Acquired Idiopathic Stiffness After Total Knee Arthroplasty

A Systematic Review and Meta-Analysis

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Background: Stiffness is a common reason for suboptimal clinical outcomes after primary total knee arthroplasty (pTKA). There is a lack of consensus regarding its definition, which is often conflated with its histopathologic subcategory—i.e., arthrofibrosis. There is value in refining the definition of acquired idiopathic stiffness in an effort to select for patients with arthrofibrosis. We conducted a systematic review and meta-analysis to establish a consensus definition of acquired idiopathic stiffness, determine its prevalence after pTKA, and identify potential risk factors for its development.

Methods: MEDLINE, Embase, Cochrane Controlled Register of Trials (CENTRAL), and Scopus databases were searched from 2002 to 2017. Studies that included patients with stiffness after pTKA were screened with strict inclusion and exclusion criteria to isolate the subset of patients with acquired idiopathic stiffness unrelated to known extrinsic or surgical causes. Three authors independently assessed study eligibility and risk of bias and collected data. Outcomes of interest were then analyzed according to age, sex, and body mass index (BMI).

Results: In the 35 included studies (48,873 pTKAs), the mean patient age was 66 years. In 63% of the studies, stiffness was defined as a range of motion of <90° or a flexion contracture of >5° at 6 to 12 weeks postoperatively. The prevalence of acquired idiopathic stiffness after pTKA was 4%, and this did not differ according to age (4%, I^2 = 95%, among patients <65 years old and 5%, I^2 = 96%, among those ≥65 years old; p = 0.238). The prevalence of acquired idiopathic stiffness was significantly lower in males (1%, I^2 = 85%) than females (3%, I^2 = 95%) (p < 0.0001) as well as in patients with a BMI of <30 kg/m^2 (2%, I^2 = 94%) compared with those with a BMI of ≥30 kg/m^2 (5%, I^2 = 97%) (p = 0.027).

Conclusions: Contemporary literature supports the following definition for acquired idiopathic stiffness: a range of motion of <90° persisting for >12 weeks after pTKA in patients in the absence of complicating factors including preexisting stiffness. The mean prevalence of acquired idiopathic stiffness after pTKA was 4%; females and obese patients were at increased risk.

Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Stiffness is a common reason for failure of primary total knee arthroplasty (pTKA), contributing to up to 58% of reoperations or repeat interventions (such as manipulation under anesthesia) and >25% of 90-day hospital readmissions in some series[1-3]. Patients who develop this complication have poor functional outcomes and increased rates of knee pain, and their symptoms often are refractory to nonoperative and even operative management[4,5]. The incidence of TKA increased from 31.2 per 100,000 person-years from 1971 to 1976 to 220.9 per 100,000 person-years from 2005 to 2008[6]. This trend, compounded by an increasing prevalence of obesity and a decreasing mean age of patients undergoing pTKA, will lead to an increased demand for revision TKAs[7-9]. It is therefore critically important to investigate and define one of the leading causes of pTKA failure.

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Arthrofibrosis is characterized histopathologically by diffuse proliferation of scar tissue and results in a painful, restricted range of motion[10]. The process is hypothesized to originate from a pro-inflammatory insult that stimulates myofibroblast and mast cell proliferation, leading to pathologic amounts of type-I collagen deposition and subsequent joint contracture[11]. Diabetes, smoking, and the patient's sex are also thought to contribute to its development. However, the precise mechanism has yet to be elucidated, and there is no definitive diagnostic test[12]. Furthermore, there is a paucity of data to support the implementation of a standardized clinical definition of arthrofibrosis[10,13]. In the absence of formal definitions, surgeons are forced to rely on clinical judgment and range-of-motion data to appropriately diagnose patients[12]. Therefore, definitions vary widely, from objective provider-obtained range-of-motion measurements to patient dissatisfaction with range of motion or pain[10,13-16]. Few authors have explicitly reported the exclusion of patients with periprosthetic joint infection, malpositioned or incorrectly sized components, ligamentous instability, patellar malalignment, an osseous block to motion, or complex regional pain syndrome from their arthrofibrotic cohort, despite the fact that these conditions may also lead to motion loss[17-20]. The terms "stiffness," "flexion contracture," and "arthrofibrosis" have often been incorrectly used interchangeably in the current literature to describe limitations of motion. This lack of consensus has led to a wide range of reported prevalences, from 0% to as high as 54%[16,21,22].

In a recent consensus study, Kalson et al.[10] developed comprehensive diagnostic and treatment guidelines for arthrofibrosis. Using 320 source studies, the authors highlighted the difficulty in studying arthrofibrosis in the absence of a widely accepted definition and generated multiple algorithms to allow clinicians to diagnose and classify these patients[10]. Additionally, a recent systematic review examined the treatment strategies for stiffness following pTKA[23]. This review included a host of etiologies and outcomes as well as common complications and reasons for revisions and reoperations. The patient cohorts from which these conclusions were drawn varied with respect to sample size, technique, diagnosis, and treatment. Furthermore, because no explicit numerical data analyses were performed, risk factors for the development of acquired idiopathic stiffness could not be determined.

We posit that a subset of patients with stiffness, specifically those for whom other identifiable causes have been ruled out, has acquired idiopathic stiffness. We hypothesize that this cohort most closely represents those who would receive the histopathologic diagnosis of arthrofibrosis. In light of the substantial patient cohort variability and absence of a concise standardized definition, we conducted a comprehensive systematic review and meta-analysis to (1) establish a range-of-motion threshold to define "acquired idiopathic stiffness" that can be used as a working clinical definition, (2) determine its prevalence after pTKA, and (3) identify potential risk factors for its development.

Materials and Methods

A protocol was designed for this systematic review and meta-analysis to define the population of interest, interventions of interest, and related outcomes. This study was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology[17].

Study Eligibility

All prospective or retrospective studies that recorded the prevalence of acquired idiopathic stiffness following TKA were included. Comparative studies with Level-I, II, or III evidence in which this disease was reported as an aseptic pTKA failure mechanism not attributable to another condition were also included. Exclusion criteria were (1) studies with non-routine inclusion criteria (e.g., only patients with organ transplants or connective-tissue disorders); (2) studies describing only patients with a preoperative flexion contracture or decreased range of motion preoperatively; (3) studies lacking a specific definition of stiffness, flexion contracture, or arthrofibrosis with numerical clinical data; and (4) studies of revision TKA without data describing overall prevalence of stiffness in the original patient cohort.

Literature Search

We searched databases, including MEDLINE, Embase, MEDLINE In-Process & Other Non-Indexed Citations, Cochrane Controlled Register of Trials (CENTRAL), Cochrane Database of Systematic Reviews, and Scopus, for studies published between January 2002 and October 2017 (see Appendix 1). We used MeSH and Emtree headings in several combinations and supplemented with free text to increase sensitivity. We manually searched the reference lists of relevant studies to identify any additional articles. The search strategy was designed and performed by an experienced librarian.

Study Selection

Three authors (M.E.T., A.K.L., and C.G.S.) independently identified all titles and abstracts using Covidence, an electronic screening form. Disagreements were resolved by consensus. Studies of patients who were <18 years of age and studies of stiffness in anatomical locations other than the knee were excluded. Editorials, reviews, symposia, basic-science papers, case reports, and case series were excluded as well.

Data Extraction

The included studies were assessed by 3 reviewers (M.E.T., A.K.L., and C.G.S.) in accordance to the Newcastle-Ottawa Scale, which detects heterogeneity within groups and outcomes[24]. The studies were assessed for quality on the basis of the duration of follow-up, cohort selection, and outcome assessment. Data were extracted manually and then were modified as necessary to fit the outcomes of interest (Table I).

Outcomes

The primary outcome of interest was the prevalence of acquired idiopathic stiffness following pTKA. We performed

TABLE I Characteristics of Included Studies*

Authors	Period of Study	Institution	Country	No. of Patients
Abdel et al., 2017[1]	2000-2013	Mayo Clinic	U.S.	
Anania et al., 2013[4]	Jan. 2006-Apr. 2011	Hospital for Special Surgery	U.S.	295
Barnes et al., 2013[43]	Sept. 2005-Apr. 2008	Hip Knee Arkansas Foundation	U.S.	755
Bawa et al., 2013[28]	1999-2007	Case Medical Center	U.S.	2,782
Bistolfi et al., 2013[52]	Jan. 1998-Sept. 2002	Adelaide Hospital	Italy	163
Boldt et al., 2006[20]	1988-1999	Orthopedic University Hospital Balgrist	Switzerland	
Cates and Schmidt, 2009[29]	2000-Jan. 2005	Tennessee Orthopaedic Clinics	U.S.	
Chalidis et al., 2011[44]	1994-2000	"G. Papanikolaou" Hospital	Greece	345
Choi et al., 2015[45]	2001-2011	Massachusetts General Hospital	U.S.	
Curtin et al., 2014[19]	(1) Jan. 1998-May 2005/ (2) June 2005-Dec. 2007	VCU/MCV West Hospital	U.S.	546 (1st study period/ 280 (2nd study period)
Dalury et al., 2003[30]	3-yr period (published Oct. 2003)	University of Maryland	U.S.	
Dzaja et al., 2015[12]	May 2001-July 2012	Western University	Canada	
Everts et al., 2007[41]		Catharina Hospital	Netherlands	85 (platelet gel and fibrin sealant/80 (no gel or sealant)
Fosco et al., 2011[31]	Mar. 1997-Aug. 2009	University of Bologna	Italy	
Gandhi et al., 2006[32]	Sept. 1998-May 2002	Henderson Hospital	Canada	
Geller et al., 2017[46]	Nov. 2005-Sept. 2015	Columbia University	U.S.	690 (sensor)/252 (no sensor)
Harvie et al., 2013[47]		Royal Perth Hospital	Australia	
Hommel and Wilke, 2017[42]	June 2011-Dec. 2013	Krankenhaus Markisch Oderland	Germany	257
Husted et al., 2015[33]	Jan. 10, 2010-May 31, 2012	Copenhagen University	Denmark	
Ipach et al., 2011[34]	Aug. 1, 2004-July 31, 2009	Ortho University Tuebingen	Germany	
Kim et al., 2004[16]	1997-2000	Hospital of the University of Pennsylvania, Philadelphia, PA	U.S.	981
Lavernia et al., 2008[35]		Orthopedic Institute, Mercy Hospital, Miami, FL	U.S.	778
McAllister and Stepanian, 2008[48]		Evergreen Orthopedic Center, Kirkland, WA	U.S.	73
McGinn et al., 2016[49]	Jan. 2013-Dec. 2014	Rubin Institute for Advanced Orthopedics, Sinai Hospital, Baltimore, MD	U.S.	127
Mitsuyasu et al., 2011[53]	Jan. 2001-July 2006	Kyushu University, Fukuoka	Japan	85 (0°/<5°/<10° flexion contracture preop.)
Quah et al., 2012[36]	2001-2006	Royal Derby Hospital	U.K.	1,626
Ritter et al., 2007[54]	1973-2002	Center for Hip and Knee Surgery, Mooresville, IN	U.S.	
Rubinstein and DeHaan, 2010[18]	1992-2007	Portland Knee Clinic	U.S.	
Sharma et al., 2008[50]	Jan. 2002-Dec. 2003	Ranawat Orthopedic Center	U.S.	251 (PCA)/ 248 (no PCA)
Smith et al., 2016[37]	2012-2013	Rothman Institute	U.S.	372
Vanlommel et al., 2017[17]	2004-2014	University Hospitals Leuven	Belgium	3,905
Walton et al., 2005[40]	Jan. 1993-Dec. 2003	Wakefield Orthopedic Clinic, Adelaide	Australia	728
White and Ranawat, 2016[51]	Jan. 2010-Nov. 2012	Hospital for Special Surgery	U.S.	
Yercan et al., 2006[38]	1987-2003	Centre Livet-Hopital Croix Rousse, Caluire	France	
Yoo et al., 2015[39]	Mar. 2000-July 2004	National Health Insurance Corporation Ilsan Hospital, Goyang	Korea	

*MUA = manipulation under anesthesia, ROM = range of motion, PT = physical therapy, PF = patellofemoral, TKA = total knee arthroplasty, FFD = fixed flexion deformity, f/u = follow-up, and PCA = patient-controlled anesthesia.

TABLE I (*continued*)

No. of Knees	% with Arthrofibrosis	Definition of Arthrofibrosis/Stiffness/Flexion Contracture	Criteria for MUA
5,098	2.1	"Stiffness": ROM <90° 6-12 wk postop.	"Stiffness" (ROM <90° 6-12 wk postop.)
319	14.4	"Flexion contracture" (loss of extension) ≥5° 6 wk postop.	
755	4.1	"Stiffness": ROM <90° 6 wk postop.	
3,244	3.7		Failure to reach 90° of flexion by 6 wk postop.; could be sooner if patient not on track to achieve this goal
200	0	"Flexion contracture" >10°	No MUA performed
3,058	1.6	"Arthrofibrosis": max. ROM <90°, flexion contracture >10°	
767	6		Flexion <100° 4-8 wk postop. or <110° with functional restrictions later in recovery
393	1.5		Flexion <90° <4 wk postop.
1,293	6.3		Flexion <90° 4-6 wk postop. and/or flexion <90° and failure to gain ROM back 2-3 mo postop.
	4.2/2.1		Flexion <90° 6 wk postop., or if flexion remained <90° up to 3 mo postop.
1,014	2.27	"Stiffness": flexion >80°-100° 3 mo postop.; severely stiff: flexion <80° 6 wk postop. and no MUA	Flexion <80° 6 wk postop.
6,043	1.2		Flexion <90° unresponsive to PT
	10/2.3	"Arthrofibrosis": painful stiffness with scarring of soft tissue, flexion <80°, PF immobility, no heterotopic bone formation	
861	4.9	"Stiff": ROM <50°	
1,216	3.7	"Stiffness": flexion <90° 1 yr postop.	
	4.9/1.6		ROM ≤90° 6-8 wk postop.
281	7.4		Mean ROM 62° (range, 30°-75°); mean extension deficit 8° (range, 5°-30°)
257	0	"Stiffness": flexion <90°	
3,145	2.2		At surgeon's discretion but all used flexion <90° and agreed to wait 6 wk (see various definitions in table on page 3/6)
867	4.5	If ROM >90° not achieved, patient kept in hospital for 14 days.	If ROM still not 90° and anatomical reasons were excluded, patient encouraged to undergo immediate MUA
1,000	1.3	"Flexion contracture" >15° or flexion <75°	
	4.8		Flexion <90° at 4 wk
89	18.0		If flexion <90° at 6 wk MUA considered; done by 3 mo if ROM had not improved; MUA done after 14% of traditional TKAs
	8.7	Need for MUA	Failure to reach 90° of flexion or 15° of extension by 6 wk postop.
48	8/0/8.7	Postop. flexion contracture in degrees (>5° was minimum)	
	9	FFD (170 patients) >5° (124 patients, 91.2%) or >15° (12 patients, 8.8%) at 6-wk f/u	
5,622	1.8	"Flexion contracture" >10°	
800	4.6		Flexion <90° 4-6 wk postop. and/or failure to gain motion over initial 2-3 mo
286/292	2.4	Patients with flexion <90°, flexion contracture >15°, or ROM <70°-80° given 2-3 wk of extensive supervised PT	No improvement after 2-3 wk of extensive supervised PT after ruling out malposition, PF overstuffing, patella baja, maltracking, infection
	3.8	If flexion contracture >10°, extension orthosis applied 2-4×/day for 30-60 min. If this failed, patient offered study enrollment	
4,568	3.9	Flexion <90° or lack of extension of >15° within 3 mo postop.	
874	9.5	Criteria for MUA defined as having arthrofibrosis according to Maloney	Flexion <80° at 6-8 wk f/u
42	38.1	Flexion <90° or flexion contracture >10° at 6-wk or 3-mo f/u visit	Infection, implant malalignment, fracture, loosening contraindications
1,188	5.3	Extension deficit >10° and/or flexion <95° 1st 6 wk postop.	Failure to achieve active knee flexion of 75° at end of 10 days and/or 95° of flexion within 3 mo postop.
329	1.2	Patients with <80° of flexion or progressive stiffness despite flexion of >80° at discharge came back for visit at 1-2 wk	Flexion <80° at 1-2-wk visit

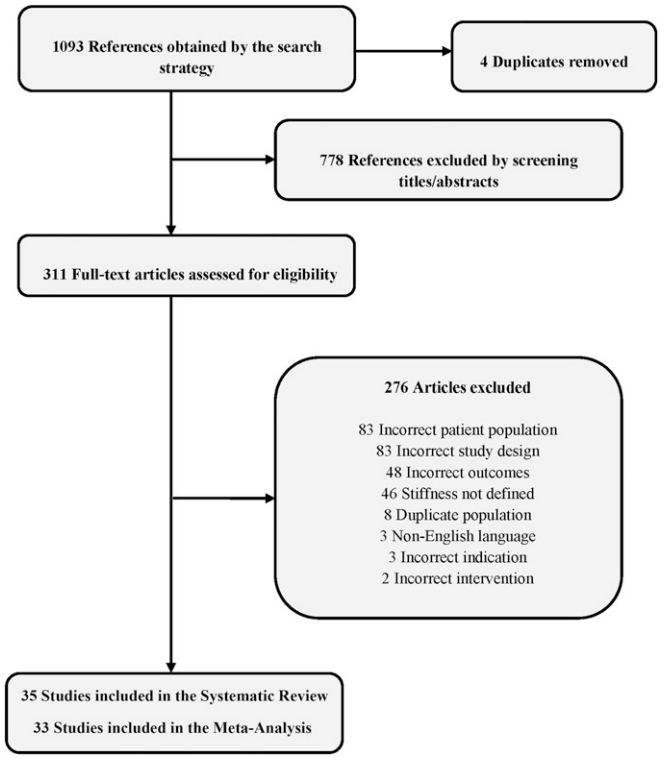

Fig. 1

Flowchart depicting PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) search strategy.

subanalyses according to the duration of follow-up (≤24 and >24 months), sex (female and male), age (<65 and ≥65 years old), and body mass index (BMI) (<30 and ≥30 kg/m^2).

Statistical Analysis

The DerSimonian and Laird conservative random-effects model was used to pool log-transformed event prevalence and estimated 95% confidence intervals (CIs)[25]. Heterogeneity was quantified using the I^2 statistic, which estimates the proportion of total variability between studies not due to chance alone[26]. Values of >50% were considered to be heterogeneous. Subgroup analyses of disease prevalence by duration of follow-up, sex, age, and BMI were also performed to further assess heterogeneity. P values of <0.05 were considered significant. All data were analyzed using STATA, version 14 (StataCorp)[27].

Results

Eligible and Included Studies

There were 1,089 potentially eligible articles; 778 were unrelated to the study question and thus excluded. The full text of 311 studies was reviewed, and 276 were excluded because of an incorrect or duplicate patient population, incorrect study design or outcomes, lack of criteria for stiffness, non-English language, and operative intervention not involving TKA. We further filtered these studies according to previously described inclusion and exclusion criteria as well as methodological quality. Ultimately, 35 studies (48,873 pTKAs) (Fig. 1) were selected for inclusion in the systematic review. Because 2 of them had no events, 33 were included in the meta-analysis. The mean patient age in the studies was 66 years.

Study Characteristics

Eighteen (51%) of the studies[4,12,16-18,20,28-39] (31,195 knees) contained sufficient data to allow analysis of age as a risk factor for developing acquired idiopathic stiffness following pTKA. This complication developed in 1,069 knees (3.4%) in patients with a mean age of 64.3 years (range among studies, 57 to 71 years). Patient sex was reported in 17 studies[4,12,17-20,28,29,31,32,34-40] (49%) with a total of 16,720 patients (27,736 knees), 10,473 (63%) of whom were female and 6,247 (37%) of whom were male. Acquired idiopathic stiffness developed in 980 (6%) of these patients, 658 (67%) of whom were female and 322 (33%) of whom were male. BMI was reported in 10 studies (21,336 knees)[4,12,17,20,28-30,32,35,39] and averaged 31 kg/m^2 (range among studies, 18 to 54 kg/m^2) for the patients who developed acquired idiopathic stiffness.

Clinical Definitions

The definition(s) of "arthrofibrosis," "stiffness," and/or "flexion contracture" utilized as inclusion criteria in each study were assessed. Of the 35 studies included in our review, 2 used the clinical term "arthrofibrosis,"[20,41] 29 used "stiffness,"[1,12,16-20,28-35,38-51] and 11 used "flexion contracture."[4,16,20,36-38,50-54] Five studies used a combination of the aforementioned clinical terminology as inclusion criteria[16,20,38,41,51]. For 12 studies[12,18,19,28,29,33,35,44-48] that did not explicitly define inclusion criteria, but instead listed range-of-motion criteria for manipulation under anesthesia, definitive criteria for manipulation under anesthesia were used as surrogate definitions.

The numerical range-of-motion cutoffs used to differentiate among the above terms varied. Details and definitions can be found in Table I.

Outcomes

Overall prevalence of acquired idiopathic stiffness following pTKA: The overall prevalence of acquired idiopathic stiffness was 4% (Fig. 2). Its prevalence was significantly (p = 0.033) lower in studies with >24 months of follow-up[1,4,12,16-18,20,28,30,31,36,38,39,44,54] (3%, I^2 = 96%) than in those with ≤24 months of follow-up[19,29,32-35,37,40,41,43,45-51,53] (4%, I^2 = 85%) (Fig. 3).

Prevalence of acquired idiopathic stiffness following pTKA by age, sex, and BMI: The prevalence of acquired idiopathic stiffness did not differ significantly (p = 0.238) between patients <65 years of age (4%, I^2 = 95%)[12,17,18,28,29,33-35,37,39] and those ≥65 years of age (5%, I^2 = 96%)[4,16,20,30-32,36,38] (Fig. 4). The prevalence was significantly lower (p < 0.001) in men[4,12,17-20,28,29,31,32,34-38,40] (1%, I^2 = 85%) than women (3%, I^2 = 95%)[4,12,17-20,28,29,31,32,34-40] (Fig. 5). Patients with a BMI of <30 kg/m^2 (2%, I^2 = 94%)[17,20,30,39] had a significantly lower prevalence (p = 0.027) than those with a BMI of ≥30 kg/m^2 (5%, I^2 = 97%)[4,12,28,29,32,35] (Fig. 6).

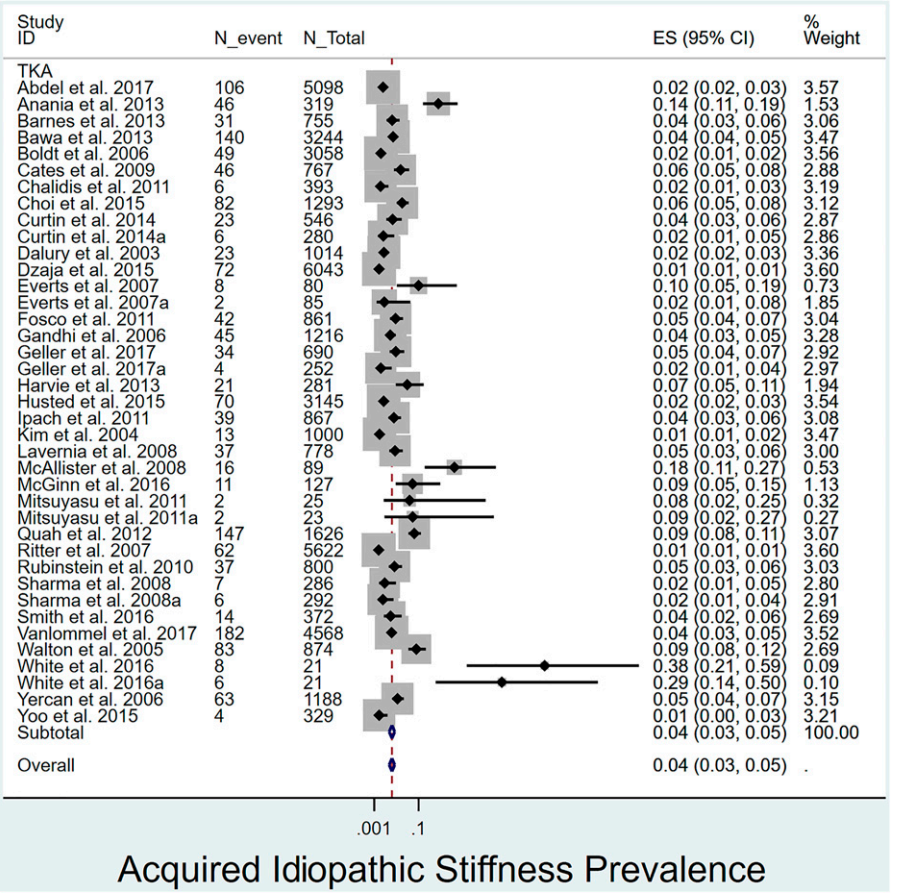

Fig. 2

Forest plot depicting the prevalence of acquired idiopathic stiffness among all included studies as well as the overall mean. ES (95% CI) = effect size (95% confidence interval). The values correspond to prevalences (expressed as decimal values rather than percentages).

Methodological quality and risk of bias assessment: All 35 studies included in this review were observational uncontrolled cohort studies and thus a high risk of bias was observed. A detailed assessment of methodological quality indicators is presented in Appendix 2. Overall, there was high statistical heterogeneity for all outcomes.

Diabetes mellitus and smoking status were examined; however, because of insufficient data reporting in the included studies, an analysis was not performed for these parameters.

Discussion

Despite being one of the most common reasons for failure of pTKA, the definition of acquired idiopathic stiffness is poorly understood and the entity probably is often misdiagnosed. The prevalence of this complication in the studies included in this review ranged from 1% to 38% (mean, 4%) even with strict inclusion criteria. Disease prevalence did not differ significantly according to age; however, female sex and a BMI of ≥30 kg/m^2 were found to be risk factors.

In the majority (63%) of the studies, a range of motion of <90° or a flexion contracture of >5° was used to define postoperative acquired idiopathic stiffness[1,12,17-20,28,32-35,38,42-46,48-51]. Previous studies have demonstrated that 105° to 110° is the minimum knee flexion required to perform most activities of daily living (ADLs) in Western societies such as rising from a chair, walking, and ascending stairs[55,56]. A more recent kinematic analysis providing additional data on activities showed donning pants and getting in and out of a bathtub to require 78° and 123° to 143° of knee flexion, respectively[57]. Despite the results of these biomechanical studies, McClelland et al.[58] recently demonstrated that patients use only 81° to 91° of their maximal passive knee flexion after TKA. Patients with a greater passive range of motion did have higher maximal flexion during ADLs but utilized only 68% to 77% of their maximal motion during more strenuous activities[58]. Several additional studies have shown that preoperative range of motion is the best predictor of final range of motion[16,17,59], which justifies the extensive exclusion criteria that we utilized to select eligible studies. In order to accurately identify only those patients with a substantial postoperative loss of range of motion leading to limitations in ADLs, we propose a threshold range of motion of <90° persisting for >12 weeks after TKA to define *acquired idiopathic stiffness*. This should exclude patients with periprosthetic joint infection, a prosthetic or osseous block to motion (including malpositioned components), aseptic loosening of components, or preoperative stiffness. Use of this definition

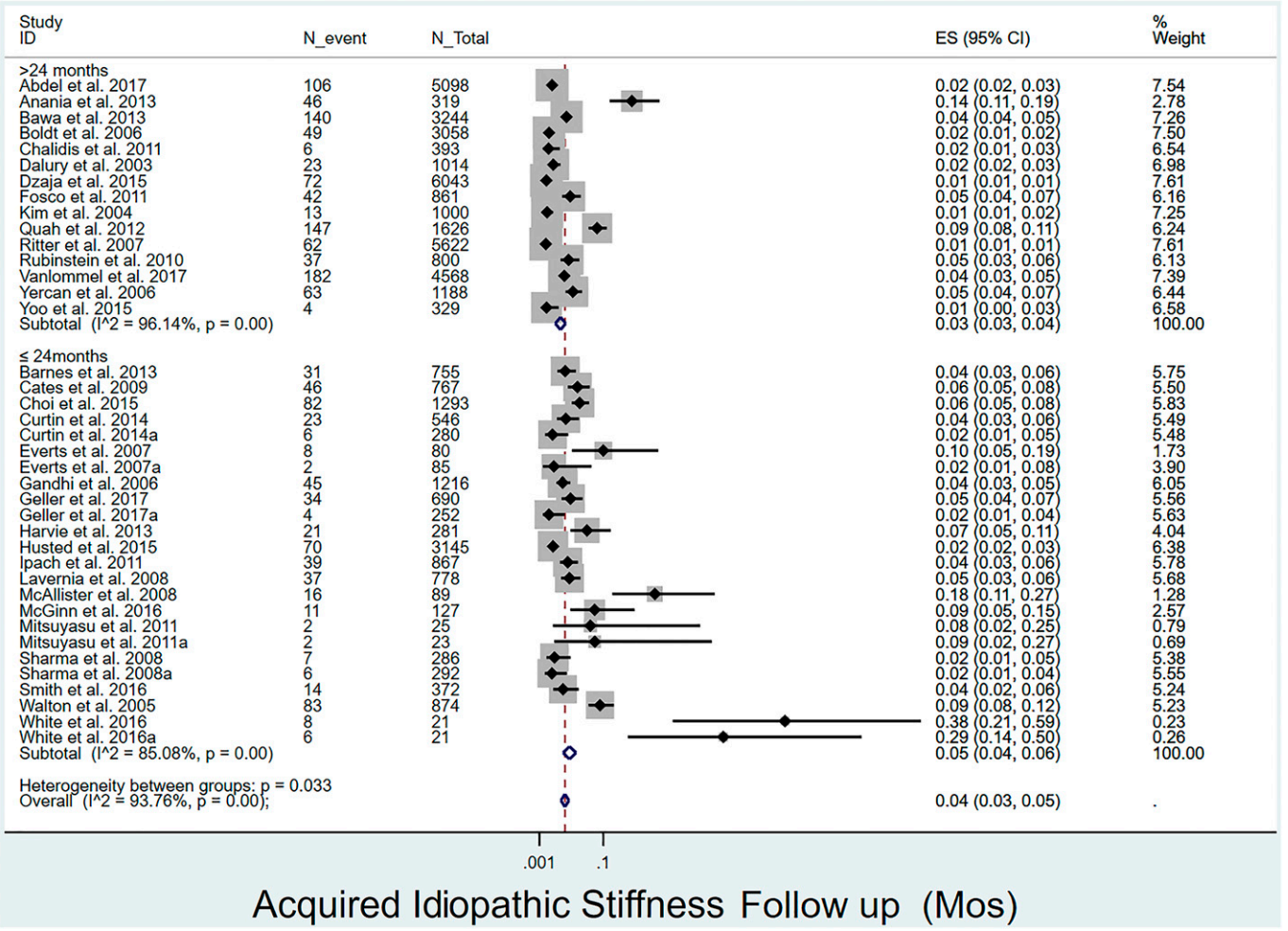

Fig. 3

Forest plot depicting the prevalence of acquired idiopathic stiffness according to duration of follow-up. ES (95% CI) = effect size (95% confidence interval). The values correspond to prevalences (expressed as decimal values rather than percentages).

clinically, and in future studies, would allow improved understanding of the characteristics of at-risk patients and would facilitate treatment and prevention of this disease. We recognize that some of the above factors that are known to cause knee stiffness may create secondary tissue changes similar or identical to those seen in acquired *idiopathic* stiffness.

We report a mean prevalence of acquired idiopathic stiffness of 4% after pTKA (Table I). The wide range of disease prevalence among the included studies (38% in 1 series[51]) can be attributed to variable and sometimes limited sample sizes. The severity of acquired idiopathic stiffness is a continuum; the authors of several studies have recognized that the time of follow-up as well as the extent of clinical intervention or rehabilitation play a large role in determining the reported prevalence of the disease. We found that the prevalence was significantly lower ($p = 0.033$) in studies with follow-up of >24 months[1,4,12,16-18,20,28,30,31,36,38,39,44,54] (3%, $I^2 = 96\%$) than in those with ≤24 months of follow-up[19,29,32-35,37,40,41,43,45-51,53] (4%, $I^2 = 85\%$). These data suggest that the disease process generates its most significant effects early; therefore, efforts to interrupt the process should be undertaken immediately postoperatively or in the perioperative period. Early clinical intervention such as intense physical therapy or manipulation under anesthesia has been advocated for patients who do not obtain at least 90° of flexion by the 4-week follow-up visit[19,26,31,44]. The decreased prevalence over time suggests that, in some patients, the stiff soft tissues eventually become more compliant, with subsequent improvements in range of motion.

Stratification by age did not demonstrate a significant difference in the prevalence of acquired idiopathic stiffness between patients ≥65 and those <65 years of age ($p = 0.238$). This corroborates the results reported by Kim et al.[16], who did not identify age as a risk factor in 1,000 consecutive TKAs, 1.3% of which were followed by development of acquired idiopathic stiffness. In a review of 18,065 TKAs for which infection and stiffness were the most common reasons for failure, Pitta et al.[60] found that increasing age was protective against TKA failure (hazard ratio [HR] = 0.61, $p < 0.01$). This is likely due to the decreased functional demands

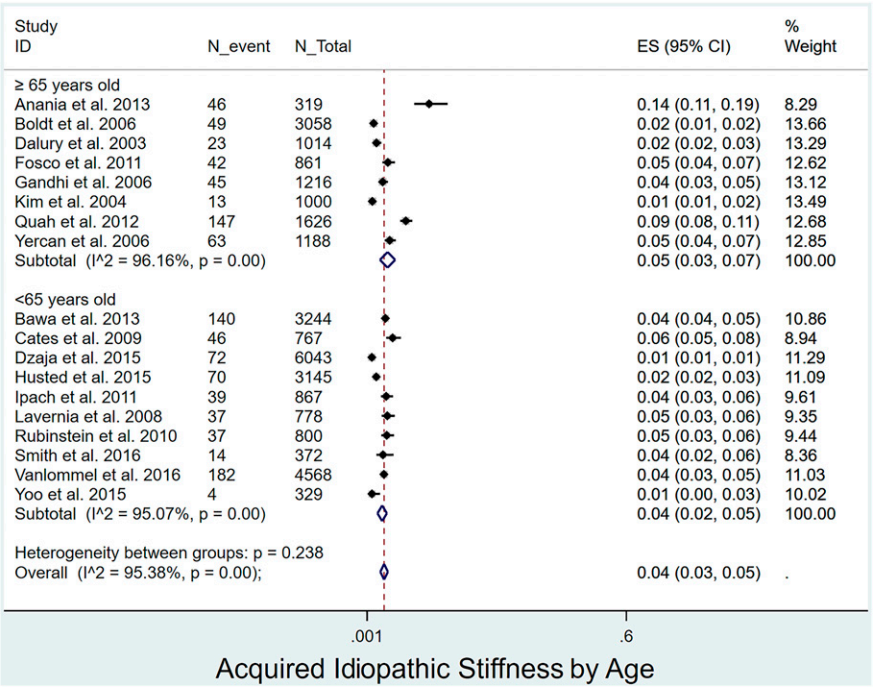

Fig. 4

Forest plot depicting the prevalence of acquired idiopathic stiffness according to age. ES (95% CI) = effect size (95% confidence interval). The values correspond to prevalences (expressed as decimal values rather than percentages).

and stresses that older patients place on implants. Conversely, elevated BMI (≥30 kg/m^2) significantly affected the prevalence of acquired idiopathic stiffness in our review (p = 0.027). While data on the prevalence of this disease in obese patients are limited, ample data have demonstrated that patients with a higher BMI have an increased risk of perioperative

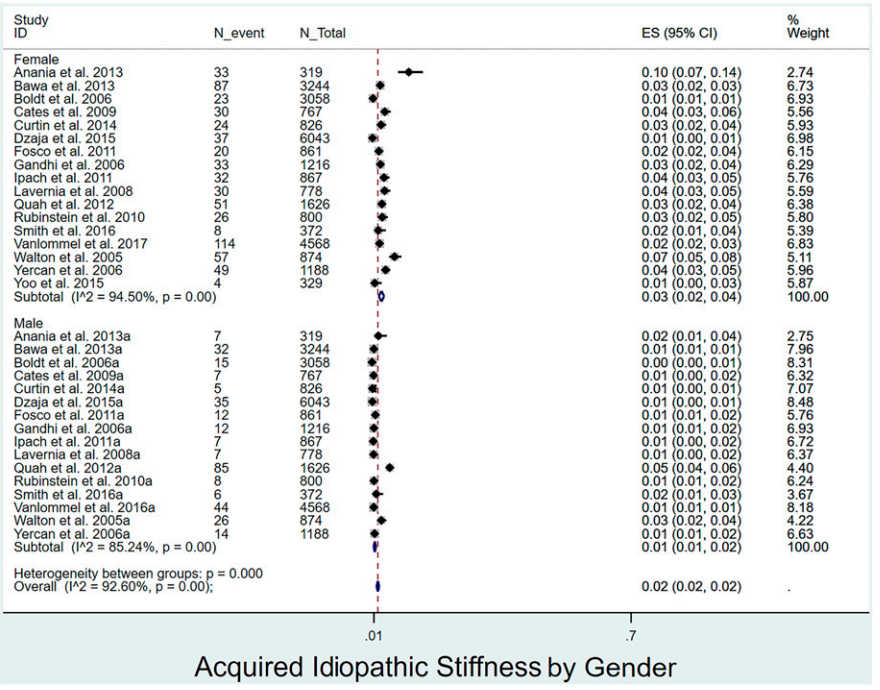

Fig. 5

Forest plot depicting the prevalence of acquired idiopathic stiffness according to sex. ES (95% CI) = effect size (95% confidence interval). The values correspond to prevalences (expressed as decimal values rather than percentages).

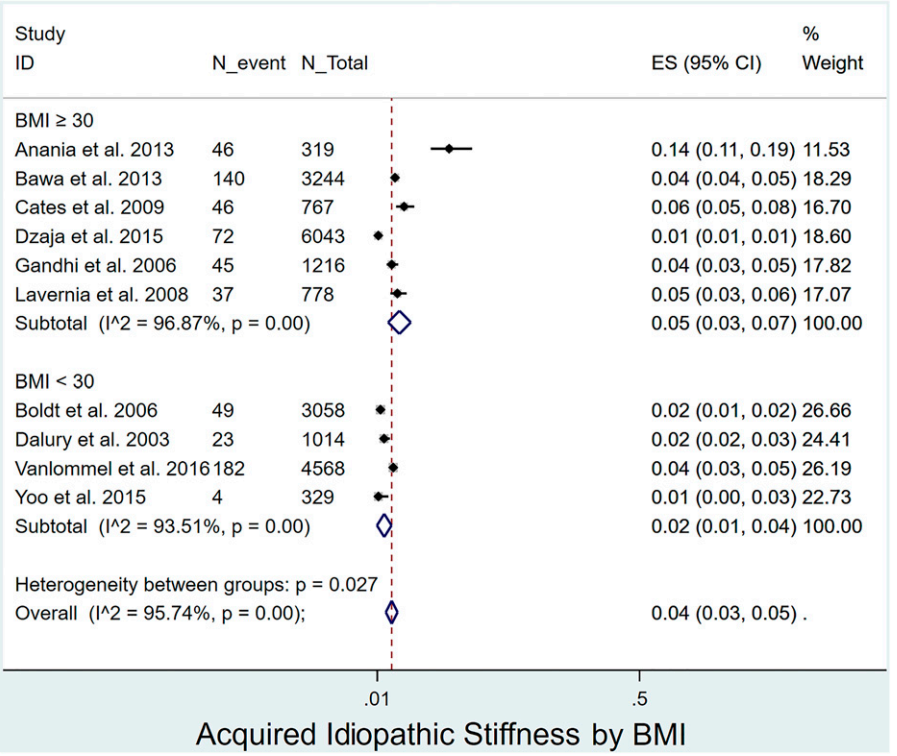

Fig. 6

Forest plot depicting the prevalence of acquired idiopathic stiffness according to BMI (kg/m^2). ES (95% CI) = effect size (95% confidence interval). The values correspond to prevalences (expressed as decimal values rather than percentages).

complications, decreased functional outcome scores, and a decreased range of motion[61,62]. Vazquez-Vela Johnson et al.[63] found that, at 10 years, obese males ≤60 years of age had an implant survival rate of 35.7% compared with 99.4% in non-obese females who were >60 years old. The prevalence among females was 3-fold greater than that among males ($p < 0.001$) in our analysis, even though few series have demonstrated an association between female sex and the development of acquired idiopathic stiffness. This may be due to the fact that most studies are underpowered to detect sex-based differences. Pooling the data and subsequently performing analyses allows detection of these smaller differences.

Our review has a number of limitations. First, we were unable to stratify outcomes according to implant type, which may have contributed to the observed heterogeneity. To reduce and explore heterogeneity, we stratified analyses by the duration of follow-up, sex, age, and BMI. Second, publication bias is common in systematic reviews of observational studies. Third, it is not clear how the authors of each study managed the definition of postoperative stiffness as it relates to preoperative stiffness (for example, a 91° range of motion preoperatively compared with 88° postoperatively) and/or BMI.

We believe that the present study represents the most comprehensive assessment of acquired idiopathic stiffness following pTKA in the literature. It identified a mean prevalence of 4% after pTKA and showed female sex and a BMI ≥30 kg/m^2 to be risk factors. It also provides a working definition for *acquired idiopathic stiffness:* a total range of motion of <90° persisting for >12 weeks after pTKA in patients with osteoarthritis in the absence of other complicating factors. This definition will allow more uniform diagnosis, treatment, and study of the disease process. Further research at the genetic, histological, and biochemical levels is necessary to determine the molecular etiology in patients with this clinical diagnosis who have the pathologic entity arthrofibrosis and to identify potential therapeutic targets.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/F317). ■

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