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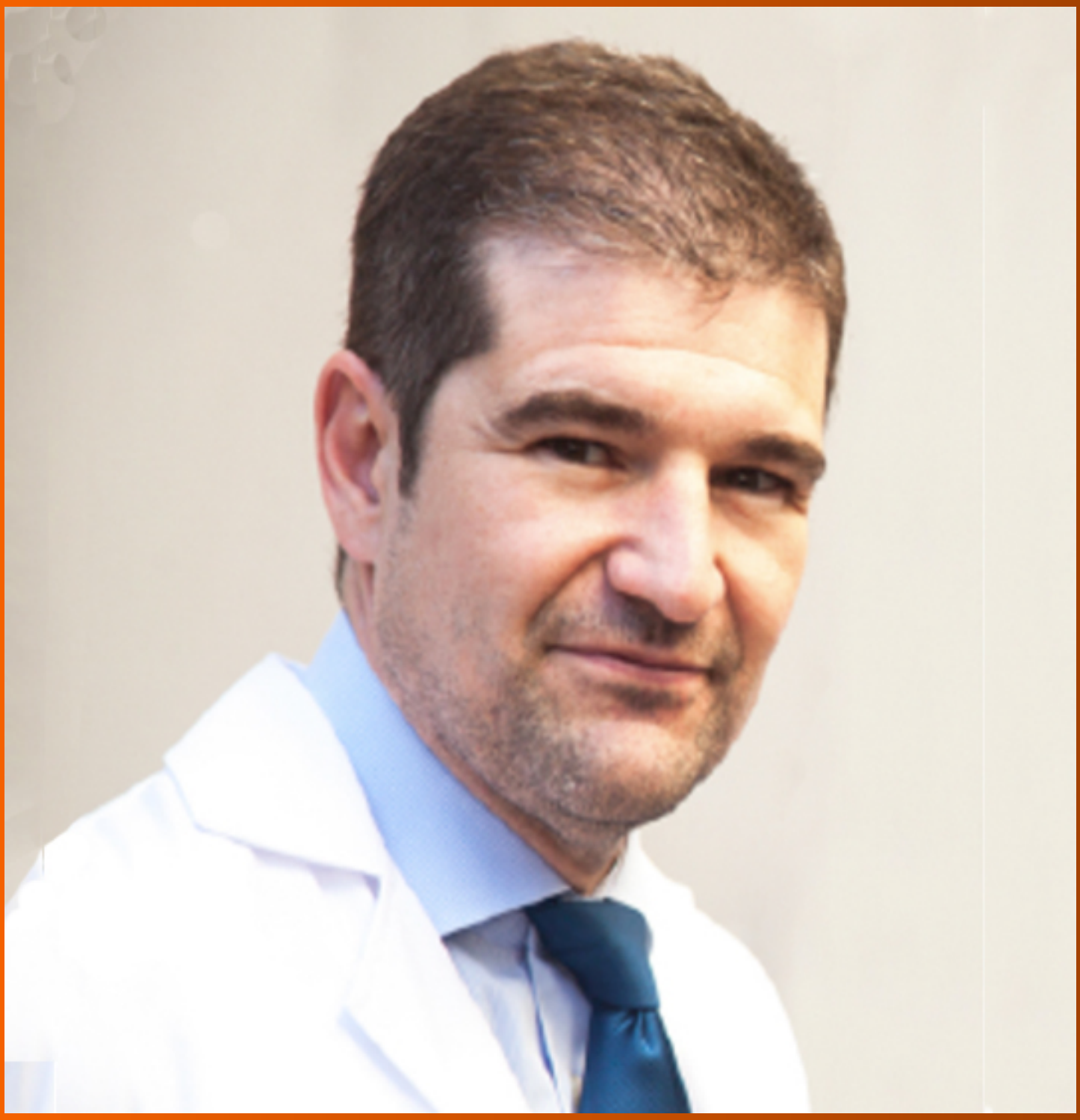

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MINIREVIEWS

Evaluating learning and change in orthopaedics: What is the evidence-base?

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Abstract

Learning and change are key elements of clinical governance and are responsible for the progression of our specialty. Although orthopaedics has been slow to embrace quality improvement, recent years have seen global developments in surgical education, quality improvement, and patient outcome research. This review covers recent advances in the evaluation of learning and change and identifies the most important research questions that remain unanswered. Research into proxies of learning is improving but more work is required to identify the best proxy for a given procedure. Learning curves are becoming commonplace but are poorly integrated into postgraduate training curricula and there is little agreement over the most appropriate method to analyse learning curve data. With various organisations promoting centralisation of care, learning curve analysis is more important than ever before. The use of simulation in orthopaedics is developing but is yet to be formally mapped to resident training worldwide. Patient outcome research is rapidly changing, with an increased focus on quality of life measures. These are key to patients and their care. Cost-utility analysis is increasingly seen in orthopaedic manuscripts and this needs to continue to improve evidence-based care. Large-scale international, multi-centre randomised trials are gaining popularity and updated guidance on sample size estimation needs to become widespread. A global lack of surgeon equipoise will need to be addressed. Quality improvement projects frequently employ interrupted time-series analysis to evaluate change. This technique's limitations must be acknowledged, and more work is required to improve the evaluation of change in a dynamic healthcare environment where multiple interventions frequently occur. Advances in the evaluation of learning and change are needed to drive improved international surgical education and increase the reliability, validity, and importance of the conclusions drawn from orthopaedic research.

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Key words: Learning; Change; Quality improvement; Orthopaedics; Surgical education

Core tip: Learning and change are integral to clinical governance. Despite orthopaedics being slow to embrace quality improvement, recent years have seen global improvements in the field. This review covers various aspects of learning and change including: proxies of learning, learning curve analysis, simulation, outcome measures, retrospective and prospective studies as well as time-series analysis. It summarises the current evidence-base and identifies research questions that remain unanswered.

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INTRODUCTION

Learning and change are key elements of clinical governance, a framework through which healthcare organisations are accountable for continuously improving the quality of their services[1]. Historically, despite a growing interest within medicine, orthopaedics has been slow to embrace quality improvement. However, in recent years there has been a global drive towards evidence-based improvement in the quality of service provision[2], surgical education[3], and outcome research[4,5].

The process of evaluating learning and change is what guides improvement strategy. We must accept that "not all change is improvement, but all improvement is change"[6]. Proxies of performance and methods to analyse the change in performance over time are core themes of current healthcare research and play a critical role in the development of our specialty. This is evident in the increasing use of patient-reported outcome measures (PROMs) to guide evidence-based care and in the use of learning curve data as an assessment metric to promote self-regulated learning[7].

The aim of this review is to provide orthopaedic surgeons with an evidence-based introduction to the evaluation of learning and change in this era of healthcare quality improvement reform.

LEARNING

Proxies of learning

In order to draw meaningful conclusions from data, learning variables need to demonstrate high validity. Validity is "the extent to which an assessment measures what it intends to measure"[8]. This is a judgment based on several factors, including whether the variable correlates with other 'gold standard' measures.

Proxies of learning are largely divided into surgical process and patient outcome variables. Surgical process variables include operative factors such as operative time, intraoperative blood loss, implant alignment, and fluoroscopy dose. Patient outcome variables include PROMs, mortality, morbidity, length of hospital stay, and transfusion requirement. A key systematic review by Ramsey and colleagues found that operative time was the most commonly used proxy of learning[9]. Although this variable is easily accessible, its validity in the context of learning is less robust. Global rating scales for surgical procedures have been increasingly used to evaluate learning in orthopaedic surgery, and are probably a better surrogate marker of learning[10]. In particular, their combination with motion analysis seems to offer a valid proficiency metric for arthroscopy simulators[11]. More work is required to directly compare the validity of different proxies of learning in different orthopaedic procedures.

Learning curves

A learning curve is a graphical representation of the relationship between learning effort and learning outcome[12]. It serves as a visual representation of the process of learning and allows researchers to employ statistical techniques to draw conclusions from the data. A typical learning curve resembles that of a negative exponential: With

experience, a greater learning effort is required to produce the same improvement in performance[13]. However, due to the high variability of surgical data, this is rarely the case in practice. Researchers are then faced with interpreting highly variable data from which to draw meaningful conclusions.

The most commonly employed technique to detect learning is the 'split-group' method[14]. The data is chronologically split into two or three consecutive groups of arbitrary size, and groups are compared by *t*-tests or equivalent. Although simple, this technique is fraught with bias and is increasingly disapproved by researchers. For example, a recent systematic review investigating the learning curve of the Latarjet procedure found that most included studies used the split-group method, and called for more rigorous, continuous learning curve modelling techniques[15].

Although other methods for modelling learning curves do exist (*e.g.*, cumulative sum methods), the widespread use of mathematically valid regression techniques in orthopaedics remains sparse[16]. Researchers have recently developed mathematically rigorous segmented linear regression techniques that test multiple learning models and applied these to investigate the learning curves austerity across healthcare systems of total knee and total hip replacements when using imageless navigation[17,18] (Figures 1 and 2). Further studies are required to ensure that mathematically rigorous learning curve techniques become commonplace when evaluating the learning curves of new orthopaedic procedures. Indeed, accurate and informative learning curve analysis is even more important in an era of centralisation of care, where difficult procedures are increasingly reserved for supra-specialist, high-volume surgeons[19].

Simulation

The ongoing emphasis on patient safety in conjunction with reduced working hours and financial austerity across healthcare systems has led to improved methods to train surgeons outside the operating room[20]. Simulation-based training has been successfully incorporated into the general surgery training curriculum in the United States[21], and randomised controlled trials (RCT) have proved its benefits[22]. The use of simulation in arthroscopy[23] and trauma[24] is increasing, though the level of evidence for simulation studies in orthopaedics remains low with a lack of focus on nontechnical skills and cost analyses[25]. There are ongoing consultations to map simulation to the trauma and orthopaedics postgraduate curriculum in the United Kingdom[26]. A stronger drive is required to formally integrate simulation training within orthopaedic residency training at an international level.

CHANGE

Change in outcomes in orthopaedics can be considered following operative intervention, and by examining time-series following system interventions. The measures of performance in both settings are similar and reflect the variables we consider to lie at the core of orthopaedic practice. Although there is a degree of overlap with variables used to measure learning, these are largely related to patient outcomes and health economics.

Outcome measures

Prior to implementing and evaluating change, researchers must identify appropriate measures to determine whether an intervention works[27]. Ideally, these should be part of routinely collected data for quality improvement purposes. An example includes the National Hip Fracture Database in the United Kingdom that routinely collects standardised outcome data[28]. It is based on this that the World Hip Trauma Evaluation (WHiTE) study has founded a reliable and organised framework for comprehensive cohort studies on fragility hip fractures[29].

Patient outcomes in orthopaedics mainly include mortality, postoperative complications, infection, performance testing, and PROMs[30]. Of these there has been a recent surge in PROMs research[31]. This is because PROMs lie at the heart of patient-centred care. There is no surprise that health-related quality of life measures such as the EuroQol are increasingly being employed to guide operative decision making in trauma[29,32]. Simultaneously, there is a trend towards including patients in setting research questions through priority setting partnerships[33], and patient and public involvement is now indispensable to healthcare research[34]. Cost-utility, the financial cost for health gain, is the variable that the National Institute for Health and Care Excellence (NICE) uses when forming guidelines for healthcare provision. It is thus very important that orthopaedic surgeons understand and incorporate cost-utility analysis in their research[35].

Variables used to evaluate an intervention are usually divided into outcome measures, process measures, and balancing measures[5,36]. Outcome measures monitor

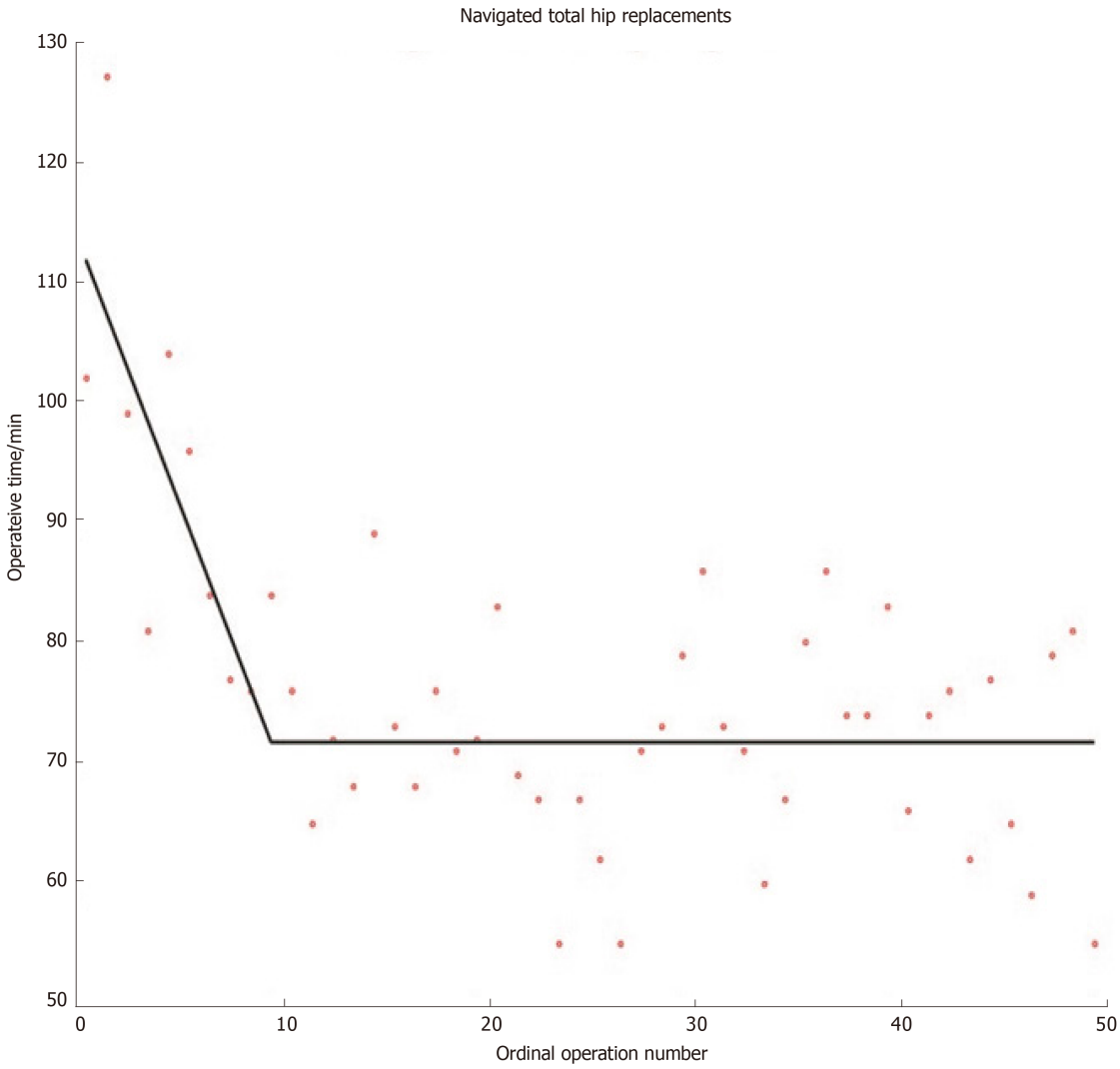

Figure 1 Learning curve for navigated total hip replacements. Segmented linear regression technique was employed to model learning[17]. Line-plateau model fits the data best, with a plateau being attained at 12 operations.

how a system is performing, process measures assess the implementation of an intervention, and balancing measures assess unintended consequences of the intervention.

Once outcome measures are identified and data is collected, analysis of the data is required to evaluate change.

Evaluating change

Operative intervention: Analysing change following operative intervention forms the basis of retrospective and prospective research studies. The level of evidence for a given study depends on a multitude of factors, most importantly study design[37]. There are three types of outcome variables: Continuous (*e.g.*, operative time), categorical (*e.g.*, presence or absence of a complication), and time-to-event (*e.g.*, time to revision of a joint replacement). Statistical tests comparing outcomes consider the type of variable and can include parametric (*t*-test) and non-parametric (Mann-Whitney) tests, crosstabs (*e.g.*, Chi-squared test and Fischer's test), and survival analysis. These tests usually output a significance value (*P*-value) which is a measure of the likelihood that the result was due to chance.

Increased focus is being placed on the minimal clinically important difference - the smallest change in an outcome that a patient would identify as important, and which would usually indicate a change in patient management. Even a very small change can be shown to be statistically significant with a large enough sample size, but this may not be important. There is significant variation in the reporting of sample size calculations in orthopaedic literature[38] and until recently, reporting guidelines were lacking. Adoption of the DELTA^2 guidance on choosing a target difference and reporting sample size in RCTs should improve this[39].

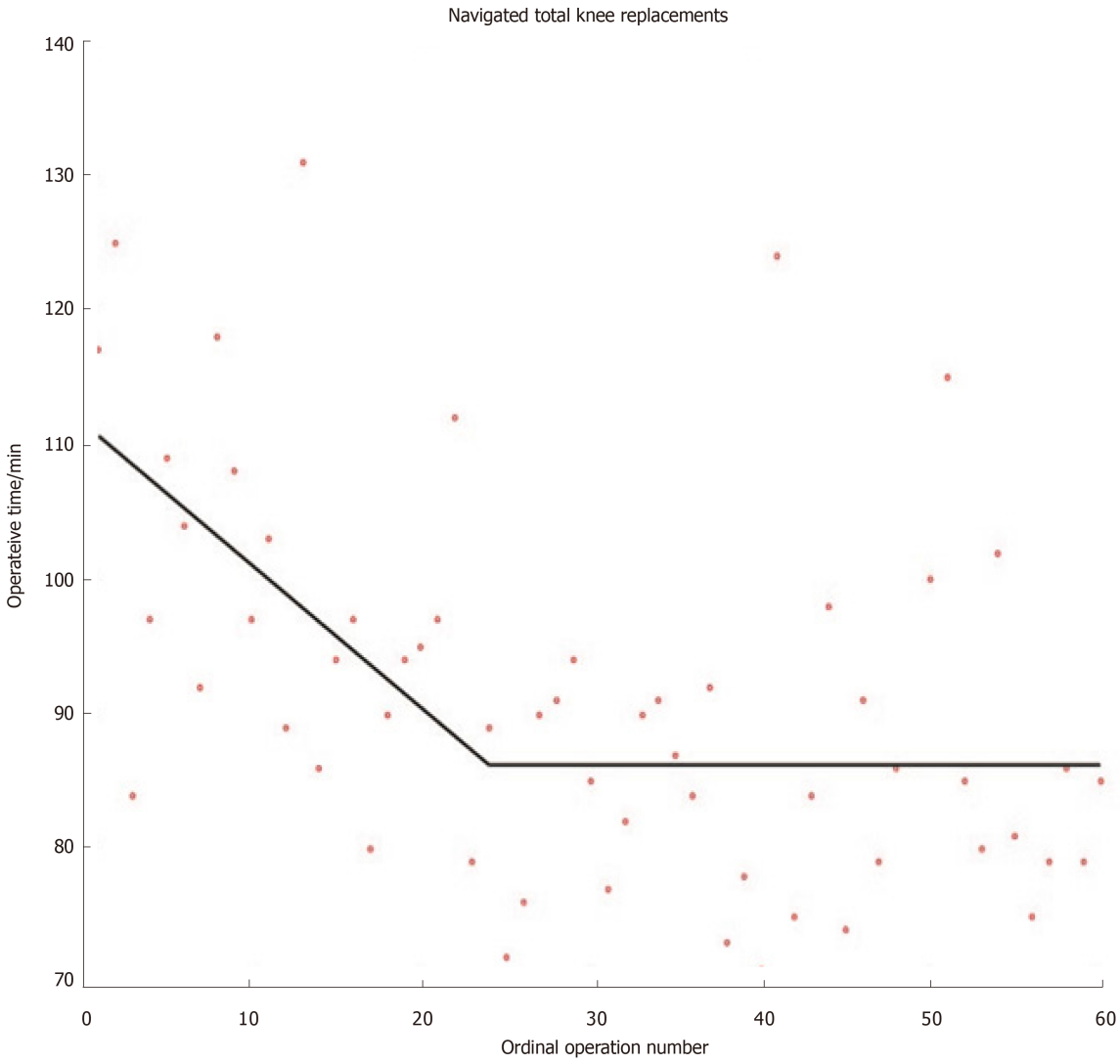

Figure 2 Learning curve for navigated total knee replacements. Segmented linear regression technique was employed to model learning[17]. Line-plateau model fits the data best, with plateau being attained at 26 operations.

RCTs are considered the gold-standard hypothesis-testing study design. This is mainly because they allow for controlling of confounding variables that complicate observational studies. Over the last decade there has been a surge in trauma trials on an international scale, starting with the CRASH-2 trial on the effectiveness of tranexamic acid in trauma[40]. Other large-scale randomised trials have followed suit, investigating fixation of intracapsular neck of femur fractures[41], fixation of distal radius fractures[42] and ongoing research on the optimal timing of hip fracture surgery[43] to mention a few.

Although RCTs are excellent for answering certain research questions, retrospective studies remain indispensable. In the era of information technology, 'Big Data' is becoming ubiquitous[44]. Using Big Data to identify research questions, guide efficient targeting of resources and subsequently address these questions with randomised trials may not be the exception in a few years. It is definitely appearing promising so far[29]. One major limitation that will need to be addressed in future if RCTs are to output the highest quality data is surgeon equipoise. Surgeons are rarely in true equipoise and they usually have a clear idea of what management option is the best for a given patient. Although few would question the importance of decision making in surgery, it can present an obstacle when patient randomisation is required[45]. This must be addressed through improved surgeon education and standardised randomisation processes.

Time-series analysis: A toolbox for detecting change: Many quality improvement projects evaluate the effectiveness of an intervention by collecting data over time. Data can be graphically displayed as control charts, also known as Shewart charts. They are a statistical process control tool used to determine whether a system is in

control and provide immediate feedback about performance[46].

Orthopaedic surgeons may be more familiar with audit cycles. Audit is a framework of quality improvement where performance is compared to a published standard[47]. Part of this process includes introducing an intervention and assessing its effectiveness by comparing performance before and after the intervention by simple statistical group tests. Although ubiquitous in clinical orthopaedics and indeed in all medical specialties, such approaches are sensitive to secular (background) trends. Interrupted time-series (ITS) analysis is a useful tool for evaluating the effectiveness of interventions where data is collected at several time-points before and after the intervention to determine whether any change could be explained by secular trends[48]. Cochrane recommends this tool to evaluate interventions[49] and several recent orthopaedic studies have employed this technique[50,51].

ITS does not come without limitations, and is known to display bias for detecting change at the time of the studied intervention where other changes at different time-points may be equally, if not more important[52,53]. Segmented linear regression models have been developed for evaluating change in retrospective studies by enabling more than one linear segment to describe the periods before and after an intervention. A recent study employing this technique revealed that improvements in time to surgery and 30-d mortality following hip fracture over a 6-year period were likely the result of a combination of surgical, anaesthetic, and procedural improvements over time, rather than due to the introduction of a dedicated hip fracture unit[53] (Figure 3). Future work is required to determine the optimal way to describe retrospective time-series: How many linear segments should be used, and how to best model binary outcomes.

CONCLUSION

Learning and change are integral to quality improvement and surgical education, and strongly influence the development of our specialty. The orthopaedic community has seen several improvements in PROMs research, learning curve analysis, randomised trial design, and time-series analysis.

Future work is required to improve and standardise learning variables and formally implement simulation in orthopaedic residency education. Global collaborative research networks are developing but integrating randomised trials with Big Data on an international scale to improve orthopaedics will require a concerted effort.

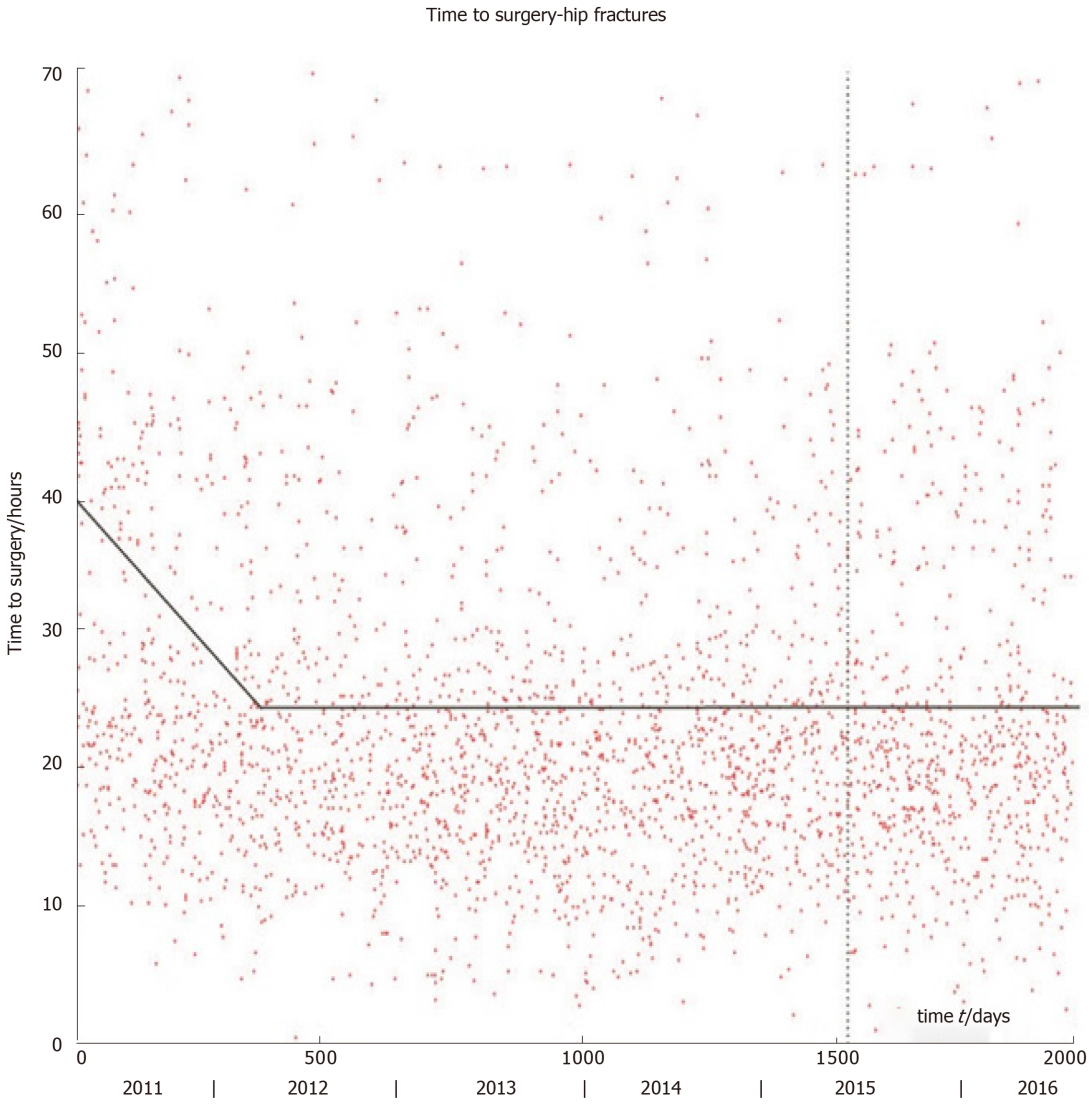

Figure 3 Time to surgery for neck of femur fractures. The vertical dashed line marks the onset of a dedicated hip fracture unit. The line-plateau is the best-fitting linear model for the entire period: the line has equation $y = -0.0414t + 40.1868$; plateau at $y = 24.7033$ reached after 375 d. The initial drop may be related to the introduction of the Best Practice Tariff. The hip fracture unit did not significantly affect time to surgery[53].

REFERENCES

1 **Scally G**, Donaldson LJ. The NHS's 50 anniversary. Clinical governance and the drive for quality improvement in the new NHS in England. *BMJ* 1998; **317**: 61-65 [PMID: 9651278 DOI: 10.1136/bmj.317.7150.61]

2 **Barratt H**, Turner S, Hutchings A, Pizzo E, Hudson E, Briggs T, Hurd R, Day J, Yates R, Gikas P, Morris S, Fulop NJ, Raine R. Mixed methods evaluation of the Getting it Right First Time programme - improvements to NHS orthopaedic care in England: study protocol. *BMC Health Serv Res* 2017; **17**: 71 [PMID: 28115018 DOI: 10.1186/s12913-017-2012-y]

3 **Nousiainen MT**, Mironova P, Hynes M, Glover Takahashi S, Reznick R, Kraemer W, Alman B, Ferguson P, Safir O, Sonnadara R, Murnaghan J, Ogilvie-Harris D, Theodoropoulos J, Hall J, Syed K, Howard A, Ford M, Daniels T, Dwyer T, Veillette C, Wadey V, Narayanan U, Yee A, Whyne C. Eight-year outcomes of a competency-based residency training program in orthopedic surgery. *Med Teach* 2018; 1-13 [PMID: 29343150 DOI: 10.1080/0142159X.2017.1421751]

4 **Sedrakyan A**, Paxton EW, Phillips C, Namba R, Funahashi T, Barber T, Sculco T, Padgett D, Wright T, Marinac-Dabic D. The International Consortium of Orthopaedic Registries: overview and summary. *J Bone Joint Surg Am* 2011; **93** Suppl 3: 1-12 [PMID: 22262417 DOI: 10.2106/JBJS.K.01125]

5 **Wolfstadt JI**, Ward SE, Kim S, Bell CM. Improving Care in Orthopaedics: How to Incorporate Quality Improvement Techniques into Surgical Practice. *J Bone Joint Surg Am* 2018; **100**: 1791-1799 [PMID: 30334891 DOI: 10.2106/JBJS.18.00225]

6 **Berwick DM**. A primer on leading the improvement of systems. *BMJ* 1996; **312**: 619-622 [PMID: 8595340 DOI: 10.1136/bmj.312.7031.619]

7 **Brydges R**, Butler D. A reflective analysis of medical education research on self-regulation in learning and practice. *Med Educ* 2012; **46**: 71-79 [PMID: 22150198 DOI: 10.1111/j.1365-2923.2011.04100.x]

8 **Downing SM**. Validity: on meaningful interpretation of assessment data. *Med Educ* 2003; **37**: 830-837

[PMID: 14506816 DOI: 10.1046/j.1365-2923.2003.01594.x]
9 **Ramsay CR**, Grant AM, Wallace SA, Garthwaite PH, Monk AF, Russell IT. Assessment of the learning curve in health technologies. A systematic review. *Int J Technol Assess Health Care* 2000; **16**: 1095-1108 [PMID: 11155830 DOI: 10.1017/S0266462300103149]
10 **Alvand A**, Logishetty K, Middleton R, Khan T, Jackson WF, Price AJ, Rees JL. Validating a global rating scale to monitor individual resident learning curves during arthroscopic knee meniscal repair. *Arthroscopy* 2013; **29**: 906-912 [PMID: 23628663 DOI: 10.1016/j.arthro.2013.01.026]
11 **Chang J**, Banaszek DC, Gambrel J, Bardana D. Global Rating Scales and Motion Analysis Are Valid Proficiency Metrics in Virtual and Benchtop Knee Arthroscopy Simulators. *Clin Orthop Relat Res* 2016; **474**: 956-964 [PMID: 26282388 DOI: 10.1007/s11999-015-4510-8]
12 **Pusic MV**, Kessler D, Szyld D, Kalet A, Pecaric M, Boutis K. Experience curves as an organizing framework for deliberate practice in emergency medicine learning. *Acad Emerg Med* 2012; **19**: 1476-1480 [PMID: 23230958 DOI: 10.1111/acem.12043]
13 **Singer JD**, Willett JB. Applied Longitudinal Data Analysis: Modeling Change and Event Occurrence. 1st ed New York; Oxford University Press. 2003.
14 **Ramsay CR**, Grant AM, Wallace SA, Garthwaite PH, Monk AF, Russell IT. Statistical assessment of the learning curves of health technologies. *Health Technol Assess* 2001; **5**: 1-79 [PMID: 11319991]
15 **Ekhtiari S**, Horner NS, Bedi A, Ayeni OR, Khan M. The Learning Curve for the Latarjet Procedure: A Systematic Review. *Orthop J Sports Med* 2018; **6**: 2325967118786930 [PMID: 30090836 DOI: 10.1177/2325967118786930]
16 **Valsamis EM**, Chouari T, O'Dowd-Booth C, Rogers B, Ricketts D. Learning curves in surgery: variables, analysis and applications. *Postgrad Med J* 2018; **94**: 525-530 [PMID: 30209180]
17 **Valsamis EM**, Golubic R, Glover TE, Husband H, Hussain A, Jenabzadeh AR. Modeling Learning in Surgical Practice. *J Surg Educ* 2018; **75**: 78-87 [PMID: 28673804 DOI: 10.1016/j.jsurg.2017.06.015]
18 **Valsamis EM**, Ricketts D, Hussain A, Jenabzadeh AR. Imageless navigation total hip arthroplasty - an evaluation of operative time. *SICOT J* 2018; **4**: 18 [PMID: 29792786 DOI: 10.1051/sicotj/2018016]
19 **Hay S**, Kulkarni R, Watts A, Stanley D, Trail I, Van Rensburg L, Little C, Samdanis V, Jenkins P, Eames M, Phadnis J, Ali A, Rangan A, Drew S, Amirfeyz R, Conboy V, Clark D, Brownson P, Connor C, Jones V, Tennent D, Falworth M, Thomas M, Rees J. The Provision of Primary and Revision Elbow Replacement Surgery in the NHS. *Shoulder Elbow* 2018; **10**: S5-S12 [PMID: 30147752 DOI: 10.1177/1758573218789849]
20 **Atesok K**, Mabrey JD, Jazrawi LM, Egol KA. Surgical simulation in orthopaedic skills training. *J Am Acad Orthop Surg* 2012; **20**: 410-422 [PMID: 22751160 DOI: 10.5435/JAAOS-20-06-410]
21 **Accreditation Council for Graduate Medical Education**. ACGME Program Requirements for Graduate Medical Education in General Surgery. Available from: https://www.unitypoint.org/desmoines/filesimages/Residency/Surgery/general_surgery_program_requirements.pdf
22 **Franzeck FM**, Rosenthal R, Muller MK, Nocito A, Wittich F, Maurus C, Dindo D, Clavien PA, Hahnloser D. Prospective randomized controlled trial of simulator-based versus traditional in-surgery laparoscopic camera navigation training. *Surg Endosc* 2012; **26**: 235-241 [PMID: 21853391 DOI: 10.1007/s00464-011-1860-5]
23 **Middleton RM**, Alvand A, Garfjeld Roberts P, Hargrove C, Kirby G, Rees JL. Simulation-Based Training Platforms for Arthroscopy: A Randomized Comparison of Virtual Reality Learning to Benchtop Learning. *Arthroscopy* 2017; **33**: 996-1003 [PMID: 28073670 DOI: 10.1016/j.arthro.2016.10.021]
24 **Bhattacharyya R**, Sugand K, Al-Obaidi B, Sinha I, Bhattacharya R, Gupte CM. Trauma simulation training: a randomized controlled trial -evaluating the effectiveness of the Imperial Femoral Intramedullary Nailing Cognitive Task Analysis (IFINCTA) tool. *Acta Orthop* 2018; **89**: 689-695 [PMID: 30326762 DOI: 10.1080/17453674.2018.1517442]
25 **Morgan M**, Aydin A, Salih A, Robati S, Ahmed K. Current Status of Simulation-based Training Tools in Orthopedic Surgery: A Systematic Review. *J Surg Educ* 2017; **74**: 698-716 [PMID: 28188003 DOI: 10.1016/j.jsurg.2017.01.005]
26 **Kellet C**. The Role of Simulation. *J Trauma Orthop* 2018; **6**: 78-79
27 **Solberg LI**, Mosser G, McDonald S. The three faces of performance measurement: improvement, accountability, and research. *Jt Comm J Qual Improv* 1997; **23**: 135-147 [PMID: 9103968 DOI: 10.1016/S1070-3241(16)30305-4]
28 **Royal College of Physicians**. National Hip Fracture Database (NHFD) Annual Report 2017. Available from: https://nhfd.co.uk/files/2017ReportFiles/NHFD-AnnualReport2017.pdf
29 **Costa ML**, Griffin XL, Achten J, Metcalfe D, Judge A, Pinedo-Villanueva R, Parsons N. World Hip Trauma Evaluation (WHiTE): framework for embedded comprehensive cohort studies. *BMJ Open* 2016; **6**: e011679 [PMID: 27797994 DOI: 10.1136/bmjopen-2016-011679]
30 **Lübbeke A**. Research methodology for orthopaedic surgeons, with a focus on outcome. *EFORT Open Rev* 2018; **3**: 160-167 [PMID: 29951252 DOI: 10.1302/2058-5241.3.170064]
31 **Joeris A**, Knoll C, Kalampoki V, Blumenthal A, Gaskell G. Patient-reported outcome measurements in clinical routine of trauma, spine and craniomaxillofacial surgeons: between expectations and reality: a survey among 1212 surgeons. *BMJ Open* 2018; **8**: e020629 [PMID: 29895649 DOI: 10.1136/bmjopen-2017-020629]
32 **Ulvik A**, Kvåle R, Wentzel-Larsen T, Flaatten H. Quality of life 2-7 years after major trauma. *Acta Anaesthesiol Scand* 2008; **52**: 195-201 [PMID: 18005377 DOI: 10.1111/j.1399-6576.2007.01533.x]
33 **Fernandez MA**, Arnel L, Gould J, McGibbon A, Grant R, Bell P, White S, Baxter M, Griffin X, Chesser T, Keene D, Kearney RS, White C, Costa ML. Research priorities in fragility fractures of the lower limb and pelvis: a UK priority setting partnership with the James Lind Alliance. *BMJ Open* 2018; **8**: e023301 [PMID: 30287674 DOI: 10.1136/bmjopen-2018-023301]
34 **National Institute for Health Research**. Going the extra mile: improving the nationâs health and wellbeing through public involvement in research. 2015. Available from: https://www.nihr.ac.uk/patients-and-public/documents/Going-the-Extra-Mile.pdf
35 **Costa M**. The Price to Pay. *J Trauma Orthop* 2018; **6**: 60-61
36 **Chiu YJ**, Chung HH, Yeh CH, Cheng JT, Lo SH. Improvement of insulin resistance by Chlorella in fructose-rich chow-fed rats. *Phytother Res* 2011; **25**: 1306-1312 [PMID: 21312306 DOI: 10.1002/ptr.3379]
37 **Howick J**, Chalmers I, Glasziou P, Greenhalgh P, Heneghan C, Liberati A. The Oxford 2011 Levels of Evidence. 2011.
38 **Sabharwal S**, Patel NK, Holloway I, Athanasiou T. Sample size calculations in orthopaedics randomised

controlled trials: revisiting research practices. *Acta Orthop Belg* 2015; **81**: 115-122 [PMID: 26280864]
39 **Cook JA**, Julious SA, Sones W, Hampson LV, Hewitt C, Berlin JA, Ashby D, Emsley R, Fergusson DA, Walters SJ, Wilson ECF, Maclennan G, Stallard N, Rothwell JC, Bland M, Brown L, Ramsay CR, Cook A, Armstrong D, Altman D, Vale LD. DELTA^2 guidance on choosing the target difference and undertaking and reporting the sample size calculation for a randomised controlled trial. *Trials* 2018; **19**: 606 [PMID: 30400926 DOI: 10.1186/s13063-018-2884-0]
40 **Roberts I**, Shakur H, Coats T, Hunt B, Balogun E, Barnetson L, Cook L, Kawahara T, Perel P, Prieto-Merino D, Ramos M, Cairns J, Guerriero C. The CRASH-2 trial: a randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients. *Health Technol Assess* 2013; **17**: 1-79 [PMID: 23477634 DOI: 10.3310/hta17100]
41 **Fixation using Alternative Implants for the Treatment of Hip fractures (FAITH) Investigators**. Fracture fixation in the operative management of hip fractures (FAITH): an international, multicentre, randomised controlled trial. *Lancet* 2017; **389**: 1519-1527 [PMID: 28262269 DOI: 10.1016/S0140-6736(17)30066-1]
42 **Costa ML**, Achten J, Parsons NR, Rangan A, Edlin RP, Brown J, Lamb SE. UK DRAFFT - a randomised controlled trial of percutaneous fixation with kirschner wires versus volar locking-plate fixation in the treatment of adult patients with a dorsally displaced fracture of the distal radius. *BMC Musculoskelet Disord* 2011; **12**: 201 [PMID: 25716883 DOI: 10.3310/hta19170]
43 **Hip Fracture Accelerated Surgical Treatment and Care Track (HIP ATTACK) Investigators**. Accelerated care versus standard care among patients with hip fracture: the HIP ATTACK pilot trial. *CMAJ* 2014; **186**: E52-E60 [PMID: 24246589 DOI: 10.1503/cmaj.130901]
44 **Perry D**. Big data – what it does, and what it doesn't. *J Trauma Orthop* 2018; **6**: 52-53
45 **Ollivere B**. Equipoise, ethics, and offering patients participation in studies. *Bone Jt 360* 2018 [DOI: 10.1302/2048-0105.76.360661]
46 **Mohsin M**. Anti-smoking campaign in Multan, Pakistan. *East Mediterr Health J* 2005; **11**: 1110-1114 [PMID: 16761682 DOI: 10.1007/s10722-011-9680-y]
47 **Fowkes FG**. Medical audit cycle. A review of methods and research in clinical practice. *Med Educ* 1982; **16**: 228-238 [PMID: 6750333 DOI: 10.1111/j.1365-2923.1982.tb01254.x]
48 **Bernal JL**, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol* 2017; **46**: 348-355 [PMID: 27283160 DOI: 10.1093/ije/dyw098]
49 **Higgins JPT**, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. 2011. Available from: http://handbook-5-1.cochrane.org/
50 **McKirdy A**, Imbuldeniya AM. The clinical and cost effectiveness of a virtual fracture clinic service: An interrupted time series analysis and before-and-after comparison. *Bone Joint Res* 2017; **6**: 259-269 [PMID: 28473333 DOI: 10.1302/2046-3758.65.BJR-2017-0330.R1]
51 **Matharu GS**, Hunt LP, Murray DW, Howard P, Pandit HG, Blom AW, Bolland B, Judge A. Is the rate of revision of 36 mm metal-on-metal total hip arthroplasties with Pinnacle acetabular components related to the year of the initial operation? an interrupted time-series analysis using data from the National Joint Registry for England and Wales. *Bone Joint J* 2018; **100-B**: 33-41 [PMID: 29305448 DOI: 10.1302/0301-620X.100B1.BJJ-2017-0625.R2]
52 **Fretheim A**, Tomic O. Statistical process control and interrupted time series: a golden opportunity for impact evaluation in quality improvement. *BMJ Qual Saf* 2015; **24**: 748-752 [PMID: 26316541 DOI: 10.1136/bmjqs-2014-003756]
53 **Valsamis EM**, Ricketts D, Husband H, Rogers BA. Segmented Linear Regression Models for Assessing Change in Retrospective Studies in Healthcare. *Comput Math Methods Med* 2019; **2019**: 9810675 [PMID: 30805023 DOI: 10.1155/2019/9810675]

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ORIGINAL ARTICLE

Observational Study

Epidemiology of syndactyly in New York State

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Abstract

BACKGROUND

There is paucity of literature focusing on the incidence and surgical management of syndactyly. In this study, we describe the incidence and rates of surgical management of patients with syndactyly in New York State.

AIM

To describe the incidence and surgical management of patients with syndactyly using an America's population-based database.

METHODS

We conducted a retrospective study using the New York State Statewide Planning and Research Cooperative System. All patients with a diagnosis of syndactyly at birth were identified and followed longitudinally to determine yearly incidence as well as demographic and surgical factors. Descriptive statistics and univariate analyses were used.

RESULTS

There were 3306 newborns with a syndactyly diagnosis between 1997 and 2014 in New York State. The overall incidence was 0.074% or 7 cases per 10000 live births. A small number of patients underwent surgical correction in New York State (178 patients, 5.4%). Among the surgical patients, most of the operations were performed before the age of two (79%). Approximately 87% of surgeries were performed at teaching hospitals, and 52% of procedures were performed by plastic surgeons. Skin grafting was performed in 15% of cases. Patients having surgery in New York State were more likely to have Medicaid insurance compared to patients not having surgery (P = 0.02).

CONCLUSION

Syndactyly occurs in approximately 7 per 10000 live births, and the majority of patients undergo surgical correction before age two. There may be several

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barriers to care including the availability of specialized hand surgeons, access to teaching hospitals, and insurance status.

Key words: Congenital hand anomaly; Epidemiology; Incidence; Syndactyly

Core tip: There is paucity of literature focusing on the incidence and surgical management of syndactyly. In our study, we found the incidence of syndactyly to be 7 cases per 10000 live births in New York State, and the majority of patients underwent surgical correction before age two. Most patients did not receive surgical care in New York State, indicating there may be barriers to care such as the availability of specialized hand surgeons, access to teaching hospitals, and insurance status. Additional study is needed to better understand outcomes after surgical management of syndactyly.

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INTRODUCTION

Syndactyly is a congenital anomaly characterized by an abnormal connection between adjacent digits[1]. Syndactyly is considered to be one of the most common hand malformations[2]; however, there is limited epidemiologic data in the literature[3]. The incidence of syndactyly is most commonly reported to be as low as 2 per 10000 live births, but it has also been reported to be as high as 1 per 2000 to 3000 live births[4-9]. However, the majority of these studies have been hospital-based or extrapolated from clinic visits[10]. A study using Swedish national registries found the incidence of differentiation anomalies to be 10.5 per 1000010, and a study from Western Australia reported the incidence of all upper extremity anomalies to be 1 in 506 with failure of differentiation being the most common anomaly[11]. However, syndactyly was not specifically identified as a subgroup in either study. A recent study found the prevalence of syndactyly to be 1.3 per 10000 in New York State; however, this study focused on disease prevalence and used a congenital malformations registry that is susceptible to underreporting[12].

Surgical management for syndactyly may be performed as early as 6 mo of age, but it is frequently performed between 12 to 18 mo of age[13]. Surgery is not recommended in children under the age of 6 mo due to the inherent anesthetic risk, but it should not be performed too late due to the potential risk of abnormal development of cerebral cortex patterns and the effect on adjacent digits[2,13,14]. While acceptable results have been reported with delaying surgery until age 4 or 5[13], surgical management is typically recommended between 2 and 3 years of age for optimal outcomes[2]. Outcomes are satisfactory in the majority of cases[15,16]. However, an increase in complications and re-operation rates has been previously associated with age, other ipsilateral hand anomalies, and split-thickness skin grafting[2,4,15]. Given the importance of timely surgical management, issues relating to access of care such as insurance status, geographic factors, and availability of specialized hand surgeons may influence patient outcomes, but these factors have not been previously studied. Several barriers to care for congenital conditions have been described in other specialties including patient education level, accessibility, and socioeconomic factors[17]. In addition, insurance status and distance to care are known to be important barriers to care in pediatric surgical care[18-20].

As a whole, there is a paucity of epidemiologic studies using modern, population-based databases. Furthermore, it is not known when these children are undergoing operative management and whether social or demographic factors limit access to care. In this study, we use a state database to describe the incidence of syndactyly in the state of New York. We also describe the age at which children are undergoing surgery, and whether insurance status or access to care is associated with operative management. We hypothesize that the disease incidence will be low and the majority of children will have surgery before age two. In addition, we hypothesize that

insurance status and access to care are potential barriers to care in patients with syndactyly.

MATERIALS AND METHODS

A retrospective study was conducted using the New York Statewide Planning and Research Cooperative System (SPARCS) database. SPARCS is a comprehensive data reporting system established in 1979 that collects patient level data for each inpatient stay, ambulatory surgery procedure, and emergency department admission from non-federal healthcare facilities in New York State.

Newborn admissions from 1997 to 2014 with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code for syndactyly (755.1X) were identified. We included patients with simple and complicated syndactyly, and excluded patients with unknown sex or non-NY residence. Data regarding patient sex and insurance status were obtained from the newborn admission record. Annual incidence for the overall study period and each year individually was calculated by dividing the number of newborns with syndactyly by the total number of live births in New York State each year. Annual live birth counts for 1997 to 2014 were obtained from the New York State Department of Health Vital Statistics website.

Current pocedural terminology (CPT) codes (26560, 26561, 26562, 28280, 28345) and ICD-9-CM procedure codes (86.85) were used to determine whether the identified newborns had a subsequent syndactyly-related procedure. Variables obtained from the surgery visit were age at time of surgery, additional procedures performed, surgeon license number, and hospital identifier. We used CPT codes (14301, 15120, 15200, 15240, 15241, 15760) and ICD-9-CM procedure codes (86.61, 86.62, 86.63, 86.69, 86.70, 86.72, 86.73, 86.89) to determine whether patients having syndactyly surgery had concomitant skin grafting procedures. In addition, surgeon license number was used to obtain surgeon specialty information by querying state and public databases or the professional and personal websites for the surgeon. Hospital identifier was used to obtain information on residency accreditation for the institution from the American Hospital Association Annual Survey database. Hospitals with residency accreditation were classified as teaching hospitals.

Univariate comparisons between syndactyly patients with and without surgical treatment were performed using the Chi-Square test. A geographic heat map of syndactyly procedure frequency was generated with SAS PROC GMAP. Data analysis were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC, United States). Significance level was set at 0.05.

RESULTS

From 1997 to 2014 there were 3306 cases of syndactyly in New York State (Table 1). The annual incidence ranged from 0.062% to 0.085% with an overall incidence of 0.074% (1 per 1350 live births) (Figure 1). There were 1164 females (35%) and 2142 males (65%) in the cohort.

Of these patients, 178 patients (5%) had a syndactyly procedure in New York State. Approximately 67% of these patients were male (119 cases) and 33% were female (59 cases). Forty-four percent of these patients had a syndactyly surgery before age one (78 cases); 35% had surgery at age one (63 cases); and 21% at or after age two (37 cases). There was an equal mix of Medicaid and private insurance (47% each).

Almost all surgeries (183) were performed in New York County (Manhattan), Monroe County (Rochester), Albany County (Albany), Westchester County, Erie County (Buffalo), Bronx, and Kings County (Brooklyn) (Figure 2). Approximately, 87% of cases were performed at teaching hospitals, and slightly more than half of syndactyly releases were performed by plastic surgeons (52%) followed by orthopaedic surgeons (42%). In addition to syndactyly release, skin grafting procedures were also performed in 35 cases (15%).

Some significant differences were noted between patients that did and did not undergo surgery in New York State (Table 1). Patients having surgery in New York State were more likely to have Medicaid insurance compared to patients who did not have surgical treatment in New York (47% *vs* 37%, $P = 0.02$). However, there were no significant differences in sex between patients that did or did not have surgery in New York State ($P = 0.55$).

Table 1 Patient demographic information of those with and without syndactyly procedures

	Syndactyly patient without release procedure in NYS		Syndactyly patient with release procedure in NYS		Total		*P* value
	n	%	*n*	%	*n*	%	
Total	3128	94.62	178	5.38	3306		
Age at surgery							-
0	-	-	78	43.82			
1	-	-	63	35.39			
2 +	-	-	37	20.79			
Sex							0.55
Male	2023	64.67	119	66.85	2142	64.79	
Female	1105	35.33	59	33.15	1164	35.21	
Insurance							0.02
Private	1779	56.87	83	46.63	1862	56.32	
Medicaid	1149	36.73	84	47.19	1233	37.3	
Other	200	6.39	11	6.18	211	6.38	

NYS: New York State.

DISCUSSION

Syndactyly occurs in 7 per 10000 live births in New York State. The reported incidence in this study is higher than some previous reports[4-8], and the higher incidence in New York State may reflect an increasing incidence, population differences, or increase in reporting of this condition. There are varying reports of syndactyly incidence in the literature ranging from 2 to 10 per 10000 live births[4-8,10,11], and this study provides an estimate of incidence in an American population.

Only 5.4% of patients had syndactyly surgery in New York State. Among the surgical patients, most of the operations were performed before the age of two, and a minority of patients needed skin grafting. While surgical release is the recommended treatment for syndactyly and re-operation rates are well-published[21-24], there is limited data on the rates of surgery. Due to the paucity of studies on rates of surgery, we are unable to compare our surgical rates to other populations.

The vast majority of patients with a diagnosis of syndactyly in New York State did not have surgery in the state. This finding suggests that patients are either not undergoing surgical repair or, more likely, they are traveling out of state for care. There are several factors that may affect access to care, including the availability of specialized hand surgeons; proximity to urban medical centers and teaching hospitals; as well as socioeconomic factors and insurance coverage. More specifically, the majority of syndactyly surgeries in New York State are performed by plastic surgeons in urban, teaching hospitals.

Furthermore, payer data shows that patients having surgery in New York State were more likely to have Medicaid insurance compared to patients not having surgery. One possible reason for this might be that patients with private insurance and possibly higher socioeconomic status may be leaving the state to receive care at specialized centers. This finding underscores the need for greater availability of surgical care for the treatment of congenital hand differences in New York State.

This study has several strengths. Firstly, it is a large study that includes all patients in New York State with a diagnosis of syndactyly at birth. This data provides an epidemiologic assessment of incidence and surgical management, and to our knowledge, this is the first study focusing specifically on the incidence of syndactyly in an American population. Recently, Goldfarb *et al*[12] reported the prevalence of congenital hand anomalies using the New York Congenital Malformations Registry, however, their study focused solely on disease prevalence; used a database that does not require confirmation of diagnosis; and they specifically note the potential for underreporting of syndactyly in their database. Furthermore, we are able to describe the surgical management for patients with syndactyly in our study, as well as explore factors that may affect management. Several of these factors have not been previously investigated, and our findings can be used to generate additional studies focusing on surgical management and access to care.

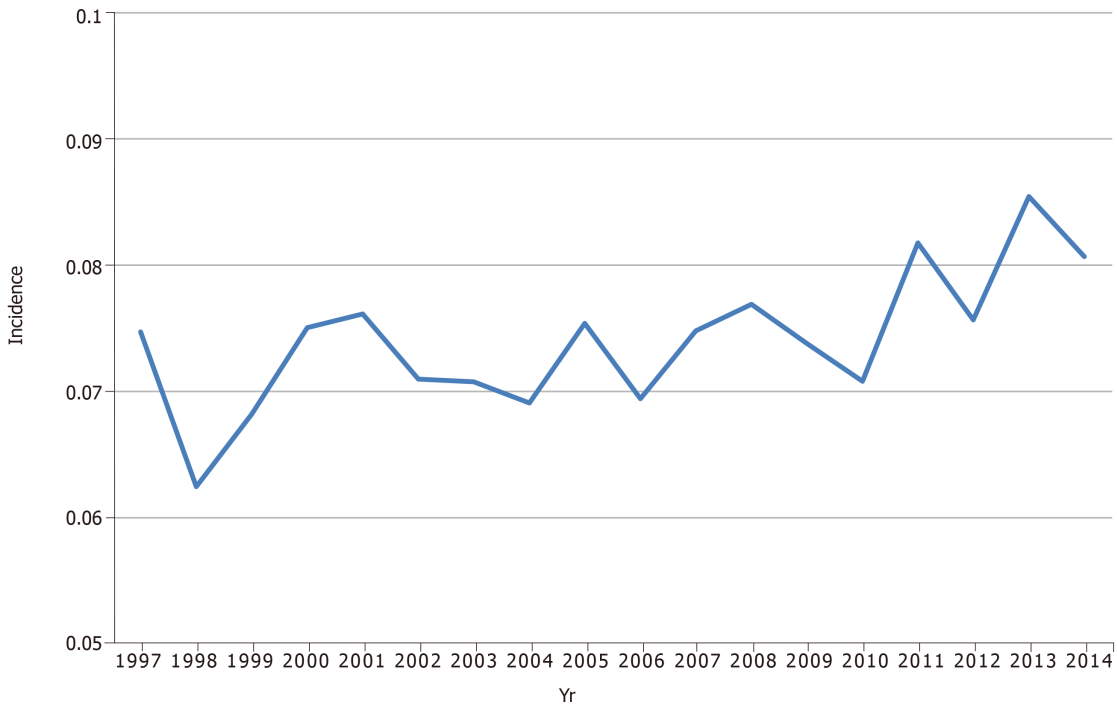

Figure 1 Syndactyly incidence over time.

However, this study has several weaknesses as well. First of all, our study is limited by the limitations of any study utilizing an administrative database. For example, our results are susceptible to errors in reporting and coding, and the available data is less granular in nature and limited to care provided in New York State. Similarly, we used syndactyly-specific CPT codes and ICD-9-CM procedure codes to identify surgical treatment, and it is possible that we did not capture all procedures for syndactyly if they were performed in conjunction with other procedures or having more procedures than are retained in the record. In addition, we do not have access to any clinical or patient-reported outcome measures to determine outcomes after surgery. However, several previous studies have investigated re-operation rates and complications associated with surgical management[22-24]. Lastly, these results are specific to patients residing in New York State and it is unclear whether these results are generalizable to other populations. However, our study provides useful information on the cohort of patients with syndactyly that were managed with surgery in New York State.

In conclusion, this study shows that the incidence of syndactyly is relatively high at 7 per 10000 live births. Most patients who underwent surgical treatment in New York State were under age two at the time of surgery; however, the majority of patients from New York State likely receive care elsewhere. The low rates of surgical management in New York State may be due to barriers to care including the availability of pediatric hand surgeons, proximity to urban medical centers and teaching hospitals, and insurance status. These factors underscore the need for specialized surgical care in New York State, and they should be considered by healthcare officials for resource management and planning. Additional research is needed to specifically understand the low rates of surgical management in New York State, as well as determine the outcomes of surgery in this population.

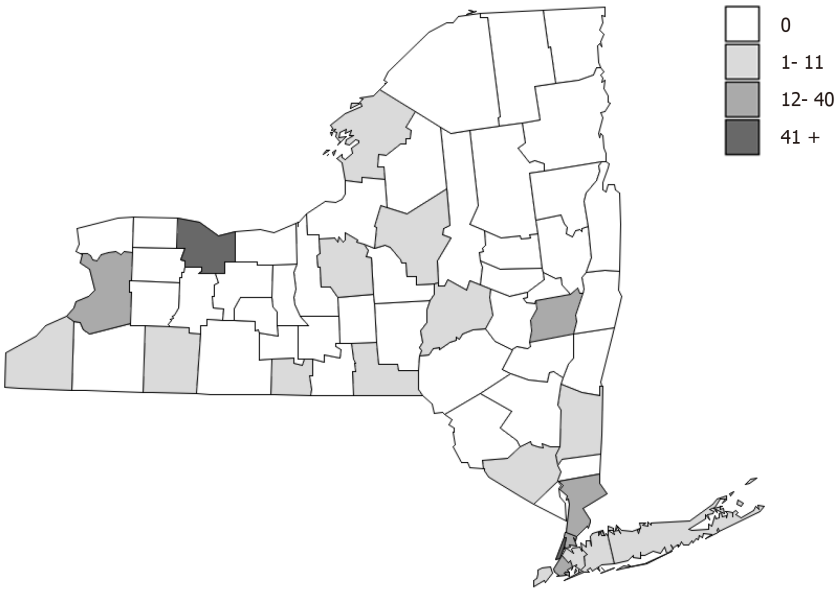

Figure 2 Geographic distribution of syndactyly procedures in New York State.

ARTICLE HIGHLIGHTS

Research background

There is paucity of literature focusing on the incidence and surgical management of syndactyly. In addition, very few epidemiologic studies have used modern, statewide databases to understand the incidence of disease in the United States.

Research motivation

It is important to understand the incidence and surgical management of an important congenital hand anomaly. It is also important to understand rates of surgical management and potential barriers to care.

Research objectives

In this study, we describe the incidence and surgical management of patients with syndactyly in New York State using a statewide database. This study helps to identify the incidence of disease, rates of surgical management, and potential barriers to care.

Research methods

We conducted a retrospective study using the New York State Statewide Planning and Research Cooperative System database. We identified newborn records with a diagnosis of syndactyly to determine annual incidence, and searched subsequent records to determine rates of surgical management. Descriptive statistics and univariate analyses were performed on demographic and surgical information contained in the database.

Research results

We identified 3306 cases of syndactyly between 1997 and 2014 in New York State. The overall incidence was 0.074% or 7 cases per 10000 live births. In total, 178 patients underwent surgical management in New York State and 79% of patients were under the age of two at the time of surgery. Approximately, 87% of surgeries were performed at teaching hospitals, and 52% of procedures were performed by plastic surgeons. Patients having surgery in New York State were more likely to have Medicaid insurance compared to patients not having surgery.

Research conclusions

Syndactyly occurs in approximately 7 per 10000 live births, and the majority of patients undergoing surgical correction are treated before age two. There may be several barriers to care including the availability of specialized hand surgeons, access to teaching hospitals, and insurance status.

Research perspectives

Additional research is needed to determine the incidence of syndactyly in other populations, understand the low rates of surgical management in New York State, and describe the outcomes of surgery in this population. Statewide databases are well-suited for these types of studies.

REFERENCES

1 **Dy CJ**, Swarup I, Daluiski A. Embryology, diagnosis, and evaluation of congenital hand anomalies. *Curr Rev Musculoskelet Med* 2014; **7**: 60-67 [PMID: 24515896 DOI: 10.1007/s12178-014-9201-7]
2 **Dao KD**, Shin AY, Billings A, Oberg KC, Wood VE. Surgical treatment of congenital syndactyly of the hand. *J Am Acad Orthop Surg* 2004; **12**: 39-48 [PMID: 14753796 DOI: 10.5435/00124635-200401000-00006]
3 **Goldfarb CA**. Congenital hand anomalies: a review of the literature, 2009-2012. *J Hand Surg Am* 2013; **38**: 1854-1859 [PMID: 23683863 DOI: 10.1016/j.jhsa.2013.03.023]
4 **Percival NJ**, Sykes PJ. Syndactyly: a review of the factors which influence surgical treatment. *J Hand Surg Br* 1989; **14**: 196-200 [PMID: 2545804 DOI: 10.1016/0266-7681(89)90125-3]
5 **Kozin SH**. Syndactyly. *J Am Soc Surg Hand* 2001; **1**: 1-13 [DOI: 10.1053/jssh.2001.21778]
6 **Eaton CJ**, Lister GD. Syndactyly. *Hand Clin* 1990; **6**: 555-575 [PMID: 2176654]
7 **Lamb DW**, Wynne-Davies R, Soto L. An estimate of the population frequency of congenital malformations of the upper limb. *J Hand Surg Am* 1982; **7**: 557-562 [PMID: 7175125 DOI: 10.1016/S0363-5023(82)80101-9]
8 **Light TR**. Congenital anomalies: syndactyly, polydactyly, and cleft hand. In: Peimer CA, eds. Surgery of the hand and upper extremity. New York, NY: McGraw-Hill; 1996; 2121-2123
9 **Dai L**, Zhou GX, Zhu J, Mao M, Heng ZC. [Epidemiological analysis of syndactyly in Chinese perinatals]. *Zhonghua Fuchanke Zazhi* 2004; **39**: 436-438 [PMID: 15347462 DOI: 10.3760/j.issn:0529-567x.2004.07.002]
10 **Ekblom AG**, Laurell T, Arner M. Epidemiology of congenital upper limb anomalies in 562 children born in 1997 to 2007: a total population study from stockholm, sweden. *J Hand Surg Am* 2010; **35**: 1742-1754 [PMID: 20961708 DOI: 10.1016/j.jhsa.2010.07.007]
11 **Giele H**, Giele C, Bower C, Allison M. The incidence and epidemiology of congenital upper limb anomalies: a total population study. *J Hand Surg Am* 2001; **26**: 628-634 [PMID: 11466636 DOI: 10.1053/jhsu.2001.26121]
12 **Goldfarb CA**, Shaw N, Steffen JA, Wall LB. The Prevalence of Congenital Hand and Upper Extremity Anomalies Based Upon the New York Congenital Malformations Registry. *J Pediatr Orthop* 2017; **37**: 144-148 [PMID: 27078227 DOI: 10.1097/BPO.0000000000000748]
13 **Comer GC**, Ladd AL. Management of complications of congenital hand disorders. *Hand Clin* 2015; **31**: 361-375 [PMID: 25934210 DOI: 10.1016/j.hcl.2015.01.011]
14 **Bauer TB**, Tondra JM, Trusler HM. Technical modification in repair of syndactylism. *Plast Reconstr Surg (1946)* 1956; **17**: 385-392 [PMID: 13335516 DOI: 10.1097/00006534-195605000-00007]
15 **Kettelkamp DB**, Flatt AE. An evaluation of syndactylia repair. *Surg Gynecol Obstet* 1961; **113**: 471-478 [PMID: 13752783]
16 **Lumenta DB**, Kitzinger HB, Beck H, Frey M. Long-term outcomes of web creep, scar quality, and function after simple syndactyly surgical treatment. *J Hand Surg Am* 2010; **35**: 1323-1329 [PMID: 20638200 DOI: 10.1016/j.jhsa.2010.04.033]
17 **Bush ML**, Hardin B, Rayle C, Lester C, Studts CR, Shinn JB. Rural barriers to early diagnosis and treatment of infant hearing loss in Appalachia. *Otol Neurotol* 2015; **36**: 93-98 [PMID: 25325844 DOI: 10.1097/MAO.0000000000000636]
18 **Skaggs DL**, Clemens SM, Vitale MG, Femino JD, Kay RM. Access to orthopedic care for children with medicaid versus private insurance in California. *Pediatrics* 2001; **107**: 1405-1408 [PMID: 11389265 DOI: 10.1542/peds.107.6.1405]
19 **Skaggs DL**, Lehmann CL, Rice C, Killelea BK, Bauer RM, Kay RM, Vitale MG. Access to orthopaedic care for children with medicaid versus private insurance: results of a national survey. *J Pediatr Orthop* 2006; **26**: 400-404 [PMID: 16670556 DOI: 10.1097/01.bpo.0000217715.87857.24]
20 **Mayer ML**, Beil HA, von Allmen D. Distance to care and relative supply among pediatric surgical subspecialties. *J Pediatr Surg* 2009; **44**: 483-495 [PMID: 19302846 DOI: 10.1016/j.jpedsurg.2008.08.015]
21 **Cortez M**, Fernandes Júnior JV, da Silva RF, Gilbert A, Valenti P, Brandt CT, Teles AA. Surgical results from treating children with syndactyly through the collective effort system at "SOS Hand Recife" between 2005 and 2009. *Rev Bras Ortop* 2014; **49**: 396-400 [PMID: 26229834 DOI: 10.1016/j.rboe.2014.07.006]
22 **Canizares MF**, Feldman L, Miller PE, Waters PM, Bae DS. Complications and Cost of Syndactyly Reconstruction in the United States: Analysis of the Pediatric Health Information System. *Hand* 2017; **12**: 327-334 [PMID: 28644945 DOI: 10.1177/1558944716668816]
23 **Deunk J**, Nicolai JP, Hamburg SM. Long-term results of syndactyly correction: full-thickness versus split-thickness skin grafts. *J Hand Surg Br* 2003; **28**: 125-130 [PMID: 12631483 DOI: 10.1016/S0266-7681(02)00306-6]
24 **Jose RM**, Timoney N, Vidyadharan R, Lester R. Syndactyly correction: an aesthetic reconstruction. *J Hand Surg Eur Vol* 2010; **35**: 446-450 [PMID: 20237190 DOI: 10.1177/1753193410362638]

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SYSTEMATIC REVIEWS

Magnetically controlled growing instrumentation for early onset scoliosis: Caution needed when interpreting the literature

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Abstract

BACKGROUND

Magnetically controlled growing rods (MCGR) are a novel treatment option for early onset scoliosis (EOS). Although the complication profile with MCGR use has been reviewed, these reviews do not take into account important implants modifications, termed iterations, that were made due to early on postoperative complications is not well reported or understood.

AIM

To assess the effect of MCGR implant iterations on post-operative complications in EOS.

METHODS

A systematic review was performed to identify studies investigating MCGR specifically for the treatment of EOS, refined to those reporting the implant iteration, specifically the incorporation of the keeper plate to the implant design. Articles with mixed implant iteration usage were excluded. Complications following surgery were recorded as well as potential risk factors and compared between implant cohorts.

RESULTS

Although 20 articles were identified for inclusion, 5 included mixed implant iteration leaving a total of 271 patients identified through 15 clinical studies that

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met inclusion criteria. The average follow-up was 25.4-mo. Pre-keeper plate implants were utilized in 3 studies with a total of 49 patients. Overall, 115 (42.4%) post-operative complications were identified, with 87% defined as major. The addition of the keeper plate significantly decreased the rate of post-operative complications per study (35.7% *vs* 80.6%, $P = 0.036$), and the rate of distraction failure (8.1% *vs* 40.8%, $P = 0.02$). Unplanned reoperation occurred in 69 (26.7%) patients but was not different between implant iteration cohorts (25.5% without keeper plate *vs* 27.1% with keeper plate, $P = 0.92$).

CONCLUSION
MCGR for EOS has a cumulative complication rate of 42.4% but this is significantly reduced to 35.7% when reviewing only keeper-plate enabled implants. However, 25% of published articles included mixed implant iterations. Future studies should discern between implants iterations when reporting on the usage of MCGR for EOS.

Key words: Complications; Early onset scoliosis; Magnetically controlled growing instrumentations; Keeper plate; Reoperation; Systematic review

Core tip: Magnetically controlled growing rods (MCGR) are a novel treatment approach for early onset scoliosis which is gaining increases clinical usage. Since its introduction, numerous modifications have been implemented to improve the performance of the construct, however, these modifications are often over-looked in current published series. This study evaluated the effect of the addition of the keeper plate to MCGR, finding that it had a significant impact on decreasing the rate of post-operative distraction failures. Despite the impact of this modification, 25% of published articles included mixed implant designs in their series, potentially inflating reported complication rates.

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INTRODUCTION

Early onset scoliosis (EOS) is a complex entity that has seen an evolution in its approach to surgical intervention from early definitive fusion, to non-fusion technique that allow and facilitate continued spinal growth[1]. Magnetically controlled growing rods (MCGR) are one such non-fusion approach that has gained interest and support since its introduction in 2007[2]. MCGR has been found to be a safe and effective non-fusion treatment for EOS[3-5], with equivalent curve correction and thoracic height growth as compared with traditional growing rods (TGR)[6]. Clinical reports, however, on the outcomes and complications of MCGR have been limited to case series and cohort studies with limited patient numbers[2-23].

Thakar *et al*[24] preformed a retrospective review of reported studies using MCGR for the treatment of EOS. From an identified 15 studies including 336 children undergoing MCGR insertion, they identified a mean complication rate of 44.5%, with 33% of children undergoing an unplanned reoperation. However, the timeline of these studies included spanned a seven year period since the introduction of the implant[24]. Over this period, the manufacturers made several alterations to the implant design, consisting first of the addition of a keeper plate in 2010 to the actuator to decrease the incidence of lost distraction, followed by alterations to the welding process in 2012, as well as expanded size options in the rod and actuator[2,25].

Early reports identified a high rate of loss of distraction due to the magnetic lengthening mechanism being unable to maintain the rod in the lengthened position. Due to the rotatory mechanism of lengthening, this inability to lock the rod in the lengthened position, the actuator was prone to unwind and shorten resulted in a loss

of distraction[2,25]. To combat this, a magnetic lock, the keeper plate, was applied around the lengthening mechanism to maintain the rod in place at its desired length and prevent the rod collapse identified in the early implant iterations, Figure 1. However, the efficacy of the keeper plate to decrease the rate of loss of distraction has not been previously reported.

The aim of this study is to examine the reported literature on the reporting of implant iterations as well as its effect on the post-operative complication rates following MCGR implantation for the treatment of EOS, specifically the effect of the addition of the keeper plate. We hypothesized that the reporting of implant iteration would be limited and the rate of postoperative complications, specifically the rate of distraction loss, would be significantly lower in children treated with implants containing a keeper plate.

MATERIALS AND METHODS

Literature search

After obtaining institutional review board approval, a comprehensive systematic review was conducted using an internet-based search beginning with queries into the MEDLINE database for all articles between January 1, 1967 and February 1, 2018. The search terms included: (1) "early onset scoliosis"; (2) "magnetically controlled growing rods"; (3) "scoliosis"; and (4) "magnetically controlled growing rods complications". The preferred reporting items for systematic reviews and meta-analyses protocol was followed for data analysis and synthesis[26].

Study selection

The abstracts of all identified articles were subsequently analyzed to determine relevance to complications associated with MCGR for early-onset scoliosis. Articles were excluded for one or more of the following criteria: Literature review or expert opinion, publication in non-English language, published prior to the year 1967, did not include pediatric patients, included fewer than 3 patients, implanted instrumentation other than MCGR. Studies reported from the same institution were further scrutinized to determine if overlapping patient cohorts were reported, excluding studies with shorter average follow-up.

A total of 49 articles were identified for further review. The full manuscripts of the remaining studies were then reviewed for the following inclusion criteria: Peer-reviewed clinical studies of level I to IV evidence, involving pediatric patients undergoing surgery for implantation of MCGR, and reporting the number of perioperative complications and unplanned procedures. The references of all articles were cross-referenced as well for any additional articles that were not found on the initial search. The patient cohorts of studies with the same authors and/or institutions were scrutinized to ensure that no redundant data was collected.

Articles were further reviewed to determine the iteration of implant utilized. Since its introduction, there have been 7 main alterations to the implant design with the earliest change being the addition of a keeper plate, introduced in 2010, to correct early issues with loss of distraction[2,25]. Articles were reviewed to delineate between series with and without the keeper plate based upon either direct report or time period reviewed in each study. For studies that did not specify the iteration of implant used, surgical dates were reviewed with years before 2010 defined as pre-Keeper plate series. Studies with mixed implants utilized were included in the analysis if they included > 80% of procedures with a specific implant. Studies with overlapping surgical dates were excluded.

Patient demographics (age, gender, curve etiology), construct design (number of rods implanted, technique, anchors placed), and the frequency and number of lengthening's were extracted from each article. Complication rates were recorded for each study. Complications were classified as either major or minor, with major complications defined as complications necessitating cessation of treatment (failure of distraction) or revision surgery (implant failure to include rod breakage, screw pull-out, proximal junctional kyphosis, deep surgical site infection, or sequela that did not resolve without significant interventions). Minor complications were defined as prominent hardware, superficial surgical site infection, or issues that required minimal intervention without repeat surgical intervention. Reoperation or need for revision surgery was recorded as a separate variable.

Data analysis was performed using SPSS statistical package version 24 (SPSS Inc, Chicago, IL, United States). Significance was set at $P < 0.05$. Descriptive statistics were generated. Univariate analyses were used to compare overall complication rates by implant iteration, specific complication rates, and to identify risk factors for post-

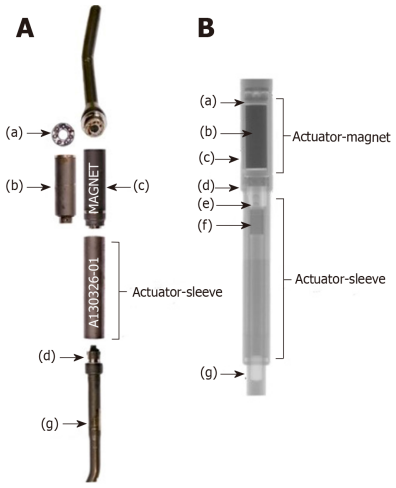

Figure 1 Clinical and radiographic image of a magnetically controlled growing rod after sectioning. A: Clinical image of a magnetically controlled growing rod after sectioning; B: Radiographic image of a magnetically controlled growing rod after sectioning. The keeper plate (label c) is seen in its position around the magnet (label b). The Figure is adapted from Panagiotopoulou *et al*[31].

operative complications.

RESULTS

A total of 49 studies were identified for manuscript review. After review of the manuscripts, 26 were excluded (7 mechanical failure studies, 6 cost comparison studies, 3 imaging studies, 2 case reports, 2 editorial, 2 non-human studies, 2 animal studies, 1 case series, and 1 review article). Of the remaining 23 clinical articles, 3 additional studies were excluded (1 each with insufficient patient number, overlapping patient samples, combined MCGR/Shilla technique) leaving 20 clinical studies for review. Of these 20 studies, an additional 5 studies were excluded due to mixed implant iterations leaving 15 studies that met inclusionary criteria, consisting of 11 case series and 4 cohort studies, Figure 2.

From the 15 clinical articles, a total of 271 children were identified (7.87 years ± 1.54 years, 46.8% male) with an average of 26.4-mo follow-up. Curve etiology is summarized in Table 1, with idiopathic (32.8%) reported as the most common, and an average curve magnitude of 61.3 degrees. Pre-keeper plate implants were utilized in 3 studies with remaining 12 post-Keeper plate implants. The majority of cases were primary MCGR implantations (74.7%) *vs* conversion procedures (25.2%). Dual rod instrumentation (76.4%) was the most common construct, with children undergoing an average of 7.85 lengthening's.

From the identified 271 children, 115 (42.4%) experienced a post-operative complication, Table 2. Of the 115 complications, 95 (82.6%) were defined as major, with an average major complication rate of 80% per study. Complications were not subdivided according to curve etiology. Failure of distraction was the most common complication, occurring in 14% of children, followed by implant failure (including rod breakage and implant failure not otherwise characterized) in 8.86%, and screw/hook pullout (8.12%), Table 2. Of the 115 children with a postoperative complication, 69 patients (27.9% of overall cohort) required an unplanned reoperation. The most common reason for reoperation was the inability to distract (n = 20), followed by proximal instrumentation pullout with or without proximal junctional kyphosis (n = 19), rod breakage (n = 19), wound dehiscence/infections (n = 6), prominent hardware (n = 2), and 3 unlisted procedures.

Univariate analysis of complications between implant iterations identified that complication rates significantly decreased with the addition of the keeper plate (35.7% *vs* 80.6%, P = 0.036, Table 2). Additionally, there was a statistically significant decrease in the rate of distraction failure in the keeper plate cohort (8.1% *vs* 40.8%, P = 0.02). There was not difference in reoperation rates between implant iteration cohorts (25.5% without keeper plate *vs* 27.1% with keeper plate, P = 0.92). Identified studies did not provide information for revision surgeries according to type of instrumentation (single rod *vs* dual road), or by proximal anchor type (rib *vs* spine) or number of proximal anchor points. Given the paucity of available data, a subgroups

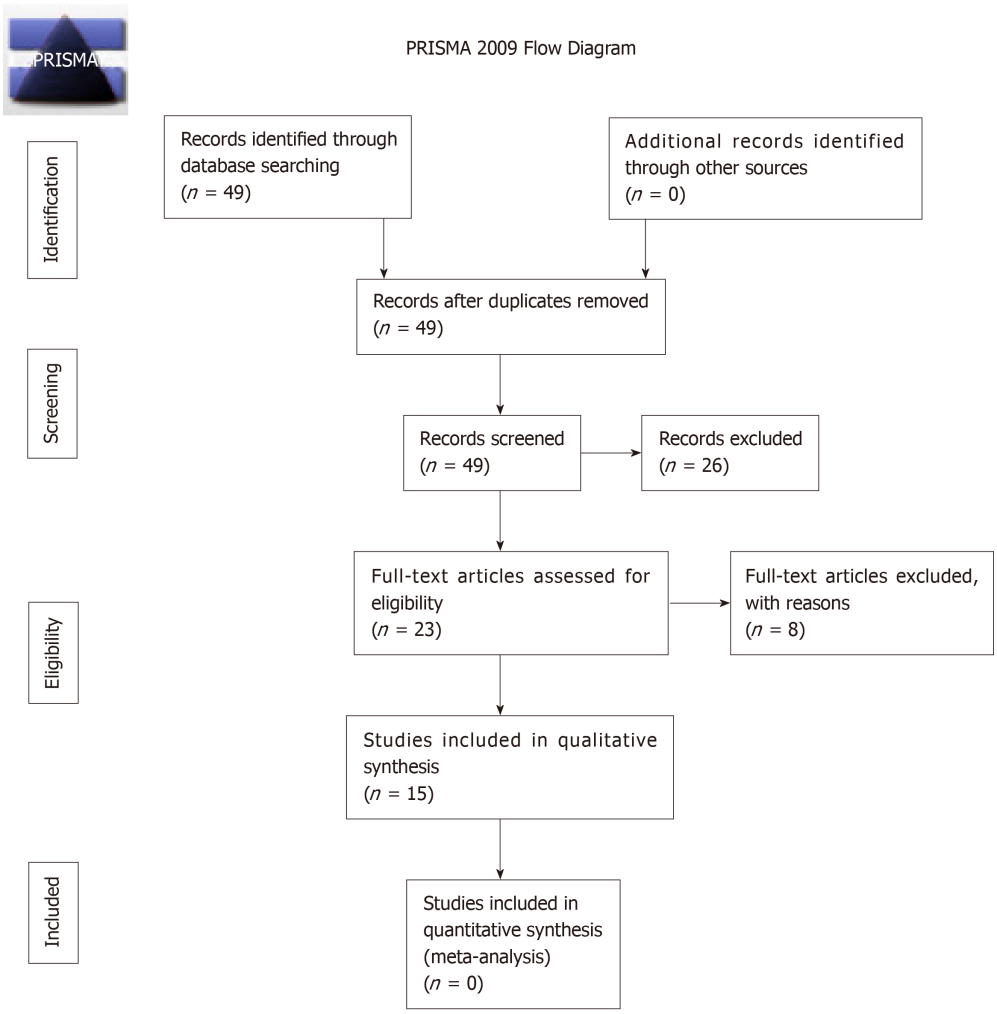

Figure 2 The preferred reporting items for systematic reviews and meta-analyses flowchart depicting protocol for reviewing studies considered for inclusion. PRISMA: Preferred reporting items for systematic reviews and meta-analyses.

analysis was foregone. Summary of articles included for analysis is shown in the Table 3.

DISCUSSION

Through this systematic review, we identified that children treated with all types of MCGR implants for EOS have a 42.4% rate of postoperative complications at an average of 26.4-mo follow-up after implantation, with failure of distraction being the most common complication seen in 14%. The implant iteration was found to significantly affect complication rates with the keeper plate-enabled implants significantly decreasing the rate of postoperative complications (35.7% *vs* 80.6%). However, of the 20 studies published at the time of this review, 25% included mixed implants iterations in their retrospective reviews.

Complications in the treatment of EOS are not infrequent, given the patient age and the necessity to accommodate continued growth of the thorax and spine. TGR instrumentation preceded MCGR in the treatment of EOS, with well-reported complication profiles. Bess *et al*[27] reported that 58% of patients developed at least one complication during their treatment duration, with higher rates of complications with the use of single rod fixation, decreasing patient age, and with each additional lengthening procedure. Yang *et al*[28] identified underlying scoliosis etiology, prior rod failure, single rod constructs, stainless steel rods, small diameter rods, and tandem connector variables as risk factors for rod failure with TGR. Additionally, the requirement for repeat surgical interventions for lengthening increase the rate of wound and other complications 24% for each additional lengthening procedure[28].

MCGR was developed in an attempt to meet the need for continued spinal growth and curve correction while attempting to decrease the risk of post-operative

Table 1 Summary of patient and surgery characteristics for identified patients undergoing magnetically controlled growing rods instrumentation, *n* (%)

Items	
Curve etiology	
Idiopathic	89 (32.8)
Congenital	43 (15.9)
Syndromic	68 (25.1)
Neuromuscular	63 (23.2)
Neurofibromatosis	8 (2.9)
Type of surgery	
Primary	195 (74.7)
Conversion	66 (25.3)
Unspecified	10
Type of instrumentation	
Single rod	64 (23.6)
Dual rod	207 (76.4)

complications. MCGR functionally lengthens the spinal construct through the application of an external magnet which induces a rotatory motion to the actuator, which is threaded, resulting in elongation[2]. Akbarnia *et al*[6] performed a case-matched comparison of children with EOS treated with MCGR and TGR, finding equivalent curve correction and thoracic height gain. Although the MCGR cohort had less overall surgical procedures, the incidence of unplanned reoperation secondary to post-operative complications was not affected, with 75% of MCGR reoperations occurring secondary to unspecified implant failures.

Unique to MCGR is the risk of rod distraction failure[29], which accounts for between 25%-35% of unplanned surgical procedures[4,29]. The current findings reinforce previous studies[24], that these instances are not isolated, with loss of distraction accounting for 33% of all complications, and 28.9% of reoperations. Numerous mechanisms for distraction failure have been identified in the literature, to include: Fracture of the actuator pin, wear of the extending bar, debris in the actuator, damage to the radial bearings, and O-ring seal failure[30,31]. Loss of distraction ranged in the reported articles, accounting for between 0% to 100% of complications, and affecting between 0% and 100% of patients/series (average 14.86% patients/series)[2-22,29,32].

The only identified risk factor for complication was the use of a pre-keeper plate implant, with an 80.6% complication rate compared with 35.7% in keeper plate enabled implants. The necessity for the keeper plate was identified early following the induction of MCGR due to tendency for the actuator to unwind and shorten resulted in a loss of distraction[2,25]. To combat this, a magnetic lock, the keeper plate, was applied around the lengthening mechanism to maintain the actuator in the desired lengthen position and prevent rod collapse[25]. With regard to distraction failure, this decreased to a rate of 8.1% from 40.8% with the introduction of the keeper plate. This data indicates that the keeper plate was successful as designed to lock the magnetic actuator in its lengthening position, resisting the tendency to unwind and shorten following distraction.

An important implication of this data is in the future reporting of clinical outcomes of MCGR and the synthesis of the current published literature in systematic reviews. Since the introduction of MCGR technology, the product has gone through a continual process of quality improvement, evident by the seven iteration changes to date[1,9]. This study is the first to report on the effect these iteration changes have on post-operative complications, specifically the introduction of the keeper plate to reduce rod distraction failure. Despite this fact, 25% of the published clinical articles included mixed implant iterations in their analysis. Given these significant differences, future studies and systematic reviews need to include implant iterations in their data reporting and analysis for postoperative complications to avoid contaminating the results of more recent MCGR implant iterations.

This study is not without its limits. As a systematic review, the strength of the findings are solely dependent on the quality and rigor of the studies included in the analysis, which in this instance is comprised largely of level IV case series and four level II cohort studies. As a newer surgical technique, there is also the risk for performance bias between the 2 study cohorts, which could also impact the rate of

Table 2 Summary of hardware related complications following magnetically controlled growing rods instrumentation for early onset scoliosis

	Complication rate	Without keeper plate	With keeper plate
Overall complication rate/study	35.6% (n = 115)	80.61% (n = 38)	35.65% (n = 77)
Major complications	n = 95	n = 32	n = 63
Cumulative Complications			
Distraction failure	14.0% (n = 38)	40.8% (n = 20)	8.1% (n = 18)
Implant failure	8.86% (n = 24)	18.36% (n = 9)	6.76% (n = 15)
Screw pull-out	8.12% (n = 22)	4.1% (n = 2)	9.0% (n = 20)
Infection	2.2% (n = 6)	2.04% (n = 1)	2.25% (n = 5)
Prominent hardware	2.58% (n = 7)	14.28% (n = 7)	0% (n = 0)
Proximal junctional kyphosis	2.58% (n = 7)	0% (n = 0)	3.15% (n = 7)
Wound dehiscence	0.74% (n = 2)	0% (n = 0)	0.9% (n = 2)

postoperative complications. This is further confounded by the temporal relationships between included studies. The concern for overlapping patients in the identified studies was mitigated by close inspection of the study methods. However, several studies reported data from multi-center databases[1,2,15,18] and as such, the risk for overlapping information is present.

A number of the identified risk factors for post-operative complications, include patient age, curve etiology, number, and type of proximal and distal fixation points, as well as type of implantation (primary *vs* conversion), were not able to be investigated due to a lack of reporting in the original studies. The average follow-up in this review consisted of 26 mo. Given that the average patient age at time of MCGR implantation was 7.87 years, these results do not account for the full extent of the child's treatment course and may underestimate the long-term complication profile. Additionally, there is no standard method for reporting complications for children treated with MCGR, leading to variable methods of reporting in the identified studies.

Given these identified deficiencies in standardized complication reporting, we recommend future studies also consider MCGR complication reporting according to patient and treatment variables (underlying diagnosis, number of rods, type of implantation, type and number of proximal anchorage points, occurrence of complication by number of lengthenings) and classify complications into the following categories: Permanent mechanical distraction failure, temporary distraction failure, rod breakage unrelated to the distraction mechanism, proximal anchorage failure, infectious/wound complication, and hardware prominence. These six categories represent the most common post-operative complications, while also identifying complications requiring an alteration in the planned treatment course.

In conclusion, this systematic review identified that 271 children undergoing MCGR implantation for the treatment of EOS, resulting in a cumulative 42.4% rate of post-operative complications, 87% of which required a cessation in the planned treatment course or a reoperation. The introduction of the keeper plate significantly decreased the rate of post-operative complications to 35.7% and the rate of distraction failure. However, of the 20 clinical articles reporting on the outcomes of MCGR in EOS, 25% included mixed implant iterations highlighting the need for strict. Further research is needed to investigate the effects of subsequent implant iterations as well as the long-term outcomes of treatment.

Table 3 Summary of articles included for analysis

First author	Yr	Keeper plate?	# Of patients	Primary surgeries	Revisions	% Male	Age at surgery (yr)	Curve magnitude
Hickey[8]	2014	Y	8	4	4	75%	4.5	59.25
Akbarnia[6]	2014	N	12	12	0	42%	6.8	59
Lebon[4]	2017	Y	30	25	5	53%	9.1	66
Akbarnia[2]	2013	N	14	14	0	50%	8.83	60
Thompson[17]	2016	Y	19	11	8	53%	9.1	62
Heydar[14]	2017	Y	16	16	0	37.5%	7.83	62
Heydar[3]	2016	Y	18	18	0	39%	7.3	68
Yılmaz[18]	2016	Y	8	5	3	25%	10.6	---
Keskinen[16]	2016	Y	50	27	23	38.4%		55.2
Hosseini[15]	2016	N	23	15	8	29.2%	7.45	55.35
La Rosa[21]	2017	Y	10	10	0	50%	7.2	64.7
Teoh[11]	2016	Y	8	4	4	---	8.2	60
Rolton[22]	2016	Y	21	10	11	52%	7.8	54
Nnadi[23]	2018	Y	10	10	0	50%	6.2	57.7
Ridderbusch[5]	2017	Y	24	24	0	33%	8.9	63

ARTICLE HIGHLIGHTS

Research background

Although the outcomes of using magnetically controlled growing rods (MCGR) to treat early onset scoliosis (EOS) has been reviewed, these studies do not take into account important implants modifications, termed iterations, that were made due to early on postoperative complications is not well reported or understood.

Research motivation

To gain a deeper understanding of how modification to MCGR after affected patients outcomes for the treatment of EOS and the implications of these effects on the reporting of future MCGR.

Research objectives

To assess the effect of MCGR implant iterations on post-operative complications in EOS.

Research methods

A systematic review was performed to identify studies investigating MCGR specifically for the treatment of EOS, refined to those reporting the implant iteration, specifically the incorporation of the keeper plate to the implant design. Articles with mixed implant iteration usage were excluded. Complications following surgery were recorded as well as potential risk factors and compared between implant cohorts.

Research results

Although 20 articles were identified for inclusion, 5 (25%) included mixed implant iteration leaving a total of 271 patients identified through 15 clinical studies that met inclusion criteria. Pre-keeper plate implants were utilized in 3 studies with a total of 49 patients. Overall, 115 (42.4%) post-operative complications were identified, with 87% defined as major. The addition of the keeper plate significantly decreased the rate of post-operative complications per study (35.7% *vs* 80.6%, $P = 0.036$), and the rate of distraction failure (8.1% *vs* 40.8%, $P = 0.02$). Unplanned reoperation occurred in 69 (26.7%) patients but was not different between implant iteration cohorts (25.5% without keeper plate *vs* 27.1% with keeper plate, $P = 0.92$).

Research conclusions

MCGR implant with Keeper plates have less post-operative distraction failures. Of the currently published studies, 25% include mixed implant designs. Future studies reporting on MCGR outcomes should include implant iteration in their analysis. MCGR implant with Keeper plates have less post-operative distraction failures. Of the currently published studies, 25% include mixed implant designs. Studies included mixed implant iterations could be artificially inflating postoperative complication rates. Have more recent implant modification exhibited similar effects on MCGR outcomes. Twenty-five percent of currently published studies on MCGR outcomes included mixed implant iterations which could be artificially inflating complication rates. The addition of the keeper plate has decreased the incidence of distraction failure in the treatment of EOS. Understanding implant design gives important insight to understanding how they affect patient outcomes.

Research perspectives

Future studies should include implant iterations in the reporting of MCGR outcomes for the treatment of EOS. Long-term follow-up of children treated with MCGR for EOS. Subdividing MCGR outcomes by implant iteration will help ensure complications rates are not artificially inflated.

REFERENCES

1 **Yang S**, Andras LM, Redding GJ, Skaggs DL. Early-Onset Scoliosis: A Review of History, Current Treatment, and Future Directions. *Pediatrics* 2016; **137** [PMID: 26644484 DOI: 10.1542/peds.2015-0709]
2 **Akbarnia BA**, Cheung K, Noordeen H, Elsebaie H, Yazici M, Dannawi Z, Kabirian N. Next generation of growth-sparing techniques: preliminary clinical results of a magnetically controlled growing rod in 14 patients with early-onset scoliosis. *Spine (Phila Pa 1976)* 2013; **38**: 665-670 [PMID: 23060057 DOI: 10.1097/BRS.0b013e3182773560]
3 **Heydar AM**, Şirazi S, Bezer M. Magnetic Controlled Growing Rods as a Treatment of Early Onset Scoliosis. *Spine* 2016; **41**: E1336-E1342 [PMID: 27831988 DOI: 10.1097/brs.0000000000001614]
4 **Lebon J**, Batailler C, Wargny M, Choufani E, Violas P, Fron D, Kieffer J, Accadbled F, Cunin V, De Gauzy JS. Magnetically controlled growing rod in early onset scoliosis: a 30-case multicenter study. *Eur Spine J* 2017; **26**: 1567-1576 [PMID: 28040873 DOI: 10.1007/s00586-016-4929-y]
5 **Ridderbusch K**, Rupprecht M, Kunkel P, Hagemann C, Stücker R. Preliminary Results of Magnetically Controlled Growing Rods for Early Onset Scoliosis. *J Pediatr Orthop* 2017; **37**: e575-e580 [PMID: 27182837 DOI: 10.1097/BPO.0000000000000752]
6 **Akbarnia BA**, Pawelek JB, Cheung KM, Demirkiran G, Elsebaie H, Emans JB, Johnston CE, Mundis GM, Noordeen H, Skaggs DL, Sponseller PD, Thompson GH, Yaszay B, Yazici M; Growing Spine Study Group. Traditional Growing Rods Versus Magnetically Controlled Growing Rods for the Surgical Treatment of Early-Onset Scoliosis: A Case-Matched 2-Year Study. *Spine Deform* 2014; **2**: 493-497 [PMID: 27927412 DOI: 10.1016/j.jspd.2014.09.050]
7 **Dannawi Z**, Altaf F, Harshavardhana NS, El Sebaie H, Noordeen H. Early results of a remotely-operated magnetic growth rod in early-onset scoliosis. *Bone Joint J* 2013; **95-B**: 75-80 [PMID: 23307677 DOI: 10.1302/0301-620X.95B1.29565]
8 **Hickey BA**, Towriss C, Baxter G, Yasso S, James S, Jones A, Howes J, Davies P, Ahuja S. Early experience of MAGEC magnetic growing rods in the treatment of early onset scoliosis. *Eur Spine J* 2014; **23** Suppl 1: S61-S65 [PMID: 24413746 DOI: 10.1007/s00586-013-3163-0]
9 **Skov ST**, Wijdicks SPJ, Bünger C, Castelein RM, Li H, Kruyt MC. Treatment of early-onset scoliosis with a hybrid of a concave magnetic driver (magnetic controlled growth rod) and a contralateral passive sliding rod construct with apical control: preliminary report on 17 cases. *Spine J* 2018; **18**: 122-129 [PMID: 28687252 DOI: 10.1016/j.spinee.2017.06.027]
10 **Teoh KH**, Winson DM, James SH, Jones A, Howes J, Davies PR, Ahuja S. Do magnetic growing rods have lower complication rates compared with conventional growing rods? *Spine J* 2016; **16**: S40-S44 [PMID: 26850175 DOI: 10.1016/j.spinee.2015.12.099]
11 **Teoh KH**, Winson DM, James SH, Jones A, Howes J, Davies PR, Ahuja S. Magnetic controlled growing rods for early-onset scoliosis: a 4-year follow-up. *Spine J* 2016; **16**: S34-S39 [PMID: 26844638 DOI: 10.1016/j.spinee.2015.12.098]
12 **Cheung JP**, Bow C, Samartzis D, Kwan K, Cheung KM. Frequent small distractions with a magnetically controlled growing rod for early-onset scoliosis and avoidance of the law of diminishing returns. *J Orthop Surg (Hong Kong)* 2016; **24**: 332-337 [PMID: 28031501 DOI: 10.1177/1602400312]
13 **Cheung KM**, Cheung JP, Samartzis D, Mak KC, Wong YW, Cheung WY, Akbarnia BA, Luk KD. Magnetically controlled growing rods for severe spinal curvature in young children: a prospective case series. *The Lancet* 2012; **379**: 1967-1974 [PMID: 22520264 DOI: 10.1016/s0140-6736(12)60112-3]
14 **Heydar AM**, Şirazi S, Okay E, Kiyak G, Bezer M. Short Segment Spinal Instrumentation in Early-onset Scoliosis Patients Treated With Magnetically Controlled Growing Rods: Surgical Technique and Mid - Short-term Outcomes. *Spine (Phila Pa 1976)* 2017; **42**: 1888-1894 [PMID: 28582331 DOI: 10.1097/BRS.0000000000002265]
15 **Hosseini P**, Pawelek J, Mundis GM, Yaszay B, Ferguson J, Helenius I, Cheung KM, Demirkiran G, Alanay A, Senkoylu A, Elsebaie H, Akbarnia BA. Magnetically controlled Growing Rods for Early-onset Scoliosis: A Multicenter Study of 23 Cases With Minimum 2 years Follow-up. *Spine (Phila Pa 1976)* 2016; **41**: 1456-1462 [PMID: 26974834 DOI: 10.1097/BRS.0000000000001561]
16 **Keskinen H**, Helenius I, Nnadi C, Cheung K, Ferguson J, Mundis G, Pawelek J, Akbarnia BA. Preliminary comparison of primary and conversion surgery with magnetically controlled growing rods in children with early onset scoliosis. *Eur Spine J* 2016; **25**: 3294-3300 [PMID: 27160822 DOI: 10.1007/s00586-016-4597-y]
17 **Thompson W**, Thakar C, Rolton DJ, Wilson-MacDonald J, Nnadi C. The use of magnetically-controlled growing rods to treat children with early-onset scoliosis: early radiological results in 19 children. *Bone Joint J* 2016; **98-B**: 1240-1247 [PMID: 27587527 DOI: 10.1302/0301-620X.98B9.37545]
18 **Yılmaz B**, Ekşi MŞ, Işik S, Özcan-Ekşi EE, Toktaş ZO, Konya D. Magnetically Controlled Growing Rod in Early-Onset Scoliosis: A Minimum of 2-Year Follow-Up. *Pediatr Neurosurg* 2016; **51**: 292-296 [PMID: 27497928 DOI: 10.1159/000448048]
19 **Yoon WW**, Sedra F, Shah S, Wallis C, Muntoni F, Noordeen H. Improvement of pulmonary function in children with early-onset scoliosis using magnetic growth rods. *Spine (Phila Pa 1976)* 2014; **39**: 1196-1202 [PMID: 24825149 DOI: 10.1097/BRS.0000000000000383]
20 **Doany ME**, Olgun ZD, Kinikli GI, Bekmez S, Kocyigit A, Demirkiran G, Karaagaoglu AE, Yazici M. Health-Related Quality of Life in Early-Onset Scoliosis Patients Treated Surgically: EOSQ Scores in Traditional Growing Rod Versus Magnetically Controlled Growing Rods. *Spine (Phila Pa 1976)* 2018; **43**: 148-153 [PMID: 28604490 DOI: 10.1097/BRS.0000000000002274]
21 **La Rosa G**, Oggiano L, Ruzzini L. Magnetically Controlled Growing Rods for the Management of Early-onset Scoliosis: A Preliminary Report. *J Pediatr Orthop* 2017; **37**: 79-85 [PMID: 26192879 DOI: 10.1097/BPO.0000000000000597]
22 **Rolton D**, Thakar C, Wilson-MacDonald J, Nnadi C. Radiological and clinical assessment of the distraction achieved with remotely expandable growing rods in early onset scoliosis. *Eur Spine J* 2016; **25**: 3371-3376 [PMID: 26358257 DOI: 10.1007/s00586-015-4223-4]

23 **Nnadi C**, Thakar C, Wilson-MacDonald J, Milner P, Rao A, Mayers D, Fairbank J, Subramanian T. An NIHR-approved two-year observational study on magnetically controlled growth rods in the treatment of early onset scoliosis. *Bone Joint J* 2018; **100-B**: 507-515 [PMID: 29629587 DOI: 10.1302/0301-620X.100B4.BJJ-2017-0813.R1]

24 **Thakar C**, Kieser DC, Mardare M, Haleem S, Fairbank J, Nnadi C. Systematic review of the complications associated with magnetically controlled growing rods for the treatment of early onset scoliosis. *Eur Spine J* 2018; **27**: 2062-2071 [PMID: 29675673 DOI: 10.1007/s00586-018-5590-4]

25 **Jenks M**, Craig J, Higgins J, Willits I, Barata T, Wood H, Kimpton C, Sims A. The MAGEC system for spinal lengthening in children with scoliosis. *Appl Health Econ Health Policy* 2014; **12**: 587-599 [PMID: 25172432 DOI: 10.1007/s40258-014-0127-4]

26 **Liberati A**, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; **339**: b2700 [PMID: 19622552 DOI: 10.1136/bmj.b2700]

27 **Bess S**, Akbarnia BA, Thompson GH, Sponseller PD, Shah SA, El Sebaie H, Boachie-Adjei O, Karlin LI, Canale S, Poe-Kochert C, Skaggs DL. Complications of growing-rod treatment for early-onset scoliosis: analysis of one hundred and forty patients. *J Bone Joint Surg Am* 2010; **92**: 2533-2543 [PMID: 20889912 DOI: 10.2106/JBJS.I.01471]

28 **Yang JS**, Sponseller PD, Thompson GH, Akbarnia BA, Emans JB, Yazici M, Skaggs DL, Shah SA, Salari P, Poe-Kochert C; Growing Spine Study Group. Growing rod fractures: risk factors and opportunities for prevention. *Spine (Phila Pa 1976)* 2011; **36**: 1639-1644 [PMID: 21738096 DOI: 10.1097/BRS.0b013e31822a982f]

29 **Kwan KYH**, Alanay A, Yazici M, Demirkiran G, Helenius I, Nnadi C, Ferguson J, Akbarnia BA, Cheung JPY, Cheung KMC. Unplanned Reoperations in Magnetically Controlled Growing Rod Surgery for Early Onset Scoliosis With a Minimum of Two-Year Follow-Up. *Spine (Phila Pa 1976)* 2017; **42**: E1410-E1414 [PMID: 28658035 DOI: 10.1097/BRS.0000000000002297]

30 **Joyce TJ**, Smith SL, Rushton PRP, Bowey AJ, Gibson MJ. Analysis of Explanted Magnetically Controlled Growing Rods From Seven UK Spinal Centers. *Spine (Phila Pa 1976)* 2018; **43**: E16-E22 [PMID: 28459777 DOI: 10.1097/BRS.0000000000002221]

31 **Panagiotopoulou VC**, Tucker SK, Whittaker RK, Hothi HS, Henckel J, Leong JJH, Ember T, Skinner JA, Hart AJ. Analysing a mechanism of failure in retrieved magnetically controlled spinal rods. *Eur Spine J* 2017; **26**: 1699-1710 [PMID: 28102447 DOI: 10.1007/s00586-016-4936-z]

32 **Choi E**, Yaszay B, Mundis G, Hosseini P, Pawelek J, Alanay A, Berk H, Cheung K, Demirkiran G, Ferguson J, Greggi T, Helenius I, La Rosa G, Senkoylu A, Akbarnia BA. Implant Complications After Magnetically Controlled Growing Rods for Early Onset Scoliosis: A Multicenter Retrospective Review. *J Pediatr Orthop* 2017; **37**: e588-e592 [PMID: 27328123 DOI: 10.1097/BPO.0000000000000803]

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CASE REPORT

Synovial chondromatosis of the foot: Two case reports and literature review

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Abstract

BACKGROUND

Primary synovial chondromatosis (PSC) is a rare arthropathy of the synovial joints characterized by the formation of cartilaginous nodules, which may detach and become loose bodies within the joint and may undergo secondary proliferation. PSC of the foot and ankle is exceedingly rare, with only a few cases reported in the literature. The diagnosis may be difficult and delayed until operative treatment, when it is confirmed by histological assessment. PSC may degenerate into chondrosarcoma. Operative treatment is the gold standard aiming to minimize pain, improve function, prevent or limit progression of arthritis. Surgical treatment consists in debridement by arthrotomic or arthroscopic management, but there is no consensus in the literature about timing of surgery and surgical technique. Thus, the aim of this study is to report the outcomes of the surgical treatment of two cases, together with a literature review.

CASE SUMMARY

We report two cases of patients affected by PSC of the foot in stage III, according to the Milgram classification: the former PSC localized in the ankle that underwent open surgery consisted of loose bodies removal; the latter in the subtalar joint, and the choice of treatment was the arthrotomy and debridement from loose bodies, in addition to the subtalar arthrodesis. Both patients returned to complete daily and working life after surgery.

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CONCLUSION
Synovial chondromatosis is a rare benign pathology, even rarer in the ankle joint and especially in the foot. Surgery should be minimal in patients with ankle PSC, choosing the correct timing, waiting if possible until stage III. More aggressive and early surgery should be performed in patients with PSC of the foot, particularly the subtalar joint, due to the high risk of arthritic evolution.

Key words: Synovial chondromatosis; Foot; Ankle; Review; Treatment; Case report

Core tip: Synovial chondromatosis of the ankle and foot is a particularly rare, benign pathology. Despite the etiology remaining unknown, it can severely impair common daily activities of affected patients because of severe pain and limitation of joint motion. Surgical treatment should be performed in patients with Milgram's stage III primary ankle synovial chondromatosis. Earlier surgery should be limited to primary synovial chondromatosis of the foot only, because of the higher frequency of subsequent degenerative pathologies.

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INTRODUCTION

Synovial chondromatosis (SC) is a rare arthropathy of the synovial joints characterized by the formation of cartilaginous nodules in the synovium[1-3]. These nodules may detach and become loose bodies within the joint, and may undergo secondary calcification and proliferation[4] .

Some authors suggested metaplastic or neoplastic origin. Nevertheless, the exact initial stimulus resulting in synovial transformation is still unknown[2,5,6].

Males in their third to fifth decades are typically affected. SC can be classified as primary (benign neoplastic process) or secondary, and associated with joint abnormalities, such as mechanical or arthritic conditions[7]; the pathogenesis of the latter being related to certain synoviocyte dysfunction. Particularly, cells like synovial macrophages, other synoviocytes and chondrocytes may produce different enzymes and cytokines, inducing inflammation and damage to articular tissues[8].

Knee (up to 65%) and hip are mostly involved, followed by elbow and shoulder; uncommon cases have been reported in wrist, interphalangeal and temporo-mandibular joints, as well as in extra-articular locations[5,7,9,10].

Primary (P) SC of the foot and ankle is exceedingly rare, with only a few cases reported in the literature worldwide: Reports include tibiotalar, calcaneocuboid, talonavicular, subtalar, navicular-cuneiform, tarsometatarsal and meta-tarsophalangeal joints[11-15].

We report two cases of patients affected by PSC of the foot: The former in the ankle, the latter in the subtalar joint. The aim of the study is to report the outcomes of the surgical treatment of those two rare cases, together with a review of the literature.

CASES PRESENTATION

Patient 1

Male, Caucasian, 50-years-old. The patient complained of pain, stiffness, crepitation and catching sensation at his right ankle for more than 1 year. No traumatic events were reported. Personal and family history were silent at the time of onset.

At admission, clinical assessment revealed swelling of the ankle and good range of motion (ROM) (dorsiflexion 10°; plantarflexion 10°). Anterior impingement with moderate pain was detected. No vascular or neurological abnormalities were referred; laboratory test, blood and urine were normal.

Radiographs are shown in Figure 1. Multiple intra-articular loose bodies were seen

around the ankle joint, suggesting possible PSC.

Patient 2

Female, Caucasian, 43-years-old. The patient complained of pain at the right rearfoot, and two crutches were necessary for walking. These symptoms have been present and worsening over the last 2 years, and a previous surgery for tarsal tunnel syndrome was reported several years before. No other significant information on personal or family history was collected.

At admission, the right ankle was swollen and aching; ROM was good (dorsiflexion 10°; plantarflexion 30°). Palpation of sinus tarsi was painful. as was its passive motion. Ipsilateral hallux valgus was present. No vascular or neurological abnormalities were referred nor seen, and all laboratory tests were normal.

Plain radiographs of the rearfoot revealed no osseous abnormality: a cavus right foot with hallux valgus, and an arthritic degeneration of the talo-navicular joint. No loose bodies or osteochondral defects were seen (Figure 2). Magnetic resonance imaging (MRI) identified a mass extending from the subtalar joint to the soft tissue posteriorly to the medial malleolus, as an arthritic formation at the subtalar joint (Figure 3).

TREATMENT

Patient 1 underwent surgery, with removal of all the intra-articular bodies; the joint was irrigated by copious amounts of normal saline. The ankle was immobilized with a cast, and weight-bearing was avoided for 1 mo (Figure 4).

Also, patient 2 did undergo operative treatment. Direct approach to the subtalar joint was performed; fibrous, scar tissue was found, probably due to the previous surgery; multiple loose bodies and arthritic degeneration were found in the subtalar joint. A medial approach was also necessary to release the tibialis posterior nerve trapped within the synovial degenerative tissue. After removal of all loose bodies, an arthrodesis of subtalar joint was performed. At the same time, Youngswick and Akin osteotomies were performed for the hallux valgus (Figure 5).

Postoperatively, the patient was immobilized in a non-weightbearing cast for a month.

FINAL DIAGNOSIS

Histological examination of surgically harvested samples from "patient 1" revealed SC, with no evidence of malignant transformation.

Histology of patient 2's loose bodies showed multiple osseous-cartilaginous fragments from the synovium.

OUTCOME AND FOLLOW-UP

At 1-year follow up, "patient 1" was pain-free with a full ROM (dorsiflexion 20°; plantarflexion 30°), and full return to his previous daily activity level. No recurrence of pathology was observed.

At the same interval follow up, patient 2 was also pain-free with a full ROM of the ankle (dorsiflexion 20°; plantarflexion 40°), and went back to her previous daily activities. Similarly, no recurrence of pathology was seen.

DISCUSSION

Epidemiology

SC shows a 1:100,000 incidence rate[16]. The disease affects males twice as often as females, with peak incidence in the third to fifth decades[17]. Secondary forms mainly affect older subjects, between the fourth and seventh decades of life[6].

SC has rarely been reported in the prepubescent age group, and only a handful of cases have been reported extra-articularly in children[18]. Mishra finally described a PSC case in a post-partum woman[19].

SC is usually a monoarticular disease[2,11]. The knee joint is the predilection site (up to 50%-65%), followed by the hip, shoulder and elbow[7,20]. In some conditions, authors referred to "snow storm knee"; larger loose bodies fragments under the force of joint

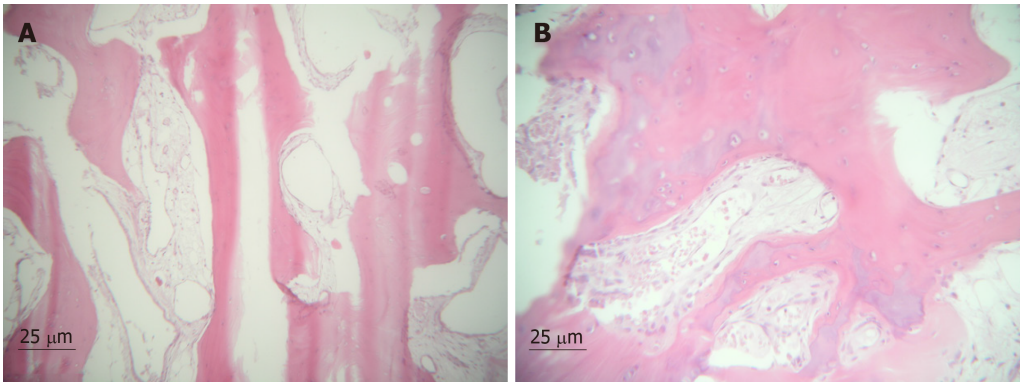

Figure 1 Histological features of synovium in chondromatosis: Trabecular and stroma, with collagen and new bone tissue forming; 10 × zoom (A) and 25 × zoom (B).

movements, giving rise to smaller bodies that may grow again in the synovium through real mitoses and matrix synthesis. This vicious circle leads to a myriad of loose bodies (from 200 to more than 1,500 bodies, often with a diameter of 1–2mm)[21]. Uncommon cases have been reported in wrist, metacarpophalangeal or interphalangeal joints, acromioclavicular, temporo-mandibular and tibiofibular articulations, as well as extra-articular locations[5,9,10]. Littrel *et al*[22] described 28 cases of PSC in the spine from 1984-2011.

PSC of the foot and ankle is exceedingly rare, with only a few cases reported in the literature worldwide. The subtalar joint is mostly affected[11,13-15]. Other reports include tibiotalar, calcaneocuboid, talonavicular, navicular-cuneiform, tarsometatarsal and metatarsophalangeal joints[1,13,15]. Recently, Isbell described a PSC case of the ankle with associated talar syndrome[23].

Pathogenesis

SC can be differentiated into primary (PSC) and secondary forms (SSC).

PSC occurs in an otherwise normal joint[10,15,18]. This form is generally thought to be progressive, more likely to recur, and may lead to severe degenerative arthritis with long term presence[15]. Primary cases are thought to be more aggressive, and a relationship with osteoarthritic processes was mentioned[24,25]. Stensby *et al*[15] reported a history of trauma in 24% of PSC cases involving the feet.

Its pathogenesis is unknown; it is considered that undifferentiated mesenchymal stem cells proliferate in the synovium, forming nodular foci of hyaline cartilage[2,5,6,21]. It is assumed that chondroid metaplasia (with high numbers of MIB-1-positive chondrocytes) occurs as a precursor of cartilaginous nodules, under the influence of bone morphogenetic protein (BMP). Cartilage develops in the synovium, leading to sessile nodules that often detach and remain as loose bodies within the synovial folds or articular cavity, being nourished by the synovial fluids, as they may calcify and even ossify over time[5,9,10,16,21,23,26]. Silva hypothesized that PSC is a secondary disorder following cartilage shedding into a joint[16].

There are rare reports of familial association (2% of cases) related to type 2 collagen abnormalities, such as those described for Wagner-Stickler syndrome. The hedgehog signaling pathway, measured by its target genes PTC1 and GLI1, may play a role in the development of PSC[20].

Several studies suggested cytogenetic implications: Mertens described complex structural chromosomal aberrations in three PSC lesions[27]. Robinson reported diploid chromosomes and expression of C-ERB B-2 in about half of the cells, indicating that the disorder is probably metaplasia of the synovium[28]. The same proto-oncogene was found in a familial case of two brothers with PSC at the ankle[20]. Apte and Athanasou[29] claimed that synovial cells in PSC express CD68 and HLA-DR. Sciot *et al*[17] reported a case of SC with clonal chromosomal changes.

Mertens reported the rearrangement of band lpl3, as loss of band IOq26 and translocations involving 12ql13-15 were as frequent as in other benign and malignant chondroid tumors[27].

Dysplasia of fibroblasts is also reported in PSC[27,30]. Pau discussed the metaplasia due to the presence of fibroblast growth factor FGF-9 and FGF receptor-3, which activate bone morphogenetic proteins 2 and 3[25]. Robinson showed changed levels of FGF-9 and FGF receptor-3, which can increase the proliferation of mesenchymal cells. The presence of FGF-9 and FGF receptor-3 creates a feedback loop that results in the continued proliferation of loose bodies[25].

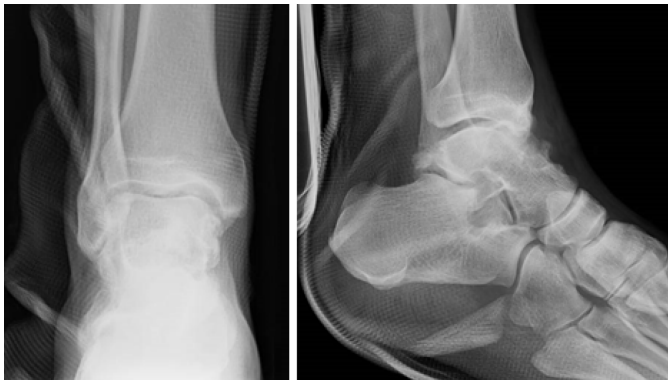

Figure 2 Radiographs of the ankle in Patient 1, after operative removal.

Although PSC is considered a benign condition (metaplasia), some authors suggested a possible neoplastic origin; indirect evidence for a neoplastic origin could be derived from the existence of well-documented cases of chondrosarcoma originating in SC[1,25,27,30,31]. Ozyurek *et al*[33] suggested neoplastic origin with chromosome 6 abnormalities[32]. In his review of 155 cases of PSC, McCarthy identified four cases of aggressive chondrosarcoma-like masses.

Secondary SC is associated with joint abnormalities, such as mechanical or arthritic conditions: Degenerative arthritis, trauma, inflammatory and non-inflammatory arthropathies, neuropathic arthropathy and avascular necrosis[20,24,34,35]. More frequent than primary chondromatosis, SSC occurs when cartilage fragments detach from articular surfaces or become embedded in the synovium. These loose bodies are nourished by the synovium, and consequently produce chondroid nodules[16,35]. Cytogenetic aberrations are absent in secondary SC[20]. SSC is not likely to recur after operative removal[10].

Clinical presentation

Diagnosis may be difficult and delayed until operative treatment, as symptoms are vague and physical assessment non-specific[6].

Although a history of ankle sprains is often described, patient may not experience any trauma, inflammatory or other joint disease[13,19,21,34].

Clinical symptoms typically include pain, swelling, stiffness and restriction of ROM[2,20,35]. Aching is described as chronic, subtle, a "catching sensation", or dull; in some cases, patients refer to "walking on pebbles"[3,10,32]. Discomfort is aggravated by physical activity, running, shoe-wearing, weight bearing and climbing stairs, which could last all-day long[10,13,23,32]. Patients may also report tingling and burning along the plantar aspect of the foot[13,23].

Physical examination demonstrated normal symmetrical alignment of the hindfoot, midfoot, and forefoot[12]. Christensen and Poulsen proposed that a clinical diagnosis may be made in the presence of any one of three diagnostic criteria: changes within the synovial membrane, metaplasia or more than three intra-articular nodules[24].

Assessment reveals focal swelling or diffuse joint enlargement, articular tenderness, articular crepitus, locking, and palpable bony nodules or a mass[18-20]. The overlying skin is usually normal, without erythema[11,18,19,36].

Movement is painful and limited[37]. Instability is normally absent as drawer ankle test negative[14,34,38].

In case of known PSC with rapid deterioration of clinical symptoms, transformation to synovial chondrosarcoma should be suspected[2].

Laboratory studies including C-reactive protein and erythrocyte sedimentation rate were normal[3,5,11,14,15].

Imaging features

Radiographs: Plain radiographs are mandatory for the diagnosis of SC.

Features of PSC include multiple intraarticular chondral bodies of uniform size distributed within the joint, with "ring-and-arc" chondroid mineralization[8,16,20]; calcified bodies are usually smooth, round and finely stippled[1,14]. Edema and calcifications of surrounding soft tissues are characteristic[36,37].

Calcifications or mineralization are common (67%-95% of cases)[1,15,20,38]. Only 29% of PSC cases presenting in the subtalar joint demonstrated mineralization, compared to 91% of cases of PSC presenting in other joints of the feet[11,12,15,24,26,39,40]. This discrepancy may in part be attributed to the average time of diagnosis from the onset of

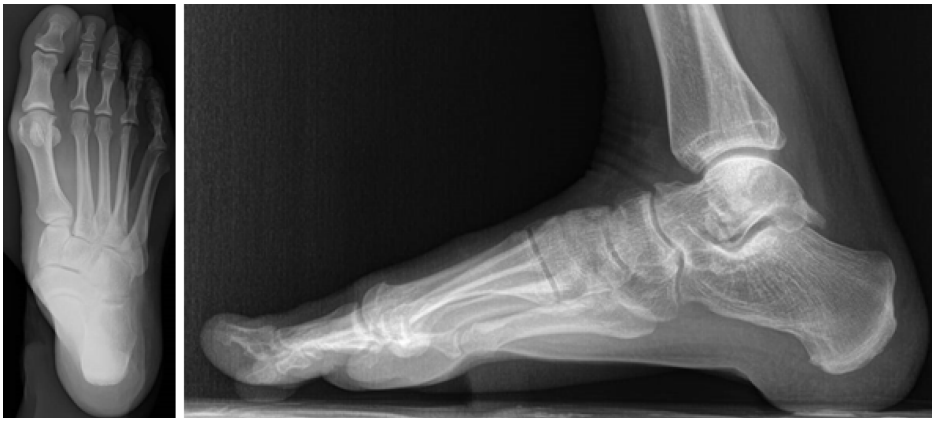

Figure 3 Pre-operative radiographs of Patient 2 with subtalar primary synovial chondromatosis.

symptoms; 12 mo in the subtalar joint and 27 mo in other joints[15].

Osseous erosion is also typical (20%-80% of all cases)[1,12,20,41]. Osseous erosions are not correlated with symptoms, while relationships with the presence of tightly adherent synovium have been reported[42].

In long-stage PSC disorders, mineralization of the nodules may evolve to enchondral ossification with peripheral calcified rim cortex and inner trabecular bone[5,41]. Although juxta-articular osteopenia may develop, bone density is usually preserved[16]. Secondary osteoarthritis may arise in more advanced untreated disease, as well as displacement or even dislocation of the joint[16,43].

SSC shows fewer osteochondral bodies with a greater variability in size, suggesting various times of origin; they exhibit several rings of calcification, in contradistinction to the single ring seen in primary disease. Osteoarthritis degeneration is usually evident as an extrinsic erosion of bone[16].

Computed tomography (CT): CT is for identifying the calcified intra-articular nodules; calcified nodules may present a "ring and arc" pattern of mineralization or a target appearance[16]. CT can also help differentiate PSC loose bodies from loose bodies that are secondary to degenerative osteoarthritis or joint destruction[1].

CT depicts document joint destruction and extrinsic bone erosion[1,20]. After intravenous administration of contrast material, peripheral and septal enhancement may be seen[16].

MRI: MRI is mandatory to assess alterations of synovium, define the stage of the disorder (Milgram's classification) and depict bone erosion. It represents the best modality to evaluate lesion extension, extrinsic bone erosion and marrow invasion[16].

Nodules of low or isointense signal on T1-weighted images and high signal on T2-weighted images, with thin peripheral and septal enhancement, are typical described; nidus of low signal intensity could be referred, depending on mineralization/ossification and joint effusion[1,16,20,36,39].

Villonodular hypertrophic synovitis is often revealed with hemosiderin deposits or mineralization, as well as calcified lesions of ankle ligaments[5,38,44].

Kramer *et al*[45] described three patterns of PSC, based on the signal intensity of the nodules. Pattern A (16% of cases) consists of lobulated homogeneous intra-articular isointense/hypointense T1-weighted and hyperintense T2-weighted nodules without mineralization. They are difficult to distinguish from the synovial fluid. If vascular supply from the synovium is present, nodules may only show peripheric gadolinium enhancement. Pattern B (75% of cases) had a similar appearance; nonetheless, foci of low signal intensity due to calcification are depicted. Pattern C (9% of cases) reveals both A and B features, but nodules are characterized by an external hypointense signal ring and fat signal core, corresponding to ossification. Among SC of the foot, pattern A is described in 44% of cases, pattern B in 33% and pattern C in 22%[15,16]. MR is also crucial to evaluate enlarging erosions, cortical destruction of bones and early marrow infiltration[33].

Other investigations: Ultrasonography may show heterogeneous avascular masses surrounded by fluid, with hyperechoic foci (cartilaginous nodules or osseous loose bodies). Posterior acoustic shadowing may be present, depending on mineralization[16]. A bone scan may be useful in determining the level of activity of the disease, and the assessment of possible recurrence after operative excision[24].

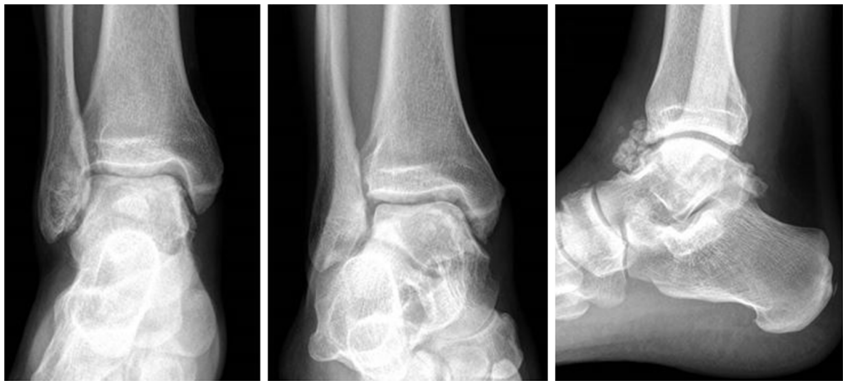

Figure 4 Radiographs of the ankle in Patient 1, showing several loose bodies at the anterior compartment.

Differential diagnosis and histopathology

The diagnosis is confirmed by histopathological examination, which reveals a «*cobblestone appearance*» of lobulated hyaline cartilage, surrounded by synovium and some degree of nuclear atypia without the presence of mitosis[9,19,20,22]. The cobblestone appearance may extend into adjacent soft tissues and bursae, as it may erode bone. Fusion or coalescence of multiple chondral bodies may occur, creating a giant conglomerate appearance; lobules of hyaline cartilage surrounded by synovial lining (a two-cell layer of cuboidal epithelium) that is usually attenuated[20].

The degree of cellularity is generally striking. Double or multiple as enlarged pleomorphic nuclei may be seen within individual chondrocytes[6]. There was no necrosis or myxoid change in the stroma. The primary and recurrent lesions showed an identical morphology[17]. Cells at the periphery of the cartilage nodules express FGFR3 and PCNA (proliferating cell nuclear antigen)[28]. DNA image cytometry suggests that chondrocytes in primary SC are active[1]. Figure 6 shows the histological pattern.

The differential diagnosis includes[5,10,18,24,31,34,38,46,47]: (1) Joint disorders: degenerative arthropathy, osteochondritis dissecans, neurotrophic, tuberculous, rheumatoid or septic arthritis, injury-related soft tissue calcification, osteochondral fractures and avascular necrosis; (2) Benign disorders: Synovial hemangioma, pigmented Villonodular synovitis, chondroma, tenosynovial giant cell tumor, calcifying aponeurotic fibroma, periosteal chondroma; and (3) Malignant disorders: Chondrosarcoma, synovial chondrosarcoma, synovial sarcoma; in case of proximity of nerves, neurofibroma, schwannoma and peripheral nerve sheath tumor.

Although PSC is considered completely benign, recent interest in diagnosis has occurred due to about 2.5%-5% relative risk for malignant degeneration[30,33,48]. Bojanic *et al*[49] reported malignant transformation to chondrosarcoma in 17%-25% of all cases, while Galat *et al*[1] reported two cases of transformation in PSC of the foot. The high rate of malignant progression could be referred to difficulty in distinguishing these two entities, and some authors argue it is simply a case of misdiagnosis[1,11]. An accurate diagnosis is based on clinical, radiographic or advanced imaging and histological evidence[10]. They appear histologically indistinguishable from low-grade chondrosarcomas; although mitotic figures were identified in the chondrosarcomas but not in cases of SC or in the enchondromas, binucleate chondrocytes were present in all cases of SC. Chondrosarcomas usually show loss of the micro-nodularity of the chondrocytes and myxoid transformation of the matrix, as chondrocyte necrosis. The most reliable histological sign consists of osseous permeation by cartilage, with the extension of cartilage matrix into the intertrabecular space[2].

Davis suggests assessing proliferative activity by Ki-67 immunohistochemical staining, since there is no detectable staining for Ki-67 protein in SC or enchondromas. Moreover, C-erb B2 staining is positive in SC, while negative in normal articular cartilage, enchondromas, or grade I chondrosarcomas. Thus, the authors concluded that detection of C-erb B-2 protein may be a more sensitive indicator of cell proliferation than nuclear expression of Ki-67 protein[48]. A DNA index of >1 has also been suggested to carry prognostic value[50].

Bertoni *et al*[31] described five features to distinguish PSC from chondrosarcoma: First, there is a typical clustering pattern with abundant matrix juxtaposed to areas in PSC cartilage, while the tumor cells were arranged in sheets. Second, there is a myxoid change in the matrix; while it appears solid in PSC, any tendency to «run» when cut into should be viewed with suspicion for malignancy. Third, hypercellularity with spindling of the nuclei at the periphery is present in sarcoma not

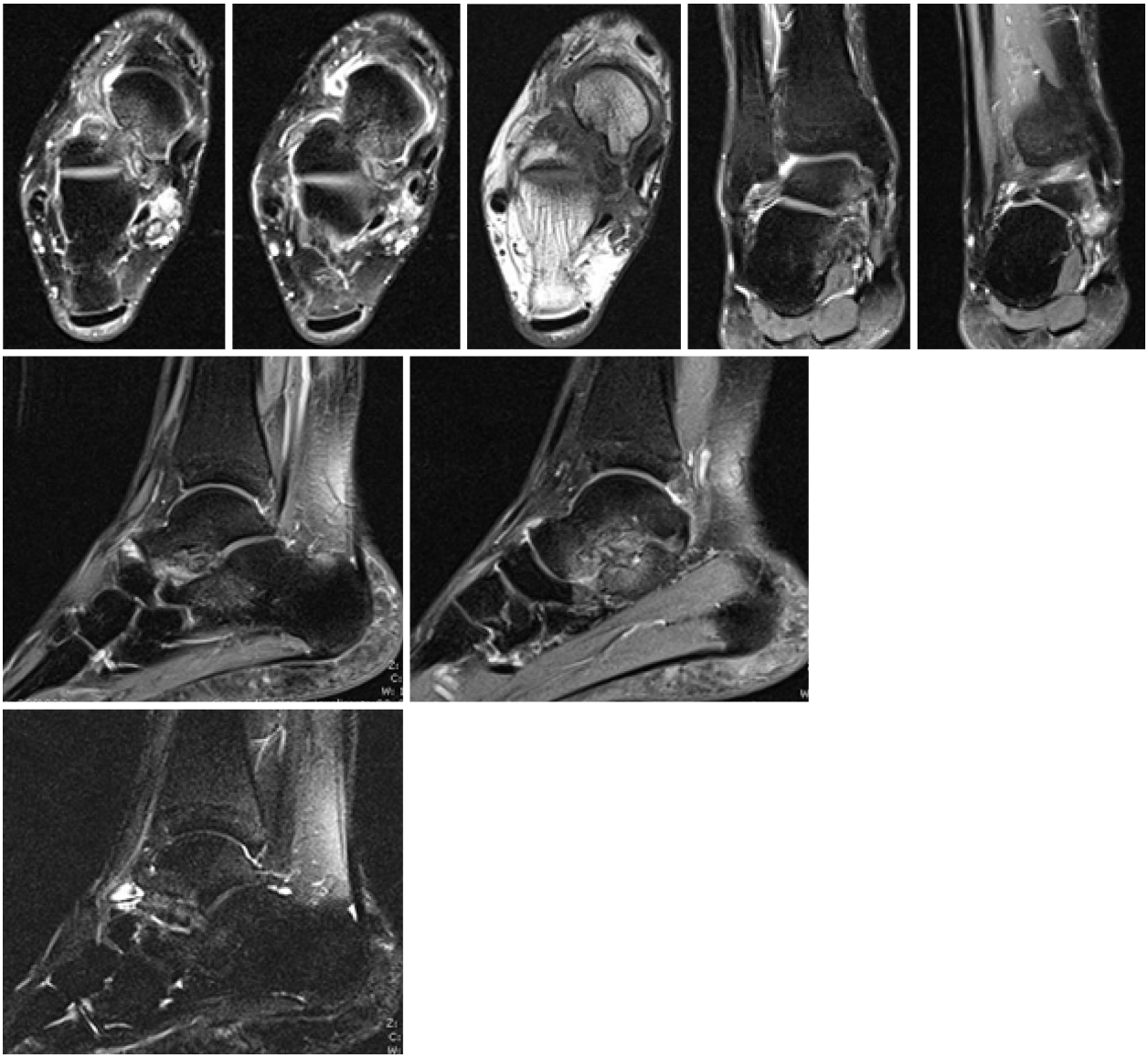

Figure 5 Magnetic resonance imaging of the ankle of Patient 2. Loose bodies and degenerative arthritis are shown.

in PSC. Fourth, necrosis cannot be considered crucial, as it is absent in PSC and very rare in chondrosarcoma. Finally, SC may erode bone and soft tissues, but when it does, the tumor usually has pushing margins. Permeation of trabecular bone with filling-up of marrow spaces should be considered a sign of malignancy[31].

Classification

In 1977, Milgram described a three-stage classification of SC, based on the position of the loose bodies and pathologic findings[41].

Phase I (early or florid stage) is characterized by metaplasia of the synovial intima, active synovitis and formation of nodules, with no calcification. Phase II (transitional stage) shows both active intra-synovial proliferation or calcification of the nodules and free loose bodies. Phase III (late or quiescent stage) demonstrates only the loose bodies, without any evidence of synovial metaplasia but occasional, slight inflammation of the membrane. Calcification or ossification of loose bodies is present only in the third phases.

Treatment

The target of treatment is to minimize pain, improve function, and prevent or limit the progression of arthritis and chondral damage[5].

SC is a benign condition with a tendency to progressive resolution[2,7]. Since SC tends to be progressive but self-limiting, indications for surgery depend on symptomatic presentation in addition to the functional demands of the patients[7,10]. In asymptomatic patients, the nodules may resorb over time and invasive procedures

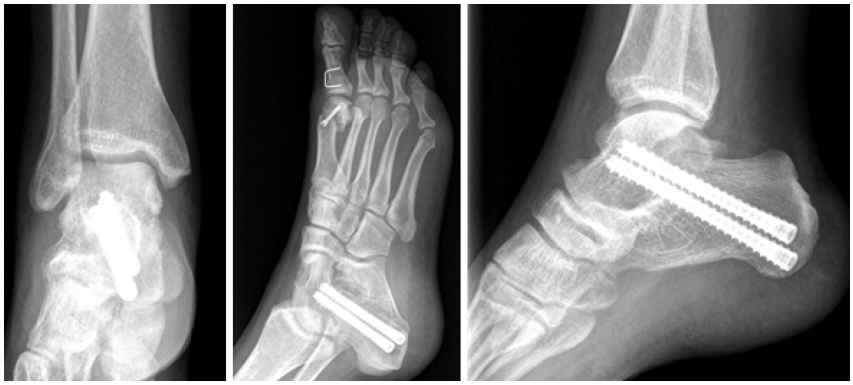

Figure 6 Post-operative radiographs of Patient 2: Synovectomy, removal of loose bodies and arthrodesis of subtalar joint is performed. Youngswick and Akin osteotomies are performed to correct hallux valgus.

should be avoided; treatment can be planned conservatively with frequent follow-up assessments. Patient age is also important for indications[51]; children should initially be treated conservatively with NSAIDs, cryotherapy and ultrasound because they are skeletally immature[18].

Indeed, surgery is considered the treatment of choice for PSC. The operative approach can vary based on the stage of disease: complete synovectomy for stage I, complete synovectomy and removal of intra articular bodies for stage II, removal of loose bodies for stage III[15,39,40]. Milgram recommended simple excision of the foreign bodies in the late inactive stages, although adding synovectomy and foreign body removal if the disease is active or transitional[40]. Some authors reported the same results by the removal of loose bodies alone, as well as synovectomy added to the removal of loose bodies[15,52].

Maurice distinguished two groups of patients, with extra- and intra-articular SC, and recommended treatment in each case: Synovectomy is recommended for both groups with localized disease; in intra-articular cases, synovectomy can be associated with removal of the loose bodies[53]. Nevertheless, for the extra-articular group, Shearer stated that surgery to extract the calcifications from the tendons would be too invasive, and that the surgeon should avoid excessively weakening tendon structure[10].

The traditional technique for the treatment of PSC of the ankle is arthrotomy and debridement. However, arthroscopy gained more and more indications in the last two decades.

Advantages of the arthroscopic approaches include decreased morbidity, wide visualization and treatment feature for intra- and extra-articular pathologies[5,34]. The excision of the loose bodies is the standard arthroscopic treatment with synovectomy[23]. Minimally invasive surgery offers a multitude of advantages in comparison with open techniques: Less local pain, swelling, infection, shorter recovery times, increased patient satisfaction, no need of immobilization post-operatively, and the patient can walk without pain[5,23,34,54]. Finally, Iossifidis[7] stated that such extensive surgery predisposes to tissue scarring and compromises articular function.

The ankle joint is entered *via* anteromedial and anterolateral arthroscopic portals during spinal anesthesia and tourniquet application, under manual traction and manipulation[5,13,34]. Bojanic also performed arthroscopy by posteromedial and posterolateral portals with patients in the prone position and by using a 4.5-mm/30-degree arthroscope[49].

Before and after closure of the wound in layers, an anterior drawer stress test should be performed to demonstrate joint stability[12]. The subtalar joint is entered by both medial and lateral approach, at the base of the position of loose bodies.

For the Lisfranc joint, Fujita performed a synovectomy and removal of the loose bodies in the dorsal, lateral, and plantar aspect of the articulation[39]. By a dorsal approach with dislocation of the fourth and fifth metatarsal bases, adequate visualization of both the dorsal and plantar aspects of the Lisfranc joint is allowed. Repair of dorsal ligamentous structures and percutaneous pinning of the Lisfranc joint is necessary for anatomic reduction at the end of surgery. The disadvantages of this approach include the possibility of postoperative instability and degenerative arthritis of the fourth and fifth Lisfranc joints. In severe cases, arthrodesis may be considered[15].

The use of intraoperative C-arm fluoroscopy is mandatory to ensure that all

calcified loose bodies are removed; they may not be found in the joint cavity because they can be encysted in bursae or in the synovium, or because they have not yet been liberated from the synovial membrane[5,9].

Before closing the articular capsule, abundant washing with normal saline is required[3]. However, Saxena suggested irrigation with 3% hydrogen peroxide for PSC and synovial tumors in the foot and ankle[30]. Hydrogen peroxide serves as a chemo-cautery by removing microscopic chemical elements; this appears to decrease recurrence[54].

Portals or wounds should be primarily closed after drain insertion. Post-operative immobilization in a cast for a varying period is usually necessary after open operative treatment. For arthroscopy, after the compressive dressing that is removed in the first post-operative day as it drains, early active motion of the joint can start. Bearing weight as tolerated is recommended for 2 wk, and is then allowed to gradually progress to full weightbearing[5,34].

Complications

In untreated patients or those without the appropriate therapy, degenerative arthritis or joint dislocation could occur in later stages of the disease[34,39].

Another usual complication of PSC is recurrence. It is thought to be related to the presence of the stimulus that caused the metaplasia, or to incomplete synovectomy[3,13,18,23,30,34,40,52]. Recurrence after loose body removal and synovectomy varies from 3%-23% of cases[1,3,16,36]. Saxena suggested irrigation with hydrogen peroxide, as used by other authors for synovial tumors in the foot and ankle, which appears to decrease recurrence[30,55].

When recurrence is associated with particularly aggressive features, such as rapid growth or destruction of joints, the surgeon should consider the potential for malignant transformation[1,56]. Surgeons ought to also consider malignancy in case of longstanding PSC after several surgeries[36]. In these patients, wide operative margin is mandatory, as the post-operative administration of radiation therapy is suggested[31,50].

SC is a rare benign monoarticular disease characterized by the presence of cartilaginous nodules in the synovium of joints, tendon sheaths and bursae, which often occur without trauma or inflammation[1,2,3,44].

Described firstly by Leannac in 1813, SC is also named chondromatosis, synoviochondrometaplasia, synovial chondrosis, synovial osteochondromatosis and articular chondrosis[9,10]. The earliest description in the literature of synovial osteochondromatosis was from Henderson and Jones in 1923[24].

CONCLUSION

SC is a rare benign disease with extremely rare presentation in foot and ankle joints. Clinical relevance to clinicians and surgeons may be summarized in the need for open or arthroscopic surgery, and subsequent to clinical assessment and imaging. Postoperative histopathological characterization should lead to a definitive diagnosis. Also, as malignant transformation may occur, surgeons should perform a complete synovectomy with wide margins, and remove all loose bodies.

REFERENCES

1 **Galat DD**, Ackerman DB, Spoon D, Turner NS, Shives TC. Synovial chondromatosis of the foot and ankle. *Foot Ankle Int* 2008; **29**: 312-317 [PMID: 18348828 DOI: 10.3113/FAI.2008.0312]
2 **Jeffreys TE**. Synovial chondromatosis. *J Bone Joint Surg Br* 1967; **49**: 530-534 [PMID: 6037566]
3 **Sedeek SM**, Choudry Q, Garg S. Synovial Chondromatosis of the Ankle Joint: Clinical, Radiological, and Intraoperative Findings. *Case Rep Orthop* 2015; **2015**: 359024 [PMID: 26177002 DOI: 10.1155/2015/359024]
4 **Adelani MA**, Wupperman RM, Holt GE. Benign synovial disorders. *J Am Acad Orthop Surg* 2008; **16**: 268-275 [PMID: 18460687]
5 **Doral MN**, Uzumcugil A, Bozkurt M, Atay OA, Cil A, Leblebicioglu G, Tetik O. Arthroscopic treatment of synovial chondromatosis of the ankle. *J Foot Ankle Surg* 2007; **46**: 192-195 [PMID: 17466247 DOI: 10.1053/j.jfas.2007.01.001]
6 **Hermann G**, Klein MJ, Abdelwahab IF, Kenan S. Synovial chondrosarcoma arising in synovial chondromatosis of the right hip. *Skeletal Radiol* 1997; **26**: 366-369 [PMID: 9229420]
7 **Iossifidis A**. Synovial chondromatosis of the ankle. *The Foot* 1995; **5**: 44-46 [DOI: 10.1016/0958-2592(95)90035-7]
8 **Zhang M**, Wang J. Epigenetics and Osteoarthritis. *Genes Dis* 2015; **2**: 69-75 [PMID: 25961070 DOI: 10.1016/j.gendis.2014.12.005]
9 **Scholl DM**, Taddie KL. Asymptomatic synovial chondromatosis of the ankle: an incidental finding. *J Foot Ankle Surg* 2010; **49**: 565.e13-565.e17 [PMID: 20851002 DOI: 10.1053/j.jfas.2010.08.002]
10 **Shearer H**, Stern P, Brubacher A, Pringle T. A case report of bilateral synovial chondromatosis of the

ankle. *Chiropr Osteopat* 2007; **15**: 18 [PMID: 18036237 DOI: 10.1186/1746-1340-15-18]
11 **Bahari S**, McKenna J. Subtalar and Extra Articular Synovial Chondromatosis. *J Case Rep* 2012; **2**: 120-124 [DOI: 10.17659/01.2012.0037]
12 **Brodsky JW**, Jung KS, Tenenbaum S. Primary synovial chondromatosis of the subtalar joint presenting as ankle instability. *Foot Ankle Int* 2013; **34**: 1447-1450 [PMID: 23687334 DOI: 10.1177/1071100713490674]
13 **Kim JB**, Song IS, Shin SY, Yoon JY. Primary synovial chondromatosis of the talonavicular joint: A case report. *Foot Ankle Surg* 2016; **22**: e25-e28 [PMID: 27810034 DOI: 10.1016/j.fas.2016.08.003]
14 **Kim SR**, Shin SJ, Seo KB, Teong CT, Hyun CL. Giant extra-articular synovial osteochondromatosis of the sinus tarsi: a case report. *J Foot Ankle Surg* 2013; **52**: 227-230 [PMID: 23318098 DOI: 10.1053/j.jfas.2012.11.017]
15 **Derek Stensby J**, Fox MG, Kwon MS, Caycedo FJ, Rahimi A. Primary synovial chondromatosis of the subtalar joint: case report and review of the literature. *Skeletal Radiol* 2018; **47**: 391-396 [PMID: 28932921 DOI: 10.1007/s00256-017-2775-6]
16 **Silva L**, Castro MOE, Santos BMQ, Bilreiro C, Aleixo F. Synovial Chondromatosis: a pictorial review. *ECR* 2014; C-1307 [DOI: 10.1594/ecr2014/C-1307]
17 **Sciot R**, Dal Cin P, Bellemans J, Samson I, Van den Berghe H, Van Damme B. Synovial chondromatosis: clonal chromosome changes provide further evidence for a neoplastic disorder. *Virchows Arch* 1998; **433**: 189-191 [PMID: 9737798]
18 **Damodaran P**, Talawadekar GD, Cornell M. Bilateral, symptomatic synovial chondromatosis of ankle in a prepubescent 7-year-old boy. *Eur J Rad Extra* 2009; **72**: e137-e139 [DOI: 10.1016/j.ejrex.2009.04.008]
19 **Mishra P**, Mishra PK, Pandey D, Tripathi BN. Primary ankle synovial chondromatosis in a young post-partum female. *J Orthop Allied Sci* 2014; **2**: 60-62 [DOI: 10.4103/2319-2585.145605]
20 **Murphey MD**, Vidal JA, Fanburg-Smith JC, Gajewski DA. From the Archives of the AFIP: Imaging of Synovial Chondromatosis with Radiologic-Pathologic Correlation. *Radio Graphics* 2007; **27**: 1465-1488 [DOI: 10.1148/RG.275075116]
21 **Mohr W**. Is synovial osteo-chondromatosis a proliferative disease? *Pathol Res Pract* 2002; **198**: 585-588 [PMID: 12440780 DOI: 10.1078/0344-0338-00306]
22 **Littrell LA**, Inwards CY, Sim FH, Wenger DE. Imaging features of synovial chondromatosis of the spine: a review of 28 cases. *Skeletal Radiol* 2016; **45**: 63-71 [PMID: 26363786 DOI: 10.1007/s00256-015-2248-8]
23 **Isbell JA**, Morris AC, Araoye I, Naranje S, Shah AB. Recurrent Extra- and Intra-articular Synovial Chondromatosis of the Ankle with Tarsal Tunnel Syndrome: A Rare Case Report. *J Orthop Case Rep* 2017; **7**: 62-65 [PMID: 28819605 DOI: 10.13107/jocr.2250-0685.752]
24 **Dawson-Bowling S**, Hamilton P, Bismil Q, Gaddipati M, Bendall S. Synovial osteochrondomatosis of the talonavicular joint: a case report. *Foot Ankle Int* 2008; **29**: 241-244 [PMID: 18315983 DOI: 10.3113/FAI.2008.0241]
25 **Pau M**, Bicsák A, Reinbacher KE, Feichtinger M, Kärcher H. Surgical treatment of synovial chondromatosis of the temporomandibular joint with erosion of the skull base: a case report and review of the literature. *Int J Oral Maxillofac Surg* 2014; **43**: 600-605 [PMID: 24314559 DOI: 10.1016/j.ijom.2013.10.019]
26 **Young-in Lee F**, Hornicek FJ, Dick HM, Mankin HJ. Synovial chondromatosis of the foot. *Clin Orthop Relat Res* 2004; **Jun;** 423: 186-190 [DOI: 10.1097/01.blo.0000127133.89704.86]
27 **Mertens F**, Jonsson K, Willén H, Rydholm A, Kreicbergs A, Eriksson L, Olsson-Sandin G, Mitelman F, Mandahl N. Chromosome rearrangements in synovial chondromatous lesions. *Br J Cancer* 1996; **74**: 251-254 [PMID: 8688330]
28 **Robinson D**, Hasharoni A, Evron Z, Segal M, Nevo Z. Synovial chondromatosis: the possible role of FGF 9 and FGF receptor 3 in its pathology. *Int J Exp Pathol* 2000; **81**: 183-189 [PMID: 10971739]
29 **Apte SS**, Athanasou NA. An immunohistological study of cartilage and synovium in primary synovial chondromatosis. *J Pathol* 1992; **166**: 277-281 [PMID: 1381426]
30 **Saxena A**, St Louis M. Synovial Chondromatosis of the Ankle: Report of Two Cases With 23 and 126 Loose Bodies. *J Foot Ankle Surg* 2017; **56**: 182-186 [PMID: 27066867 DOI: 10.1053/j.jfas.2016.02.009]
31 **Bertoni F**, Unni KK, Beabout JW, Sim FH. Chondrosarcomas of the synovium. *Cancer* 1991; **67**: 155-162 [PMID: 1985712]
32 **Ozyurek S**, Atik A, Sivrioglu AK, Ege T. Primary synovial osteochondromatosis of the ankle. *BMJ Case Rep* 2013; **2013**: pii: bcr2013009046 [PMID: 23531938 DOI: 10.1136/bcr-2013-009046]
33 **McCarthy C**, Anderson WJ, Vlychou M, Inagaki Y, Whitwell D, Gibbons CL, Athanasou NA. Primary synovial chondromatosis: a reassessment of malignant potential in 155 cases. *Skeletal Radiol* 2016; **45**: 755-762 [PMID: 26919862 DOI: 10.1007/s00256-016-2353-3]
34 **Ozmeric A**, Aydogan NH, Kocadal O, Kara T, Pepe M, Gozel S. Arthroscopic treatment of synovial chondromatosis in the ankle joint. *Int J Surg Case Rep* 2014; **5**: 1010-1013 [PMID: 25460460 DOI: 10.1016/j.ijscr.2014.10.083]
35 **Peh WC**, Shek TW, Davies AM, Wong JW, Chien EP. Osteochondroma and secondary synovial osteochondromatosis. *Skeletal Radiol* 1999; **28**: 169-174 [PMID: 10231916]
36 **Brucher N**, Faruch-Bilfeld M, Molinier F, Brouchet-Gomez A, Lapegue F, Sans N. Primary synovial osteochondromatosis of the first interphalangeal joint of the foot: A case report. *Diagn Interv Imaging* 2014; **95**: 451-453 [PMID: 24231342 DOI: 10.1016/j.diii.2013.10.003]
37 **Santiago T**, Mariano C. Primary synovial chondromatosis of the ankle joint presenting as monoarthritis. *BMJ Case Rep* 2013; **2013**: pii: bcr2013202186 [PMID: 24326442 DOI: 10.1136/bcr-2013-202186]
38 **Kyriakopoulos CK**, Mavrogenis AF, Benetos IS, Koulalis D, Mitsou A, Papagelopoulos PJ. Arthroscopic treatment of synovial chondromatosis of the ankle. *Eur J Orthop Surg Traumatol* 2006; **16**: 75-79 [DOI: 10.1007/s00590-005-0021-8]
39 **Fujita I**, Matsumoto K, Maeda M, Kizaki T, Okada Y, Yamamoto T. Synovial osteochondromatosis of the Lisfranc joint: a case report. *J Foot Ankle Surg* 2006; **45**: 47-51 [PMID: 16399560]
40 **Milgram JW**. Synovial osteochondromatosis: a histopathological study of thirty cases. *J Bone Joint Surg Am* 1977; **59**: 792-801 [PMID: 908703]
41 **Wittkop B**, Davies AM, Mangham DC. Primary synovial chondromatosis and synovial chondrosarcoma: a pictorial review. *Eur Radiol* 2002; **12**: 2112-2119 [PMID: 12136332 DOI: 10.1007/s00330-002-1318-1]
42 **Norman A**, Steiner GC. Bone erosion in synovial chondromatosis. *Radiology* 1986; **161**: 749-752 [PMID: 3786727 DOI: 10.1148/radiology.161.3.3786727]
43 **Harish S**, Saifuddin A, Cannon SR, Flanagan AM. Synovial chondromatosis of the foot presenting with

Lisfranc dislocation. *Skeletal Radiol* 2005; **34**: 736-739 [PMID: 15990990 DOI: 10.1007/s00256-005-0923-x]
44 **Hocking R**, Negrine J. Primary synovial chondromatosis of the subtalar joint affecting two brothers. *Foot Ankle Int* 2003; **24**: 865-867 [PMID: 14655893 DOI: 10.1177/107110070302401111]
45 **Kramer J**, Recht M, Deely DM, Schweitzer M, Pathria MN, Gentili A, Greenway G, Resnick D. MR appearance of idiopathic synovial osteochondromatosis. *J Comput Assist Tomogr* 1993; **17**: 772-776 [PMID: 8370833]
46 **Duymus TM**, Yucel B, Mutlu S, Tuna S, Mutlu H, Komur B. Arthroscopic treatment of synovial chondromatosis of the shoulder: A case report. *Ann Med Surg (Lond)* 2015; **4**: 179-182 [PMID: 26005571 DOI: 10.1016/j.amsu.2015.05.001]
47 **Taglialavoro G**, Moro S, Stecco C, Pennelli N. [Bilateral synovial chondromatosis of the first metatarsophalangeal joint: a case report]. *Reumatismo* 2003; **55**: 263-266 [PMID: 14872226]
48 **Davis RI**, Hamilton A, Biggart JD. Primary synovial chondromatosis: a clinicopathologic review and assessment of malignant potential. *Hum Pathol* 1998; **29**: 683-688 [PMID: 9670824 DOI: 10.1016/S0046-8177(98)90276-3]
49 **Bojanic I**, Bergovec M, Smoljanovic T. Combined anterior and posterior arthroscopic portals for loose body removal and synovectomy for synovial chondromatosis. *Foot Ankle Int* 2009; **30**: 1120-1123 [PMID: 19912726 DOI: 10.3113/FAI.2009.1120]
50 **Sah AP**, Geller DS, Mankin HJ, Rosenberg AE, Delaney TF, Wright CD, Hornicek FJ. Malignant transformation of synovial chondromatosis of the shoulder to chondrosarcoma. A case report. *J Bone Joint Surg Am* 2007; **89**: 1321-1328 [PMID: 17545437 DOI: 10.2106/JBJS.F.00511]
51 **Yu GV**, Zema RL, Johnson RW. Synovial osteochondromatosis. A case report and review of the literature. *J Am Podiatr Med Assoc* 2002; **92**: 247-254 [PMID: 11961091]
52 **Shpitzer T**, Ganel A, Engelberg S. Surgery for synovial chondromatosis. 26 cases followed up for 6 years. *Acta Orthop Scand* 1990; **61**: 567-569 [PMID: 2281768]
53 **Maurice H**, Crone M, Watt I. Synovial chondromatosis. *J Bone Joint Surg Br* 1988; **70**: 807-811 [PMID: 3192585]
54 **Kunzler DR**, Shazadeh Safavi P, Warren BJ, Janney CF, Panchbhavi V. Arthroscopic Treatment of Synovial Chondromatosis in the Ankle Joint. *Cureus* 2017; **9**: e1983 [PMID: 29503777 DOI: 10.7759/cureus.1983]
55 **Goni V**, Gopinathan NR, Radotra BD, Viswanathan VK, Logithasan RK, S B. Giant cell tumour of peroneus brevis tendon sheath--a case report and review of literature. *BMJ Case Rep* 2012; **2012**: pii: bcr0120125703 [PMID: 22802558 DOI: 10.1136/bcr.01.2012.5703]
56 **Jonckheere J**, Shahabpour M, Willekens I, Pouliart N, Dezillie M, Vanhoenacker F, De Mey J. Rapid malignant transformation of primary synovial chondromatosis into chondrosarcoma. *JBR-BTR* 2014; **97**: 303-307 [PMID: 25597214]

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