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International consensus on the definition and classification of fibrosis of the knee joint

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Aims

The aim of this consensus was to develop a definition of post-operative fibrosis of the knee.

Patients and Methods

An international panel of experts took part in a formal consensus process composed of a discussion phase and three Delphi rounds.

Results

Post-operative fibrosis of the knee was defined as a limited range of movement (ROM) in flexion and/or extension, that is not attributable to an osseous or prosthetic block to movement from malaligned, malpositioned or incorrectly sized components, metal hardware, ligament reconstruction, infection (septic arthritis), pain, chronic regional pain syndrome (CRPS) or other specific causes, but due to soft-tissue fibrosis that was not present pre-operatively. Limitation of movement was graded as mild, moderate or severe according to the range of flexion (90° to 100°, 70° to 89°, < 70°) or extension deficit (5° to 10°, 11° to 20°, > 20°). Recommended investigations to support the diagnosis and a strategy for its management were also agreed.

Conclusion

The development of standardised, accepted criteria for the diagnosis, classification and grading of the severity of post-operative fibrosis of the knee will facilitate the identification of patients for inclusion in clinical trials, the development of clinical guidelines, and eventually help to inform the management of this difficult condition.

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Fibrosis affecting joints is a well-recognised pathological process that involves diffuse scarring within a joint and the surrounding soft tissues, leading to limitation of movement and pain.^{1,2} It may be a devastating complication of surgery involving the knee that might require further surgery with debridement, with associated morbidity, risk of adverse effects and a significant risk of recurrence.^{3–5}

Tissue from fibrotic knee joints is composed of a dense, disorganised extracellular matrix of collagen fibrils⁶ interspersed with α -smooth muscle actin containing myofibroblast cells.⁷ Well defined intra-articular fibrous bands may be seen at arthroscopy.^{5,8}

Various clinical criteria have been used to diagnose post-traumatic fibrosis, including specific limitations of movement^{9,10} and the presence of fibrotic tissue seen at operation.^{5,11,12} The lack of a consistent, widely accepted definition of the condition is reflected in the wide range of the incidence reported in the literature for fibrosis after

total knee arthroplasty (TKA), which varies between 1% and 15%.^{1,5,6,13,14}

There are also no standardised accepted clinical guidelines for the investigation and management of fibrosis of the knee. Consequently, recommendations on the use of CT scans, MRI and ultrasound imaging and the role of aspiration in making the diagnosis are inconsistent.^{3,5,14} The role and timing of treatment, such as manipulation under anaesthetic (MUA), is also debated and different guidelines to management have been proposed.^{3,5,14}

The lack of a precise definition of fibrosis of the knee after surgery presents a challenge for research in this area. Whilst our understanding of the cellular pathology is progressing, our ability to identify affected patients consistently is hindered by a lack of agreement about the diagnostic criteria, grading, role of imaging techniques and forms of treatment. The aim of this study was to develop a definition of post-operative fibrosis of the

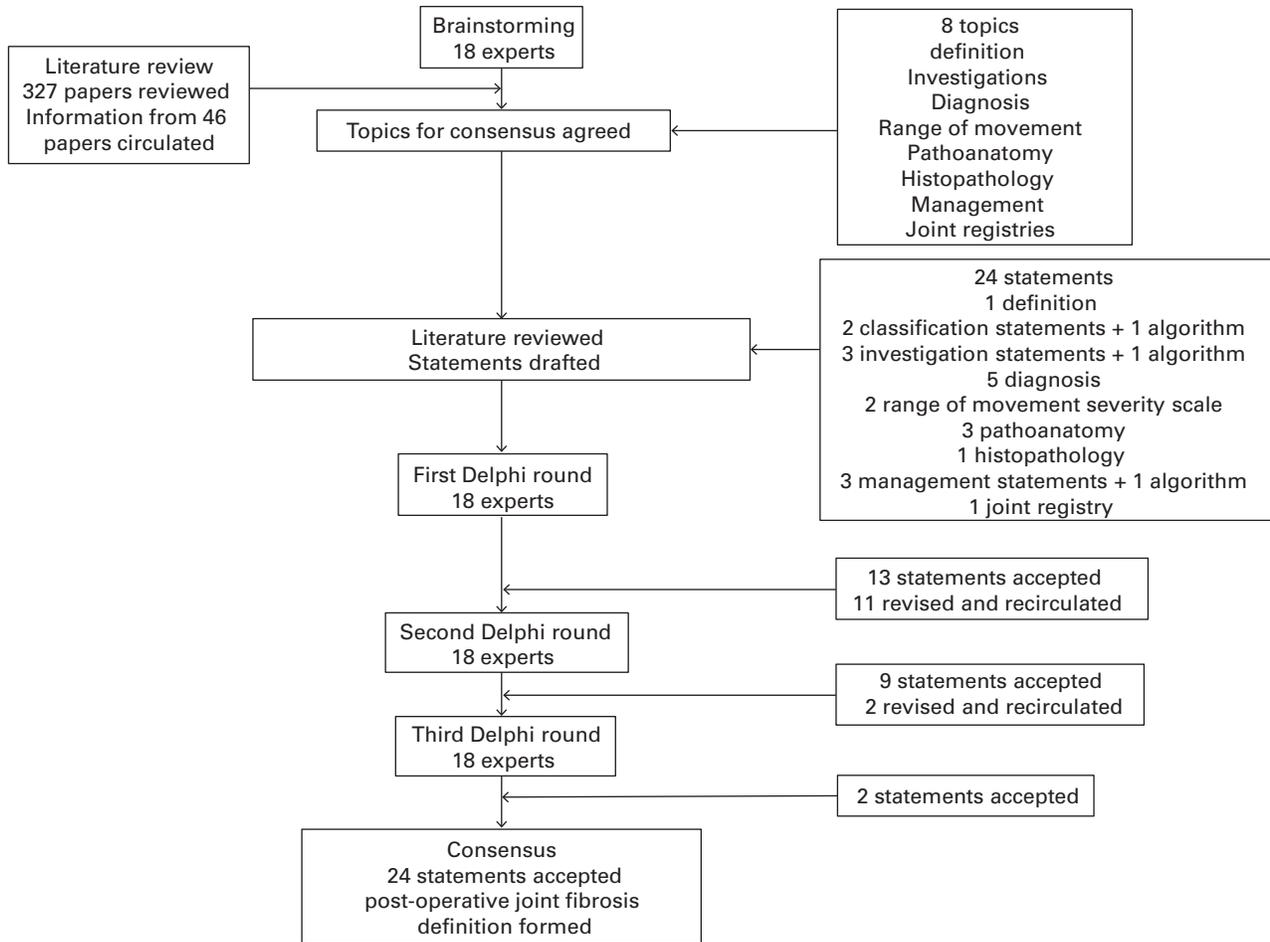


Fig. 1

The Delphi Consensus Process followed in the formation of consensus statements on post-operative knee fibrosis.

knee with diagnostic criteria and a classification, using a recognised formal consensus process.

Patients and Methods

A Delphi process (brainstorming, narrowing down, quantification)¹⁵ was applied based on previously published consensus statements¹⁶ and followed guidelines set out by the NHS Research and Development Health Technology Assessment programme¹⁷ and the British Medical Journal.¹⁸ The process which was applied is outlined in Figure 1.

An expert panel that included knee surgeons, rheumatologists, basic scientists working on fibrosis, pathologists and musculoskeletal physiologists was selected based on publication record in these areas. Key individuals involved in the diagnosis of arthrofibrosis,^{19,20} the analysis, management and revision of TKA,²¹ the investigation and treatment of post-surgical fibrosis^{1,5,13,14,22-33} and basic research on fibrosis³⁴⁻³⁶ formed the Joint Fibrosis Consensus Working Group. Founding members (SH) and Presidents and Past-Presidents of the European Knee Society (JB, JA), the Past-President of the International Society of Arthroplasty Registries (OF), members of the Knee Society (MM, JN, JB, FH), the Head of the Norwegian Knee Arthroplasty

Register (OF), the Past-President of the Arthroplasty Society of Australia (PL), the Deputy Director of the Australian Orthopaedic Association National Joint Replacement Registry (PL), and a member of the British Association for Knee Surgery Research Board (AT) were part of the group. Previous participants in an international consensus group on prosthetic joint infection (MM, FH, RMJ) were also included. Several members have also chaired instructional courses for stiffness of the knee and the management of contracture (MM, AB, PL).

Members of the working group initially identified specific topics that required the formation of a consensus (brainstorming). A literature review was undertaken (NK) focusing on key areas requiring consensus and this was circulated to the panel for comments. A search was done of Medline (via PubMed), Embase and Cochrane databases for papers on fibrosis of the knee which were published in English between 1950 and June 2015. These formed the start of the Delphi process. The following search terms were used: 'arthrofibrosis', 'fibrosis', 'knee', 'arthroplasty', 'knee replacement', 'ligament reconstruction'. Overall, 320 papers were reviewed and information on key topics (definition, classification, diagnosis, investigation,

Table I. Consensus statements - Definition and Classification

Consensus statements
Post-surgical knee joint fibrosis is defined as restricted ROM, in flexion or extension, that is not attributable to osseous or prosthetic block to movement from malpositioned or incorrectly sized components, metal hardware, ligament reconstruction, infection (septic arthritis), pain, CRPS or other specific causes, and is due to soft-tissue fibrosis that was not present pre-operatively.
Joint fibrosis may be spontaneous (primary) or following an insult such as surgery or trauma (secondary).
Spontaneous knee joint fibrosis, in the absence of trauma or surgery, is extremely rare. Post-trauma or post-surgery knee fibrosis is much more clinically important.
This classification can be further sub-categorised into post-arthroplasty joint fibrosis, post-ligament reconstruction fibrosis etc., according to the algorithm in Figure 2.
ROM, range of movement; CRPS, chronic regional pain syndrome

management) from 47 reports was circulated to the group. The rejected 273 papers were not relevant to post-surgical knee joint fibrosis (e.g. different anatomical site, post-traumatic or spontaneous fibrosis etc.). Feedback was used to define key areas for consensus and to draft initial statements (NK, DJD).

Draft consensus statements were circulated for rating with a scale of 1 (disagree) to 10 (agree), and comments. An online survey tool³⁷ was used throughout this process. These inputs were integrated, and the amended consensus statements were prepared with a detailed explanation for each revision. Anonymised results from the first round were recirculated for scoring, comments, and proposed revisions for statements that scored 7 or less in the first round. Three rounds were required before final revisions were derived. A predetermined mean score of 7 or more (with three or fewer outliers: defined as scores less than 4) was used to define consensus.

Results

Consensus findings. Consensus was reached on 24 statements that fulfilled the criteria for acceptance. They were grouped into eight key categories (Definition and Classification, Investigations, Diagnosis, Range of Movement, Patho-anatomy, Histology, Prevention and Management and Joint Registries).

Definition and classification. Post-surgical fibrosis of the knee was defined as limited range of movement (ROM) of the knee, in flexion and/or extension, that is not attributable to a bony or prosthetic block to movement from malaligned or malpositioned components, hardware, ligament reconstruction, infection (septic arthritis), pain, complex regional pain or other specific causes, and is due to fibrosis of the soft tissues which was not present pre-operatively (Table I). Pain is a possible cause of stiffness; this can be demonstrated by examination under anaesthesia. The term post-surgical fibrosis of the knee was selected by the panel, rather than arthrofibrosis, which is commonly used in the literature, as a precise name for the deposition of fibrotic tissue in the knee following surgery. Post-surgical fibrosis of the knee may follow ligament reconstruction and arthroplasty. Fibrosis following trauma was considered as a separate condition. It was recognised that fibrosis of the knee may be primary (spontaneous) if it occurs without

preceding injury, infection or surgery, but the overwhelming majority of cases occur following either trauma, infection (septic arthritis) or surgery (secondary). The classification of fibrosis of the knee as primary or secondary reflects this consensus (Fig. 2).

Investigations. The principal aim of investigation in a patient with a stiff, painful knee and suspected fibrosis following surgery is to exclude other causes of stiffness. These include, but are not exclusively limited to, osseous or prosthetic block to movement from malpositioned or incorrectly sized components, metal hardware, ligament reconstruction or infection or chronic regional pain syndrome (CRPS). Plain films and CT scans are useful for identifying mal-positioning of components or a bony block to movement, such as heterotopic ossification (Table II, Fig. 3). Infection must be excluded and laboratory evaluation of inflammatory markers (CRPS, white blood cell count and differential) and aspiration of the joint for microbiological culture and cell count is strongly recommended. Criteria set out by the Musculoskeletal Infection Society (MSIS) should be used to rule out infection.³⁸ There may not be any fluid available on attempted aspiration of a stiff knee. In this situation injection of saline and re-aspiration is not recommended by the Philadelphia Consensus Meeting on periprosthetic joint infection.^{39,40}

Undertaking TKA for the wrong indication may result in a painful and stiff knee.⁴¹ Evaluation of pre-operative radiographs may confirm this without the need for further sophisticated tests. In addition to intra-articular scarring, a fibrotic or non-elastic extensor mechanism can cause stiffness and pain in the knee. Once more, the evaluation of pre-operative radiographs can be used to find evidence for conditions of the extensor mechanism. Removal of intra-articular scarring will be ineffective in restoring movement in these cases.

Fibrosis may be present with other causes of stiffness and pain in the knee after surgery, and may be triggered by them (e.g. by infection or mechanical conflict). When fibrosis occurs in association with another pathology causing stiffness, this was not considered true post-surgical fibrosis.

At present, fibrosis cannot be diagnosed confidently by, MR imaging, however, it may be useful in the future as metal artifact reducing sequences are being developed for this purpose. In the future, the basis of objective measure-

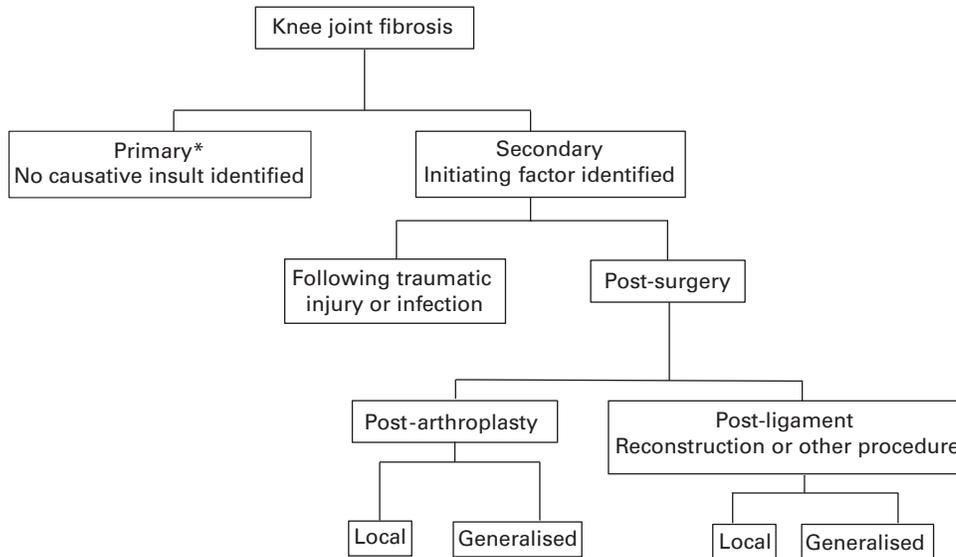


Fig. 2

Classification system for fibrosis of the knee. * Extremely rare in the knee

Table II. Consensus statements – Investigations

Consensus statements

There is no definitive diagnostic imaging test available for diagnosing post-surgical knee fibrosis.

Knees should be investigated by plain radiographs (which may show patella infera). CT scans can help identify component malpositioning.

The purpose of radiological and CT imaging is to rule out causes of stiffness post-surgery (e.g. implant malalignment, component sizing issues). There is currently not enough evidence for the routine use of MRI in diagnosing fibrosis.

We propose an algorithm for investigation of patients with stiff knee joints post-surgery (Fig. 3).

ments of fibrosis on MRI scans may allow the measurement of perisynovial thickness or the quantification of fibrotic tissue in the parapatellar gutters.

Diagnosis. Post-surgical fibrosis of the knee is a clinical diagnosis that can only be made when investigations have been performed to exclude other causes (Table III). The clinical diagnosis may be supported by direct visualisation of fibrosis at surgery, either arthroscopically or by open techniques. Laboratory evaluations and aspiration for microbiological culture should be performed to rule out infection according to the MSIS criteria.³⁸ A bone scan alone is not recommended to rule out infection. Histological criteria have been proposed,^{19,20} but biopsy is not required to make a diagnosis. Tissue taken at the time of débridement may be sent for histopathological evidence of fibrosis to support the diagnosis.

Range of movement of the knee. Reduction in flexion and/or extension is required for a diagnosis of fibrosis (Table IV). The severity of loss of movement can be graded. This criterion is active rather than passive ROM, as examiners may apply varying degrees of pressure. For simplicity, an absolute ROM is used for grading of severity. Comparison with pre-operative ROM and with the contralateral knee may be useful clinically, but these comparisons can be affected by pre-operative stiffness and the presence or absence of contralateral disease. The goal of TKA includes the establish-

ment of a good ROM, therefore absolute limitation of movement forms part of the criteria for the diagnosis of fibrosis. Three levels of severity were agreed according to the amount of restriction (mild, moderate and severe). Extreme loss of movement, with global ROM < 30° in total, which may happen in ankylosis following septic arthritis as described by Bae et al,⁴² does not form part of the classification of the severity of post-surgical fibrosis of the knee. The severity of fibrosis is not solely due to the degree of limitation of movement; other factors including pain, are important.

Pathological anatomy. Information about the pathological location can be gained from clinical examination and correlation with areas of swelling or a particular deficit in movement (Table V). However, direct visualisation is the benchmark for the determination of the location of fibrosis. MRI may become a useful tool for identifying areas of fibrosis. Focal fibroses such as infra-patella contraction syndrome (IPCS)⁴³ do not generally cause severe limitation of movement. Thorpe et al⁴⁴ described a syndrome of painful patellofemoral dysfunction, without limitation of movement, following TKA in 11 of 635 patients. Intra-articular lesions were found transversely on the patella, or between the patella and the fat pad or the intercondylar notch. The symptoms resolved following arthroscopic removal of these lesions without a change in active ROM. Without a limitation of ROM

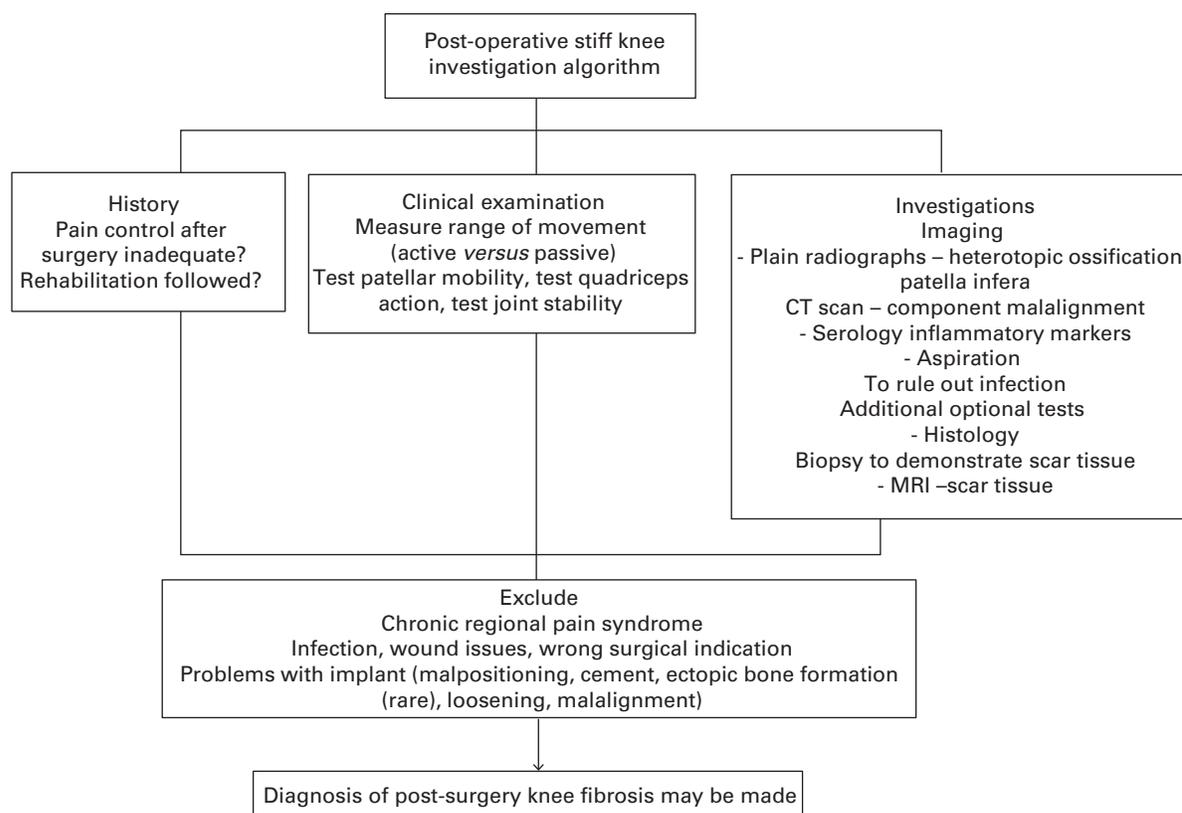


Fig. 3

Investigation algorithm for patients with suspected fibrosis following total knee arthroplasty (ROM, range of movement). Note that not all investigations are mandated, clinical judgement is required and the diagnosis may be made clinically with support of plain radiographs.

Table III. Consensus statements – Diagnosis

Consensus statements

A clinical diagnosis of joint fibrosis may be made after excluding other causes of stiffness.

The clinical diagnosis may be confirmed surgically (either through open or arthroscopic visualisation of the joint), but surgery is only warranted as an intervention and is not justified for diagnosis alone.

Tissue biopsy is not required to make the diagnosis.

Further research into radiological measures of fibrosis (e.g. perisynovial tissue thickness, knee circumference) is required before their widespread use in diagnosis.

Further research is required to identify robust predictors of fibrosis. These may include serum biomarkers.

these lesions do not form part of the definition of post-surgical fibrosis.

Histopathology. Criteria for a tissue diagnosis have been proposed.^{19,20} Histopathologically, post-surgical fibrosis of the knee is characterised by a varying degree of cellularity of fibroblasts.²⁰ In one report, a count of β -catenin positive cells above a threshold level of > 20 per high power field, 0.307 mm^2 allows, in conjunction with the clinical information, the histopathological diagnosis of fibrosis. Histopathological analysis of tissue taken during surgery performed to débride fibrotic lesions is useful to support the diagnosis, but biopsy is not required for the diagnosis,

particularly as it requires an invasive procedure that may cause infection (Table VI).

Prevention and management. There is some evidence that aggressive rehabilitation regimes can reduce the incidence of fibrosis, but in some patients this may precipitate or worsen fibrosis. There is evidence that optimised post-operative pain control can reduce the requirement for MUA after TKA.⁴⁵ The pharmaceutical modulation of inflammation with steroids⁴⁶ and the interleukin-1 receptor antagonist Anakinra⁴⁷ has been used to reduce the inflammatory response and decrease the formation of fibrotic tissue and pain⁴⁸ post-operatively.

Table IV. Consensus statements – Range of Movement restriction**Consensus statements**

A restricted range of movement in flexion or extension, or both flexion and extension must be present for a diagnosis of knee joint fibrosis. The severity may be graded according to loss of movement based on the deviation from full flexion or extension as mild, moderate and severe extension restriction (5° to 10°, 11° to 20°, > 20°) or flexion range (90° to 100°, 70° to 89°, < 70°).

Table V. Consensus statements – Patho-anatomy**Consensus statements**

The anatomical location of fibrosis can be demonstrated during open or arthroscopic surgery. Current imaging modalities (e.g. ultrasound, MRI) are not yet validated for visualising fibrosis.

The location of the scar tissue may be as follows:- infrapatellar (Hoffa) fibrosis - medial or lateral parapatellar fibrosis or scarring (gutter)- suprapatellar pouch fibrosis, scarring or obliteration - patellar tendon shortening- posterior fibrosis - quadriceps muscle fibrosis/scarring (vastus intermedius) - intrasubstance fibrosis of the knee joint capsule - diffuse fibrosis or scarring involving a combination of the above.

Local fibroses such as infrapatellar contraction syndrome or discrete bands of adhesions that do not cause restricted range of movement are not sufficient for a diagnosis of knee joint fibrosis, and are considered local fibrosis.

Table VI. Consensus statements – Histopathology**Consensus statements**

Further research is needed to determine a histological definition of fibrosis.

Table VII. Consensus statements – Prevention and Management**Consensus statements**

Early fibrosis, less than three to six months post-operatively, may respond to treatment with physiotherapy and rehabilitation therapy and manipulation under anaesthesia (MUA), whereas established, 'late' fibrosis is relatively resistant to physiotherapy and MUA.

There is some evidence that successful post-operative pain control can reduce the incidence of post-surgical fibrosis of the knee,⁴⁹ although further research into the prevention of this condition is required.

Further research is also required to develop an evidence-based management algorithm to prevent post-surgical fibrosis.

We propose an algorithm for management of diagnosed post-surgical fibrosis of the knee (Fig. 4).

The management of fibrosis depends on its staging. Early fibrosis, which often has a 'soft endpoint' to movement of the knee, may be treated successfully with physiotherapy and manipulation. Analgesia and relaxation techniques may be helpful.⁴⁹ In addition, mechanical soft-tissue stimulation using instruments such as Astym (Performance Dynamics Inc., Muncie, Indiana) that provides topical administration of pressure and shear force designed to stimulate regeneration of damaged tissues and breakdown of scar tissue, has shown good early results in stiff TKAs.²⁸ Established fibrosis, typically present three to six months after surgery, often has a hard endpoint to movement of the knee. There is evidence that MUA performed within three months post-operatively is more effective than that performed after three months.^{24,50} The risk of iatrogenic fracture should be borne in mind when considering MUA, particularly in patients with inflammatory conditions such as rheumatoid arthritis. The timing of MUA was debated within the group; some members felt that MUA is safe and effective up to six months post-operatively. This debate is reflected in the range of time after surgery that MUA is considered an option (three to six months) although it is emphasised that efforts should be made to exclude other

causes of stiffness as soon post-operatively as possible to allow MUA to be performed before fibrosis becomes established (Table VII, Fig. 4).

MUA should be performed at a time of maximum muscle relaxation by flexing the hip to 90° and grasping the tibia proximally to avoid leverage on the joint. The knee is flexed slowly and gently until palpable and audible separation of adhesions no longer occurs, as described by Fox and Poss.⁵¹ Consensus was reached that established fibrosis requires arthroscopic or open débridement. Revision of the components may be required to re-establish movement.

Joint registries and fibrosis. Joint replacement registries do not currently allow sufficiently granular identification of patients with post-surgical fibrosis of the knee (Table VIII). 'Arthrofibrosis' or stiffness is often used as an umbrella term for stiff knees, lack of movement and true fibrosis (intra-articular scarring causing restricted ROM), thus it is difficult to define patients with true fibrosis. Furthermore, procedures for treating stiffness caused by fibrosis, such as MUA and arthroscopic debridement, where open surgery is not performed and components are not changed, are not recorded in most registries.

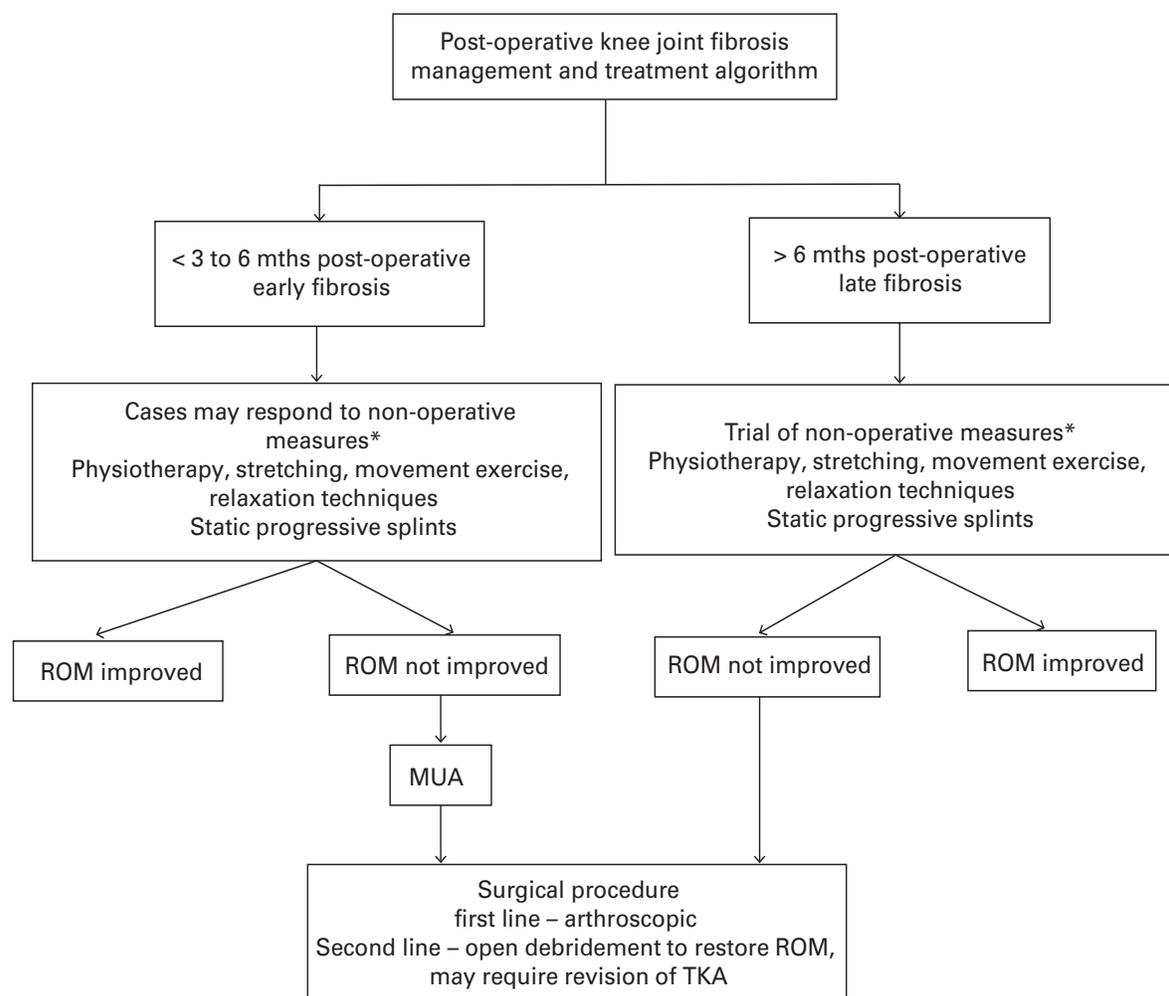


Fig. 4

Management algorithm for post-operative fibrosis of the knee (ROM, range of movement; MUA, manipulation under anaesthesia; TKA, total knee arthroplasty). *Important to investigate patient to exclude causes of stiff TKA whilst non-operative treatments are employed.

Table VIII. Consensus statements – Joint Registries

Consensus statements

Registries in their current form do not provide a robust resource for identifying patients who have post-surgical joint fibrosis due to several limitations, including lack of a current, accepted disease definition and diagnostic criteria and most national registries do not include re-operations without component removal or change or closed procedures.

Discussion

This international consensus provides agreement amongst a multi-disciplinary panel for the definition, classification and diagnostic criteria of post-surgical fibrosis of the knee. This is considered to be a clinical diagnosis characterised by limitation of movement of the knee. The severity of fibrosis may be graded according to the degree of limitation of movement and a scale is proposed from mild, moderate to severe according to the degree of restriction of ROM. The diagnosis may be supported by direct visualisation of fibrosis at surgery and by the histopathological analysis of tissue from the knee, although formal biopsy is not indicated or required.

Post-surgical fibrosis presents both a diagnostic and therapeutic challenge. It is considered a diagnosis of exclusion that requires thorough investigation to establish that the symptoms do not have another cause. The list of possible causes is long, but infection and malalignment of components or surgical error in particular must be excluded. Investigation algorithms have been presented for the analysis of the stiff TKA.⁵² A significant proportion of failed TKAs are due to malrotation of components, and this must be ruled out before making a diagnosis of fibrosis.⁵³ The cornerstones of investigation remain clinical examination, aspiration of the knee and laboratory evaluation to rule out infection, and plain films and CT scan to analyse the

alignment of the components.³ MRI scans with artifact reducing sequences may in the future provide a non-invasive method of describing intra-articular fibrosis.

Fibrosis may co-exist with other conditions such as following trauma⁵⁴ or mechanical conflict caused by malalignment of components, and may be triggered by them.⁵⁵ Fibrosis in this context was not considered post-operative fibrosis, which currently has an unknown aetiology. Tissue from fibrotic joints is composed of a dense, disorganised extracellular matrix of collagen fibrils⁶ interspersed with α -smooth muscle actin containing myofibroblast cells⁷ which form intra-articular fibrous bands.^{5,8} The molecular mechanism underlying the development of post-traumatic fibrosis is not known. It is likely that different triggers converge on a common 'fibrotic pathway',⁵⁶ involving myofibroblasts⁷ and transforming growth factor (TGF)- 1β signalling.⁵⁷ Furthermore, there is some evidence that fibrotic conditions are heritable.³⁴

There may be several different locations of the fibrosis, but it must be sufficient to cause limitation of movement. Limited pathology in local fibroses that do not cause limitation of movement, such as IPCS syndrome, is not considered to be fibrosis of the knee.

Alongside imaging, aspiration of the knee is recommended to rule out infection. Provided that this is performed in sterile conditions, the risk of introducing infection is outweighed by the need to establish whether stiffness is due to infection. Histopathology may be used to support the diagnosis of fibrosis, and recent publications have provided diagnostic criteria, such as the number of β -catenin staining cells, but these criteria need validation before biopsy can be recommended to establish a diagnosis.^{19,20}

There was considerable debate about the limitation of movement and whether this should be measured relative to pre-operative values or to those of the contralateral knee. Several grading systems have been proposed.^{9,10,58} Agreement was reached on the grading of the severity by absolute limitation of movement irrespective of pre-operative stiffness or the ROM of the contralateral knee. The limitation of the grading which was chosen is that knees with reduced ROM pre-operatively often do not regain ROM post-operatively. The important message is that some degree of limitation of movement in either flexion, extension, or both is absolutely required for a diagnosis of post-surgical fibrosis. It is also important to note that to judge success solely on ROM achieved would miss the main reason for TKA, namely reduction in pain.

Rehabilitation protocols aimed at restoring movement have reduced the incidence of stiffness post-operatively, particularly following anterior cruciate ligament reconstruction (ACL),^{13,49,59,60} but the optimum regime remains unknown. Similarly, the management of the stiff TKA remains challenging and evidence for particular forms of treatment is not available. There is evidence that optimised pain control can reduce the requirement for MUA in stiff knees following TKA.⁴⁵ One critical concept in the

approach to fibrosis is of early *versus* late fibrosis. The fibrotic condition is a disease spectrum, and early fibrosis is amenable to physiotherapy, whereas established fibrosis, which usually occurs after between three and six months is refractory to physiotherapy and manipulation runs the risk of iatrogenic fracture and should be avoided.⁵⁰ There was considerable debate over the timing of MUA. A consensus was reached that MUA more than six months post-operatively is not indicated. There is limited evidence that MUA is most effective less than three months after surgery.²⁴ Consensus agreement over the timing of MUA was challenging due to the lack of clear evidence and the risk of iatrogenic injury. Consensus was reached on MUA being an appropriate intervention between three and six months post-operatively.

Patients resistant to non-operative treatment require arthroscopic or open surgical procedures to excise and remove the soft-tissue contractures.³ Arthroscopic release may be used as an initial approach of choice. Kim, Gill and Millett⁴ provided an algorithm for this procedure following ACL reconstruction involving capsular distension with fluid, medial and lateral retinacular releases, graft debridement and posterior joint release. Open surgery for fibrosis is reserved for knees resistant to arthroscopic procedures (2% of cases)⁶¹ and often requires large incisions with extensive exploration of the joint and surrounding extra-capsular soft tissues.¹² The outcomes of surgically treated post-traumatic fibrosis of the knee are poor, with most patients unable to return to pre-injury level of function.^{12,62} Currently, available treatments work by stretching or surgically removing the fibrotic tissue; they do not address the biological basis of disease. This may contribute to recurrence of post-traumatic fibrosis, which is a frequent problem.^{5,10}

The role of arthroplasty registries in research into fibrosis was considered. Population level studies of patients with fibrosis would allow identification of risk factors, provide more precise data about the incidence, and inform management strategies. Currently, the identification of patients with fibrosis in National Registries is difficult; as a reason for revision it forms one group in the Australian registry⁶³, while the England, Wales and Northern Ireland registry⁶⁴ uses stiffness, despite the range of different pathologies that this encompasses. Furthermore, only patients having a formal revision procedure involving the exchange, removal or introduction of components are captured by registries, significantly underestimating the number of patients with fibrosis who are treated with non-operative measures or debridement only. A way forward for registries might be to use this consensus statement as a definition and include fibrosis after TKA as an indication for revision and also include open revision procedures not involving exchange of components and closed procedures such as MUA.

This consensus process has provided a definition, classification and diagnostic criteria for fibrosis of the knee after surgery. The aim was not to provide clinical guidelines on

the management of these patients. An international, multi-disciplinary working group reviewed the existing literature on fibrosis of the knee and further research into the prevention and management of this condition is required. A major challenge is the accurate diagnosis and stratification of patients with fibrosis of the knee to allow robust clinical studies. The definition of the disease and diagnostic criteria presented here may be used to diagnose, select and stratify patients accurately in future clinical studies for this poorly understood condition. These statements should now undergo a period of validation to allow the definition and classification to be improved upon and modified.



Take home message:

This definition will be used to identify patients and stratify them accurately in future clinical investigations, and ultimately improve our understanding and treatment of this challenging clinical problem.

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References

- Gollwitzer H, Burgkart R, Diehl P, Grading R, Bühren V. Therapy of arthrofibrosis after total knee arthroplasty. *Orthopade* 2006;35:143–152. (In German)
- Petsche TS, Hutchinson MR. Loss of extension after reconstruction of the anterior cruciate ligament. *J Am Acad Orthop Surg* 1999;7:119–127.
- Magit D, Wolff A, Sutton K, Medvecky MJ. Arthrofibrosis of the knee. *J Am Acad Orthop Surg* 2007;15:682–694.
- Kim DH, Gill TJ, Millett PJ. Arthroscopic treatment of the arthrofibrotic knee. *Arthroscopy* 2004 Jul 187–194.
- Seyler TM, Marker DR, Bhave A, et al. Functional problems and arthrofibrosis following total knee arthroplasty. *J Bone Joint Surg [Am]* 2007;89-A:59–69.
- Freeman TA, Parvizi J, Dela Valle CJ, Steinbeck MJ. Mast cells and hypoxia drive tissue metaplasia and heterotopic ossification in idiopathic arthrofibrosis after total knee arthroplasty. *Fibrogenesis Tissue Repair* 2010;3:17.
- Unterhauser FN, Bosch U, Zeichen J, Weiler A. Alpha-smooth muscle actin containing contractile fibroblastic cells in human knee arthrofibrosis tissue. Winner of the AGA-DonJoy Award 2003. *Arch Orthop Trauma Surg* 2004;124:585–591.
- Jerosch J, Aldawoudy AM. Arthroscopic treatment of patients with moderate arthrofibrosis after total knee replacement. *Knee Surg Sports Traumatol Arthrosc* 2007;15:71–77.
- Blauth W, Jaeger T. Arthrolysis of the knee joint. *Orthopade* 1990;19:388–399. (In German)
- Shelbourne KD, Patel DV, Martini DJ. Classification and management of arthrofibrosis of the knee after anterior cruciate ligament reconstruction. *Am J Sports Med* 1996;24:857–862.
- Sprague NF III, O'Connor RL, Fox JM. Arthroscopic treatment of postoperative knee fibroarthrosis. *Clin Orthop Relat Res* 1982;166:165–172.
- Wang JH, Zhao JZ, He YH. A new treatment strategy for severe arthrofibrosis of the knee. A review of twenty-two cases. *J Bone Joint Surg [Am]* 2006;88-A:1245–1250.
- Bonutti PM, Marulanda GA, McGrath MS, Mont MA, Zywiol MG. Static progressive stretch improves range of motion in arthrofibrosis following total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2010;18:194–199.
- Toms AD, Mandalia V, Haigh R, Hopwood B. The management of patients with painful total knee replacement. *J Bone Joint Surg [Br]* 2009;91:143–150.
- Biondo PD, Nekolaichuk CL, Stiles C, Fainsinger R, Hagen NA. Applying the Delphi process to palliative care tool development: lessons learned. *Support Care Cancer* 2008;16:935–942.
- Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011;12:489–495.
- Murphy MK, Black NA, Lamping DL, et al. Consensus development methods, and their use in clinical guideline development. *Health Technol Assess* 1998;2:i–iv–1–88.
- Jones J, Hunter D. Consensus methods for medical and health services research. *BMJ* 1995;311:376–380.
- Krenn V, Morawietz L, Perino G, et al. Revised histopathological consensus classification of joint implant related pathology. *Pathol Res Pract* 2014;210:779–786.
- Ruppert M, Theiss C, Knöß P, et al. Histopathological, immunohistochemical criteria and confocal laser-scanning data of arthrofibrosis. *Pathol Res Pract* 2013;209:681–688.
- Leta TH, Lygre SHL, Skredderstuen A, Hallan G, Furnes O. Failure of aseptic revision total knee arthroplasties. *Acta Orthop* 2015;86:48–57.
- Walton NP, Jahromi I, Dobson PJ, et al. Arthrofibrosis following total knee replacement; does therapeutic warfarin make a difference? *Knee* 2005;12:103–106.
- Witvrouw E, Bellemans J, Victor J. Manipulation under anaesthesia versus low stretch device in poor range of motion after TKA. *Knee Surg Sports Traumatol Arthrosc* 2013;21:2751–2758.

24. **Issa K, Kapadia BH, Kester M, et al.** Clinical, objective, and functional outcomes of manipulation under anesthesia to treat knee stiffness following total knee arthroplasty. *J Arthroplasty* 2014;29:548–552.
25. **Costa CR, McElroy MJ, Johnson AJ, Lamm BM, Mont MA.** Use of a static progressive stretch orthosis to treat post-traumatic ankle stiffness. *BMC Res Notes* 2012;5:348.
26. **Ibrahim MI, Johnson AJ, Pivec R, et al.** Treatment of adhesive capsulitis of the shoulder with a static progressive stretch device: a prospective, randomized study. *J Long Term Eff Med Implants* 2012;22:281–291.
27. **McElroy MJ, Johnson AJ, Zywiell MG, Mont MA.** Devices for the prevention and treatment of knee stiffness after total knee arthroplasty. *Expert Rev Med Devices* 2011;8:57–65.
28. **Chughtai M, Mont MA, Cherian C, et al.** A Novel, Nonoperative Treatment Demonstrates Success for Stiff Total Knee Arthroplasty after Failure of Conventional Therapy. *J Knee Surg* 2016;29:188–193.
29. **McGrath MS, Mont MA, Siddiqui JA, Baker E, Bhave A.** Evaluation of a custom device for the treatment of flexion contractures after total knee arthroplasty. *Clin Orthop Relat Res* 2009;467:1485–1492.
30. **Seyler TM, Jinnah RH, Koman LA, et al.** Botulinum toxin type A injections for the management of flexion contractures following total knee arthroplasty. *J Surg Orthop Adv* 2008;17:231–238.
31. **Ulrich SD, Bhave A, Marker DR, Seyler TM, Mont MA.** Focused rehabilitation treatment of poorly functioning total knee arthroplasties. *Clin Orthop Relat Res* 2007;464:138–145.
32. **Mont MA, Seyler TM, Marulanda GA, Delanois RE, Bhave A.** Surgical treatment and customized rehabilitation for stiff knee arthroplasties. *Clin Orthop Relat Res* 2006;446:193–200.
33. **Bhave A, Mont M, Tennis S, et al.** Functional problems and treatment solutions after total hip and knee joint arthroplasty. *J Bone Joint Surg [Am]* 2005;87-A:9–21.
34. **Williams FM, Kalson NS, Fabiane SM, Mann DA, Deehan DJ.** Joint Stiffness Is Heritable and Associated with Fibrotic Conditions and Joint Replacement. *Reilly G, ed. PLoS One* 2015;10:0133629.
35. **Dixon D, Coates J, del Carpio Pons A, et al.** A potential mode of action for Anakinra in patients with arthrofibrosis following total knee arthroplasty. *Sci Rep* 2015;5:16466.
36. **Abdul N, Dixon D, Walker A, et al.** Fibrosis is a common outcome following total knee arthroplasty. *Sci Rep* 2015;5:16469.
37. No authors listed. Willkommen bei SoSci Survey. www.sosci.de (date last accessed 23 August 2016).
38. **Parvizi J, Zmistowski B, Barbari EF, et al.** New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res* 2011;469:2992–2994.
39. **Parvizi J, Gehrke T, International Consensus Group on Periprosthetic Joint Infection.** Definition of periprosthetic joint infection. *J Arthroplasty* 2014;29:1331.
40. **Gehrke T, Parvizi J.** Proceedings of the International Consensus Meeting on Periprosthetic Joint Infection. *J Arthroplasty* 2014;2:4.
41. **Dowsey MM, Nikpour M, Dieppe P, Choong PFM.** Associations between preoperative radiographic changes and outcomes after total knee joint replacement for osteoarthritis. *Osteoarthritis Cartilage* 2012;20:1095–1102.
42. **Bae DK, Yoon KH, Kim HS, Song SJ.** Total knee arthroplasty in stiff knees after previous infection. *J Bone Joint Surg [Br]* 2005;87-B:333–336.
43. **Paulos LE, Rosenberg TD, Drawbert J, Manning J, Abbott P.** Infrapatellar contracture syndrome. An unrecognized cause of knee stiffness with patella entrapment and patella infera. *Am J Sports Med* 1987;15:331–341.
44. **Thorpe CD, Bocell JR, Tullos HS.** Intra-articular fibrous bands. Patellar complications after total knee replacement. *J Bone Joint Surg [Am]* 1990;72-A:811–814.
45. **Lavernia C, Cardona D, Rossi MD, Lee D.** Multimodal pain management and arthrofibrosis. *J Arthroplasty* 2008;23:74–79.
46. **Irrgang JJ, Harner CD.** Loss of motion following knee ligament reconstruction. *Sports Med* 1995;19:150–159.
47. **Brown CA, Toth AP, Magnussen B.** Clinical benefits of intra-articular anakinra for arthrofibrosis. *Orthopedics* 2010;33:877.
48. **Lunn TH, Kristensen BB, Andersen LØ, et al.** Effect of high-dose preoperative methylprednisolone on pain and recovery after total knee arthroplasty: a randomized, placebo-controlled trial. *Br J Anaesth* 2011;106:230–238.
49. **Cosgarea AJ, Sebastianelli WJ, DeHaven KE.** Prevention of arthrofibrosis after anterior cruciate ligament reconstruction using the central third patellar tendon autograft. *Am J Sports Med* 1995;23:87–92.
50. **Mamarelis G, Sunil-Kumar KH, Khanduja V.** Timing of manipulation under anaesthesia for stiffness after total knee arthroplasty. *Ann Transl Med* 2015;3:316.
51. **Fox JL, Poss R.** The role of manipulation following total knee replacement. *J Bone Joint Surg [Am]* 1981;63-A:357–362.
52. **Hofmann S, Seitlinger G, Djahani O, Pietsch M.** The painful knee after TKA: a diagnostic algorithm for failure analysis. *Knee Surg Sports Traumatol Arthrosc* 2011;19:1442–1452.
53. **Bédard M, Vince KG, Redfern J, Collen SR.** Internal rotation of the tibial component is frequent in stiff total knee arthroplasty. *Clin Orthop Relat Res* 2011;469:2346–2355.
54. **Haller JM, Holt DC, McFadden ML, Higgins TF, Kubiak EN.** Arthrofibrosis of the knee following a fracture of the tibial plateau. *Bone Joint J* 2015;97-B:109–114.
55. **Luck JV.** Traumatic arthrofibrosis; the fibroplastic response of joints to trauma. *Bull Hosp Joint Dis* 1951;12:394–403.
56. **Mann J, Mann DA.** Epigenetic regulation of wound healing and fibrosis. *Curr Opin Rheumatol* 2013;25:101–107.
57. **Watson RS, Gouze E, Levings PP, et al.** Gene delivery of TGF-β1 induces arthrofibrosis and chondrometaplasia of synovium in vivo. *Lab Invest* 2010;90:1615–1627.
58. **Schiavone Panni A, Cerciello S, Vasso M, Tartarone M.** Stiffness in total knee arthroplasty. *J Orthop Traumatol* 2009;10:111–118.
59. **DeHaven KE, Cosgarea AJ, Sebastianelli WJ.** Arthrofibrosis of the knee following ligament surgery. *Instr Course Lect* 2003;52:369–381.
60. **Noyes FR, Berrios-Torres S, Barber-Westin SD, Heckmann TP.** Prevention of permanent arthrofibrosis after anterior cruciate ligament reconstruction alone or combined with associated procedures: a prospective study in 443 knees. *Knee Surg Sports Traumatol Arthrosc* 2000;8:196–206.
61. **Noyes FR, Mangine RE, Barber SD.** The early treatment of motion complications after reconstruction of the anterior cruciate ligament. *Clin Orthop Relat Res* 1992;277:217–228.
62. **Millett PJ, Williams RJ III, Wickiewicz TL.** Open debridement and soft tissue release as a salvage procedure for the severely arthrofibrotic knee. *Am J Sports Med* 1999;27:552–561.
63. **No authors listed.** Australian Orthopaedic Association National Joint Replacement Registry. <https://aoanjrr.sahmri.com/> (date last accessed 23 August 2016).
64. **No authors listed.** National Joint Registry. <http://www.njrcentre.org.uk/njrcentre/default.aspx> (date last accessed 23 August 2016).