

# Manipulation under anesthesia for stiffness after total knee replacement: A systematic review

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## ABSTRACT

**Introduction:** Stiffness following total knee replacement (TKR) is a debilitating complication. Manipulation under anesthesia (MUA), arthroscopy, and open arthrolysis are used to treat the stiffness. **Objectives:** The aim of the review was to answer the following questions. What is the gain in range of motion (ROM) after MUA for stiffness following TKR? Is the gain in ROM after MUA for stiffness following TKR retained at the last follow-up? What is the gender distribution amongst the patients presenting for MUA following TKR? What is the mean age of the patients presenting for MUA following TKR? What is the influence of timing of MUA following TKR on the ROM? The review was aimed towards establishing the current available evidence regarding MUA for stiffness. **Materials and Methods:** A systematic review of the current available literature was performed and the relevant studies were critically appraised. **Results:** Nine studies were identified to be relevant to the review (1-Level 2; 2-Level 3; 6-Level 4). It was found that there was a gain in the ROM after MUA and it was retained at the final follow-up. The patients presenting for MUA were younger and were predominantly females. Early MUA was found to be more effective, although late MUA was also beneficial. **Conclusions:** With limited and low quality of evidence, it is not possible to draw any conclusions.

**Keywords:** Manipulation, stiffness, total knee replacement

## Introduction

Total knee replacement (TKR) gives satisfactory results in most patients with advanced degenerative changes in the knee.<sup>[1]</sup> The most common indications for this surgical procedure are osteoarthritis (OA) and rheumatoid arthritis (RA).<sup>[2]</sup> Postoperative knee stiffness is a known and debilitating complication.<sup>[3]</sup> The definition of stiffness has been changing with time. This is because of the increasing expectations of the patients and the

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physicians.<sup>[4]</sup> It is defined as flexion contracture equal or greater than 10 or the arc of motion less than 95°.<sup>[5]</sup>

Early treatment of resistant cases of stiffness requires manipulation under anesthesia (MAU).<sup>[6,7]</sup> The aim of this review was to integrate the information available from the studies related to this topic. To this end, the relevant studies were evaluated with a view to know the gain in ROM after MUA. Also, an effort was made to know if the gain in ROM is retained or not. The complications following the MUA were evaluated as well.

In recent years, gender specific implants have been introduced and this has led to the debate if these implants really had any potential benefits.<sup>[8]</sup> It was noted that women had more pain than men at 1 and 2 year follow-up.<sup>[9]</sup> Also, it was demonstrated that women had better outcome scores and had a lower rate of revision surgery as compared to the men.<sup>[10]</sup> It must be noted that anthropometric gender differences have been reported in the knee.<sup>[11-13]</sup> The anthropometric differences have been cited as the precise reason for gender specific implants. However, lack of enough evidence to show the difference in the outcome raises doubts about their need.<sup>[14]</sup> The intention of this review was to gain information about the gender distribution of the patients presenting for MUA.

It has been suggested that the patients in the older age group did better as far as outcomes of TKR are concerned.<sup>[15,16]</sup> Also, it is reported that one of the risk factor for poor outcome in primary

and revision TKR is younger age.<sup>[8]</sup> Others have suggested no relation between age and outcomes of TKR.<sup>[17]</sup> One of the aims of the review would be to identify the mean age for patients presenting with stiffness. Knowing the gender preponderance and the mean age of patients with stiffness will thus suggest patient characteristics with worse outcomes. Also, it will help in identifying the patients at risk for stiffness after TKR. It has been suggested that this data will be useful for policy makers, epidemiologists, and many surgeons.<sup>[8]</sup>

The specific objectives for conducting the systematic review were as follows:

- To assess the gain in the ROM after MUA for stiffness following a TKR
- To verify if the gain in the ROM after MUA was retained or not
- To know the ratio of male and female amongst the patients presenting for MUA
- To assess the mean age of the patients presenting for MUA following TKR
- To assess the influence of the timing of MUA on increase in the ROM.

## Materials and Methods

The search was structured using the patient, intervention, comparison, outcome (PICO) format.<sup>[18]</sup>

### Inclusion and exclusion criteria

#### Inclusion criteria

Adult participants (over 18 years) with stiffness of the knee after the TKR who underwent MUA were included in the study. Patients who had primary MUA were included in the study.

#### Exclusion criteria

Participants with revision surgery, infected TKR, MUA after primary MUA, arthrolysis before or after the MUA, and a follow-up of less than 1 year after MUA were excluded from the study.

### Search strategy

The searches were carried out between 14<sup>th</sup> November 2011 and 30<sup>th</sup> November 2011. Databases such as MEDLINE (1950 to 30<sup>th</sup> November, 2011), EMBASE (1980 to 30<sup>th</sup> November, 2011) and Cumulative Index to Nursing and Allied Health (CINAHL) (1981 to 30<sup>th</sup> November, 2011) were searched via National Health Service (NHS) Evidence ([www.library.nhs.uk](http://www.library.nhs.uk)).

Keywords such as ‘arthroplasty’, ‘range of motion’, ‘manipulation’, ‘anesthesia’, and relevant synonyms were used for the search. Boolean operators such as AND and OR were used to combine the terms. The \* truncation operator was used to retrieve variations of terms (e.g., Stiff would retrieve stiff, stiffness, etc.). Thesaurus terms relevant to each database were also utilized. Studies were limited to humans and adults over the age of 18 years.

The titles and the abstracts of these articles were viewed electronically with a view to select the articles for the search. If the title or the abstract was not clear, the article was retrieved and reviewed. Relevant and applicable articles were selected from the identified titles and abstracts and if necessary from the full text.

The Cochrane Library was used to highlight any Cochrane Reviews (Cochrane Database for Systematic Reviews) and any non-Cochrane reviews were identified through the Database of Abstracts and Reviews. The Cochrane library did not reveal any relevant review. A search through the Database of Abstracts and Reviews showed one review. In addition, the Cochrane Central Register of Controlled Trials (CENTRAL) was searched for relevant trials.

Also, additional databases like Tripdatabase ([www.tripdatabase.com/](http://www.tripdatabase.com/)) and Aggressive Research Intelligence Facility (ARIF) Database ([www.arif.bham.ac.uk/](http://www.arif.bham.ac.uk/)) were searched.

### Other sources

Reference lists of included studies were also reviewed for other appropriate publications. Citation searching using studies identified as relevant to the review was undertaken using the Science Citation Index ([www.isinet.com/](http://www.isinet.com/)).

Dissertations and theses were searched using the ProQuest Dissertations and Theses Database website-[www.proquest.co.uk/en-UK/catalogs/databases/detail/pqdt.shtml](http://www.proquest.co.uk/en-UK/catalogs/databases/detail/pqdt.shtml) (Higgins and Green, 2011).<sup>[18]</sup>

### Research registers

To identify ongoing and unpublished trials, Current Controlled Trials were searched.

### Grey literature

Databases like OpenSIGLE (System for Information on Grey Literature) launched by Institute for Scientific and Technical Information (INIST), the National Technical Information Service ([www.ntis.gov/search](http://www.ntis.gov/search)) and British National Bibliography for Report Literature ([www.bl.uk/](http://www.bl.uk/)) were searched to identify additional grey literature.<sup>[18]</sup>

### Search restrictions

The search was limited to humans only and restricted to patients over 18 years of age.

## Results

Nine studies were selected for the systematic review. Six studies were not included in the review. Five articles were rejected because the patients in these studies had a follow-up of less than 1 year. One of the studies was regarding stiffness unresponsive to standard methods of MUA, that is, refractory to primary MUA and hence was not included in the review.

Each article was read carefully. A data extraction sheet was formulated. It included prevalence of stiffness, diagnosis of the patients presenting for manipulation, mean age, and gender distribution. It included details regarding the intervention like indications; description of the MUA, anesthesia used, and any other protocols used during or after the MUA. The data extraction sheet also comprised of questions to know the degrees of ROM before, during, and after MUA. Also, the length of follow-up and the timing of MUA were looked at. This data is presented in the form of charts.

The level of evidence of the nine studies was decided using the guidance provided by Centre for Evidence Based Medicine, Oxford, United Kingdom (<http://www.cebm.net/index.aspx?o=1025>). One study<sup>[19]</sup> was a level 2 study. Two studies<sup>[6,20]</sup> were designated as level 3 case control studies. The remaining six studies were level 4 retrospective case series. This was followed by quality appraisal of the studies.

The prevalence of patients presenting for MUA varies from 1.8<sup>[20]</sup> to 23%.<sup>[21]</sup> The predominant diagnosis in the patients presenting for MUA was OA.

In all the studies, it was found that the patients presenting for MUA following a TKR were predominantly females. The mean age of patients in the nine studies was between 53 and 71 years.

The technique of MUA was similar across all the studies. Some of the studies used an additional intra-articular injection of steroid/epinephrine/local anesthetic or a combination during the MUA.<sup>[22-24]</sup> Post manipulation different protocols like ice, continuous passive motion (CPM), physiotherapy (PT) steroid tablets, pain control measures, etc., were used by different authors. The procedure was predominantly done under general anesthesia (GA) with an additional muscle relaxant in some studies.

In all the studies considered for the review, there was a definite gain in the ROM. This was variable from 26<sup>[22]</sup> to 47°.<sup>[5]</sup>

The post manipulation ROM was not reported in three studies.<sup>[22,23,25]</sup> The range of motion (ROM) gained at MUA was retained at final follow-up in four studies.<sup>[5,6,19,24]</sup> Patients in three studies gained motion.<sup>[6,19,24]</sup> In three studies, the gain in ROM was lost at final follow-up.<sup>[20,21,24]</sup> Keating *et al.*, (2007)<sup>[20]</sup> have noted a mean loss of 6° of flexion. However, there was no clarity if this loss of ROM was statistically significant or not. The population mix (predominantly rheumatoid) for the TKR in the study by Fox and Poss (1981)<sup>[21]</sup> was not a representative of the general population.

The results of these studies suggest a relationship between the timing of MUA and the gain in ROM. Five studies have indicated that early manipulation is more effective than late manipulation.<sup>[5,6,19,22,23]</sup> It must be noted that they the late group patients also benefitted from the MUA.

Six studies have not reported any complications.<sup>[5,6,19,22-24]</sup> In their

study, Daluga *et al.*,<sup>[6]</sup> found that the knees that underwent MUA were significantly more predisposed to heterotopic ossification. They further, found that the overall flexion was better in the patients with heterotopic ossification than the rest of the patients who had MUA. Fox and Poss (1981)<sup>[21]</sup> in their study had five patients with complications following MUA (three hemarthroses, one wound dehiscence, one fatal pulmonary embolism). Keating *et al.*, (2007)<sup>[20]</sup> found one complication in the form of a supracondylar fracture in their study. One patient, in the study by Rubinstein and DeHaan (2010),<sup>[25]</sup> had a superficial wound dehiscence.

### Fox and Poss, 1981<sup>[21]</sup>

This retrospective case series reviewed the results of 81 patients who had MUA for stiffness following TKR.

The primary objective of the study is stated clearly. The study protocol is well-defined. There is no mention of any inclusion/exclusion criteria for this study. It is unclear if the patients were recruited consecutively. There was no effort at blinding the outcome assessors. However, it is felt that another outcome measure (in addition to ROM) in the form of a knee score which focuses on the function and pain would have been useful. Also, it is not clear if the outcome was measured prospectively/retrospectively. It is not clear if the participants had signed an informed consent or not. Also, it is not mentioned that any ethical committee had approved the study. It is noted that the participants enrolled for the TKR were predominantly suffering from RA. Thus they do not represent the population, in general.

From the strength point of view, it is a weak design. Because of the retrospective nature of the study there may have been a selection bias. It can only generate hypothesis and clinical questions. However, it is not possible to arrive at any conclusion.

### Scranton, 2001<sup>[23]</sup>

This is an observational study of 26 patients who had stiffness following TKR performed in a single center. It was treated using MUA, arthroscopy, and open arthrolysis.

Methodology: The recruitment criterion for the study is well-defined. The techniques of manipulation, arthroscopic debridement and modified open release are well described. An informed consent was taken from the participants before exposing them to any of the procedures. All the patients were followed-up for at least 1 year after the procedure. However, finally, only 19 patients were included in the study dealing with MUA. They were further divided into two groups depending on the timing of the manipulation. In essence, all these have adversely affected the power of the study. This design is susceptible to selection bias.

There is a lack of clarity regarding the objectives, inclusion and exclusion criteria, outcome measures, and the assessors. Taking into consideration the biases involved, the power of the study and thus the applicability of the study, it is not possible to draw any conclusion.

### **Sharma et al., 2008<sup>[24]</sup>**

This is an observational study where two groups of patients who had TKR were exposed to different protocols for pain management and the results were compared. In addition, the patients in these groups who developed stiffness were exposed to different protocols during the MUA.

It is a well-designed and retrospective study. There is an attempt made by the authors to limit bias by reporting in detail about the intervention and the post intervention protocols. Patients were enrolled consecutively and there was a long follow-up without losing any patients to follow up. The outcome measures included validated outcome measure like Knee Society Score. To be noted that by its inherent nature a retrospective study is exposed to a selection bias. There is no mention of blinding of the assessors. Without a control group, it is not possible to reach to any conclusion from this study. In addition, as the power of the second component of the study is low, it is not possible to draw any conclusion.

### **Rubinstein and Dehaan, 2010<sup>[25]</sup>**

This retrospective review of 37 patients with stiff knees following TKR was conducted to establish if there was any association between pre-TKR and post-MUA ROM.

**Methodology:** It is a retrospective study. The participants seemed to represent the population. All the participants were recruited in the study at the same time. The patients were selected consecutively. The outcome was measured prospectively. The protocol of the study was defined elaborately. The intervention of manipulation has been described adequately. It was carried out by an experienced surgeon and was done in appropriate surroundings. The follow-up was long enough to detect important effects. None of the patients were lost to follow-up.

The only outcome measure utilized for the study was the ROM. An additional outcome measure which takes into consideration pain and function of the knee would have been appropriate. It has been noted that the chart (details) of one patient were not available. This increases the chances of an attrition bias in the study.

The design of the study is reasonable. It is an observational study. It is a retrospective case series. The authors would have to depend on the accuracy and availability of medical records. As the authors have selected the cases themselves, it introduces an obvious selection bias. In addition, in this experiment, there is no use of control subjects. Inability to blind the participants and the clinicians introduces performance and measurement biases in the study. Given the number of biases that the study is prone to, the conclusions drawn from the study cannot be generalized. The conclusions drawn from the study should be used to generate a hypothesis which needs to be tested by more robust prospective study designs.

### **Cates and Schmidt, 2009<sup>[22]</sup>**

This retrospective case series reviewed the case records of 37 patients to establish any predictors of manipulation outcomes.

It is retrospective observational study. The sample participants represent the patient population. The inclusion and exclusion criteria were used to include 37 participants out of a potential 46. The selection of the patients was consecutive and all the subjects entered the study at a similar point as far as their ROM was concerned. The procedure of manipulation is well described in detail. It was carried out by the surgeon with an assistant in safe surroundings. The participants were followed-up for a year which is long enough to detect important effects of the intervention. None of the participants were lost to follow-up. None of the authors had any financial gains to be achieved from the study.

As the participants were selected by the authors, there is an element of selection bias associated with the study. ROM was the only clinical outcome used for the study. As there is no blinding of the outcome measure assessors, the likelihood of introducing a performance bias becomes high. To be noted that the outcome data was collected retrospectively. Nine patients were excluded from the study as the data on their ROM was incomplete. This increases the likelihood of introducing attrition bias.

With this study, it is difficult to establish cause and effect. At best, the conclusions drawn from the study can be used to lay down a hypothesis.

### **Yercan et al., 2006<sup>[5]</sup>**

This is an observational study where the authors reviewed the results of 67 patients who had MUA for stiffness over a period of 18 years in a single center.

It is a retrospective observational study. It is not clarified where the data was collected from. However, it can be safely implied that the data was retrieved from the case records. The participants seem to represent the patient population. The selection of the patients was consecutive and they were selected for manipulation at the same time. The outcome measures used for the study included ROM and Knee Society Pain Score. Inclusion of an outcome measure to assess the function of the knee would have been more helpful. It has been clarified that the authors did not benefit in any manner from the study.

The design of the study is weak. The aims and objectives are not clearly mentioned. Although the protocol following the MUA is described, there is no actual description of the intervention (MUA). It is not clear how the details of the participants were collected. There are no inclusion or exclusion criteria for the study. The data collection for the outcomes is retrospective. It is not mentioned if the outcome assessors were blinded or not. It must be noted that six patients with stiff knees were not included in the study as three died before the time of review and three were lost to follow-up.

It is a poorly designed study. There are no clear objectives. The inclusion and exclusion criteria are absent. The outcomes are not measured prospectively. By its inherent nature, this retrospective study is prone to a selection bias. In addition, dependence on

the medical records for the accuracy of the results increases the bias. No measures, whatsoever, have been taken to minimize the bias. There is no mention of blinding of the outcome assessors. This enhances the possibility of introducing a performance/measurement bias in the study. As three patients were lost to follow-up and three others died before the review could be completed, the chances of an attrition bias affecting the study comes into play. This, in turn, will have an effect on the validity of the study. It is not possible to draw any conclusions from the study.

### **Keating *et al.*, 2007<sup>[20]</sup>**

This observational study reviewed the results of 90 patients who underwent MUA for stiffness. The aim of the study was to analyze the results of the MUA and to identify any predictors of the need for MUA.

There is a precise definition of the cases. The cases were recruited taking into account the ROM that they achieved at 2 months postoperatively. They were incident cases and seemed to represent a defined population. A sufficient number of cases were selected with a relevant time frame. The selection of the controls is not clearly defined. The outcome measures used by the authors are adequate.

The authors have failed to mention if this was a prospective or a retrospective study. It is not clear if the data was collected from medical records or not. The number of participants allocated to the controls is not clear. It is unclear if the controls were selected randomly or by a matching procedure. The outcome assessors were not blinded. It is not mentioned if any confounding factors were accounted for.

This is a case control study. It has weaknesses in study design and analysis. There is no clarity regarding collection of data, selection of controls, number of controls, confounding factors, or the blinding of assessors. These factors increase the chances of selection and information biases in the study. There is no mention if any measures were taken into account for any confounding factors. There is no discussion about the odds ratio or confidence interval. It is presumed that if anything regarding the design or analysis is not reported, it was not considered by the authors. Because of these obvious flaws, the validity of the study becomes questionable and it is difficult to draw any conclusion.

### **Daluga *et al.*, 1991<sup>[6]</sup>**

The aim of this case control study was to identify the prognostic indicators for MUA. To this end, the data of 60 patients who presented for MUA for stiffness was compared with the data of 28 patients assigned to the control group.

It is clearly mentioned that it is a retrospective study. The patients who developed stiffness after TKR were included as cases. A total of 94 cases were selected for the study. They were precisely defined. They were representatives of the defined population. They were incident cases. The time frame of the study is relevant

to the development of stiffness after TKR. The controls were selected from the same population who had a TKR and did not develop stiffness. They were not matched for any characteristics. The details about the cases and controls were obtained from the medical records. The outcome measures were assessed objectively from the medical notes, radiographs, and measurements of ROM and Hospital for Special Surgery (HSS) knee scoring system. The outcome measures used were comprehensive. These measures were similar for the cases and controls.

The authors have not made any effort to limit the confounding in the design by matching the controls with the cases. As the details of the patients were obtained from the case notes, the accuracy of these details relies on the exactness of the medical records. Thus, there is an increased chance of introducing bias in the study. It is not clear if the outcome measure assessors were blinded or not which in turn can introduce bias. Regression analysis was used for the analysis in an attempt to limit confounding.

It is well-designed retrospective study. It had definite objectives. The study protocol was strictly adhered to. The selection of cases and controls was done appropriately. A comprehensive list of outcome measures was assessed. Overall, the study has a reasonable validity. It can be considered to be reliable. Although, it is difficult to ascertain a cause and effect from this study, it does help to generate a hypothesis. This needs to be tested by using a robust prospective study.

### **Esler *et al.*, 1999<sup>[19]</sup>**

This prospective study reviewed the results of 47 patients who had MUA for stiffness and compared them with the results of patients with stiffness who declined MUA.

**Methodology:** It is a prospective study. All the participants who entered the study were accounted for at the end of the study. Participants in both the groups were followed-up in a similar way for 2 years. The participants were allocated to two groups. There was no randomization in the allocation of the patients to each group. The patients who did not achieve 80° of flexion after intensive physiotherapy were recruited for the study. Of these, the participants who were ready to undergo MUA were allocated to one group. The rest of the participants who refused the intervention were allocated to the other group. ROM is the outcome measure used for the study. It is felt that an outcome measure taking into account the pain and function components in addition to the ROM would have been more appropriate. The outcome measure assessors have not been mentioned clearly. There was no effort towards blinding the assessors or the participants. There is no power calculation. There is no mention if the patients were consented for the procedure or not. There is no involvement of any ethical committee.

The allocation of the patients to the two groups is not satisfactory. The authors have themselves admitted that it is difficult to classify the second group as a 'control' group. Their refusal for MUA might indicate a low level of motivation. In any case, this

kind of allocation would increase the chances of introducing a selection bias. As there was no blinding of the outcome measure assessors, the chances of introducing a detection bias in the study are increased. Also, inclusion of more outcome measures would have helped. In effect, the internal validity of the study is affected adversely. It is difficult to arrive at any conclusion from the study. At best, it is possible to generate a hypothesis which needs to be verified by more robust prospective study.

## Discussion

A systematic search of the literature revealed nine articles.

The reporting of the findings of different studies had its drawbacks. Scranton (2001) did not mention about the diagnosis, gender ratio, mean pre MUA ROM, post MUA ROM or the ROM at final follow-up. Yercan *et al.*, (2006) did not inform the reader about the intervention itself. Two other studies did not report about the ROM after the MUA.<sup>[22,25]</sup> Most of the studies had similar technique for MUA. However, the intra and post MUA protocols were not the same. Some of the studies used an intra-articular injection in addition to the MUA.<sup>[22-24]</sup> As a part of the post MUA protocol, PT was common to almost all the studies. The other options used in different studies were CPM, cryotherapy, epidural injections, and steroid tablets. The reporting of the complications was poor. There were six studies in which the complications were not reported.<sup>[5,6,19,22-24]</sup>

The reporting of outcome measures was variable. Only two studies used a scoring system to assess the pain and function of the patients.<sup>[6,20]</sup> Yercan *et al.*, (2006) used pain score of the Knee Society Score. In all the studies, the motion in the knee was measured. However, it was reported as flexion in some studies.<sup>[6,19,20,21]</sup> In others, it was reported as ROM.<sup>[5,22,23,25]</sup>

Six studies have looked into the effect of timing of MUA on the ROM by dividing patients into early and late groups.<sup>[5,6,19,22,23]</sup> However, cut-off timing between these groups is not the same for the six studies.

As the checklists did not have a scoring system and our exclusion criteria did not have a quality check, poor quality studies may have been included in the review.

From the systematic review, the following hypotheses are made.

- There is a gain in the ROM after MUA for stiffness following TKR
- The gain in ROM for stiffness following MUA is retained at the final follow-up
- The patients presenting for MUA were predominantly females
- The need for manipulation after TKR was associated with a younger age
- The predominant diagnosis of patients presenting for MUA is OA

- If the MUA for stiffness following TKR is performed early, it is more effective.

Late MUA is still beneficial.

As the data regarding the complications is sparsely reported, it is difficult to know the rate of the complications.

## Conclusion

It must be noted that this systematic review is based on literature which mainly comprises of level 4 studies and a few level 3 and level 2 studies. No direct conclusions or recommendations for treatment can be made. At best, this can lead to generating hypotheses. Further randomized control trials are needed to validate these hypotheses.

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