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REVIEW

Skeletal muscle mitochondrial health and spinal cord injury

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Abstract

Mitochondria are the main source of cellular energy production and are dynamic organelles that undergo biogenesis, remodeling, and degradation. Mitochondrial dysfunction is observed in a number of disease states including acute and chronic central or peripheral nervous system injury by traumatic brain injury, spinal cord injury (SCI), and neurodegenerative disease as well as in metabolic disturbances such as insulin resistance, type Ⅱ diabetes and obesity. Mitochondrial dysfunction is most commonly observed in high energy requiring tissues like the brain and skeletal muscle. In persons with chronic SCI, changes to skeletal muscle may include remarkable atrophy and conversion of muscle fiber type from oxidative to fast glycolytic, combined with increased infiltration of intramuscular adipose tissue. These changes contribute to a proinflammatory environment, glucose intolerance and insulin resistance. The loss of metabolically active muscle combined with inactivity predisposes individuals with SCI to type Ⅱ diabetes and obesity. The contribution of skeletal muscle mitochondrial density and electron transport chain activity to the development of the aforementioned comorbidities following SCI is unclear. A better understanding of the mechanisms involved in skeletal muscle mitochondrial dynamics is imperative to designing and testing effective treatments for this growing population. The current editorial will review ways to study mitochondrial function and the importance of improving skeletal muscle mitochondrial health in clinical populations with a special focus on chronic SCI.

Key words: Mitochondria; Spinal cord injuries; Body composition; Diabetes mellitus; Obesity; Metabolism

Core tip: Mitochondria are the main source of cellular energy production and have decreased function in many disease states. After spinal cord injury (SCI) there is a dramatic deterioration of body composition including

increased adipose tissue deposition, skeletal muscle atrophy and conversion from oxidative to glycolytic skeletal muscle fibers. These changes put persons with SCI at a high risk for developing cardiovascular disease and type Ⅱ diabetes. How skeletal muscle mitochondrial function is impacted after human SCI has yet to be determined. The current editorial will discuss the importance of studying skeletal muscle mitochondrial function after SCI.

INTRODUCTION

Mitochondria produce over 95% of ATP through the process of oxidative phosphorylation. Under physiological conditions, mitochondria undergo a dynamic process of biogenesis, remodeling and degradation. Dysregulation of this balance results in decreased energy production, increased reactive oxygen species (ROS) and in some cases cell death. Mitochondrial dysfunction is observed with normal aging, as well as in many disease states. It is well established that damage to the central nervous system (CNS) by traumatic brain injury, spinal cord injury (SCI) and neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis) is associated with mitochondrial dysfunction[1]. Recent studies have suggested that metabolic disorders including atherosclerosis, hypertension, cancer, insulin resistance, type Ⅱ diabetes and obesity is associated with decreased mitochondrial function as well[2-4]. A better understanding of the mechanisms involved in mitochondrial dynamics and ways to improve mitochondrial health could be important for designing and testing effective treatments for these clinical populations. In this editorial we will discuss the importance of studying skeletal muscle mitochondrial health and function in persons with chronic SCI.

SCI is a devastating medical condition that results from direct or indirect damage to the spinal cord. This damage can be caused by trauma or by several pathological conditions. There are approximately 12000 new cases of SCI each year in the United States and nearly half of these individuals are between the ages of 16 and 30[5]. Because of the near-normal life expectancy of persons with SCI, the estimated lifetime cost of health care and living expenses for a person with a cervical SCI is over \$3 million, not including lost income[5]. After SCI, patients undergo severe body composition deterioration and skeletal muscle changes that predispose them to metabolic disorders like type Ⅱ diabetes and cardiovascular disease[6-8].

MITOCHONDRIAL DYNAMICS AND ENERGY PRODUCTION

Cellular energy production

Mitochondria are double membraned organelles. The outer mitochondrial membrane (OMM) allows the passage of small molecules through voltage-dependent anion channels; however, access to the inner mitochondrial membrane (IMM) is much more tightly regulated[9]. The electron transport chain (ETC) consists of IMM-bound protein complexes Ⅰ-Ⅳ and functions to maintain the electrochemical gradient across the IMM that is necessary to make ATP[10] (Figures 1 and 2). This electrochemical gradient is achieved by the pumping of protons (H^+) from the mitochondrial matrix into the intermembrane space (IMS) by complexes Ⅰ, Ⅲ, and Ⅳ (Figure 2). Disruption of this gradient results in decreased ATP synthesis and causes electrons to leak from the ETC and react with molecular oxygen in the matrix to create the ROS superoxide (O_2^-)[11].

The main source of electrons for the ETC is the reduced form of nicotinamide adenine dinucleotide (NADH) produced by the citric acid (Kreb's) cycle and the oxidation of fatty acids (β-oxidation; Figure 1). Another source of electrons is succinate, a byproduct of the Kreb's cycle. Electrons enter the ETC through complex Ⅰ (NADH dehydrogenase) or complex Ⅱ (succinate dehydrogenase) and are then transferred to complex Ⅲ (cytochrome bc1 complex) through a lipid soluble carrier molecule, coenzyme Q (Figure 2). Electrons then move between complex Ⅲ and Ⅳ by way of a water soluble carrier molecule, cytochrome c. Molecular oxygen is reduced and water is produced by complex Ⅳ, cytochrome c oxidase. The movement of electrons through the ETC is coupled to ATP production by ATP synthase, or complex Ⅴ. This protein complex converts ADP to ATP and is coupled to proton movement from the IMS back into the matrix. This process of synthesizing ATP in the mitochondria is called oxidative phosphorylation.

Electrons can leak from the ETC and react with molecular oxygen to create ROS like O_2^- (Figure 2). Complex Ⅰ and Ⅲ are the primary sites of electron leak and are sensitive to ROS injury[11]. ROS play an important role in skeletal muscle plasticity and activate many signaling cascades including increasing peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), the master regulator of mitochondrial biogenesis[12,13]. Cells have antioxidants in the cytoplasm and mitochondrial matrix in order to neutralize ROS. However, if the balance between antioxidants and ROS is disturbed, large amounts of ROS can result in the oxidation of proteins, lipids and DNA. As discussed above, access across the IMM is tightly regulated and disruption of the electrochemical gradient across it results in decreased ATP synthesis and increased ROS production. In addition to mitochondrial ROS production, in skeletal muscle, superoxide is also produced

Figure 1 Cellular energy production. In skeletal muscle, glucose enters the cell through glucose transporter type 1 or 4 (GLUT1 or GLUT4, respectively). Glucose is converted to pyruvate in the glycolysis pathway. Pyruvate is transported across the outer and inner mitochondrial membranes (OMM and IMM, respectively) and into the mitochondrial matrix where it is converted into acetyl-coA. Fatty acids undergo β-oxidation in the mitochondria, creating acetyl-coA and NADH. Acetyl-coA is utilized by the Kreb's cycle, creating NADH and succinate which enter the electron transport chain (ETC) at complex I and II, respectively. The movement of electrons through the ETC is coupled to the production of ATP in a process called OXPHOS. IMS: Intermembrane space; OXPHOS: Oxidative phosphorylation.

Figure 2 The electron transport chain is located on the inner mitochondrial membrane. Electrons (e-) enter through complex I or II and are transferred to complex III by coenzyme Q (Q). Electrons then move between complex III and IV by cytochrome c (c). Electrons can leak from the chain and react with oxygen to create superoxide (O2·-). The movement of electrons is coupled to the pumping of protons (H+) from the mitochondrial matrix into the intermembrane space (IMS). This gradient is then used by ATP synthase, or complex V, to generate ATP.

in the sarcoplasmic reticulum, transverse tubules, sarcolemma, and the cytosol[14].

Mitochondrial biogenesis

Mitochondrial biogenesis includes transcription of genes by the nuclear and mitochondrial genomes. Mitochondrial DNA (mtDNA) is circular and encodes 13 proteins essential for ETC function. MtDNA is susceptible to damage by ROS because it is not protected by histones like nuclear DNA. Deletions in mtDNA are observed in several diseases and may result in a decrease in gene expression of mitochondrial encoded genes important for ETC function, resulting in increased ROS production and decreased ATP production.

Mitochondrial biogenesis is regulated, in part, by the master regulator PGC-1α and varies based on the energy needs of the cell. After translation and mitochondrial import, proteins of the ETC are assembled into protein complexes and generate ATP through oxidative phosphorylation[13].

Mitochondrial dynamics

Remodeling of mitochondria occurs by fission and fusion. Fusion of mitochondria results in a large mitochondrial network, while fission pinches off a part of this network. After fission, mitochondrial fragments can be tagged for degradation by a specialized type of autophagy, termed mitophagy, or they can rejoin the mitochondrial network by fusion. When there is a scarcity of nutrients the mitochondrial network is fused in order to increase mitochondrial bioenergetic efficiency, while an abundance of nutrients results in a fragmented mitochondrial network[15]. Mitochondria also make contact with other subcellular organelles, including the endoplasmic reticulum. These endoplasmic reticulum mitochondria-associated membranes play an important role in cellular functions including mitochondrial division, apoptosis, and lipid and calcium regulation[15,16].

METHODS FOR STUDYING MITOCHONDRIA

There are multiple techniques that can be used to measure mitochondrial dynamics and function. These include measuring mRNA or protein expression, enzyme activity, and oxygen consumption by respirometry. Skeletal muscle biopsies are most commonly used in human studies since spinal cord and brain tissue is inaccessible.

mRNA and protein expression

mRNA and protein expression of molecules involved in mitochondrial biogenesis, remodeling and degradation can be observed by quantitative (real-time) polymerase chain reaction (qPCR) and western blot. This is the easiest way to detect changes in cellular signaling cascades and allows for the elucidation of where in the cascade there is a potential defect caused by disease or injury. Western blot analysis of ETC proteins and other mitochondrial proteins can be assayed as an estimate of respiratory chain function and mitochondrial mass, respectively. However, this type of analysis assumes that the proteins will then be imported into the mitochondria and properly assembled into the ETC complexes. There is also the assumption that a change in the expression of one protein from each complex is representative of the whole complex when in fact there are multiple proteins in each complex. For example, the mammalian complex I contains 45 different proteins[17].

Enzyme activity

One way to estimate mitochondrial function is to measure the activity of individual ETC complexes using a spectro-photometer. This can be done by measuring specific donor-acceptor oxidoreductase activities as previously described[18,19]. By using specific substrates and inhibitors each complex can be assayed individually. Linked activity between complexes can be measured by adding either NADH (for complex I) or succinate (for complex II) and measuring the reduction of cytochrome c by complex III[18,19]. Other key enzymes of the citric acid cycle (*i.e.,* citrate synthase) and β-oxidation pathways [*i.e.,* β-hydroxyacyl-CoA dehydrogenase (β-HAD)] can also be measured spectrophotometrically[18,20].

The benefit of spectrophotometric analysis is that it uses a small amount of tissue, samples can be previously frozen, and spectrophotometers are common lab equipment[19]. A limitation of spectrophotometric analysis is that it shows maximum capacity of individual complexes and does not necessarily represent physiological function. However, with the limited sample size obtained by human skeletal muscle biopsy and the need by many labs to freeze tissue, this may be a good option for many research groups.

Previous research has used human biopsy or autopsy specimens from tissues such as skeletal muscle, liver and skin[21]. Studies have been conducted using both tissue homogenates and isolated mitochondria from previously frozen human skeletal muscle[22,23]. Isolating mitochondria is ideal for understanding mechanism; however, the cellular context is lost. Also, more tissue is needed compared to running tissue homogenates because some mitochondria will be lost in the isolation process. A benefit of analyzing tissue homogenates is that the mitochondria remain in their cellular context, giving a more physiological reading. A limitation of analyzing tissue homogenates is the high non-mitochondrial NADH oxidase activity of some tissues[24].

Respirometry

Measuring oxygen consumption of isolated mitochondria or permeabilized cells by respirometry is currently the gold standard for assaying mitochondrial function. Respiration shows that the ETC is functioning because oxygen is necessary for ATP synthesis. The addition of substrates and inhibitors allows assessment of individual ETC complexes and coupling to ATP synthesis. Respiration can determine mitochondrial dysfunction not identified by spectrophotometric analysis, including impairment in mitochondrial membrane transport, problems with substrate utilization, and defects in fatty acid metabolism[25]. Protocols have recently been developed to analyze mitochondrial function from as little as 20-50 mg of muscle tissue[26]. However, this technique is labor intensive and samples cannot be previously frozen because freezing uncouples the ETC from ATP synthesis.

CHANGES IN BODY COMPOSITION AND METABOLISM AFTER SCI

SCI is usually a result of trauma to the spine, resulting

in damage to cells that send messages to and from the brain. Damage can be to the upper motor neurons that project from the brain to the spinal cord or lower motor neurons that project from the spinal cord to the muscles. The location and severity of the injury largely determines the extent of impairment. Injuries resulting in motor and sensory impairment distal to the level of injury are classified as either complete or incomplete SCI, with incomplete injury resulting in spared sensation and/or motor function. The loss of peripheral nervous system control below the level of injury results in decreased mobility. This immobility, combined with hormonal changes and poor dietary habits result in decreased muscle mass and increased adipose deposition[6,7,27]. These changes put individuals with SCI at a high risk for developing cardiovascular disease, type II diabetes, and obesity[7,28,29]. Recent studies have shown a link between the deterioration in body composition and the impaired metabolic profile after SCI[30,31]. However, there are still many questions that remain unanswered at the cellular level.

Body composition after SCI

Drastic changes in body composition follow SCI[8]. Skeletal muscle atrophy combined with inactivity and poor diet contributes to the increased prevalence of obesity in this population[32]. Excess body fat, particularly around the waist, is a risk factor for a number of conditions including cardiovascular and metabolic disease[31,33]. Measurements of body mass index (BMI) do not take into account regional distribution of adipose tissue and underestimate fat mass in persons with SCI[34]. Waist circumference measurements do not distinguish between subcutaneous adipose tissue and ectopic [visceral adipose tissue (VAT)]. It is important to distinguish between these two adipose tissue types, as an increase in VAT is a risk factor for cardiovascular and metabolic disease[35]. Waist circumference measurements underestimate the amount of VAT in individuals with SCI. Increased waist circumference is correlated with the amount of VAT in able bodied (AB) individuals but this is not the case in the SCI population[36]. SCI individuals have more VAT than AB individuals with the same waist circumference[37]. Collectively, these data suggest that there adipose tissue deposition is increased after SCI and that the distribution is altered compared to AB individuals. For a review on this topic, see[8].

In addition to increased adipose tissue disposition, individuals with SCI experience significant changes to their skeletal muscle. These changes include significant muscle atrophy, conversion of muscle fiber type from oxidative to fast glycolytic, and an increase in intramuscular fat (IMF). Both complete and incomplete SCI results in substantial atrophy of muscles below the level of injury. Incomplete SCI resulted in a 33% decrease in thigh muscle cross sectional area and an increase in IMF six weeks post-injury compared to AB controls[32]. The conversion of muscle fiber type to fast glycolytic results in an quickly fatigued

muscle that can be damaged easily[38]. Additionally, an increase in fast glycolytic muscle fibers decreases insulin sensitivity and may lead to diabetes[39].

As discussed above, increased VAT, but not sub-cutaneous adipose tissue, is a risk factor for cardiovascular disease, glucose intolerance, insulin resistance, and hyperlipidemia[35]. This may be due to the infiltration of immune cells into VAT and subsequent secretion of inflammatory cytokines including tumor necrosis factor α (TNFα), interleukin-1β (IL-1β) and IL-6. Previous research suggests that inflammatory cytokines released by adipose tissue accelerate skeletal muscle atrophy[40-42]. A recent study investigating the interactions between adipose tissue and skeletal muscle revealed that VAT adipocytes from obese subjects decreased cultured myotube thickness and resulted in a gene expression profile suggestive of muscle atrophy[41]. The proposed mechanism is through the release of IL-1β and IL-6 and decreased insulin growth factor signaling, resulting in insulin resistance. Another type of adipose tissue that is similar to VAT, IMF, is increased after SCI and may be a contributing factor to the development of insulin resistance[32,43]. The mechanisms underlying the interplay between adipose tissue and skeletal muscle are just beginning to be understood.

Metabolism after SCI

In addition to changes in body composition, metabolism is disrupted after SCI. As many as 55% of individuals with SCI have metabolic syndrome, which is characterized by three or more of the following conditions: Obesity, high blood pressure, insulin resistance, high triglycerides, and low high-density lipoprotein (HDL) cholesterol levels[44]. Impaired glucose tolerance was observed in 56% of persons with SCI, compared with only 18% of AB controls[45]. Individuals with SCI also have increased low-density lipoprotein (LDL) cholesterol[46,47]. These conditions worsen with age and put individuals at risk for developing cardiovascular disease and type II diabetes.

MITOCHONDRIAL HEALTH STATUS AFTER SCI

CNS mitochondrial health after SCI

The immediate damage to the spinal cord, including damage to axons and cells at the injury site is called primary injury. Models of SCI have shown an increase in intracellular sodium, chloride and calcium 15-60 min after injury[48]. An increase in intracellular calcium may result in apoptosis if the excess calcium taken up by mitochondria triggers mitochondrial permeability transition pore opening. Following this initial insult is a secondary injury, characterized by invasion of inflammatory cells and more cell death as cells invade not only the injury site, but also the spared nervous tissue. Neuronal death leads to loss of motor or sensory function and loss of oligodendrocytes leads to axonal demyelination[49].

Mitochondrial respiration in the spinal cord through

complexes I and II is decreased and oxidative stress is increased at 12 and 24 h, but not after 6 h after SCI in a rat model[50]. In another study respiration and complex I and IV enzyme activity was decreased in the spinal cord after SCI[51]. In this study mitochondrial function was improved by treatment with an antioxidant. Complex I, complex IV, and pyruvate dehydrogenase are mitochondrial enzymes that are particularly vulnerable to damage by ROS and are decreased after SCI[52]. Decreasing ROS or increasing function of these enzymes may improve functional outcomes after SCI.

Skeletal muscle mitochondrial health after SCI

There is limited knowledge about the changes in mitochondrial function following SCI in humans. However, indirect evidence of mitochondrial function using near-infrared resonance spectroscopy to measure tissue oxygenation revealed that muscle oxidative capacity was decreased 50%-60% in participants with SCI 2.7-22 years after injury compared to AB controls[53]. A similar deficit was observed using histochemistry to measure succinate dehydrogenase (SDH) activity in muscle biopsy samples from paralyzed muscle 2-11 years post injury compared to AB controls[54,55]. In contrast, a study analyzing SDH and GAPDH activity, markers of complex II and glycolytic capacity, respectively, 6-24 wk after injury found increased activity despite greater fatigability of muscles[38]. The reason for these discrepant results in unclear, but it could be that early after injury muscle atrophy and fiber type changes results in a compensatory increase in oxidative and glycolytic enzymes but long periods of muscle inactivity result in reduced activity of oxidative and glycolytic pathways[38,54,55]. More research is needed to determine the effect of SCI on mitochondrial function.

Mitochondria are also dysfunctional in a number of metabolic diseases including type II diabetes and obesity. A large network of fused mitochondria is observed in healthy skeletal muscle, while muscle from obese and type II diabetics is fragmented[56]. Skeletal muscle mitochondrial function is decreased as well, with a 2-3 fold decrease in NADH oxidase (complex I) activity normalized to mitochondrial content in obese and type II diabetics compared to control[57].

Exercise interventions have been shown to increase skeletal muscle mitochondrial function and improve insulin sensitivity in obesity, diabetes, and aging[58,59]. Some options for exercise intervention after SCI include neuromuscular electrical stimulation-induced weight lifting and functional electrical stimulation (FES) cycling. Sixteen weeks of electrical stimulation-induced resistance training increased muscle mass and improved mitochondrial function by 25% in patients with SCI[60]. FES cycling has also been shown to increase mitochondrial function in patients with SCI. Eight weeks of FES cycling resulted in an increase in citrate synthase, a marker of mitochondrial mass[61]. Similarly, studies found increased citrate synthase as well as increased function of enzymes involved in

glycolysis and β-oxidation[62,63]. Finally, SDH was increased after 4 wk of training, suggesting that complex II activity is increased with exercise[64]. Similarly, a recent study showed that a single session of low frequency electrical stimulation increased genes involved in muscle metabolism, including PGC-1α[65]. Collectively, these studies suggest that paralyzed skeletal muscle is malleable and can increase mitochondrial function in response to exercise. Additionally, IMF has been shown to decrease after resistance exercise training[66]. This would provide additional benefit to skeletal muscle and may improve insulin sensitivity.

SIGNIFICANCE AND FUTURE DIRECTIONS

Mitochondria are vital for energy production and play a role in a number of cellular processes including cell signaling, cell cycle progression, calcium regulation and cell death. These organelles are dynamic, and undergo changes in activity and number in response to cellular energy needs. A decrease in neuron and skeletal muscle mitochondrial function is observed in a number of disease and injury states including CNS trauma, neurodegenerative disease, type II diabetes and obesity[1-3]. However, we know very little about mitochondrial function in patients with chronic SCI. We are just beginning to understand the role of mitochondria in insulin resistance and how skeletal muscle mitochondrial function is disrupted in patients with SCI. Future research needs to be done using functional assays to assess activity of individual ETC complexes, as well as its coupling to ATP synthesis.

Increasing mitochondrial function by pharmacological activation of mitochondrial biogenesis is an active area of research[67]. There are a number of FDA approved medications as well as naturally occurring substances that activate mitochondrial biogenesis. For example, resveratrol, which is found in red wine, activates sirtuin 1 (SIRT1) and increases PGC-1α activity and mitochondrial function and was shown to improve insulin resistance in diabetic patients[68,69]. Small molecules that activate SIRT1 with improved bioavailability and potency have been developed and are currently being tested in humans. FDA approved pharmacological activators of mitochondrial biogenesis include the β_2-adrenergic receptor agonist formoterol[70], the anti-diabetic drug metformin[71], the phosphodiesterase inhibitor sildenafil[72], the PPARγ agonist rosiglitazone[73], the mitochondrial permeability transition pore inhibitor cyclosporine A[74], and the angiotensin-converting enzyme inhibitor captropril[75], among others. Although these compounds are thought to exert their effects at least in part by increasing mitochondrial biogenesis, there are currently no specific activators of mitochondrial biogenesis. Future studies need to investigate the safety and efficacy of systemically increasing mitochondrial biogenesis, as well as optimizing dosing in order to maximize the therapeutic benefit.

In order to study mitochondrial function after disease

or injury or to assess the efficacy of mitochondrial targeted therapies, skeletal muscle biopsies could be used because of the inaccessibility of the brain and spinal cord in humans. However, recent studies have suggested that the bioenergetic profile of blood cells is associated with physical function and inflammation as well[76,77]. Indeed, mitochondrial dysfunction is seen in blood from patients with a number of diseases including neurodegenerative diseases and type Ⅱ diabetes[78,79]. Peripheral blood mononuclear cells from patients with type Ⅱ diabetes and chronic kidney disease have increased inflammatory cytokines, decreased mitochondrial function and increased ROS production[80]. These studies suggest that blood cell bioenergetics may predict systemic mitochondrial function and may act as biomarkers for metabolic stress and surrogate markers for the severity of disease progression and the efficacy of therapeutics[80,81]. This represents an intriguing possibility, as obtaining blood samples are much less invasive than biopsies and could be taken more frequently in order to better characterize the time course of therapeutic intervention.

There are a number of different techniques for analyzing cellular signaling pathways and mitochondrial function. Researchers should carefully weigh the convenience of non-invasive techniques with the mechanistic detail provided by analyzing biopsy tissue. If choosing to analyze biopsy tissue, care should be taken to obtain the proper amount of tissue required for the assay and to prepare it properly in order to preserve mitochondrial function. For samples that need to be frozen, spectrophotometric analysis may be the best option for analyzing mitochondrial function, while respiration will be ideal for fresh tissue samples. Another research consideration is whether or not to isolate mitochondria and this may depend on the sample size.

As discussed above, both resistance training and FES cycling has been shown to increase mitochondrial function in persons with SCI. In addition, electrical stimulation-induced resistance training reduced VAT and IMF and increased insulin sensitivity while increasing muscle mass[66]. FES cycling has been shown to improve insulin sensitivity as well, but the effect on muscle size and body composition were minimal to modest[82]. It is unknown if conditioning the muscles with resistance training prior to FES cycling would result in greater mitochondrial and metabolic outcomes.

CONCLUSION

There is limited knowledge regarding skeletal muscle mitochondrial health following SCI. Challenges may stem from difficulties in capturing muscle biopsies and running biochemical analysis to determine mitochondrial mass or activity by spectroscopy or respiration. Non-invasive procedures like near-infrared resonance spectroscopy may reflect mitochondrial activity; however, mechanistic dysfunctions inclivdual of complexes may be limited.

A better understanding of how mitochondrial function

is impacted in patients with chronic SCI is critical for developing interventions to increase mitochondrial function and improve metabolic outcomes. Skeletal muscle or blood cell bioenergetics may predict overall mitochondrial health and therefore be a surrogate marker of disease progression and treatment efficacy. Increasing mitochondrial function immediately following SCI may decrease cell death and improve functional outcomes. Improvement in mitochondrial function by exercise or pharmacological interventions in chronic SCI may decrease comorbidities. This will result in better health for patients and a lower financial burden for their health care. A better understanding of mitochondrial biology may also translate to a number of other diseases in which mitochondrial are dysfunctional, particularly insulin resistance, type Ⅱ diabetes, and obesity.

REFERENCES

1 **Itoh K**, Nakamura K, Iijima M, Sesaki H. Mitochondrial dynamics in neurodegeneration. *Trends Cell Biol* 2013; **23**: 64-71 [PMID: 23159640 DOI: 10.1016/j.tcb.2012.10.006]

2 **Chan DC**. Mitochondria: dynamic organelles in disease, aging, and development. *Cell* 2006; **125**: 1241-1252 [PMID: 16814712 DOI: 10.1016/j.cell.2006.06.010]

3 **Zhao J**, Zhang J, Yu M, Xie Y, Huang Y, Wolff DW, Abel PW, Tu Y. Mitochondrial dynamics regulates migration and invasion of breast cancer cells. *Oncogene* 2013; **32**: 4814-4824 [PMID: 23128392 DOI: 10.1038/onc.2012.494]

4 **Phielix E**, Mensink M. Type 2 diabetes mellitus and skeletal muscle metabolic function. *Physiol Behav* 2008; **94**: 252-258 [PMID: 18342897 DOI: 10.1016/j.physbeh.2008.01.020]

5 **National Spinal Cord Injury Statistical Center**. Spinal cord injury facts and figures at a glance. *J Spinal Cord Med* 2013; **36**: 1-2 [PMID: 23433327 DOI: 10.1179/1079026813Z.000000000136]

6 **Kocina P**. Body composition of spinal cord injured adults. *Sports Med* 1997; **23**: 48-60 [PMID: 9017859]

7 **Gater DR**. Obesity after spinal cord injury. *Phys Med Rehabil Clin N Am* 2007; **18**: 333-351, vii [PMID: 17543776 DOI: 10.1016/j.pmr.2007.03.004]

8 **Gorgey AS**, Dolbow DR, Dolbow JD, Khalil RK, Castillo C, Gater DR. Effects of spinal cord injury on body composition and metabolic profile - part I. *J Spinal Cord Med* 2014; **37**: 693-702 [PMID: 25001559 DOI: 10.1179/2045772314Y.0000000245]

9 **Lemasters JJ**, Holmuhamedov E. Voltage-dependent anion channel (VDAC) as mitochondrial governator--thinking outside the box. *Biochim Biophys Acta* 2006; **1762**: 181-190 [PMID: 16307870 DOI: 10.1016/j.bbadis.2005.10.006]

10 **Saraste M**. Oxidative phosphorylation at the fin de siècle. *Science* 1999; **283**: 1488-1493 [PMID: 10066163]

11 **Turrens JF**. Mitochondrial formation of reactive oxygen species. *J Physiol* 2003; **552**: 335-344 [PMID: 14561818 DOI: 10.1113/jphysiol.2003.049478]

12 **Hoppeler H**, Baum O, Lurman G, Mueller M. Molecular mechanisms of muscle plasticity with exercise. *Compr Physiol* 2011; **1**: 1383-1412 [PMID: 23733647 DOI: 10.1002/cphy.c100042]

13 **Scarpulla RC**, Vega RB, Kelly DP. Transcriptional integration of mitochondrial biogenesis. *Trends Endocrinol Metab* 2012; **23**: 459-466 [PMID: 22817841 DOI: 10.1016/j.tem.2012.06.006]

14   **Powers SK**, Ji LL, Kavazis AN, Jackson MJ. Reactive oxygen species: impact on skeletal muscle. *Compr Physiol* 2011; **1**: 941-969 [PMID: 23737208 DOI: 10.1002/cphy.c100054]

15   **Schrepfer E**, Scorrano L. Mitofusins, from Mitochondria to Metabolism. *Mol Cell* 2016; **61**: 683-694 [PMID: 26942673 DOI: 10.1016/j.molcel.2016.02.022]

16   **Vance JE**. MAM (mitochondria-associated membranes) in mammalian cells: lipids and beyond. *Biochim Biophys Acta* 2014; **1841**: 595-609 [PMID: 24316057 DOI: 10.1016/j.bbalip.2013.11.014]

17   **Carroll J**, Fearnley IM, Skehel JM, Shannon RJ, Hirst J, Walker JE. Bovine complex I is a complex of 45 different subunits. *J Biol Chem* 2006; **281**: 32724-32727 [PMID: 16950771 DOI: 10.1074/jbc.M607135200]

18   **Brass EP**, Hiatt WR, Gardner AW, Hoppel CL. Decreased NADH dehydrogenase and ubiquinol-cytochrome c oxidoreductase in peripheral arterial disease. *Am J Physiol Heart Circ Physiol* 2001; **280**: H603-H609 [PMID: 11158957]

19   **Spinazzi M**, Casarin A, Pertegato V, Salviati L, Angelini C. Assessment of mitochondrial respiratory chain enzymatic activities on tissues and cultured cells. *Nat Protoc* 2012; **7**: 1235-1246 [PMID: 22653162 DOI: 10.1038/nprot.2012.058]

20   **Morash AJ**, Kotwica AO, Murray AJ. Tissue-specific changes in fatty acid oxidation in hypoxic heart and skeletal muscle. *Am J Physiol Regul Integr Comp Physiol* 2013; **305**: R534-R541 [PMID: 23785078 DOI: 10.1152/ajpregu.00510.2012]

21   **Hoppel CL**, Kerr DS, Dahms B, Roessmann U. Deficiency of the reduced nicotinamide adenine dinucleotide dehydrogenase component of complex I of mitochondrial electron transport. Fatal infantile lactic acidosis and hypermetabolism with skeletal-cardiac myopathy and encephalopathy. *J Clin Invest* 1987; **80**: 71-77 [PMID: 3110216 DOI: 10.1172/JCI113066]

22   **Kelly NA**, Ford MP, Standaert DG, Watts RL, Bickel CS, Moellering DR, Tuggle SC, Williams JY, Lieb L, Windham ST, Bamman MM. Novel, high-intensity exercise prescription improves muscle mass, mitochondrial function, and physical capacity in individuals with Parkinson's disease. *J Appl Physiol* (1985) 2014; **116**: 582-592 [PMID: 24408997 DOI: 10.1152/japplphysiol.01277.2013]

23   **Menshikova EV**, Ritov VB, Fairfull L, Ferrell RE, Kelley DE, Goodpaster BH. Effects of exercise on mitochondrial content and function in aging human skeletal muscle. *J Gerontol A Biol Sci Med Sci* 2006; **61**: 534-540 [PMID: 16799133]

24   **Trounce IA**, Kim YL, Jun AS, Wallace DC. Assessment of mitochondrial oxidative phosphorylation in patient muscle biopsies, lymphoblasts, and transmitochondrial cell lines. *Methods Enzymol* 1996; **264**: 484-509 [PMID: 8965721]

25   **Puchowicz MA**, Varnes ME, Cohen BH, Friedman NR, Kerr DS, Hoppel CL. Oxidative phosphorylation analysis: assessing the integrated functional activity of human skeletal muscle mitochondria-case studies. *Mitochondrion* 2004; **4**: 377-385 [PMID: 16120399 DOI: 10.1016/j.mito.2004.07.004]

26   **Bharadwaj MS**, Tyrrell DJ, Lyles MF, Demons JL, Rogers GW, Molina AJ. Preparation and respirometric assessment of mitochondria isolated from skeletal muscle tissue obtained by percutaneous needle biopsy. *J Vis Exp* 2015; Epub ahead of print [PMID: 25741892 DOI: 10.3791/52350]

27   **Bauman WA**, Spungen AM. Metabolic changes in persons after spinal cord injury. *Phys Med Rehabil Clin N Am* 2000; **11**: 109-140 [PMID: 10680161]

28   **Duckworth WC**, Solomon SS, Jallepalli P, Heckemeyer C, Finnern J, Powers A. Glucose intolerance due to insulin resistance in patients with spinal cord injuries. *Diabetes* 1980; **29**: 906-910 [PMID: 7429029]

29   **Lavela SL**, Weaver FM, Goldstein B, Chen K, Miskevics S, Rajan S, Gater DR. Diabetes mellitus in individuals with spinal cord injury or disorder. *J Spinal Cord Med* 2006; **29**: 387-395 [PMID: 17044389]

30   **Gorgey AS**, Gater DR. Regional and relative adiposity patterns in relation to carbohydrate and lipid metabolism in men with spinal cord injury. *Appl Physiol Nutr Metab* 2011; **36**: 107-114 [PMID: 21326384 DOI: 10.1139/H10-091]

31   **Gorgey AS**, Mather KJ, Gater DR. Central adiposity associations

32   **Gorgey AS**, Dudley GA. Skeletal muscle atrophy and increased intramuscular fat after incomplete spinal cord injury. *Spinal Cord* 2007; **45**: 304-309 [PMID: 16940987 DOI: 10.1038/sj.sc.3101968]

33   **Nakamura T**, Tokunaga K, Shimomura I, Nishida M, Yoshida S, Kotani K, Islam AH, Keno Y, Kobatake T, Nagai Y. Contribution of visceral fat accumulation to the development of coronary artery disease in non-obese men. *Atherosclerosis* 1994; **107**: 239-246 [PMID: 7980698]

34   **Spungen AM**, Adkins RH, Stewart CA, Wang J, Pierson RN, Waters RL, Bauman WA. Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. *J Appl Physiol* (1985) 2003; **95**: 2398-2407 [PMID: 12909613 DOI: 10.1152/japplphysiol.00729.2002]

35   **Jensen MD**. Role of body fat distribution and the metabolic complications of obesity. *J Clin Endocrinol Metab* 2008; **93**: S57-S63 [PMID: 18987271 DOI: 10.1210/jc.2008-1585]

36   **Gorgey AS**, Mather KJ, Poarch HJ, Gater DR. Influence of motor complete spinal cord injury on visceral and subcutaneous adipose tissue measured by multi-axial magnetic resonance imaging. *J Spinal Cord Med* 2011; **34**: 99-109 [PMID: 21528633 DOI: 10.1179/107902610X12911165975106]

37   **Edwards LA**, Bugaresti JM, Buchholz AC. Visceral adipose tissue and the ratio of visceral to subcutaneous adipose tissue are greater in adults with than in those without spinal cord injury, despite matching waist circumferences. *Am J Clin Nutr* 2008; **87**: 600-607 [PMID: 18326597]

38   **Castro MJ**, Apple DF, Staron RS, Campos GE, Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 mo of injury. *J Appl Physiol* (1985) 1999; **86**: 350-358 [PMID: 9887150]

39   **Simoneau JA**, Kelley DE. Altered glycolytic and oxidative capacities of skeletal muscle contribute to insulin resistance in NIDDM. *J Appl Physiol* (1985) 1997; **83**: 166-171 [PMID: 9216960]

40   **Hoppeler H**. Molecular networks in skeletal muscle plasticity. *J Exp Biol* 2016; **219**: 205-213 [PMID: 26792332 DOI: 10.1242/jeb.128207]

41   **Pellegrinelli V**, Rouault C, Rodriguez-Cuenca S, Albert V, Edom-Vovard F, Vidal-Puig A, Clément K, Butler-Browne GS, Lacasa D. Human Adipocytes Induce Inflammation and Atrophy in Muscle Cells During Obesity. *Diabetes* 2015; **64**: 3121-3134 [PMID: 25695947 DOI: 10.2337/db14-0796]

42   **Kelley DE**, Goodpaster BH. Stewing in Not-So-Good Juices: Interactions of Skeletal Muscle With Adipose Secretions. *Diabetes* 2015; **64**: 3055-3057 [PMID: 26294424 DOI: 10.2337/db15-0403]

43   **Elder CP**, Apple DF, Bickel CS, Meyer RA, Dudley GA. Intramuscular fat and glucose tolerance after spinal cord injury-a cross-sectional study. *Spinal Cord* 2004; **42**: 711-716 [PMID: 15303112 DOI: 10.1038/sj.sc.3101652]

44   **Nelson MD**, Widman LM, Abresch RT, Stanhope K, Havel PJ, Styne DM, McDonald CM. Metabolic syndrome in adolescents with spinal cord dysfunction. *J Spinal Cord Med* 2007; **30** Suppl 1: S127-S139 [PMID: 17874698]

45   **Bauman WA**, Spungen AM. Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: a model of premature aging. *Metabolism* 1994; **43**: 749-756 [PMID: 8201966]

46   **Nash MS**, Mendez AJ. A guideline-driven assessment of need for cardiovascular disease risk intervention in persons with chronic paraplegia. *Arch Phys Med Rehabil* 2007; **88**: 751-757 [PMID: 17532897 DOI: 10.1016/j.apmr.2007.02.031]

47   **Bauman WA**, Spungen AM, Zhong YG, Rothstein JL, Petry C, Gordon SK. Depressed serum high density lipoprotein cholesterol levels in veterans with spinal cord injury. *Paraplegia* 1992; **30**: 697-703 [PMID: 1448297 DOI: 10.1038/sc.1992.136]

48   **LoPachin RM**, Gaughan CL, Lehning EJ, Kaneko Y, Kelly TM, Blight A. Experimental spinal cord injury: spatiotemporal characterization of elemental concentrations and water contents in axons and neuroglia. *J Neurophysiol* 1999; **82**: 2143-2153 [PMID:

to carbohydrate and lipid metabolism in individuals with complete motor spinal cord injury. *Metabolism* 2011; **60**: 843-851 [PMID: 20870252 DOI: 10.1016/j.metabol.2010.08.002]

10561394]

49   **Rabchevsky AG**, Patel SP, Springer JE. Pharmacological interventions for spinal cord injury: where do we stand? How might we step forward? *Pharmacol Ther* 2011; **132**: 15-29 [PMID: 21605594 DOI: 10.1016/j.pharmthera.2011.05.001]

50   **Sullivan PG**, Krishnamurthy S, Patel SP, Pandya JD, Rabchevsky AG. Temporal characterization of mitochondrial bioenergetics after spinal cord injury. *J Neurotrauma* 2007; **24**: 991-999 [PMID: 17600515 DOI: 10.1089/neu.2006.0242]

51   **Patel SP**, Sullivan PG, Pandya JD, Goldstein GA, VanRooyen JL, Yonutas HM, Eldahan KC, Morehouse J, Magnuson DS, Rabchevsky AG. N-acetylcysteine amide preserves mitochondrial bioenergetics and improves functional recovery following spinal trauma. *Exp Neurol* 2014; **257**: 95-105 [PMID: 24805071 DOI: 10.1016/j.expneurol.2014.04.026]

52   **McEwen ML**, Sullivan PG, Rabchevsky AG, Springer JE. Targeting mitochondrial function for the treatment of acute spinal cord injury. *Neurotherapeutics* 2011; **8**: 168-179 [PMID: 21360236 DOI: 10.1007/s13311-011-0031-7]

53   **Erickson ML**, Ryan TE, Young HJ, McCully KK. Near-infrared assessments of skeletal muscle oxidative capacity in persons with spinal cord injury. *Eur J Appl Physiol* 2013; **113**: 2275-2283 [PMID: 23703066 DOI: 10.1007/s00421-013-2657-0]

54   **Martin TP**, Stein RB, Hoeppner PH, Reid DC. Influence of electrical stimulation on the morphological and metabolic properties of paralyzed muscle. *J Appl Physiol* (1985) 1992; **72**: 1401-1406 [PMID: 1534322]

55   **Grimby G**, Broberg C, Krotkiewska I, Krotkiewski M. Muscle fiber composition in patients with traumatic cord lesion. *Scand J Rehabil Med* 1976; **8**: 37-42 [PMID: 132700]

56   **Kelley DE**, He J, Menshikova EV, Ritov VB. Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. *Diabetes* 2002; **51**: 2944-2950 [PMID: 12351431]

57   **Ritov VB**, Menshikova EV, Azuma K, Wood R, Toledo FG, Goodpaster BH, Ruderman NB, Kelley DE. Deficiency of electron transport chain in human skeletal muscle mitochondria in type 2 diabetes mellitus and obesity. *Am J Physiol Endocrinol Metab* 2010; **298**: E49-E58 [PMID: 19887598 DOI: 10.1152/ajpendo.00317.2009]

58   **Toledo FG**, Goodpaster BH. The role of weight loss and exercise in correcting skeletal muscle mitochondrial abnormalities in obesity, diabetes and aging. *Mol Cell Endocrinol* 2013; **379**: 30-34 [PMID: 23792186 DOI: 10.1016/j.mce.2013.06.018]

59   **Lanza IR**, Nair KS. Muscle mitochondrial changes with aging and exercise. *Am J Clin Nutr* 2009; **89**: 467S-471S [PMID: 19056588 DOI: 10.3945/ajcn.2008.26717D]

60   **Ryan TE**, Brizendine JT, Backus D, McCully KK. Electrically induced resistance training in individuals with motor complete spinal cord injury. *Arch Phys Med Rehabil* 2013; **94**: 2166-2173 [PMID: 23816921 DOI: 10.1016/j.apmr.2013.06.016]

61   **Chilibeck PD**, Bell G, Jeon J, Weiss CB, Murdoch G, MacLean I, Ryan E, Burnham R. Functional electrical stimulation exercise increases GLUT-1 and GLUT-4 in paralyzed skeletal muscle. *Metabolism* 1999; **48**: 1409-1413 [PMID: 10582549]

62   **Kjaer M**, Mohr T, Biering-Sørensen F, Bangsbo J. Muscle enzyme adaptation to training and tapering-off in spinal-cord-injured humans. *Eur J Appl Physiol* 2001; **84**: 482-486 [PMID: 11417439]

63   **Crameri RM**, Weston A, Climstein M, Davis GM, Sutton JR. Effects of electrical stimulation-induced leg training on skeletal muscle adaptability in spinal cord injury. *Scand J Med Sci Sports* 2002; **12**: 316-322 [PMID: 12383078]

64   **Rochester L**, Barron MJ, Chandler CS, Sutton RA, Miller S, Johnson MA. Influence of electrical stimulation of the tibialis anterior muscle in paraplegic subjects. 2. Morphological and histochemical properties. *Paraplegia* 1995; **33**: 514-522 [PMID: 8524604 DOI: 10.1038/sc.1995.112]

65   **Petrie M**, Suneja M, Shields RK. Low-frequency stimulation regulates metabolic gene expression in paralyzed muscle. *J Appl Physiol* (1985) 2015; **118**: 723-731 [PMID: 25635001 DOI: 10.1152/japplphysiol.00628.2014]

66   **Gorgey AS**, Mather KJ, Cupp HR, Gater DR. Effects of resistance training on adiposity and metabolism after spinal cord injury. *Med Sci Sports Exerc* 2012; **44**: 165-174 [PMID: 21659900 DOI: 10.1249/MSS.0b013e31822672aa]

67   **Whitaker RM**, Corum D, Beeson CC, Schnellmann RG. Mitochondrial Biogenesis as a Pharmacological Target: A New Approach to Acute and Chronic Diseases. *Annu Rev Pharmacol Toxicol* 2016; **56**: 229-249 [PMID: 26566156 DOI: 10.1146/annurev-pharmtox-010715-103155]

68   **Lagouge M**, Argmann C, Gerhart-Hines Z, Meziane H, Lerin C, Daussin F, Messadeq N, Milne J, Lambert P, Elliott P, Geny B, Laakso M, Puigserver P, Auwerx J. Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1alpha. *Cell* 2006; **127**: 1109-1122 [PMID: 17112576 DOI: 10.1016/j.cell.2006.11.013]

69   **Brasnyó P**, Molnár GA, Mohás M, Markó L, Laczy B, Cseh J, Mikolás E, Szijártó IA, Mérei A, Halmai R, Mészáros LG, Sümegi B, Wittmann I. Resveratrol improves insulin sensitivity, reduces oxidative stress and activates the Akt pathway in type 2 diabetic patients. *Br J Nutr* 2011; **106**: 383-389 [PMID: 21385509 DOI: 10.1017/S0007114511000316]

70   **Wills LP**, Trager RE, Beeson GC, Lindsey CC, Peterson YK, Beeson CC, Schnellmann RG. The β2-adrenoceptor agonist formoterol stimulates mitochondrial biogenesis. *J Pharmacol Exp Ther* 2012; **342**: 106-118 [PMID: 22490378 DOI: 10.1124/jpet.112.191528]

71   **Kukidome D**, Nishikawa T, Sonoda K, Imoto K, Fujisawa K, Yano M, Motoshima H, Taguchi T, Matsumura T, Araki E. Activation of AMP-activated protein kinase reduces hyperglycemia-induced mitochondrial reactive oxygen species production and promotes mitochondrial biogenesis in human umbilical vein endothelial cells. *Diabetes* 2006; **55**: 120-127 [PMID: 16380484]

72   **Whitaker RM**, Wills LP, Stallons LJ, Schnellmann RG. cGMP-selective phosphodiesterase inhibitors stimulate mitochondrial biogenesis and promote recovery from acute kidney injury. *J Pharmacol Exp Ther* 2013; **347**: 626-634 [PMID: 24042162 DOI: 10.1124/jpet.113.208017]

73   **Pardo R**, Enguix N, Lasheras J, Feliu JE, Kralli A, Villena JA. Rosiglitazone-induced mitochondrial biogenesis in white adipose tissue is independent of peroxisome proliferator-activated receptor γ coactivator-1α. *PLoS One* 2011; **6**: e26989 [PMID: 22087241 DOI: 10.1371/journal.pone.0026989]

74   **Osman MM**, Lulic D, Glover L, Stahl CE, Lau T, van Loveren H, Borlongan CV. Cyclosporine-A as a neuroprotective agent against stroke: its translation from laboratory research to clinical application. *Neuropeptides* 2011; **45**: 359-368 [PMID: 21592568 DOI: 10.1016/j.npep.2011.04.002]

75   **Yanagishita T**, Tomita M, Itoh S, Mukae S, Arata H, Ishioka H, Geshi E, Konno N, Katagiri T. Protective effect of captopril on ischemic myocardium. *Jpn Circ J* 1997; **61**: 161-169 [PMID: 9070972]

76   **Tyrrell DJ**, Bharadwaj MS, Van Horn CG, Kritchevsky SB, Nicklas BJ, Molina AJ. Respirometric Profiling of Muscle Mitochondria and Blood Cells Are Associated With Differences in Gait Speed Among Community-Dwelling Older Adults. *J Gerontol A Biol Sci Med Sci* 2015; **70**: 1394-1399 [PMID: 25030980 DOI: 10.1093/gerona/glu096]

77   **Tyrrell DJ**, Bharadwaj MS, Van Horn CG, Marsh AP, Nicklas BJ, Molina AJ. Blood-cell bioenergetics are associated with physical function and inflammation in overweight/obese older adults. *Exp Gerontol* 2015; **70**: 84-91 [PMID: 26226578 DOI: 10.1016/j.exger.2015.07.015]

78   **Zharikov S**, Shiva S. Platelet mitochondrial function: from regulation of thrombosis to biomarker of disease. *Biochem Soc Trans* 2013; **41**: 118-123 [PMID: 23356269 DOI: 10.1042/BST20120327]

79   **Ladd AC**, Keeney PM, Govind MM, Bennett JP. Mitochondrial oxidative phosphorylation transcriptome alterations in human amyotrophic lateral sclerosis spinal cord and blood. *Neuromolecular Med* 2014; **16**: 714-726 [PMID: 25081190 DOI: 10.1007/s12017-014-8321-y]

80   **Ravi S**, Mitchell T, Kramer PA, Chacko B, Darley-Usmar VM. Mitochondria in monocytes and macrophages-implications for translational and basic research. *Int J Biochem Cell Biol* 2014; **53**:

202-207 [PMID: 24863362 DOI: 10.1016/j.biocel.2014.05.019]

81 **Chacko BK**, Kramer PA, Ravi S, Benavides GA, Mitchell T, Dranka BP, Ferrick D, Singal AK, Ballinger SW, Bailey SM, Hardy RW, Zhang J, Zhi D, Darley-Usmar VM. The bioenergetic health index: A new concept in mitochondrial translational research. *Clin Sci* (Lond)

2014; **127**: 367-373 [PMID: 24895057 DOI: 10.1042/CS20140101]

82 **Gorgey AS**, Dolbow DR, Dolbow JD, Khalil RK, Gater DR. The effects of electrical stimulation on body composition and metabolic profile after spinal cord injury--Part II. *J Spinal Cord Med* 2015; **38**: 23-37 [PMID: 25001669 DOI: 10.1179/2045772314Y.0000000244]

REVIEW

Magnetic resonance imaging after anterior cruciate ligament reconstruction: A practical guide

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Abstract

Anterior cruciate ligament (ACL) reconstruction is one of the most common orthopedic procedures performed worldwide. In this regard, magnetic resonance imaging (MRI) represents a useful pre-operative tool to confirm a disruption of the ACL and to assess for potential associated injuries. However, MRI is also valuable post-operatively, as it is able to identify, in a non-invasive way, a number of aspects and situations that could suggest potential problems to clinicians. Graft signal and integrity, correct tunnel placement, tunnel widening, and problems with fixation devices or the donor site could all compromise the surgical outcomes and potentially predict the failure of the ACL reconstruction. Furthermore, several anatomical features of the knee could be associated to worst outcomes or higher risk of failure. This review provides a practical guide for the clinician to evaluate the post-surgical ACL through MRI, and to analyze all the parameters and features directly or indirectly related to ACL reconstruction, in order to assess for normal or pathologic conditions.

Key words: Anterior cruciate ligament reconstruction; Magnetic resonance imaging; Graft; Tunnel; Failures; Complications; Anatomic

Core tip: There are several original studies and reviews in the literature that discuss magnetic resonance imaging (MRI) evaluation after anterior cruciate ligament (ACL) reconstruction. However, these are mostly focused on a single aspect such as graft signal intensity, tunnel

placement, joint anatomy, or complications. This is a first known review to summarize all the aspects that should be evaluated through MRI after an ACL reconstruction, in order to perform a complete and global assessment of the post-operative status. The iconographic sections with practical and detailed explanation of measurements will serve as a useful reference for the MRI evaluation after ACL reconstruction in daily clinical practice.

INTRODUCTION

Anterior cruciate ligament (ACL) reconstruction is one of the most common orthopedic procedures performed worldwide. It is considered the standard of care for young active patients who wish to return to sport practice after ACL injury[1]. Despite the lack of clear evidence of its ability to reduce the onset and progression of knee osteoarthritis (OA), ACL reconstruction is expected to prevent further meniscal and cartilage lesions that could occur in the ACL-deficient knee[2,3]. Usually, ACL reconstruction is performed arthroscopically (occasionally combined with extra-articular plasty/augmentation) using autologous graft such as Gracilis and Semitendinosus tendons (HS), bone-patellar tendon bone (BPTB), and Quadriceps Tendon (QT), or allogenic grafts such as BPTB, Achilles Tendon, and Posterior or Anterior Tibialis tendons. Graft fixation is obtained through a wide range of fixation devices, different in function, shape, size, material, biomechanical proprieties and positioning. The outcomes of ACL reconstruction are generally good; however, graft rupture or clinical failure can occur in 6%-12% of the cases[4].

In the field of ACL injury and reconstruction, magnetic resonance imaging (MRI) represents a useful pre-operative tool to confirm a disruption of the ACL and to assess for potential associated injuries. However, MRI is also valuable post-operatively to assess graft healing and maturation, to determine its position, and to evaluate potential complications or re-injury[5-7]. For example, a survey among expert surgeons of the German Arthroscopy Association (AGA) showed that MRI represents one of the decision-making criteria for return to sport activity in only 4% of those interviewed[8].

The purpose of this review is to provide a practical guide for the clinician to evaluate the post-surgical ACL through MRI, and to analyze all the parameters and features directly or indirectly related to ACL reconstruction, in order to assess normal or pathologic conditions.

Figure 1 Various graft signal intensity. The signal intensity is usually calculated through the SNQ (signal-digital noise ratio), which is obtained through the following formula: SNQ = (ACL graft signal - PCL graft signal)/background signal. According to these measurements, we could have a hyperintense graft (A), a graft with reduced intensity signal but not yet analogous to native ACL (B) and a graft iso-intense to PCL (C). PCL: Posterior cruciate ligament; SNQ: Symbol of national quality; ACL: Anterior cruciate ligament.

GRAFT SIGNAL

The signal evaluation of the neo-ligament, whose intensity is generally evaluated with a combined score (Table 1) or with software (Figure 1), represents a dynamic field of research.

General healing process

From the biological point of view, the intra-articular graft undergoes a maturation and remodeling process lasting even beyond 24 mo, and consists of 4 steps: The initial avascular necrosis, the revascularization, cellular proliferation, and final remodeling[9]. It is generally agreed that initially the graft undergoes necrosis, showing hypocellularity especially in its central part. Cytokines are released as a consequence of necrosis, which then trigger growth factors for cell migration, proliferation, extracellular matrix (ECM) synthesis, and revascularization[10]. Maximum cellularity is observed during the proliferation phase as the cell number surpasses that of the intact ACL in numerous animal models[11]. Cell numbers then regress towards the intact ACL cellularity at the end of the proliferation phase. The tissue remodeling phase is started with cell-mediated restructuring of the extracellular matrix as an adaptive response to mechanical loading on the

tendon graft. This whole process from tendon graft toward the acquisition of histologic and biomechanical properties similar to the native ACL is known as "ligamentization".

This process could be indirectly monitored through MRI, as it has been proved that poor biomechanical properties and an incomplete graft maturation are related to a hyperintense graft signal on MRI[5,7]. Weiler et al[12] demonstrated in an animal model that a significantly elevated graft signal was present between the 6th and 12th weeks, and this condition was correlated to the lowest tensile stress of the graft (estimated around the 7%-16% of the initial values). However, from the 6th to the 24th month, the signal did not differ from that of the native ACL and the tensile stress increased, reaching around the 60% of the time-zero values. Furthermore, contrast-enhanced MRI with gadolinium showed the return to a graft signal similar to the native ACL by the 24th month, thus suggesting a late remodeling period. From the histological point of view, hyperintense signal was correlated to the presence of new hypervascular and hypercellular reparative tissue.

Despite the normal maturation process, it is important to know that an increase of signal intensity of the new-ACL, especially on the distal two-thirds, may also be due to graft impingement. This complication occurs when the grafts contacts the intercondylar notch during the extension of the knee. This has been implicated in the pathogenesis of the so-called "Cyclops lesion", which consist of a fibrous injury to the anterior side of the graft, close to the site of greatest friction within the notch[5,13].

BPTB autograft
The structural composition of the graft and the presence or absence of the bone plugs has been shown to present different maturation behaviors and presentations with MRI. When BPTB autograft tendons are used, in the first month the graft usually presents a low-intensity signal in T1 and T2 sequences, similar to the original patellar tendon, mirroring the relatively avascular nature of the donor structure. Subsequently, during the remodeling phase, the graft is wrapped by synovial tissue and vascularized (Figure 2), with the consequent increase of MRI signal up to 16-18 mo. After this period, the graft will shortly reach a signal very similar to original ACL[5-7].

HS autograft
When Gracilis and Semitendinosus autograft tendons are used, in the 1st month it is possible to not necessarily observe a hypointense signal as with the BPTB graft, because of the multiple layer configuration of the graft that could cause an accumulation of a thin liquid stratum (hyperintense at the MRI) between the individual layers. This finding, sometimes combined with small liquid deposits in the tunnel-graft interface, can remain in the first post-operative year. After that, the maturation process continues similarly to that of the patellar tendon[5-7]. However, in a recent study on 26 patients undergoing single-bundle ACL reconstruction, it has been

Figure 2 Successful anterior cruciate ligament reconstruction with Gracilis and Semitendinosus autograft with a normal healing process. At the 6th month, it is possible to appreciate in the T2-Fast recovery sat-spin echo (FRFSE) MRI a hyperintense line within the graft body. The graft is surrounded by an intermediate signal intensity tissue (red arrows), representing vascularization and synovialization (A). At the 12th month, the periligamentous signal has disappeared and the graft signal decreased resembling that of PCL (B). PCL: Posterior cruciate ligament; ACL: Anterior cruciate ligament; MRI: Magnetic resonance imaging.

shown that the Gracilis and Semitendinosus autograft demonstrated slower maturation at 6 mo compared to an autograft quadriceps tendon with bone block, when measured with the signal/noise quotient[14]. The authors proposed the possibility of needing to modify rehabilitation according to the extent of graft maturation to prevent re-injury and maximize patient function.

Allografts
Even allografts exhibit a similar behavior; however, it has been demonstrated that they have a much longer maturating process[15-17]. This has been confirmed by the persistence of a higher signal intensity compared to autografts for up to 2 years following ACL reconstruction[18].

In summary, the MRI evaluation of the neo-ligament signal indirectly allows us to obtain valuable information of the state of maturation, giving the clinician precious insight that can help guide rehabilitation and physical activity.

GRAFT INTEGRITY
Apart from incorrect tunnel placement, one of the most common causes of ACL reconstruction failure is a new injury. A new disruption of the reconstructed ligament appears on MRI as increased signal intensity in the T2 sequence within the graft body[7,19] (Figure 3). However, this should be combined with a concordant clinical examination and a clear medical history of a new trauma. In fact, the mere MRI evaluation could sometimes be misleading, because of the discordance between clinical examination and MRI evaluation. In a series of 50 revision ACL reconstructions with a graft lesion confirmed by arthroscopy and clinical examination, the graft was read intact on MRI evaluation in 24% of cases. The discordance between MRI and clinical evaluation,

Figure 3 Three years after an anterior cruciate ligament reconstruction with Gracilis and Semitendinosus autograft in a 26-year-old-male. The intercondylar space is occupied by mixoid tissue with slightly hyperintense signal in proton density turbo-shin echo weighted images (white arrows). It is not possible to distinguish the regular course of the graft.

Figure 4 On the sagittal plane, the front border of the tibial tunnel. It should be localized behind a line that is tangential to the Blumensaat line (line b); however, without going beyond the midpoint of the proximal tibia with the knee in full extension. The femoral tunnel should be located at the intersection of the posterior femoral cortex (line a) and the lateral wall of the intercondylar notch (line b). The position of the tibial tunnel entrance is measured as following: the total antero-posterior diameter of the tibial plateau (line c) is measured in the sagittal slice where the tibial entrance is better visualized. The location of the anterior margin of the tunnel is obtained dividing the distance from the anterior tibial plateau margin and the most anterior part of the tunnel entrance (point 1) for the total AP diameter (line c) and multiplying for 100. The location of the posterior margin (point 3) and the center of the tunnel (point 2) are obtained similarly (A). Sagittal view with a tibial tunnel positioned anterior to the midpoint of the tibial plateau diameter, resulting in an increased risk of impingement (B). Sagittal view with a tibial tunnel positioned too posterior, resulting in a vertical graft (C). The native ACL is located between the 31% and 63% of the tibial plateau diameter, with its center at 48%. ACL: Anterior cruciate ligament.

and between MRI and arthroscopic evaluation was 52% and 44% respectively, especially in the cases of an insidious-onset mechanism of injury[19]. With arthroscopic evaluation as the diagnostic standard, the sensitivity of MRI to diagnose an ACL graft tear was 60%, and specificity 87%.

Therefore, it is possible to see an apparently normal graft on MRI but clinically or arthroscopically injured or elongated. To avoid this discrepancy and to improve the diagnostic power, some authors suggest the use of MR-arthrography, which can increase the sensitivity and specificity toward values near 100%[5]. Nevertheless the MRI should be considered an additional and not exclusive tool for the assessment of the post-operative ACL.

TUNNEL POSITION

The correct positioning of the femoral and tibia tunnel represents a key technical step for the success of ACL reconstruction surgery. The MRI provides important information about those aspects, especially regarding the graft inclination.

Sagittal plane position

On the sagittal plane of the MRI the front border of the tibial tunnel should be localized behind a line that is tangential to the Blumensaat line (which is the line tangential to the intercondylar roof), without going beyond the midpoint of the proximal tibia with the knee in full extension (Figure 4A). The tibial tunnel center should ideally be located around the 42% mark of the entire sagittal distance of the tibial plateau as measured from the anterior edge of the tibia[20] (Figure 4A). It has been demonstrated that the native ACL is located between the 28% and 63% mark of the tibial plateau's antero-posterior diameter, with the center at 46%[21]. If the tunnel is too forward, the risk of impingement of the graft with the intercondylar notch increases, possibly causing extension deficit or a Cyclops lesion (Figure

4B), while a tunnel too posterior could lead to a vertical graft (Figure 4) responsible of an incomplete control of knee antero-posterior and rotatory stability[22]. A controversial matter of debate is the correct positioning of the femoral tunnel. Despite the fact that the most accurate evaluation is obtained through arthroscopy, MRI could be helpful to identify gross malpositioning. It is generally accepted that the femoral tunnel should be located at the intersection of the posterior femoral cortex and the lateral wall of the intercondylar notch[23] (Figure 4A).

Regarding the bi-dimensional sagittal inclination, considering that the native ACL sagittal inclination ranges between 50°-60°[24], the graft inclination after ACL reconstruction should not exceed 60° (Figure 5A). A greater laxity could be linked to ACL reconstructions with sagittal graft inclination > 60° (Figure 5B).

Coronal plane position

Similarly, on the coronal plane, the graft inclination should be less than 75° (Figure 6A), as an excessively vertical graft sub-optimally controls rotatory laxity compared with a more horizontally placed graft[25] (Figure 6B). Usually, the coronal position of the tibial tunnel entrance does not represent an issue in the MRI evaluation after ACL reconstruction, as it is generally in the correct position under the femoral notch in the vast majority of the cases thanks to intra-operative anatomical landmarks; such as the anterior horn of lateral meniscus and the medial tibial eminence.

Figure 5 Measurement of the sagittal obliquity of the graft. The inclination is calculated measuring the angle between the perpendicular line (line c and d) to the proximal tibial axis (line a and b), and the line which best defines the course of intra-articular part of the graft (line e and f). A high angle represents a vertical graft in the sagittal plane (A). Vertically positioned graft, with an angle of 78°, far higher than the normal range 50°-60° (B).

Figure 6 Measurement of the coronal obliquity of the graft. The inclination is calculated measuring the angle between the tangent line to the tibial plateau (a and b) and the line which best defines the course of the intra-articular part of the graft (c and d). A high angle represents a vertical graft in the coronal plane (A). Vertically positioned graft, with an angle of 88°, far higher than the normal value < 75° (B).

Tunnel inclination could therefore be correlated with success or failure of ACL reconstruction. Hosseini *et al*[26], reported a mean sagittal graft inclination of 69° in patients with failed ACL reconstruction scheduled for a revision procedure. Similarly, Mall *et al*[24] reported greater laxity in knees with sagittal graft inclination > 60° (Figure 5B); however, this did not affect general outcomes and the ability of these National Football League (NFL) athletes to return to high level sports practice. Furthermore, Fujimoto *et al*[27] found a mean coronal graft inclination of 79.5° in patients with grade 3 laxity after ACL reconstruction. Several factors could influence graft inclination, such as surgical experience, knee anatomy, and surgical technique. It has been demonstrated that trans-tibial (TT) femoral tunnel drilling tended to result in more vertical grafts in the sagittal plane compared to anteromedial portal (AMP) drilling (72° *vs* 53°)[28] or other methods of independent femoral tunnel drilling.

TUNNEL ENLARGEMENT

Tunnel morphology and possible enlargement should be evaluated appropriately using radiographs, computed tomography (CT), or MRI[29]. It has been demonstrated that intra-observer kappa scores for CT, radiographic and MRI evaluation of tunnel enlargement were 0.66, 0.50 and 0.37 respectively, and inter-observer kappa scores were 0.65, 0.39 and 0.32 respectively. Thus, MRI is considered a sub-optimal and not reliable tool to evaluate the progression of tunnel enlargement, while the CT represents the most reliable one. A precise

tunnel measurement is in fact mandatory, as it could represent an indication for a staged revision procedure (usually with a tunnel diameter > 15 mm). However, through MRI it is possible to identify liquid collection and cyst formation inside the tibial tunnel, responsible of potential tunnel widening (Figure 7). Usually in Gracilis and Semitendinosus ACL reconstruction, such situations could occur within the first post-operative year. A hyperintense signal due to liquid collection in the tendon-tunnel interface could be present; however, with the tendency for spontaneous resolution[5-7]. Usually, tunnel enlargement occurs within the first 3 month and tends to remain stable up to 2 years if no tunnel malpositioning or graft lack of healing is present.

The exact etiology of tunnel widening is unknown[30], despite the fact that it has been related to several factors such as mechanical or biological mechanisms. Size mismatch between tunnel and graft dimension could allow sagittal micromotion at the graft-tunnel interface: This phenomenon, known as the "windshield wiper effect", has been indicated as a potential cause of tunnel enlargement especially in the tibia, proximal to the fixation site. Similarly, longitudinal elongation, known as the "bungee cord effect" could also play a role. The use of a Gracilis and Semitendinosus graft coupled with cortical devices, that produce a low stiffness construct with a long tunnel length, have been demonstrated to be subjected to this phenomenon, leading to tunnel enlargement in the femoral side[31]. Furthermore, tunnel malposition could generate abnormal stresses and motion of the graft, leading to tunnel lysis. As tunnel enlargement has been noted to stabilize after the first 3 month post-operative,

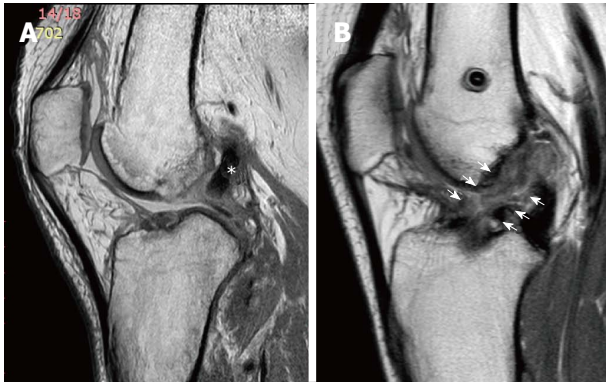**Figure 7 Coronal slice of a proton density spectral attenuated inversion recovery weighted mri 3.5 years after anterior cruciate ligament reconstruction with gracilis and semitendinosus autograft in a 29-year-old female.** It shows tibial tunnel macroscopic enlargement (A). In the sagittal T1 Turbo-Spin Echo weighted image, it is possible to note a cyst with hyperintense signal (B).

Figure 8 Proton density fat saturation coronal magnetic resonance imaging. The metal interference screw on the femoral side (black asterisk) is responsible of marked artifact that could hinder the evaluation of tunnel placement, differently from the bioabsorbable interference screw on the tibial side (white asterisk).

it is believed that the bone-to-bone or the tendon-to-bone healing within the tunnel could also influence the mechanical behavior of the graft. For the aforementioned reasons, early and aggressive rehabilitation, could potentially contribute to this phenomenon as well.

Regarding biological factors, it has been proposed that tunnel enlargement has been associated with allograft use secondary to a subclinical immunologic reaction[32], and to the presence of inflammatory cytokines within synovial fluid between the bone-graft tunnel interfaces, because of their osteolytic activity. Finally, a 12% increase size of the graft due to swelling has been reported through MRI after ACL reconstruction, and the consequent increased pressure within the tunnel could be responsible for necrosis and further cytokine release.

Despite the fact that tunnel enlargement does not appear to adversely affect clinical outcomes in the short term, the long-term relationship with potential knee laxity or increased traumatic failure is unknown[30]. Moreover, large tunnels could seriously complicate the revision procedure, especially regarding graft placement and fixation, sometimes requiring a staged procedure.

FIXATION DEVICES

Fixation devices can be an issue in ACL post-operative MRI evaluation, because metallic devices could be responsible for disturbing artifacts (Figure 8). However, artifacts derived from metallic devices such as interference screws can be managed with software techniques to reduce metallic-hardware artifacts, reduction of slice thickness, and use of interecho spacing or short tau inversion recovery (STIR) techniques[33]. The use of bioabsorbable devices reduce the problems related to artifacts. However, despite possible artifacts due to fixation devices, their macroscopic mobilization, migration or rupture could be easily evidenced on MRI, and represent the cause of a potential reconstruction failure. Interference screws can migrate inside the joint damaging articular cartilage; suspensory extra-cortical systems can move inside

the tunnel causing reduction of graft tensioning; cross pin fixation can migrate inside the soft tissues irritating muscles or tendons; while bioabsorbable materials can generate foreign-body inflammatory reaction. The latter circumstance could represent a severe event, due to an immune-mediate response. The production of inflammatory cytokine and the creation of a granuloma inside the bone around the screw or even in the surrounding soft-tissues, could possibly compromise the trabecular architecture weakening the bone[34]. Normally, bioabsorbable screws made in Poly-L-lactide (PLLA) or hydroxyapatite-PLLA have been reported to reabsorb slowly, necessitating up to 4 years to degrade[35]. Poly-D-L-lactide (PDLLA) screws have been reported clearly visible with MRI at 6-8 mo, show fragmentation and connective tissue ingrowth at 12-16 mo, and can be fully reabsorbed after 22 mo[36]. Differently, Polyglycolic Acid (PGA) screws have been shown to be completely reabsorbed even after 6-12 mo[37].

DONOR SITE PATHOLOGY

The MRI could be considered a precious tool also to evaluate aspects not directly relating to the neo-ACL, but closely related to reconstruction surgery, as those deriving from graft harvesting.

BPTB autograft

For example, the patellar tendon after the harvesting of its middle third, could appear thickened with enhanced signal in T1 and T2 sequences[38] (Figure 9). A gap between the medial and lateral third of the patellar tendon could be present, despite the fact it tends to disappear with time (Figure 10). In this regard, MRI studies have revealed the permanence of the tendon gap even after 10 years from reharvesting, and an increase of tendon thickness from 2 to 10 years, significantly higher compared to normal tendon[39]. Although rare, a patellar fracture, patellar tendon tears, bursitis or hematoma, especially after BPTB graft reharvesting, can be observed.

Figure 9 Anterior cruciate ligament reconstruction with bone-patellar tendon bone autograft in a 30-year-old male at 2 years of follow-up. Donor site pathology is displayed as a hyperintense signal (asterisk) in the proton-density fat saturation axial images surrounding the split patellar tendon (A). In the sagittal proton density weighted slice, the post-operative patellar tendinopathy is displayed as an increase of signal intensity within the tendon itself (asterisk), that resulted in an enlarged and swollen tendon (B).

Figure 10 Natural history of bone-patellar tendon bone harvesting in a 21-year-old male. It is possible to appreciate a bone defect (asterisk) on the anterior surface of the patella (A), the split hypointense patellar tendon (asterisk) (B), and another squared bone defect (asterisk) at the level of the central part of the anterior tibial tubercle (C).

Figure 11 Sagittal proton density weighted images of anterior cruciate ligament reconstruction with Gracilis and Semitendinosus Autograft in a 26-year-old male at 1.5 years follow-up. It is possible to appreciate a localized area of low to intermediate signal intensity extending anterior to the distal anterior cruciate ligament graft (black arrows) consistent with local arthrofibrosis.

Sometimes, the Hoffa fat-pad could present an inflammatory reaction, highlighted by a hyperintense T2 signal at MRI fat-suppression sequences, due to hypertrophy and edema.

Another relatively frequent complication that can occur in the anterior knee compartment often related to graft harvesting is arthrofibrosis (Figure 11). Defined as a generic condition of post-operative stiffness (either extension or flexion), arthrofibrosis is believed to occur from ACL reconstruction being performed before post-traumatic inflammation has subsided or secondary to prolonged immobilization after ACL reconstruction. The arthrofibrosis can be diffuse or focal, and presents as an area of low-intermediate signal intensity extending anterior to the distal ACL[6] (Table 1).

HS autograft

Regarding the "pes-anserinus", it occasionally is subjected

Figure 12 Natural history of Gracilis and Semitendinosus harvesting. Two years after anterior cruciate ligament reconstruction in a 21-year-old male, in the axial view it is possible to appreciate a well represented "pes anserinus" with regenerated Sartorius fascia (black asterisk), Gracilis tendon (red asterisk) and hypertrophic Semitendinosus tendon (white asterisk) (A). Conversely, seven years after anterior cruciate ligament reconstruction in a 35-year-old male, it is possible to identify the Sartorius fascia (black asterisk) with a thin and hypotrophic Gracilis (red asterisk) and Semitendinosus (white asterisk) tendons (B).

Table 1 Figueroa's score

Item	Points
Integration: Synovial fluid at tunnel-graft interface	
Positive	1
Negative	2
Ligamentization: Graft signal pattern (> 50%)	
Hypointense	3
Isointense	2
Hyperintense	1
Characterization of graft	
Poor	2
Adequate	3-5

The Figueroa score is based on the sum of the points achieved in the 2 items: 2-points represents an insufficiently mature graft, while a score between 3 and 5 points represents a good ligamentization process and graft integration.

to donor-site pathology. A light fluid collection along the donor site can be present in the first post-operative month, until its complete disappearance around 12-18 mo. Tendon regeneration has been documented to occur through the so-called "lizard's tail effect", even if the quality for reharvesting could be questioned[40]. A 2014 systematic review of 18 publications demonstrated a mean regeneration rate for the semitendinosus and gracilis tendons of 70% or higher[41]. However, more recent literature supports a complete regeneration of the Semitendinosus during the 3rd-6th month in 60% of the cases, while Gracilis regeneration has been reported to be present after its harvesting in 30% of the cases (Figure 12). Complete regeneration of the whole "pes anserinus" was only noted in 10% of the cases, often with an ectopic re-insertion 1-2 cm below the joint line at the level of Sartorius fascia or medial head of Gastrocnemius. In 15% of the cases, complete absence of both tendons was noted. An initial hypertrophy, followed by a progressive volume reduction was described along the first 2 post-operative years, accompanied by muscular atrophy, retraction and fatty infiltration in up to 90% of the cases[42].

JOINT MORPHOLOGY AND ACL RECONSTRUCTION

Tibial slope
Christensen *at al*[43] evaluated the MRI of 35 patients with early ACL failure and 35 with no evidence of ACL graft failure, particularly medial (Figure 13A) and lateral (Figure 13B) tibial plateau sagittal slope. They found a higher lateral tibial plateau slope in patients that experienced graft failure (8.4° *vs* 6.5°). They estimated an odd ratio for graft failure of 1.6, 2.4 and 3.8 with a slope increase of 2°, 4° and 6° respectively. These findings were more evident in females. A similar conclusion was presented by Webb *et al*[44] using lateral radiographs. They described an incidence near 60% of graft re-rupture or contralateral ACL injury in patients with tibial slope > 12°. An increased tibial slope, especially the posterior slope of the lateral tibial plateau, is in fact a recognized risk factor for non-contact ACL injury[45]. However, there are some controversies in the literature, as some studies describing increased medial tibial plateau being the more important risk factor to ACL injury. Others believe the meniscal slope is a more accurate measure rather than the bony tibial plateau slope. Furthermore, different landmarks for measuremet, knee or long-leg X-ray, use of MRI, and other features, increase the variability of the measurement and the absence of complete agreement regarding this issue. However, despite the controversy in the literature, it is well accepted that increasing the posteriorslope overall increases risk of ACL injury or graft failure.

Notch shape
Notch shape is also considered a risk factor for non-contact ACL injury. A narrow notch has been measured in ACL-deficient patients, probably accounting for a smaller and weaker ACL compared to healthy patients with a wider notch[46]. Furthermore, in the setting of ACL reconstruction, Fujii *et al*[13] found a smaller notch cross-sectional area (Figure 14) in patients that developed the "cyclops lesion" due to notch impingement compared to complication-free patients (251.7 mm^2 *vs* 335.6 mm^2).

Anterior subluxation
Tanaka *et al*[47] reported an abnormal tibiofemoral relationship at MRI in patients with failed ACL recon-struction. An average of 5.7 mm of anterior tibial subluxation within the lateral compartment was reported, with a value greater than 15 mm in 12.5% of cases (Figure 15). The magnitude of anterior subluxation was 3.9 mm and 3.1 mm greater than the values of normal

Figure 13 The medial tibial plateau slope is calculated in a sagittal slice passing through the middle-portion of the tibial plateau. As the angle between the perpendicular line (line c and d) to the proximal tibial axis (line a and b) and the line tangent to the tibial plateau (line e and f) (A); the lateral tibial plateau slope is calculated similarly (B). For a correct identification of the proximal tibial axis, it should pass mid-way on two antero-posterior tibial diameters drawn at a distance of 5 cm and 15 cm from the joint line.

Figure 14 The femoral notch cross sectional area is measured as follows. The coronal slice passing at the middle point of the Blumensaat Line is chosen. The width of the notch (red dotted line) is measured on a line passing through the popliteal groove (line c and d) parallel to the femoral joint surface (line a and b). The height of the notch is the distance between the joint surface and the top of the intercondylar notch. The cross sectional area (red box) is obtained multiplying the width (mm) by the height (mm).

Figure 15 The tibial anterior subluxation with respect to the femur is measured as follow. With the magnetic resonance imaging acquired in extension and external rotation, the sagittal slice passing through the insertion of the medial gastrocnemius (medial side) or through the most medial cut of the fibula at the tibiofibular joint (lateral side) is selected. Then, a circle over the subchondral line of the posterior condyle (circle a) and a line tangential to the tibial plateau (line b and c) are drawn. The distance (red asterisk) between a perpendicular line to the tibial plateau passing through its posterior margin (line d and e) and a parallel line tangent to the circle (line f and g) is measured.

Figure 16 Tibial plateau anatomy is best evaluated by selecting the coronal slice where both tibial spines are visible. Lateral Femoral Condyle (line a) and Medial Femoral Condyle (line b) diameters are measured from borders of corresponding articular cartilage. Lateral Tibial Plateau (line c) and Medial Tibial Plateau (line d) diameters are measured from the intercondylar spine to the border of the corresponding tibial plateau.

knees and knees with acute ACL tears, respectively. No noteworthy findings were reported for the medial compartment. This association between anterior displacement and failed ACL reconstruction may provide a mechanical explanation of suboptimal clinical results of ACL revision reconstruction.

Tibial plateau and femoral condyles geometry
In the ACL-deficient condition, Musahl *et al*[48] noted a narrower lateral tibial plateau in patients with grade Ⅱ pivot-shift compared to patients with grade Ⅰ pivot-shift, (35.5 mm *vs* 30.3 mm) (Figure 16). However, this finding was significant only in female patients. No other anatomical parameters seemed to affect the pre-operative laxity. The authors suggested that bony anatomy contributes to the magnitude of knee laxity in the ACL-deficient knee; therefore, it could be argued that patients with specific anatomical features could represent

patients with a higher risk of sub-optimal results of ACL reconstruction. In these cases of higher pre-operative laxity, the association of a lateral extra-articular plasty could be indicated[49] (Figure 17).

CONCLUSION

MRI represents an important tool for the post ACL reconstruction evaluation, due to its abilities to identify, in a non-invasive manner, a number of aspects and situations that could suggest potential problems to clinicians. Graft signal and integrity, correct tunnel placement or widening, and problems with fixation devices or donor site could all compromise the surgical outcomes and potentially determine the failure of the ACL reconstruction. However, this tool must not be used in isolation when assessing the post ACL reconstruction status. It should always

Figure 17 Magnetic resonance imaging evaluation of an anterior cruciate ligament reconstruction with a single-bundle plus lateral extra-articular plasty/augmentation using Gracilis and Semitendinosus Autograft. In the coronal view, it is possible to identify the intra-articular part of the graft (black arrows) that continue proximally above the lateral femoral condyle (red arrows) in the "over-the-top" position (A). The lateral extra-articular plasty (asterisk) could be identified both in axial (B) and coronal view (C) beneath the iliotibial band, extending from the lateral femoral condyle to Gerdy's tubercle.

be integrated with a careful clinical and medical history evaluation, as only an integrated approach to graft status and functionality is most effective in reducing potential diagnostic mistakes.

REFERENCES

1   **Irarrzaval S**, Kurosaka M, Cohen M, Fu FH. Anterior cruciate ligament reconstruction. *ISAKOS* 2016; **1**: 38-52 [DOI: 10.1136/jisakos-2015-000001]

2   **Fabricant PD**, Lakomkin N, Cruz A, Spitzer E, Lawrence JTR, Marx RG. Early ACL reconstruction in children leads to less meniscal and articular cartilage damage when compared with conservative or delayed treatment. *ISAKOS* 2016; **1**: 10-15 [DOI: 10.1136/jisakos-2015-000012]

3   **Fabricant PD**, Lakomkin N, Cruz A, Spitzer E, Marx RG. ACL reconstruction in youth athletes results in an improved rate of return to athletic activity when compared with non-operative treatment: a systematic review of the literature. *ISAKOS* 2016; **1**: 2059-7762 [DOI: 10.1136/jisakos-2015-000013]

4   **Crawford SN**, Waterman BR, Lubowitz JH. Long-term failure of anterior cruciate ligament reconstruction. *Arthroscopy* 2013; **29**: 1566-1571 [PMID: 23820260 DOI: 10.1016/j.arthro.2013.04.014]

5   **Gnannt R**, Chhabra A, Theodoropoulos JS, Hodler J, Andreisek G. MR imaging of the postoperative knee. *J Magn Reson Imaging* 2011; **34**: 1007-1021 [PMID: 22002752 DOI: 10.1002/jmri.22672]

6   **Kulczycka P**, Larbi A, Malghem J, Thienpont E, Vande Berg B, Lecouvet F. Imaging ACL reconstructions and their complications. *Diagn Interv Imaging* 2015; **96**: 11-19 [PMID: 24910463 DOI: 10.1016/j.diii.2014.04.007]

7   **Naraghi A**, White L. MRI evaluation of the postoperative knee: special considerations and pitfalls. *Clin Sports Med* 2006; **25**: 703-725 [PMID: 16962423 DOI: 10.1016/j.csm.2006.06.007]

8   **Petersen W**, Zantop T. Return to play following ACL reconstruction: survey among experienced arthroscopic surgeons (AGA instructors). *Arch Orthop Trauma Surg* 2013; **133**: 969-977 [PMID: 23604790 DOI: 10.1007/s00402-013-1746-1]

9   **Janssen RP**, Scheffler SU. Intra-articular remodelling of hamstring tendon grafts after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 2102-2108 [PMID: 23982759 DOI: 10.1007/s00167-013-2634-5]

10   **Lui PP**, Lee YW, Mok TY, Cheuk YC, Chan KM. Alendronate reduced peri-tunnel bone loss and enhanced tendon graft to bone tunnel healing in anterior cruciate ligament reconstruction. *Eur Cell Mater* 2013; **25**: 78-96 [PMID: 23325540]

11   **Unterhauser FN**, Bail HJ, Höher J, Haas NP, Weiler A. Endoligamentous revascularization of an anterior cruciate ligament graft. *Clin Orthop Relat Res* 2003; **(414)**: 276-288 [PMID: 12966303 DOI: 10.1097/01.blo.0000079442.64912.51]

12   **Weiler A**, Peters G, Mäurer J, Unterhauser FN, Südkamp NP. Biomechanical properties and vascularity of an anterior cruciate ligament graft can be predicted by contrast-enhanced magnetic resonance imaging. A two-year study in sheep. *Am J Sports Med* 2001; **29**: 751-761 [PMID: 11734489]

13   **Fujii M**, Furumatsu T, Miyazawa S, Okada Y, Tanaka T, Ozaki T, Abe N. Intercondylar notch size influences cyclops formation after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 1092-1099 [PMID: 24549261 DOI: 10.1007/s00167-014-2891-y]

14   **Ma Y**, Murawski CD, Rahnemai-Azar AA, Maldjian C, Lynch AD, Fu FH. Graft maturity of the reconstructed anterior cruciate ligament 6 months postoperatively: a magnetic resonance imaging evaluation of quadriceps tendon with bone block and hamstring tendon autografts. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 661-668 [PMID: 25223969 DOI: 10.1007/s00167-014-3302-0]

15   **Amendola A**, Stolley MP. What do we really know about allografts? *Clin Sports Med* 2009; **28**: 215-222, vii-viii [PMID: 19306731 DOI: 10.1016/j.csm.2008.10.002]

16   **Ekdahl M**, Wang JH, Ronga M, Fu FH. Graft healing in anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2008; **16**: 935-947 [PMID: 18633596 DOI: 10.1007/s00167-008-0584-0]

17   **Gulotta LV**, Rodeo SA. Biology of autograft and allograft healing in anterior cruciate ligament reconstruction. *Clin Sports Med* 2007; **26**: 509-524 [PMID: 17920950 DOI: 10.1016/j.csm.2007.06.007]

18   **Li H**, Tao H, Cho S, Chen S, Yao Z, Chen S. Difference in graft maturity of the reconstructed anterior cruciate ligament 2 years postoperatively: a comparison between autografts and allografts in young men using clinical and 3.0-T magnetic resonance imaging evaluation. *Am J Sports Med* 2012; **40**: 1519-1526 [PMID: 22495290 DOI: 10.1177/0363546512443050]

19   **Waltz RA**, Solomon DJ, Provencher MT. A Radiographic Assessment

of Failed Anterior Cruciate Ligament Reconstruction: Can Magnetic Resonance Imaging Predict Graft Integrity? *Am J Sports Med* 2014; **42**: 1652-1660 [PMID: 24821755 DOI: 10.1177/0363546514532335]

20 **Howell SM**, Berns GS, Farley TE. Unimpinged and impinged anterior cruciate ligament grafts: MR signal intensity measurements. *Radiology* 1991; **179**: 639-643 [PMID: 2027966 DOI: 10.1148/radiology.179.3.2027966]

21 **Frank RM**, Seroyer ST, Lewis PB, Bach BR, Verma NN. MRI analysis of tibial position of the anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1607-1611 [PMID: 20563557 DOI: 10.1007/s00167-010-1192-3]

22 **Lee S**, Kim H, Jang J, Seong SC, Lee MC. Intraoperative correlation analysis between tunnel position and translational and rotational stability in single- and double-bundle anterior cruciate ligament reconstruction. *Arthroscopy* 2012; **28**: 1424-1436 [PMID: 22717211 DOI: 10.1016/j.arthro.2012.03.027]

23 **Tomczak RJ**, Hehl G, Mergo PJ, Merkle E, Rieber A, Brambs HJ. Tunnel placement in anterior cruciate ligament reconstruction: MRI analysis as an important factor in the radiological report. *Skeletal Radiol* 1997; **26**: 409-413 [PMID: 9259098 DOI: 10.1007/s002560050256]

24 **Mall NA**, Matava MJ, Wright RW, Brophy RH. Relation between anterior cruciate ligament graft obliquity and knee laxity in elite athletes at the National Football League combine. *Arthroscopy* 2012; **28**: 1104-1113 [PMID: 22421564 DOI: 10.1016/j.arthro.2011.12.018]

25 **Saupe N**, White LM, Chiavaras MM, Essue J, Weller I, Kunz M, Hurtig M, Marks P. Anterior cruciate ligament reconstruction grafts: MR imaging features at long-term follow-up--correlation with functional and clinical evaluation. *Radiology* 2008; **249**: 581-590 [PMID: 18769016 DOI: 10.1148/radiol.2492071651]

26 **Hosseini A**, Lodhia P, Van de Velde SK, Asnis PD, Zarins B, Gill TJ, Li G. Tunnel position and graft orientation in failed anterior cruciate ligament reconstruction: a clinical and imaging analysis. *Int Orthop* 2012; **36**: 845-852 [PMID: 21826407 DOI: 10.1007/s00264-011-1333-4]

27 **Fujimoto E**, Sumen Y, Deie M, Yasumoto M, Kobayashi K, Ochi M. Anterior cruciate ligament graft impingement against the posterior cruciate ligament: diagnosis using MRI plus three-dimensional reconstruction software. *Magn Reson Imaging* 2004; **22**: 1125-1129 [PMID: 15527999 DOI: 10.1016/j.mri.2004.08.007]

28 **Hantes ME**, Zachos VC, Liantsis A, Venouziou A, Karantanas AH, Malizos KN. Differences in graft orientation using the transtibial and anteromedial portal technique in anterior cruciate ligament reconstruction: a magnetic resonance imaging study. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 880-886 [PMID: 19238359 DOI: 10.1007/s00167-009-0738-8]

29 **Marchant MH**, Willimon SC, Vinson E, Pietrobon R, Garrett WE, Higgins LD. Comparison of plain radiography, computed tomography, and magnetic resonance imaging in the evaluation of bone tunnel widening after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1059-1064 [PMID: 19953224 DOI: 10.1007/s00167-009-0952-4]

30 **Wilson TC**, Kantaras A, Atay A, Johnson DL. Tunnel enlargement after anterior cruciate ligament surgery. *Am J Sports Med* 2004; **32**: 543-549 [PMID: 14977688 DOI: 10.1177/0363546504263151]

31 **Clatworthy MG**, Annear P, Bulow JU, Bartlett RJ. Tunnel widening in anterior cruciate ligament reconstruction: a prospective evaluation of hamstring and patella tendon grafts. *Knee Surg Sports Traumatol Arthrosc* 1999; **7**: 138-145 [PMID: 10401649]

32 **Fahey M**, Indelicato PA. Bone tunnel enlargement after anterior cruciate ligament replacement. *Am J Sports Med* 1994; **22**: 410-414 [PMID: 8037283 DOI: 10.1177/036354659402200318]

33 **White LM**, Buckwalter KA. Technical considerations: CT and MR imaging in the postoperative orthopedic patient. *Semin Musculoskelet Radiol* 2002; **6**: 5-17 [PMID: 11917267 DOI: 17.10.1055/s-2002-23160]

34 **Konan S**, Haddad FS. Femoral fracture following knee ligament reconstruction surgery due to an unpredictable complication of bioabsorbable screw fixation: a case report and review of literature. *J Orthop Traumatol* 2010; **11**: 51-55 [PMID: 20016925 DOI: 10.1007/s10195-009-0079-x]

35 **Ma CB**, Francis K, Towers J, Irrgang J, Fu FH, Harner CH. Hamstring anterior cruciate ligament reconstruction: a comparison of bioabsorbable interference screw and endobutton-post fixation. *Arthroscopy* 2004; **20**: 122-128 [PMID: 14760343 DOI: 10.1016/j.arthro.2003.11.007]

36 **Achtnich A**, Forkel P, Metzlaff S, Zantop T, Petersen W. Degradation of poly-D-L-lactide (PDLLA) interference screws (Megafix ®). *Arch Orthop Trauma Surg* 2014; **134**: 1147-1153 [PMID: 24899253 DOI: 10.1007/s00402-014-2013-9]

37 **Fink C**, Benedetto KP, Hackl W, Hoser C, Freund MC, Rieger M. Bioabsorbable polyglyconate interference screw fixation in anterior cruciate ligament reconstruction: a prospective computed tomography-controlled study. *Arthroscopy* 2000; **16**: 491-498 [PMID: 10882444 DOI: 10.1053/jars.2000.4633]

38 **Peterson RK**, Shelton WR, Bomboy AL. Allograft versus autograft patellar tendon anterior cruciate ligament reconstruction: A 5-year follow-up. *Arthroscopy* 2001; **17**: 9-13 [PMID: 11154360 DOI: 10.1053/jars.2001.19965]

39 **Lidén M**, Ejerhed L, Sernert N, Bovaller A, Karlsson J, Kartus J. The course of the patellar tendon after reharvesting its central third for ACL revision surgery: a long-term clinical and radiographic study. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 1130-1138 [PMID: 16951974 DOI: 10.1007/s00167-006-0167-x]

40 **Yoshiya S**, Matsui N, Matsumoto A, Kuroda R, Lee S, Kurosaka M. Revision anterior cruciate ligament reconstruction using the regenerated semitendinosus tendon: analysis of ultrastructure of the regenerated tendon. *Arthroscopy* 2004; **20**: 532-535 [PMID: 15122146 DOI: 10.1016/j.arthro.2004.01.031]

41 **Suijkerbuijk MA**, Reijman M, Lodewijks SJ, Punt J, Meuffels DE. Hamstring Tendon Regeneration After Harvesting: A Systematic Review. *Am J Sports Med* 2015; **43**: 2591-2598 [PMID: 25548149 DOI: 10.1177/0363546514562169]

42 **Tsifountoudis I**, Bisbinas I, Kalaitzoglou I, Markopoulos G, Haritandi A, Dimitriadis A, Papastergiou S. The natural history of donor hamstrings unit after anterior cruciate ligament reconstruction: a prospective MRI scan assessment. *Knee Surg Sports Traumatol Arthrosc* 2015; Epub ahead of print [PMID: 26239861 DOI: 10.1007/s00167-015-3732-3]

43 **Christensen JJ**, Krych AJ, Engasser WM, Vanhees MK, Collins MS, Dahm DL. Lateral Tibial Posterior Slope Is Increased in Patients With Early Graft Failure After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2015; **43**: 2510-2514 [PMID: 26320223 DOI: 10.1177/0363546515597664]

44 **Webb JM**, Salmon LJ, Leclerc E, Pinczewski LA, Roe JP. Posterior tibial slope and further anterior cruciate ligament injuries in the anterior cruciate ligament-reconstructed patient. *Am J Sports Med* 2013; **41**: 2800-2804 [PMID: 24036571 DOI: 10.1177/0363546513503288]

45 **Bisson LJ**, Gurske-DePerio J. Axial and sagittal knee geometry as a risk factor for noncontact anterior cruciate ligament tear: a case-control study. *Arthroscopy* 2010; **26**: 901-906 [PMID: 20620789 DOI: 10.1016/j.arthro.2009.12.012]

46 **Sonnery-Cottet B**, Archbold P, Cucurulo T, Fayard JM, Bortolletto J, Thaunat M, Prost T, Chambat P. The influence of the tibial slope and the size of the intercondylar notch on rupture of the anterior cruciate ligament. *J Bone Joint Surg Br* 2011; **93**: 1475-1478 [PMID: 22058297 DOI: 10.1302/0301-620X.93B11.26905]

47 **Tanaka MJ**, Jones KJ, Gargiulo AM, Delos D, Wickiewicz TL, Potter HG, Pearle AD. Passive anterior tibial subluxation in anterior cruciate ligament-deficient knees. *Am J Sports Med* 2013; **41**: 2347-2352 [PMID: 23928320 DOI: 10.1177/0363546513498995]

48 **Musahl V**, Ayeni OR, Citak M, Irrgang JJ, Pearle AD, Wickiewicz TL. The influence of bony morphology on the magnitude of the pivot shift. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1232-1238 [PMID: 20376621 DOI: 10.1007/s00167-010-1129-x]

49 **Marcacci M**, Zaffagnini S, Marcheggiani Muccioli GM, Neri MP,

Bondi A, Nitri M, Bonanzinga T, Grassi A. Arthroscopic intra- and extra-articular anterior cruciate ligament reconstruction with gracilis and semitendinosus tendons: a review. *Curr Rev Musculoskelet Med* 2011; **4**: 73-77 [PMID: 21594691 DOI: 10.1007/s12178-011-9075-x]

MINIREVIEWS

Treatment of the ulnar nerve for overhead throwing athletes undergoing ulnar collateral ligament reconstruction

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Abstract

Ulnar nerve (UN) injuries are a common complaint amongst overhead athletes. The UN is strained during periods of extreme valgus stress at the elbow, especially in the late-cocking and early acceleration phases of throwing. Although early ulnar collateral ligament (UCL) reconstruction techniques frequently included routine submuscular UN transposition, this is becoming less common with more modern techniques. We review the recent literature on the sites of UN compression, techniques to evaluate the UN nerve, and treatment of UN pathology in the overhead athlete. We also discuss our preferred techniques for selective decompression and anterior transposition of the UN when indicated. More recent studies support the use of UN transpositions only when there are specific preoperative symptoms. Athletes with isolated ulnar neuropathy are increasingly being treated with subcutaneous anterior transposition of the nerve rather than submuscular transposition. When ulnar neuropathy occurs with UCL insufficiency, adoption of the muscle-splitting approach for UCL reconstructions, as well as using a subcutaneous UN transposition have led to fewer postoperative complications and improved outcomes. Prudent handling of the UN in addition to appropriate surgical technique can lead to a high percentage of athletes who return to competitive sports following surgery for ulnar neuropathy.

Key words: Ulnar nerve; Neuropathy; Ulnar collateral ligament reconstruction; Management; Athletes

Core tip: Ulnar nerve (UN) injuries frequently plague overhead athletes due to the strain caused by extreme valgus stress across the elbow during throwing. In this paper, we review common locations of UN compression

and keys to the evaluation. We also discuss the recent literature on treatment of injuries to the UN in overhead athletes and our preferred techniques for addressing UN symptomatology during concomitant UCL reconstruction. Athletes are increasingly being treated with subcutaneous anterior UN transpositions only when appreciable neurologic symptoms are present preoperatively.

Figure 1 Ulnar nerve anatomy at the elbow. The ulnar nerve courses posterior to the intermuscular septum and adjacent to the triceps. It passes posterior to the medial epicondyle before entering into the cubital tunnel.

INTRODUCTION

Ulnar nerve (UN) injuries in the overhead athlete often occur as a result of overuse of the arm during throwing and may exist in isolation or in association with other pathologic processes such as ulnar collateral ligament (UCL) insufficiency[1-4]. Because of its course along the medial elbow, the UN can be strained in the cubital tunnel (CT) secondary to the extreme valgus stress experienced by the elbow during throwing[1,2]. Secondary causes of ulnar neuropathy include a traction neuritis as a result of valgus stress, osteophytes, compression caused by adhesions, flexor muscle hypertrophy, or repetitive friction secondary to subluxation of the nerve[5]. As the second most common entrapment neuropathy of the upper extremity, CT syndrome (CTS) has even been reported in adolescent baseball players in elementary and middle school[6,7].

Reconstruction of the UCL also places the UN at risk. When Dr. Jobe *et al*[8] first published his series of UCL reconstructions with concomitant submuscular UN transposition in 16 elite throwing athletes in 1986, he reported postoperative UN complications in five patients, of which, two required a subsequent surgery for neurolysis. However, changes in surgical technique including selective, subcutaneous transposition of the UN have led to improved outcomes in UCL reconstruction and fewer postoperative neurologic complications[5,9].

UN ANATOMY AND SITES OF COMPRESSION

The UN begins in the anterior compartment of the upper arm before entering the posterior compartment at the arcade of Struthers. At the elbow, the nerve resides in the CT just posterior to the medial epicondyle and exits the CT between the dual heads of the flexor carpi ulnaris muscle (FCU) and into the anterior compartment of the forearm (Figure 1). Nerve compression may occur at numerous sites throughout its course. Additionally, the UN is susceptible to the "double crush" phenomenon,

which is found when the it is compressed at more than one level[10]. This occurs because nerves compressed at one site are more easily damaged at another[11].

The arcade of Struthers, a band that travels from the medial head of the triceps to the medial intermuscular septum in the upper arm, is another common site of compression for the UN. Located approximately 8 cm proximal to the medial epicondyle, the arcade of Struthers present in 70% of the population[3,9,12,13]. Failure to relieve compression at the arcade of Struthers can lead to persistent UN symptoms despite cubital tunnel release[3,9,10,12,13]. The UN can also be compressed in patients with a hypertrophy medial triceps, which is commonly observed in throwing atheltes[9]. In a recent series of six adolescent throwers with CTS and a hypertrophic medial triceps, all six patients demonstrated UN compression when the elbow was flexed greater than 90°[7].

After traversing the arcade of Struthers, the nerve enters the CT as it passes behind the medial epicondyle. The floor of the CT is formed by the olecranon, posteromedial elbow capsule, and UCL, while the roof is created by the CT retinaculum (or arcuate ligament). It has been reported that the space available for the UN within the CT decreases by as much as 55% during elbow flexion[10]. Additionally, the CT can be narrowed in the presence of a hypertrophic arcuate ligament or anconeus epitrochlearis muscle[9,14]. Bony abnormalities such as prominent osteophytes near the medial epicondyle or the olecranon can impinge on the nerve in the CT resulting in UN irritation[9].

Upon exiting the CT, the UN passes between the dual muscle bellies of the FCU. Compression can also occur at the aponeurosis of the FCU. Additionally, repetitive microtrauma can lead to osteophyte formation and hypertrophy of the sublime tubercle at the UCL insertion, which can subsequently compress the nerve at this site[9].

UN hypermobility leading to subluxation or dislocation anteriorly over the medial epicondyle may also produce symptoms[6,9]. Subluxation of the UN typically occurs during elbow flexion[6]. Asymptomatic nerve dislocation

has been reported in 16% of individuals[15]. Chronic friction as a result of repeated subluxations of the UN in overhead athletes may lead to inflammation and neuropathy[16].

The valgus stress experienced by the elbow during overhead throwing may also lead to traction neuropathy of the UN. During late-cocking and early acceleration, the valgus force at the elbow has been estimated to be well over 60 N*m with compressive forces exceeding 500 N at the radiocapitellar joint[17]. This valgus stress, in combination with elbow extension, results in a tensile stress across structures of the medial elbow including the UCL and UN[5]. Repetitive microtrauma to the UCL can eventually lead to attenuation or failure of the ligament[5]. The laxity caused by UCL insufficiency may permit increased medial soft tissue stretching that predisposes these athletes to ulnar neuritis[5]. Aoki *et al*[18] found that the maximum strain during the acceleration phase of throwing may lead to nerve injury and compromise its vascular supply. The resultant decreased circulation to the nerve during overhead throwing may be an important factor contributing to ulnar neuropathy.

Additionally, traction on the UN that occurs when the extended elbow is flexed may contributed to nerve injury[10]. An additional 5.1 mm of UN excursion has been reported as the elbow moves from 10 to 90 degrees[19]. This longitudinal traction may compromise neural function and increase the likelihood of irritation[10].

EVALUATNG OF THE UN IN THE THROWING ATHLETE

The diagnosis of ulnar neuropathy in the overhead athlete is predominantly based on history and exam. Early symptoms may include diminished sensation, tingling, or a burning type sensation in the small and ring fingers, especially during or after throwing[5,9]. Elbow flexion may also exacerbate the patient's symptoms[6]. Athletes may endorse pain along the medial elbow and limitation of elbow extension despite prolonged periods of rest[7]. Motor symptoms including weakness or atrophy of the intrinsic muscles of the hand are typically late findings seen only in severe or chronic cases[9]. Symptoms are generally worsened by repetitive valgus stress, and after several innings of throwing, pitchers may complain of heaviness or clumsiness of the hands and fingers[9]. Patients who suffer from UN subluxation may report a snapping or popping sensation at the medial elbow that occurs with flexion, extension, or throwing[9].

Physical examination in the throwing athlete must include the entire length of the UN. A thorough assessment of the cervical spine needs to be performed to look for evidence of radiculopathy or degenerative changes[9]. Neural or vascular compression at the thoracic outlet should also be ruled out. Afterwards, the examiner can shift focus to the medial elbow. Elbow instability as a result of UCL injury or insufficiency is an important underlying cause of ulnar neuritis[5]. Thus, UCL

evaluation in athletes with suspected UN compression is essential. Valgus laxity should be assessed, and the Moving Valgus Stress Test is one the more reliable examination maneuvers for UCL insufficiency[5]. Palpation of the medial elbow may elicit UN tenderness in the cubital tunnel and may be useful to identify coexisting medial epicondylitis or UN subluxation out of the condylar groove, especially as the elbow is flexed and extended[9,10]. The examiner should ensure that any patient with a subluxating UN does not also have a snapping medial triceps[20]. This generally presents as a second "snap" that follows the nerve subluxation. Tinel's test involves tapping the nerve from distal to proximal, and a positive test occurs when there is an unpleasant sensation at a site along the course of the nerve, especially if this recreates the patient's symptoms[10]. In throwing athletes with suspected ulnar neuropathy, special attention should be directed towards the cubital tunnel[9]. In addition, the elbow flexion test is a provocative maneuver that can be used to reproduce UN symptoms. To perform the elbow flexion test, the elbow is flexed, while the forearm is supinated and the wrist is extended for several minutes[9]. The elbow flexion test is positive if the UN symptoms are aggravated in this position[9].

Distally, a full neurovascular examination should be performed. Loss of static two-point discrimination when compared to the contralateral hand, weakness in grip strength, and weakness in pinch strength can all be signs of ulnar neuropathy[7]. Froment's sign, in which the patient grasps a piece of paper between the thumb and index finger while resisting the examiner's attempt to pull the object from the patient's hand, may be used to test UN function[10]. Weakness in the hand's intrinsic muscles may be subtle but often presents before changes in forearm extrinsic weakness and grip strength[9].

Imaging should begin with elbow in multiple planes (anteroposterior, lateral, and oblique views)[5]. X-rays are evaluated for osteophytes or degenerative changes that may impinge on the UN as well as any previous bony injury, loose bodies, or abnormal calcification[9]. Magnetic resonance imaging is often utilized to evaluate the soft tissue structures of the elbow such as: The UN, UCL, and possible space occupying lesions or bone spurs[9]. Electrophysiologic investigations may occasionally be useful to confirm the diagnosis and the location of compression in equivocal cases[10]. Additionally, electrodiagnostic testing may reveal a secondary compression site ("double crush" phenomenon). Because these studies have a false negative rate reported to be 10% or even higher, they cannot be solely relied on to identify ulnar neuropathy in the throwing athlete[16].

TREATMENT OF UN COMPRESSION
Conservative management
Initial management of ulnar neuropathy with conservative treatment is appropriate for the overhead throwing

athlete[5]. Anti-inflammatory medications, cryotherapy, and physical therapy are the mainstays of non-operative treatment[5]. The athlete should be instructed to avoid throwing or any other activities that cause pain[5]. The elbow may be splinted, especially at night, for six weeks to immobilize the UN, and the cubital tunnel may be protected using an elbow pad to avoid pressure to the region[9]. Before returning to sport, deficiencies in throwing mechanics must be identified and corrected[9]. A gradual interval-throwing program is initiated, and a stretching program for the posterior capsule is often indicated[9]. Additionally, participation in a strength-training program focusing on dynamic elbow stabilizers is an important part of rehabilitation[9]. The athlete should be followed clinically for progression of symptoms. For patients who fail to demonstrate improvement following a comprehensive course of conservative management, surgical options may be considered.

Surgical management

Surgical options for ulnar neuropathy at the cubital tunnel include *in situ* decompression, subcutaneous anterior transposition, or in rare cases, submuscular transposition. UN entrapment syndrome was initially treated with submuscular anterior transposition, and Del Pizzo *et al*[21] demonstrated successful return to play at 3 to 58 mo postoperatively in nine of fifteen (60%) baseball players treated in this fashion. Similarly, the original technique for UCL reconstruction described by Dr. Jobe *et al*[8] consisted of release of the flexor-pronator mass from its insertion and concomitant UN submuscular transposition. However, of the sixteen elite throwing athletes included in the initial cohort, UN symptoms persisted in five patients post-operatively[8]. A follow-up series by Conway *et al*[22] of 71 athletes (including the sixteen athletes from the original study), who underwent UCL reconstruction and concomitant submuscular nerve transposition found postoperative ulnar neuropathy in 15 (21%) patients, and 9 of these patients went on to require further decompression surgery. Subsequent changes in surgical technique led to improved handling of the nerve and alterative strategies that did not require release of the flexor-pronator muscle origin[9].

Rettig and Ebben[23] demonstrated excellent outcomes with anterior subcutaneous UN transposition in twenty athletes who had failed non-operative treatment. The athletes were followed for an average of 19 mo postoperatively, and 19 of 20 (95%) patients were asymptomatic at that time[23]. The patients returned to play at an average of 12.6 wk[23]. Similarly, Andrews and Timmerman[24] published their results on an anterior subcutaneous transfer in eight professional athletes in 1995. They reported postoperative ulnar neuropathy in only 11% of cases, and seven of the athletes (88%) returned to their previous level of play for a minimum of one year[24]. Azar *et al*[25] reported only one case of postoperative transient ulnar neuropathy in 91 throwing athletes following UCL reconstruction and subcutaneous UN transposition. They

found that 90% (9 of 10) of athletes with preoperative symptoms of ulnar neuritis demonstrated resolution of those symptoms postoperatively[25]. Another study in high school aged baseball players undergoing subcutaneous UN transposition reported a 7% incidence of transient ulnar neuropathy and 74% of these athletes were able to of return to their previous level of sport for at least a year[26]. Although no studies have directly compared subcutaneous and submuscular transposition of the UN, the reported rates of postoperative complications appear to be lower in the subcutaneous group.

More recently, many authors have recommended against obligatory UN transposition[1,27-29]. In one study of 83 athletes who underwent UCL reconstruction without nerve transposition, transient neurogenic symptoms were reported in only 4 (5%) patients post-operatively, and all resolved completely with non-operative care[27]. In this work, 20 (24%) patients had preoperative UN symptoms[27]. They hypothesized that not exposing or dissecting the UN minimized the risk of nerve injury[27]. Other authors only consider transposition of if neurologic symptoms are present preoperatively[28,29]. Koh *et al*[28] and Paletta *et al*[29] both reported low rates of postoperative UN complications (5% and 4%, respectively). Between the two studies, only one patient required subsequent UN transposition[28]. A more recent systematic review of 378 patients undergoing UCL reconstruction did not support obligatory UN transposition[1]. In this work, those treated with routine nerve transposition demonstrated a lower rate of "excellent" results (75% *vs* 89%) and were twice as likely to demonstrate signs of postoperative ulnar neuropathy compared with those treated without transposition[1]. However, some authors feel that *in situ* decompression should not be used in the overhead athlete because it fails to address the increased tension experienced during the throwing motion[9].

AUTHORS' PREFERRED TECHNIQUES FOR ADDRESSING THE UN DURING UCL RECONSTRUCTION

In patients without UN symptomatology, we do not routinely expose, decompress, or transpose the UN during UCL reconstruction. For the UCL reconstruction, we utilize the docking technique for humeral fixation and a muscle splitting approach to access the ligament[30]. Because the docking technique utilizes a socket on the humeral side, the *in situ* nerve is at less risk for injury than it would be when drilling full tunnels as described in the Modified Jobe technique. Great care is taken throughout the procedure to ensure that the course of the UN is well understood, and the nerve is protected during every step, especially during drilling. For patients with UN symptoms, we generally decompress and subcutaneously transpose the nerve during UCL reconstruction. Submuscular transposition is generally reserved for rare cases that have failed a prior subcutanetous transposition despite adequate proximal

Figure 2 Dissection of the ulnar nerve. The ulnar nerve is identified proximal to the cubital tunnel and posterior to the medial intermuscular septum. Dissection of the nerve begins proximally at the arcade of Struthers and is continued distally to the two heads of the flexor carpi ulnaris muscle.

Figure 4 Anterior subcutaneous transposition of the ulnar nerve in flexion. A band of medial intermuscular septum is used as a sling to hold the nerve in place. One end of the band is excised beginning 8 cm proximal to the medial epicondyle, and the other end is left attached to the medial epicondyle. The strip is sutured onto the fascia overlying the flexor-pronator musculature.

Figure 3 Protection of ulnar nerve. The surgeon must be aware of the anatomy of the ulnar nerve and protect it until the ulnar collateral ligament reconstruction is complete.

Figure 5 Anterior subcutaneous transposition of the ulnar nerve in extension. The inverted V-shaped sling prevents the nerve from falling behind the medial epicondyle.

and distal decompression.

Subcutaneous transposition is accomplished using the V-sling technique as of Tan *et al*[31]. After identifying the UN posterior to the intermuscular septum and proximal to the cubital tunnel, it is carefully dissected free proximally and distally (Figure 2). If transposition is planned, we decompress the nerve at least 10 cm proximally and 10 cm distally from the elbow joint. The nerve is then protected until the UCL reconstruction is complete (Figure 3). Following the UCL procedure, the UN is transposed anterior to the medial epicondyle and thoroughly inspected for any sites of compression such as the medial triceps tendon proximally or the FCU fascia distally. Further decompression is completed as needed. Once it is completely free in the transposed position, a thin slip of the medial intermuscular septum is harvested to serve as a sling to hold it in place. This thin band is excised form the septal fascia beginning 8 cm above the epicondyle. It is dissected distally but is left attached at its distal insertion on the medial epicondyle. The strip is subsequently sutured to the flexor-pronator fascia in an inverted V-shape, which prevents the nerve from migrating behind the epicondyle (Figures 4 and 5).

The postoperative rehabilitation protocol following transposition of the UN with concomitant UCL reconstruction is determined by the reconstructive procedure rather than the nerve decompression. In these cases of UCL reconstruction, we place the patient in a split post-operatively. The splint is replaced with a hinged elbow brace one week following surgery. While wearing the brace, elbow ROM is initially permitted from 30° to 90°, and this is advanced to 15° to 105° from weeks 3 to 5. At week 6, the brace is discontinued, and formal physical therapy is initiated. From weeks 6 to 12, the focus of PT is on elbow ROM, and shoulder and wrist strength and ROM. This is advanced as tolerated. Beginning at 16th week, a formal throwing program is initiated if the patient has met all milestones up to this point. Throwing begins at a distance of 45 feet on flat ground and is slowly advanced as tolerated. If the patient is able to throw 180 feet on flat ground without pain at the 7- to 9-mo mark, throwing from the mound is permitted. This is slowly advanced over the next 3 mo with the goal of returning the athlete to competitive pitching from a mound between 12 and 18 mo.

CONCLUSION

Recent trends in the treatment of UN injuries in the overhead athlete favor reserving nerve decompression and transposition for instances in which there are appreciable UN symptoms present prior to surgery[1,27-29]. In cases of isolated ulnar neuropathy in athletes, *in situ* decompression or subcutaneous anterior transposition appear to have more favorable outcomes than submuscular transposition although the techniques have not yet been compared head to head. As the surgical approach for UCL reconstructions has evolved from flexor-pronator detachment to a more tissue friendly muscle-splitting approach, patients with UN symptoms who are undergoing UCL reconstruction are better suited with *in situ* decompression or subcutaneous transposition rather than submuscular transposition. These changes have led to fewer postoperative UN complications and improved outcomes in these high-demand athletes.

Because the UN lies in close proximity to the operative field during the UCL reconstruction, the surgeon must take great care to protect it throughout the duration of the case. Obtaining a diligent history, performing a detailed physical exam, and proper surgical technique are all critical steps needed to successfully treat throwing athletes with UN symptoms. When appropriate steps are followed, the vast majority of athletes can be expected to return to competitive sports.

REFERENCES

1   **Vitale MA**, Ahmad CS. The outcome of elbow ulnar collateral ligament reconstruction in overhead athletes: a systematic review. *Am J Sports Med* 2008; **36**: 1193-1205 [PMID: 18490476 DOI: 10.1177/0363546508319053]

2   **King JW**, Brelsford HJ, Tullos HS. Analysis of the pitching arm of the professional baseball pitcher. *Clin Orthop Relat Res* 1969; **67**: 116-123 [PMID: 5361189 DOI: 10.1097/0003086-196911000-00018]

3   **Keefe DT**, Lintner DM. Nerve injuries in the throwing elbow. *Clin Sports Med* 2004; **23**: 723-742, xi [PMID: 15474232 DOI: 10.1016/j.csm.2004.04.012]

4   **Treihaft MM**. Neurologic injuries in baseball players. *Semin Neurol* 2000; **20**: 187-193 [PMID: 10946738 DOI: 10.1055/s-2000-9827]

5   **Cain EL**, Dugas JR, Wolf RS, Andrews JR. Elbow injuries in throwing athletes: a current concepts review. *Am J Sports Med* 2003; **31**: 621-635 [PMID: 12860556 DOI: 10.1177/0363546506295026]

6   **Spinner RJ**. Nerve Entrapment Syndromes. In: Morrey BF, editor. Its Disord. 4th edition. Philadelphia: Saunders Elsevier, 2009: 1090-1118 [DOI: 10.1016/B978-1-4160-2902-1.50085-1]

7   **Aoki M**, Kanaya K, Aiki H, Wada T, Yamashita T, Ogiwara N. Cubital tunnel syndrome in adolescent baseball players: a report of six cases with 3- to 5-year follow-up. *Arthroscopy* 2005; **21**: 758 [PMID: 15944636 DOI: 10.1016/j.arthro.2005.03.030]

8   **Jobe FW**, Stark H, Lombardo SJ. Reconstruction of the ulnar collateral ligament in athletes. *J Bone Joint Surg Am* 1986; **68**: 1158-1163 [PMID: 3771597]

9   **Gee AO**, Angeline ME, Dines JS, Altchek DW. Ulnar nerve issues in throwing athletes. In: Dines JS, Altchek DW, editors. Ulnar Collat. Ligament Inj. A Guid. to Diagnosis Treat. New York: Springer, 2015: 179-188 [DOI: 10.1007/978-1-4899-7540-9_21]

10   **Hayton M**, Talwalkar S. Nerve entrapment around the elbow. In: Stanley D, Trail I, editors. 1st edition. Elsevier, 2012: 455-473 [DOI: 10.1016/B978-0-7020-3099-4.00031-X]

11   **Upton AR**, McComas AJ. The double crush in nerve entrapment syndromes. *Lancet* 1973; **2**: 359-362 [PMID: 4124532 DOI: 10.1016/S0140-6736(73)93196-6]

12   **Bencardino JT**, Rosenberg ZS. Entrapment neuropathies of the shoulder and elbow in the athlete. *Clin Sports Med* 2006; **25**: 465-487, vi-vii [PMID: 16798138 DOI: 10.1016/j.csm.2006.03.005]

13   **Glousman RE**. Ulnar nerve problems in the athlete's elbow. *Clin Sports Med* 1990; **9**: 365-377 [PMID: 2183951]

14   **Li X**, Dines JS, Gorman M, Limpisvasti O, Gambardella R, Yocum L. Anconeus epitrochlearis as a source of medial elbow pain in baseball pitchers. *Orthopedics* 2012; **35**: e1129-e1132 [PMID: 22784916 DOI: 10.3928/01477447-20120621-39]

15   **Childress HM**. Recurrent ulnar-nerve dislocation at the elbow. *Clin Orthop Relat Res* 1975; **(108)**: 168-173 [PMID: 1139823 DOI: 10.1097/00003086-197505000-00027]

16   **Zemel NP**. Ulnar neuropathy with and without elbow instability. *Hand Clin* 2000; **16**: 487-495, x [PMID: 10955221]

17   **Fleisig GS**, Andrews JR, Dillman CJ, Escamilla RF. Kinetics of baseball pitching with implications about injury mechanisms. *Am J Sports Med* 1995; **23**: 233-239 [PMID: 7778711 DOI: 10.1177/036354659502300218]

18   **Aoki M**, Takasaki H, Muraki T, Uchiyama E, Murakami G, Yamashita T. Strain on the ulnar nerve at the elbow and wrist during throwing motion. *J Bone Joint Surg Am* 2005; **87**: 2508-2514 [PMID: 16264128 DOI: 10.2106/JBJS.D.02989]

19   **Wright TW**, Glowczewskie F, Cowin D, Wheeler DL. Ulnar nerve excursion and strain at the elbow and wrist associated with upper extremity motion. *J Hand Surg Am* 2001; **26**: 655-662 [PMID: 11466640 DOI: 10.1053/jhsu.2001.26140]

20   **Spinner RJ**, Goldner RD. Snapping of the medial head of the triceps and recurrent dislocation of the ulnar nerve. Anatomical and dynamic factors. *J Bone Joint Surg Am* 1998; **80**: 239-247 [PMID: 9486730]

21   **Del Pizzo W**, Jobe FW, Norwood L. Ulnar nerve entrapment syndrome in baseball players. *Am J Sports Med* 1977; **5**: 182-185 [PMID: 907029 DOI: 10.1177/036354657700500502]

22   **Conway JE**, Jobe FW, Glousman RE, Pink M. Medial instability of the elbow in throwing athletes. Treatment by repair or reconstruction of the ulnar collateral ligament. *J Bone Joint Surg Am* 1992; **74**: 67-83 [PMID: 1734015]

23   **Rettig AC**, Ebben JR. Anterior subcutaneous transfer of the ulnar nerve in the athlete. *Am J Sports Med* 1993; **21**: 836-839; discussion 839-840 [PMID: 8291635 DOI: 10.1177/036354659302100613]

24   **Andrews JR**, Timmerman LA. Outcome of elbow surgery in professional baseball players. *Am J Sports Med* 1995; **23**: 407-413 [PMID: 7573648 DOI: 10.1177/036354659502300406]

25   **Azar FM**, Andrews JR, Wilk KE, Groh D. Operative treatment of ulnar collateral ligament injuries of the elbow in athletes. *Am J Sports Med* 2000; **28**: 16-23 [PMID: 10653538 DOI: 10.1016/s1048-6666(01)80036-7]

26   **Petty DH**, Andrews JR, Fleisig GS, Cain EL. Ulnar collateral ligament reconstruction in high school baseball players: clinical results and injury risk factors. *Am J Sports Med* 2004; **32**: 1158-1164 [PMID: 15262637 DOI: 10.1177/0363546503262166]

27   **Thompson WH**, Jobe FW, Yocum LA, Pink MM. Ulnar collateral ligament reconstruction in athletes: muscle-splitting approach without transposition of the ulnar nerve. *J Shoulder Elbow Surg* 2001; **10**: 152-157 [PMID: 11307079 DOI: 10.1067/mse.2001.112881]

28   **Koh JL**, Schafer MF, Keuter G, Hsu JE. Ulnar collateral ligament reconstruction in elite throwing athletes. *Arthroscopy* 2006; **22**: 1187-1191 [PMID: 17084295 DOI: 10.1016/j.arthro.2006.07.024]

29   **Paletta GA**, Wright RW. The modified docking procedure for elbow ulnar collateral ligament reconstruction: 2-year follow-up in elite throwers. *Am J Sports Med* 2006; **34**: 1594-1598 [PMID: 16832125 DOI: 10.1177/0363546506289884]

30   **Rohrbough JT**, Altchek DW, Hyman J, Williams RJ, Botts JD. Medial collateral ligament reconstruction of the elbow using the docking technique. *Am J Sports Med* 2002; **30**: 541-548 [PMID: 12130409]

31   **Tan V**, Pope J, Daluiski A, Capo JT, Weiland AJ. The V-sling: a modified medial intermuscular septal sling for anterior transposition of the ulnar nerve. *J Hand Surg Am* 2004; **29**: 325-327 [PMID: 15043909 DOI: 10.1016/j.jhsa.2003.11.011]

MINIREVIEWS

Posterior ankle impingement syndrome: A systematic four-stage approach

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Abstract

Posterior ankle impingement syndrome (PAIS) is a common injury in athletes engaging in repetitive plantarflexion, particularly ballet dancers and soccer players. Despite the increase in popularity of the posterior two-portal hindfoot approach, concerns with the technique remain, including; the technical difficulty, relatively steep learning curve, and difficulty performing simultaneous anterior ankle arthroscopy. The purpose of the current literature review is to provide comprehensive knowledge about PAIS, and to describe a systematic four-stage approach of the posterior two-portal arthroscopy. The etiology, clinical presentation, diagnostic strategies are first introduced followed by options in conservative and surgical management. A detailed systematic approach to posterior hindfoot arthroscopy is then described. This technique allows for systematic review of the anatomic structures and treatment of the bony and/or soft tissue lesions in four regions of interest in the hindfoot (superolateral, superomedial, inferomedial, and inferolateral). The review then discusses biological adjuncts and postoperative rehabilitation and ends with a discussion on the most recent clinical outcomes after posterior hindfoot arthroscopy for PAIS. Although clinical evidence suggests high success rates following posterior hindfoot arthroscopy in the short- and mid-term it may be limited in the pathology that can be addressed due to the technical skills required, but the systematic four-stage approach of the posterior two-portal arthroscopy may

improve upon this problem.

Key words: Posterior ankle impingement syndrome; Arthroscopy; Endoscopy; Review; Os trigonum

Core tip: A systematic four-stage approach was developed to standardize technical variety of posterior two-portal hindfoot arthroscopy for the treatment of posterior ankle impingement syndrome (PAIS). After making two-portals using the "nick and spread" technique, hindfoot strictures are divided into 4 regions of interest (superolateral, superomedial, inferomedial, and inferolateral) based on the intermalleolar ligament. In each region, anatomical structures are systematically reviewed and treated in regards to the presence of mechanical impingement and inflammation. Clinical evidence suggests high success rates following arthroscopic approach in short- and mid-term follow-up. This technique can help the surgeons optimize the outcomes following two-portal hindfoot arthroscopy for PAIS.

INTRODUCTION

Posterior ankle impingement syndrome (PAIS) is a spectrum of clinical disorders characterized by posterior ankle pain during plantar flexion or hyper flexion[1]. PAIS has become more commonly recognized, particularly in athletes because of heightened awareness[2-4] and more advanced imaging[5-7]. Conservative treatment may be indicated in the early stage of PAIS, however; approximately 40% patients eventually require surgical intervention due to intractable hindfoot pain.

The traditional open surgical treatment of PAIS through a lateral or medial approach has had good results, however complication rates are high[8]. Since its introduction in 2000[1], the posterior two portal hindfoot approach has been adopted by many surgeons for treatment of PAIS. Recently, a systematic review by Zwiers *et al*[9] highlighted the advantages of the endoscopic approach over the open approach including lower complication rates, shorter recovery time, less blood loss, less postoperative pain, and comparable functional outcomes. However, concerns with the technique remain; including the technical difficulty, relatively steep learning curve, and difficulty performing simultaneous anterior ankle arthroscopy[3].

This review discusses the etiology of PAIS, the spectrum of clinical disorders it encompasses, its clinical presentation and management. The review provides

Table 1 Posterior ankle impingement syndrome pathology

Osseus lesions	Soft tissue lesions
Stieda process	Flexor hallux longus tenosynovitis
Os trigonum	Synovitis
Osteophytes	Impingement of the joint capsule
Osteochondral lesion	Impingement of the anomalous muscles
Loose bodies	
Chondromatosis	
Subtalar coalition	

an up-to date assessment of the clinical evidence for the treatment of PAIS and describes a systematic four-stage approach of the posterior two-portal hindfoot arthroscopy.

ETILOGY

PAIS pathology can be due to both osseous and/or soft tissue lesions and anatomic variants (Table 1)[10]. Osseous lesions include a Stieda process (elongated protuberance)[10], pathological os trigonum (non-fused ossicle found in up to 25% of the normal adult population)[11], osteophytes, osteochondral lesion (OCL), loose bodies, chondromatosis, and subtalar coalition. In soft tissue lesions, flexor hallux longus (FHL) tenosynovitis, synovitis, impingement of the joint capsule, and impingement of the anomalous muscles[12] are described.

CLINICAL PRESENTATION AND DIAGNOSIS

PAIS is characterized by deep posterior ankle pain caused by plantar flexion of the ankle joint[13]. Pain is described as consistent, sharp, dull and radiating, however, it is usually hard for patients to indicate the exact location of the pain in the hindfoot. It is most commonly seen in athletes who participate in sports that require repetitive plantar flexion such as ballet dancers, soccer players, and downhill runners[14]. In these athletes PAIS may present acutely after a forced plantar flexion injury or chronically due to overuse. After an acute injury, patients have a robust inflammatory response leading to pain and swelling that manifests in the hindfoot 3-4 wk after the injury. More commonly, PAIS develops over time in these athletes because repetitive flexion causes increased compression and forces on the anatomic structures between the calcaneus and the posterior part of the distal tibia. In these athletes who present with chronic hindfoot pain, the clinician must have a heightened suspicion for PAIS as these symptoms may mimic posterior capsulitis and rheumatoid arthritis. Clinically, it is less common to see PAIS in the non-athletic population or athletes who perform plantar flexion of ankle joint less frequently. In patients who present with chronic hindfoot pain and do not engage in activities with repetitive flexion, anatomic variants may be implicated in the development of PAIS.

A full history and physical examination is critical in the

diagnosis of PAIS. Physical examination should include a complete neurovascular examination as well strength and range of motion assessment. Hindfoot pain aggravated by plantar flexion of the ankle indicates a positive plantar flexion test. A negative plantar flexion test makes a diagnosis of PAIS significantly less likely, but no studies have reported on the specificity or sensitivity of the plantar flexion test in the diagnosis of PAIS. Patients may also be tender over the posteromedial (PM) aspect of the ankle joint. The clinician must pay special attention to the exact location of tenderness, as pain over the posterior tibial tendon may indicate posterior tibial tendon tenosynovitis or dysfunction and not PAIS. To further clarify the location of the pain, the clinician may passively flex and extend the great toe. If the patient is tender during passive or active ROM, it may indicate pathology involving the FHL tendon. A neurologic examination should be performed to exclude tarsal tunnel syndrome, as the pain may be caused by Valleix's sign[15].

Standard plain X-rays[6], computed tomography (CT), and magnetic resonance imaging (MRI) are useful for diagnosis and preoperative planning[7]. In standard plain X-rays, anteroposterior (AP), mortise, and lateral views of ankle joint are commonly used. The lateral view is the most useful view to observe osseous lesions of hindfoot (*e.g.*, Stieda process, os trigonum, osteophytes, loose bodies, chondromatosis, subtalar coalition). Recently, the posterior impingement (PIM) view has been recommended instead of a conventional lateral view for symptomatic hindfoot pain. The PIM view is a lateral, 25-degree external rotation, oblique view of the ankle, which has shown significant superior diagnostic accuracy compared with the lateral view in the detection of os trigonum[16].

Compared with radiographs, multi-slice helical CT is more useful to evaluate osseous pathologies. CT provides fine detail regarding the size, location, and number of anatomical bony abnormalities[17]. Many surgeons prefer CT to examine the osteophyte of the tibia that sometimes co-exists with PAIS[18] and thus often use it to determine whether the anterior or posterior scope would be performed[18].

MRI is more useful to evaluate soft tissue lesions of the ankle. Of note, the presence and location of anomalous muscles should be evaluated. These anomalous muscles cause PAIS, but also increase the difficulty of operative treatment[12]. The peroneus quartus is the most commonly reported anomalous muscle, with between 7% and 22% of the population having them, other anomalous muscles such as flexor digitorum accessorius longus only occur in between 1% and 8% of the population[12].

After the positive plantar flexion test is elicited, the authors prefer to evaluate the condition of the hindfoot structures using standard plain X-ray and MRI. Then, we perform an ultrasound diagnostic injection using a local anesthetic to confirm the diagnosis (Figure 1).

TREATMENT

Conservative treatment
Conservative treatment includes rest, modification of activity, physiotherapy, anti-inflammatory drugs, and ultrasound-guided injections[19]. Ultrasound-guided injections may be useful in high-level athletes to allow them to finish the season[20]. Although no substantial evidence has published the success rate with conservative treatment[19], a small cohort study reported approximately 60% success rates following conservative treatment in PAIS[21].

Surgical indications
Surgical management is indicated for patients following failure to address symptoms after 3 mo of conservative treatment. However, if athletic patients want to return to athletic activity promptly, then surgical intervention can be recommended early in the treatment process. Options include open treatment or arthroscopic intervention[3,22,23]. The advantages of arthroscopic procedures for PAIS are that they are less invasive, have a lower risk of postoperative complications, and shorter recovery time for returning to full activity. However, the technical difficulty and relatively steep learning curve are disadvantages[3]. Additionally, it is difficult to perform simultaneous treatments for anterior ankle pathologies using a posterior two-portal approach, while subtalar arthroscopy or conventional ankle arthroscopy with posterolateral (PL) portal are more available[24].

For patients who have isolated PAIS, the authors utilize posterior hindfoot arthroscopy. For patients who require operative intervention for both PAIS and ankle anterior pathologies (*e.g.*, anterior impingement syndrome, anterior OCL, degenerative ankle arthritis), the authors prefer to treat anterior pathologies in the supine position with traditional anterior arthroscopic portals, then, switch to the prone position for posterior hindfoot arthroscopy.

Posterior hindfoot arthroscopy - a systematic four-stage approach[9]
The senior author (John G Kennedy) uses the original posterior two-portal technique, similar to the 21-point systematic surgical approach in anterior ankle arthroscopic surgery[25]. The senior author utilizes a systematic four-stage approach for posterior hindfoot arthroscopy beginning with a systematic evaluation of the anatomical structures and subsequent operative treatment for pathological abnormalities.

Equipment
Typical arthroscopy equipment used in anterior ankle arthroscopy is required for posterior hindfoot arthroscopy. A 2.7/4.0 mm arthroscope with 30/70 degree viewing angle, a 3.5/4.5 mm shaver for soft tissue debridement, a 4.0 mm aggressive shaver or burr for bony resection,

Figure 1 Untrosound guided diagnostic injection. AT: Achilles tendon; FHL: Flexor hallucis longus tendon; T.N: Tibial nerve.

Figure 2 The posterolateral and posteromedial arthroscopic portals.

osteotomy, and fluoroscopy (optional) are used. Sizes of arthroscopes can be selected depending on the surgeon's preference. A thigh tourniquet is necessary to obtain good visualization of hindfoot anatomical structures. Additionally, an irrigation system is useful. The fluid pressure is usually set to 50-60 mmHg, and fluid flow is 0.5 L/min. Although dorsiflexion of hindfoot is usually applied for providing good visualization of the ankle and subtalar joints, a non-invasive distractor is may be applied to assist with visualization.

Patient position
The patient should be positioned in the prone or sloppy lateral position. The senior authors have found that general or spinal anesthesias with a regional block are most effective. The operative foot should be elevated using a support or cushion placed underneath the lower leg, so that the leg is raised approximately 15 cm above the contralateral leg. This position can prevent contact of the arthroscope or instruments with the contralateral side in the operative procedure.

Technique
Marking anatomical landmarks and portal sites: In posterior hindfoot arthroscopy, a PL and PM portal are most commonly utilized. Prior to incision, landmarks including lateral malleoli (LM), medial malleoli (MM) and Achilles tendon should be marked using a sterile surgical marker. Portal sites should then be marked out.

The portal sites are 1.0 mm anterior to the borders of Achilles tendon and at the level between the horizontal lines running from the inferior poles of MM and tip of LM (Figure 2). The sural nerve can be palpated and its course marked to avoid iatrogenic nerve injury.

Establishing portals: After all anatomic landmarks and portal sites have been identified and marked, a #11 blade should be used to make 1 cm vertical incisions at the labeled portal sites for the PM and PL portals. Then, subcutaneous blunt dissection using a mosquito clamp is performed *via* both portals. At this time, care must be taken to avoid damage to the sural nerve. The "nick and spread" technique is important to avoid sural neurovascular damages. A 2.7-mm arthroscope sleeve with trocar is carefully advanced *via* a PL portal to touch the posterior aspect of the talus by directing it towards the first interdigital web space. All instruments should be directed towards first interdigital web space to prevent iatrogenic neurovascular bundle injury in the hindfoot. Once the bone can be palpated with the trocar, it is switched out for a 2.7-mm arthroscope.

Creating working space: Initial visualization is poor because of the fat tissue located behind the posterior aspect of talus. After the shaver blade is confirmed in arthroscopic view, soft tissue is debrided to expose the intermalleolar (IM) ligament using a 3.5 or 4.0 mm aggressive shaver. The shaver blade must always be maneuvered very gently under arthroscopic visualization to avoid iatrogenic injury to healthy tissue.

Systematic four-stage approach to visualization of the hindfoot: The systematic approach in posterior ankle arthroscopy allows for a full assessment of all structures at the posterior ankle and subtalar joint (Figure 3). The anatomic landmark for defining the quadrants is the IM ligament that has been well described previously[26,27] based on the IM ligament, the hindfoot structures are divided into 4 regions of interest (superolateral, superomedial, inferomedial, and inferolateral). The authors prefer to start the inspection from the superolateral quadrant and then proceed to the other regions in a counterclockwise fashion for right ankles and a clockwise fashion for left ankles.

Figure 3 Hindfoot extra-articular structures divided into quadrants as defined by the intermalleolar ligament. (1) Fibula, (2) tibia, (3) posterior-inferior tibiofibular ligament (transverse ligament), (4) flexor hallucis longus tendon, (5a) intermalleolar ligament, (5b) superior tibial insertion of the intermalleolar ligament, (6) tibiotalar joint, (7) subtalar joint, (8) posterolateral talar process, (9) flexor hallucis longus retinaculum, (10) calcaneofibular ligament, and (11) posterior talofibular ligament. Illustration is a copyright of and reproduced with permission from Kennedy JG, MD. Reproduction without express written consent is prohibited.

This quadrant contains the posterior inferior tibio-fibular ligament, transverse ligament, and IM ligament. The IM ligament may be associated with PIM[8,27]. During inspection of the superolateral quadrant, the ankle should be passively plantarflexed to see if any of these ligaments are impinged under direct visualization[26]. If impingement is present, the related structures should be debrided using a shaver or punch.

The FHL tendon and its associated fibro-osseous tunnel are found in this quadrant. Of note, the neurovascular bundle lies just medial to FHL tendon. It is therefore essential that any instruments should be maneuvered in the area lateral to FHL tendon. Additionally, surgeons should evaluate if the anomalous muscles particularly the peroneous qaurtus are present[13]. It is sometime difficult to expose the FHL tendon because of soft tissue cicatrization. In these cases, moving (passive flexion/extension) the great toe may help surgeons identify the FHL tendon.

Tenosynovitis around FHL tendon is a typical finding in patients with hindfoot pain (63% to 85%)[8,28]. By moving the great toe, impingement of the tendon in its sheath can be identified and resected using a 4.5-mm shaver. A low-lying muscle of FHL can be found, which may cause impingement between the associated bony or soft tissues. Any tenosynovitis or identified impingement should be debrided.

A Stieda process or separate os trigonum can be observed in this region. These bony structures are removed using osteotomes or shaver, with care taken to avoid causing iatrogenic cartilage lesions in the subtalar joint. The scope and shaver are switched in order to gain optimal access to achieve adequate debridement. The posterior talofibular ligament (PTFL) that attaches to these structures may need to be released, however the authors prefer to preserve as much as possible of the posterior talofibular ligament.

Once those osseous structures are removed, the arthroscope is advanced into the fibro-osseous tunnel, which allows full visualization of the FHL tendon. Any pathology restricting smooth passive movement of the FHL tendon in the fibro-osseous tunnel such as vincula, nodules, or cicatrization should be debrided and removed.

The PTFL and the calcaneofibular ligament (CFL) are found in this region. The PTFL may be thickened and hypertrophied, requiring debridement. In the case of an ankle history of chronic lateral ankle instability, attenuation or scarring of the CFL may be found. Any tenosynovitis or identified impingement should be debrided.

Intra-articular inspection of the talocrural and subtalar joints: The talocrural joint and subtalar joint are inspected following visualization of all four quadrants of the hindfoot. Both joints can be visualized using same standard portals. Ankle dorsiflexion can allow full visualization of joint surfaces, however, soft tissue distractors are sometimes used to obtain better visualization[29]. Any pathology detected including OCLs, synovitis, osteophytes, and hypertrophic capsule should be addressed. For OCLs, the authors recommend bone marrow stimulation using a microfracture pic or drilling to produce fibrocartilage repair tissue.

Biologics

Biologics including platelet-rich plasma (PRP) and con-centrated bone marrow aspirate (CBMA) may be used at the time of the surgery. These biologic augments are becoming recognized as promising adjuvants that may improve the quality of regenerative tissue and decrease inflammatory responses[30]. For PAIS, PRP and CBMA are injected into the degenerative tendon or bed of the lesion after irrigation water is stopped. The authors also recommend injecting these biological adjuvants into the joint after the wound is closed to limit the inflammatory response.

Postoperative rehabilitation

A compression bandage is applied after surgery and patients are allowed to be weightbearing as tolerated immediately after surgery. Patients may also begin ranging their ankle as tolerated. The goal of early ROM and weightbearing is to prevent post-operative stiffness and hopefully limit the delay in return to sport[13,30]. Typically, ankle immobilization is not necessary, unless patients had more significant osseous injury, which may require modifications of the above protocol.

Clinical outcomes following posterior hindfoot arthroscopy

Several clinical studies have reported good short-term clinical results following posterior two-portal hindfoot arthroscopy for PAIS (Table 2)[28,29,31-41]. A majority

Table 2 Reported clinical outcomes following hindfoot arthroscopy

Ref.	Year	No. of cases (*n*)	LoE	Follow-up (mo)	Primary outcome measure	Pre-operative score	Post-operative score	Return to sport (wk)
Jerosch *et al*[32]	2006	10	IV	28 (6-61)	AOFAS	43	87	12
Tey *et al*[33]	2007	15	IV	3 (15-63)	AOFAS	84.4	98.5	14.1
Horibe *et al*[34]	2008	11	IV	33.8 (12-58)	AOFAS	71	99	12
Scholten *et al*[28]	2008	55	IV	38 (24-54)	AOFAS	71.1	90	18.9
Willits *et al*[31]	2008	16	IV	3 (6-74)	AOFAS	N/A	91	63
Calder *et al*[35]	2010	27	IV	23 (15-49)	N/A	N/A	N/A	5.9
Noguchi *et al*[36]	2010	12	IV	9.7 (6-14)	AOFAS	68	98.3	5.9
Galla *et al*[37]	2011	30	IV	9.7 (6-14)	AOFAS	60	90	N/A
Ogut *et al*[38]	2011	14	IV	31.6 (8-75)	AOFAS	53.6	84.2	30.6
Nikisch *et al*[39]	2012	80	IV	15.4 (5-59)	N/A	N/A	N/A	N/A
van Dijk *et al*[29]	2009	55	IV	90 (24-480)	AOFAS	75	90	N/A
Lopez-Valerio *et al*[40]	2015	20	IV	78.6 (24-120)	VAS	7.5	0.8	6.7
Dinato *et al*[41]	2015	17	III	N/A	AOFAS	62.9	92.3	15.6
		15				67.9	94	16.3

AOFAS: American Orthopedic Foot and Ankle Society (AOFAS) Score; VAS: Visual Analogue Scale; N/A: Not applicable.

of studies have reported post-operative American Orthopaedic Foot and Ankle Society (AOFAS) Scores greater than 85[28,29,31-34,36,37,39,41] at short-term follow-up. A recent systematic review by Zwiers *et al*[9] demonstrated that the mean time to return to full activity was on average 11.3 wk (5.9-12.9 wk) following arthroscopic treatment. Complication rates after posterior hindfoot arthroscopy were also low with 1.8% of patients suffering a major complication and 5.4% of patients suffering a minor complication[9]. However, the current literature is limited by long-term follow-up studies evaluating the outcomes after posterior hindfoot arthroscopy for PAIS.

CONCLUSION

PAIS is a clinical spectrum of both soft tissue and osseous pathology that is common in athletes who repetitively plantar flex their ankle. Patients who do not respond to conservative management may require operative intervention. While open treatments have showed good success in the short-term for PAIS, posterior hindfoot arthroscopy may lead to equivalent outcomes with less morbidity. Performing two-portal hindfoot arthroscopy in the described systematic four-stage approach allows for standardized evaluation of the anatomic structures of the hindfoot and ultimately to address any pathology that may be present. Clinical outcomes after posterior hindfoot arthroscopy for PAIS are very good in the short-term with low complication rates, however future long-term studies are warranted.

REFERENCES

1   **van Dijk CN**, Scholten PE, Krips R. A 2-portal endoscopic approach for diagnosis and treatment of posterior ankle pathology. *Arthroscopy* 2000; **16**: 871-876 [PMID: 11078550 DOI: 10.1053/jars.2000.19430]
2   **van Dijk CN**, van Bergen CJ. Advancements in ankle arthroscopy. *J Am Acad Orthop Surg* 2008; **16**: 635-646 [PMID: 18978286]
3   **Coetzee JC**, Seybold JD, Moser BR, Stone RM. Management of Posterior Impingement in the Ankle in Athletes and Dancers. *Foot Ankle Int* 2015; **36**: 988-994 [PMID: 26163559 DOI: 10.1177/1071100715595504]
4   **Nault ML**, Kocher MS, Micheli LJ. Os trigonum syndrome. *J Am Acad Orthop Surg* 2014; **22**: 545-553 [PMID: 25157036]
5   **Sofka CM**. Posterior ankle impingement: clarification and confirmation of the pathoanatomy. *HSS J* 2010; **6**: 99-101 [PMID: 20012503 DOI: 10.1007/s11420-009-9147-2]
6   **Wiegerinck JI**, Vroemen JC, van Dongen TH, Sierevelt IN, Maas M, van Dijk CN. The posterior impingement view: an alternative conventional projection to detect bony posterior ankle impingement. *Arthroscopy* 2014; **30**: 1311-1316 [PMID: 25023737 DOI: 10.1016/j.arthro.2014.05.006]
7   **Hayashi D**, Roemer FW, D'Hooghe P, Guermazi A. Posterior ankle impingement in athletes: Pathogenesis, imaging features and differential diagnoses. *Eur J Radiol* 2015; **84**: 2231-2241 [PMID: 26239710 DOI: 10.1016/j.ejrad.2015.07.017]
8   **Hamilton WG**, Geppert MJ, Thompson FM. Pain in the posterior aspect of the ankle in dancers. Differential diagnosis and operative treatment. *J Bone Joint Surg Am* 1996; **78**: 1491-1500 [PMID: 8876576]
9   **Zwiers R**, Wiegerinck JI, Murawski CD, Smyth NA, Kennedy JG, van Dijk CN. Surgical treatment for posterior ankle impingement. *Arthroscopy* 2013; **29**: 1263-1270 [PMID: 23541613 DOI: 10.1016/j.arthro.2013.01.029]
10   **Maquirriain J**. Posterior ankle impingement syndrome. *J Am Acad Orthop Surg* 2005; **13**: 365-371 [PMID: 16224109 DOI: 10.5435/00124635-200510000-00001]
11   **Lawson JP**. Symptomatic radiographic variants in extremities. *Radiology* 1985; **157**: 625-631 [PMID: 4059550 DOI: 10.1148/radiology.157.3.4059550]
12   **Best A**, Giza E, Linklater J, Sullivan M. Posterior impingement of the ankle caused by anomalous muscles. A report of four cases. *J Bone Joint Surg Am* 2005; **87**: 2075-2079 [PMID: 16140823 DOI: 10.2106/JBJS.D.01916]
13   **Smyth NA**, Murawski CD, Levine DS, Kennedy JG. Hindfoot arthroscopic surgery for posterior ankle impingement: a systematic surgical approach and case series. *Am J Sports Med* 2013; **41**: 1869-1876 [PMID: 23720445 DOI: 10.1177/0363546513489489]
14   **Smyth NA**, Zwiers R, Wiegerinck JI, Hannon CP, Murawski CD, van Dijk CN, Kennedy JG. Posterior hindfoot arthroscopy: a review. *Am J Sports Med* 2014; **42**: 225-234 [PMID: 23868522 DOI: 10.1177/0363546513491213]
15   **Umans H**. Ankle impingement syndromes. *Semin Musculoskelet Radiol* 2002; **6**: 133-139 [PMID: 12077702 DOI: 10.1055/s-2002-32359]
16   **Wiegnerinck JI**, Kerkhoffs GMM, Struijs PAA, van Dijk CN. The

posterior impingement-view: An alternative conventional projection to detect bony posterior ankle impingement. *Arthroscopy* 2014; **30**: 1311-1316 [PMID: 25023737 DOI: 10.1016/j.arthro.2014.05.006]

17   **Burghardt AJ**, Link TM, Majumdar S. High-resolution computed tomography for clinical imaging of bone microarchitecture. *Clin Orthop Relat Res* 2011; **469**: 2179-2193 [PMID: 21344275 DOI: 10.1007/s11999-010-1766-x]

18   **Niek van Dijk C**. Anterior and posterior ankle impingement. *Foot Ankle Clin* 2006; **11**: 663-683 [PMID: 16971256 DOI: 10.1016/j.fcl.2006.06.003]

19   **Ribbans WJ**, Ribbans HA, Cruickshank JA, Wood EV. The management of posterior ankle impingement syndrome in sport: a review. *Foot Ankle Surg* 2015; **21**: 1-10 [PMID: 25682399 DOI: 10.1016/j.fas.2014.08.006]

20   **Roche AJ**, Calder JD, Lloyd Williams R. Posterior ankle impingement in dancers and athletes. *Foot Ankle Clin* 2013; **18**: 301-318 [PMID: 23707179 DOI: 10.1016/j.fcl.2013.02.008]

21   **Hedrick MR**, McBryde AM. Posterior ankle impingement. *Foot Ankle Int* 1994; **15**: 2-8 [PMID: 7981792 DOI: 10.1177/107110079401500102]

22   **Marumoto JM**, Ferkel RD. Arthroscopic excision of the os trigonum: a new technique with preliminary clinical results. *Foot Ankle Int* 1997; **18**: 777-784 [PMID: 9429879 DOI: 10.1177/107110079701801205]

23   **Allegra F**, Maffulli N, Cerza F, Delianni E. Postero-medial approach procedure in the supine position for one-step anterior and posterior ankle arthroscopy. *Sports Med Arthrosc* 2009; **17**: 185-189 [PMID: 19680115 DOI: 10.1097/JSA.0b013e3181b12745]

24   **Ferkel RD**. In which position do we perform arthroscopy of the hindfoot--supine or prone? Commentary on an article by Florian Nickisch, MD, et al.: "Postoperative complications of posterior ankle and hindfoot arthroscopy". *J Bone Joint Surg Am* 2012; **94**: e33 [PMID: 22398746 DOI: 10.2106/JBJS.K.01634]

25   **Ferkel RD**, Fischer SP. Progress in ankle arthroscopy. *Clin Orthop Relat Res* 1989; **240**: 210-220 [PMID: 2917435 DOI: 10.1097/00003086-198903000-00027]

26   **Golanó P**, Vega J, de Leeuw PA, Malagelada F, Manzanares MC, Götzens V, van Dijk CN. Anatomy of the ankle ligaments: a pictorial essay. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 557-569 [PMID: 20309522 DOI: 10.1007/s00167-010-1100-x]

27   **Oh CS**, Won HS, Hur MS, Chung IH, Kim S, Suh JS, Sung KS. Anatomic variations and MRI of the intermalleolar ligament. *AJR Am J Roentgenol* 2006; **186**: 943-947 [PMID: 16554561 DOI: 10.2214/AJR.04.1784]

28   **Scholten PE**, Sierevelt IN, van Dijk CN. Hindfoot endoscopy for posterior ankle impingement. *J Bone Joint Surg Am* 2008; **90**: 2665-2672 [PMID: 19047712 DOI: 10.2106/JBJS.F.00188]

29   **van Dijk CN**, de Leeuw PA, Scholten PE. Hindfoot endoscopy for posterior ankle impingement. Surgical technique. *J Bone Joint Surg Am* 2009; **91** Suppl 2: 287-298 [PMID: 19805591 DOI: 10.2106/JBJS.I.00445]

30   **Cassano JM**, Kennedy JG, Ross KA, Fraser EJ, Goodale MB, Fortier LA. Bone marrow concentrate and platelet-rich plasma differ in cell distribution and interleukin 1 receptor antagonist protein concentration. *Knee Surg Sports Traumatol Arthrosc* 2016 Feb 1; Epub ahead of print [PMID: 26831858 DOI: 10.1007/s00167-016-3981-9]

31   **Willits K**, Sonneveld H, Amendola A, Giffin JR, Griffin S, Fowler PJ. Outcome of posterior ankle arthroscopy for hindfoot impingement. *Arthroscopy* 2008; **24**: 196-202 [PMID: 18237704 DOI: 10.1016/j.arthro.2007.08.025]

32   **Jerosch J**, Fadel M. Endoscopic resection of a symptomatic os trigonum. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 1188-1193 [PMID: 16763849 DOI: 10.1007/s00167-006-0089-7]

33   **Tey M**, Monllau JC, Centenera JM, Pelfort X. Benefits of arthroscopic tuberculoplasty in posterior ankle impingement syndrome. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 1235-1239 [PMID: 17589829 DOI: 10.1007/s00167-007-0349-1]

34   **Horibe S**, Kita K, Natsu-ume T, Hamada M, Mae T, Shino K. A novel technique of arthroscopic excision of a symptomatic os trigonum. *Arthroscopy* 2008; **24**: 121.e1-121.e4 [PMID: 18182212 DOI: 10.1016/j.arthro.2007.04.019]

35   **Calder JD**, Sexton SA, Pearce CJ. Return to training and playing after posterior ankle arthroscopy for posterior impingement in elite professional soccer. *Am J Sports Med* 2010; **38**: 120-124 [PMID: 19966105 DOI: 10.1177/0363546509346390]

36   **Noguchi H**, Ishii Y, Takeda M, Hasegawa A, Monden S, Takagishi K. Arthroscopic excision of posterior ankle bony impingement for early return to the field: short-term results. *Foot Ankle Int* 2010; **31**: 398-403 [PMID: 20460066 DOI: 10.3113/FAI.2010.0398]

37   **Galla M**, Lobenhoffer P. Technique and results of arthroscopic treatment of posterior ankle impingement. *Foot Ankle Surg* 2011; **17**: 79-84 [PMID: 21549977 DOI: 10.1016/j.fas.2010.01.004]

38   **Ogut T**, Ayhan E, Irgit K, Sarikaya AI. Endoscopic treatment of posterior ankle pain. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 1355-1361 [PMID: 21311860 DOI: 10.1007/s00167-011-1428-x]

39   **Nickisch F**, Barg A, Saltzman CL, Beals TC, Bonasia DE, Phisitkul P, Femino JE, Amendola A. Postoperative complications of posterior ankle and hindfoot arthroscopy. *J Bone Joint Surg Am* 2012; **94**: 439-446 [PMID: 22398738 DOI: 10.2106/JBJS.K.00069]

40   **López Valerio V**, Seijas R, Alvarez P, Ares O, Steinbacher G, Sallent A, Cugat R. Endoscopic repair of posterior ankle impingement syndrome due to os trigonum in soccer players. *Foot Ankle Int* 2015; **36**: 70-74 [PMID: 25249322 DOI: 10.1177/1071100714552078]

41   **Dinato MC**, Luques IU, Freitas Mde F, Pereira Filho MV, Ninomiya AF, Pagnano RG, Etchebehere M. Endoscopic treatment of the posterior ankle impingement syndrome on amateur and professional athletes. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 1396-1401 [PMID: 26264381 DOI: 10.1007/s00167-015-3747-9]

ORIGINAL ARTICLE

Retrospective Cohort Study

Effect of body mass index on functional outcome in primary total knee arthroplasty - a single institution analysis of 2180 primary total knee replacements

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Abstract

AIM
To evaluate the effect of body mass index (BMI) on short-term functional outcome and complications in primary total knee arthroplasty.

METHODS
All patients undergoing primary total knee arthroplasty at a single institution between 2007 and 2013 were identified from a prospective arthroplasty database. 2180 patients were included in the study. Age, gender, BMI, pre- and post-operative functional scores [Western Ontario and McMaster University Arthritis Index (WOMAC) and SF-36], complications and revision rate were recorded. Patients were grouped according to the WHO BMI classification. The functional outcome of the normal weight cohort (BMI < 25) was compared to the overweight and obese (BMI $\geq$ 25) cohort. A separate sub-group analysis was performed comparing all five WHO BMI groups; Normal weight, overweight, class 1 obese, class 2 obese and class 3 obese.

RESULTS
With a mean age of 67.89 (28-92), 2180 primary total knee replacements were included. 64.36% (1403) were female. The mean BMI was 31.86 (18-52). Ninty-three percent of patients were either overweight or obese. Mean follow-up 19.33 mo (6-60 mo). There was no significant difference in pre or post-operative WOMAC score in the normal weight (BMI < 25) cohort compared to patients with a BMI $\geq$ 25 (P > 0.05). Sub-group analysis revealed significantly worse WOMAC scores in class 2 obese 30.80 compared to overweight 25.80 (P < 0.01) and class 1

obese 25.50 ($P < 0.01$). Similarly, there were significantly worse SF-36 scores in class 2 obese 58.16 compared to overweight 63.93 ($P < 0.01$) and class 1 obese 63.65 ($P < 0.01$) There were 32 (1.47%) superficial infections, 9 (0.41%) deep infections and 19 (0.87%) revisions overall with no complications or revisions in the normal weight cohort (BMI < 25).

CONCLUSION
Post-operative functional outcome was not influenced by BMI comparing normal weight individuals with BMI > 25. Patients should not be denied total knee arthroplasty based solely on weight alone.

Key words: Total knee replacement; Body mass index; Total knee arthroplasty

Core tip: We assessed the effect of body mass index (BMI) on short-term functional outcome of 2180 patients that underwent primary total knee arthroplasty at a single institution. Functional outcome was assessed using the Western Ontario and McMaster University Arthritis Index and SF-36 outcome tools. Patients were stratified according to BMI using the WHO classification and results compared. We found no statistical difference in our primary outcome measure, functional outcome of normal weight individuals compared to those with a BMI greater than 25.

INTRODUCTION

Total knee arthroplasty (TKA) is an effective surgical treatment of osteoarthritis of the knee, with 700000 procedures performed in the United States annually with the demand for TKA projected to increase 673% by 2030[1]. Occurring in tandem with this increase in demand is the exponential increase in obesity in society. Currently in Ireland, 36% of the population are overweight and 14% obese and this is estimated to increase further in the future[2]. It is well established that obesity confers an increased risk for a number of medical conditions including ischaemic heart disease, diabetes and stroke[3]. It has also been shown that obesity increases the risk of development of osteoarthritis, particularly in the knee, which has potential implications for the demand for TKA in the future[4].

Obesity has a number of implications for surgery in general, but in particular for elective surgery such as TKA. Obesity is an independent risk factor for a number of perioperative complications including acute coronary syndrome, wound infection and urinary tract infection[5]. The outcome of obese patients that undergo TKA as compared to non-obese patients is of particular interest. Currently the evidence is unclear with some studies indicating that obese patients achieve inferior outcomes[6] with others showing equivalent functional outcome[7,8].

The aim of this study was to assess the effect of body mass index (BMI) on functional outcome in primary total knee arthroplasty.

MATERIALS AND METHODS

Patients that underwent primary total replacement were identified from a prospectively collected joint registry at a single institution. Ethical approval was obtained for the establishment of the joint registry and for on going research. The joint registry is maintained by a full time clinical nurse specialist and all demographic and clinical information for each arthroplasty procedure performed at the institution is prospectively anonymously recorded. Two thousand one hundred and eighty patients were identified during the period 2007-2013. Demographic data including age and gender were collated for each patient. Body mass index (BMI) was calculated for each patient at pre-operative assessment using the standardised formula; weight in kilograms squared, divided by height in metres squared. Functional outcome scores, the Western Ontario and McMaster University Arthritis Index (WOMAC) and the Short Form 36 (SF-36) were collected pre-operatively and 6 mo post operatively. Complications including revision, superficial and deep infection, deep venous thrombosis (DVT) and pulmonary embolism (PE) were recorded prospectively in the postoperative period.

Patients were divided into two comparative groups for the purpose of the study, those with a normal BMI (less than or equal to 25) Group 1 and those who were overweight or obese (greater than 25) Group 2 according to the WHO BMI classification[9]. A separate sub-group analysis was performed comparing all five WHO BMI groups; Normal weight, overweight, class 1 obese, class 2 obese and class 3 obese.

The Primary outcomes assessed were pre-operative and six-month post-operative WOMAC and the SF-36 scores. The WOMAC score is a validated self-administered questionnaire that assesses the condition of patients with hip and knee arthritis. It has a scale of 0 to 100, with a higher score equalling more pain, stiffness and functional limitation[10]. The SF-36 is also a self-administered questionnaire that assesses quality of life. It has a scale of 0 to 100, with a higher score equating to a greater quality of life[11]. Secondary outcomes assessed included

Distribution of BMI

Figure 1 Distribution of patients according to World Health Organization body mass index classification. BMI: Body mass index.

Table 1 World Health Organization body mass index classification	
WHO BMI classification	
Underweight	< 18.5
Normal range	18.5-25
Overweight	⩾ 25
Obese	⩾ 30
Class 1 obese	30-34.9
Class 2 obese	35-39.9
Class 3 obese	⩾ 40

WTO: World Health Organization; BMI: Body mass index.

Table 2 Pre- and post-operative functional outcome scores	Group 1 (BMI < 25)	Group 2 (BMI > 25)	
WOMAC scores			
Pre-operative	52.7 (1-84)	53.7 (3-96)	$P = 0.5$
6 mo post-operative	29.7 (1-83)	27 (1-95)	$P = 0.075$
SF-36 Scores			
Pre-operative	48.8 (10.4-90.6)	48.25 (3.3-94.6)	$P = 0.83$
6 mo post-operative	61.34 (1-83)	62.15 (7.3-99.4)	$P = 0.7$

WOMAC: Western Ontario and McMaster University Arthritis Index; BMI: Body mass index.

complications revision, superficial and deep infection, DVT and PE.

Statistical analysis

Statistical analysis was performed using STATA Version 12.1. All data was collated on a Microsoft Excel© (Microsoft Corporation, Seattle WA, United States) spreadsheet. Results were analyzed and are presented as mean, percentage and standard deviation for each BMI group according to the WHO classification as appropriate. Statistical significance between the main study groups (normal weight BMI < 25 *vs* BMI > 25) was assessed using the student *t* test, with significance set at $P < 0.05$.

Further sub-group analysis was performed comparing each of the WHO BMI sub-groups. Initially a One-way ANOVA analysis was performed to assess any difference between the groups. Further *post-hoc* Tukey HSD (honest significance test) analysis was then performed, comparing each of the sub-groups with significance set at $P < 0.05$. Statistical analysis was performed by Shane O'Neill MD.

RESULTS

A total of 2180 primary total knee replacements were performed at the institution between 2007 and 2013. The mean age was 67.9 years (28-92), with 36% Male and 64% Female. The mean follow up was 19.3 mo, with a range of 6 mo to 5 years. The distribution according to BMI group is shown in Figure 1. The mean BMI was 31.9 (18-52) with 63% obese, 30% overweight and 7% normal weight. The two comparative study groups consisted of Group 1 (*n* = 162 patients) and Group 2 (*n* = 2018 patients).

Functional outcome

There was no significant difference in the pre-op WOMAC scores between Group 1; 52.7 (1-84) and Group 2; 53.7 (3-96) ($P = 0.5$). Similarly, there was no significant difference in the post op scores between the two groups, 29.7 (1-83) and 27 (1-95) ($P = 0.075$) respectively. There was no significant difference in either the pre-operative ($P = 0.83$) or post-operative ($P = 0.7$) SF-36 scores. The complete functional outcome scores are presented in Tables 1 and 2.

Sub-group analysis

Table 3 outlines 6-mo post operative functional scores arranged by WHO BMI sub-group in tabular format.

WOMAC: Initial One-way ANOVA analysis of the six-month post operative WOMAC scores between the 5 groups revealed a P-value < 0.01, suggesting a significant difference between one or more groups. Further *post-hoc* Tukey HSD testing revealed significant differences in the 6 mo postoperative WOMAC scores

	BMI < 25 Normal	BMI 25-29 Overweight	BMI 30-34 Class 1 obese	BMI 35-39 Class 2 obese	BMI > 40 Class 3 obese
Table 3 Sub-group analysis of post-operative functional outcome scores					
WOMAC scores					
6 mo post-operative	29.67	25.8	25.5	30.8	28.6
SF-36 Scores					
6 mo post-operative	61.34	63.93	63.65	58.16	58.47

WOMAC: Western Ontario and McMaster University Arthritis Index; BMI: Body mass index.

comparing BMI 25-29 (overweight) 25.80 *vs* BMI 35-39 (class 2 obese) 30.80 ($P < 0.01$) and BMI 30-34 (class 1 obese) 25.50 *vs* BMI 35-39 (class 2 obese) 30.80 ($P < 0.01$). There was no significant difference in post operative WOMAC scores in the other BMI subgroup analysis.

SF-36: Initial One-way ANOVA analysis of the six month post operative SF-36 scores between the 5 groups revealed a P-value < 0.01, suggesting a significant difference between one or more groups. Further post-hoc Tukey HSD Testing revealed significant differences in the six month postoperative SF-36 scores comparing BMI 25-29 (overweight) 63.93 *vs* BMI 35-39 (class 2 obese) 58.16 ($P < 0.01$) and BMI 30-34 (class 1 obese) 63.65 *vs* BMI 35-39 (class 2 obese) 58.16 ($P < 0.01$). There was no significant difference in post operative SF-36 scores in the other BMI sub-group analysis.

Complications

There were no complications in Group 1 ($n = 162$) at latest follow-up. There were 19 (0.87%) revisions, 32 (1.47%) superficial infections, 9 (0.41%) deep infections, 10 (0.46%) DVTs and 9 (0.41%) PEs in Group 2 ($n = 2018$) over the same mean follow-up. The absolute number of complications was not sufficient to perform a meaningful statistical analysis.

DISCUSSION

Overall the study revealed no significant difference in short-term post-operative functional outcome in patients with a normal BMI as compared to overweight or obese patients. Sub-group analysis found significantly lower functional outcome scores in class 2 obese patients (BMI 35-39.9) compared to both overweight and class 1 obese patient.

The study highlights that, the vast majority of patients now presenting to our institution for total knee replacement, 93% are either overweight or obese. This is significantly higher than the baseline levels in the general population, where 50% are either overweight or obese[2]. This finding is mirrored in previous studies, which also revealed a considerable proportion of patients undergoing total knee arthroplasty are now obese[12]. According to the latest National joint registry in the United Kingdom (NJR) figures (2013), the mean

BMI of patients undergoing TKA in the United Kingdom is now 30.8 (Class 1 obese)[13]. This underlines the significant burden that this increase in BMI will place on orthopaedic services now and in the future.

The principle finding in this study of equivalent functional outcome comparing normal weight BMI < 25 individuals with BMI > 25 is in keeping with a recent study of 13673 primary total knee replacements by Baker *et al*[14] using NJR data. They found that the improvement of patient reported outcomes (PROMs) were similar irrespective of BMI. Similarly, Desmukh *et al*[15] revealed no correlation with BMI and functional outcome at 1 year. However, a consensus has yet to be reached in the literature, as there is also evidence that increasing BMI, particularly greater than 40 results in inferior clinical outcomes. Collins *et al*[16] reviewed 445 total knee replacements and found inferior clinical outcome scores in individuals with a BMI greater than 30 at 9 years follow up. Interestingly, although obese patients achieved lower outcome scores as compared to non-obese patients, they achieved significant absolute functional improvement and the authors concluded that they "found no reason to limit access to total knee replacement in obese patients". While there was no difference in our main outcome measure, the sub-group analysis revealed significantly worse functional outcomes in the class 2 obese cohort compared to both the overweight and class 1 obese cohort. Interestingly the class 3 obese cohort did not demonstrate any significant difference in functional outcome scores. All cohorts achieved significant absolute improvements in functional outcome measures compared to preoperative values. The significance of our finding of inferior outcomes in the class 2 cohort is unclear. While we have included a relatively large cohort in this study (2180), perhaps larger numbers found in registry studies are necessary to define clear sub-group differences.

Despite no difference in functional outcome, the incidence of all complications was higher in the overweight and obese cohort as compared to the normal weight cohort. The evidence in the literature is clear in relation to the increased risk of perioperative complications with increasing BMI in TKA. The aetiology behind this is multifactorial. Wound healing and the development of both superficial and deep peri-prosthetic joint infections are significantly more common with increasing BMI. A recent meta-analysis

by Kerkhoffs *et al*[17] revealed an odds ratio of 1.9 for all infection and 2.38 for deep infection in obese patients as compared to non-obese patients in an analysis of 15276 and 5061 patients respectively. Obese patients are also at a higher risk of thromboembolic disease post operatively[18]. It is imperative that patients are counselled in detail regarding the increased risk of perioperative complications with increasing BMI. While it would seem intuitive that patients should attempt to lose weight prior to surgery, some recent evidence suggests that obese patients that lose a significant proportion of bodyweight preoperatively, actually have a higher rate of surgical site infection compared to control[19]. Further research is needed in relation to perioperative weight management, however it raises interesting questions about the best way to manage this ever-expanding cohort of overweight and obese patients.

Due to the current demographics of our patient cohort, there were relatively few normal weight individuals presenting for surgery and therefore available for inclusion in the study. Similarly, larger studies using registry data may be necessary to elucidate clear sub-group differences. While the patient numbers were sufficient to statistically compare the functional outcome scores, there was an insufficient incidence of complications to draw any statistical conclusions in relation to complication differences. We acknowledge that early functional outcome may not correspond to long-term functional outcome and further research in this area is required.

In conclusion, overall there was no difference in early post-operative functional outcome comparing normal weight individuals with those of a BMI > 25 in a cohort of 2080 primary total knee replacements. Patients should be counselled regarding the potential increased risk of complications with increasing BMI, however they should not be denied TKA based solely on weight if medically fit to undergo the procedure.

COMMENTS

Background
The demand for total knee arthroplasty is increasing year on year and is projected to increase further in the future. Parallel to this the average weight of individuals is also increasing year on year. This directly corresponds to an increase in demand for total knee replacement (TKR), as increasing weight is associated with increased risk of symptomatic degenerative change in the knee. It is therefore imperative that the authors study the efficacy and safety of performing TKR on this patient cohort.

Research frontiers
The author's group perform high volume multi-surgeon arthroplasty at a single dedicated unit. This paper provides evidence for the efficacy for TKR in this patient cohort irrespective of body mass index (BMI).

Innovations and breakthroughs
Recent innovations in perioperative pain management and the enhanced recovery protocol have had a positive impact in decreasing length of stay and rehab potential for patients undergoing this procedure. This is particularly relevant to overweight and obese individuals for whom it imperative that they

mobilise early to try and minimise the risk of perioperative complications.

Applications
Patients with severe degenerative change affecting their quality of life and mobility can benefit from total knee arthroplasty. The procedure can transform a patient's life, relieving them of chronic pain and improving mobility.

Terminology
TKR involves the replacement of the worn surfaces of the distal femur and proximal tibia and replacement with prosthetic implants, which can be secured with or without cement.

Peer-review
This is an interesting clinical study concerning the effect of BMI on functional outcome and complications in primary total knee arthroplasty.

REFERENCES

1   **Kurtz S**, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; **89**: 780-785 [PMID: 17403800 DOI: 10.2106/JBJS.F.00222]

2   **Morgan KMH**, Watson D, Perry I, Barry M, Shelley E, Harrington J, Molcho M, Layte, RTN, van Lente E, Ward M, Lutomski J, Conroy R, Brugha R. SLAN 2007 Survey of lifestyle attitudes and nutrition in Ireland. Main Report. Dublin: Department of Health and Children, 2007

3   **Bray GA**. Overweight is risking fate. Definition, classification, prevalence, and risks. *Ann N Y Acad Sci* 1987; **499**: 14-28 [PMID: 3300479 DOI: 10.1111/j.1749-6632.1987.tb36194.x]

4   **Felson DT**, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med* 1988; **109**: 18-24 [PMID: 3377350 DOI: 10.7326/0003 -4819-109-1-18]

5   **Bamgbade OA**, Rutter TW, Nafiu OO, Dorje P. Postoperative complications in obese and nonobese patients. *World J Surg* 2007; **31**: 556-560; discussion 561 [PMID: 16957821 DOI: 10.1007/ s00268-006-0305-0]

6   **Foran JR**, Mont MA, Rajadhyaksha AD, Jones LC, Etienne G, Hungerford DS. Total knee arthroplasty in obese patients: a comparison with a matched control group. *J Arthroplasty* 2004; **19**: 817-824 [PMID: 15483795 DOI: 10.1016/j.arth.2004.03.017]

7   **Amin AK**, Patton JT, Cook RE, Brenkel IJ. Does obesity influence the clinical outcome at five years following total knee replacement for osteoarthritis? *J Bone Joint Surg Br* 2006; **88**: 335-340 [PMID: 16498007 DOI: 10.1302/0301-620X.88B3.16488]

8   **Spicer DD**, Pomeroy DL, Badenhausen WE, Schaper LA, Curry JI, Suthers KE, Smith MW. Body mass index as a predictor of outcome in total knee replacement. *Int Orthop* 2001; **25**: 246-249 [PMID: 11561501 DOI: 10.1007/s002640100255]

9   **WHO**. Global database on Body Mass Index: BMI Classification. Geneva: World Health Organization, 2006

10 WOMAC Osteoarthritis Index User Guide. Version V. Australia: Brisbane, 2002

11 **Ware JE**, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30**: 473-483 [PMID: 1593914 DOI: 10.1097/00005650 -199206000-00002]

12 **Kremers HM**, Visscher SL, Kremers WK, Naessens JM, Lewallen DG. The effect of obesity on direct medical costs in total knee arthroplasty. *J Bone Joint Surg Am* 2014; **96**: 718-724 [PMID: 24806008 DOI: 10.2106/JBJS.M.00819]

13 **National Joint Registry**. National Joint Registry Annual Report, 2014. Available from: URL:http://www.hqip.org.uk/resources/ national-joint-registry-annual-report-2014/

14 **Baker P**, Petheram T, Jameson S, Reed M, Gregg P, Deehan D. The association between body mass index and the outcomes of total knee arthroplasty. *J Bone Joint Surg Am* 2012; **94**: 1501-1508

[PMID: 22992819 DOI: 10.2106/JBJS.K.01180]

15   **Deshmukh RG**, Hayes JH, Pinder IM. Does body weight influence outcome after total knee arthroplasty? A 1-year analysis. *J Arthroplasty* 2002; **17**: 315-319 [PMID: 11938508 DOI: 10.1054/arth.2002.30776]

16   **Collins RA**, Walmsley PJ, Amin AK, Brenkel IJ, Clayton RA. Does obesity influence clinical outcome at nine years following total knee replacement? *J Bone Joint Surg Br* 2012; **94**: 1351-1355 [PMID: 23015559 DOI: 10.1302/0301-620X.94B10.28894]

17   **Kerkhoffs GM**, Servien E, Dunn W, Dahm D, Bramer JA, Haverkamp D. The influence of obesity on the complication rate and outcome of total knee arthroplasty: a meta-analysis and systematic literature review. *J Bone Joint Surg Am* 2012; **94**: 1839-1844 [PMID: 23079875 DOI: 10.2106/JBJS.K.00820]

18   **Mantilla CB**, Horlocker TT, Schroeder DR. Risk factors for clinically relevant pulmonary embolism and deep venous thrombosis in patients undergoing primary hip or knee arthroplasty. *Anesthesiology* 2003; **99**: 552-560 [PMID: 12960538]

19   **Inacio MC**, Kritz-Silverstein D, Raman R, Macera CA, Nichols JF, Shaffer RA, Fithian DC. The risk of surgical site infection and re-admission in obese patients undergoing total joint replacement who lose weight before surgery and keep it off post-operatively. *Bone Joint J* 2014; **96-B**: 629-635 [PMID: 24788497 DOI: 10.1302/0301-620X.96B5.33136]

ORIGINAL ARTICLE

Retrospective Study

Outcome of repair of chronic tear of the pectoralis major using corkscrew suture anchors by box suture sliding technique

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Abstract

AIM

To assess the functional and clinical results of repair of chronic tears of pectoralis major using corkscrew and sliding suture technique.

METHODS

In this retrospective study, we reviewed the results of pectoralis major repair in 11 chronic cases (> 6 wk) done between September 2011 and December 2014 at our institute. In all cases repair was done by same surgeon using corkscrew suture anchors and box suture sliding technique. At 6 mo, after surgery magnetic resonance imaging was done to see the integrity of the repair. Functional evaluation was done using Penn and ASES scores. Pre and postoperative Isokinetic strength was measured.

RESULTS

Average follow-up was 48.27 ± 21.0 mo. The Wilcoxon signed rank test was used to evaluate the outcome scores. The average ASES score increased from an average of 54.63 ± 13.0 preoperatively to 95.09 ± 2.60 after surgery at their last follow-up. The average Penn score also increased from 5.72 ± 0.78, 2.81 ± 1.32 and 45.81 ± 1.72 to 9.36 ± 0.80, 8.27 ± 0.90 and 59 ± 1.34 for pain, satisfaction and function respectively. Follow up magnetic resonance imaging (MRI) (at 6 mo) showed continuity and the bulk of pectoralis major muscle in all cases. Average isokinetic strength deficiency in horizontal

adduction at 60° was 13.63% ± 6.93% and at 120° was 10.18% ± 4.93% and in flexion at 60° was 10.72% ± 5.08% and at 120° was 6.63% + 3.74%. Results showed that both ASES and Penn score improved significantly (2 tailed *P* value = 0.0036).

CONCLUSION
We could conclude from this series that pectoralis major repair even in chronic cases using 5.5 mm corkscrew anchors give excellent functional and cosmetic results. In chronic cases the repairable length of the tendon is not available and sliding suture technique allows for fixation of worn out tendomuscular junction to bone without letting cutting through the muscle.

Key words: Pectoralis major tear; Corkscrew suture anchors; Chronic tears; Bench press; Tendon repair

Core tip: We are presenting the results of repair of rare chronic tears of pectoralis major. This is one of the longest series of repair of chronic pectoralis major tears by corkscrew suture anchors with midterm follow-up. In chronic tears hardly any repairable length of the tendon is available and what available is largely musculotendinous unit. We used a new technique to prevent cutting through of sutures from retracted musculotendinous unit in chronic tears. We have obtained excellent results with this technique.

INTRODUCTION

Pectoralis major tear is a relatively rare and extremely traumatic orthopedic injury. Recently there has been an increase in reporting of such cases, especially in young, athletic males between 20 to 40 years of age, who are into body building or weightlifting sports[1]. Pectoralis major muscle has 2 heads of origin, sternocostal and clavicular. Sternocostal part forms the deeper posterior lamina and inserts more proximally on humerus and clavicular part forms the anterior lamina and inserts distally. Sternocostal part primarily internally rotates and adducts the shoulder whereas clavicular part forward flexes and adducts the shoulder. Traditionally, pectoralis major tear were being managed conservatively, but recently the surgical management of pectoralis major repair especially in young athletes has been recommended[2]. Cases of repair of both acute and

chronic tear of pectoralis major have been reported. Tietjen[3] classified these injuries into three classes: (1) sprain; (2) partial tear; and (3) complete tear. Complete tear is further classified into tear of (1) muscle origin; (2) muscle belly; (3) musculotendinous junction and of tendon itself (4) recently, two more subclasses have been added[4-8]; (5) bony flake avulsion of the tendon; and (6) intratendinous ruptures. Chronic tears of pectoralis major are different from acute tears as the repairable length of the tendon is hardly available for fixation. This makes fixation difficult as cutting through the retracted musculo-tendinous junction of sutures is likely. This led us to develop a new technique which resulted in excellent results in chronic cases of this rare injury.

In this article we are reporting our experience of repair of chronic tendon rupture of pectoralis major muscles in 11 cases where we assessed clinical, functional and cosmetic results and incidence of re-rupture.

MATERIALS AND METHODS

In this retrospective study, we reviewed the results of the pectoralis major repair in 11 cases (Table 1) done between September 2011 and December 2014 at our institute. The inclusion criteria were all chronic cases (> 6 wk) of pectoralis major tear repair who had minimum 2-year follow up with the availability of all medical records. All patients presented with common complaints of weakness of involved shoulder and loss of shape/bulge of axillary border. All cases felt sudden tearing sensation and pain in the axilla at time of injury. This was followed by development of bruises and swelling in the axilla. All were managed conservatively for at least 6 wk by local practitioner before presentation (range 1.5-4 mo). On examination, there was a weakness of adduction and internal rotation strength on the involved side compared to the other side and there was a loss of the anterior axillary fold (Figure 1). No patient gave a history of the use of anabolic steroids or any local injections. Diagnosis was confirmed by radiologist in all cases on MRI scan. Multi-planar coronal oblique and axial scans (T2-weighted fat-suppressed and proton density-weighted fat-suppressed images) were taken in all cases. Interstitial edema, retracted tendons and tear with fluid signal were considered positive findings to make the diagnosis. All patients were managed surgically.

Patients were followed up at 2, 6, 12 and 24 wk and subsequently at 3 monthly intervals and assessed clinically by range of motion and strength measurement. After surgery, shoulder was immobilized in a sling for 3 wk. Passive forward flexion and abduction were started after 2 wk. External rotation was restricted to 15 degrees in 1st 6 wk. Range of motion was gradually increased to achieve full range of motion by 3 mo. Strengthening exercises were started by the end of 2 mo and gradually increased from isometric exercises to

Table 1 Details of patients and functional assessment

S/N Profession	Age/sex	Mode of injury	Type of tear	Time between injury and surgery	Follow up	ROM	Penn Score pre surgery	Penn Score (at final follow up)	ASES		Cosmetic appearance
									Pre-surgery	Post-surgery	
1 Student	24/M	Bench press, 190 kg	Both heads avulsion at bony insertion on the humerus	4 mo	82 mo	Full	Pain-6 Satisfaction- 3 Function-45	Pain-10 Satisfaction-9 Function- 60	40	98.33	No complaints
2 Wrestler	25/M	Bench press, 180 kg	Sternal head avulsion at bony insertion on humerus	3 mo	80 mo	Full	Pain-5 Satisfaction- 4 Function-46	Pain-10 Satisfaction- 9 Function- 60	43.33	98.33	No complaints
3 Gym trainer	27/M	Bench press	Sternal head avulsion at bony insertion on humerus	3 mo	68 mo	Full	Pain-7 Satisfaction- 3 Function-44	Pain-9 Satisfaction-9 Function-58	45	91.66	No complaints
4 Kabaddi player	25/M	While playing Kabaddi (Forceful abduction and extension)	Both heads avulsion at bony insertion on the humerus	1.5 mo	56 mo	Full	Pain-6 Satisfaction- 3 Function-45	Pain-8 Satisfaction-7 Function-58	42.77	96.1	No complaints
5 Wrestler	30/ M	Bench press, 150 kg	Both heads avulsion at bony insertion on the humerus	3 mo	50 mo	Full	Pain-5 Satisfaction- 3 Function-45	Pain-8 Satisfaction-7 Function-56	40	91.66	Not fully satisfied with cosmetic appearance (Changed profession due to pain in carrying weight)
6 Wrestler	27/M	Bench press	Sternal head avulsion at bony insertion on humerus	2 mo	44 mo	Full	Pain-6 Satisfaction- 3 Function-45	Pain-9 Satisfaction- 8 Function-60	68.32	93.33	No complaints
7 Weightlifter	25/M	Bench press, 170 kg	Sternal head avulsion at bony insertion on humerus	3 mo	40 mo	Full	Pain-6 Satisfaction- 3 Function-45	Pain-9 Satisfaction-7 Function-60	78.32	98.33	Not fully satisfied with cosmetic appearance
8 Wrestler	28/M	While wrestling	Both heads avulsion at bony insertion on the humerus	2 mo	32 mo	Full	Pain-4 Satisfaction-0 Function-44	Pain-10 Satisfaction-8 Function-58	61.66	95	No complaints
9 Weightlifter	20/M	Bench press 165 kg	Sternal head avulsion at bony insertion on humerus	1.5 mo	30 mo	Full	Pain-6 Satisfaction-3 Function-48	Pain-10 Satisfaction-9 Function-59	63.31	93.33	No complaints
10 Student	27/M	Bench press	Sternal head avulsion at bony insertion on humerus	3.5 mo	25 mo	Full	Pain-6 Satisfaction-5 Function-48	Pain-10 Satisfaction-9 Function-60	61.64	98.33	No complaints
11 Weightlifter	23/M	Bench press 160 kg	Sternal head avulsion at bony insertion on humerus	2 mo	24 mo	Full	Pain-6 Satisfaction-1 Function-49	Pain-10 Satisfaction-9 Function-60	56.66	96.66	No complaints

M: Male; F: Female.

isotonic exercises. Postoperatively results were assessed by American shoulder and elbow assessment (ASES) score, Penn scores and bilateral isokinetic strength testing by Humac™ (CSMI, Stoughton, MA). Deficit in strength was calculated as the percent difference between the higher and lower peak torque of the two limbs divided by the highest peak torque at 60 degrees

and 120 degrees. The Wilcoxon signed rank test was used to assess the difference in pre and post-operative ASES and Penn scores and isometric strength.

Surgical technique
Patients were operated in the beach chair position. An incision of 5 cm was given in distal part of deltopectoral

Figure 1 Preoperative physical appearance with loss of anterior axillary fold (black arrow).

Figure 2 Magnetic resonance imaging report showing near complete tear (arrow) of Pectoralis major muscle.

Figure 3 Torn pectoralis major tendon Sternal head identified and whip sutured (A); and a complete tear of both sternal and clavicular heads, held separately with forceps after mobilization (B).

groove. Torn tendon of pectoralis major was identified and mobilized (Figures 2 and 3). The lateral lip of bicipital groove was exposed and its base was roughened with a rasp and drilling. Two double loaded 5.5 mm corkscrew anchors (Arthrex, Naples, United States) were deployed into the lateral lip proximally and distally at the insertion site of the tendon (Figure 4). Pectoralis major tendon was then attached to the lateral lip of bicipital groove with the help of anchors. The suturing was done in a box like fashion in the musculotendinous area to have a broader fixation and sliding knots followed by the half hitches were applied with post being the free thread (not through the muscle tendon).This brings the broad bulk of muscular tissue in approximation to the insertion site. The technique (box suture-sliding technique, Figure 5) holds good for these types of chronic cases where the torn tendon often gets attrition and it is difficult to achieve secure fixation in the worn out tendon.

RESULTS

All patients were young and active (mean age 25.54 ± 2.60 years). Mean follow up was 48.27 ± 21.0 mo.

Figure 4 Exposure of bicipital groove (A), Biceps tendon is protected. Corkscrew anchors (double loaded) are deployed into the lateral lip of bicipital groove (B).

Figure 5 Box sliding technique. Musculotendinous unit was whipstiched (this makes like a box covering the broad area of delicate muscle to prevent cutting through the musclotendinous unit) and sliding Nikky's knot was used to push the tendon to bone (A). A final picture after the torn tendon has been secured to the lateral lip of bicipital groove with anchors (B).

Mean time from injury to surgery was 2.59 ± 0.83 mo. Nine cases sustained injury while doing bench press exercise in the gymnasium, one patient sustained injury while playing Kabaddi (A popular contact sport in South Asia) and one patient while wrestling. MRI showed near complete tear of the pectoralis major at axillary fold level in four cases and tear of Sternal head in seven cases (Figure 2).

All patients achieved their pre injury exercise level in gymnasium between 9 and 12 mo postoperatively and returned to their previous occupation except one patient (wrestler) who changed the profession due to pain in overhead activity and difficulty in carrying weight. All patients were happy with the cosmetic result regarding the appearance of axillary fold, compared to the other side (Figure 6C) except two patients. At 6 mo, all cases were able to do bench press with minimum 70 kg weight. There was no complication till last follow up. No patient suffered re-tear of the repair till last follow-up.

The average ASES score increased from an average of 54.63 ± 13.0 preoperatively to 95.09 ± 2.60 after

Figure 6 Magnetic resonance imaging at 6 mo follow up showing excellent continuity (arrow) and the bulk of pectoralis major muscle after repair (A, B); restoration of the anterior axillary fold after surgery (C).

surgery at their last follow-up. The average Penn score also increased from 5.72 ± 0.78, 2.81 ± 1.32 and 45.81 ± 1.72 to 9.36 ± 0.80, 8.27 ± 0.90 and 59 ± 1.34 for pain, satisfaction and function respectively. Follow up MRI (at 6 mo) showed continuity and the bulk of pectoralis major muscle in all cases (Figure 6A and B). Average isokinetic strength deficiency in horizontal adduction at 60° was 13.63% ± 6.93% and at 120° was 10.18% ± 4.93% and in flexion at 60° was 10.72% ± 5.08% and at 120° was 6.63% ± 3.74%.

Statistical analysis: The Wilcoxon signed rank test was used to assess the difference in pre and post-operative ASES and Penn scores and isometric strength. Improvement in ASES score and all components of Penn scores were significant (Two tailed $P = 0.0036$, $P < 0.05$).

DISCUSSION

Athletes usually sustain pectoralis major injury as a result of violent, eccentric contraction of the muscle during athletic activities. Sudden forceful abduction and external rotation of contracted muscle is the usual mode of injury. Bench-pressing weights has been reported as the most common mode of injury[4,8]. Other common modes of injury include rugby, football, wrestling and water skiing[5-7]. Type ⅢD (tendon tear) tear is the most common with a rate of 65%, followed by the type Ⅲ C tears[8]. To date just over 60 articles and 350 cases have been reported in English literature[9]. Although first case was reported in 1822 more than 75% cases have been reported in last 20 years[9]. This simply reflects the advancement of diagnostic modalities and our understanding of these injuries. Use of anabolic steroids has been reported as a risk factor in weightlifters in such cases[10]. Sternocostal part stretches when the arm is abducted, externally rotated and extended and it fails more often before the clavicular part[11].

Wolf *et al*[11] in a cadaveric study showed that lower fibers of the sternocostal part are disproportionately lengthened and stressed in the last 30 degrees of extension. This explains why sternocostal part ruptures more often and before clavicular part. Females are less commonly exposed to high velocity sports and high end muscle building exercises. In addition to this larger tendon to muscle diameter in women has also been suggested[12] for almost no incidence of pectoralis major tear in females.

Since the reporting of the 1st case of pectoralis major muscle tear by Patissier[13] in 1822 its treatment has evolved from conservative to surgical management. Now most of the tears are treated surgically except for tears in elderly patients, those with sedentary lifestyles and minor muscle belly rupture[7,14]. While conservative treatment has shown poor results[15,16] surgical treatment has produced excellent outcomes[7,8,13,15] and is the preferred treatment now. In a large series of surgical repair of pectoralis major tear, Äärimaa *et al*[12] showed that early surgical repair has better outcomes than delayed repair. Eight weeks have been reported as an ideal time for surgery of pectoralis major tear[15]. Patients who are treated conservatively show good relief in pain and achieve range of motion compared to surgically treat patients, but they fail to achieve their pre injury level of functional strength and have cosmetic deformity. Surgical management usually involves reattachment of the tendon to humerus by drill holes and tying sutures over a bone bridge[15] anchors[16-25], and staples[23]. Three main techniques of re-attachment of tendon to humerus are bone tunnel technique, bone trough technique and suture anchor technique. In bone tunnel technique sutures are passed using a curved suture passer through curved/angled bone tunnels and tendon are tied over a bone bridge reattaching the tendon to humerus. In bone trough technique drill holes are made into the bone trough at the site of tendon

Figure 7 In acute cases reparable length of the tendon may be available for repair, but in chronic cases it is mainly muscle, which remains available to be attached back to the bone (Figure 3).

insertion. Suture anchors are being increasingly used in recent years, probably due to increasing familiarity of surgeons with these anchors and almost all the case series of repair with suture anchors have been reported after 2004[2,17-19,25]. Care should be taken not to injure the biceps tendon while making trough or drill holes in the bicipital groove.

Due to the rarity of injury no fixation method has been reported to give superior results compared to other methods, however drill holes fixation with or without trough remain the most common method of repair in most of the reported case series. Recently few cadaveric studies have given the results of biomechanical studies of common methods of pectoralis major repair. Sherman *et al*[21] and Hart *et al*[22] concluded that suture anchor repair and trans osseous repair of pectoralis major confer the same biomechanical integrity, whereas Rabuck *et al*[20] found a bone trough repair of the pectoralis major tendon was stronger than suture anchor repair. More studies are needed to reach a conclusion to recommend one method over another. We used suture anchors to fix the tendon to bone as these are easy to use and give firm anchorage in hard young cortical bone.

Although, excellent results have been reported in most cases of late presentation, the main differences in management of acute and chronic cases from the surgery point of view, is the available length of the tendon for repair. In a cadaveric study at our centre (unpublished data) we have seen that the approximate length of pectoralis major tendon from musculotendinous junction is 2.5 cm (Figure 7). In chronic cases the repairable length of the tendon is hardly available and it is mostly muscle/musculotendinous junction, which is anchored to bone (Figure 3). In our technique we used sliding knot, to prevent cutting through of suture through the muscle. Tendon mobilization may be a problem in chronic cases due to adhesions and scars. After incision of these peri-tendinous adhesions it may be possible to bring the tendon to the insertion site at humerus without tension[2]. If the sufficient excursion of the tendon is not possible use of allograft or autograft is necessary[24]. In our series we did not find any difficulty in the mobilization

and fixation of pectoralis major tendon by corkscrew anchors and achieved excellent results.

The only limitation of this study is that the sample size is small, but due to the rarity of the tear of pectoralis major, results are worth reporting. As such, few cases of chronic tears have been reported and there is no consensus for a surgical repair method for chronic tears. We could conclude from this series that pectoralis major repair can be done even in chronic cases using 5.5 mm corkscrew anchors and it gives excellent functional and cosmetic results. Surgery should be done in all such active persons who want to get back to pre-injury activity level.

COMMENTS

Background

Pectoralis major tears are rare injuries with reporting of just over 350 cases in English literature. Pectoralis major muscle has 2 heads of origin, sternocostal and clavicular. The Sternocostal part is mainly internal rotator and adductor of the shoulder whereas the clavicular part is mainly forward flexor and adductor of the shoulder. Management of these tears has been changed over the years from conservative to surgical and now most of the pectoralis major tears are being managed surgically, especially in young athletes. Tears are classified into sprain, partial and complete tears. The most common type of complete tears are tears of tendon itself and tears at musculotendinous junction. Many surgical repair methods have been published for both acute and chronic cases with no published reports of superiority of one method over others.

Research frontiers

In chronic retracted tear of the pectoralis major muscle, repairable length of the tendon is hardly available and mostly it is the musculotendinous unit which remains left. In these cases cutting of suture through the retracted musculotendinous unit is likely while pulling it towards the humerus. To overcome this difficulty the authors used specially designed box suture sliding technique with corkscrews.

Innovation and breakthrough

Sliding knots with suture anchors are commonly used in arthroscopic surgeries. Their study describes the useful role of sliding knot and corkscrew suture anchors in repair of chronic tears of pectoralis major muscle.

Application

The results of this study describe the valuable role of corkscrew suture anchors and sliding knot in repair of chronic tears of the pectoralis major.

Peer-review

The authors of this paper evaluated the results of repair of chronic tears of the pectoralis major muscle using corkscrews and a specially devised sliding knot in 11 patients. They obtained excellent results with significant improvement in ASES score, Penn score and isokinetic strength testing.

REFERENCES

1   **Potter BK**, Lehman RA, Doukas WC. Pectoralis major ruptures. *Am J Orthop* (Belle Mead NJ) 2006; **35**: 189-195 [PMID: 16689519]

2   **Petilon J**, Carr DR, Sekiya JK, Unger DV. Pectoralis major muscle injuries: evaluation and management. *J Am Acad Orthop Surg* 2005; **13**: 59-68 [PMID: 15712983 DOI: 10.5435/00124635-200501000-00008]

3   **Tietjen R**. Closed injuries of the pectoralis major muscle. *J Trauma* 1980; **20**: 262-264 [PMID: 7359604 DOI: 10.1097/00005373-198003000-00015]

4   **Hasegawa K**, Schofer JM. Rupture of the pectoralis major: a case report and review. *J Emerg Med* 2010; **38**: 196-200 [PMID: 18818044 DOI: 10.1016/j.jemermed.2008.01.025]

5   **Hanna CM**, Glenny AB, Stanley SN, Caughey MA. Pectoralis major tears: comparison of surgical and conservative treatment. *Br J Sports Med* 2001; **35**: 202-206 [PMID: 11375884 DOI: 10.1136/bjsm.35.3.202]

6   **Connell DA**, Potter HG, Sherman MF, Wickiewicz TL. Injuries of the pectoralis major muscle: evaluation with MR imaging. *Radiology* 1999; **210**: 785-791 [PMID: 10207482 DOI: 10.1148/radiology.210.3.r99fe43785]

7   **Schepsis AA**, Grafe MW, Jones HP, Lemos MJ. Rupture of the pectoralis major muscle. Outcome after repair of acute and chronic injuries. *Am J Sports Med* 2000; **28**: 9-15 [PMID: 10653537]

8   **Bak K**, Cameron EA, Henderson IJ. Rupture of the pectoralis major: a meta-analysis of 112 cases. *Knee Surg Sports Traumatol Arthrosc* 2000; **8**: 113-119 [PMID: 10795675 DOI: 10.1007/s001670050197]

9   **ElMaraghy AW**, Devereaux MW. A systematic review and comprehensive classification of pectoralis major tears. *J Shoulder Elbow Surg* 2012; **21**: 412-422 [PMID: 21831661 DOI: 10.1016/j.jse.2011.04.035]

10 **März J**, Novotný P. [Pectoralis maior tendon rupture and anabolic steroids in anamnesis--a case review]. *Rozhl Chir* 2008; **87**: 380-383 [PMID: 18810933]

11 **Wolfe SW**, Wickiewicz TL, Cavanaugh JT. Ruptures of the pectoralis major muscle. An anatomic and clinical analysis. *Am J Sports Med* 1992; **20**: 587-593 [PMID: 1443329 DOI: 10.1177/036354659202000517]

12 **Aärimaa V**, Rantanen J, Heikkilä J, Helttula I, Orava S. Rupture of the pectoralis major muscle. *Am J Sports Med* 2004; **32**: 1256-1262 [PMID: 15262651 DOI: 10.1177/0363546503261137]

13 **Patissier P**. Traite des maladies des artisans. *Paris* 1882; **2**: 162-164

14 **Beloosesky Y**, Grinblat J, Weiss A, Rosenberg PH, Weisbort M, Hendel D. Pectoralis major rupture in elderly patients: a clinical study of 13 patients. *Clin Orthop Relat Res* 2003; **(413)**: 164-169 [PMID: 12897606 DOI: 10.1097/01.blo.0000076803.53006.12]

15 **Kretzler HH**, Richardson AB. Rupture of the pectoralis major muscle. *Am J Sports Med* 1989; **17**: 453-458 [PMID: 2782527 DOI: 10.1177/036354658901700401]

16 **de Castro Pochini A**, Ejnisman B, Andreoli CV, Monteiro GC, Silva AC, Cohen M, Albertoni WM. Pectoralis major muscle rupture in athletes: a prospective study. *Am J Sports Med* 2010; **38**: 92-98 [PMID: 19880715 DOI: 10.1177/0363546509347995]

17 **Merolla G**, Campi F, Paladini P, Porcellini G. Surgical approach to acute pectoralis major tendon rupture. *G Chir* 2009; **30**: 53-57 [PMID: 19272235]

18 **Kakwani RG**, Matthews JJ, Kumar KM, Pimpalnerkar A, Mohtadi N. Rupture of the pectoralis major muscle: surgical treatment in athletes. *Int Orthop* 2007; **31**: 159-163 [PMID: 16847645 DOI: 10.1007/s00264-006-0171-2]

19 **Samitier GS**, Marcano AI, Farmer KW. Pectoralis major transosseous equivalent repair with knotless anchors: Technical note and literature review. *Int J Shoulder Surg* 2015; **9**: 20-23 [PMID: 25709241 DOI: 10.4103/0973-6042.150219]

20 **Rabuck SJ**, Lynch JL, Guo X, Zhang LQ, Edwards SL, Nuber GW, Saltzman MD. Biomechanical comparison of 3 methods to repair pectoralis major ruptures. *Am J Sports Med* 2012; **40**: 1635-1640 [PMID: 22679296 DOI: 10.1177/0363546512449291]

21 **Sherman SL**, Lin EC, Verma NN, Mather RC, Gregory JM, Dishkin J, Harwood DP, Wang VM, Shewman EF, Cole BJ, Romeo AA. Biomechanical analysis of the pectoralis major tendon and comparison of techniques for tendo-osseous repair. *Am J Sports Med* 2012; **40**: 1887-1894 [PMID: 22781500 DOI: 10.1177/0363546512452849]

22 **Hart ND**, Lindsey DP, McAdams TR. Pectoralis major tendon rupture: a biomechanical analysis of repair techniques. *J Orthop Res* 2011; **29**: 1783-1787 [PMID: 21538507 DOI: 10.1002/jor.21438]

23 **Egan TM**, Hall H. Avulsion of the pectoralis major tendon in a weight lifter: repair using a barbed staple. *Can J Surg* 1987; **30**:

434-435 [PMID: 3664412]

24   **Zafra M**, Muñoz F, Carpintero P. Chronic rupture of the pectoralis major muscle: report of two cases. *Acta Orthop Belg* 2005; **71**: 107-110 [PMID: 15792217]

25   **Mooers BR**, Westermann RW, Wolf BR. Outcomes Following Suture-Anchor Repair of Pectoralis Major Tears: A Case Series and Review of the Literature. *Iowa Orthop J* 2015; **35**: 8-12 [PMID: 26361438]

ORIGINAL ARTICLE

Observational Study

Is there a weekend effect in hip fracture patients presenting to a United Kingdom teaching hospital?

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Abstract

AIM

To compare mortality and time-to-surgery of patients admitted with hip fracture to our teaching hospital on weekdays *vs* weekends.

METHODS

Data was prospectively collected and retrospectively analysed for 816 hip fracture patients. Multivariate logistic regression was carried out on 3 binary outcomes (time-to-surgery < 36 h; 30-d mortality; 120-d mortality), using the explanatory variables time-of-admission; age; gender; American Society of Anesthesiologist (ASA) grade; abbreviated mental test score (AMTS); fracture type; accommodation admitted from; walking ability outdoors; accompaniment outdoors and season.

RESULTS

Baseline characteristics were not statistically different between those admitted on weekdays *vs* weekends. Weekend admission was not associated with an increased time-to-surgery ($P = 0.975$), 30-d mortality ($P = 0.842$) or 120-d mortality ($P = 0.425$). Gender ($P = 0.028$), ASA grade ($P < 0.001$), AMTS ($P = 0.041$) and accompaniment outdoors ($P = 0.033$) were significant co-variates for 30-d mortality. Furthermore, age ($P < 0.001$),

gender ($P = 0.011$), ASA grade ($P < 0.001$), AMTS ($P < 0.001$) and accompaniment outdoors ($P = 0.033$) all significantly influenced mortality at 120 d. ASA ($P < 0.001$) and season ($P = 0.014$) had significant effect on the odds of undergoing surgery in under 36 h.

CONCLUSION
Weekend admission was not associated with increased time-to-surgery or mortality in hip fracture patients. Demographic factors affect mortality in accordance with previous published reports.

Key words: Weekend; Hip; Fracture; Mortality; Season

Core tip: The weekend effect is gaining academic and political interest. It is important to consider departmental set ups that avoid potentially increased mortality in sick patients admitted on the weekend. Here we evaluate hip fracture patients admitted to a United Kingdom teaching hospital prior to the recent media and political interest, in a centre that had been commended for its care of hip fracture patients. There is no increased mortality in those admitted on a weekend - confirming that it is possible to negate a "weekend effect" with the appropriate infrastructure for hip fracture patients.

INTRODUCTION

Hip fractures related to fragility account for a significant clinical and economic burden on the NHS, especially in an ageing population. There are an estimated 70000 such fractures annually in the United Kingdom, commanding a cost of almost £2 billion a year[1]. These patients have a high prevalence of co-morbidities reflected by the high level of mortality associated with hip fractures - up to 10% of patients die within 30 d[2]. In recent years there have been many steps taken to optimise the quality of care in this group of patients. This includes the distribution of the joint British Orthopaedic Association (BOA)-British Geriatric Society (BGS) "blue book"[1], the setting up of the United Kingdom National Hip Fracture Database (NHFD)[3], the government initiative of a best practice tariff (BPT)[4], and recent publication of NICE guideline CG124[5].

The literature has highlighted some concern over the management of patients admitted over weekends, which represent periods of time involving lower staffing levels and potential shortfalls in care[6]. North American and Australasian studies have found patients with certain medical and surgical diagnoses admitted over the weekend had higher risk-adjusted mortality than patients admitted on weekdays[6-8]. This potential "weekend effect" may be exaggerated in teaching hospitals[7]. In addition, a recent Dr. Foster report suggested that within the United Kingdom, "access to treatment over a weekend is a weak link in the management of hip fractures"[9]. This observation must be addressed, as "early surgery" is associated with significantly reduced risk of mortality[10], and thus any delays linked to timing of admission may have important consequences.

Patients admitted with hip fracture often have multiple co-morbidities and can present with concomitant medical pathologies such as ischaemic heart disease, electrolyte imbalances, renal impairment and sepsis. The effective management of these, medical optimisation and access to timely surgery are key factors in the effective treatment of hip fractures and prevention of further complications. Thus, the objective of our study was to examine the potential "weekend effect" on patients presenting with acute fragility hip fracture to a United Kingdom teaching hospital. Our aim was to compare patients admitted on weekdays *vs* weekends to elucidate any differences in: (1) Time-to-surgery (within 36 h, or not); (2) 30-d mortality; and (3) 120-d mortality.

Our null hypothesis was that there would be no difference in time to surgery or mortality between weekday and weekend groups. In addition, we planned to analyse the effect of 9 other variables on the above outcomes: Age; gender; American Society of Anesthesiologist (ASA) grade; abbreviated mental test score (AMTS); fracture type; type of accommodation admitted from; walking ability outdoors; need for accompaniment outdoors and season.

MATERIALS AND METHODS

Between 1st April 2009 and 30th September 2011, 883 patients were admitted to our hospital with primary fragility hip fracture. Hip fracture was defined as "a fracture occurring in the area between the edge of the femoral head and 5 cm below the lesser trochanter". All these patients had detailed records prospectively created on the NHFD. We excluded those whose records were incomplete to avoid unknown confounders (missing data included details on where the patient was admitted from, preoperative mobility and cognitive status and adequate follow up). This left us a study sample of 816 patients with 100% complete datasets, who were all included in our study. The NHFD is an internet-based audit tool that collates a variety of details on patients admitted with acute hip fracture, including patient characteristics, fracture type, operative details and times of admission to A&E, admission to orthopaedic ward and time of surgery. Accurate dates of death were attained from electronic hospital patient records. The resulting dataset was then used to extrapolate accurate values for time-to-surgery (hours) and 30- and 120-d mortality rates. Of the 816

Table 1 Baseline characteristics, grouped by time of week admitted

Explanatory variable	Classification	Time of week	
		Weekday	Weekend
Age, yr	46.4-100.9	83.1 (8.4)	82.6 (9.3)
mean (SD)	(P = 0.779)[2]		
Gender	Male	169	65
	Female	412	170
	(Female %) (P = 0.733)[1]	(70.90%)	(72.30%)
ASA grade	1-5	3 (1)	3 (1)
median (IQR)	(P = 0.282)[2]		
AMTS	0-10	8 (5)	8 (5)
median (IQR)	(P = 0.924)[2]		
Fracture type	Intertrochanteric	217	92
	Intracapsular - displaced	287	99
	Intracapsular - undisplaced	48	31
	Subtrochanteric	29	13
	(% Intracapsular-displaced) (P = 0.097)[1]	(49.40%)	(42.10%)
Admitted from	Own home	417	191
	Other	110	44
	(% Own home) (P = 1.00)[1]	(81.10%)	(81.30%)
Ability to walk outdoors	Wheelchair/bedbound/electric buggy Never goes outdoors	173	65
	Two aids	54	20
	One aids	154	60
	No aids	200	90
	(% Wheelchair, *etc.*) (P = 0.780)[1]	(29.80%)	(27.70%)
Accompaniment outdoors	Wheelchair/bedbound/electric buggy Never goes outdoors	88	31
	Yes	193	86
	No	300	118
	(% Wheelchair, *etc.*) (P = 0.604)[1]	(15.10%)	(13.20%)
Season	Spring	133	61
	Summer	183	54
	Autumn	160	73
	Winter	105	47
	(% Winter) (P = 0.108)[1]	(18.10%)	(20.00%)
Time of week	Weekday	581	0
	Weekend	0	235

[1]Fisher's Exact test; [2]Mann-Whitney *U* test. SD: Standard deviation; IQR: Interquartile range.

patients, 20 did not have surgery and thus were excluded from the analysis for time-to-surgery (*n* = 796).

Definitions
Patients who were admitted to A and E from Monday 8:00 AM and Friday 5:59 PM were placed in the "weekday" group. Those admitted between Friday 6:00 PM and Monday 7:59 AM were categorised as the "weekend" group, in line with the trust out-of-hours rota.

Statistical analysis
Baseline characteristics between the two groups were compared using Fisher's exact test (for categorical co-variates) or Mann - Whitney *U* test (for continuous co-variates).

Logistic regression was carried out on 3 outcomes of interest (all binary outcomes), using 10 explanatory variables: (1) the proportion of patients receiving surgery in less than 36 h; (2) 30-d mortality; and (3) 120-d mortality.

The co-variates used were: day of admission (weekday *vs* weekend); age; gender; ASA grade; AMTS; type of accommodation admitted from; type of fracture; ability to walk outdoors, need for accompaniment outdoors and season. Logistic regression models were fitted and the "Enter" method was used in the regression models to incorporate the time of week variable, as this was the main interest of the study; forward model selection was then applied to the remaining nine covariates in order to select the most parsimonious model. A *P*-value < 0.05 was considered as significant. The statistical methods of this study were reviewed by Rebecca Harvey of the Centre for Applied Medical Statistics, University of Cambridge.

RESULTS
A total of 796 patients were included for the final analysis. The average age of these patients was 83.0 ± 8.7 years, with a gender ratio of 2.5:1 (581 females; 235 males). During the study period there were 581 admissions during weekdays and 235 during weekend periods. Baseline characteristics of the two groups were not statistically

Table 2 Time-to-surgery and mortality and of patients admitted with hip fracture, grouped and compared by time of week

Outcome variable	Classification	Time of week	
		Weekday	Weekend
Time to surgery	< 36 h	334	138
(*n* = 796)	> 36 h	233	91
	(%< 36 h) *P* > 0.05	(58.90%)	(60.30%)
30-d mortality	No	548	224
(*n* = 816)	Yes	33	11
	(%Yes) *P* > 0.05	(5.70%)	(4.70%)
120-d mortality	No	497	207
(*n* = 816)	Yes	84	28
	(%Yes) *P* > 0.05	(14.50%)	(13.50%)

Table 3 Estimated model coefficients for the multivariate logistic regression model - time to surgery

Outcome 1	Time to surgery (< 36 h)		*n* = 796	
Variable	Level	OR	95%CI	*P*-value
ASA grade	1-5	0.68	0.54, 0.85	0.001
Season	Winter (reference)			0.014
	Spring	1.89	1.21, 2.94	0.005
	Summer	1.7	1.11, 2.61	0.014
	Autumn	1.9	1.23, 2.92	0.004
Time of week	Weekday (reference)			
	Weekend	1.01	0.73, 1.39	0.975

ASA: American Society of Anesthesiologist.

Figure 1 There was no significant difference in time-to-surgery < 36 h (*P* = 0.975) 30-d mortality (*P* = 0.842) or 120-d mortality (*P* = 0.425) between acute hip fracture patients admitted on weekdays (red bars) *vs* weekends (grey bars). All *P*-values derived from logistic regression model.

different in any of the measured fields (Table 1). The most common type of fracture seen during our study period was the intracapsular and displaced neck of femur fracture (*n* = 386; 47.9%). Most patients (*n* = 662; 70.9%) were living in their own home and around a third (*n* = 290; 35.6%) of patients walked outdoors without the use of aids prior to injury.

None of the outcome measures were significantly different between the weekday and the weekend groups (Figure 1 and Table 2).

Outcome 1 - Time-to-surgery < 36 h (Table 3)

There was statistically no difference in the odds of time-to-surgery being less than 36 h between weekend and weekday patients (*P* = 0.975). As ASA increases by one unit, the expected odds of having a time-to-surgery of less than 36 h are reduced by 32% (*P* = 0.001; 95%CI: 0.54, 0.85) (Figure 2). The season also has a significant effect on undergoing surgery within 36 h (*P* = 0.014). Patients who were admitted in spring, summer or autumn all have greater odds of having a time to surgery of less than 36 h compared to the patients admitted in winter.

Outcome 2 - 30-d mortality

There was statistically no difference in the odds of mortality within 30 d between hip fracture patients admitted during the weekdays *vs* weekends (*P* = 0.842) (Table 4). ASA was a strongly significant covariate in

this model. As ASA grade increases by one unit, it is expected that the odds of dying by 30 d to be almost 2.7 times greater (*P* < 0.001) (Figure 2). Male patients had higher odds of mortality at 30 d than female patients [odds ratio (OR) 2.12; 95%CI: 1.09, 4.15] (Figure 3). It is expected that the 30-d mortality odds are lower as AMTS increases by one unit (*P* = 0.041); as AMTS increases by 1, the odds of dying at 30 d are reduced by 10% (95%CI: 0.81, 1.00) (Figure 4). Patients requiring accompaniment outdoors (*P* = 0.015) and those using a wheelchair or never go outdoors (*P* = 0.011) both have higher odds of mortality at 30 d compared with those who do not need any accompaniment outside (Figure 5). Wheelchair-bound patients have the greatest odds relative to those not requiring accompaniment outdoors - they are expected to have 5 times the odds of 30-d mortality. Other co-variates were not significant on this outcome.

Outcome 3 - 120-d mortality

There is no difference in odds of 120-d mortality between the weekend and the weekday groups (*P*-value = 0.425) (Table 4). As ASA increases by one unit, we would expect the odds of 120-d mortality to be 2 times greater (*P* < 0.001) (Figure 2). At 120 d, male patients have greater odds of dying but the expected increase in odds is lower than at 30 d. Male patients are expected to have 1.85 greater odds of mortality at 120 d (95%CI: 1.15, 2.98) (Figure 3). As AMTS increases by a unit, it would be expected that the odds of death at 120 d decrease by around 11% (*P* = 0.001) (Figure 4).

As age increases by one year, the odds of dying at 120 d are 1.06 times greater, *i.e.*, an age increase of one year yields a 6% increase in 120-d mortality (95%CI: 1.03, 1.10). Patients who require a wheelchair to go outdoors or patients who don't go outside have more than twice the odds of 120-d mortality than patients who don't need accompaniment outdoors (*P* = 0.022) (Figure 5). There is however statistically no

Table 4 Estimated model coefficients for the multivariate logistic regression model - mortality

Outcome 2 30-d mortality		*n* = 816			Outcome 3 120-d mortality		*n* = 816		
Variable		OR	95%CI	*P*-value			OR	95%CI	*P*-value
Gender	Female (reference)				Female (reference)				
	Male	2.12	1.09, 4.15	0.028	Male		1.86	1.15, 2.99	0.011
ASA grade	1-5	2.68	1.55, 4.62	< 0.001	1-5		2.03	1.39, 2.95	< 0.001
AMTS	0-10	0.9	0.81, 1.00	0.041	0-10		0.89	0.83, 0.95	0.001
Age (yr)					46-101		1.06	1.03, 1.10	< 0.001
Accompanied	No (reference)			0.033	No (reference)				0.033
outdoors	Yes	4.22	1.32, 13.47	0.015	Yes		1.29	0.70, 2.36	0.423
	Wheelchair/bedbound/electric buggy/does not go out	5.14	1.46, 18.09	0.011	Wheelchair/bedbound/electric buggy/does not go out		2.22	1.12, 4.38	0.022
Time of week	Weekday (reference)				Weekday (reference)				
	Weekend	0.93	0.44, 1.94	0.842	weekend		0.82	0.50, 1.34	0.425

AMTS: Abbreviated Mental Test Score; ASA: American Society of Anesthesiologist.

Figure 2 American Society of Anesthesiologist grade of patients admitted with hip fracture had a significant effect on 30-d mortality (*P* < 0.001), 120-d mortality (*P* < 0.001) and time to surgery (*P* = 0.001). As ASA increased, the mortality rate at 30- and 120-d increased, whilst the percentage of patients undergoing surgery within 36 h decreased. Percentages are expressed as means. All *P*-values derived from logistic regression model. ASA: American Society of Anesthesiologist.

Figure 3 Gender of patients admitted with acute hip fracture had a significant influence on 30-d mortality (*P* = 0.028) and 120-d mortality (*P* = 0.011), with males having an increased risk of death at the two time cut-offs. Percentages are expressed as means. All *P*-values derived from logistic regression model.

difference in odds of dying between non wheelchair bound patients who need accompaniment outdoors and patients who do not require accompaniment outdoors. Other co-variates were not significant on this outcome

DISCUSSION

This study examines the potential weekend effect in patients with a hip fracture in a single teaching hospital within the United Kingdom; it reveals no statistical difference in either 30- or 120-d mortality between patients admitted to our tertiary referral hospital on weekdays *vs* weekends. In addition, patients admitted on the weekend were equally likely to undergo surgery within 36 h.

Hip fractures represent a common and serious injury in older people. Surgery is the main stay of treatment, with over 98% of patients undergoing operative fixation[3]. The association of early surgery

with lower mortality rates in these patients has been widely published[10]. Whilst national NICE guidelines recommend that surgery be performed "on the day of, or the day after admission"[5], the government has introduced the "BPT"[4]. The BPT offers hospitals a £1335 "bonus" payment per hip fracture patient that is managed according to a set of quality indicators, which include performing surgery within 36 h of admission, in combination with orthogeriatric led medical care in the acute phase and secondary fracture prevention. The BPT aims to financially incentivise best clinical practice in hip fracture management and thus enable targeted investment back into local hip fracture services. Accordingly, it has become a target for orthopaedic departments across the country to achieve surgery within the 36-h window and thus we chose that cut-off for this study.

Previous studies

Admissions over the weekend and other out-of-hour periods have been associated with undesirable

Figure 4 As Abbreviated Mental Test Score increased, 30-d mortality (*P* = 0.041) and 120-d mortality (*P* = 0.001) decreased in patients admitted with acute hip fracture. Percentages expressed as means. All *P*-values derived from logistic regression model. AMTS: Abbreviated Mental Test Score.

Figure 5 Requirement for accompaniment outside in hip fracture patients significantly influenced 30-d (*P* = 0.033) and 120-d mortality (*P* = 0.033). At 30 d, patients who are wheelchair bound, bedbound or do not go outside have a higher risk of death than 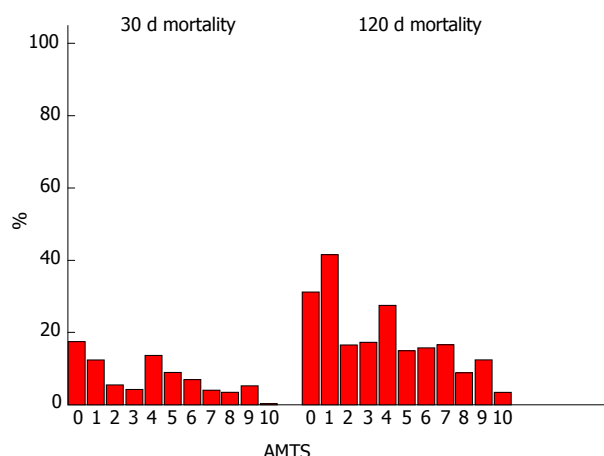those requiring no accompaniment outdoors, at 30 d and 120 d. In addition, patients requiring accompaniment outdoors have a higher at 30-d mortality than those who do not (*P* = 0.015), but this difference is abolished by 120 d (*P* = 0.423). Percentages are expressed as mean. All *P*-values derived from logistic regression model.

delays in investigations and procedures for certain conditions. A report recently published by the Agency for Healthcare Research and Quality (AHRQ) suggested that patients admitted over the weekend in the United States had significantly longer waits for various major procedures[11]. The 2011 Dr. Foster report highlighted that there may be significant delays to hip fracture surgery associated with timing of admission in the United Kingdom, highlighting that many trusts are significantly worse at operating at the weekend[9].

In addition, past research has shown that weekend admission is associated with increased mortality in certain diagnoses, attributing their findings to lower staffing levels and unreliable access to clinical services. Studies from Canada, United States and Australia have shown patients with ruptured abdominal aortic aneurysm (AAA)[6], pulmonary embolism[6], duodenal ulcers[7] and ischaemic heart disease[7,8] have a significantly increased risk of mortality if admitted during the weekend rather than weekday. More recently, evidence of a weekend effect for emergency conditions has also been reported in the United Kingdom[12]. These studies did not observe an increase in mortality in hip fracture patients. However, a Danish study looking at 600 patients presenting with acute hip fracture, did find a significantly higher rate of mortality for those admitted over holiday periods[13], another time group with limitations in human resources. One previous study has observed a potential weekend effect for hip fracture patients in a different United Kingdom teaching hospital[14]. However, following reports of no weekend effect at national level in the United States[15], it was clear that this may not be the case at other similar United Kingdom institutions and it is essential that this is shown.

Interpretation of results
Our data shows that being admitted with a hip fracture on the weekend has no negative impact on whether

patients undergo surgery within 36 h, at our centre. This is likely to be due to the fact this hospital runs a dedicated trauma list, with an allocated anaesthetist and on call theatre radiographer 7 d/wk. In centres where this in not available, the potential improvement in surgical delay with the addition of extra trauma theatre time has been emphasized[16,17]. In addition we have a trauma nurse specialist heavily involved with the management of patients and organisation of trauma lists on every Saturday, in addition to weekdays. Despite these resources available, we found that around 16% of our cases are still delayed whilst awaiting trauma list space underlining the considerable room for further improvement[3]. Indeed, only around 60% of patients achieve surgery within 36 h - however, this is a relatively new target that was introduced in April 2010, and the NHFD report shows this number to be improving nationwide since then[3].

Our study also reveals an inverse relationship between the ASA grade and the time to surgery. This probably translates to patients with more co-morbidities requiring longer to undergo appropriate tests prior to transfer and achieve pre-operative optimization. Indeed, the NHFD report for 2010-2011 suggested that almost 1/3 of the fragility hip fracture patients in the United Kingdom who did not receive an operation within 36 h were delayed because they were awaiting medical review, investigation or stabilization[3]. The number of patients falling into this group may be greater on weekends in some smaller United Kingdom centres where there are potentially only one or two general medical registrars on site; our centre is fortunate to have subspeciality medical registrars (*e.g.*, cardiology, respiratory) on call as well during the weekends. Thus speciality review and special investigations may have a greater probability of being achieved on admission,

which could reduce potential delays in optimisation for surgery.

Interestingly, we found that patients admitted during spring, summer or autumn were statistically more likely to go for surgery within 36 h than those who presented in winter. Higher fracture rates during winter have been reported for various types fracture in the United Kingdom, including hip fractures[18,19]. It may be that patients admitted with hip fracture over winter are more likely to have an acute medical illness which has predisposed them to an increase risk of falls. Additionally, adverse weather conditions may have led to an increase in other non hip fractures, which may be reflected by longer time-to-surgery for patients in our study.

Our model did not find any significant difference in 30- or 120-d mortality between those admitted on weekends when compared with weekday admissions, supporting the null hypothesis. However, logistic regression of our data revealed that patients who were older, male, or had a higher ASA grade or lower AMTS at admission had a significantly higher risk of mortality, which correlates with previous observations[20]. In addition, those who were wheelchair bound or did not go outside had a significantly increased odd of mortality, which may reflect the severity of co-morbidities in these patients. Baseline characteristics were not different between the two groups. Early surgery following hip fracture has been shown to significantly reduce morbidity and mortality when compared with delayed surgery[13]. Thus, the fact there was no statistical difference between weekday and weekend groups in time-to-surgery within 36 h, nor mortality, suggests the outcomes are likely to be linked in our study. Whilst significant blood loss following hip fracture has been reported[21], and such injuries may occur as a result of cardiorespiratory deterioration, it is not a diagnosis that is as susceptible to delays in definitive treatment as those mentioned above that do exhibit a weekend effect. These diagnoses, such as ruptured AAA, PE, and MI would be expected to have a much faster, more dramatic effect on haemodynamic stability.

Messages for clinicians and policy makers
Our data reveals that the overall 30-d mortality for patients presenting with hip fractures to our unit between April 2009-September 2011 was 5.4%. This is notably better than the widely reported figure of 10%[3]; this lower rate has been previously acknowledged and commended[22]. We have an established orthogeriatric service which directs peri- and post-operative medical optimisation of these patients. Regular medical input by such a team allows a continuity of care not afforded by previous systems where issues were dealt with by the on-call medical registrar of the day. In addition, our multidisciplinary rehabilitation team includes regular input from trauma nurse specialists, and 7 d/wk physiotherapy and occupational therapy service,

with emphasis placed on providing falls assessment and commencing bone protection medication during the admission. This highlights the potential positives of adhering to the indicators set out by the BPT[4].

The aim of the BPT, which offers £1335 more than base tariff per case, is to financially incentivise best clinical practice in hip fracture management and thus enable targeted investment back into local hip fracture services. This should "stimulate better quality service provision which is more cost effective"[4]. Our findings suggest that such funding would be well spent in developing additional trauma theatre time and further enhancing services over the weekend including physiotherapy, orthogeriatrics, trauma anaesthetists and theatre radiographers. Whilst guidelines encourage surgery to be performed during "normal working hours", there may be an argument to routinely extend the length of trauma lists to the twilight period to achieve better outcomes and aid qualification for the economic incentive described above.

Limitations
Our study does have limitations. The NHFD is an internet-based data collection system that was set up in 2007 following the long term success of databases such as the Scottish Hip fracture audit[23]. It collates a wealth of information making it a powerful clinical audit tool, especially as data is collected prospectively. As with any database the information available is subject to error during data entry. Some fields such as were missing for certain patients resulting in exclusion of patients from our study. Importantly, baseline characteristics were not statistically different between weekday and weekend groups, either prior to or following exclusion though. The risk of future missing data has been minimised by appointment of an elderly trauma nurse specialist whose role includes ensuring accuracy, appropriateness and completeness of database entries.

We chose to maximise the number of patients we could analyse by including all patients who we could ascertain 120-d mortality data. In addition, it was necessary to amalgamate some groups to allow analysis, as individual groups (*e.g.*, those with ASA 4 or 5) would not have contained sufficient patients otherwise. Future studies should aim to explore if any difference exists in the longer term, for instance at 1 year, and should be of sufficient size to have adequate numbers in each category for analysis.

Future work
The management of hip fracture and resources available at different trusts vary considerably; it was the recognition of this fact which initiated the immense nationwide effort towards clinical governance outlined in this paper. Accordingly, it would be naïve to infer that the findings described at our tertiary referral centre hold true for all other hospitals in the United Kingdom. Previous studies have suggested that weekend effects

are amplified in teaching hospitals[7]. This may not be the case in hip fracture surgery, if indeed there is a weekend effect to be found in other hospitals. The NHFD does however represent a useful instrument with which to analyse this potential weekend effect on a national basis, perhaps including a comparison between outcomes at teaching *vs* district general hospitals, as has previously been done in other countries[7].

ACKNOWLEDGMENTS

COMMENTS

Background

The weekend effect is gaining academic and political interest. Here we evaluate hip fracture patients admitted to a United Kingdom teaching hospital prior to the recent media and political interest, in a centre that had been commended for its care of hip fracture patients. Departments in the United Kingdom are encouraged to aim to medically optimise and operate on all hip fracture patients within 36 h if medically stable. However, hospitals around the country are very heterogeneous in their infrastructure. It is important to consider departmental set ups that avoid potentially increased mortality in sick patients admitted on the weekend.

Research frontiers

The weekend effect refers to the differential on mortality between patients admitted on a weekday with a given diagnosis, when compared with those admitted on a weekend with the same diagnosis. It is encouraged that hip fracture patients are operated on within 36 h of admission in the United Kingdom. This is financially incentivized as this time target is one of the criteria for the best practice tariff (BPT) (see terminology).

Innovations and breakthroughs

Whilst large population studies are incredibly useful at exploring the presence of weekend effect within a whole system, it is also important to check for its presence within heterogeneous departments within that overall system. This allows comparison and elucidation of potential targets to attenuate such differences. This study shows no weekend effect at this United Kingdom teaching hospital for hip fracture patients, in contrast with findings from other teaching hospitals. Increased orthogeriatrics involvement and 7 d/wk orthopaedic trauma lists are likely factors that negate the weekend effect.

Applications

Departments should explore the weekend effect in their departments to highlight areas for service improvement.

Terminology

BPT - the United Kingdom government has introduced the BPT. The BPT offers hospitals a £1335 "bonus" payment per hip fracture patient that is managed according to a set of quality indicators, which include performing surgery within 36 h of admission, in combination with orthogeriatric led medical care in the acute phase and secondary fracture prevention. The BPT aims to financially incentivise best clinical practice in hip fracture management and thus enable targeted investment back into local hip fracture services.

Peer-review

Authors compared mortality and time-to-surgery of patients admitted with hip fracture to their teaching hospital on weekdays *vs* weekends. As an observational report, it is an interesting study of weekend effect on hip fracture patients. Experiments are generally well conducted and the manuscript is well written.

REFERENCES

1   The care of patients with a fragility fracture. Published by the British Orthopaedic Association, 2007. [accessed 2011 Nov 21]. Available from: URL: http://www.fractures.com/pdf/BOA-BGS-Blue-Book.pdf
2   **Roche JJ**, Wenn RT, Sahota O, Moran CG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ* 2005; **331**: 1374 [PMID: 16299013 DOI: 10.1136/bmj.38643.663843.55]
3   The National Hip Fracture Database National Report 2011. [accessed 2011 Dec 4]. Available from: URL: http://www.nhfd.co.uk/003/hipfracrureR.nsf/NHFDNationalReport2011_Final.pdf
4   Best Practice Tariff for Hip Fracture- Making ends meet. British Geriatrics Society. [accessed 2011 Nov 28]. Available from: URL: http://www.bgs.org.uk/index.php?option=com_content&view=article&id=700: tariffhipfracture&catid=47: fallsandbones&Itemid=307
5   Hip fracture: the management of hip fracture in adults. NICE clinical guideline CG124; issued June 2011. [accessed 2011 Nov 27]. Available from: URL: http://www.nice.org.uk/nicemedia/live/13489/54919/54919.pdf
6   **Bell CM**, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001; **345**: 663-668 [PMID: 11547721 DOI: 10.1056/NEJMsa003376]
7   **Cram P**, Hillis SL, Barnett M, Rosenthal GE. Effects of weekend admission and hospital teaching status on in-hospital mortality. *Am J Med* 2004; **117**: 151-157 [PMID: 15276592 DOI: 10.1016/j.amjmed.2004.02.035]
8   **Clarke MS**, Wills RA, Bowman RV, Zimmerman PV, Fong KM, Coory MD, Yang IA. Exploratory study of the 'weekend effect' for acute medical admissions to public hospitals in Queensland, Australia. *Intern Med J* 2010; **40**: 777-783 [PMID: 19811554]
9   Inside your hospital - Dr Foster Hospital Guide 2001-2011. [accessed 2011 Dec 7]. Available from: URL: http://drfosterintelligence.co.uk/wpcontent/uploads/2011/11/Hospital_Guide_2011.pdf
10 **Simunovic N**, Devereaux PJ, Sprague S, Guyatt GH, Schemitsch E, Debeer J, Bhandari M. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. *CMAJ* 2010; **182**: 1609-1616 [PMID: 20837683 DOI: 10.1503/cmaj.092220]
11 **Ryan K**, Levit K, Hannah Davis PH. Characteristics of Weekday and Weekend Hospital Admissions. Rockville, MD, HCUP Statistical Brief #87. Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project (HCUP) Statistical Briefs [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006-2010 Mar [PMID: 21452494]
12 **Freemantle N**, Richardson M, Wood J, Ray D, Khosla S, Shahian D, Roche WR, Stephens I, Keogh B, Pagano D. Weekend hospitalization and additional risk of death: an analysis of inpatient data. *J R Soc Med* 2012; **105**: 74-84 [PMID: 22307037 DOI: 10.1258/jrsm.2012.120009]
13 **Foss NB**, Kehlet H. Short-term mortality in hip fracture patients admitted during weekends and holidays. *Br J Anaesth* 2006; **96**: 450-454 [PMID: 16443639 DOI: 10.1093/bja/ael012]
14 **Thomas CJ**, Smith RP, Uzoigwe CE, Braybrooke JR. The weekend effect: short-term mortality following admission with a hip fracture. *Bone Joint J* 2014; **96-B**: 373-378 [PMID: 24589794 DOI: 10.1302/0301-620X.96B3.33118]
15 **Boylan MR**, Rosenbaum J, Adler A, Naziri Q, Paulino CB. Hip Fracture and the Weekend Effect: Does Weekend Admission Affect Patient Outcomes? *Am J Orthop* (Belle Mead NJ) 2015; **44**: 458-464 [PMID: 26447407]
16 **Marsland D**, Chadwick C. Prospective study of surgical delay for hip fractures: impact of an orthogeriatrician and increased trauma capacity. *Int Orthop* 2010; **34**: 1277-1284 [PMID: 19838708 DOI:

10.1007/s00264-009-0868-0]

17   **Bhattacharyya T**, Vrahas MS, Morrison SM, Kim E, Wiklund RA, Smith RM, Rubash HE. The value of the dedicated orthopaedic trauma operating room. *J Trauma* 2006; **60**: 1336-1340[PMID: 16766980 DOI: 10.1097/01.ta.0000220428.91423.78]

18   **Crawford JR**, Parker MJ. Seasonal variation of proximal femoral fractures in the United Kingdom. *Injury* 2003; **34**: 223-225 [PMID: 12623255 DOI: 10.1016/S0020-1383(02)00211-5]

19   **O'Neill TW**, Cooper C, Finn JD, Lunt M, Purdie D, Reid DM, Rowe R, Woolf AD, Wallace WA. Incidence of distal forearm fracture in British men and women. *Osteoporos Int* 2001; **12**: 555-558 [PMID: 11527052 DOI: 10.1007/s001980170076]

20   **Gunasekera N**, Boulton C, Morris C, Moran C. Hip fracture audit: the Nottingham experience. *Osteoporos Int* 2010; **21**: S647-S653 [PMID: 21058005 DOI: 10.1007/s00198-010-1426-8]

21   **Smith GH**, Tsang J, Molyneux SG, White TO. The hidden blood loss after hip fracture. *Injury* 2011; **42**: 133-135 [PMID: 20236640 DOI: 10.1016/j.injury.2010.02.015]

22   Hospital Guide 2010: What makes a good hospital. [accessed 2011 Nov 28]. Available from: URL: http://www.drfosterhealth.co.uk/docs/ospital-guide-2010.pdf

23   Scottish Hip fracture Audit: Report 2008. Information and statistics division NHS services Scotland. [accessed 2012 Jan 12]. Available from: URL: http://www.show.scot.nhs.uk/shfa

ORIGINAL ARTICLE

Randomized Controlled Trial

Volar locking distal radius plates show better short-term results than other treatment options: A prospective randomised controlled trial

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Abstract

AIM
To compare the outcomes of displaced distal radius fractures treated with volar locking plates and with immediate postoperative mobilisation with the outcomes of these fractures treated with modalities that necessitate 6 wk wrist immobilisation.

METHODS
A prospective, randomised controlled single-centre trial

was conducted with 56 patients who had a displaced radius fracture were randomised to treatment either with a volar locking plate (n = 29), or another treatment modality (n = 27; cast immobilisation with or without wires or external fixator). Outcomes were measured at 12 wk. Functional outcome scores measured were the Patient-Rated Wrist Evaluation (PRWE) Score; Disabilities of the Arm, Shoulder and Hand and activities of daily living (ADLs). Clinical outcomes were wrist range of motion and grip strength. Radiographic parameters were volar inclination and ulnar variance.

RESULTS
Patients in the volar locking plate group had significantly better PRWE scores, ADL scores, grip strength and range of extension at three months compared with the control group. All radiological parameters were significantly better in the volar locking plate group at 3 mo.

CONCLUSION
The present study suggests that volar locking plates produced significantly better functional and clinical outcomes at 3 mo compared with other treatment modalities. Anatomical reduction was significantly more likely to be preserved in the plating group. Level of evidence: Ⅱ.

Key words: Volar locking distal radius plate; Prospective randomised controlled; Postoperative mobilisation; Distal radius fracture; Short-term outcome

Core tip: The present study suggests that the treatment of distal radius fractures with volar locking distal radius plates and immediate postoperative mobilisation produces better functional, radiological and clinical outcomes at three months compared with other treatment modalities which necessitate six weeks immobilisation post fracture. Short term outcomes are very important in our view, as early mobility potentially means earlier return to activities of daily life and return to work for younger patients and remaining functionally independent for the elderly. Future studies should focus on cost savings gained by earlier return to activities of daily living.

INTRODUCTION
Distal radius fractures are the most common type of fracture of the human skeleton, with about ten percent of the population sustaining a fracture at some point in their life[1-3]. Despite the lack of clear evidence, the treatment of distal radius fractures with volar locking distal radius plates (VLDRPs) has become increasingly popular in the last decade[4-8]. The driving force behind the development of VLDRPs was dissatisfaction with the results of conventional treatment modalities. Volar locking plates are expensive[9-11], but they are the only modality that allows distal radius fracture treatment without postoperative immobilisation. All other treatments necessitate between four and eight weeks of wrist immobilisation. Several studies show that these theoretical advantages of VLDRP seem to be equalized after twelve to 24 mo[12-22]. The data on short-term benefits are still unclear, because patients treated with VLDRP still often have their wrists immobilised postoperatively, rather than being allowed to use as tolerated[12-22]. There are only a few studies that specifically allow immediate postoperative mobilisation[23,24], however they did not report on short-term outcomes. The aim of our study was to evaluate short-term results of distal radius fracture treatment with VLDRP and with immediate postoperative wrist mobilisation as tolerated compared to treatment modalities with six weeks immobilisation (closed reduction and casting; Kirschner (K-) wires and casting; external fixation).

MATERIALS AND METHODS
Study design
We carried out a randomised controlled single-centre trial involving patients presenting with distal radial fractures. The study was approved by the Queensland Health ethics committee (approval No. EC00407) and was registered with Clinical Trials.gov (NCT00809861; DCDRS00407).

Setting and participants
The study was conducted at a regional general hospital in Mackay, Queensland, Australia, between June 2009 and December 2013.

The study participants were recruited by two of the study authors (Herwig Drobetz and Lidia Koval). Consecutive patients presenting with distal radial fractures were invited to take part in the trial. The principle researcher was responsible for collecting data. Demographic information was collected for all patients, as well as clinical information regarding presence of osteoporosis, diabetes, or any other predetermined significant medical conditions. Fracture type was recorded. At the end of the recruitment period the principle and associate investigators re-examined hospital records to fill in any missing data.

Eligibility criteria
All patients over the age of 18 years presenting to the Emergency Department or Fracture clinic with a distal radial fracture were eligible to participate in the study. Patients who had bilateral wrist fractures, compound fractures, a concurrent ipsilateral upper limb injury, a past
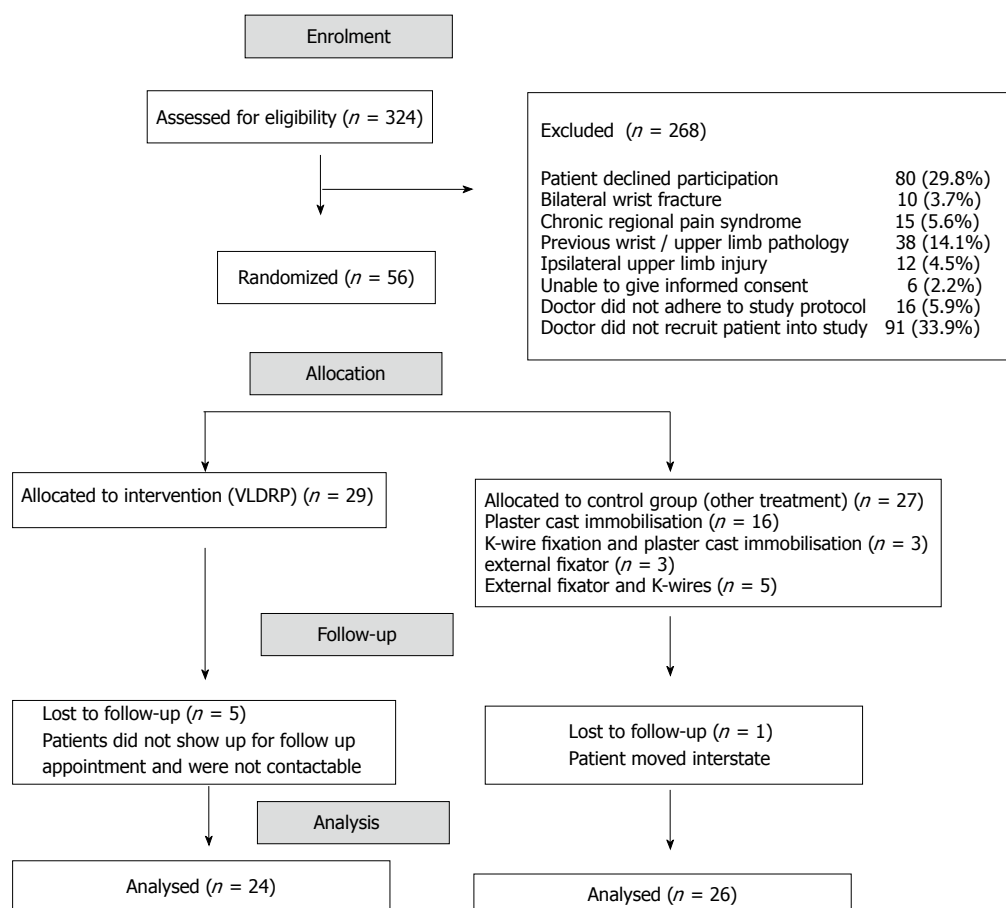
Figure 1 Consort flowchart of enrolment, exclusion, randomisation and follow up of patients. Patients were not recruited because they were overseas tourists or travelling or planning to move within the next twelve weeks.

history of chronic pain syndrome or history of pathology of ipsilateral extremity (including ipsilateral wrist) or who were unable to give informed consent were excluded from the study. Patients were also not included if the treating doctors concluded that they could not adhere to the study protocol (Figure 1).

Technique
All operations were performed by three consultant surgeons (including the principal investigator) at the Mackay Base Hospital Department of Orthopaedic surgery. The following technique was used.

Intervention (VLDRP): The fracture was approached using a volar Henry approach, reduced under fluoroscopic guidance and stabilised with a volar locking distal radius plate. All plates used were Synthes® (Synthes GmbH, Solothurn, Switzerland) VLDRPs, although different models (fixed and variable locking plates with either single or multiple distal screw holes). No bone graft or other void fillers were used. Postoperatively, patients were allowed to immediately use their wrist as tolerated without splinting or any other form of immobilisation. Patients were usually discharged from the hospital the day after the operation and were referred to a physiotherapist. The patients were seen at 2, 6 and 12

wk postoperatively.

Control group (non-operative, K-wire fixation and external fixator): The patients in the control group received either: Closed reduction and casting ($n = 16$); closed reduction, K-wire fixation and casting ($n = 3$); or closed reduction and external fixation with ($n = 5$) or without ($n = 3$) additional K-wires (Figure 1). The same cohort of surgeons who performed the operations in the intervention group also treated the patients in the control group and were free to choose the control group treatment modality. All patients in the control group had their wrist immobilised for six weeks. K-wires and/or external fixators were removed at six weeks. The patients were seen weekly for cast checks/changes or pin checks. Patients were referred for physiotherapy after removal of the cast or external fixator. All patients were then seen again at 12 wk.

Recruitment and randomisation
All patients gave written informed consent before enrolling in the study. After agreeing to participate, patients were randomised using computer generated random numbers and opaque sealed envelopes. The principle investigator enrolled patients and assigned participants to their groups. All participating patients received written instructions on

post-operative care.

Outcomes
Follow up was conducted at 12 wk and comprised patient reported (functional), clinical and radiological outcomes. Only the principle investigator performed the assessments.

Functional assessment: Two self-administered standard questionnaires were given to the study participants [Disabilities of the Arm Shoulder and Hand (DASH) Outcome Measure[25] and Patient Rated Wrist Evaluation (PRWE)][26] to measure disability at the three-month visit. Patients were assessed for their ability to perform activities of daily life (ADL) by being asked if they had resumed driving, and if employed if they had resumed working. They were further asked to grade their ability to perform ADLs into five categories (Group 1 = 100%; Group 2 = 75%-100%; Group 3 = 50%-75%; Group 4 = 25%-50%; Group 5 = 0%-25%). Not being able to drive or work at the 3 mo mark immediately precluded patients from classification into group 1 or 2. The measurement of ADLs was considered to be a secondary outcome measurement.

Clinical assessment: The range of movement of the wrist was assessed with use of a standard goniometer. Wrist strength was measured with use of a dynamometer (Jamar Hydraulic Hand Dynamometer; Lafayette Instrument®, Lafayette, IN, United States). All clinical assessments were performed by the principle investigator (Herwig Drobetz) to reduce inter-observer variability.

Radiological assessment: Radiographs of the wrist taken pre-operatively, post reduction/postoperatively and at three months were assessed for study purposes. Volar tilt of the distal radius joint surface and anterior-posterior radial inclination were measured in degrees and ulnar variance as an indicator of radius shortening was measured in millimetres. Negative values for volar tilt represent dorsal tilt, and negative values for ulnar variance represent an ulna that is shorter than the radius. All radiological measurements were made by an independent assessor (Paula Jeffries) and validated by a radiologist. It was pre-determined that any inter-observer discrepancy of > 15% would trigger another review.

Sample size
Sample size was calculated on the basis of the validated DASH scale, in which a 20-point difference is considered to be clinically significant. Group sample sizes of 21 and 21 achieve 82% power to detect a difference of 20.0 between the null hypothesis assuming that both group means are 40.0 and the alternative hypothesis that the mean of group 2 is 20.0 with estimated group standard deviations of 20.0 and 20.0 and with a significance level (alpha) of 0.025 using a two-sided two-sample *t*-test. Therefore 21 patients were required in the intervention

and control groups. The sample size was set to a total of 46 patients to allow for drop out. The sample size calculation was based on the clinically significant difference for DASH in 2008 being considered to be 20.

Statistical analysis
All analysis was based on the intention-to-treat principal. Depending on the distribution, numerical data was described as mean value and SD or median value and inter-quartile range (IQR). Comparisons between intervention and control groups were conducted using bivariate statistical tests of the statistical programme SPSS (SPSS for Windows, version 22, SPSS Inc., Chicago, IL, United States). *P*-values less than 0.05 were considered to be statistically significant.

RESULTS
Of the total of 324 patients who presented with distal radial fractures during the study period from November 2009 to December 2013, 268 patients were excluded. Of the remaining 56 patients, 29 patients were randomised to the intervention (VLDRP) group, and 27 to the control (other treatments) group. A total of six patients were eventually lost to follow up because they failed to return for the 3-mo review. Follow up was completed in 50/56 (89%) randomised patients (Figure 1). Patients who completed the trial did not differ demographically, clinically or in terms of fracture severity from the group who were eligible for recruitment.

Comparisons at baseline
There were no significant differences between the intervention and the control groups at baseline (Table 1). Fracture types were comparable between groups.

Functional/clinical outcomes
The PRWE scores were significantly better in the VLDRP group than the control group at three months. The mean score in the VLDRP group was 21 compared to a mean score of 47 in the control group. This is also clinically significant as the minimum clinically important difference (MCID) is between 11 and 14 for the PRWE score[27,28]. ADLs were significantly better at three months in the VLDRP group. Twenty patients were able to drive or work at 3 mo (group 1 or 2) in the VLDRP group compared with 15 patients in the control group (Table 2). The DASH scores were also better but this did not reach statistical significance. Wrist extension was significantly better in the VLDRP group as well as grip strength.

Radiological outcomes
At 3 mo, all radiological parameters were significantly better in the VLDRP group than in the control group (Table 3).

Complications
In the VLDRP group we observed five complications in five patients at the three month follow up visit:

Table 1 Baseline comparisons of intervention (volar locking distal radius plate) and control (other treatments) group

	Intervention group n = 24	Control group n = 26
Patient characteristics		
Mean age (SD)	51.1 (16.0)	52.5 (16.5)
Gender F (M)	15 (9)	13 (13)
% Osteoporosis	43	47
% Diabetes mellitus	5	4
% With medical condition[1]	25	29
Dominant hand	9	12
Fracture classification		
A2	0	2
A3	4	7
B2	3	3
C1	7	6
C2	8	7
C3	2	1

[1]Medical conditions recorded were COPD (3), Patient on aspirin or clopidogrel (5); oral steroids (1); continuous inhaled steroids (2); ischaemic heart disease (2). F: Female; M: Male.

Table 2 Functional and clinical outcomes at 3 mo

	VLDRP group n = 24	Control group n = 26	*P*-value
DASH (points)	40 (12)	50 (24)	0.063
PRWE (points)	21 (20)	47 (40)	0.007[1]
Grip strength (% of grip strength of uninjured limb)	64 (29)	42 (32)	0.012[1]
Range of motion (in degrees)			
Flexion	60 (21)	49 (22)	0.072
Extension	65 (48)	48 (27)	0.021[1]
Pronation	70 (31)	68 (26)	0.805
Supination	82 (25)	79 (24)	0.677
ADLs			
Grade 1	19	10	0.036[1]
Grade 2	1	5	
Grade 3	4	7	
Grade 4	0	2	
Grade 5	0	2	

The values are given as the mean and (standard deviation). [1]Indicates significant result. The DASH is a validated, self-reported thirty item metric of upper-extremity function based on a 100 point scale, with 0 points indicating no disability and 100 points indicating maximum disability. The PRWE is a 15-item questionnaire designed to measure wrist pain and disability in activities of daily living. The PRWE allows patients to rate pain and disability from 0 to 10, with 10 being worst pain/unable to perform an activity. ADL: Activities of daily life; VLDRP: Volar locking distal radius plate; DASH: Disabilities of the Arm Shoulder and Hand; PRWE: Patient-Rated Wrist Evaluation.

Flexor tendon rupture, *n* = 1 (patient refused tendon reconstruction); carpal tunnel syndrome, *n* = 1 (patient underwent nerve release after 6 mo); Chronic Regional Pain Syndrome (CRPS), *n* = 1. Two patients did not like "having a plate inside my body" and the plates were subsequently removed 4 mo postoperatively. There were no intra-operative or immediate postoperative complications.

In the control group we observed seven complications

Table 3 Radiological parameters at presentation, post reduction, and 3 mo follow-up

	VLDRP group n = 24	Control group n = 26	*P*-value
Injured wrist at presentation			
Volar slope (degrees)	-17.2 (17.2)	-13.4(14.4)	0.241
Radial inclination (degrees)	8.7 (7.6)	14.2 (9.4)	0.02[1]
Ulnar variance (mm)	2.5 (2.2)	2.3 (3.3)	0.285
Injured wrist post-reduction			
Volar slope (degrees)	4.7 (5.4)	0.08(7.25)	0.01[1]
Radial inclination (degrees)	19.6 (4.5)	18.69(4.52)	0.45
Ulnar variance (mm)	0.1 (0.6)	0.4 (1.4)	0.146
Injured wrist 3 mo			
Volar slope (degrees)	3.5 (4.6)	-5.4 (11.6)	0.001[1]
Radial inclination (degrees)	19.3 (4.4)	15.37 (7.0)	0.054[1]
Ulnar variance (mm)	0.9 (1.3)	2.1 (1.9)	0.011[1]

The values are given as the mean and (standard deviation). [1]Indicates significant result. VLDRP: Volar locking distal radius plate.

in seven patients: Malunion, *n* = 2 (1 of which subsequently had a corrective osteotomy due to functional deficits); CRPS, *n* = 2; infected K-wires which had to be removed early, *n* = 3.

DISCUSSION

The results of our study suggest that clinical and radiological outcomes are superior in the VLDRP group when compared to treatment modalities that necessitate six weeks of wrist immobilisation at the 3-mo mark.

Currently there are no clear evidence based guidelines for the best treatment of distal radius fractures[28]. There have been many encouraging results with the use of VLDRPs[29-34] but other authors reported similar favourable results with other treatment modalities[13,16,21,22,35].

As mentioned in the introduction, many studies show that after one to two years the results of all treatment modalities are similar and there are no longer any significant differences. This fact is often used as an argument against the use of VLDRPs. We do not agree, as the short-term outcomes of treatments are important for patient quality of life and morbidity. Getting back to work 6 wk earlier or, for elderly patients, staying independent can make a significant difference. This might also have an economical impact, as the Medicare savings with earlier return to ADLs can potentially offset the costs for the more expensive treatment with VLDRPs.

Furthermore, it holds true for almost every fracture we treat that long-term outcomes are similar regardless of the treatment, but short-term outcomes are favourable for the more invasive treatment modalities. Tibial shaft fractures treated with intramedullary nails show excellent functional short-term results. After 12 to 24 mo, however, the results are not significantly different from treatment of these fractures with cast immobilisation or an external fixator, both of which are significantly cheaper options[36]. However, due to increased patient demands, the ability

to mobilise early and the fact that the overall short-term benefits are significantly greater, intramedullary nailing of tibial shaft fractures has become the gold-standard treatment.

There are several limitations to our study. Various factors influence the outcomes of distal radius fractures and although information on as many variables as possible was recorded, it proved difficult to ensure that baseline data was comparable. For example, the prevalence of osteopenia or osteoporosis was not verified by a computer tomography or bone densitometry but we used information from the patient's history or GP. Surgical training and technique of the surgeons involved is a potential confounder, which would be difficult to quantify and was not recorded. The study was not blinded, as the nature of surgical procedures, and related postoperative care cannot realistically be masked to patients and staff, and resulting scars preclude the blinding of a blinded independent outcome assessor.

DASH and PRWE, although validated questionnaires, are still subjective scores and especially the DASH has a lower specificity in reporting wrist problems[37,38]. The clinical measurements may be subject to inter and intra-observer variation, although one clinician completed all measurements to reduce inter-observer error. Radiological measurements may also be subject to intra and inter-observer error. Two observers including a radiologist checked all radiographs to reduce errors.

We asked the study participants to subjectively rate their ability to perform specific ADLs with their injured wrist, compare them to their uninjured wrist and then quantify them. We are aware that this is not a validated score but to our knowledge there is no validated wrist specific ADL score available yet[39]. The number of patients reporting full return to ADLs after twelve weeks in the VLDRP was, however, significantly higher than in the control group.

Another limitation is that the study had three different treatment types in the control arm. However, we felt it was unethical to use a single treatment modality as the control group for the purposes of the study, and we feel that this heterogeneous control group represents the "real-life" situation. Our main outcome measure was to see the effect of six weeks immobilization *vs* immediate mobilization.

There are some important strengths of this study. To our knowledge this is the first study that looked at immediate mobilisation *vs* immobilisation for the treatment of distal radius fractures. The study showed that distal radius fractures treated with VLDRP can be treated with immediate postoperative mobilisation without secondary loss of reduction. In a setting like Northern Queensland, where many patients live up to 600 km away from the hospital this constitutes an important factor as the number of follow up visits can potentially be significantly reduced. Treatment with plaster cast or external fixator necessitates more follow up visits and is generally more involved. While recent European studies[10,11] show significant cost savings with the use of K-wires over volar locking plates, this might be different in a regional Australian setting.

In conclusion, the evidence for using VLDRPs for the treatment of distal radius fractures is still a matter of debate and in addition to efficacy; costs and adverse effects should be taken into account. However, our study showed that in the short-term, the functional, clinical and radiological outcomes were superior in the VLDRP group in comparison to other treatment methods. We strongly believe we should concentrate on the early outcomes of distal radius fracture treatment with VLDRPs and not resign ourselves to the fact that "after time, they are all the same". Therefore, the results of this study could encourage the judicial use of VLDRPs for the treatment of distal radius fractures. Future studies should focus on cost savings gained by earlier return to ADLs.

COMMENTS

Background
Despite the lack of clear evidence, the treatment of distal radius fractures with volar locking distal radius plates (VLDRPs) has become increasingly popular in the last decade VLDRPs are the only treatment which allows distal radius fracture fixation without the need for postoperative immobilisation. Several studies show that advantages of VLDRP seem to be equalized after 12 to 24 mo, but there are little data available on short-term benefits of VLDRPs when combined with early mobilisation.

Research frontiers
The treatment of distal radius fractures with VLDRPs has been an area of increased research interest in the last ten years. Recently, many authors have focused on the fact that outcomes when compared with non-operative treatment are similar after 12 to 24 mo. There have also been recent publications showing that volar plating is significantly more expensive when compared to other treatment modalities. There are, however only very limited data on return to work and function in the short term. Earlier return of function and ability to work, which is potentially possible with volar locking plates could mean significant overall cost savings when compared to other treatment options which necessitate 6 wk of immobilisation.

Innovations and breakthroughs
The study showed that VDRLP produced significantly better functional and clinical outcomes at 3 mo compared with other treatment modalities. The study also showed that VLDRP patients can perform activities of daily life significantly earlier than patients who need 6 wk of wrist immobilisation. The study is the only study to the knowledge which allowed immediate postoperative wrist mobilisation after plating with VLDRPs. This allows accurate determination of early functional results, which in our opinion are crucial. All other studies the authors looked at immobilised the wrist for 2 to 4 wk postoperatively.

Applications
Short term benefits are very important, as they translate into the ability for patients to return to work earlier, improve patient quality of life and might have overall cost savings when patients can return to work potentially 6 wk earlier than patients treated with casts or external fixators.

Terminology
VLDRPs have been in clinical use since 1997. The difference to traditional plates is that the screws are connected to the plate in an angle stable fashion, mostly by a thread in the plate hole and in the screw head. This effectively creates a rake like construct. The stiffness of the construct and its ability to withstand deforming forces are therefore not dependant of the bone quality

anymore, as opposed to traditional plates, which need friction between bone and plate to create sufficient construct stiffness. This allows treatment of fractures from the "biomechanically wrong" volar side of the wrist - easier approach and better soft tissue coverage of the implants. It also allows immediate postoperative mobilisation of the wrist, a unique feature of VLDRPs.

Peer-review

It is a random controlled study involving patients presenting with distal radial fractures. Based on better functional, clinical and radiological outcomes at short-term follow-up, the authors encourage the use of volar locking plates for the treatment of distal radius fractures. The study is well designed and the data is reliable.
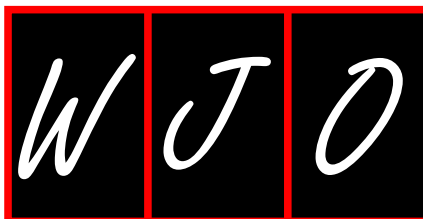
REFERENCES

1   **Graff S**, Jupiter J. Fracture of the distal radius: classification of treatment and indications for external fixation. *Injury* 1994; **25** Suppl 4: S-D14-S-D25 [PMID: 7868191]

2   **Jupiter JB**. Fractures of the distal end of the radius. *J Bone Joint Surg Am* 1991; **73**: 461-469 [PMID: 2002085]

3   **Tscherne H**, Jähne J. [Current status of the treatment of distal radius fracture]. *Unfallchirurg* 1990; **93**: 157-164 [PMID: 2189226]

4   **Chung KC**, Shauver MJ, Birkmeyer JD. Trends in the United States in the treatment of distal radial fractures in the elderly. *J Bone Joint Surg Am* 2009; **91**: 1868-1873 [PMID: 19651943 DOI: 10.2106/JBJS.H.01297]

5   **Mattila VM**, Huttunen TT, Sillanpää P, Niemi S, Pihlajamäki H, Kannus P. Significant change in the surgical treatment of distal radius fractures: a nationwide study between 1998 and 2008 in Finland. *J Trauma* 2011; **71**: 939-942; discussion 942-943 [PMID: 21986738 DOI: 10.1097/TA.0b013e3182231af9]

6   **Chen NC**, Jupiter JB. Management of distal radial fractures. *J Bone Joint Surg Am* 2007; **89**: 2051-2062 [PMID: 17768207 DOI: 10.2106/JBJS.G.00020]

7   **Tarallo L**, Mugnai R, Zambianchi F, Adani R, Catani F. Volar plate fixation for the treatment of distal radius fractures: analysis of adverse events. *J Orthop Trauma* 2013; **27**: 740-745 [PMID: 23515129 DOI: 10.1097/BOT.0b013e3182913fc5]

8   **Mellstrand-Navarro C**, Pettersson HJ, Tornqvist H, Ponzer S. The operative treatment of fractures of the distal radius is increasing: results from a nationwide Swedish study. *Bone Joint J* 2014; **96-B**: 963-969 [PMID: 24986952 DOI: 10.1302/0301-620X.96B7.33149]

9   **Dzaja I**, MacDermid JC, Roth J, Grewal R. Functional outcomes and cost estimation for extra-articular and simple intra-articular distal radius fractures treated with open reduction and internal fixation versus closed reduction and percutaneous Kirschner wire fixation. *Can J Surg* 2013; **56**: 378-384 [PMID: 24284144 DOI: 10.1503/cjs.22712]

10 **Karantana A**, Scammell BE, Davis TR, Whynes DK. Cost-effectiveness of volar locking plate versus percutaneous fixation for distal radial fractures: Economic evaluation alongside a randomised clinical trial. *Bone Joint J* 2015; **97-B**: 1264-1270 [PMID: 26330595 DOI: 10.1302/0301-620X.97B9.35560]

11 **Tubeuf S**, Yu G, Achten J, Parsons NR, Rangan A, Lamb SE, Costa ML. Cost effectiveness of treatment with percutaneous Kirschner wires versus volar locking plate for adult patients with a dorsally displaced fracture of the distal radius: analysis from the DRAFFT trial. *Bone Joint J* 2015; **97-B**: 1082-1089 [PMID: 26224825 DOI: 10.1302/0301-620X.97B8.35234]

12 **Wilcke MK**, Abbaszadegan H, Adolphson PY. Wrist function recovers more rapidly after volar locked plating than after external fixation but the outcomes are similar after 1 year. *Acta Orthop* 2011; **82**: 76-81 [PMID: 21281262 DOI: 10.3109/17453674.2011.552781]

13 **Wei DH**, Raizman NM, Bottino CJ, Jobin CM, Strauch RJ, Rosenwasser MP. Unstable distal radial fractures treated with external fixation, a radial column plate, or a volar plate. A prospective randomized trial. *J Bone Joint Surg Am* 2009; **91**: 1568-1577 [PMID:

14 **Egol K**, Walsh M, Tejwani N, McLaurin T, Wynn C, Paksima N. Bridging external fixation and supplementary Kirschner-wire fixation versus volar locked plating for unstable fractures of the distal radius: a randomised, prospective trial. *J Bone Joint Surg Br* 2008; **90**: 1214-1221 [PMID: 18757963 DOI: 10.1302/0301-620X.90B9.20521]

15 **Wright TW**, Horodyski M, Smith DW. Functional outcome of unstable distal radius fractures: ORIF with a volar fixed-angle tine plate versus external fixation. *J Hand Surg Am* 2005; **30**: 289-299 [PMID: 15781351 DOI: 10.1016/j.jhsa.2004.11.014]

16 **Rozental TD**, Blazar PE, Franko OI, Chacko AT, Earp BE, Day CS. Functional outcomes for unstable distal radial fractures treated with open reduction and internal fixation or closed reduction and percutaneous fixation. A prospective randomized trial. *J Bone Joint Surg Am* 2009; **91**: 1837-1846 [PMID: 19651939 DOI: 10.2106/JBJS.H.01478]

17 **Koshimune M**, Kamano M, Takamatsu K, Ohashi H. A randomized comparison of locking and non-locking palmar plating for unstable Colles' fractures in the elderly. *J Hand Surg Br* 2005; **30**: 499-503 [PMID: 16061315 DOI: 10.1016/j.jhsb.2005.04.018]

18 **Chung KC**, Squitieri L, Kim HM. Comparative outcomes study using the volar locking plating system for distal radius fractures in both young adults and adults older than 60 years. *J Hand Surg Am* 2008; **33**: 809-819 [PMID: 18656749 DOI: 10.1016/j.jhsa.2008.02.016]

19 **Chung KC**, Watt AJ, Kotsis SV, Margaliot Z, Haase SC, Kim HM. Treatment of unstable distal radial fractures with the volar locking plating system. *J Bone Joint Surg Am* 2006; **88**: 2687-2694 [PMID: 17142419 DOI: 10.2106/JBJS.E.01298]

20 **Karantana A**, Davis TR. Extra-articular fractures of the distal radius--a European view point. *Hand Clin* 2012; **28**: 145-150 [PMID: 22554657 DOI: 10.1016/j.hcl.2012.03.001]

21 **Costa ML**, Achten J, Parsons NR, Rangan A, Griffin D, Tubeuf S, Lamb SE. Percutaneous fixation with Kirschner wires versus volar locking plate fixation in adults with dorsally displaced fracture of distal radius: randomised controlled trial. *BMJ* 2014; **349**: g4807 [PMID: 25096595 DOI: 10.1136/bmj.g4807]

22 **Karantana A**, Downing ND, Forward DP, Hatton M, Taylor AM, Scammell BE, Moran CG, Davis TR. Surgical treatment of distal radial fractures with a volar locking plate versus conventional percutaneous methods: a randomized controlled trial. *J Bone Joint Surg Am* 2013; **95**: 1737-1744 [PMID: 24088965 DOI: 10.2106/JBJS.L.00232]

23 **Shetty MS**, Kumar MA, Kiran K, Kini AR. Locking distal radius plate--early results from India. *J Trauma* 2011; **71**: 1359-1363 [PMID: 21460739 DOI: 10.1097/TA.0b013e3182127c57]

24 **Osada D**, Kamei S, Masuzaki K, Takai M, Kameda M, Tamai K. Prospective study of distal radius fractures treated with a volar locking plate system. *J Hand Surg Am* 2008; **33**: 691-700 [PMID: 18590852 DOI: 10.1016/j.jhsa.2008.01.024]

25 **Hudak PL**, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG) *Am J Ind Med* 1996; **29**: 602-608 [PMID: 8773720 DOI: 10.1002/(SICI)1097-0274(199606)29: 6<602: : AID-AJIM4>3.0.CO; 2-L]

26 **MacDermid JC**, Turgeon T, Richards RS, Beadle M, Roth JH. Patient rating of wrist pain and disability: a reliable and valid measurement tool. *J Orthop Trauma* 1998; **12**: 577-586 [PMID: 9840793 DOI: 10.1097/00005131-199811000-00009]

27 **Walenkamp MM**, de Muinck Keizer RJ, Goslings JC, Vos LM, Rosenwasser MP, Schep NW. The Minimum Clinically Important Difference of the Patient-rated Wrist Evaluation Score for Patients With Distal Radius Fractures. *Clin Orthop Relat Res* 2015; **473**: 3235-3241 [PMID: 26040969 DOI: 10.1007/s11999-015-4376-9]

28 **Sorensen AA**, Howard D, Tan WH, Ketchersid J, Calfee RP. Minimal clinically important differences of 3 patient-rated outcomes instruments. *J Hand Surg Am* 2013; **38**: 641-649 [PMID: 23481405 DOI: 10.1016/j.jhsa.2012.12.032]

29 **Lichtman DM**, Bindra RR, Boyer MI, Putnam MD, Ring D, Slutsky DJ, Taras JS, Watters WC, Goldberg MJ, Keith M, Turkelson CM, Wies JL, Haralson RH, Boyer KM, Hitchcock K, Raymond L. Treatment of distal radius fractures. *J Am Acad Orthop Surg* 2010; **18**: 180-189 [PMID: 20190108 DOI: 10.5435/0 0124635-201003000-00007]

30 **Matschke S**, Marent-Huber M, Audigé L, Wentzensen A. The surgical treatment of unstable distal radius fractures by angle stable implants: a multicenter prospective study. *J Orthop Trauma* 2011; **25**: 312-317 [PMID: 21464738 DOI: 10.1097/ BOT.0b013e3181f2b09e]

31 **Lattmann T**, Meier C, Dietrich M, Forberger J, Platz A. Results of volar locking plate osteosynthesis for distal radial fractures. *J Trauma* 2011; **70**: 1510-1518 [PMID: 21057334 DOI: 10.1097/ TA.0b013e3181f13c6a]

32 **Jupiter JB**, Marent-Huber M. Operative management of distal radial fractures with 2.4-millimeter locking plates. A multicenter prospective case series. *J Bone Joint Surg Am* 2009; **91**: 55-65 [PMID: 19122079 DOI: 10.2106/JBJS.G.01498]

33 **Arora R**, Lutz M, Fritz D, Zimmermann R, Oberladstätter J, Gabl M. Palmar locking plate for treatment of unstable dorsal dislocated distal radius fractures. *Arch Orthop Trauma Surg* 2005; **125**: 399-404 [PMID: 15891921 DOI: 10.1007/s00402-005-0820-8]

34 **Orbay JL**, Fernandez DL. Volar fixed-angle plate fixation for unstable distal radius fractures in the elderly patient. *J Hand Surg Am* 2004; **29**: 96-102 [PMID: 14751111 DOI: 10.1016/ j.jhsa.2003.09.015]

35 **Hull P**, Baraza N, Gohil M, Whalley H, Mauffrey C, Brewster M, Costa ML. Volar locking plates versus K-wire fixation of dorsally displaced distal radius fractures--a functional outcome study. *J Trauma* 2011; **70**: E125-E128 [PMID: 20693924 DOI: 10.1097/ TA.0b013e3181e32714]

36 **Sarmiento A**. A functional below-the-knee brace for tibial fractures: a report on its use in one hundred and thirty-five cases. 1970. *J Bone Joint Surg Am* 2007; **89** Suppl 2 Pt.2: 157-169 [PMID: 17768212 DOI: 10.2106/JBJS.G.00188]

37 **Changulani M**, Okonkwo U, Keswani T, Kalairajah Y. Outcome evaluation measures for wrist and hand: which one to choose? *Int Orthop* 2008; **32**: 1-6 [PMID: 17534619 DOI: 10.1007/s00264-007-0368-z]

38 **Mellstrand Navarro C**, Ponzer S, Törnkvist H, Ahrengart L, Bergström G. Measuring outcome after wrist injury: translation and validation of the Swedish version of the patient-rated wrist evaluation (PRWE-Swe). *BMC Musculoskelet Disord* 2011; **12**: 171 [PMID: 21781287 DOI: 10.1186/1471-2474-12-171]

39 **Goldhahn J**, Beaton D, Ladd A, Macdermid J, Hoang-Kim A. Recommendation for measuring clinical outcome in distal radius fractures: a core set of domains for standardized reporting in clinical practice and research. *Arch Orthop Trauma Surg* 2014; **134**: 197-205 [PMID: 23728832 DOI: 10.1007/s00402-013-1767-9]

CASE REPORT

Laminar screw fixation in the subaxial cervical spine: A report on three cases

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Abstract

Although laminar screw fixation is often used at the C2 and C7 levels, only few previous case reports have presented the use of laminar screws at the C3-C6 levels. Here, we report a novel fixation method involving the use of practical laminar screws in the subaxial spine. We used laminar screws in the subaxial cervical spine in two cases to prevent vertebral artery injury and in one case to minimize exposure of the lamina. This laminar screw technique was successful in all three cases with adequate spinal rigidity, which was achieved without complications. The use of laminar screws in the subaxial cervical spine is a useful option for posterior fusion of the cervical spine.

Key words: Laminar screw; Instrumentation; Subaxial cervical spine

Core tip: Laminar screw fixation is often used at the C2 and C7 levels, however, only few previous case reports have presented the use of laminar screws at the C3-C6 levels. In this article, the authors describe a novel fixation method involving the use of laminar screws in the subaxial spine with adequate spinal rigidity, which was achieved without complications.

INTRODUCTION

Posterior surgical stabilization for instability of the cervical spine can be achieved using various techniques. Traditionally, posterior wiring methods have been used[1,2]. Recently, methods involving the use of screws and rods, including pedicle[3], lateral mass[4], and transarticular screws[5], have been widely applied because of the resulting biomechanically rigid stabilization. However, screw insertion is associated with a high risk of injury to the vertebral artery because of differences in the position of the foramen transversarium of the cervical spine, the size of the pedicle of the vertebral arch, and the course of the vertebral arteries among patients. Furthermore, the malposition of these screws can cause serious complications, including massive hemorrhage, neurological deficits, and possible death[6-8]. Here, we describe a novel fixation method involving the use of laminar screws in the subaxial spine for posterior fusion of the cervical spine.

CASE REPORT

Case 1

A 32-year-old man with neck pain had an asymptomatic dumbbell-shaped schwannoma with highly destructive changes observed on radiography (Figure 1). Preoperative magnetic resonance imaging (MRI) showed narrowing of the right vertebral artery due to pressure from the tumor. Subsequently, tumor resection was performed using a posterior approach with total facetectomies of the right C2-3 through C6-7 levels. Reconstruction was achieved using C2-C6 laminar screw fixation (3.5 mm in diameter); the screws were placed in the left lamina to avoid injuring the vertebral artery on the dominant side. Minimal canal invasion by the screw at the C6 level without any resulting neurological deficit was noted. The remaining screws were appropriately placed (Figure 1).

The patient's post-surgical course was uneventful. At 5 years postoperatively, his neck pain disappeared and solid bone fusion was achieved with no instrumentation failure (Figure 1).

Case 2

A 15-year-old girl had a Ewing's sarcoma that involved the right C7 and C8 nerve roots. She began to feel right arm numbness at 12 years of age, and she was diagnosed with a cervical tumor on MRI. In the same year, hemilaminectomy of the right C6 and C7 levels, medial facetectomies of the right C6-7 and Th1 levels, and tumor resection were performed. Pathology of the resected tissues confirmed Ewing's sarcoma. Postoperatively, chemotherapy and radiotherapy were

Figure 1 Case 1. A: A magnetic resonance imaging scan image showing a dumbbell-shaped schwannoma at the C3 level; B, C: Computed tomography images showing an appropriately inserted C4 laminar screw (B) and a C6 laminar screw with minimal canal invasion (C); D: A roentgenogram showing solid bone fusion after C2-6 laminar screw fixation.

repeated.

Two years postoperatively, recurrence of the tumor was detected on MRI. However, no neurological deficits
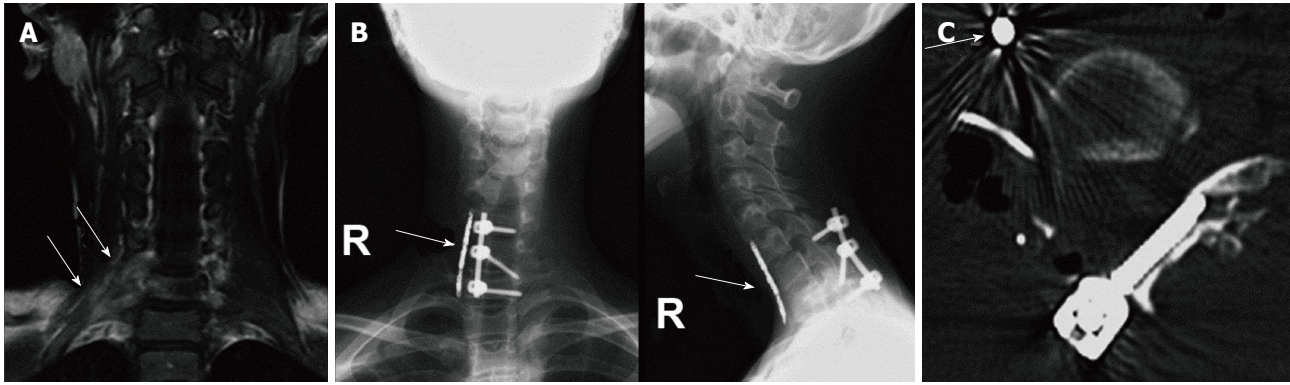
Figure 2 Case 2. A: A magnetic resonance imaging scan image showing a Ewing's sarcoma involving the right C7 and C8 nerve roots (arrows); B: Roentgenograms showing the laminar screws, which are placed at the C6–Th1 levels with a preoperative embolic coil in the right vertebral artery (arrows); C: A computed tomography image showing a C6 laminar screw penetrating the facet joint and a preoperative embolic coil (arrows).
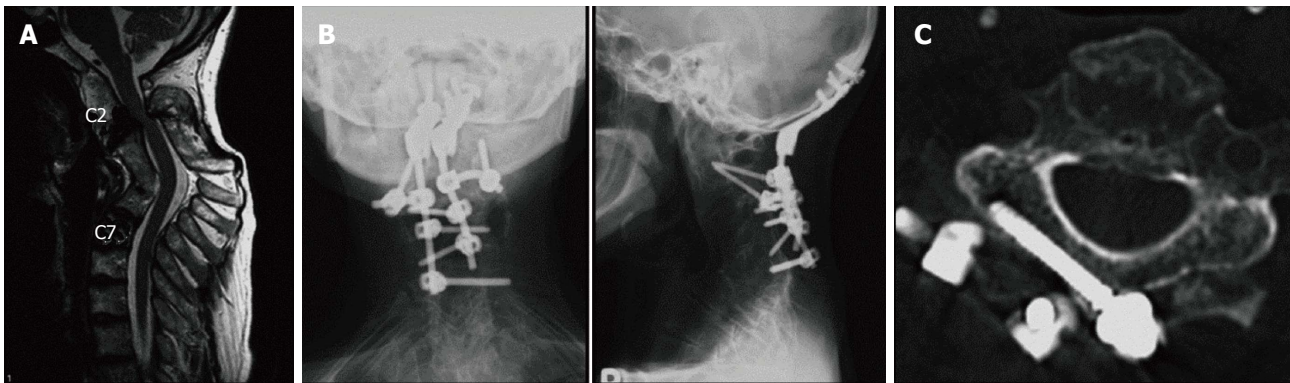

Figure 3 Case 3. A: A magnetic resonance imaging scan image showing severe cervical kyphosis with junctional canal stenosis at the C2-3 levels; B: Roentgenograms showing posterior arthrodesis performed using occipital plates, C2 pedicle screws, and laminar screws at the C3-C6 levels; C: A computed tomography image showing an appropriately inserted C3 laminar screw.

were observed. The tumor was dumbbell-shaped and was located in the intra- and extra-foraminal areas of the C6-7 and C7-Th1 levels (Figure 2). Revision surgery was performed after embolization of the right vertebral artery. Using the posterior approach, laminar screws were inserted at the left C6-Th1 levels to avert the risk of injuring the dominant vertebral artery (Figure 2). Total facetectomies of the right C6-7 and Th1 levels and tumor resection of the right C7 and C8 nerve roots were performed. Additional tumor resection using an anterolateral approach was performed according to the method described by Hodgson[9].

From the day after the operation, she could walk with a soft neck brace, and she exhibited no neurological deficits other than a dropped finger. Two years after the second operation, recurrence of the tumor was detected, and it was treated with chemotherapy. The laminar screws continued to remain rigidly fixed.

Case 3

A 61-year-old woman experienced neck pain and loss of fine motor control of her hand, and 1 year later, she was referred to our hospital for treatment. She had a history of tuberculosis at 8 years of age, which was

conservatively treated for 4 years. She had cervical myelopathy due to an unstable C2-3 joint with marked kyphosis at the C3-6 levels (Figure 3). Because the laminae were very thick, a laminar screw system was selected for cervical fixation. After decompression with partial laminectomy at the C2-3 level, posterior cervical spinal arthrodesis was performed using occipital plates, C2 pedicles, and laminar screws at the C3-C6 levels (3.5 mm screws) with less exposure outside of the lateral mass.

Postoperatively, the patient was mildly immobilized with a soft neck brace, and her post-surgical course was uneventful. At 4 years postoperatively, her neck pain greatly improved and excellent postoperative stability was noted (Figure 3).

DISCUSSION

Here, we reported a novel fixation method involving the use of practical laminar screws in the subaxial spine. Posterior cervical fixation has often been used for stabilizing the cervical spine, correcting deformities, and easing the symptoms of degenerative diseases. Recently, fixation methods involving screws and rods
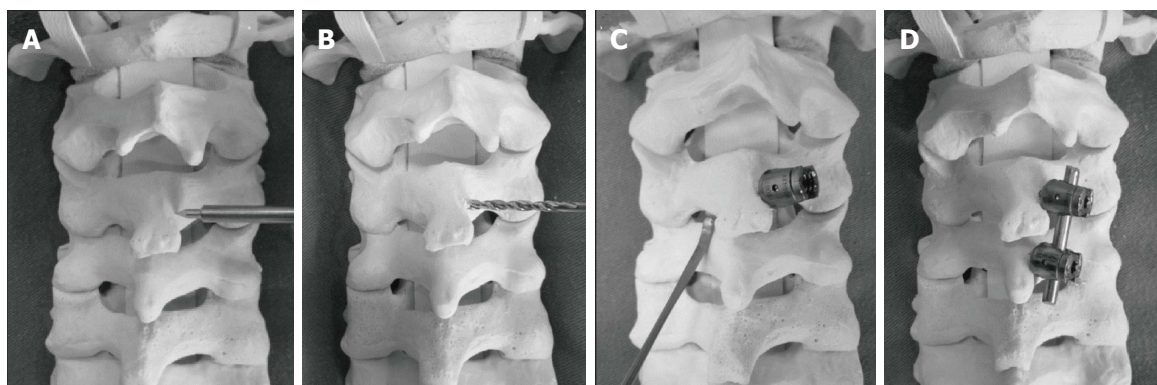
Figure 4 Surgical procedures. A: Create a small cortical window at the junction of the C3 spinous process and the lamina on the right; B: Using a hand drill, carefully drill along the length of the contralateral (left lamina), with the drill visually aligned among the angle of the exposed contralateral laminar surface; C: Insert a 3.5 mm diameter polyaxial screw along the same trajectory in the left C3 lamina. Palpate the ventral lamina with a Penfield dissector to verify that no cortical breakthrough into the spinal canal has occurred; D: Using the same technique as above, insert a 3.5 mm diameter polyaxial screw into the left C4 lamina. Place appropriate rods into the screw heads and attach to C3 and C4 screws.

have become standard, because greater advantages with regard to stabilization and fusion rates of the posterior cervical spine were noted with screw fixation methods than with posterior wiring methods[3,10-12].

Although cervical pedicle screws are the most biomechanically stable screws[13], their use requires an advanced surgical technique and they are associated with the risk of neurovascular complications[14]. To prevent injuring the vertebral artery, pedicle screws should not be used in cases involving the dominant side (*e.g.,* cases 1 and 2). Although the risk of vertebral arterial injury is lower with lateral mass and transarticular screws than with pedicle screws, lateral mass and transarticular screws are difficult to use after facetectomy. Moreover, unilateral use of these screws does not provide sufficient rigidity.

A laminar screw method, which was first reported by Wright[15] in 2004, uses two screws that are inserted crosswise into the lamina of the axis to prevent vertebral artery injuries and safely perform fixation. Although some authors have reported the use of this method in the subaxial lamina of C7[16-18], only two previous studies are present on the use of laminar screws elsewhere in the cervical spine[19,20]. These previous studies did not report sufficient rigidity because thin 1.6 or 2.0 mm mini-screws[19] were used with a mini-plate for fixing the open lamina at the C3-6 levels or an auxiliary laminar screw[20] was inserted at the tip of the C3 lamina accompanied with rigid bilateral C1 lateral mass screws. To our knowledge, our case report is the first to describe the use of practical laminar screws in the subaxial cervical spine. Surgical procedures of subaxial laminar screwing are illustrated in Figure 4.

This new laminar screw technique has four advantages. First, it precludes the risk to the vertebral artery, because the path of the screw is present only in the posterior elements. Second, it is less invasive because of the limited lateral cervical exposure. Third, biomechanical stability with laminar screws is similar to that with pedicle screws, as determined previously by the measurement

of pullout forces[16]. Additionally, surgeons can obtain good rigidity by penetrating the facet joints as shown in cases 1 and 2, and using laminar screws with lateral mass screws as shown in case 3. Fourth, intraoperative navigation systems are not needed, because the screws can be inserted into the lamina under direct vision.

Nakanishi *et al*[21] have pointed out that the laminar screw technique poses a risk to the ventrally located spinal canal that is not easily observed. However, we believe that this risk may be reduced by using a Penfield dissector to detect canal violation following the removal of the flavum ligaments between the laminae. Another disadvantage is that laminar screws with a diameter of 3.5 mm cannot be used at the C3-7 levels in all patients. Cardoso *et al*[16] measured the diameter of the vertebral arch using a computed tomography (CT) navigation system and reported that the insertion of screws with a diameter of 3 mm was only possible in 2%-39% of male and 0%-26% of female patients at the C3-7 cervical spine[21]. However, other authors reported significantly greater C7 laminar thickness with caliper measurements than CT measurements. Therefore, the underestimation of laminar thickness using CT may provide a margin of safety when placing screws into laminae that measure close to 3.5 mm on CT.

Preoperative measurements of the laminar diameter and evaluation of the vertebral arteries by using CT and magnetic resonance angiography are important. We believe that the use of laminar screws in the subaxial cervical spine is a viable salvage option for cases that have failed pedicle screw fixation. The accumulation of further data from the treatment of additional cases is required to clarify the indications for and limitations of using the laminar screw technique at the C3-6 levels.

In conclusion, the findings in our cases suggest that the use of the laminar screw technique in the subaxial cervical spine is feasible, as it provides sufficient spinal rigidity. Laminar screws are considered useful for avoiding arterial injuries, and the laminar screw technique is a viable salvage technique.

COMMENTS

Case characteristics

Three cases are discussed with reports of posterior surgical stabilization for instability of the cervical spine.

Clinical diagnosis

Tumor was diagnosed for the first two cases. Cervical myelopathy was the clinical diagnosis for the third case.

Imaging diagnosis

Magnetic resonance imaging was done to for all cases to establish the cause of the problem.

Pathological diagnosis

Pathology analysis was conducted for the 15-year-old female case for confirming the diagnosis of Ewing's sarcoma.

Treatment

For the first case, a 32-year-old male, tumor resection was performed and reconstruction was done using screw fixation. For the 15-year-old female case, tumor resection was performed and postoperatively chemotherapy and radiotherapy was performed. For the 61-year-old female case, cervical fixation was done.

Experiences and lessons

A novel fixation method has been reported with use of practical laminar screws in the subaxial cervical spine. This method reduces the risk to the vertebral artery, is less invasive, provides biomechanical stability and the screws can be inserted with direct vision. Additional cases are needed to clarify the indications and limitations for using laminar screw technique.

Peer-review

This is a good case report with medium term result in one patient and will add to the body of literature for posterior cervical fusion.

REFERENCES

1   **Brooks AL**, Jenkins EB. Atlanto-axial arthrodesis by the wedge compression method. *J Bone Joint Surg Am* 1978; **60**: 279-284 [PMID: 348703]

2   **Dickman CA**, Sonntag VK, Papadopoulos SM, Hadley MN. The interspinous method of posterior atlantoaxial arthrodesis. *J Neurosurg* 1991; **74**: 190-198 [PMID: 1988587 DOI: 10.3171/jns.1991.74.2.0190]

3   **Abumi K**, Itoh H, Taneichi H, Kaneda K. Transpedicular screw fixation for traumatic lesions of the middle and lower cervical spine: description of the techniques and preliminary report. *J Spinal Disord* 1994; **7**: 19-28 [PMID: 8186585 DOI: 10.1097/00002517-199407010-00003]

4   **Taniguchi M**, Maruo S. Posterior Lower Cervical Spine Arthrodesis with Lateral Mass Fixation. *Spine & Spinal Cord* 1998; **11**: 217-224

5   **Jeanneret B**, Magerl F. Primary posterior fusion C1/2 in odontoid fractures: indications, technique, and results of transarticular screw fixation. *J Spinal Disord* 1992; **5**: 464-475 [PMID: 1490045 DOI: 10.1097/00002517-199212000-00012]

6   **Coric D**, Branch CL, Wilson JA, Robinson JC. Arteriovenous fistula as a complication of C1-2 transarticular screw fixation. Case report and review of the literature. *J Neurosurg* 1996; **85**: 340-343 [PMID: 8755766 DOI: 10.3171/jns.1996.85.2.0340]

7   **Madawi AA**, Casey AT, Solanki GA, Tuite G, Veres R, Crockard HA. Radiological and anatomical evaluation of the atlantoaxial transarticular screw fixation technique. *J Neurosurg* 1997; **86**: 961-968 [PMID: 9171174 DOI: 10.3171/jns.1997.86.6.0961]

8   **Wright NM**, Lauryssen C. Vertebral artery injury in C1-2 transarticular screw fixation: results of a survey of the AANS/CNS section on disorders of the spine and peripheral nerves. American Association of Neurological Surgeons/Congress of Neurological Surgeons. *J Neurosurg* 1998; **88**: 634-640 [PMID: 9525707 DOI: 10.3171/foc.1998.4.2.2]

9   **Hodgson AR**. An approach to the cervical spine (C-3 TO C-7). *Clin Orthop Relat Res* 1965; **39**: 129-134 [PMID: 14288168 DOI: 10.1097/00003086-196500390-00012]

10 **An HS**, Gordin R, Renner K. Anatomic considerations for plate-screw fixation of the cervical spine. *Spine* (Phila Pa 1976) 1991; **16**: S548-S551 [PMID: 1801270 DOI: 10.1097/00007632-199110001-00019]

11 **Harris BM**, Hilibrand AS, Nien YH, Nachwalter R, Vaccaro A, Albert TJ, Siegler S. A comparison of three screw types for unicortical fixation in the lateral mass of the cervical spine. *Spine* (Phila Pa 1976) 2001; **26**: 2427-2431 [PMID: 11707704 DOI: 10.1097/00007632-200111150-00006]

12 **Ludwig SC**, Kramer DL, Vaccaro AR, Albert TJ. Transpedicle screw fixation of the cervical spine. *Clin Orthop Relat Res* 1999; **(359)**: 77-88 [PMID: 10078131 DOI: 10.1097/00003086-199902000-00009]

13 **Jones EL**, Heller JG, Silcox DH, Hutton WC. Cervical pedicle screws versus lateral mass screws. Anatomic feasibility and biomechanical comparison. *Spine* (Phila Pa 1976) 1997; **22**: 977-982 [PMID: 9152447 DOI: 10.1097/00007632-199705010-00009]

14 **Taneichi H**. Placement technique of cervical screws and prevention of its complications. *Spine & Spinal Cord* 2005; **18**: 1043-1052

15 **Wright NM**. Posterior C2 fixation using bilateral, crossing C2 laminar screws: case series and technical note. *J Spinal Disord Tech* 2004; **17**: 158-162 [PMID: 15260101 DOI: 10.1097/00024720-200404000-00014]

16 **Cardoso MJ**, Dmitriev AE, Helgeson MD, Stephens F, Campbell V, Lehman RA, Cooper P, Rosner MK. Using lamina screws as a salvage technique at C-7: computed tomography and biomechanical analysis using cadaveric vertebrae. Laboratory investigation. *J Neurosurg Spine* 2009; **11**: 28-33 [PMID: 19569937 DOI: 10.3171/2009. 3.SPINE08648]

17 **Hong JT**, Yi JS, Kim JT, Ji C, Ryu KS, Park CK. Clinical and radiologic outcome of laminar screw at C2 and C7 for posterior instrumentation--review of 25 cases and comparison of C2 and C7 intralaminar screw fixation. *World Neurosurg* 2010; **73**: 112-118; discussion e15 [PMID: 20860937 DOI: 10.1016/j.surneu.2009.06.010]

18 **Şenoğlu M**, Özkan F, Çelik M. Placement of C-7 intralaminar screws: a quantitative anatomical and morphometric evaluation. *J Neurosurg Spine* 2012; **16**: 509-512 [PMID: 22339053 DOI: 10.3171/2012.1.SPINE111048]

19 **Hong JT**, Sung JH, Son BC, Lee SW, Park CK. Significance of laminar screw fixation in the subaxial cervical spine. *Spine* (Phila Pa 1976) 2008; **33**: 1739-1743 [PMID: 18628706 DOI: 10.1097/BRS.0b013e31817d2aa2]

20 **Jea A**, Johnson KK, Whitehead WE, Luerssen TG. Translaminar screw fixation in the subaxial pediatric cervical spine. *J Neurosurg Pediatr* 2008; **2**: 386-390 [PMID: 19035682 DOI: 10.3171/PED.2008.2.12.386]

21 **Nakanishi K**, Tanaka M, Sugimoto Y, Misawa H, Takigawa T, Fujiwara K, Nishida K, Ozaki T. Application of laminar screws to posterior fusion of cervical spine: measurement of the cervical vertebral arch diameter with a navigation system. *Spine* (Phila Pa 1976) 2008; **33**: 620-623 [PMID: 18344855 DOI: 10.1097/BRS.0b013e318166aa76]

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