Prognostic factors that predict failure of manipulation under anesthesia for the stiff total knee arthroplasty: A systematic review

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ABSTRACT

Purpose: Prognostic factors associated with Manipulation under anesthesia (MUA) failure remain unknown.

Methods: A systematic review of the literature was performed to identify studies that reported prognostic factors associated with MUA for postoperative stiffness.

Results: 7 studies analyzing prognostic factors associated with MUA outcomes were included. Several studies note pre-MUA ROM to be a significant prognostic factor affecting post-MUA ROM at final follow-up. Knees with < 70° of flexion pre-MUA had less final flexion arc than those with > 70°.

Conclusions: The strongest prognostic factor for decreased ROM after MUA is severe pre-MUA stiffness.

1. Introduction

Stiffness following total knee arthroplasty (TKA) remains a common challenge for healthcare professionals and patients.^{1,2} Stiffness is characterized by limited range of motion (ROM), frequently associated with pain and knee dysfunction. Multiple definitions of post-operative stiffness have been presented. A recent International Consensus publication categorized knee stiffness as mild, moderate or severe according to the range of flexion (90°–100°, 70°–89°, < 70°) or extension deficit (5°–10°, 11°–20°, > 20°).³

Multiple patient-specific factors are thought to contribute to the risk for post-operative stiffness. These include poor preoperative range of motion, body habitus, preoperative diagnosis (i.e. post-traumatic), socio-economic status, ethnicity, poor pain tolerance, and lack of compliance with rehabilitation protocols.^{4–10} In addition, technical errors related to the thickness of bony resections, flexion-extension gap mismatch, component sizing errors and component malrotation can all lead to stiffness after TKA. In a small subset of patients, arthrofibrosis may occur post-operatively. According to the International Consensus in 2016, post-operative arthrofibrosis is defined as a limited ROM in flexion and/or extension that is not attributable to an osseous or prosthetic block to movement, but due to soft-tissue fibrosis that was not present pre-operatively.³

The initial conservative treatment for knee stiffness after TKA

include intensive physiotherapy and continuous passive motion devices, although the efficacy of the latter has recently been challenged.¹¹ If knee ROM does not improve with these treatments, a manipulation under anesthesia (MUA) is commonly performed to address suspected early post-operative arthrofibrosis. Several studies have evaluated the risk factors associated with an increased risk of requiring MUA post TKA; however, there is limited available evidence on the patient specific variables associate with inferior ROM gains after MUA. We therefore performed a systematic review of the literature to specifically evaluate the variables that negatively impact ROM outcomes after MUA. The purpose of the study was to determine whether there are prognostic factors that affect patient outcomes after MUA. We performed a systematic review of the literature and examined the following variables: Pre-MUA ROM, Pre-TKA ROM, prior history of knee surgery, BMI, age, DM status, gender, and smoking.

2. Methods

2.1. Search criteria

The US National Library of Medicine (PubMed/MEDLINE), SCOPUS, and the Cochrane Database of Systematic Reviews were queried for publications from January 1980 to December 2016 utilizing keywords pertinent to manipulation under anesthesia, stiffness, and total knee

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arthroplasty.

2.2. Search terms

1. (“Total Knee Arthroplasty” [All Fields])
2. AND Stiffness
3. AND Manipulation under Anesthesia

Only abstracts that evaluated the clinical outcomes of primary MUA were reviewed.

2.3. Inclusion and exclusion criteria

The inclusion criteria were: 1) Studies describing human subjects of any age and gender. 2) Studies that include a population of at least ten patients who underwent MUA for post-TKA stiffness. 3) Studies that follow patients for a minimum of 10 days after total knee arthroplasty. 4) Studies that analyze at least one prognostic factor in relation to pre- and post- MUA outcome. The exclusion criteria were: 1) Review articles. 2) Case studies. 3) Studies examining concomitant treatments of stiffness. 4) Studies stratifying patients based on perioperative management (anesthesia protocol, limitation of blood loss, surgical technique, prosthesis type, etc.) in which allocation of patients who previously underwent manipulation under anesthesia is not specified. 5) Studies in which no subjects underwent manipulation under anesthesia. 6) Non-English language publications. For articles that met these criteria, the reference lists were screened for additional studies not captured using the initial search terms.

2.4. Data collection

Two authors independently conducted the described search. Both authors compiled a list of papers not excluded after application of the inclusion and exclusion criteria. Discrepancies between the list compiled by two authors were resolved by discussion. During initial review of the data, the following information was collected for each study: title, author, study design, number of patients, number of knees, BMI, gender, ROM changes after MUA, pre-TKA flexion, pre-MUA flexion, prior knee surgeries, smoking status, diabetes, and complications.

3. Results

3.1. Study selection

The search resulted in 727 abstracts that were examined to determine the efficacy of MUA for post-TKA stiffness (Fig. 1). Following elimination of duplicate articles, predetermined inclusion and exclusion criteria were applied. In total, 9 articles met the inclusion criteria. Two articles were excluded as they only reviewed revision TKA. Overall, 7 articles were included in this analysis (Table 1). Each study included analyzed at least one prognostic factor for ROM response post-MUA. Indications for MUA in each study are described in Table 2. Additional anesthesia protocols are described in Table 3. Consensus on which articles would be analyzed in the present study was achieved by discussion between the reviewers based on the predetermined inclusion and exclusion criteria described above.

3.2. Prognostic factors evaluated

3.2.1. Pre-TKA stiffness and MUA outcome

Four studies^{14–17} analyzed whether ROM before primary TKA predicts response to MUA. Among patients who required MUA after TKA, Keating et al. found that those with pre-TKA flexion less than 90° had significantly less absolute flexion gain following MUA ($p = 0.001$) at five-year follow-up than those with greater pre-TKA flexion requiring MUA.¹⁵ Rubenstein et al. found that, for knees requiring MUA after

TKA, those with less than 115° of flexion before TKA had less total flexion ($p = 0.004$) at long-term follow-up than those with greater than 115° of flexion before TKA.¹⁴ In contrast, Yeoh et al. used a cutoff of 90° to delineate MUA study groups and found that pre-TKA ROM did not significantly affect absolute flexion at one-year follow-up after MUA ($p = 0.06$).¹⁷ Similarly, Choi et al. found that pre-TKA ROM was not associated with achieving a satisfactory outcome ($> 90^\circ$ ROM) after MUA ($p = 0.42$).¹⁶ Based on the available evidence, it is unclear if pre-TKA absolute flexion has any impact on MUA outcome.

3.2.2. Pre-MUA stiffness and MUA outcome

Two studies^{12,13} analyzed the prognostic value of ROM prior to MUA. Ipach et al. found that knees with a pre-MUA flexion of less than 70° had significantly less absolute flexion ($p = 0.04$) at six-week follow-up than those with pre-MUA flexion of greater than 70°.¹³ Cates et al. found no difference in absolute flexion ($p = 0.35$) at one-year follow-up between knees with a pre-MUA flexion of less than 90° compared to those with greater than 90°.¹² Ipach et al. reported a significantly greater gain in total flexion if pre-MUA flexion was less than 70° compared to those with pre-MUA flexion of greater than 70°.¹³ Similarly, Cates et al. reported that pre-MUA flexion of less than 90° had a significantly greater gain in total flexion compared to those with flexion of greater than 90°.¹² Combining the result of these two studies suggests that patients with severe post-operative stiffness (ROM $< 70^\circ$) achieve significant gains in ROM gains but fail to achieve similar absolute flexion as patients with mild or moderate stiffness (ROM 70–90°) undergoing MUA.

3.2.3. BMI and risk of MUA failure

Association between BMI and development of post-operative stiffness was evaluated in three studies.^{12,13,16} Ipach et al. found no difference in final ROM when stratifying post-MUA patients into 18.5–25, 25–30, and 30 + BMI groups ($p = 0.33$).¹³ Choi et al. found that BMI did not affect the likelihood of achieving final ROM of greater than or less than 90° ($p = 0.58$).¹⁶ Cates et al. found no difference in flexion or extension gains when comparing a post-MUA group with a BMI less than 30 to a group with a BMI greater than 30.¹² In general, BMI is not shown to be a risk factor for worse outcomes after MUA.

3.2.4. Age

Association between age and stiffness post-TKA was evaluated in three studies.^{12,15,16} Choi et al. found that age, using a cutoff of 65 years to stratify groups, was not significantly different between patients achieving post-MUA ROM greater than 90 and patients failing to achieve post-MUA ROM greater than 90 [$p = 0.87$; 16]. Cates et al. found no difference in MUA outcome for those less than or greater than 60 years old.¹² However, Keating et al. observed that patients requiring MUA (average age of 65) were significantly younger than patients not requiring MUA (average age of 71; $p < 0.0001$).¹⁵ Overall, age is not associated with success or failure after MUA.

3.2.5. Gender

Gender was analyzed in two studies.^{12,16} Choi et al. found no difference in gender prevalence when analyzing a cohort with greater than 90° of ROM at final follow-up compared to a cohort with less than 90° of ROM at final follow-up [$p = 0.8$; 16]. Cates et al. found no significant difference between men and women in flexion ($p = 0.2$) or extension gain ($p = 0.4$) at one year following MUA.¹² Based on this evidence it does not appear that gender is a risk factor for poor outcomes after MUA.

3.2.6. Diabetes mellitus

Current literature regarding the effect of diabetes mellitus on MUA outcome is inconclusive.^{16,18} While Bawa et al. reported that subjects with diabetes achieve less ROM after MUA than non-diabetics,¹⁸ this may not be functionally significant as another study found no

Fig. 1. Systematic review flow diagram. Flow diagram describing the systematic review of literature on prognostic factors for manipulation under anesthesia after total knee arthroplasty.

Table 1
Included studies.

Study ID	Year Published	Study Type	CEBM Evidence Level
Choi et al.	2014	Retrospective	3
Bawa et al.	2012	Retrospective	3
Yeoh et al.	2011	Retrospective	3
Ipach et al.	2011	Retrospective	3
Rubinstein et al.	2010	Retrospective	3
Cates et al.	2009	Retrospective	3
Keating et al.	2007	Retrospective	3

association between diabetic status and achieving a post-MUA ROM greater than 90°. ¹⁶ Based on these conflicting results, diabetes should not be considered a good predictor of MUA success.

3.2.7. Smoking

Only Cates et al. analyzed the impact of smoking, finding no difference in flexion or extension gains between smokers and non-smokers ($p > 0.05$). ¹²

3.2.8. Prior procedures

Two studies analyzed the association of prior procedures with MUA efficacy. ^{12,13} Ipach et al. determined that patients with at least one prior knee surgery prior to MUA had less absolute gain in flexion post-MUA than those who had none. ($p = 0.04$). ¹³ Cates et al. found no

Table 2

Indications for MUA.

Choi et al.	Failure to achieve flexion of $\geq 90^\circ$ at 4–8 weeks post-TKA
Bawa et al.	Failure to achieve flexion of $\geq 90^\circ$ within 6 weeks of TKA
Yeoh et al.	Failure to achieve flexion of $\geq 80^\circ$ despite 3 weeks of physiotherapy
Ipach et al.	Failure to achieve flexion of $\geq 90^\circ$ within 2 weeks
Rubenstein et al.	Failure to achieve flexion of $\geq 90^\circ$ at 4–6 weeks post-operatively and/or failure to progress with gaining knee motion over the initial 2–3-month post-operative period
Cates et al.	Failure to achieve flexion of $\geq 100^\circ$ by 4–8 weeks post-operatively or flexion of $\geq 110^\circ$ with functional restrictions later in recovery
Keating et al.	Failure to achieve flexion of $\geq 90^\circ$ by 2 months post-operatively. If patient declined initial MUA procedure, they were offered supervised physical therapy if they had not entered one previously. If knee flexion did not increase after one month in this program, patients were again encouraged to undergo MUA.

significant difference in final gain in flexion or extension when comparing a cohort with at least one prior surgery to another cohort with no prior surgeries ($p > 0.05$).¹² Currently, the evidence is mixed as to whether prior knee surgery impacts ROM gains after MUA. Additional studies are needed that control for the type of knee surgery and number of surgeries when evaluating the impact of prior surgery on MUA outcomes.

4. Discussion

MUA is generally perceived as an effective and low-risk treatment option for knee stiffness after TKA. While many studies support this notion, it is important to identify patients who are most likely to benefit from MUA and those at highest risk for failure. Identifying these patients prior to MUA may help guide patient expectations and encourage more intense adjuvant therapy for these higher risk groups.

One common area of study is the impact of pre-TKA and pre-MUA stiffness on MUA outcomes. Patients with more severe flexion limitation pre-MUA experience a greater total gain in ROM from the procedure.^{12,13} However, patients with severe stiffness ($< 70^\circ$) have the most restricted final ROM after MUA.¹³ In practice, those with pre-MUA flexion of less than 70° should still undergo MUA as patients will achieve significant ROM gains. Patients with pre-MUA ROM $< 70^\circ$ may have a more longstanding pathological etiology for knee stiffness that may not respond as well to mechanical disruption of knee fibrosis.¹⁹ The literature does support performing an MUA on patients with severe stiffness, but patients should be educated on inferior absolute flexion.

Studies have also evaluated whether stiffness before primary TKA predicts response to MUA. The literature is inconclusive with some studies^{14,15} showing that more severe pre-TKA flexion deficits are associated with decreased flexion after MUA and others finding no association.^{16,17} Based on this data, pre-TKA stiffness is not generally a useful predictor of response to MUA. Intuitively, a knee with pre-TKA stiffness has a long-standing range of motion loss that is not related to early post-operative adhesions. Patient with pre-TKA stiffness that is related more to soft tissue contracture rather than osseous mechanical impingement would seemingly have inferior outcomes with MUA. More research is needed to better categorize patients with pre-TKA stiffness as mechanical or potentially arthrofibrotic prior to TKA and to better differentiate the severely stiff knee ($< 70^\circ$) vs moderate stiffness

(70° – 90°). Arthrofibrosis can be established prior to TKA in the native knee as Freeman et al. found increased fibrotic tissue in the posterior capsule in knees with stiffness undergoing TKA.²⁰

Patients with multiple prior knee surgeries appear to have worse outcomes after MUA. Having an additional prior knee surgery was associated with decreased MUA efficacy.¹³ However, another study found no association when stratifying patients between no prior surgeries and at least one prior knee procedure.¹² While additional trauma to the knee caused by further surgical interventions would realistically result in increased risk of arthrofibrosis, the current literature does not support nor refute this.

Of studies evaluating BMI,^{12,13,16} age,^{12,16} gender,^{12,16} diabetes mellitus and smoking status,¹² there has been no association with MUA outcomes. In general, BMI may be a poor marker as BMI is often a poor surrogate marker for circumference of the limb and soft tissue impingement; which act as the real drivers of reduced ROM in these patients. Of note, other studies in the literature found that patients who undergo MUA tend to be significantly younger than those that do not.^{15,21} At this time, BMI, age, gender, and smoking status should not be used to determine if a patient would benefit from MUA and do not appear to negatively impact ROM outcomes after MUA.

There were several limitations to this study. We were limited by the quality of the original studies, the variability in inclusion criteria and methods for reporting the evaluated variables, and the number of patients analyzed. The methodology of the present study did not allow for the identification of unpublished literature on MUA and thus is limited by potential publication bias. Lastly, we did not separate those with under 70° of flexion from those with 70° – 90° of flexion for purposes of comparison in final outcome to those with over 90° of flexion. This may result in a potential type 2 error, as those with $< 70^\circ$ and 70° – 90° of flexion may have been combined into one category. Despite these limitations, this study was able evaluate prognostic factors from the largest patient sample to date, which should help to guide future research.

Based on this literature review, the strongest prognostic factor for decreased ROM after MUA is severe pre-MUA stiffness. However, even among this challenging group of patients, a substantial gain in function is still expected with MUA. The effect of other prognostic factors is likely small and should not preclude patients who would otherwise benefit from MUA from undergoing the procedure. More research is

Table 3

Anesthesia and adjuvant therapies for MUA.

Study	Anesthesia Protocol	Adjunct therapies to MUA
Choi et al. (2014)	General anesthesia (n = 120), Epidural (n = 18), Spinal (n = 5)	Inpatient: CPM with local ice pack. Outpatient: Physiotherapy only
Bawa et al. (2012)	General or regional anesthesia with complete muscle relaxation	Inpatient and outpatient physiotherapy
Yeoh et al. (2011)	General anesthesia	Inpatient and outpatient physiotherapy, CPM used at surgeon's discretion
Ipach et al. (2011)	General Anesthesia, 3- in-1 Nerve Block Until post-operative day #3	CPM, physiotherapy and cryotherapy
Rubinstein et al. (2010)	General anesthesia	Six days of methylprednisolone
Cates et al. (2009)	Epidural or general anesthesia with local marcaine and epinephrine	Physiotherapy
Keating et al. (2007)	General anesthesia, with 24% of patients also receiving an epidural catheter for 24 h	Immediate active and active assisted ROM, cryotherapy with ice packs and outpatient physiotherapy

necessary to elucidate prognostic factors that affect MUA results and how postoperative decision-making can be guided by these factors and allow for better guidance of patient expectations following MUA.

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Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Appendix A. Supplementary data

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