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Hip hemi-arthroplasty for neck of femur fracture: What is the current evidence?

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evidence (meta-analyses and Cochrane reviews) relating to the use of hip hemi-arthroplasty for neck of femur fractures. Regarding the optimal surgical approach, two recent meta-analyses have found that posterior approaches are associated with: higher rates of dislocation compared to lateral and anterior approaches; and higher rates of re-operation compared to lateral approaches. Posterior approaches should therefore be avoided when performing hip hemi-arthroplasty procedures. Assessing the optimal prosthesis head component, three recent meta-analyses and one Cochrane review have found that while unipolar hemi-arthroplasty can be associated with increased rates of acetabular erosion at short-term follow-up (up to 1 year), there is no significant difference between the unipolar hemi-arthroplasty and bipolar hemi-arthroplasty for surgical outcome, complication profile, functional outcome and acetabular erosion rates at longer-term follow-up (2 to 4 years). With bipolar hemi-arthroplasty being the more expensive prosthesis, unipolar hemi-arthroplasty is the recommended option. With regards to the optimal femoral stem insertion technique, three recent meta-analyses and one Cochrane Review have found that, while cemented hip hemi-arthroplasties are associated with a longer operative time compared to uncemented Hip Hemi-arthroplasties, cemented prostheses have lower rates of implant-related complications (particularly peri-prosthetic femoral fracture) and improved post-operative outcome regarding residual thigh pain and mobility. With no significant difference found between the two techniques for medical complications and mortality, cemented hip hemi-arthroplasty would appear to be the superior technique. On the topic of wound closure, one recent meta-analysis has found that, while staples can result in a quicker closure time, there is no significant difference in post-operative infections rates or wound healing outcomes when comparing staples to sutures. Therefore, either suture or staple wound closure techniques appear equally appropriate for hip hemi-arthroplasty procedures.

Abstract

This editorial reviews and summarises the current

Key words: Hemi-arthroplasty; Prosthesis; Stem; Head; Hip; Femoral; Neck; Fracture; Cement

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Core tip: From the current evidence on hip hemi-arthroplasty, the following conclusions can be drawn: posterior approaches are associated with higher rates of dislocation and should be avoided; there is no significant difference between unipolar and bipolar hemi-arthroplasty for surgical outcome, complication profile, functional outcome and long-term acetabular-erosion rates, therefore unipolar hemi-arthroplasty, the cheaper prosthesis, is the recommended option; cemented hemi-arthroplasty, the recommended option, has lower rates of implant-related complications and residual thigh pain compared to uncemented hemi-arthroplasty, with no significant difference in medical complications or mortality; there is no significant difference in wound-infections rates or healing outcomes between staples and sutures.

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INTRODUCTION

Hip fractures in the elderly represent a major public health concern^[1-7]. These account for a quarter of all fractures in patients aged 75 years and over^[3]. With a global incidence of 1.7 million hip fractures in 1990, this is targeted to reach 6.3 million in 2050^[7].

The management of hip fractures is based on the location of the fracture: the two main categories being intra and extra-capsular fractures^[8]. Intra-capsular fractures comprise around 60% of all hip fractures, with up to 80% of these being displaced^[1,9]. Fracture displacement increases the risk of disruption to the femoral head blood supply, and so, is associated with increased rates of osteo-necrosis of femoral head, non-union, delayed union and failure of fracture fixation procedures^[10-15]. As such, the current treatment guidelines for hip fractures advise that "displaced intracapsular neck of femur fractures be treated with arthroplasty procedures"^[16]. There are two main arthroplasty procedures available for the treatment of displaced intracapsular neck of femur fractures: hip hemi-arthroplasty and total hip replacement^[17-22]. Hip hemi-arthroplasty is the recommended option in the frail, low mobility population as the large diameter hemi-arthroplasty "head" component reduces the risk of dislocation: total hip replacement is the recommended option in the more active population as it can provide a better functional outcome^[17-22]. The current guidelines from the "National Institute for Health and Care Excellence" (NICE) advice for orthopaedic surgeons to consider total hip

arthroplasty over hip hemi-arthroplasty as treatment of displaced neck of femur fractures in patients who are: independently mobile out-doors, requiring one stick or less for support; cognitively intact; and considered suitably healthy to undergo the operation by both the orthopaedic and anaesthetic teams. When such criteria are not met, a hip hemi-arthroplasty is indicated^[16]. The current registry data suggests that around 90% of displaced intra-capsular fractures are treated with hip hemi-arthroplasty, with 10% treated with total hip replacements^[1,2,23].

Despite the perceived simplicity of the hip hemi-arthroplasty procedure, there are a number of variations to the procedure^[15,24-26]. These include the approach^[26-28], the type of prosthesis head^[25,29-31], the method of stem insertion^[25,32-34], and the type of prosthesis assembly^[35]. The optimal selection for each of these factors remains to be determined^[15,24-26].

This editorial reviews and summarises the current evidence (meta-analyses and Cochrane reviews) relating to the use of hip hemi-arthroplasty for neck of femur fractures.

SURGICAL APPROACH - LATERAL VS POSTERIOR VS ANTERIOR APPROACHES

Surgical approaches to the hip for hip hemi-arthroplasty can be divided into three main categories: lateral approaches (LA), posterior approaches (PA) and anterior approaches (AA).

LAs commonly involve (partial or complete) division or retraction of the hip abductor muscles (gluteus medius and minimus) to enable access to the hip capsule^[26,27]. These include the Hardinge (direct lateral), the transgluteal and the Watson-Jones (anterolateral) approach^[26,27].

PAs commonly involve a trans-gluteus-maximus approach, followed by division of the tendons of the short external rotators, to enable access to the hip joint^[26,27]. These include the Moore, the Southern, the true posterior and the posterolateral approaches^[26,27].

AAs commonly involve use the inter-nervous plane between the femoral and the superior gluteal nerves (the superficial interval between sartorius and tensor fasciae latae; and the deep interval between rectus femoris and gluteus medius) to enable access to the anterior hip capsule^[26-28]. These include the direct anterior and the Smith-Petersen approaches^[26-28].

There are two recent meta-analyses^[27,28] and one Cochrane review^[26] comparing outcomes of hip hemi-arthroplasty by type of approach used.

The most recent meta-analysis is that by van der Sijp *et al*^[27]. The authors performed a systematic database search, until October 2017, to identify all studies on hip hemi-arthroplasty for fracture, which compared outcome by approach used^[27]. Twenty-one studies were included in the meta-analysis [3 randomized controlled trials (RCT), 7 prospective and 11 retrospective cohort studies],

with a synthesis cohort of 61487 patients^[27]. On meta-analysis, PAs were found to have a significantly higher rate of dislocation compared to AAs (OR = 2.61; 95%CI: 1.26 to 5.43; $P < 0.01$); and LAs (OR = 2.90; 95%CI: 1.63 to 5.14; $P < 0.0003$)^[27]. PAs also had a higher risk of re-operation (*i.e.*, revision procedures, relocation of dislocations, intra-operative fracture fixation, and repair of capsule for repetitive instability) compared to LAs (OR = 1.25; 95%CI: 1.12 to 1.41; $P < 0.0001$); however no significant difference was found when comparing the re-operation rates of LAs and AAs (OR = 1.54; 95%CI: 0.50 to 4.77; $P = 0.45$)^[27]. There was insufficient data to allow meta-analysis comparison of the re-operation rates of PAs and AAs^[27]. On further meta-analysis between the three approaches, no significant differences was found for rates of surgical site infection, intra-operative fracture, and length of hospital stay^[27]. It was not possible to perform meta-analysis on the "functional outcome" data between the three approaches^[27]. The authors concluded that PAs are associated with a higher rate of dislocation and further operations in comparison to LAs and AAs in hip hemiarthroplasty for fracture^[27].

The other recent meta-analysis is that by Kunkel *et al.*^[28]: this compared the direct anterior approach (DAA) for hip hemi-arthroplasty to all other approaches for this procedure. The authors performed a systematic database search, until October 2016, identifying RCTs and cohort studies on hip hemi-arthroplasty for fracture, which compared the DAA to other surgical approaches (lateral, anterolateral, posterior, posterolateral)^[28]. Nine studies were included in the meta-analysis (3 prospective randomised studies, 3 prospective non-randomised studies and 3 retrospective cohort studies)^[28]. The synthesis cohort comprised a total of 698 hips (direct anterior approach $n = 330$; posterior approach $n = 108$, posterolateral approach $n = 114$; anterolateral approach $n = 57$; lateral approach $n = 89$)^[28]. On meta-analysis, PAs were found to have a significantly higher dislocation rate compared to the DAA (OR = 0.18; 95%CI: 0.05 to 0.63; $P = 0.007$)^[28]. However, there was no significant difference in dislocation rate between the DAA and LAs (OR = 0.19; 95%CI: 0.01 to 4.03; $P = 0.29$)^[28]. On further meta-analysis, no significant difference was found between the approaches for intra-operative blood loss, perioperative fracture, duration of procedure, post-operative pain levels, length of hospital stay, post-operative infection rate, further operation rate, total complication rate and mortality^[28]. The authors concluded that for fracture-related hip hemi-arthroplasty, PAs are associated with a significantly higher rate of dislocation in comparison to the DAA^[28].

Prior to this, Parker *et al.*^[26] performed a Cochrane review in 2002 assessing the influence of surgical approaches on outcome from hip hemiarthroplasty. The authors performed a systematic database search, until February 2002, to identify all RCTs comparing outcome from different surgical approaches in fracture-related hip hemi-arthroplasty^[26]. Only one RCT was identified that was suitable for inclusion: this comprised 114 hip

fracture patients who were managed with a cemented Thompson hemi-arthroplasty, either through an anterolateral or a posterior approach^[26]. Unfortunately, the study was found to be of sub-optimal quality to allow for reliable analysis, owing to selection bias, insufficient patient follow-up and insufficient results reporting^[26]. The authors concluded that, at that time, the evidence from RCTs was inadequate to decide which approach was most effective for hip hemi-arthroplasty in femoral neck fractures^[26].

Of the available National Guidelines which provide recommendations on the practice of hip hemiarthroplasty for hip fracture: the NICE Guidelines currently advise clinicians to favour the anterolateral approach over the posterior approach for hip hemiarthroplasty surgery^[16]; and the Scottish Intercollegiate Guidelines Network (SIGN) Guidelines advise "the anterolateral approach is recommended for hemiarthroplasty surgery"^[36].

The current evidence would suggest that, in hip hemi-arthroplasty for fracture, PAs are associated with a higher rate of post-operative dislocation compared to LAs and AAs, and a higher risk of reoperation compared to LAs. There appears no significant difference between LAs and AAs in terms of post-operative dislocation rates and re-operation rates. Thus, PAs should be avoided when performing hip hemi-arthroplasty for femoral neck fracture.

PROSTHESIS HEAD COMPONENT

- UNIPOLAR VS BIPOLAR HEMI-ARTHROPLASTY

There are two main categories of hemi-arthroplasty prosthesis, when assessing head component utilised: unipolar hemi-arthroplasty (UH) (Figure 1A) and bipolar arthroplasty (BH) (Figure 1B)^[25,29-31]. An UH comprise a large single endo-prosthetic head component, while BH has both an endo-prosthetic "bipolar" head component and an inner metal bearing^[25,29-31]. The theoretical benefit of the BH design, with its mobile bearing concept, is to reduce component-induced wear on the acetabulum^[25,29-31]. Other theoretical benefits include improved range of hip motion, decreased risk of dislocation and improved hip function, to provide a better clinical outcome over UH^[25,29-31]. However, the proven benefits of BH over UH remain to be confirmed^[25,29-31].

There are three recent meta-analyses^[29-31] and one Cochrane review^[25] which compare the outcomes of unipolar to bipolar hip hemi-arthroplasties for femoral neck fracture.

The most recent meta-analysis is by Zhou *et al.*^[29]. The authors performed a systematic database search, till April 2014, to identify all RCTs which compare UH to BH, as treatment of displaced femoral neck fractures^[29]. Eight RCTs were included in the meta-analysis, providing a synthesis cohort of 1100 patients^[29]. On meta-analysis, no significant difference was found



Figure 1 A hip hemi-arthroplasty with a unipolar component head (A); a hip hemi-arthroplasty with a bipolar component head (B); a hip hemi-arthroplasty with an uncemented femoral stem (C); and a hip hemi-arthroplasty with a cemented femoral stem (D).

between UH and BH for acetabular erosion rates (RR = 2.29; 95%CI: 0.85 to 6.12; $P = 0.10$), rate of dislocation (RR = 1.20; 95%CI: 0.47 to 3.07; $P = 0.71$), rate of reoperation (RR = 0.64; 95%CI: 0.33 to 1.26; $P = 0.19$), mortality (RR = 0.85; 95%CI: 0.63 to 1.13; $P = 0.26$), post-operative complication rates (RR = 1.05; 95%CI: 0.70 to 1.56; $P = 0.82$), and post-operative Harris Hip Scores (WMD -1.32; 95%CI: 3.29 to 0.65; $P = 0.19$)^[29]. The authors concluded that there was no apparent difference in clinical results between UH and BH, when used as treatment for displaced intra-capsular neck of femur fractures^[29].

The second of the recent meta-analyses was that by Jia *et al.*^[30]. The authors performed a systematic literature search, until April 2014, to identify all RCTs which compared UH to BH as treatment of displaced intra-capsular neck of femoral fractures^[30]. The meta-analysis comprised ten RCTs, providing a synthesis cohort of 1190 patients^[30]. On systematic review of the included studies, the authors found descriptive evidence that BH was superior to UH for post-operative hip function, quality of life and post-operative hip pain; however on meta-analysis, there was no significant difference in post-operative Harris Hip Scores between UH and BH (MD, -0.51, 95%CI: -4.43 to 3.42, $P = 0.80$)^[30]. UH was also found to have increased rates of acetabulum erosions at one year post-surgery, in comparison to BH (RR = 0.24; 95%CI: 0.06 to 0.89; $P = 0.03$); however there was no significant difference between the two groups for acetabular erosion rates at four months post-surgery (RR = 0.35; 95%CI: 0.10 to 1.21; $P = 0.10$), two years post-surgery (RR = 0.46; 95%CI: 0.20 to 1.10; $P = 0.08$), or four years post-surgery (RR = 0.48; 95%CI: 0.20 to 1.19; $P = 0.12$)^[30]. On further meta-analysis, no significant difference was found between UH and BH for: mortality (RR = 0.92; 95%CI: 0.59 to 1.44; $P = 0.71$); reoperation rates (RR = 0.98; 95%CI: 0.42 to 2.27; $P = 0.95$); dislocation rates (RR = 0.76; 95%CI: 0.30 to 1.93; $P = 0.57$); implant-related complications (RR = 0.84; 95%CI: 0.39 to 1.81; $P = 0.66$); general complications (RR = 0.65; 95%CI: 0.28 to 1.49; $P = 0.31$)^[30]. Furthermore,

two of the RCTs which reported on cost of prosthesis both noted that BH was more expensive than UH^[30]. The authors concluded that, comparing UH to BH, no significant difference could be found between post-operative result and longer term rates of acetabular erosion; however BH was consistently noted to be the more expensive implant^[30].

The last of the recent meta-analyses was that by Yang *et al.*^[31]. The authors performed a systematic database search, till July 2013, to identify all prospective RCTs that compare UH to BH for the treatment of neck of femur fractures in patients aged 65 years and over^[31]. Six RCTs were included in the meta-analysis, with a combined cohort of 982 patients^[31]. On meta-analysis, the acetabular erosion rates was noted to be significantly increased in the UH group (5.5%) compared to the BH group (1.2%) (OR = 0.22; 95%CI: 0.07 to 0.74; $P = 0.01$)^[31]. However, there was no significant difference between the two groups for: rate of mortality (OR = 1.08; 95%CI: 0.71 to 1.65; $P = 0.72$), overall post-operative complication rates (OR = 1.00; 95%CI: 0.67 to 1.50; $P = 1.00$), post-operative rate of dislocation (OR = 0.87; 95%CI: 0.29 to 2.60; $P = 0.80$), rate of infection (OR = 1.36; 95%CI: 0.60 to 3.09; $P = 0.47$), rate of reoperation (OR = 1.56; 95%CI: 0.66 to 3.68; $P = 0.31$), Harris hip scores (SMD -0.03; 95%CI: -0.23 to 0.17; $P = 0.76$) and return to pre-fracture function (OR = 1.36; 95%CI: 0.94 to 1.96; $P = 0.10$)^[31]. The authors concluded that there was no significant difference noted in clinical outcome for UH compared to BH when used as treatment of displaced intra-capsular neck of femur fractures in patients aged 65 or over^[31]. Given the similar clinical outcomes, they advised that unipolar implants appear the more economical prosthesis^[31].

Lastly, the most recent Cochrane review on the topic is that Parker *et al.*^[25]. The authors performed a systematic database search till September 2008, to identify all RCTs and quasi-RCTs comparing the use of different arthroplasty prostheses as management of femoral neck fractures^[25]. In total, twenty-three studies were included, with a synthesis cohort of 2861

patients^[25]. A sub-group analysis was performed, assessing all studies which compared UH to BH: this comprised seven studies, with a combined cohort of 857 patients (863 fractures^[25]). On meta-analysis, no significant differences was found between UH and BH for: dislocation rate (RR = 1.09; 95%CI: 0.36 to 3.31; $P = 0.88$), acetabular erosion rate (RR = 3.83; 95%CI: 0.81 to 18.15; $P = 0.090$), acetabular erosions requiring revision (RR = 2.97; 95%CI: 0.47 to 18.85; $P = 0.25$), rate of deep wound infection (RR = 1.34; 95%CI: 0.50 to 3.62; $P = 0.56$), reoperation rate (RR = 1.41; 95%CI: 0.54 to 3.69; $P = 0.49$), deep vein thrombosis (RR = 0.71; 95%CI: 0.03 to 16.45), mortality at 6 months (RR = 1.13; 95%CI: 0.73 to 1.76; $P = 0.58$); mortality at 1 to 2 years (RR = 0.90; 95%CI: 0.64 to 1.26; $P = 0.54$) and recovery of pre-fracture mobility (RR = 0.94; 95%CI: 0.40 to 2.16)^[25]. The authors concluded that from the available evidence, UH and BH implants demonstrated no significant clinical difference when used as treatment for displaced femoral neck fractures^[25].

Of the current National Guidelines, the SIGN Guidelines recommend that "BH should not be performed in preference to UH, as there is limited evidence of any clinical benefit"^[2]. In keeping with this, data from the recent English hip fracture audit has found that 79% of all hip hemi-arthroplasties performed in England in 2017 were UH^[1].

From the current evidence, it would appear, that while UH can be associated with increased rates of acetabular erosion at short-term follow-up (up to 1 year), there is no significant difference between the two prosthesis types for surgical outcome, complication profile, functional outcome and acetabular erosion rates at longer-term follow-up (2 to 4 years). Thus, with BH being the more expensive prosthesis, UH would appear to be the recommended option.

TECHNIQUE OF FEMORAL STEM INSERTION - CEMENTED VS UNCEMENTED HEMI-ARTHROPLASTY

The optimal technique for femoral stem implantation, using either an uncemented (Figure 1C) or a cemented (Figure 1D) femoral stem remains another keenly debated topic^[25,32-34]. In theory, a cemented femoral stem is more uniformly and more securely fixed within the femoral canal; this has been postulated to result in lower rates of post-operative thigh pain and reduced revision rates from aseptic loosening^[25,32-34]. However, the use of cement intra-operatively potentially confers the risks of cardiac arrhythmias and cardio-respiratory compromise, secondary to fat embolism and cement reaction phenomena^[25,32-34]. Revision of a cemented hemi-arthroplasty is also considered more challenging than that of an uncemented hemi-arthroplasty^[25,32-34]. Uncemented hemi-arthroplasties theoretically incur a shorter operating time, due to the lack of cementation

required; they also have been noted to be the cheaper of the two prosthesis types^[25,32-34]. As such, the optimal technique for femoral stem insertion remains to be decided^[25,32-34].

There are three recent meta-analyses^[32-34] and one Cochrane review^[25] which compare the outcomes of cemented to uncemented hip hemi-arthroplasties for femoral neck fracture.

The most recent meta-analysis is that by Veldman *et al.*^[32]. The authors performed a systematic database search, till April 2016, to identify all RCTs comparing outcomes for cemented versus uncemented hemi-arthroplasties for femoral neck fracture, which used contemporary generation femoral stems only^[32]. Five RCTs were included in the meta-analysis, with a synthesis cohort of 950 patients (950 hips)^[32]. Complications were categorised as: prosthesis-related (dislocation, aseptic prosthesis loosening, peri-prosthetic fractures); cardiovascular-related; local (deep and superficial wound infections); and other general complications^[32]. On meta-analysis, cementless hemi-arthroplasties had higher rates of overall complications compared cemented hemi-arthroplasties (OR = 1.61; 95%CI: 1.12 to 2.31; $P = 0.01$), especially implant-related complications (OR = 3.15; 95%CI: 1.55 to 6.41; $P = 0.002$)^[32]. However, cementless hemi-arthroplasties were associated with a shorter operating time compared to cemented hemi-arthroplasties (WMD -9.96 mins; 95%CI: -12.93 to -6.98; $P < 0.001$)^[32]. On further meta-analysis, there was no significant difference between the two methods of femoral stem insertion for: cardio-vascular complications (OR = 0.54; 95%CI: 0.24 to 1.20; $P = 0.13$); local complications (OR = 0.71; 95%CI: 0.27 to 1.86; $P = 0.49$); general complications (OR = 1.09; 95%CI: 0.62 to 1.91; $P = 0.76$); number of re-operations (OR = 1.24; 95%CI: 0.53 to 2.88; $P = 0.62$); length of hospital stay (WMD 0.36 d; 95%CI: -1.13 to 1.85; $P = 0.63$); intra-operative blood loss (WMD -36.19 mL; 95%CI: -89.45 to 17.07; $P = 0.18$)^[32]. It was not possible to perform meta-analysis on the "functional outcome" data^[32]. The authors concluded that, for fracture-related hip hemiarthroplasty using contemporary femoral stems, cemented hemi-arthroplasties were associated with fewer prosthesis-related complications, though with similar mortality rates, as compared to uncemented hemi-arthroplasties^[32].

However, it must be noted that the data regarding implant-related complications, in this meta-analysis, was heterogeneous^[32]. Review of the three studies, which reported on implant-related complications, revealed the most common complication was peri-prosthetic femoral fracture^[32]. However, no formal break-down of the individual implant-related complications was provided in the meta-analysis^[32]. As such, a more detailed meta-analysis is required to properly define the increased risk posed by uncemented prostheses. Nevertheless, the current evidence suggests that the cemented technique is safer.

The second most recent meta-analysis is that by

Ning *et al*^[33]. The authors performed a systematic database search, till March 2012, to identify all RCTs which compared cemented to uncemented hemi-arthroplasty for fracture, including all available prosthesis types^[33]. Twelve RCTs were included in the meta-analysis, providing a synthesis cohort of 1805 patients^[33]. On meta-analysis, cemented hip hemi-arthroplasties were associated with a prolonged operative time when compared to uncemented hemi-arthroplasties (SMD -0.43; 95%CI: -0.56 to -0.30; $P < 0.001$)^[33]. However, no significant difference was found between the two techniques for: intra-operative blood loss (SMD -0.12; 95%CI: -0.33 to 0.10; $P = 0.291$); length of hospital stay (SMD -1.21; 95%CI: -0.05 to 0.22; $P = 0.224$), overall complications (OR = 0.82; 95%CI 0.63 to 1.08; $P = 0.163$); post-operative pain (OR = 1.42; 95%CI: 0.99 to 2.03; $P = 0.056$) and mortality rates (OR = 1.08; 95%CI: 0.88 to 1.34; $P = 0.469$)^[33]. The authors concluded that the outcomes of uncemented and cemented hip hemiarthroplasty for femoral neck fracture, showed no significant difference^[33].

The last of the recent meta-analyses was that by Luo *et al*^[34]. The authors performed a systematic database search, till December 2010, to identify all RCTs comparing uncemented and cemented hip hemiarthroplasty (all prosthesis types included), as treatment for neck of femur fractures^[34]. Eight RCTs were included in the meta-analysis, providing a synthesis cohort of 1175 hips^[34]. On meta-analysis, uncemented hemi-arthroplasties were noted to have higher rates of post-operative pain 1-year post-surgery compared to cemented hemi-arthroplasties (RR = 0.69; 95%CI: 0.53 to 0.90; $P = 0.007$). There was however no significant difference between the two techniques for: peri-operative mortality (RR = 0.92; 95%CI: 0.58 to 1.45; $P = 0.71$), 1-year mortality (RR = 0.89; 95%CI: 0.73 to 1.09; $P = 0.26$), rates of reoperation (RR = 0.75; 95%CI: 0.44 to 1.25; $P = 0.27$), general medical complications (RR = 0.83; 95%CI: 0.61 to 1.14; $P = 0.25$) and local complications (comprising dislocation, wound infection, periprosthetic fracture and radiographic prosthesis loosening) (RR = 0.85; 95%CI: 0.58 to 1.23; $P = 0.38$)^[34]. Meta-analysis could not be performed for the "functional outcome" data^[34]. The authors concluded that, while the cemented prostheses were associated with lower rates of post-operative pain as compared to the uncemented prostheses, the two types of hemi-arthroplasty showed no significant difference in complication rates, reoperation rates and mortality rates^[34].

Lastly, the most recent Cochrane review on the topic is by Parker *et al*^[25], as described in "Prosthesis Head Component" section. On sub-group analysis, six studies were identified which compared cemented to uncemented hemi-arthroplasties for neck of femur fracture, providing a synthesis cohort of 899 participants^[25]. All prosthesis types were included in the review^[25]. On meta-analysis, cemented hemi-arthroplasties had a significantly prolonged operation time (MD 7.24 min; 95%CI: 4.75

to 9.73 min; $P < 0.00001$), though had reduced rates peri-operative of femoral fracture (RR = 0.09; 95%CI: 0.02 to 0.44; $P = 0.0031$), lower rates of residual hip pain at both three-month follow-up (RR = 0.77; 95%CI: 0.60 to 0.98; $P = 0.034$) and longer term follow-up (RR = 0.55; 95%CI: 0.40 to 0.75; $P = 0.00017$), and improved recovery of post-operative mobility scores (RR = -0.80; 95%CI: -1.23 to -0.37)^[25]. No significant difference was found between the two techniques in mortality rates at any of the follow-up time intervals: 1-mo post-surgery (RR = 0.84; 95%CI: 0.38 to 1.84; $P = 0.66$); one to three months post-surgery (RR = 0.98; 95%CI: 0.68 to 1.41; $P = 0.90$); 1-year post-surgery (RR = 0.90; 95%CI: 0.71 to 1.13; $P = 0.35$); and 3-years post-surgery (RR = 1.13; 95%CI: 0.76 to 1.67)^[25]. Similarly, no significant difference was found between the two techniques for: peri-operative blood loss (RR = 49.00; 95%CI: -22.10 to 120.10); requirement of blood transfusion (RR = 0.12; 95%CI: -0.04 to 0.27; $P = 0.13$); occurrence of medical complications (RR = 0.82; 95%CI: 0.59 to 1.13; $P = 0.23$); rate of re-operation (RR = 0.55; 95%CI: 0.27 to 1.14; $P = 0.11$); duration of hospital stay (RR = -1.42; 95%CI: -3.15 to 0.32; $P = 0.11$); percentage of patients who were able to return to their pre-injury place of residence (RR = 0.62; 95%CI: 0.34 to 1.12; $P = 0.11$) and restore their pre-injury mobility levels (RR = 0.84; 95%CI: 0.64 to 1.11; $P = 0.23$)^[25]. The authors concluded that cemented hip hemi-arthroplasties can reduce the risk of peri-operative femoral fracture, reduce post-operative pain levels and provide improved post-operative mobility, when compared to uncemented hip hemi-arthroplasties for displaced femoral neck fractures, with no significant difference between the two techniques for mortality at any of the follow-up time points^[25].

Of the available National Guidelines: the NICE Guidelines currently recommend "the use cemented implants in (hip fracture) patients undergoing surgery with arthroplasty"^[16]; and the SIGN Guidelines recommend that "cement should be used when undertaking hemiarthroplasty, unless there are cardiorespiratory complications, particularly in frail older patients"^[36]. In keeping with this, data from the recent Scottish and English Hip Fracture Audits have found that 90% and 87% of all hip hemi-arthroplasties, from Scotland and England in 2017 respectively, were performed with a cemented femoral stem^[1,2].

The current evidence would suggest that while uncemented hemi-arthroplasties can allow for a shorter operative time, cemented hemi-arthroplasties are associated with lower rates of prosthesis-related complications (particularly peri-prosthetic femoral fracture) and improved post-operative results in terms of residual thigh pain and mobility. In addition, there appears to be no significant difference between the two techniques for intra-operative blood loss, medical complications and mortality (peri-operative and 1-year). In accordance with the current literature, a cemented hip hemi-

arthroplasty would appear to be the superior technique.

TYPE OF PROSTHESIS ASSEMBLY - MONOBLOCK VS MODULAR HEMI- ARTHROPLASTY

There are two main types of prosthesis assembly that can be used in hip hemi-arthroplasty: monoblock prosthesis and modular prosthesis^[35].

A monoblock hemi-arthroplasty is produced as a single unit, with variations in prosthesis size based on the diameter of the patient's femoral head^[35]. The most commonly used monoblock implant is the collared Thompson Hemi-Arthroplasty^[35]. Given the pre-fabricated nature of this prosthesis, there is limited ability to adjust the prosthesis intra-operatively to accommodate for variations in femoral neck offset or leg length: thus, such implants often poorly recreate the patient's original hip geometry^[35]. A modular hemi-arthroplasty is produced in individual components: stem, neck and head components^[35]. On assembling these intra-operatively, the surgeon is able to alter component size, and so better recreate the patient's original hip geometry^[35]. However, the theoretical benefits of modular prostheses in hip hemi-arthroplasty as treatment of femoral neck fractures remain to be confirmed^[35].

There is one recent meta-analysis^[35] which compare the outcomes of monoblock to modular hip hemi-arthroplasties for treatment of femoral neck fractures.

The available meta-analysis is that by Sims *et al.*^[35]. The authors performed a systematic database review, until September 2015, identifying all RCTs, well-designed case control studies, retrospective cohort studies and prospective cohort studies, which compared outcomes between Thompson hemi-arthroplasties and modular unipolar hemi-arthroplasties for femoral neck fracture^[35]. Four studies were included in the review (1 RCT, 2 Retrospective Cohort Studies, 1 Swedish Joint Registry Paper), providing a synthesis cohort of 21017 patients^[35]. On meta-analysis, the odds ratio favoured modular designs for both mortality (OR = 1.3; 95%CI: 0.78 to 2.46) and post-operative complications (OR = 1.1; 95%CI: 0.79 to 1.55); however no significant difference was noted for either factor, between the prosthesis types^[35]. On review of the study quality of the included studies, the authors found these all to be subject to potential bias with significant heterogeneity noted in the methods and results^[35]. Thus the authors concluded that there is insufficient evidence at present to accurately compare monoblock to modular hemi-arthroplasty prosthesis for patients with femoral neck fractures^[35].

To note, the same authors subsequently published a multi-centre, pragmatic RCT comparing the outcome of the Thompson monoblock cemented hemi-arthroplasty to a modular hemi-arthroplasty using a cemented Exeter femoral stem and a Unitrax hemi-arthroplasty head (The WHITE 3: Hemi Trial) (2018)^[37]. The initial

recruitment cohort comprised 964 patients (monoblock group $n = 482$; modular group $n = 482$); however four-month follow-up data was only available for 482 patients (50%)^[37]. Outcome assessment was performed using the EuroQol questionnaire (EQ-5D-5L)^[37]. At four-month follow-up, the modular cohort had a marginally improved mean EQ-5D-5L (mean EQ-5D-5L for modular cohort 0.379; mean EQ-5D-5L for monoblock cohort 0.321); however, this difference did not meet the minimum required clinical difference of 0.08, nor was it statistically significant (MD = 0.037; 95%CI: -0.014 to 0.087; $P = 0.156$). Other factors which failed to show significant difference between the two groups included: mortality (OR = 1.02; 95%CI: 0.72 to 1.46; $P = 0.911$); post-operative walking ability (OR = 0.76; 95%CI: 0.54 to 1.06; $P = 0.107$); local complications (*i.e.*, wound complications; revision procedures; structural injury; deep vein thrombosis; dislocation) (OR = 1.50; 95%CI: 0.828 to 2.741; $P = 0.179$); requirement for blood transfusion (OR = 1.51; 95%CI: 0.530 to 4.316; $P = 0.439$); and medical complications (OR = 0.95; 95%CI: 0.665 to 1.358; $P = 0.779$). Length of hospital stay was marginally higher in the monoblock group (mean stay for monoblock group = 9.67 d; mean stay for modular group = 9 d; $P = 0.039$). There was no significant difference in post-operative radiographic femoral offset between the two groups (mean neck length for monoblock group = 3.01 mm; mean neck length for modular group = 2.91 mm; $P = 0.834$). The authors concluded that, accounting for the limited follow-up, there was no significant difference detected in clinical outcome between the two prosthesis types, when used as treatment for femoral neck fractures.

Of the current National Guidelines, the NICE guidelines advise to "use a proven femoral stem design (*i.e.*, those with an Orthopaedic Data Evaluation Panel rating of 10A, 10B, 10C, 7A, 7B, 5A, 5B, 3A or 3B) rather than Austin Moore or Thompson Stems for arthroplasties"^[16]. However, such guidance is directed from evidence in primary total hip arthroplasty and expert opinion^[35].

Thus, despite clear recommendations from NICE, the current evidence which compares monoblock to modular hemi-arthroplasty prosthesis for femoral neck fracture remains limited and equivocal. Despite the logical bio-mechanical advantage of the modular prosthesis, further research is required in this area to confirm their clinical benefit.

WOUND CLOSURE TECHNIQUES - SUTURES VS STAPLES

Wound closure technique remains a controversial area in hip hemi-arthroplasty surgery^[38]. The two most common skin closure methods are staples and sutures^[38]. Historically, it has been felt that staples were more time efficient, though associated with a higher rate of post-operative infection^[38]. This belief was strengthened by a systematic review and meta-

analysis on the topic, from 2010, which reported that the rate of post-operative infection following orthopaedic surgery, was over three times greater for staple wound closure compared to suture wound closure^[39]. However, the recent evidence provides a more balanced perspective^[38].

There is one recent meta-analysis comparing the outcomes of skin closure techniques (sutures vs staples) in orthopaedic surgery, with a sub-group analysis on hip surgery procedures^[38].

This meta-analysis is that by Krishnan *et al.*^[38]. The authors performed a systematic database review, until January 2015, identifying all RCTs and observational studies which compared the outcome of suture to staple wound closure technique following orthopaedic surgery^[38]. The rate of post-operative wound infection was the primary outcome measure, with secondary outcome measures comprising time of closure, wound dehiscence, inflammation, post-operative pain, length of hospital stay, necrosis, abscess formation, discharge, allergic reaction^[38]. Thirteen studies were included meta-analysis (ten RCTs, three observational studies), with a combined cohort of 1255 patients (suture group = 563 patients, staple group = 692 patients)^[38]. Six of the studies comprised patients undergoing hip surgery (suture group = 164 patients, staple group = 245 patients)^[38]. On meta-analysis, no significant difference was found in post-operative infection rates between sutures and staples (RR = 1.06; 95%CI: 0.46 to 2.44; $P = 0.89$)^[38]. On sub-group analysis, for the patients who underwent hip surgery, no significant difference was also found in post-operative infection rates between sutures and staples (RR = 0.48; 95%CI: 0.10 to 2.45; $P = 0.38$)^[38]. On further meta-analysis of the total cohort, closure time was found to be quicker for staples compared to sutures (MD = 5.84; 95%CI: 4.52 to 7.15; $P < 0.001$)^[38]. However, there was no significant difference between the two techniques for all other outcome measures: wound dehiscence (RR = 0.96; 95%CI: 0.32 to 2.84; $P = 0.94$), inflammation (RR = 0.22; 95%CI: 0.00 to 12.07; $P = 0.46$), discharge (RR = 0.66; 95%CI: 0.14 to 3.23; $P = 0.61$), necrosis (RR = 0.51; 95%CI: 0.07 to 3.88; $P = 0.52$), allergic reaction (RR = 1.37; 95%CI: 0.22 to 8.60; $P = 0.74$), abscess formation (RR = 1.86; 95%CI: 0.22 to 15.71; $P = 0.57$)^[38]. The authors concluded that, apart from time of closure, no significant difference was found between suture and staple wound closure techniques^[38].

The current orthopaedic literature, particularly with regards to hip-related procedures, provides an equivocal conclusion on the optimal wound closure technique. From the available evidence, either suture or staple wound closure techniques appear equally appropriate for hip hemi-arthroplasty procedures.

is a cemented modular bipolar hemi-arthroplasty, through an antero-lateral approach. The wound closure technique varies, as per the preference of the responsible surgeon, with either skin clips or sub-cuticular sutures used. At present, there is a randomised controlled trial being run in this unit between cemented modular bipolar hemi-arthroplasty prostheses and cemented modular UH prostheses: the result from this may influence the future choice of prosthesis head component selection in the institution.

The second author manages this fracture with a cemented, monoblock hemiarthroplasty through an antero-lateral approach, using a triple wound closure technique, which comprises monocryl, staples and glue.

CONCLUSIONS

From the current evidence on Hip Hemi-Arthroplasty, the following conclusions can be drawn: (1) posterior approaches are associated with: a higher rate of dislocation compared to lateral and anterior approaches; and a higher rate of re-operation compared to lateral approaches. Thus for fracture-related hip hemi-arthroplasty, posterior approaches should be avoided; (2) while UH can be associated with increased rates of acetabular erosion at short-term follow-up (up to 1 year), there is no significant difference between unipolar and bipolar hemi-arthroplasty for surgical outcome, complication profile, functional outcome and acetabular erosion rates at longer-term follow-up (2 to 4 years). Thus, with bipolar hemi-arthroplasty being the more expensive prosthesis, UH is the recommended option; (3) while cemented hip hemi-arthroplasties are associated with a longer operative time compared to uncemented hip hemi-arthroplasties, cemented prostheses have lower rates of implant-related complications (particularly peri-prosthetic femoral fracture) and improved post-operative outcome regarding residual thigh pain and mobility. No other significant difference has been found between the two techniques, regarding medical complications and mortality. As such, cemented hip hemi-arthroplasty appear to be the superior technique; (4) there is insufficient evidence at present to accurately compare the outcome of modular to monoblock hemi-arthroplasty prostheses for femoral neck fractures. However, based on evidence from total hip arthroplasty and expert opinion, current recommendations advocate for "a proven femoral stem design" with a modular prosthesis, as opposed to a monoblock prosthesis; and (5) while staples can result in a quicker closure time, there is no significant difference in post-operative infection rates or wound healing outcomes when comparing staples to sutures. Thus, either suture or staple wound closure techniques appear equally appropriate for hip hemi-arthroplasty procedures.

AUTHORS' CURRENT PRACTICE

Within the affiliated institution of the first author, the default choice for fracture-related hip hemi-arthroplasty

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Biomechanics of posterior shoulder instability - current knowledge and literature review

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Abstract

Posterior instability of the shoulder is a rare condition and represents about 10% of shoulder instability. It has become more frequently recognized in the last year, even though it is more difficult to diagnose than anterior shoulder instability. As this form of shoulder pathology is somewhat rare, biomechanical knowledge is limited. The purpose of our study was to perform an extensive literature search, including PubMed and Medline, and to give an overview of the current knowledge on the biomechanics of posterior shoulder instability. The PubMed/Medline databases were utilized, and all articles related to posterior shoulder instability and biomechanics were included to form a comprehensive compilation of current knowledge. A total of 93 articles were deemed relevant according to our inclusion and exclusion criteria. As expected with any newly acknowledged pathology, biomechanical studies on posterior shoulder instability remain limited in the literature. Current biomechanical models are performed in a static manner, which limits their translation for explaining a dynamic pathology. Newer models should incorporate dynamic stabilization of both the rotator cuff and scapulothoracic joint. There is a current lack of knowledge with regards to the pathomechanism of posterior shoulder instability, with no consensus on appropriate treatment regimens. Further investigation is therefore required at both basic science and clinical levels.

Key words: Posterior shoulder instability; Anatomy; Shoulder complex; Scapula; Humerus; Glenohumeral

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Core tip: Posterior shoulder instability is an infrequent

type of injury, and there is limited discussion of this topic within the literature. Other authors have acknowledged the current paucity of papers on this topic. To our knowledge, no comparable literature review has been performed showing the interactions of the individual shoulder parts, including the osseous structures, capsule, labrum, ligaments and muscles^[1]. This article aspires to help develop new protocols to investigate shoulder instability and inform clinicians about the importance of this topic in daily practice.

Bäcker HC, Galle SE, Maniglio M, Rosenwasser MP. Biomechanics of posterior shoulder instability - current knowledge and literature review. *World J Orthop* 2018; 9(11): 245-254 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i11/245.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i11.245>

INTRODUCTION

The shoulder joint is the least congruent joint in the human body and thus has a tremendous potential range of motion with daily activities. These movements are a well-balanced and complex interplay between the osseous structures (scapula, humeral head and clavicle) and the surrounding soft tissue, consisting of shoulder capsule, ligamentous, labral and muscular stabilizers. Dysfunction of one or more of these components through injury, degeneration or congenital abnormalities may lead to shoulder instability with concomitant pain and dysfunction. Anterior laxity or dislocation occurs more commonly than the posterior equivalent and is thus more discussed in the literature. However, posterior instability is an equally important cause of patients pain and loss of shoulder function.

The first reported case of posterior shoulder instability was published by White *et al* in 1741^[2], followed by a case study in 1839^[3] and a clinical case series in 1855^[4]. A variety of pathologies have been described regarding posterior shoulder instability, such as atraumatic lesions in ligamentous laxity, repetitive microtrauma (especially in overhead-throwing athletes or the active duty military population) and traumatic posterior luxation^[5,6]. In repetitive microtrauma, shearing forces may cause a loss of chondrolabral containment (e.g., frank labral tear)^[7,8].

Classifications for recurrent posterior subluxation have been established according to its anatomical and biomechanical properties. It can be distinguished between volitional (ability to subluxate the shoulder using abnormal patterns of muscular activity), dysplastic (due to glenoid retroversion or humeral head retrotorsion) and acquired posterior shoulder dislocation (caused by soft tissue deficiency, bony deficiency or scapula-thoracic dysfunction)^[5,9].

LITERATURE SEARCH

A comprehensive literature search was conducted using PubMed/MEDLINE databases (US National Library of

Medicine, National Institutes of Health) for shoulder instability and biomechanics/anatomy of the shoulder between 1957 and 2017. The search terms were intentionally broad to maximize capture of the relevant literature. The following keywords were used: "posterior shoulder instability" (*n* = 1026), "shoulder biomechanics" (*n* = 1389) and "posterior shoulder instability anatomy" (*n* = 295). Articles in English, German and French were included. All papers that both evaluated the biomechanics on posterior shoulder instability as well as described the anatomy in patients who suffered from posterior shoulder instability were included. Exclusion criteria included duplicate results, non-relevant articles that did not involve posterior shoulder instability or biomechanical studies, and letters to the editors or comments.

In total, 2710 abstracts were reviewed, of which 40 articles were duplicates and further 2542 did not investigate shoulder instability or the biomechanics of the shoulder complex. One hundred-twenty-eight full text articles were reviewed, of which 35 studies were excluded as these ones did not meet inclusion criteria. Finally, leaving 93 studies for our review. These included papers describing the biomechanics of anterior and posterior shoulder instability, the anatomy of the shoulder complex, as well as the clinical aspects.

CLINICAL PRESENTATION OF POSTERIOR SHOULDER INSTABILITY

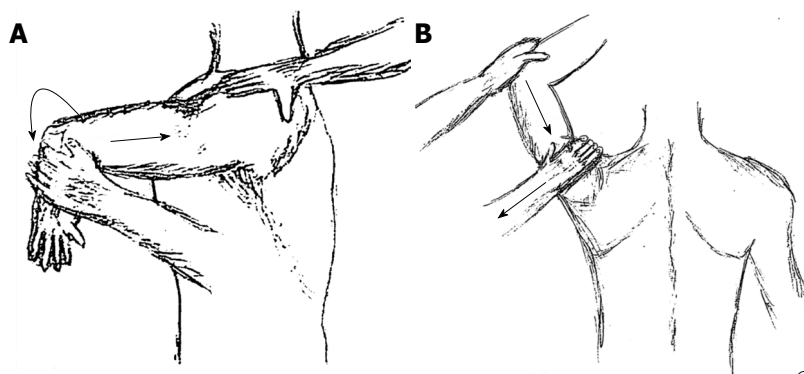
Incidence

The incidence of posterior shoulder instability is between 2%-5% of all shoulder dislocations^[10]. According to the literature, it may be under- or mis-diagnosed due to the lack of both awareness and experience of treating physicians. A significant proportion (62.5%) of patients who failed surgery and suffered from ongoing instability were diagnosed with unidirectional, posterior shoulder instability. Those patients demonstrated signs of inferior or multi-directional instability prior to revision surgery, which may be related to the capsular laxity. This appears to be an underestimation - 75% of these patients did not show labral tear, yet would have required more aggressive stabilization^[11].

Current knowledge of biomechanics

In the beginning of the investigation, the mechanism was simply believed to be the counterpart to anterior shoulder instability^[12-14]. Later on, this paradigm was questioned by several researchers, who described the posterior shoulder instability as a unique injury condition^[15-17].

Generally, posterior shoulder dislocation has been described in the setting of 90° forward elevation, adduction and internal rotation of the humerus^[17-19]. Assumingly, the humerus then dislocates either posteriorly through rupture of the posterior band of the inferior glenohumeral ligament (IGHL) or posterior inferiorly through rupture of the whole posteriorIGHL^[20]. Unfortunately, the exact biomechanical mechanism of posterior shoulder instability is not well



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Figure 1 Jerk test and Kim test. A: Jerk test: The patient is sitting, their arm is flexed to 90° and internally rotated. An axial loading and horizontal adduction is applied; B: Kim test: The patient is sitting and the arm is abducted to 90° at the beginning. The examiner elevates the arm approximately 45° while applying postero-inferior force to the upper arm and axial load to the elbow. In a positive test, a subluxation of the glenohumeral joint can be observed.

understood or described to date.

Clinical presentation

Posterior shoulder dislocation patients present with generalized symptoms about the shoulder and commonly include an intense discomfort with inability to mobilize the shoulder joint. This may be related to excessive stretching of the muscles or the joint capsule during the dislocation itself^[21]. For clinical examination, the Kim test shows the highest sensitivity of 80% and specificity of 90%. Further examinations like the Jerk test, posterior apprehension test and stress test are useful to estimate the stability and dislocation tendency. The Jerk test is the most reliable diagnostic examination, however may only be pathologic in 4 of 50 patients suffering from posterior shoulder instability^[22]. When performing the anterior apprehension test, patients may feel inconvenienced with a slight anterior subluxation. However, this test is neither sensitive nor specific^[23]. The Kim test and Jerk test are illustrated in Figure 1.

Radiographic signs

X-ray and computed tomography: To exclude any osseous lesions and diagnose posterior shoulder dislocation, an anteroposterior, lateral and axillary radiograph should be performed. Furthermore, computed tomography (CT) may help identify injuries of the shoulder complex, such as reverse Bankart lesions or, when performing with intraarticular contrast, labral lesions. Displacement of the humeral head in relation to the glenoid, reverse Hill Sachs lesions or posterior Bankart/glenoid lesions may be pathognomonic for posterior shoulder instability but not necessarily present in all cases.

Magnetic resonance imaging: Magnetic resonance imaging (MRI) is an invaluable tool to assess soft tissue lesions about the shoulder. In patients who have suffered a posterior shoulder dislocation, a labral tear of the posterior wall or edema in the posterior humeral head is typically present. Furthermore, other patholo-

gical conditions can be excluded, such as superior, anterior posterior labral lesions or rotator cuff tears masquerading as posterior instability (Figure 2 provided by Dr. Charles M. Jobin). When comparing conventional MRI with MR arthrography, MR arthrography is superior to assess glenohumeral pathology, Perthes lesions and labral tears^[24].

The rigor of MRI and CT arthrograms in posterior shoulder instability is summarized in Table 1.

SHOULDER JOINT COMPLEX IN POSTERIOR SHOULDER DISLOCATION

The glenohumeral, scapulothoracic, acromioclavicular and sternoclavicular joints can be summarized as the shoulder complex. A full range of motion, including protraction/retraction, elevation/depression, anterior/posterior tilt, internal/external and upward/downward rotation can only be achieved in combination with each individual joint^[25]. The complex can be divided into osseous and soft tissue structures, enabling stability and facilitating anatomic motion.

Osseous

Scapula: The scapula lies on ribs two through seven and has a triangular shape^[26,27]. It is solely stabilized by soft tissue restraints through a series of bursal and muscular planes. Its position is obliquely in between the frontal and sagittal planes. Besides a slight abduction by 3°, it is located 30°-45° anterior to the coronal plane, with a slight anterior tilt between 9°-20° in the sagittal plane in relation to the vertical line of the spine^[25].

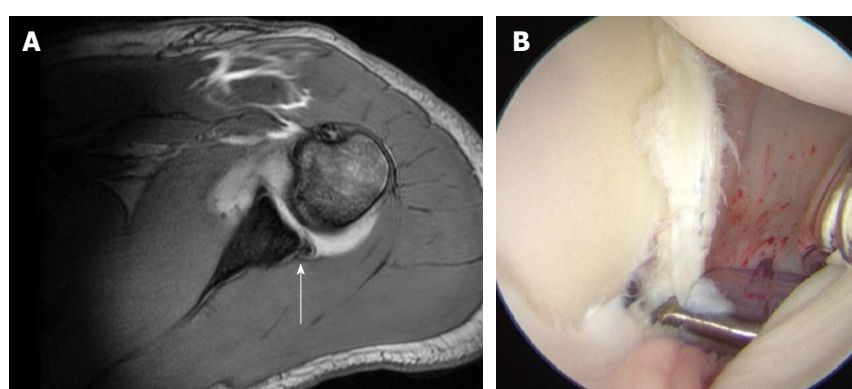
Multiaxial articulation can be enabled by the scapulothoracic joint between the humerus and the thorax. When elevating the humerus above 90° in the coronal plane, the scapular mainly rotates laterally in the coronal plane with less protraction in all three planes. At 30° and 40° of humeral elevation, a significant backward tilt occurs in the sagittal plane.

The glenoid cavity, which forms the articular surface of the glenohumeral joint, is concave in shape and

Table 1 The role of computed tomography scans, magnetic resonance imaging arthrograms and diagnostic rigor

	CT arthrography	MRI arthrography
Sensitivity	82%-100% ^[75]	48%-89% ^[76,77]
Specificity	96%-100% ^[75]	93% ^[77]
Advantage	Identifying bony lesions, severity of fractures, assessing humeral and glenoid version ^[78]	Identifying the soft tissue from labrum to the rotator cuff ^[80] , good for preoperative classification of labroligamentous injuries ^[81]
Disadvantage	lower inter-examiner reliability ^[79]	Limited in elderly patients ^[80]
Pathologies	Radiation Small soft tissue lesions ^[82] Bony lesions/ fractures (Bankart fragments, Hill-Sachs Lesion) ^[82,83] Accurate in labroligamentous, cartilaginous lesions ^[75]	Avulsion of posterior periosteum ^[82] Medial displacement of the labrum (posterior labro-scapular sleeve avulsion) ^[84] Kim lesion - incomplete and concealed superficial tear in the posterior glenoid labrum Glenoid rim articular divot lesion ^[7] Chondral loose bodies ^[85]

CT: Computed tomography scans; MRI: Magnetic resonance imaging.



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Figure 2 Posterior labral tear. A: Posterior labral tear in magnetic resonance arthrography; B: Intraoperative finding of a posterior labral tear and posterior SLAP tear.

slightly retroverted 6.2° ^[28]. An abnormal glenoid shape, such as higher retroversion or smaller cavities, leads to a higher glenohumeral index (the relationship between the humeral head and glenoid). This may predispose posterior shoulder instability^[29-31], although some authors were unable to reproduce this finding^[32].

The most important osseous feature of the scapula is the coracoid process, which is tilted approximately 120° - 160° anterolaterally^[33]. It has several attachments, which have major impact on posterior instability: the coracobrachial muscle, the short head of the biceps brachii muscle, the pectoralis minor muscle, the coracohumeral ligament (although in a few cases they insert in the pectoralis minor muscle^[34]), the coracoacromial ligament, as well as the coracoclavicular ligament. The individual function and mechanism of stabilization are discussed in full detail below.

The most frequent osseous lesion of the scapula involved during a posterior shoulder dislocation is the reverse Bankart lesion. It is located mainly in the posterior-inferior quarter of the glenoid (86%), and leads to an 86% increase in posterior translation and 31% increase in inferior translation of the humerus in the sulcus position. In patients with posterior capsular tears or posterior Bankart lesions, a bidirectional instability must be suspected^[35].

In large glenoid defects, a posterior bone block

transfer can be performed to extend the glenoid surface rather than reconstruct the glenoid anatomically. Additional indications for posterior bone block transfer include glenoid erosions, failure of primary capsular plication or congenital abnormalities. This procedure can be considered the counterpart to the Latarjet procedure, and was first described by Hindenach in 1947^[36].

Overall, the posterior bone block transfer procedure shows poor results, with a high rate of osteoarthritis in long-term follow-up, although three of 11 patients were pleased with it^[36].

In patients who suffer from higher glenoid retroversion (more than 15° - 20°) with intact soft tissue, an open wedge osteotomy may be the treatment of choice. DeLong *et al.*^[37] performed a systematic literature review, stating that posterior glenoid osteotomy does not show any good results in terms of return to pre-injury athletic level^[22,38].

Humeral head: The humeral head presents anatomically with a retroversion of 25° - 35° (related to the condyles of the elbow) and an inclination of about 130° related to the shaft^[39,40]. It consists of hyaline cartilage (thickest in the center) and forms a true sphere^[41,42]. Tendinous and ligamentous attachments form a ring to tighten and centralize the humeral head, placing it in the middle of the glenoid cavity^[43,44]. Even though no

data exist, it is likely that retroversion of $> 35^\circ$ in the humeral head may predispose posterior luxation, similar to retroversion of the glenoid.

Glenohumeral joint: The glenohumeral joint permits movement with many degrees of freedom, including flexion-extension, abduction-adduction, circumduction and medial-lateral rotation. Humeral motion is possible in the frontal, coronal/sagittal and scapular planes^[25,45].

Damage of articular cartilage and reverse Hill Sachs lesions, also called Malgaigne fractures, are rather infrequent complications of posterior shoulder instability. In high traumatic injuries, Malgaigne fractures may lead to painful clicking or catching in movements, which may worsen the damage and lead to further injuries.

Surgical correction of a reverse Hill Sachs lesion includes the McLaughlin procedure, where the subscapularis tendon is transferred into the bony defect. Other procedures include implantation of bone allograft or humeral osteotomy when the retroversion may be suspected to predispose the instability. Rotational osteotomies have shown fair results, and one paper demonstrated a 50% return to a pre-injury level of activity^[46].

Clavicle: The clavicle is less important than the scapula for posterior shoulder instability. Nevertheless, the S-shape bone does provide some elasticity, some component of shock absorption and forms a strut holding the glenohumeral joint in the parasagittal plane. At rest, it is tilted slightly superior by 10° - 12° ^[25]. Major impact on the rotation in the coronal plane could be observed which increases from 3° - 20° to 21° - 150° of humeral elevation. Clavicle posterior rotation was increased by elevation in the sagittal plane between 20° at 90° to 27° at 150° of elevation as well as protraction from -17° to -45° ^[47].

The acromioclavicular joint is a synovial joint allowing anterior/posterior and internal/external rotation over the lateral end of the clavicle^[48]. The sternoclavicular joint enables elevation and depression of the clavicle as well as protraction and retraction^[48,49].

In an intact clavicle, the degree of freedoms are external rotation, upward rotation and posterior tilting, which are greatest in the sagittal plane, thus enabling more stabilization and support in glenohumeral joint motion^[50].

According to Poppen *et al*^[45], the relation between the glenohumeral and scapulothoracic movement has a ratio of 4.3:1, with an upward translation of 3 mm. When abducting the humerus, a counterclockwise rotation of the scapula in the frontal plane is accompanied. Hereby, a rotation of the clavicle can be noted up to a taut costoclavicular ligament. After initial abduction by 30° , the glenohumeral and scapulothoracic joint movements occur simultaneously and facilitate elevation. Approximately 40° of abduction is enabled by the sternoclavicular joint, and 20° by the acromioclavicular joint^[25,51].

Soft tissue

With regards to the pathology of posterior shoulder instability, resistance to injury is provided substantially by the soft tissue. Most important are the subscapularis muscle, the coracohumeral ligament in neutral rotation, the coracohumeral ligament and the posterior band of the IGHL in internal rotation^[20].

Shoulder capsule: It is believed that posterior instability is initiated by insufficiency of the capsule, which secondarily leads to laxity of the joint. Various angles of humerus abduction have been investigated, and emphasize the importance of the posterior capsule and the IGHL as significant stabilizers^[52,53]. About 90% of patients show a rupture of the posterior capsule mainly on the scapular side after posterior shoulder dislocation. Ovesen *et al*^[17,54] noted that between 40° - 90° of abduction of the major stability is conferred by the entire posterior capsule. When sectioning posterior structures such as the teres minor, infraspinatus muscles and proximal half of the posterior capsule, there was a significant increase in posterior displacement.

Tears of the lower and proximal half of the posterior capsule have only little impact on stability in internal rotation (mainly above 40° of abduction). An entire rupture of the posterior capsule increases displacement in the last part of abduction, though not significantly. In cases of posterior structure trauma, an increase in anterior instability can also be seen^[54].

On the other hand, lesions of the anterior capsule show even more impact on the posterior stability. The anterior capsule strengthens the glenohumeral ligaments by close adherence of the coracohumeral ligaments (superiorly), as well as the teres minor and infraspinatus tendons (posteriorly), and tightens in various positions. When sectioning the entire anterior capsule, posterior displacement significantly increases in abduction between 0° - 90° ^[17].

Labrum: The labrum is a circumferential soft tissue extension of the bony glenoid rim, which is loosely attached to the surrounding capsule. It allows compressing forces, called "concavity compression", for stabilization and enables centralization of the humeral head^[55]. In 52%-66%, a posterior labrum defect (also called posterior/reverse Bankart lesion) can be found after traumatic posterior shoulder dislocation^[56]. No consensus exists on the association between posterior capsular laxity and reverse Bankart lesions^[53,57].

Ligaments: There are several ligaments that provide passive glenohumeral stabilization and help control the external forces on glenohumeral articulation.

The coracohumeral ligament is divided into a superficial and deep layer. The deep layer inserts into the rotator interval. It consists of fibers originating from the coracoid process and crisscrossing the supraspinatus and subscapularis muscles. These fibers form the pulley

system that stabilizes the long head of the biceps at the entrance into the sulcus bicipitalis^[57,58]. It allows external rotation and resists inferior and posterior translation in the suspended shoulder, which enables resistance to posterior subluxation in the neutral position^[20,58].

Three main strands build the glenohumeral ligament: the superior, middle and IGHL. The influence of the IGHL on shoulder stability is well-described. It is a thickening of the capsule with a prominent anterior band (between 2-4 o'clock)^[59] and a less prominent posterior branch. Typically, the posterior band or IGHL ruptures (posterior inferior part) in posterior dislocation (23 Blasier 1997), which can be provoked by elevation to 90° and abduction of internal rotation.

Today, most stabilization procedures are performed arthroscopically and target the capsulolabral complex. Surgical techniques can be divided into those inclusive or exclusive of suture anchor capsulolabral repair.

Bradley *et al.*^[60] suggests using suture-anchor capsulolabral repair in completely- or partially-detached labral injury patterns. He stated a success rate of 92% and 68%, respectively, returning to baseline sport when using suture anchors; otherwise, 84% and 48%, respectively, without suture anchors. The overall satisfaction is stated to be 94%, as measured using the American Shoulder and Elbow Surgeons Shoulder (ASES) score^[60]. Savoie *et al.*^[53] published a study stating that the success rate was 97% based on the Neer Foster rating scale in 92 patients after arthroscopically capsulolabral repair. The overall satisfaction in those patients who returned to sport at a pre-injury level was approximately 63.5%, and the mean ASES score improved from 45.9 to 85.1^[53,60]. Unfortunately, arthroscopic methods are somewhat limited, as the technique is not able to address severe erosions of the glenoid bone or retroversion of the glenoid exceeding 15°-20°, nor volitional instability^[30,61].

A rather infrequent method is capsulorrhaphy, which shows good to excellent results in 73.3%; however 3 patients experienced recurrent instability according to Bisson *et al.*^[62]. It should be noted that surgical indications in this study were very closely controlled, as only patients with isolated posterior instability without labral detachment underwent this technique.

Muscles: There are 17 muscles with origins or insertions at the scapula, and these can be classified according to their function and location. Three main groups exist: Scapular stabilizers ($n = 6$), Rotator cuff ($n = 4$) and Scapulohumeral muscles ($n = 6$). The omohyoid muscle is not included in this simple classification, as it originates from the superior border of the scapula yet functionally depresses the larynx and hyoid. All tendons of the rotator cuff interact intricately with the fibrous capsule, which allows dynamic stabilization and movement of the glenohumeral joint. This group includes the infraspinatus, subscapularis, supraspinatus and teres minor. After posterior shoulder dislocation, a rupture of the teres minor and infraspinatus tendon is

present in most of the cases (90% partial, 10% total rupture)^[25].

Biomechanical investigations after teres minor tenotomy demonstrate an increase of internal rotation by 7° at 30°-40° of humeral abduction compared to an intact glenohumeral joint. Similarly, infraspinatus tenotomies show a significant increase in internal rotation between 0° and 30°-50° of abduction^[32,54,63].

The scapular stabilizers include the levator scapulae (elevates and rotates the scapula), the pectoralis minor (protracts, rotates downwards and depresses the scapula), the major and minor rhomboid muscles (retract and elevate the scapula to depress the glenoid cavity, the serratus anterior (performs protraction and upward scapular rotation) and the trapezius muscle (a passive and dynamic scapular stabilizer, active elevator of the lateral scapular angle, scapular retractor and rotator). The pectoralis major, which does not attach the scapula, potentiates the scapulothoracic stabilization of the latissimus dorsi and deltoid muscle. This leads to a space in scapulothoracic articulation between the surface of the posterior thoracic cage and the subscapular fossa^[25,58], thus facilitating gliding movement.

The last group includes the scapulohumeral muscles, which are responsible for stabilizing the humeral head. The biceps brachii muscle attaches with both heads to the scapula, the long and short head which work as elbow flexors and forearm supinators. Its antagonist muscle is the triceps brachii muscle long head, which extends the elbow as well as acts as an adductor of the elbow and of the humerus. Flexion and adduction of the humerus is performed by the coracobrachial muscle, and the prime mover of the glenohumeral abduction, flexion, extension and adduction of the humerus is the deltoid muscle. The latissimus dorsi and teres major muscles perform adduction, internal rotation of the humerus, rotation of the trunk (latissimus dorsi) and extension of the humerus (teres major)^[44,64].

Treatment

In the literature, several different treatment algorithms have been developed based on bony defects, osteoarthritis and the physical state of patients^[65-68]. In athletes, authors tend to be a bit more aggressive in terms of surgical procedures. Guehring *et al.*^[69] additionally considers the time interval between trauma and surgery. Conservative therapy is a reasonable initial treatment, as one study demonstrated a subjective improvement after 6 mo in 70%-89% of patients. To avoid repetitive dislocation, certain exercises (internal rotation and horizontal adduction) and activities should be avoided for life^[70-72].

Directly after trauma, the shoulder should be kept in slight external or neutral rotation to avoid any stress to the posterior capsule. In physical therapy, a general strengthening of the dynamic muscular stabilizers is essential. This includes the rotator cuff (with focus on external rotation), infraspinatus muscle, teres minor,

Table 2 Different therapeutic options and considerations of posterior shoulder instability

Procedure	Consideration	Success rate
Conservative	Leads to loss of rotation and deformity of the shoulder, mainly performed in elderly patients	68%-77%, however only in isolated posterior shoulder instability; recurrence rate up to 96% ^[38,86]
Capsular-labral repair (<i>i.e.</i> , post. - inf. capsular shift) or reverse Bankart repair	In isolated unidirectional posterior instability	96% in post. - inf. capsular shift ^[73] 91% in posterior capsulorrhaphy in isolated post. instability ^[5] Posterior Bankart repair – 93% ^[87]
Other procedures not/or rarely performed:		
Thermal capsulorrhaphy	High recurrence rate	57%, capsular insufficiency 33% ^[88,89]
Posterior bone block or posterior wedge osteotomy	After failed capsular plication, or congenital formations	Posterior glenoid transfer: 53%; 41% complication rate ^[22,90] Posterior bone block: 45%; 36% osteoarthritis ^[36]
McLaughlin's procedure	In patients with locked posterior shoulder dislocation from reverse Hill-Sachs lesions	improvement in average constant scoring system from 16 preoperatively to 72 postoperatively ^[91]
Humeral head allograft	Alternative option to McLaughlin's procedure	Complication rate between 25%-50% ^[92,93]

periscapular muscles (for scapulohumeral rhythm) and posterior deltoid muscle^[73]. The aim of physiotherapeutic exercises is to compensate for the injured static structures of bone and tissue^[68,74].

For postoperative care, various protocols have been described. The shoulder is immobilized with an orthosis in 30° of abduction and 0° of rotation to prevent internal rotation. Cryotherapy is recommended and active elevation should be avoided for at least 4 wk. In the following weeks, passive and active assisted movements are recommended, followed by full passive and active range of motion 2 to 3 mo after. When the muscle strength is at least 80% of the contralateral side, a sport-specific rehabilitation program can be pursued, which is generally 6 mo post-operatively^[36,60,74].

As there are only a few evidence-based studies regarding treatment protocols and techniques, it is difficult to develop a uniform algorithm. The different treatment options, such as conservative and operative treatment, and success rates are summarized in Table 2.

CONCLUSION

Posterior shoulder instability seems to be underdiagnosed due to its complexity and limited diagnostic examinations in general practice. So far, no real consensus on classification of posterior shoulder instability exists. Moreover, the correct mechanism of injury is not well understood, which has led to a lack of consensus regarding treatment regimens and general awareness by physicians.

Posterior shoulder instability can be provoked according to the Kim/Jerk test in forward flexion, adduction and internal rotation. A variety of reasons for posterior shoulder instability have been described. The most important ones are capsular lesions, especially anterior ones as well as ruptures of the IGHL. Patients who suffered from posterior shoulder dislocation mostly suffer from a rupture of the posterior capsule, loosening of the posterior labrum, and a rupture of the teres minor and/or infraspinatus tendon. This increases the risk of recurrent posterior shoulder instability, especially in abduction between 0°-90°. Further predisposing conditions, which

have not yet been well investigated, include retroversion of the glenoid or humeral head.

Current treatment options vary in outcome in long-term follow-up. Currently, the best results have been observed using arthroscopic capsulolabral repair in conjunction with a careful postoperative management, with a delay in return to sport of about 4-6 mo.

With regards to the current biomechanical literature describing posterior shoulder dislocations, the predominant form of experimentation has used a static glenohumeral model. To our knowledge, no dynamic model yet exists to investigate the entire shoulder complex, including the scapulothoracic joint.

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Recently highlighted nutraceuticals for preventive management of osteoarthritis

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Abstract

Osteoarthritis (OA) is a chronic degenerative disease of articular cartilage with limited treatment options. This reality encourages clinicians to suggest preventive measures to delay and contain the outbreak of the pathological conditions. Articular cartilage and synovium suffering from OA are characterised by an inflammatory state and by significant oxidative stress, responsible for pain, swelling and loss of mobility in the advanced stages. This review will focus on the ability of olive oil to exert positive effects on the entire joint to reduce pro-inflammatory cytokine release and increase lubricin synthesis, olive leaf extract, since it maintains lubrication by stimulating high molecular weight hyaluronan synthesis in synovial cells, curcumin, which delays the start of pathological cartilage breakdown, sanguinarine, which downregulates catabolic proteases, vitamin D for its capacity to influence the oxidative and pro-inflammatory environment, and carnitine as an inducer of heme oxygenase-1, which helps preserve cartilage degeneration. These molecules, considered as natural dietary supplements, appear like a cutting-edge answer to this tough health problem, playing a major role in controlling homeostatic balance loss and slowing down the pathology progression. Natural or food-derived molecules that are able to exert potential therapeutic effects are known as "nutraceutical", resulting from the combination of the words "nutrition" and "pharmaceutical". These compounds have gained popularity due to their easy availability, which represents a huge advantage for food and pharmaceutical industries. In addition, the chronic nature of OA implies the use of pharmacological compounds with proven long-term safety, especially because current treatments like nonsteroidal anti-inflammatory drugs and analgesics

improve pain relief but have no effect on degenerative progression and can also cause serious side effects.

Key words: Osteoarthritis; Nutraceuticals; Prevention; Diet; Inflammation; Oxidative stress

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Core tip: Osteoarthritis involves the significant expression of inflammatory cytokines, matrix proteins and proteolytic enzymes. For this reason, anti-inflammatory molecules play a major role in controlling the adverse effects of cartilage homeostatic balance loss. Olive oil, olive leaf extract, curcumin and sanguinarine have been studied as supplements with anti-inflammatory properties. Moreover, chondrocytes undergo senescence and cell death in the presence of oxidative stress. Potential targets involved in this mechanism are counteracted by anti-oxidant molecules like vitamin D and carnosic acid.

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INTRODUCTION

Osteoarthritis (OA) is a very complex and multifactorial disease of articular cartilage, which represents a leading cause of joint pain and disability worldwide^[1]. The entire synovial joint is affected by the progression of this pathology, including the underlying bone, synovium, meniscus, ligaments/tendons, and cartilage^[2,3]. OA is characterized by the degradation of the articular cartilage, which can be used as hallmark of pathological advancement beyond changes in subchondral bone, osteophyte formation, joint space narrowing and chronic synovial inflammation^[4]. In normal joints, cartilage covers and cushions the ends of bones, reducing friction and absorbing shocks. Its destruction progress leads to stiffness, pain, mobility limitations and compromised overall quality of life^[5,6]. Some of the most important risk factors include aging, inflammatory state, muscle atrophy, injury and metabolic disorders^[7].

The management of OA focuses on alleviating its secondary effects since there is currently no resolutive cure. Nonsteroidal anti-inflammatory drugs and analgesics are generally prescribed to patients to reduce pain and improve joint function, but they fail in modifying disease progression in terms of prevention and chondroprotection^[8]. The chronic nature of OA forces the use of pharmacological approaches that can be considered safe for long term use and, at the same time, might be able to slow its progression. The basis

of articular damage relies on impaired balance between anabolic and catabolic mechanisms, which can be influenced by dietary compounds like nutraceuticals^[9]. Due to their minimal side effects, especially in the long term, their easy extraction and low costs of production, they may represent a valid preventive management of OA.

Forty-seven percent of people who suffer from OA use complementary medications including nutraceuticals due to their anti-inflammatory and antioxidant activities^[10]. Herbal and natural products have been used since ancient times. A 5000-year-old Sumerian clay tablet is the first proof of plants use as medicament, especially to treat pain and inflammation^[11].

During the 19th century, improvement in chemical technologies allowed for the extraction of active substances from medicinal plants such as alkaloids, tannins, saponosides, etheric oils, vitamins and glycosides, isolated in pure form^[12]. The term "nutraceutical", resulting from the combination of the words "nutrition" and "pharmaceutical", is used to define any natural or food-derived molecule able to exert a potential therapeutic effect that could be integrated into a daily diet^[13].

Statutory law of these type of medicaments differ by country. For example, in the United States, they are considered dietary supplements by the Dietary Supplement Health and Education Act of 1994^[14]. The Food and Drug Administration is in charge of reviewing and approving any health claims about these products. In some countries of the European Union, nutraceuticals may require registration whereas in others, they could be easily sold as food preparations^[15].

This review will summarize natural-based approaches for chondroprotection, highlighting the peculiarity of some molecules whose positive effect in preserving cartilage health has recently been discovered. This approach may be useful both to prevent OA onset and to slow down its progression.

ANTI-INFLAMMATORY APPROACH

The involvement of an inflammatory component, marked by joint pain, swelling and stiffness, is now well recognized in the pathogenesis of OA. Indeed, chondrocytes undergo a loss of homeostatic balance, which includes expression of inflammatory cytokines, matrix proteins such as collagen and lubricin and proteolytic enzymes^[16]. The most important pro-inflammatory cytokines involved are interleukin (IL)-1 β and tumour necrosis factor (TNF)- α ^[17]. Some of the consequences of the development of an inflammatory scenario are as follows: downregulation of structural components, including type II collagen and proteoglycans^[18-21], upregulation of proteolytic enzymes, such as matrix metalloproteinases (MMPs)-1, -3, -13, and a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS)^[22-24] and stimulation of inflammatory mediators like prostaglandin E2 (PGE2), cyclooxygenase-2 (COX-2), and Reactive oxygen species (ROS)^[25,26].

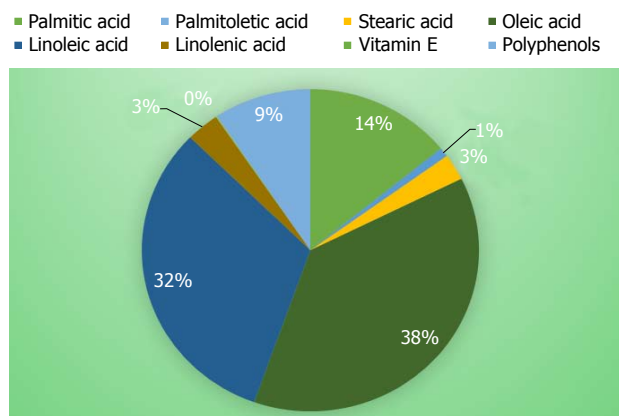


Figure 1 Composition of fatty acids, vitamin E and polyphenols in a Sicilian extra virgin olive oil-supplemented diet. Palmitic acid (16:0) (mg/kg) 9002; palmitoleic acid (16:1) (mg/kg) 579; stearic acid (18:0) (mg/kg) 1689; oleic acid (18:1) (mg/kg) 24047; linoleic acid (18:2) (mg/kg) 20352; linolenic acid (18:3) (mg/kg) 2018; vitamin E (mg/kg) 72.167; polyphenols (mg/kg) 5.960.

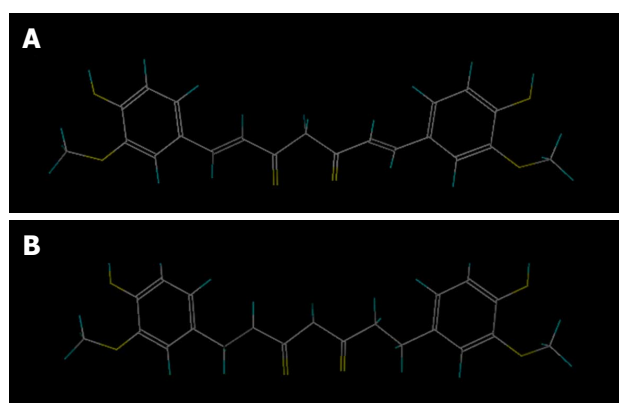


Figure 2 Chemical structure of curcumin and tetrahydrocurcumin. A: Curcumin, $C_{21}H_{20}O_6$; B: Tetrahydrocurcumin, $C_{21}H_{24}O_6$.

Recently, our lab carried out studies to determine the chondroprotective role of phytoactive molecules [e.g., polyphenols and monounsaturated fatty acids naturally present in olive tree-derived products, olive oil (-OO-) and olive leaf extract (-OLE-)] able to preserve the articular cartilage and skeletal muscle condition, in the context of early development of OA because of their antioxidant and anti-inflammatory properties^[7]. In addition, the study examined differences between three types of oils in term of origin and polyphenol contents: Sicilian extra virgin olive oil (S-EVOO), Tunisian extra virgin olive oil (T-EVOO) and Tunisian extra virgin olive oil and leaves extract (T-enriched-EVOO), concluding that the first variety of oil (S-EVOO) is the best in exerting positive effects on the entire joint, remarkably reducing IL-6 release and increasing lubricin synthesis, compared to the other diet protocols (Figure 1). The effects of physical activity were also analysed in combination with the diet^[27]. The studies demonstrated that an olive oil supplemented diet plus physical activity improved cartilage recovery after anterior cruciate ligament transection by lowering IL-6 and IL-1 expression and

by increasing lubricin expression, suggestive of chondroprotective activity. Lubricin is a glycoprotein released by type B synoviocytes and chondrocytes from the superficial layer of articular cartilage, and its functions are to lubricate and nourish articular cartilage^[28].

Another recent study that confirms the healthy effect of OLE was presented by Maruyama *et al.*^[29], which addressed the main activity of hydroxytyrosol [4-(2-hydroxyethyl)-1, 2-benzenediol] (HT), an OLE polyphenol. STR/ort mice were used as a model for knee OA, and 100 mg/kg OLE was orally administered every day for 8 wk. The chondroprotective effect of the extract was proven by Mankin scores of the non-OA control group, OA control group and OLE-treated group, which were 3.50, 11.13 and 7.20, respectively. Moreover, the study suggests that these natural molecules were able to impair cartilage damage and, consequently, the pathology progression, since they stimulated the synthesis of high molecular weight hyaluronan in synovial cells *in vitro*. High molecular weight hyaluronan is involved in maintaining joint moisture and lubrication^[30]. The authors suggested that OLE administration can effectively help suppress OA progression.

Traditionally used as an anti-inflammatory treatment in Chinese and Ayurvedic medicine, Curcuma longa is a plant rich in phytochemicals, which are responsible for its most impressive and wide-ranging health benefits. Some of its active components, curcumin and tetrahydrocurcumin (THC), a major metabolite of curcumin, have been studied because of their anti-inflammatory, antioxidant, chemopreventive, anti-aging and anti-bacterial activities^[31,32]. Park *et al.*^[33] analysed the effects of long-term THC administration and curcumin in OA progression in rats with oestrogen deficiency. Ovariectomized obese rats underwent monoiodoacetate injections into the knee to simulate OA conditions, and then curcumin and THC were fed to prevent postmenopausal and OA symptoms. One of the most significant findings of the study was the differences between the two molecules. The chemical structures of curcumin involved in exerting the main activities are methoxy, hydroxyl, α,β -unsaturated carbonyl, and diketone groups, whereas its metabolite lacks the presence of the α,β -unsaturated carbonyl group, changing its functionality and efficacy (Figure 2). Park *et al.*^[33] found that both natural products showed similar abilities to decrease expression of TNF- α , IL-1 β , IL-6 and MMP3 and MMP13, but only THC could enhance glucose tolerance, allowing it to decrease advanced glycation end products in articular cartilage, delaying the start of the pathological process of cartilage breakdown.

Furthermore, Ma *et al.*^[34] demonstrated for the first time the anti-inflammatory effect of sanguinarine (SA), a benzophenanthridine alkaloid isolated from the roots of *Sanguinaria canadensis*, on the pathogenesis of OA, *in vitro*, *ex vivo* and *in vivo*. Evaluation of the potential cytotoxicity of SA revealed that this compound does not affect cell viability at concentrations lower than 1.25 μ mol/L. As stimulation of IL-1 β increased the mRNA expression of MMP1a, MMP3, MMP13, and ADAMTS-5,

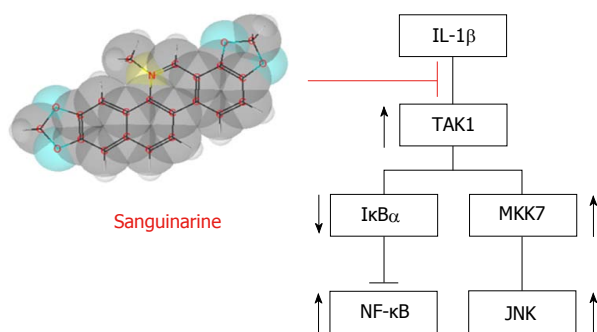


Figure 3 Anti-inflammatory effect of sanguinarine. Sanguinarine acts as suppressor of IL-1 β , targeting the pathways involved in JNK activation and the degradation of I κ B α , an inhibitory subunit of NF- κ B. IL: Interleukin; I κ B α : Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha; NF- κ B: Nuclear factor kappa B; JNK: c-Jun N-terminal kinases; MKK7: Dual specificity mitogen-activated protein kinase kinase 7.

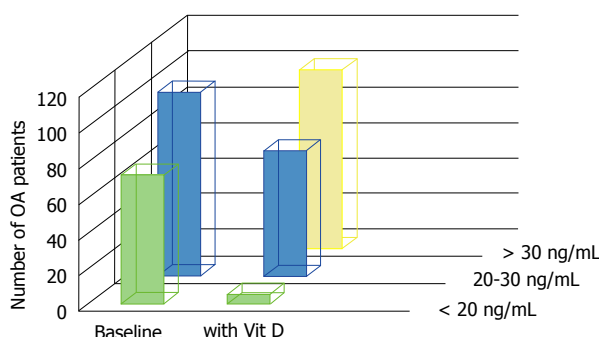


Figure 4 Vitamin D levels in osteoarthritis patients at baseline and after vitamin D2 supplementation. At baseline, 72 participants had vitamin D deficiency (< 20 ng/mL) and 103 patients had vitamin D insufficiency (20-30 ng/mL). After 40000 IU of vitamin D2 supplementation per week for 6 mo, 100 knee OA participants achieved concentration above 30 ng/mL, 70 knee OA participants had vitamin D insufficiency, and only 5 patients had vitamin D deficiency. Vit D: Vitamin D; OA: Osteoarthritis.

SA downregulated these catabolic proteases through a dose-dependent manner indicative of IL-1 β activity. More specifically, the anti-inflammatory molecule acts as suppressor of phosphorylation of the c-Jun N-terminal kinases (JNK) and nuclear factor kappa B (NF- κ B) (Figure 3). These *in vitro* analyses were followed by *ex vivo* evaluation of SA's effects on cartilage matrix degradation, which were consistent with the previous results. Intra-articular administration of different SA concentrations was used to determine whether the molecule could slow down the progression of ACLT-induced OA in mice. The hypothesis was finally and positively confirmed by immunochemistry results, evaluation of protease mRNA levels and Osteoarthritis Research Society International scoring.

ANTIOXIDANT APPROACH

It is well established that oxidative stress-induced ROS production (commonly experienced because of post-traumatic events or aging) is a crucial mediator

of OA disease progression^[35]. As a consequence, chondrocytes experience more significant senescence and cell death^[36,37]. In addition, cartilage and joint fluid are not able to counteract this scenario because superoxide dismutase antioxidant levels are consistently decreased in OA^[38]. This is the reason why an effective preventive approach to this pathology should consider boosting antioxidant shields to enhance the potency of constitutive defences such as the antioxidants catalase, superoxide dismutase, glutathione peroxidase and glutathione reductase.

A study about dietary supplementation in OA by Manoy *et al.*^[39] highlighted the role of the commonly used antioxidant vitamin D. Even though the correlation between this vitamin and musculoskeletal diseases is still not clear, low levels of 25-hydroxyvitamin D [25(OH)D] have been observed in OA patient serum. In fact, evidence suggests that vitamin D deficiency is a co-factor for OA pathogenesis^[40]. The study involved 175 primary knee OA patients who received 40000 IU vitamin D (ergocalciferol) per week. Six months after the first administration, the patients experienced ameliorated grip strength, physical performance and improved quality of life (Figure 4). Moreover, to confirm its anti-oxidant activity, analysis of protein carbonyl levels was performed to obtain information about oxidative damage. The results confirmed that vitamin D supplementation remarkably decreased carbonyl levels, and as a consequence, stress and the pro-inflammatory environment that can affect protein function and DNA. The underlying mechanism for this vitamin D activity may be explained by evidences for the downregulation of nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase), IL-6, TNF- α , NF- κ B and p38^[41,42].

Heme oxygenase-1 (HO-1) is another potential target that can be used in an anti-oxidant strategy against OA. Constitutive expression of HO-1 in chondrocytes and the meniscus in mice has been linked to preserve cartilage degeneration^[43]. For this reason, Hiroyuki *et al.*^[44] explored the effect of carnosic acid (CA) as an inducer of HO-1 upregulation in preventing OA progress. This molecule is a natural diterpene commonly found in rosemary and common sage, and it has demonstrated protective qualities in pathologies like cancer, diabetes and neurodegenerative disease^[45]. Immunoblotting assays were used to test whether CA affected HO-1 expression in articular chondrocytes. The results showed that CA increased enzyme levels in a dose-dependent manner. More specifically, the best treatment seemed to require 10 to 50 μ mol/L of CA. In addition, it was able to restore HO-1 levels under IL-1 β treatment, which specifically inhibits the anti-oxidant effects of the enzyme. According to this study, the mechanisms by which this natural compound acts rely on downregulation of MMP-13 and ADAMTS-5, activation of nuclear factor erythroid 2-related factor 2 (Nrf2), regulation of the Kelch-like ECH-associated protein 1/nuclear factor erythroid 2-related factor 2 (KEAP1/NRF2) transcriptional pathway and an increase in

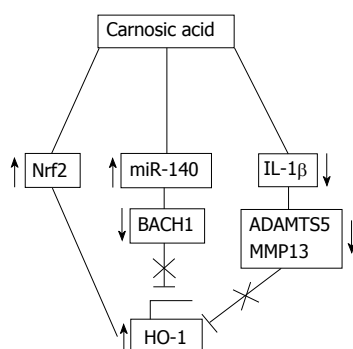


Figure 5 Mechanisms of heme oxygenase-1 upregulation by carnosis acid. CA induces the expression of HO-1 by: Activation of the Nrf2 transcription factor, downregulation of Bach1 via miR-140 and downregulation of the IL-1 β -induced expression of extracellular matrix degrading enzymes such as MMP-13 and ADAMTS-5. CA: Carnosis acid; HO-1: Heme oxygenase-1; Nrf2: Nuclear factor erythroid 2-related factor 2; IL: Interleukin; MMP: Matrix metalloproteinase; ADAMTS: A disintegrin and metalloproteinase with thrombospondin motifs; miR-140: MicroRNA 140.

microRNA 140 (miR-140) binding to the 3'UTR of Bach1 (an HO-1 repressor) in articular chondrocytes (Figure 5).

Furthermore, our lab examined the relationship between oxidative stress and physical activity or a sedentary lifestyle, suggesting therapeutic solutions that involve natural dietary supplements. One study analysed the effects of oleic acid on ROS production induced by exhaustive physical activity in rat skeletal muscle^[46]. The results highlight the importance of extra-virgin olive oil as a protective agent against oxidative stress following physical efforts. The group of rats subjected to exhaustive exercise but fed with a diet rich in oleic acid experienced a decrease in hydroperoxides and thiobarbituric acid reactive substances and an increase in antioxidant defences, rated as non-enzymatic antioxidant capacity and levels of 70 kDa heat shock proteins (Hsp70). OA cannot be completely prevented, but some precautions can help delay the progression of the pathology and manage the risk of its progression^[47]. Since sarcopenia and sedentary life are possibly associated with knee OA^[48], another study is worth citing because it evaluated whether different dietary profiles, containing or not containing vitamin D, could exert some effects on muscle fibres^[49]. The study found that muscle fibres of rats fed with high-fat extra-virgin olive oil-based diets were hypertrophic compared to those of the regular diet group. These data confirmed that this natural supplement does not impair muscle fibre metabolism, unlike high-fat butter-based diets. In addition, Vitamin D exerted a trophic action on muscle fibres both in rats fed regular diets and in those fed a diet enriched with extra-virgin olive oil, suggesting that insulin-like growth factor-1 (IGF-1) and dickkopf-1 (DKK-1) may be involved in this mechanism.

CONCLUSION

When physical activity and a healthy lifestyle are not enough, anti-inflammatory drugs and painkillers are

commonly used to alleviate pain, but sometimes rehabilitation and surgical intervention are unavoidable. For these reasons, trying to preserve the cartilage joint is imperative.

The use of natural approaches is a cutting-edge strategy. Nutraceuticals offer a wide range of molecules able to exert positive effects at different joint structures with several mechanisms of actions. In particular, this review focused on the anti-inflammatory and antioxidant properties of compounds that ameliorate cartilage conditions, suggesting that they should be integrated into a framework of prevention.

The presented studies offer thorough evaluations of olive oil, demonstrating that it reduces IL-6 release and increases lubricin synthesis, of olive leaf extract, as a stimulator of high molecular weight hyaluronan synthesis in synovial cells, of curcumin, addressing its ability to decrease TNF- α , IL-1 β , IL-6 and MMP3 and MMP13 expression, of SA, as a downregulator of catabolic proteases through interaction with IL-1 β , of vitamin D, since it influences the oxidative and pro-inflammatory environment and of CA, as an inducer of HO-1, preserving cartilage degeneration even under IL-1 β treatment.

From a general analysis, it is worth noting that a common positive element of all these molecules is their availability in nature, which represents a huge advantage for food and pharmaceutical industries, and their low side effects, allowing for a broad range of safe uses for the derived products.

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Should antibiotics be administered before arthroscopic knee surgery? A systematic review of the literature

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Abstract

AIM

To explore the current evidence surrounding the administration of prophylactic antibiotics for arthroscopic knee surgery.

METHODS

Databases were searched from inception through May of 2018 for studies examining prophylactic antibiotic use and efficacy in knee arthroscopy. Studies with patient data were further assessed for types of arthroscopic procedures performed, number of patients in the study, use of antibiotics, and outcomes with the intention of performing a pooled analysis. Data pertaining to "deep tissue infection" or "septic arthritis" were included in our analysis. Reported data on superficial infection were not included in our data analysis. For the pooled analysis, a relative risk ratio was calculated and χ^2 tests were used to assess for statistical significance between rates of infection amongst the various patient groups. *Post hoc* power analyses were performed to compute the statistical power obtained from our sample sizes. Number needed to treat analyses were performed for statistically significant differences by dividing 1 by the difference between the infection rates of the antibiotic and no antibiotic groups. An alpha value of 0.05 was used for our analysis. Study heterogeneity was assessed by Cochrane's *Q* test as well as calculation of the I^2 value.

RESULTS

A total of 49682 patients who underwent knee ar-

throscopy for a diverse set of procedures across 19 studies met inclusion criteria for pooled analysis. For those not undergoing graft procedures, there were 27 cases of post-operative septic arthritis in 34487 patients (0.08%) who received prophylactic antibiotics and 16 cases in 10911 (0.15%) who received none [risk ratio (RR) = 0.53, 95% confidence interval (CI): 0.29-0.99, $P = 0.05$]. A sub-group analysis in which bony procedures were excluded was performed which found no significant difference in infection rates between patients that received prophylactic antibiotics and patients that did not ($P > 0.05$). All anterior cruciate ligament reconstruction studies used prophylactic antibiotics, but two studies investigating the effect of soaking the graft in vancomycin in addition to standard intravenous (IV) prophylaxis were combined for analysis. There were 19 cases in 1095 patients (1.74%) who received IV antibiotics alone and no infections in 2034 patients who received IV antibiotics and had a vancomycin soaked graft (RR = 0.01, 95%CI: 0.001-0.229, $P < 0.01$).

CONCLUSION

Prophylactic antibiotics are effective in preventing septic arthritis following simple knee arthroscopy. In procedures involving graft implantation, graft soaking reduces the rate of infection.

Key words: Knee arthroscopy; Antibiotics; Systematic review; Vancomycin; Anterior cruciate ligament

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Core tip: Our study is the first to demonstrate prophylactic antibiotics are effective in preventing septic arthritis following simple arthroscopic procedures of the knee, though given the large number needed to treat, the clinical significance of this finding is unclear. There is little to no debate that antibiotics should be used prophylactically for arthroscopic surgeries involving graft implantation. However, our findings indicate that the addition of graft soaking further reduces the rate of infection. Further study is warranted to identify patient populations and arthroscopic procedures in which the use of prophylactic antibiotics may not be necessary.

Carney J, Heckmann N, Mayer EN, Alluri RK, Vangsness Jr. CT, Hatch III GF, Weber AE. Should antibiotics be administered before arthroscopic knee surgery? A systematic review of the literature. *World J Orthop* 2018; 9(11): 262-270 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i11/262.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i11.262>

INTRODUCTION

Antibiotics have been administered prophylactically in major orthopaedic surgeries for decades^[1]. Their use has been shown to reduce rates of local and systemic

infection, which leads to better patient outcomes when used in combination with proper sterile surgical technique^[2]. Failure to provide adequate infection prophylaxis prior to elective knee arthroscopy may result in septic arthritis, a devastating complication which has been shown to delay recovery time and diminish functional outcomes^[3]. The most common pathogen responsible for septic arthritis is *Staphylococcus aureus*; though other pathogens have been identified as well^[4,5]. It is accepted within the orthopaedic community that prophylactic antibiotics, typically cephalosporins or vancomycin, should be administered prior to major orthopaedic surgeries^[6]. However, the use of routine prophylactic antibiotics prior to less invasive surgeries such as hand procedures and elective arthroscopic surgeries has not been established. The wide range of rates of antibiotic administration in the published literature, ranging from as low as 5% to as high as 80.5%, highlights the lack of understanding of the role of antibiotic prophylaxis^[7-13]. The use of prophylactic antibiotics is not without risk; allergic reaction, development of resistant organisms, and side effects specific to the chosen antibiotic can be a burden to patients and health care providers alike.

There is published data that demonstrate that prophylactic antibiotics may be unnecessary for minimally invasive non-bony procedures such as carpal tunnel release^[14]. As of 2009, the American Academy of Orthopedic Surgeons published guidelines on carpal tunnel release that did not mandate the use of prophylactic antibiotics, but rather stated their use was an option for physicians to consider^[14]. There is evidence to suggest that, like carpal tunnel release, patients undergoing knee arthroscopy may receive little to no benefit from receiving prophylactic antibiotics. A recent study by Wyatt *et al*^[8] found no significant difference in cases of deep infection between patients that received prophylactic antibiotics prior to knee arthroscopy and those who did not in a study that included 40810 patients. This study is in agreement with other studies on this topic, which similarly found no difference in infection rates if prophylactic antibiotics are used or withheld^[7,12,15-17]. Although the study by Wyatt *et al*^[8] contained large cohort of patients, other studies are relatively small and may be too underpowered to draw meaningful conclusions.

The purpose of this systematic review is to summarize current literature with regards to the efficacy of antibiotic prophylaxis in arthroscopic knee surgery and to pool available studies to better determine the true infection risk in knee arthroscopy. This study is the first to our knowledge that attempts to combine data from published studies to better understand the role of antibiotic prophylaxis in knee arthroscopy. We hypothesize that there is no evidence to support the routine administration of prophylactic antibiotics in arthroscopic knee surgery.

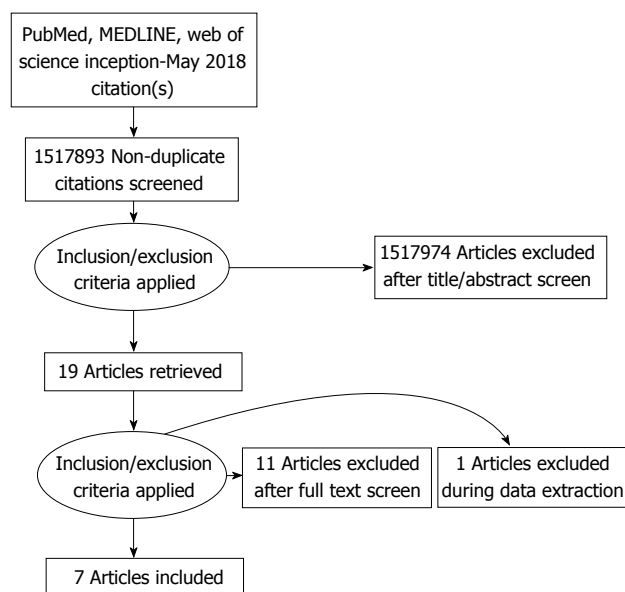


Figure 1 PRISMA flow diagram of methods for study inclusion.

MATERIALS AND METHODS

Two reviewers completed a comprehensive search of PubMed, MEDLINE, and Web of Science to identify studies pertaining to the use of antibiotic prophylaxis in knee arthroscopy from inception to May of 2018. Search strategies were customized for each database to produce the highest yield of possible results (Appendix A). Randomized control trials, prospective and retrospective studies, case-control studies, and systematic reviews were included. Review articles and surveys discussing the use of prophylactic antibiotics in arthroscopy were excluded from use in a pooled analysis, but were included for discussion purposes. Case reports, animal studies, and cadaveric studies were also excluded. The references of each study were also assessed for eligibility for our review. Studies with patient data were further assessed for types of arthroscopic procedures performed, number of patients in the study, use of antibiotics, and outcomes with the intention of performing a pooled analysis. Data pertaining to "deep tissue infection" or "septic arthritis" were included in our analysis. Reported data on superficial infection were not included in our data analysis.

Statistical analysis

For the pooled analysis, a relative risk ratio was calculated and χ^2 tests were used to assess for statistical significance between rates of infection amongst the various patient groups. *Post hoc* power analyses were performed to compute the statistical power obtained from our sample sizes. Number needed to treat analyses were performed for statistically significant differences by dividing 1 by the difference between the infection rates of the antibiotic and no antibiotic groups. An alpha value of 0.05 was used for our analysis. Study heterogeneity was assessed by Cochrane's Q test as

well as calculation of the I^2 value.

RESULTS

Our initial search yielded 1517893 studies. Nineteen studies satisfied inclusion criteria: 3 randomized control trials, 7 retrospective case control studies, 4 retrospective case series studies, 2 surveys, and 4 review articles (Table 1). These studies were further analyzed to determine if their data could be pooled for further analysis. Studies with data comparing infectious outcomes in knee arthroscopy procedures between groups that received prophylaxis and those that did not were included in our grouped analysis while studies with data not specific to the knee joint or not limited to arthroscopy were excluded.

Eight studies met inclusion criteria for pooled analysis. Upon closer review however, it was determined that two studies likely utilized the same patient database to achieve their results^[18,19]. We established correspondence with one of the authors to confirm this finding. Upon confirmation the more recent and higher powered of the two was included while the other was excluded from data analysis, leaving 7 studies for pooled analysis (Figure 1). From these studies, there were a total of 49682 patients who underwent an arthroscopic procedure. Arthroscopic procedures included diagnostic arthroscopy, joint debridement, synovectomy, partial or complete meniscectomy, meniscus repair, microfracture repair, lateral retinacular release, loose body removal, and anterior cruciate ligament reconstruction.

Five of the 7 studies had similar designs that allowed us to perform a pooled analysis of prophylactic antibiotic efficacy in arthroscopic procedures that do not involve the implantation of a graft (Table 2)^[7,8,12,15,17]. Out of a total of 45398 patients, 34487 received prophylactic antibiotics prior to arthroscopy while 10991 did not. All authors used a first generation cephalosporin such as cefazolin for primary prophylaxis, except in cases of known drug allergy. The antibiotic group had a total of 27 cases of septic arthritis (0.08%) while the no antibiotic group had 16 cases of septic arthritis (0.15%). The differences in infection rates was found to be significant [risk ratio (RR) = 0.53, 95% confidence interval (CI): 0.29 to 0.99, $P = 0.05$, *post hoc* power = 53%]. Based on these findings, the number of patients needed to treat with IV antibiotics in order to prevent 1 infection is 1463.

Regarding study heterogeneity, the Cochrane Q value was calculated to be 2.40 ($P = 0.49$) while the I^2 value was calculated to be 0% (95%CI: 0.00 to 83.11). Study heterogeneity is illustrated in Figure 2.

A subgroup analysis of this group was conducted and excluded studies that involved bony procedures (microfracture repair, procedures requiring bone tunnels, etc.), which have been demonstrated to have an increased risk of infection^[20,21]. Two studies excluded bony procedures and were included in a separate

Table 1 Summary of literature review results

Study name	Study type	No. of Patients	Procedures done	Findings/results/conclusions
Wyatt <i>et al</i> ^[6]	Retrospective Review	40810	Diagnostic arthroscopy, joint debridement, synovectomy, partial or complete meniscectomy, meniscus repair, microfracture, and lateral retinacular release	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Bert <i>et al</i> ^[7]	Retrospective Review	3231	Arthroscopic meniscectomy, arthroscopic meniscal repair, loose body removal, lateral retinacular release, and arthroscopic debridement	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Qi <i>et al</i> ^[27]	Retrospective Review	1326	Arthroscopic diagnosis, debridement, partial or complete meniscectomy, arthroscopic shaving and microfracture, removal of loose bodies, synovectomy and lateral retinacular release	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Ghmait <i>et al</i> ^[13]	Randomized control trial	180	Diagnostic arthroscopy, meniscus repair	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Rose <i>et al</i> ^[12]	Retrospective Review	302	Meniscectomies, arthroscopic debridement, arthroscopic meniscal repair, arthroscopic shaving and microfracture, removal of loose bodies, arthroscopic synovectomy, arthroscopic lateral retinacular release and diagnostic arthroscopic	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Wieck <i>et al</i> ^[16]	Randomized control trial	437	Unspecified arthroscopy	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Phegan <i>et al</i> ^[18]	Retrospective Review	1585	ACL reconstruction with graft	Vancomycin soaked grafts have a lower infection rate than non-soaked grafts
Vertullo <i>et al</i> ^[19]	Retrospective Review	1135	ACL reconstruction with graft	Vancomycin soaked grafts have a lower infection rate than non-soaked grafts
Pérez-Prieto <i>et al</i> ^[22]	Retrospective Review	1544	ACL reconstruction with graft	Vancomycin soaked grafts have a lower infection rate than non-soaked grafts
Yazdi <i>et al</i> ^[31]	Randomized control trial	360	ACL reconstruction with graft	Using gentamicin in irrigating solutions during arthroscopic ACL reconstruction surgery does not statistically decrease post-operation septic arthritis
Formaini <i>et al</i> ^[10]	Retrospective Review	2330	Unspecified arthroscopy	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Armstrong <i>et al</i> ^[11]	Retrospective Review	4256	Unspecified arthroscopy	Infection following knee arthroscopy was associated with prolonged operation time and corticosteroid use, not presence or absence of prophylactic antibiotics
D'Angelo and Ogilvie-Harris ^[24]	Retrospective Review	9	Unspecified arthroscopy	Antibiotic prophylaxis may reduce hospital costs by reducing spending on treating septic arthritis based on a 9 case review of patients with septic arthritis following arthroscopy
Babcock <i>et al</i> ^[23]	Retrospective Review	27	Unspecified arthroscopy	In a case series review of septic arthritis patients, shaving and corticosteroids were found to be significant risk factors, but not antibiotics
Lubowitz <i>et al</i> ^[25]	Review Article	NA	NA	There is not enough evidence to conclude whether or not antibiotics should be administered prophylactically in knee arthroscopy. However, the results of articles like Bert <i>et al</i> should be further examined and studied
Kurzweil ^[27]	Review Article	NA	NA	There is not enough evidence to conclude whether or not antibiotics should be administered prophylactically in knee arthroscopy. However, they should still be used as a measure to reduce the risk of post procedure infection

Onyema <i>et al</i> ^[24]	Review Article	NA	NA	Prophylactic antibiotics should not be used for knee arthroscopy
Prokuski ^[6]	Review Article	NA	NA	Cephalosporins are the drug of choice for most orthopedic surgeries. However, there is a lack of evidence supporting their efficacy in arthroscopic surgery
Müller-Rath <i>et al</i> ^[9]	Survey	110 physicians	NA	62% of the surgeons reported the use of an antibiotic prophylaxis in every arthroscopic case, while 19% administer antibiotics only occasionally
Mini <i>et al</i> ^[3]	Survey	166 hospitals	NA	57.1% of orthopedic surgeons routinely use antibiotic prophylaxis for arthroscopy

ACL: Anterior cruciate ligament; NA: Not available.

analysis (Table 3)^[7,15]. A study by Bert *et al*^[7] examined 3231 patients undergoing various arthroscopic procedures, and analyzed meniscectomies separately, of which 933 (34%) received antibiotic prophylaxis and 1847 (66%) did not. A second study by Ghnaimat *et al*^[15] randomized 180 patients undergoing either partial meniscectomy, plica excision, synovial biopsy, or diagnostic arthroscopy into two groups, of which 90 (50%) received antibiotic prophylaxis and 90 (50%) did not. From a total of 2960 patients, 1023 (35%) received antibiotics and 1937 (65%) did not. There was 1 (0.10%) case of septic arthritis in the antibiotic group and 3 (0.15%) cases of septic arthritis in the group that did not receive antibiotics, however this difference was not statistically significant (RR = 0.63, 95%CI: 0.07 to 6.06, $P = 0.69$, *post hoc* power = 5%).

Two of the 7 studies were pooled for data analysis to analyze arthroscopic anterior cruciate ligament (ACL) reconstruction (Table 4)^[18,22]. Both studies investigated the role of soaking the ACL autograft in vancomycin prior to implantation. Of 3129 patients, 1095 received intravenous (IV) antibiotics alone prior to arthroscopic ACL reconstruction, while 2034 patients received IV antibiotics and had their ACL graft soaked in vancomycin. There were 19 cases of infection in the IV antibiotics alone group (1.74%) and 0 infections in the IV antibiotics with vancomycin soaked graft group (0%). The difference in rates was found to be significant (RR = 0.01, 95%CI: 0.001 to 0.229, $P < 0.01$, *post hoc* power = 99.8%). Given these infection rates, the number need to treat with vancomycin soaked grafts to prevent 1 infection is 57.0. Analysis of heterogeneity was not performed in this dataset given the rates of infection in treatment groups were equal at 0%.

DISCUSSION

The results of our systematic review demonstrate that there is evidence supporting the use of prophylactic antibiotics in knee arthroscopic procedures to prevent postoperative infections ($P = 0.05$). The statistical significance may be attributed to knee arthroscopic procedures in which the subchondral bone is manipulated. Given the *post hoc* power analyses of our general population as well as our bone manipulation subgroup (53% and 5%, respectively), our findings should not be interpreted as a definitive answer to the question of whether antibiotic prophylaxis is appropriate in knee arthroscopy not involving a graft. However, in cases of graft implantation, particularly ACL autograft reconstruction, antibiotics appear to have a substantial protective effect particularly when antibiotics are used both locally (*i.e.*, autograft soaked in vancomycin) and systemically. Furthermore, while our findings for the pooled group were statistically significant, the clinical utility of these differences is in question as reflected by the needed to treat of approximately 1400 patients.

Arthroscopy without graft Implantation

The findings of this systematic review are in juxtaposition with current literature on this subject. A study by Babcock *et al*^[23] investigated an outbreak of septic arthritis following arthroscopy at a community hospital from 1994 to 1996. The study concluded that preoperative skin shaving and intra-articular corticosteroid injection significantly increased risk of infection, but found no link between infection and use of prophylactic antibiotics. A review of 4256 knee arthroscopies with 15% receiving prophylactic antibiotics by Armstrong *et al*^[11] similarly found that antibiotic use was not linked to a lower infection rate. Rather, corticosteroid use and prolonged operation time were the two greatest risk factors.

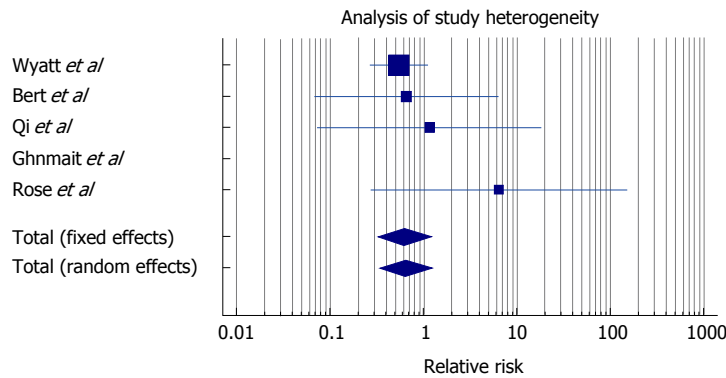
Our literature search found five studies of similar design that did not include the use of a graft and could be pooled for analysis. This pooled analysis demonstrated that

Table 2 Comparison of infection rates in simple arthroscopy patients receiving prophylactic antibiotics

Study name	Total patients	Patients receiving antibiotics	Patients not receiving antibiotics	No. of septic arthritis cases: Antibiotic group	No. of septic arthritis cases: No antibiotic group	Septic arthritis rate: Antibiotic group (%)	Septic arthritis rate: No antibiotic group (%)	P value
Wyatt <i>et al</i> ^[8]	40810	32836	7974	25	11	0.08	0.14	
Bert <i>et al</i> ^[7]	2780	933	1847	1	3	0.15	0.16	
Qi <i>et al</i> ^[17]	1326	614	712	1	1	0.16	0.14	
Ghnmait <i>et al</i> ^[15]	180	90	90	0	0	0	0	
Rose <i>et al</i> ^[12]	302	14	288	0	1	0	0.35	
Total	45398	34487	10911	27	16	0.08	0.15	0.05

Table 3 Comparison of infection rates in simple arthroscopy patients receiving prophylactic antibiotics, excluding bony procedures

Study name	Total patients	Patients receiving antibiotics	Patients not receiving antibiotics	No. of septic arthritis cases: Antibiotic group	No. of septic arthritis cases: No antibiotic group	Septic arthritis rate: Antibiotic group (%)	Septic arthritis rate: No antibiotic group (%)	P value
Bert <i>et al</i> ^[7]	2780	933	1847	1	3	0.11	0.16	
Ghnmait <i>et al</i> ^[15]	180	90	90	0	0	0	0	
Total	2960	1023	1937	1	3	0.1	0.15	0.69



Study name	Infection rate in no antibiotics group	Infection rate in no antibiotics group	Relative risk	95%CI	P value
Wyatt <i>et al</i> ^[8]	0.08	0.14	0.55	0.27-1.12	0.1
Bert <i>et al</i> ^[7]	0.15	0.16	0.66	0.07-6.34	0.72
Qi <i>et al</i> ^[17]	0.16	0.14	1.16	0.07-18.50	0.92
Ghnmait <i>et al</i> ^[15]	0	0	1	0.02-49.86	1
Rose <i>et al</i> ^[12]	0	0.35	6.42	0.27-151.12	0.25
Total	0.08	0.15	0.54	0.29-0.99	0.05
Cochrane's Q	2.4				
Significance Level	P = 0.49				
I ²	0.00%				
95%CI for I ²	0.00 to 83.84				

Figure 2 Comparison of odds ratio for simple arthroscopy.

there was a significant difference in infection rates between knee arthroscopy patients who received antibiotics and those who did not. Of these five studies, Wyatt *et al*^[8] was substantially larger in size ($n = 40810$) than the others, and thus our results are largely dominated by the findings of this study. Although they concluded that there was no difference in infection rate, they reported a P value that approached statistical significance ($P = 0.10$). Pooling their cases with those of the other studies was able to tip the scale towards significance and show that there is a difference in infection rate between those that do and do not receive prophylactic antibiotics.

Regarding the rigour of these studies, we feel confident in the results as investigation of infection rates was the primary focus of each study. Furthermore, each study analyzed similar patient groups and used similar methods of antibiotic prophylaxis (cephalosporins) that are consistent with contemporary guidelines. Our analysis of study heterogeneity confirms that the findings amongst studies are consistent ($I^2: 0.00\%$). Thus, we believe the results of this systematic review to be both accurate and applicable to current orthopaedic practice. There were other studies identified during our search that were excluded from our pooled analysis, but are worth mentioning in regards to our findings. Wieck

Table 4 Comparison of infection rates in arthroscopic anterior cruciate ligament reconstruction with *vs* without vancomycin graft soaking

Study name	Total patients	IV prophylaxis alone	IV prophylaxis + vancomycin	Number infected IV alone	Number infected IV + vancomycin	Infection rate IV alone (%)	Infection rate IV + vancomycin (%)	P value
Phegan <i>et al</i> ^[18]	1585	285	1300	4	0	1.4	0	
Pérez-Prieto <i>et al</i> ^[22]	1544	810	734	15	0	1.85	0	
Total	3129	1095	2034	19	0	1.74	0	< 0.001

et al^[16] investigated the role of antibiotic prophylaxis in 437 patients who underwent an arthroscopic procedure, not limited to the knee, and found no cases of deep infection in either arm of their study. A retrospective study of pediatric patients undergoing minimally invasive orthopedic procedures, including arthroscopy, by Formaini *et al*^[10] found no evidence to suggest that antibiotic prophylaxis reduced infection rates. Review articles by Onyema *et al*^[24], Lubowitz *et al*^[25], and Prokusi^[6] all highlighted the lack of evidence with regards to prophylactic antibiotic administration in arthroscopy and noted that their use may not be necessary. Our review differs from the aforementioned articles in that we reviewed new literature as well as included our own data analysis, which provided a large enough population size to show significant differences in infection rates. Our study is the first to our knowledge to demonstrate the efficacy of prophylaxis at the alpha = 0.05 level. Thus, we emphasize the need for further study and confirmation of our findings before they can be translated into clinical practice.

There were two publications identified that recommended prophylactic antibiotics and thus are in agreement with our findings. One was a retrospective review of septic arthritis cases following arthroscopy by D'Angelo and Ogilvie-Harris^[26] in which the authors recommended that prophylaxis be used to prevent deep tissue infections. However, the authors' rationale for the efficacy of antibiotic prophylaxis in arthroscopy is based on a paper on general orthopedic surgeries, not arthroscopy^[11]. A 2006 opinion article by Kurzweil^[27] argued that although current evidence does not demonstrate the efficacy of antibiotic prophylaxis in knee arthroscopy, there is still not enough evidence to argue for its discontinuation. Kurzweil^[27] stated that although a perfectly performed arthroscopic procedure on a healthy patient may not be affected by the use of antibiotics, they may serve as a safety net for physician errors or breaks in protocol as well as both known and unknown health-related risk factors of patients. Despite our significant findings, we agree that more evidence is needed to better understand the role of antibiotic prophylaxis in arthroscopy before a strong recommendation for or against their use can be made.

Arthroscopic ACL reconstruction with graft implantation

After a review of the literature, we determined that ACL reconstruction needed to be considered separate from other arthroscopic procedures, as our search did

not yield any publications related to ACL reconstruction that did not use antibiotic prophylaxis. Rather, studies varied in the type of antibiotic prophylaxis utilized. In arthroscopic ACL reconstruction, the graft presents additional infection risk as it is inserted into the joint space from the outside environment. It has been demonstrated that the source of infection can come from direct contamination of the graft or from skin flora^[28].

A 2013 study by Torres-Claramunt *et al*^[29] found an infection rate of 1.8% following ACL reconstruction with prophylactic administration of either cefazolin or vancomycin. However, three retrospective reviews found significantly reduced rates of septic arthritis when ACL grafts were soaked in vancomycin prior to insertion into the joint space^[18,19,22]. Our combined analysis of two of these studies strengthens these authors' individual findings. It is particularly important to note that in all three of these studies the infection rate was reduced to 0%. This highlights the important role of local prophylactic antibiotics during ligament reconstruction, which has been demonstrated in other orthopaedic procedures^[30]. An alternative method of irrigating knee joints with a solution containing gentamycin was tested in a randomized control trial by Yazdi *et al*^[31], but found to have no significant impact on infection rates.

The main weakness of this systematic review was the small number of studies that directly compared patients receiving antibiotic prophylaxis in arthroscopy to controls. Also, even in simple arthroscopic procedures without grafts, there may be many variations that affect infection risk (e.g., type of meniscal repair, whether additional incisions were made as in for an inside-out approach, etc.). Furthermore, our findings with regards to simple arthroscopy are largely dominated by one study. Three of the four studies used in the pooled analysis were multi-surgeon retrospective cohort studies and criteria for determining which patients received prophylactic antibiotics was left to individual surgeon discretion. The controlled trial performed by Ghnaimat *et al*^[16] only semi-randomized antibiotic prophylaxis by allotting according to admission number (even admission numbers received antibiotics). Additional studies are needed to better understand the role antibiotic prophylaxis plays in the development of septic arthritis. Being able to identify procedures and patient groups that do not require antibiotic prophylaxis offers the potential to reduce hospital costs, reduce the risk of allergic reaction to medication, and slow the development of drug resistant organisms. Thus, further study of this topic is

warranted.

Our study is the first to demonstrate prophylactic antibiotics are effective in preventing septic arthritis following simple arthroscopic procedures of the knee, though given the large number needed to treat, the clinical significance of this finding is unclear. Our findings regarding the addition of graft soaking indicate that further steps can be taken to reduce the rate of infection in procedures involving graft implantation. Further studies are needed to better understand when withholding prophylaxis may be appropriate.

ARTICLE HIGHLIGHTS

Research background

The administration of prophylactic antibiotics prior to knee arthroscopy is a common practice in the orthopaedic community.

Research motivation

There are no studies to date that demonstrate that the use of antibiotic prophylaxis in arthroscopic surgery of the knee is effective.

Research objectives

The purpose of this study is to analyze the literature on the effect on antibiotic prophylaxis in knee arthroscopy on rates of septic arthritis.

Research methods

We conducted a literature review of PubMed, MEDLINE, and Web of Science from inception to May of 2018. Data from studies meeting inclusion criteria were pooled for analysis. Risk-ratios were calculated to determine the effect of antibiotic prophylaxis on rates of septic arthritis in knee arthroscopy.

Research results

Nineteen studies met inclusion criteria for pooled analysis. For those not undergoing graft procedures, there were 27 cases of post-operative septic arthritis in 34487 patients (0.08%) who received prophylactic antibiotics and 16 cases in 10911 (0.15%) who received none [risk ratio (RR) = 0.53, 95% confidence interval (CI): 0.29-0.99, $P = 0.05$]. A sub-group analysis in which bony procedures were excluded was performed which found no significant difference in infection rates between patients that received prophylactic antibiotics and patients that did not ($P > 0.05$). All ACL reconstruction studies used prophylactic antibiotics, but two studies investigating the effect of soaking the graft in vancomycin in addition to standard intravenous (IV) prophylaxis were combined for analysis. There were 19 cases in 1095 patients (1.74%) who received IV antibiotics alone and no infections in 2,034 patients who received IV antibiotics and had a vancomycin soaked graft (RR = 0.01, 95%CI: 0.001-0.229, $P < 0.01$).

Research conclusions

Our study is the first to demonstrate prophylactic antibiotics are effective in preventing septic arthritis following simple arthroscopic procedures of the knee, though given the large number needed to treat, the clinical significance of this finding is unclear. Our literature search demonstrates that there is little to no debate that antibiotics should be used prophylactically for arthroscopic surgeries involving graft implantation. However, our findings indicate that the addition of graft soaking further reduces the rate of infection.

Research perspectives

Further prospective studies on this topic will help further elucidate this conclusion.

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Analysis of a ten step protocol to decrease postoperative spinal wound infections

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Abstract

AIM

To define a ten-step protocol that reduced the incidence of surgical site infection in the spine surgery practice of the senior author and evaluate the support for each step based on current literature.

METHODS

In response to unexplained increased infection rates at our institution following spine surgery, a ten-step protocol was implemented: (1) preoperative glycemic management based on hemoglobin A1c (HbA1c); (2) skin site preoperative preparation with 2% chlorhexidine gluconate disposable cloths; (3) limit operating room traffic; (4) cut the number of personnel in the room to the minimum required; (5) absolutely no flash sterilization of equipment; (6) double-gloving with frequent changing of outer gloves; (7) local application of vancomycin powder; (8) re-dosing antibiotic every 4 h for prolonged procedures and extending postoperative coverage to 72 h for high-risk patients; (9) irrigation of subcutaneous tissue with diluted povidone-iodine solution after deep fascial closure; and (10) use of DuraPrep skin preparation at the end of a case before skin closure. Through an extensive literature review, the current data available for each of the ten steps was evaluated.

RESULTS

Use of vancomycin powder in surgical wounds, routine irrigation of surgical site, and frequent changing of surgical gloves are strongly supported by the literature. Preoperative skin preparation with chlorhexidine wipes is similarly supported. The majority of current literature supports control of HbA1c preoperatively to reduce risk of infection. Limiting the use of flash sterilization is supported, but has not been evaluated in spine-specific surgery. Limiting OR traffic and number of personnel in the OR are supported although without level 1 evidence. Prolonged use of antibiotics postoperatively

is not supported by the literature. Intraoperative use of DuraPrep prior to skin closure is not yet explored.

CONCLUSION

The ten-step protocol defined herein has significantly helped in decreasing surgical site infection rate. Several of the steps have already been shown in the literature to have significant effect on infection rates. As several measures are required to prevent infection, instituting a standard protocol for all the described steps appears beneficial.

Key words: Wound infections; Spine; Ten step protocol; Surgical site infections

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Core tip: The rates of infection following spine surgery have been reported to range from less than 1% to 10.9% depending on the type of case. Several factors have been identified as risk for surgical site infection. In response to an increasing number of surgical site infections at the authors' institution, a new surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source. Institution of this bundle returned surgical site infection rates to historic level of < 1%.

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INTRODUCTION

Surgical site infection in spinal surgery is associated with significantly increased morbidity and costs^[1]. Surgical site infections (SSIs) are the most common hospital acquired infections and are usually seen in the early postoperative period^[2]. The rates of infection following spine surgery have been reported to range from less than 1% to 10.9% depending on the type of case^[3].

A variety of measures have been initiated and evaluated in the literature to reduce the occurrence of SSIs. The surgical setting is a multi-faceted environment with numerous variables and control of all risk factors associated with infection can be challenging. In addition to identifying and eliminating known factors, prophylactic treatments are available to help reduce the overall incidence of surgical site infection. Patient risk factors and prophylactic measures have often been evaluated separately, but evaluation of risk factors and interventions as a bundle may be a more appropriate approach given the dynamic environment of the surgical suite.

In response to an increasing number of SSIs at the

authors' institution, a new surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source. In addition to standard perioperative intravenous antibiotics (within 1 h preoperative administration with continuation for 24 h) and sterile operating preparation, a new 10 step protocol was instituted after extensive review of surgical and infection control literature as well as consultation with spine, total joint surgeons in the authors' and other institutions in addition to input from division of infection disease. The postoperative SSI rate in the period preceding the implementation of the ten-step protocol climbed to 10%. Institution of this bundle returned SSI rates to historic level of < 1%. The purpose of this paper is to present this protocol with an overview and evaluation of the literature for validity of each of step.

Briefly, this "Ten Step" surgical bundle is as follow: (1) preoperative glycemic management based on hemoglobin A1c (HbA1c); (2) skin site preoperative preparation the night before surgery and in the preoperative suite with disposable cloths moistened with 2% chlorhexidine gluconate (CHG) antiseptic solution; (3) limitation of operating room traffic by closure of the front door of the room with tape once the patient is in the room and until wound closure. The door through the sterile core remains available if needed; (4) decreasing the number of personnel in the room to the minimum required; (5) absolutely no flash sterilization of equipment; (6) double-gloving with frequent changing of outer gloves for the surgeon, assistant and scrub nurse throughout the case and after any step that may contaminate the gloves; (7) vancomycin powder mixed in with bone graft and applied locally to the wound after fascial closing; (8) antibiotic re-dosing every 4 h for prolonged procedures and extending postoperative coverage to 72 h for high-risk patients; (9) irrigation of the wound with diluted povidone-iodine solution; and (10) use of DuraPrep skin preparation at the end of a case to clean the skin before skin closure.

MATERIALS AND METHODS

A systematic computerized Medline literature search was performed using Pubmed. The electronic databases were searched from 1990 to October 2014. Searches were performed using the terms "surgical site infection" in conjunction with each of the following sets of terms; "spine," "hemoglobin A1c," "glycemic control," "skin preparation," "DuraPrep," "chlorhexidine cloths," "operating room traffic," "door opening," "flash sterilization," "double gloving," "glove exchange," "vancomycin powder," "postoperative antibiotics," and "wound irrigation." Abstracts were reviewed for content. Articles that included the use of one of the 10 aforementioned steps with associated outcomes for SSIs were included in the review. Where substantial information was available for a specific protocol step, only articles following outcomes for spine specific

surgeries were included. If no results for spine surgery were available on a topic, the available literature across surgical specialties was reviewed. Each manuscript was evaluated for level of evidence, number of patients included, outcome and, statistical significance.

RESULTS

Preoperative glycemic management based on HbA1c

Decreasing postoperative infection rates begins during the preoperative evaluation with the identification of patients at increased risk for infection. Diabetes mellitus is a well-known independent risk factor for SSIs. Approximately 25% of patients with diabetes are unaware that they have diabetes, which highlights the need for careful preoperative testing^[4]. HbA1c provides a good marker of a patient overall glucose management over a 2-3 mo period. An elevation in HbA1c identifies those patients with more chronic hyperglycemia and is an important indicator of poor glucose control. If HbA1c is related to risk of infection, it may represent a modifiable factor prior to proceeding with elective surgery.

The initial reports on the effects of elevated HbA1c were in the field of urology. In 1992, Bishop *et al*^[5] prospectively evaluated the influence of HbA1c on SSIs in 90 patients receiving penile implants. They found a significantly increased rate of SSI in diabetics with HbA1c greater than 11.5%. The authors recommended denying elective surgery to patients with HbA1c > 11.5% which was subsequently adopted as the standard of care. However, Wilson *et al*^[6] refuted the findings in 1998 after following 389 patients with the same surgery in which they failed to find a significant increase in infection rates with elevated HbA1c.

Since that time, there has been only slight variability in the surgical literature. Although Latham *et al*^[7] found no association between SSI and HbA1c, several other studies have found a significantly increased risk of SSIs with elevated preoperative HbA1c^[8-13]. Still others found an increased rate of infection with high HbA1c but were unable to achieve significance. Rawlins *et al*^[14] evaluated diabetics undergoing Roux-en-Y gastric bypass and Knapik *et al*^[15] looked at those having coronary artery surgery. Both found elevated rates of infection with HbA1c $\geq 7.0\%$ but did not reach statistical significance.

Several studies have been published in the orthopaedic literature since 2009 evaluating the effect of HbA1c on surgical outcomes (Table 1)^[16-23]. Many of these studies focus on total joint arthroplasty. Marchant *et al*^[16] performed the largest study by utilizing the Nationwide Inpatient Sample (NIS) database in which glycemic control and outcomes after total joint arthroplasty for over 1 million patients was evaluated. The sheer population size gave the study the power to detect small differences. Among other findings, they found a significantly increased rate of postoperative infections in diabetics with HbA1c $\geq 7.0\%$ compared

to either patients without diabetes or diabetics with HbA1c < 7.0%. Iorio *et al*^[17] and Jämsen *et al*^[18] came to a similar conclusion using a smaller group. Myers *et al*^[19] also found increased rates of infection with HbA1c > 7 in patients undergoing ankle and hindfoot fusions. Lamloum *et al*^[20] retrospectively reviewed all orthopaedic procedures in their hospital and found a slightly increased infection rate without statistical significance with HbA1c $\geq 7.0\%$. Adams *et al*^[21] and Harris *et al*^[22] similarly evaluated HbA1c and infection rate in total joint arthroplasty and found no significant association, although Harris did find an increased overall rate of complications in patients with uncontrolled diabetes.

Specific to effects of HbA1c in spine surgery, Hikata *et al*^[23] retrospectively reviewed the results of elective posterior instrumented thoracic and lumbar arthrodesis in 345 consecutive patients. Thirty-six of these patients had preexisting diabetes with preoperative HbA1c values available. In these patients, the presence of diabetes and diabetics with HbA1c ≥ 7.0 were both independent risk factors for surgical site infection. Although not looking specifically at infections, Takahashi *et al*^[24] reviewed functional results after lumbar surgery in patients and found that patients with HbA1c $\geq 6.5\%$ showed poor improvement in low back pain.

Preoperative skin preparation with CHG cloths

During the preoperative clinic appointment, each patient is given a preoperative skin preparation kit and written instructions for use. The skin preparation is done with disposable cloths moistened with a rinse-free, 2% CHG antiseptic solution. The patient is instructed to shower one hour prior to prepping, then wash with the cloths. The skin is then prepped again with a second set of cloths in the preoperative holding area. The goal of the preoperative preparation is to decrease bacterial colonization.

It has been shown that preoperative cleansing the night before surgery and the morning of with CHG decreases the bacterial colonization on the skin. Murray *et al*^[25] found that 66% of patients were colonized with microbes after prepping with CHG compared to 94% for those who showered alone preoperatively.

The data supporting the effectiveness of CHG preparation is based heavily on cohort studies. Johnson *et al*^[26] performed a cohort study comparing infection rates in patients who performed CHG preoperative prepping the night before surgery and in the preoperative area, and those who were noncompliant with prepping. They found no infections in the compliant CHG group, and 14 (1.6%) infections in the non-compliant group. Similarly, Zywił *et al*^[27] compared compliant, partially compliant, and non-compliant patients with regard to CHG preparation. They found no infections in the group that appropriately prepared with CHG, 1 (1.5%) infections in the partial compliance group, and 21 (3%) in the noncompliant group.

Table 1 Studies from orthopedic literature evaluating preoperative hemoglobin A1c and surgical site infections

Ref.	Study design (level of evidence)	Surgery performed	Groups	Main outcome	Significance
Hikata <i>et al</i> ^[23] (2013)	Retrospective cohort (IV)	Adult elective posterior instrumented thoracic and lumbar spinal arthrodesis	Non-diabetics ($n = 309$), Controlled diabetics ($\text{HbA1c} < 7.0$; $n = 19$), Uncontrolled diabetics ($\text{HbA1c} \geq 7.0$; $n = 17$)	10 (3.2%) SSI in non-diabetic group, No SSI in controlled diabetic group, 6 (35.3%) SSIs in uncontrolled diabetic group	Diabetes was an independent risk factor for SSI ($P = 0.0005$), Significantly higher rate of infection in diabetics with $\text{HbA1c} \geq 7.0$ ($P = 0.006$)
Adams <i>et al</i> ^[21] (2013)	Retrospective cohort (II)	Primary total knee arthroplasty	Non-diabetics ($n = 32924$), Controlled diabetics ($\text{HbA1c} < 7.0$; $n = 5042$), Uncontrolled diabetics ($\text{HbA1c} \geq 7.0$; $n = 2525$)	216 (0.7%) deep infections in non-diabetics, 58 (1.2%) in controlled diabetics, and 13 (0.5%) in uncontrolled diabetics	No significant association between HbA1c level and deep infection
Harris <i>et al</i> ^[22] (2013)	Retrospective cohort (IV)	Total joint arthroplasty	Controlled diabetics ($\text{HbA1c} < 7.0$; $n = 3961$), Uncontrolled diabetics ($\text{HbA1c} \geq 7.0$; $n = 2127$)	Identical percentage of patients in both groups developed superficial and deep infections	Significant increase in overall complications ($P = 0.028$), but not infections, for diabetics with $\text{HbA1c} \geq 7.0$
Iorio <i>et al</i> ^[17] (2012)	Retrospective cohort (IV)	Primary or revision total hip or knee arthroplasty	Controlled diabetics ($\text{HbA1c} < 7.0$; $n = 191$), Uncontrolled diabetics ($\text{HbA1c} \geq 7.0$; $n = 85$)	5 (2.6%) infections in controlled diabetics, 5 (5.9%) infections in uncontrolled diabetics	Increased rate of infections in uncontrolled diabetics without statistical significance ($P = 0.293$)
Myers <i>et al</i> ^[19] (2012)	Retrospective cohort (III)	Ankle and hindfoot fusions	Non-diabetics ($n = 74$), Controlled diabetics ($\text{HbA1c} < 7.0$; $n = 30$), Uncontrolled diabetics ($\text{HbA1c} \geq 7.0$; $n = 44$)	1 (1.4%) SSI in non-diabetics, 2 (6.7%) SSI in controlled diabetics, 12 (27.3%) SSI in uncontrolled diabetics	Significantly higher rate of SSI in uncontrolled vs controlled diabetics ($P < 0.05$)
Jämsen <i>et al</i> ^[18] (2010)	Retrospective cohort (IV)	Primary total knee arthroplasty	Patients with $\text{HbA1c} < 6.5$ ($n = 205$), Patients with $\text{HbA1c} \geq 6.5$ ($n = 176$)	No infections in patients with $\text{HbA1c} < 6.5$, 5 infections in patients with $\text{HbA1c} \geq 6.5$ (2.84%)	Significant increase in infection rate in patients with $\text{HbA1c} \geq 6.5$ ($P = 0.015$)
Lamloum <i>et al</i> ^[20] (2009)	Retrospective cohort (IV)	Any orthopaedic surgical procedure	Controlled diabetics ($\text{HbA1c} < 7.0$; $n = 80$), Uncontrolled diabetics ($\text{HbA1c} \geq 7.0$; $n = 238$)	10 SSIs in controlled diabetics (12.5%), 33 SSIs in uncontrolled diabetics (13.9%)	No significant difference in SSI occurrence between the two groups ($P > 0.05$)
Marchant <i>et al</i> ^[16] (2009)	Retrospective cohort (III)	Total joint arthroplasty	Non-diabetics ($n = 92055$), Controlled diabetics ($\text{HbA1c} < 7.0$; $n = 105485$), Uncontrolled diabetics ($\text{HbA1c} \geq 7.0$; $n = 3973$)	3807 (0.41%) non-diabetics with infection, 405 (0.38%) controlled diabetics with infection, 47 (1.18%) uncontrolled diabetics with infection	Uncontrolled diabetics had a statistically significant increased rate of infection compared to patients without or with controlled diabetes ($P = 0.002$)

HbA1c: Hemoglobin A1C; SSI: Surgical site infections.

Veiga *et al*^[28] conducted a randomized controlled trial to assess the effect of preoperative chlorhexidine showers on skin colonization and postoperative infection rates associated with plastic surgical procedures involving the trunk. Chlorhexidine showers were effective in reducing skin colonization with coagulase-negative staphylococci and yeasts, but there was no difference in postoperative infection rates. Two systematic reviews evaluated the clinical effectiveness of preoperative skin antiseptic preparations and the prevention of SSIs^[29,30]. Kamel *et al*^[29] reviewed 20 studies and concluded that the evidence suggests that preoperative antiseptic showers reduce bacterial colonization and may be effective at preventing SSIs. Webster and Osborne^[30] additionally reviewed 3 studies that included 7791 participants comparing CHG cloth bathing vs placebo. In their systemic review, they concluded that there is no

statistically significant benefit for preoperative showering or bathing with chlorhexidine over other wash products to reduce surgical site infection.

Limiting operative room traffic

One of the strategies implemented in this bundle to decrease SSIs involved limiting traffic in the operating room. In order to achieve this, the front door to the operating room is taped off once the patient is in the room. Only necessary door openings were performed, all of which occurred through the sterile core rather than the main operating room door.

An operating room is an isolated environment designed to recirculate air through filtered ventilation ducts. Frequent opening of the operating room door has been shown to disrupt this airflow system^[31,32]. Scaltriti *et al*^[32] studied the air quality in the operating room and

compared this with multiple parameters. They found that increased door openings and personnel changes were a positive predictor of raised bacterial counts in a room. Ritter similarly found a correlation between number of operating door openings and increased colony forming unit (CFU) counts in the operating room^[33].

In addition to affecting the air quality, door openings and increased traffic have been identified as major surgical distractors. Using an observational tool to record distraction and interruption in the operating room, Healey *et al.*^[34] found that interference levels significantly correlated with frequency of door openings. In addition unwanted distractions may lead to mistakes beyond just SSIs.

In response to an unexplained increase in SSIs at one institution, Lynch *et al.*^[35] studied operating room foot traffic. They found that their spinal fusion cases had the highest rate of door openings at 50 per hour. Additionally, when investigating the reasons for door openings, they found the most common reason for door openings was to request information from outside the room, which could feasibly be done *via* telephone or other electronic means.

In an attempt to evaluate the risk to the patient, Young and O'Reagan^[36] performed a prospective cross-sectional study in forty-six consecutive cardiac operations. An electronic door counter calculated the frequencies and rates of door openings during each surgery. Everyone was blinded to the counters except the practicing surgeons. They showed a trend toward an increased frequency of door openings per case in those patients that developed a surgical site infection vs those who had not. However, the difference did not achieve statistical significance. Additionally, there was a positive correlation between length of case and frequency of door opening.

Limit number of personnel in the operative room

Spine surgery, much like any other surgery, requires a multidisciplinary effort. In light of that fact, there is often a considerable number of people in the operating room at any given time, the attending surgeon, resident or surgical assistant, anesthesia team, surgical scrub technician, circulating nurse, radiology technician, technician for neurological monitoring, and oftentimes an equipment representative. At a teaching hospital, there is the potential for a student in the room at any of these positions as well.

Pryor *et al.*^[37] attempted to find an association between surgical site infection and increased number of personnel in the operating room. Although there was an association of increased surgical site infection with the number of people in the OR, the results were not statistically significant. The increased number of people was also associated with length of the case.

In a prognostic level III evidence study, Olsen *et al.*^[38] found that one of the factors that was significantly associated with an increased risk of surgical site in-

fection during spinal operations was the participation by two or more surgical residents. As suggested by the author, this was likely a proxy for the duration and complexity of the procedure rather than a direct cause for infection.

Although not yet clearly demonstrated, an increasing number of people present in the operating room may increase the risk of contamination and subsequently increased surgical site infection. With that in mind the authors have made efforts to limit the number of people in the operating room to the minimum. The minimum staff present includes the attending surgeon and assistant, surgical technician, anesthesiologist, nurse circulator, radiology technician, equipment representative, and spinal cord monitoring technician. In a teaching hospital reducing the number of the students in the room can be a challenge. However, in the authors' current protocol, no more than one student of any kind (medical, nursing, radiologist, or anesthesia) is allowed in the room. These practices require further evaluation for their effectiveness.

No flash sterilization of surgical equipment

Instrument reprocessing technique plays a vital role in maintaining a sterile surgery. Flash sterilization has often been utilized in order to turn over equipment quickly when additional sterile equipment is unavailable. As part of our policy, absolutely no flash sterilization may be used in spine surgery. An adequate number of sterile surgical trays are on the shelf prior to surgery to avoid any flash sterilization.

From the International Conference on Healthcare-Associated Infections, Lopansri *et al.*^[39] demonstrated their experience with SSIs and sterilization techniques. They identified 14 cases of surgical site infection after arthroscopy over a 21 mo span. Thirteen of the infections were from an individual surgeon, representing a 2.4% infection rate, while 8 other surgeons had a total of 1 infection in the same span, representing an infection rate of 0.06%. The surgeon with the larger infection rate was the only one whose equipment underwent flash sterilization. Additionally, this same surgeon operated at a separate facility that did not use flash sterilization and experienced an infection rate of 0.3% over a 4-year span. This represented a relative risk for infection after arthroscopy of 6.7 for this individual surgeon while working at a facility that used flash sterilization as opposed to one that did not.

Tosh *et al.*^[40] explored an outbreak of pseudomonas aeruginosa SSIs after arthroscopic procedures. In this retrospective case-control study, there were 7 patients with surgical site infection after arthroscopy with isolates that were indistinguishable from each other. On endoscopic examination of equipment that was flash sterilized during these cases, residual tissue was seen in the lumens of the arthroscopic equipment.

Although available literature on flash sterilization and the primary outcome of surgical site infection is

limited, it can be identified as a possible avoidable cause of infection. To our knowledge, there is no literature available evaluating the use of flash sterilization in spine surgery. Additional investigations as to the benefit of reducing utilization of flash sterilization may be of benefit.

Frequent changing of surgical gloves

It is vital to attempt to maintain a completely sterile environment in the surgical field. An important factor in surgery, which can easily transmit bacteria, is the surgical glove. Instituting a policy of double gloving with frequent changes of the outer gloves may assist in decreasing surgical infection rates. In the authors' current protocol, the surgeon, assistant, and scrub nurse change their outer gloves after steps that may contaminate the gloves such as after draping the patient and using the surgical microscope. The policy also includes changing the outer gloves prior to instrumentation and before closure.

Ritter *et al.*^[41] reported that contamination of outer gloves is common among all scrubbed personnel and occurs at a rate of 33%. It has been shown by McCue^[42] in a study evaluating frequent outer glove changes in total hip arthroplasties that gloves used at draping were the most frequently contaminated. This highlighted the draping portion as an important step for glove changes.

Ward *et al.*^[43] performed an experiment to determine risk of bacterial contamination associated with changing gloves with 251 prospectively randomized surgical team members in 142 cases in which all members were double gloved. Cultures were taken from the dominant palms at 1 h into the case at which time selected randomized individuals changed their outer gloves. A repeat culture was taken from the dominant palm 15 min later. They found a significant decrease in the number of positive cultures for the group exchanging their gloves ($P = 0.0419$). This represented nearly 2 times greater odds of being contaminated if gloves were not exchanged. However, they did not assess subsequent infection rates.

Although several studies have been published on various double gloving techniques and rates of perforation, there is very little literature on changing of gloves and the primary outcome, SSIs. Rehman *et al.*^[44] in a retrospective cohort study, compared infection rates in two groups undergoing lumbar spine fusion. The control group of 179 patients underwent surgery with the standard surgical protocol and the treatment group of 210 patients, after double gloving, the outer gloves were removed prior to instrumentation. They found a significantly decreased infection rate at 1 year postoperatively when outer gloves were removed in this manner (3.35% in control vs 0.48% in treatment; $P = 0.0369$). Additional investigations to back up this data may be beneficial as this may be a simple and cost effective step in reducing surgical infections.

Local application of vancomycin powder

The use of antibiotics has been very important in decreasing the rates of infection. Administration of systemic intravenous antibiotics perioperatively is standard^[45]. Additionally, topical vancomycin powder has recently been evaluated in the literature. Vancomycin powder has a slow resorption rate which provides a very low rate of systemic effects and excellent local coverage against the common gram positive bacteria associated with surgical site infection, with no evidence of local or systemic toxicity^[46].

The authors' protocol for the use of vancomycin powder is two-fold. When performing a fusion surgery, 1 g of vancomycin powder is mixed in with the bone graft before placement. Additionally, after closure of the deep fascia, another 1 g of vancomycin powder is applied directly onto the surgical wound and subcutaneous tissue prior to skin closure.

Sweet *et al.*^[46] first reported the benefits of using vancomycin powder during spine surgery. They performed a retrospective cohort study on a consecutive series of patients undergoing posterior instrumented thoracic and lumbar spine surgery. This study looked at a total of 1732 patients, 911 of which received 2 g of vancomycin powder, in the protocol listed dose, one gram was mixed with bone graft and 1 g was applied directly to the surgical wound. There was a statistically significant reduction in infection rate in those treated with vancomycin powder and intravenous prophylaxis as compared to intravenous antibiotic prophylaxis alone (0.2% vs 2.6%; $P < 0.0001$).

Fourteen studies were identified that evaluated post-operative infection rates and the use of topical vancomycin powder intraoperatively during spine surgery (Table 2)^[46-59]. Surgical site infection rates in these studies ranged from 0%-6.7%. Of these studies, 11 included a control group in which no vancomycin powder was applied. All groups in all of these studies received standard preoperative intravenous antibiotic prophylaxis. Infection rates without the use of vancomycin powder ranged from 1.2%-13%. The vast majority of these studies showed a significant decrease in overall infection rate when using vancomycin powder in addition to standard preoperative IV prophylaxis.

Kanj *et al.*^[60] evaluated vancomycin prophylaxis at the surgical site in clean orthopaedic surgery. Several of the studies reviewed here were included in their analysis^[46,47,49,54]. Specific to spine surgery, they calculated that a patient is 4 times more likely to develop a deep infection without vancomycin powder prophylaxis than with ($P < 0.001$).

As outlined above, there is an extensive amount of literature available on the use of vancomycin powder for infection prophylaxis in surgical wounds. The majority of the evidence points toward vancomycin powder as a significant factor in reducing SSIs.

Table 2 Studies evaluating the use of vancomycin powder intraoperatively

Ref.	Study design (level of evidence)	Surgery performed	Groups	Main outcome	Significance
Chobrial <i>et al</i> ^[56] (2014)	Retrospective case series (IV)	Spinal procedures for degenerative disease, trauma, pain and scoliosis	Vancomycin powder (range from 1-6 g) applied to subfascial and epifascial layers but not to bone graft (<i>n</i> = 981)	66 infections identified (6.7%) A number of gram-negative infections were encountered	Vancomycin may increase the incidence of gram-negative or polymicrobial spinal infections
Hill <i>et al</i> ^[55] (2014)	Retrospective cohort (III)	Instrumented or non-instrumented posterior spine surgery in adults	Patients receiving 1-2 g vancomycin powder in surgical bed (<i>n</i> = 150), No vancomycin powder (<i>n</i> = 150)	5 superficial infections in vancomycin powder group (3.3%), 5 superficial and 6 deep infections in control group (7.3%)	Significantly fewer deep infections in patients treated with vancomycin powder (<i>P</i> = 0.0297)
Theologis <i>et al</i> ^[50] (2014)	Retrospective cohort (III)	Complex adult spinal deformity reconstruction	Patients receiving 1-2 g vancomycin powder in subfascial space (<i>n</i> = 151), No vancomycin powder (<i>n</i> = 64)	4 infections in first 90 d in treatment group (2.6%), 7 infections in first 90 d in control (10.9%)	Significantly fewer hospital readmissions within 90 d of surgery when using vancomycin powder (<i>P</i> = 0.01)
Caroom <i>et al</i> ^[49] (2013)	Retrospective comparative study of prospectively collected data (II)	Multilevel posterior decompression and instrumentation for cervical spondylitic myelopathy	1 g vancomycin powder applied subfascially along bone graft and instrumentation (<i>n</i> = 40), No vancomycin powder (<i>n</i> = 72)	Zero infections in vancomycin powder group (0%), 11 infections in control (15%)	Significant decrease in infection rate with use of vancomycin powder (<i>P</i> = 0.007)
Gans <i>et al</i> ^[58] (2013)	Therapeutic retrospective cohort (II)	Pediatric spinal deformity surgery (fusion, growing rods, vertical expandable prosthetic titanium rib)	Patients received 1g vancomycin powder in surgical wound (<i>n</i> = 87)	3 surgical site infections identified (3.4%) The postoperative systemic vancomycin levels remained undetectable. None of the patients experienced nephrotoxicity or red man syndrome	Local application of vancomycin powder is safe without significant changes in creatinine level or systemic vancomycin level
Kim <i>et al</i> ^[57] (2013)	Retrospective cohort (IV)	Instrumented spinal fusion	Patients receiving 1 g vancomycin powder in surgical wound (<i>n</i> = 34), No vancomycin powder (<i>n</i> = 40)	Zero infections in vancomycin powder group (0%)	Significant decrease in infection rate with use of vancomycin powder (<i>P</i> < 0.033)
Martin <i>et al</i> ^[53] (2013)	Retrospective cohort (II)	Adult posterior thoracolumbar or lumbar instrumented fusion for spinal deformity	Patients receiving 2 g vancomycin powder in surgical wound (<i>n</i> = 156), No vancomycin powder (<i>n</i> = 150)	5 infections in control (12.5%), 8 infections in vancomycin powder group (5.1%), 8 infections in control (5.3%)	No significant difference in infection rate with use of vancomycin powder (<i>P</i> = 0.944)
Pahys <i>et al</i> ^[50] (2013)	Therapeutic retrospective cohort (II)	Posterior cervical spine surgery	Group 1: Perioperative antibiotics alone (<i>n</i> = 483), Group 2: addition of alcohol foam prep and drain (<i>n</i> = 323), Group 3: group 2 plus vancomycin powder in wound (<i>n</i> = 195)	9 infections in group 1 (1.86%), 1 infection in group 2 (0.3%), No infections in group 3 (0%)	Significant decrease in infections in both group 2 (<i>P</i> = 0.047) and group 3 (<i>P</i> = 0.048) compared to group 1
Strom <i>et al</i> ^[48] (2013)	Retrospective cohort (IV)	Instrumented and non-instrumented posterior lumbar laminectomy and fusion	Patients receiving 1 g vancomycin powder in surgical wound (<i>n</i> = 156), No vancomycin powder (<i>n</i> = 97)	Zero infections in vancomycin powder group (0%), 11 infections in control (11%)	Significant decrease in infection rate with use of vancomycin powder (<i>P</i> = 0.000018)
Strom <i>et al</i> ^[51] (2013)	Retrospective cohort (IV)	Posterior cervical fusion	Patients receiving 1 g vancomycin powder in surgical wound (<i>n</i> = 79), No vancomycin powder (<i>n</i> = 92)	2 infections in vancomycin powder group (2.5%), 10 infections in control (10.9%)	Significant decrease in infection rate with use of vancomycin powder (<i>P</i> = 0.0384)
Tubaki <i>et al</i> ^[52] (2013)	Prospective randomized controlled trial (II)	Any primary spine surgery excluding biopsy or minimally invasive procedure	Patients receiving 1 g vancomycin powder in surgical wound (<i>n</i> = 433), No vancomycin powder (<i>n</i> = 474)	7 infections in vancomycin powder group (1.61%), 8 infections in control (1.68%)	No significant difference in infection rate with use of vancomycin powder
Molinari <i>et al</i> ^[54] (2012)	Retrospective case series (IV)	Any spine surgery	Patients receiving 1 g vancomycin powder in surgical wound (<i>n</i> = 1512)	Fifteen infections identified (0.99%)	Low rate of deep spinal wound infection for both instrumented and uninstrumented cases

Sweet <i>et al</i> ^[46] (2011)	Retrospective cohort (IV)	Thoracic or lumbar posterior instrumented fusion	Patients receiving 1 g vancomycin powder in bone graft and 1 g applied directly to deep and superficial wound (<i>n</i> = 911).	Two infections in vancomycin powder group (0.2%), Twenty-one infection in control (2.6%)	Significant decrease in infection rate with use of vancomycin powder (<i>P</i> < 0.0001)
O'Neill <i>et al</i> ^[47] (2011)	Retrospective cohort (IV)	Instrumented posterior spine fusion for traumatic injury	No vancomycin powder (<i>n</i> = 821) Patients receiving 1 g vancomycin powder in surgical wound (<i>n</i> = 54), No vancomycin powder (<i>n</i> = 56)	Zero infections in vancomycin powder group (0%), Seven infections in control (13%)	Significant decrease in infection rate with use of vancomycin powder (<i>P</i> = 0.02)

Re-dosing and prolonged postoperative antibiotic course

It is standard for all of our patients undergoing surgery to receive a dose of 1-2 g of cefazolin and 1-2 g vancomycin intravenous within 1 h of incision, depending on patient weight and allergies. This is in accordance with recommendations from the North American Spine Society^[45]. For short, uncomplicated cases, no additional IV antibiotics are required. In various studies, length of surgery has been associated with surgical site infection rate. For that reason, prolonged cases are re-dosed with antibiotics at 4-h intervals during surgery. Additionally, it is the authors' protocol to extend antibiotic coverage with either cefazolin or vancomycin for a full 72 h in high-risk patients. High-risk patients include diabetics, obese patients (body mass index > 30), history of previous postoperative wound infection, complex revision or deformity surgeries lasting more than 6 h.

Little data has been published on extended postoperative antibiotic prophylaxis in spine surgery. Two studies to our knowledge have explored the effects. Ohtori *et al*^[61] in a comparative cohort study evaluated two statistically similar groups undergoing lumbar spine decompression and fusion. Group 1 received 2 d of postoperative IV antibiotics, and group 2 received 9 d IV antibiotics. There was one infection in group 1 (1/70) and no infections in group 2 (0/65), but these results were not significant. The only significant findings were that longer courses of antibiotics resulted in longer hospital stays and longer time to normalize body temperature after surgery.

In a separate retrospective cohort study, Takahashi *et al*^[62] evaluated 4 different prophylaxis measures. One group had 7 d of postoperative antibiotics and no preoperative antibiotic (group 1). The remaining 3 groups all received appropriate preoperative antibiotics as well as postoperative antibiotics for 4 d (group 2), 2 d (group 3), or 1 d postoperatively (group 4). Groups 1, 2, 3 and 4 saw infection rates of 2.6% (14/539), 0.9% (5/536), 0% (0/257) and 0% (0/83) respectively. Although this showed an increase in infection rate with shorter antibiotic duration, there were significant differences among the groups with regard to age, preoperative hospitalization duration, and proportion of patients considered to be compromised hosts.

At this time, current evidence-based guidelines from the North American Spine Society only state that prolonged regimens may be considered when significant comorbidities or complex situations exist^[45]. Comorbidities and complex situations considered applicable include obesity, diabetes, neurologic deficits, incontinence, preoperative serum glucose of > 125 mg/dL or a postoperative serum glucose level of > 200 mg/dL, trauma and prolonged multilevel instrumented surgery. A randomized prospective analysis of postoperative prophylactic antibiotic duration and surgical site infection rate may provide better evidence. The current recommendations additionally provide for repeated dosing of antibiotics intraoperatively at 3-4 h intervals for prolonged cases to maintain therapeutic antibiotic levels throughout the procedure. The superiority of one drug has not been demonstrated in the literature.

Wound irrigation with diluted povidone-iodine solution

The current infection prevention protocol involves irrigation of the surgical wound with diluted povidone-iodine solution (150 mL of saline + 5 mL of betadine aqueous solution which contains 10% povidone-iodine).

Irrigation of a surgical wound is a commonplace practice prior to closure. There is limited amount of orthopedic literature directly evaluating irrigation solutions and techniques in a clean, primary surgery. Bhandari *et al*^[63] evaluated the efficacy of various irrigating solutions in removing adherent bacteria from bone in a mice model. They found that the fewest number of residual colony-forming units were found after exposure to povidone-iodine, chlorhexidine-gluconate, and soap solutions. Normal saline was the least effective. When low-pressure pulsatile lavage was added, no growth was observed after wash with soap solution, and there was near complete removal of adherent bacteria with the povidone-iodine and chlorhexidine-gluconate solutions. As it pertains to orthopaedic clinical practice, four studies were identified in whose

Table 3 Clinical orthopedic studies evaluating surgical wound irrigation before closure

Ref.	Study design (level of evidence)	Surgery performed	Groups	Main outcome	Significance
Yazdi <i>et al</i> ^[64] (2014)	Prospective randomized controlled trial (I)	Arthroscopic ACL reconstruction	Irrigation with 0.9% normal saline and 80 mg/L gentamicin (<i>n</i> = 180), Irrigation with 0.9% normal saline (<i>n</i> = 180)	One infection in gentamicin group (0.57%), Four infections in normal saline alone group (2.2%)	Decreased rate of infection when using gentamicin in irrigating solution (<i>P</i> = 0.4)
Brown <i>et al</i> ^[65] (2012)	Retrospective cohort (IV)	Primary total hip or total knee arthroplasty	Soak wound with 500 mL 0.35% povidone-iodine followed by 1 L NS pulse lavage prior to closure (<i>n</i> = 688), Pulse lavage with 1 L NS only prior to closure (<i>n</i> = 1862)	One infection in betadine group (0.15%), Eighteen infections in saline alone group (0.97%)	Significant decrease in 90-d infection rate when soaking surgical wound with betadine solution prior to closure (<i>P</i> = 0.04)
Chang <i>et al</i> ^[66] (2006)	Prospective randomized controlled trial (I)	Instrumented lumbosacral posterolateral fusion for degenerative spinal disorder with segmental instability	Wounds irrigated with 0.35% povidone-iodine (<i>n</i> = 120), Wounds irrigated with normal saline (<i>n</i> = 124)	No infections in povidone-iodine group, 4.8% infection rate in saline group	Overall infection rate was statistically significant when comparing betadine solution group with no betadine group (<i>P</i> = 0.029)
Cheng <i>et al</i> ^[67] (2005)	Prospective randomized controlled trial (I)	Spinal decompression with or without fusion	Wounds irrigated with 0.35% povidone-iodine (<i>n</i> = 208), Wounds irrigated with normal saline (<i>n</i> = 206)	No infections in povidone-iodine group, 3.5% infection rate in saline group	Overall infection rate was statistically significant when comparing betadine solution group with no betadine group (<i>P</i> = 0.007)

ACL: Anterior cruciate ligament.

main goal was measuring outcomes of irrigating surgical wounds with antimicrobial solutions and comparing to normal saline irrigation (Table 3)^[64-67].

Most notably, as it relates to spine, Chang *et al*^[66] and Cheng *et al*^[67] performed prospective randomized controlled studies comparing intraoperative wound irrigation using normal saline to 0.35% povidone-iodine solutions. Both studies found a statistically significant decrease in post-operative infections with the use of povidone-iodine solution.

Yazdi *et al*^[64] evaluated the effect of gentamicin in irrigating solutions during arthroscopic anterior cruciate ligament (ACL) reconstructions in a prospective randomized controlled study. Although infection rates were lower for the group receiving gentamicin as opposed to normal saline alone, statistical significance was not achieved.

Brown *et al*^[65] retrospectively reviewed total knee and hip arthroplasties before and after initiating a protocol to soak the surgical wound with 0.35% povidone-iodine solution prior to closure. They found a significant decrease in 90-d postoperative infection rate when using the betadine solution.

Based on these studies, it appears that there is a significant advantage for infection prophylaxis when irrigating a surgical wound with a povidone-iodine solution.

Duraprep prior to skin closure

The final intraoperative step occurs just prior to skin closure. There is often significant handling of the skin at closure, which could potentially contaminate the surgical site. As a safeguard, prior to skin closure, DuraPrep is

used over any exposed skin as a prophylactic measure.

In a level I prospective randomized study evaluating the efficacy of both ChlorPrep (2% CHG and 70% isopropyl alcohol) and DuraPrep (0.7% iodine and 74% isopropyl alcohol) in lumbar spine surgery, Savage *et al*^[68] found that both skin preparations significantly reduced bacterial flora growths after application. Cultures were taken from the skin before application, after application, and after skin closure for 100 consecutive patients randomly assigned to one of the two preparations. They found that for the ChlorPrep and DuraPrep groups, positive cultures were found, respectively, in 84% and 80% pre-preparation, 0% and 6% post-preparation, and 34% and 32% after closure. As outlined, there was a significant increase in the number of positive cultures following skin closure. It is unclear whether this is from recolonization or possibly disruption of the natural skin flora beneath the epidermis during surgery. The bio-burden on the skin at the end of a case is not the same as in the beginning. It has not been shown that this increase results in an increased rate of postoperative infection. Further studies are needed to evaluate the effectiveness of intraoperative reapplication of a skin prep solution before skin closure.

DISCUSSION

Several factors have been identified as risk for surgical site infection. Although multiple reviews have addressed these risk factors and prophylactic measures individually, it is difficult to control for and evaluate all factors affecting an individual patient. In response to an increasing number of SSIs at the authors' institution,

a new surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source. In view of the absence of a clear cause of the increased infection rate, the authors decided to implement the ten-step protocol targeting areas highlighted by the literature search. The purpose of the current study was analyzed the literature for each of the 10 steps and evaluated our own experience. As to which factor or factors affected the decreased infection rate is an area of future research.

The use of vancomycin powder has been studied extensively in the literature. We have employed the routine use of 1 g mixed in with bone graft when used and an additional 1 g spread directly over the surgical site after closure of the deep fascia. Only two of the 11 studies comparing use of vancomycin powder in spine surgery to a control failed to show a significant difference. The vast majority of the literature has found significantly lower rates of infection with routine use of vancomycin powder. Its use in spine surgery is well supported by several studies and routine use is more than acceptable.

Also strongly supported is routine irrigation of surgical wounds. Irrigation of the surgical wound has been evaluated in several surgical settings. Chang *et al*^[66] and Cheng *et al*^[67] both evaluated the use of 0.35% povidone-iodine solution irrigation in spine patients. Both studies were prospective randomized controlled studies and provided strong evidence that irrigation with 0.35% povidone-iodine significantly reduces surgical site infection in spine surgery. Also supported is the use of CHG cloths in a preoperative setting. Their use for preoperative cleansing has showed a significant reduction in skin bacterial colonization. Additionally, in a systematic review, CHG cloths have been shown to reduce the incidence of surgical site infection.

One of the measures employed in this current report is double gloving with frequent changing of outer gloves. The majority of the available literature on gloving techniques focuses on double gloving and perforation rates. It has been shown in several studies that double gloving reduces rate of perforation to the inner gloves. With respect to infection, Rehman *et al*^[44] had perhaps the most relevant study. In a retrospective study on spine fusions in which one group the surgeon removed outer gloves prior to instrumentation, there was a significant decrease in infection rates with removing outer gloves. It was also shown by Ward *et al*^[43] that changing outer gloves during a case significantly reduces contamination of gloves as seen by bacterial cultures taken from the gloves. This practice was largely adopted from reports in arthroplasty cases. Changing of the outer gloves prior to implanting total hips was shown to decrease infection rates. The routine changing of outer gloves at distinct points in a case to reduce infection is strongly supported.

HbA1c has been studied as a possible marker for increased infection risk. Although early studies identified

elevated HbA1c as a significant risk factor for infection, there has been some variation in the literature. The majority of finding point to an increased infection rate with high HbA1c, but some has found no correlation. It is possible that perioperative and intraoperative glucose levels or even absolute diabetic status are more significant. It remains to be seen if an individual's risk changes with improving their HbA1c preoperatively. The literature is lacking a level I prospective randomized study discussing the relationship between preoperative HbA1c and the risk of elective spine surgery postoperative wound infection. Ethically such a study cannot be done, as one simply cannot take a patient with poor diabetic control to an elective spine surgery. Therefore, it remains to be seen whether the postoperative spine wound infection risk changes if a diabetic is able to bring down HbA1c prior to an elective procedure. However, with the current available data, adoption of a protocol that tightly controls preoperative HbA1c to 7.0 makes sense as, in general, it improves the patient health status and may reduce the risk of postoperative wound infection.

Keeping an operating room door taped shut is an idea that has not yet been evaluated in the literature. Although Young and O'Reagan^[36] showed a trend of increased infection rate in cardiac surgery with increasing numbers of door openings, the effect of limiting traffic remains to be seen. The available studies appear to support the practice limiting the number of openings of the main operating room door in order to reduce the postoperative spine wound infection especially in a long spine cases.

Similarly, there is insufficient evidence as of yet in the literature to define the risk of surgical site infection based on number of personnel in the operating room. As seen by Olsen *et al*^[38] there was a trend towards increased number of infections based on increasing personnel in the operating room. As they pointed out though, this was likely a proxy of case length and complexity. But with the thought in mind that more people means more possibilities of contamination, it is still possible that limiting the number of personnel in the operating room can be protective against surgical site infection. This practice seems to be supported but is lacking higher level evidence.

Flash sterilization, although useful if equipment needs reprocessed quickly, may present some risk to the patient. Spine surgery deals with very durable bone and soft tissue that can potentially persist on the equipment with insufficient cleaning. Tosh *et al*^[40] showed that residual tissue was commonly seen in arthroscopic equipment under endoscopic evaluation after flash sterilization. The Fifth Decennial International Conference on Healthcare-Associated Infections identified flash sterilization as a likely source of increased infection rate at one institution. Although available literature on flash sterilization and the primary outcome of surgical site infection is limited, it can be identified as a possible avoidable cause of infection. To

our knowledge, there is no literature available evaluating the use of flash sterilization in spine surgery. Additional investigations as to the benefit of reducing utilization of flash sterilization may be of benefit to support or refute the utility of restricting its use.

The use of preoperative antibiotic prophylaxis has become an important part of infection prevention. Current recommendations additionally advise on repeated dosing every 3-4 h during prolonged cases. Extending antibiotics beyond 24 h postoperatively has been evaluated, but no level 1 evidence exists. The current literature has not shown any benefit with extended antibiotics. A prospective randomized study may better help identify if there is utility in extending antibiotics in specific patients.

The final measure explored here is use of DuraPrep on exposed skin prior to wound closure. As was shown by Savage *et al.*^[68] the use of DuraPrep significantly reduces the chances of obtaining a positive culture from the skin at the start of a case. However, cultures at the end of a case show a drastic increase in positive growth. Although it has not been evaluated in the literature, we have employed routine repeat cleansing of the skin prior to closure. It is thought that this theoretically reduces the bacterial load while closing. Since this is a time with significant handling of the skin, it is plausible that this may decrease contamination of the surgical wound and thus surgical site infection.

In conclusion, several details surrounding surgery have been evaluated in the literature as both patient risk factors and prophylactic measures for decreasing rates of SSIs. With the multivariable setting that is inherent in spine surgery, it is difficult to evaluate changes in all variables simultaneously. The authors attempted to control for 10 factors and found support in the literature for the majority of the 10 steps taken. This protocol resulted in a significant reduction in SSIs in the senior author's practice. Postoperative surgical site infection will remain a matter of concern for patients, surgeons and healthcare providers. Future prospective randomized studies that include some or all of the 10 steps discussed in this report are necessary to confirm whether the 10 steps adopted by the authors were in fact science or fiction in the battle for infection control.

ARTICLE HIGHLIGHTS

Research background

Surgical site infections (SSIs) are the most common hospital acquired infections. The rates of infection following spine surgery have been reported to range from less than 1% to 10.9%. Surgical site infection in spinal surgery is associated with significantly increased morbidity and costs.

Research motivation

In response to an increasing number of SSIs at the authors' institution, a new ten step surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source.

Research objectives

To define a ten-step protocol that reduced the incidence of surgical site infection

in the spine surgery practice of the senior author and evaluate the support for each step based on current literature.

Research methods

Ten-step protocol was implemented. (1) Preoperative glycemic management based on hemoglobin A1c (HbA1c); (2) skin site preoperative preparation with 2% chlorhexidine gluconate disposable cloths; (3) Limit operating room traffic; (4) cut the number of personnel in the room to the minimum required; (5) absolutely no flash sterilization of equipment; (6) double-gloving with frequent changing of outer gloves; (7) local application of vancomycin powder; (8) re-dosing antibiotic every 4 h for prolonged procedures and extending postoperative coverage to 72 h for high-risk patients; (9) irrigation of subcutaneous tissue with diluted povidone-iodine solution after deep fascial closure; and (10) use of DuraPrep skin preparation at the end of a case before skin closure. Through an extensive literature review, the current data available for each of the ten steps was evaluated.

Research results

Use of vancomycin powder in surgical wounds, routine irrigation of surgical site, and frequent changing of surgical gloves are strongly supported by the literature. Preoperative skin preparation with chlorhexidine wipes is similarly supported. The majority of current literature supports control of HbA1c preoperatively to reduce risk of infection. Limiting the use of flash sterilization is supported, but has not been evaluated in spine-specific surgery. Limiting OR traffic and number of personnel in the OR are supported although without level 1 evidence. Prolonged use of antibiotics postoperatively is not supported by the literature. Intraoperative use of DuraPrep prior to skin closure is not yet explored.

Research conclusions

Several details surrounding surgery have been evaluated in the literature as both patient risk factors and prophylactic measures for decreasing rates of SSIs. The authors attempted to control for 10 factors and found support in the literature for the majority of the 10 steps taken. This protocol resulted in a significant reduction in SSIs in the senior author's practice.

Research perspectives

In the current era of pay per performance, there is a major drive in all hospitals to reduce postoperative infection to the minimum. A variety of measures have been initiated and evaluated in the literature to reduce the occurrence of SSIs. Postoperative surgical site infection will remain a matter of concern for patients, surgeons and healthcare providers. Future prospective randomized studies that include some or all of the 10 steps discussed in this report are necessary to confirm whether the 10 steps adopted by the authors were in fact science or fiction in the battle for infection control.

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