



## Original article

# Younger age is associated with increased odds of manipulation under anesthesia for joint stiffness after total knee arthroplasty



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## ABSTRACT

**Introduction:** Limited range of motion (ROM) after total knee replacement (TKR) is associated with low function and might require manipulation under anaesthesia (MUA). In order to identify factors associated with a limited ROM we investigated predictors for MUA. We hypothesized that older age was associated with higher MUA due to limited ROM post TKR.

**Methods:** In a case control study we investigated all patients undergoing primary TKR at a University Hospital in Sweden between 2007–2012. We registered background factors and compared those between the group who underwent MUA and those who did not. Odds ratios (OR) were calculated in a univariate analysis and an adjusted regression analysis.

**Results:** Of the total of 669 TKRs performed, 31 patients who had undergone MUA were identified. The prevalence of MUA was 4.6%. The mean increase in ROM after MUA was 27 degrees at final minimum one-year follow-up. After controlling for confounders, patients with good health and young age had increased OR for MUA. OR decreased 0.93 (CI 0.93–0.97) per increased age year in the multiple regression analysis. Diabetes mellitus, BMI and sex did not have a significant effect on the odds ratio for MUA.

**Discussion:** Young patients undergoing TKR has earlier been identified as a group with a higher grade of dissatisfaction and complications. We found an association between young age and MUA after TKR indicating an additional, rather unknown complication for this group of patients. The background and reasons for this has to be further investigated.

**Level of evidence:** II, cohort study/case control study (case control is level III).

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## 1. Introduction

One uncommon complication to total knee replacement (TKR) is a postoperative unexpected limited range of motion (ROM). The reported prevalence (between 1.3% to 5.3%) is highly variable [1,2]. The inability to achieve a functional ROM impairs activities of daily living and thereby decreases general quality of life [3]. While the majority of those with a limited postoperative ROM evolve favourably some require manipulation under anaesthesia (MUA). The indication and timing for MUA is still debated but in general the commonly accepted indication is a ROM less than 90 degrees

of flexion at 6 weeks [4–7]. Some factors such as sex, age, pre-operative ROM, obesity, diabetes mellitus (DM) and comorbidities have earlier been associated with post TKR stiffness [2,8–12]. However, earlier reports have small sample size or do not account for confounding variables [13].

The aim of the present study was to identify possible predictors for MUA after TKR. Further we report the results of MUA in terms of improved ROM and the effect of early versus late MUA.

## 2. Materials and methods

### 2.1. Study design

We performed a case control study using ICD-10 codes to identify all patients that underwent TKR during 2007–2012 at a University Hospital in Stockholm, Sweden. Patients that underwent

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TKR and MUA (study group) were compared to patients without MUA (control group). All patients were operated by five senior consultants and received cemented total knee arthroplasty components (PFC Sigma, de Puy, New Jersey, USA or Thriathlon, Stryker Orthopedics, New Jersey, USA). About ninety percent were operated with cruciate retaining (CR) components without resurfacing the patella.

## 2.2. Eligibility criteria and data

Excluded were patients who underwent MUA secondary to infection. In cases when the patient received bilateral TKR only the first TKR was included for analyses. In order to avoid repeated measurements in within-subjects (dependent observations) and bias we decided to include only one measurement per subject, the first knee operated.

## 2.3. Variables

Our outcome of interest was patients undergoing MUA due to limited ROM, defined as flexion less than 90 degrees and 10 degrees of extension deficit at a minimum of 6 weeks after a TKR. Identified known risk factors for joint stiffness and subsequent MUA were used as covariates and included sex, age, body mass index (BMI), diabetes mellitus (DM) and general health measured by ASA [14] (Table 1). We then assessed the statistical difference in the rate of exposure to defined risk factors between the groups and used the outcome measure as odds ratio. Age was calculated from the Swedish national identification number and year at the time of the index intervention (TKR) collected from the Swedish Knee Arthroplasty Registry (SKAR) and used as a continuous variable. The patients were subsequently divided into young (less than 65 years) and old (65 years or more) to calculate the relative risk or risk ratio. Data regarding indication for TKR and earlier operations were recorded as well as mean ROM before and after TKR and MUA. Also, the time elapsed between TKR and MUA was recorded and defined as early (< 12 weeks after TKR) or late (> 12 weeks after TKR) [15], in our clinic we don't have a time limit for MUA, but patients with joint stiffness over one year are unlikely to be MUA. In addition, the numbers of MUA per patient and postoperative complications were registered. Two experienced orthopedic surgeons classified in consensus the radiographic severity of osteoarthritis (OA) in all patients undergoing MUA according to the Ahlback classification [16].

## 2.4. MUA

All manipulations were performed in the operation theater under spinal anesthesia in combination with an epidural anesthesia (EDA) for postoperative use during the three days in hospital. The

**Table 1**  
Baseline demographics for the patients manipulated under anesthesia (MUA) after total knee replacement and those who were not (controls) in mean (SD).

	MUA group	Control group	P-value
n	31	638	
Female sex n (%)	18 (58.1)	415 (65.0)	0.445
Age	58.35 (7.96)	68.41 (10.23)	< 0.001
ASA n (%)			< 0.001
1	18 (58.1)	69 (10.9)	
2	6 (19.4)	289 (45.6)	
3	7 (22.6)	268 (42.3)	
4	0 (0.0)	8 (1.3)	
BMI	29.03 (3.95)	29.52 (5.53)	0.629
Diabetes mellitus	2 (6.5)	100 (15.8)	0.206

ASA: American Society of Anesthesiologists; BMI: body mass index.

manipulations were performed with the patient in supine position and after adequate anesthesia the hip was flexed 90 degrees and the knee joint gently flexed to the maximum possible degree. Postoperatively the use of a continuous passive motion device was applied for three days in hospital in combination with physiotherapy performed by an experienced physiotherapist who also measured ROM with a goniometer. Rehabilitation included early weight-bearing, quadriceps strengthening and range of motion exercises in combination with non-steroidal inflammatory medication and analgesics in order to reduce inflammation and pain.

## 3. Statistical analysis

We used SPSS 18.0 and R 3.3.2 for statistical analyses. A significance level was set at  $p < 0.05$ . Descriptive statistics were calculated for baseline data and presented as mean with their standard deviations (SD). 95% confidence intervals (CI) described estimation uncertainty. Two-sample Welch's t-test was used for comparison of demographic data between case and control groups. Student's t-test was used to compare ROM in early and late MUA as well as ROM post MUA in younger and older patients. Age and BMI were used as continuous variables. Categorical variables were reported as proportions and Fischer's Exact test was used for comparison between groups. In order to calculate unadjusted and adjusted odd ratios (OR) logistic regression models were fitted, with adjustment for relevant confounders (age, sex, BMI, ASA and DM). Continuous variables were kept continuous in order not to weaken the precision of statistical analyses.

The relative risk for MUA was analyzed descriptively by calculating the proportions between age (< 65 and  $\geq 65$  y) groups and ASA (ASA < 1 and ASA  $\geq 2$ ) groups.

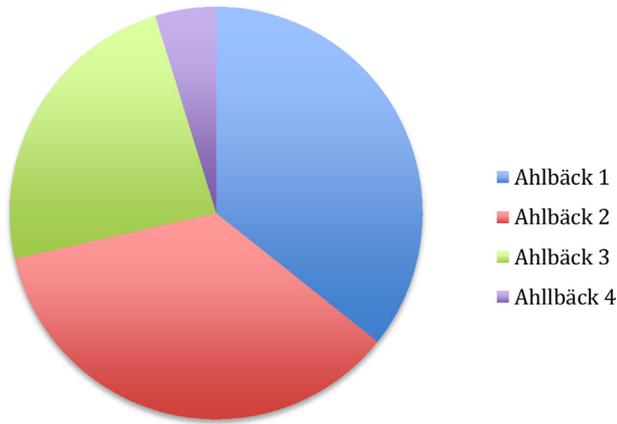
## 4. Ethics

The study was approved by the local ethics committee (Dnr. 2015/978-31).

## 5. Results

ICD-10 disclosed 817 patients who underwent TKR during the period 2007–2012. The primary diagnosis for TKR was OA in 73.8% of the cases, posttraumatic arthritis in 9.5%, rheumatoid arthritis in 7.14%, and other reasons in 9.5% (haemophilia, osteonecrosis) and 13.5% of patients had had previous surgery in the knee (SKAR). For the MUA group the distribution of primary diagnosis was as follows; OA in 73% of the cases, posttraumatic arthritis in 8%, rheumatoid arthritis and psoriasis arthritis in 2%, and other reason in 14% (osteonecrosis and mechanical complications). The mean age was 58.4 years (7.9) in the case group and 68.4 years (10.2) in the control group (Table 1). After adjusting for duplicates and inaccurate diagnosis a total of 762 TKR were identified, 43 MUA (cases) and 719 controls. We included only the first TKR per patient, resulting in a total of 669 patients, giving 31 cases and 638 controls and a prevalence of 4.6% for MUA. Three patients (10%) had previous knee surgeries before index TKR, one meniscectomy and two cruciate ligament reconstructions. These patients (with previous surgeries and MUA) did not differ in results from MUA regarding mean gain in ROM, although this group is too small to draw further statistical analysis. There was no difference in sex distribution between groups (MUA and controls) ( $p = 0.547$ ). The time elapsed between the TKR and first MUA was in median 15 weeks (range 5–53). The mean ROM before index operation (TKR) was 107 degrees and the mean ROM before MUA was 64 degrees. Nine patients had preoperative stiffness i.e. before index TKR (ROM 90 degrees or less of whom 4 patients had a ROM 0–90 degrees) with no difference in

### OA stage



**Fig. 1.** Graph showing the distribution of knee osteoarthritis stage (Ahlback 1–4) in the group mobilized under anesthesia.

**Table 2**  
Unadjusted odds ratios with 95% confidence intervals for manipulation under anesthesia after TKA in relation to age, sex, diabetes mellitus (DM), body mass index (BMI) and ASA score.

Univariate logistic regression analysis			
	Odds ratio	95% CI	P-value
Age (years)	0.91	0.88–0.95	< 0.001
Sex <sup>a</sup>	0.74	0.36–1.54	0.43
BMI	0.98	0.90–1.06	0.63
DM <sup>b</sup>	0.36	0.09–1.56	0.18
ASA 2 <sup>c</sup>	0.08	0.03–0.20	< 0.001
ASA 3 <sup>c</sup>	0.1	0.04–0.25	< 0.001

<sup>a</sup> The reference value is male sex.

<sup>b</sup> The reference value is DM = 0.

<sup>c</sup> The reference value is ASA = 1

proportions between younger and older patients. At the time of the final follow-up (at least one year after MUA), the mean extension was 4 degrees (7) range 0–30 degrees, the mean flexion 95 degrees (15) range 75–125 and the mean final ROM was 91 degrees (19) range 60–125 degrees. Finally a mean net gain in ROM was 27 degrees (21) range 5–90. There was no statistical significant difference in the final ROM between younger and older patients ( $p=0.068$ ) and no difference in final ROM between early and late MUA ( $p=0.18$ ). One complication was noted in a patient who suffered an undislocated periprosthetic femoral fracture during the MUA.

Post-hoc analysis disclosed that 72% of the patients undergoing MUA had low grade OA (Ahlback I-II), (Fig. 1).

#### 5.1. Univariate analysis

Younger and healthier patients (ASA I and II) had higher odds ratio (OR) for MUA. DM was not associated with increased OR for MUA after TKR (OR = 0.36, 95% CI: 0.09–1.56). In addition, increasing BMI and sex showed no increased odds for MUA (Table 2).

#### 5.2. The adjusted regression analysis

The adjusted regression model (Table 3) showed lower OR for increasingly aging patients (OR 0.93, 95% CI: 0.93–0.97,  $p=0.001$  per year) and patients with ASA II-IV showed lower OR compared to patients with ASA I (OR 0.18, 95% CI: 0.07–0.52,  $p=0.001$ ), (Fig. 2). An interaction between age and ASA was found. For the healthy

**Table 3**

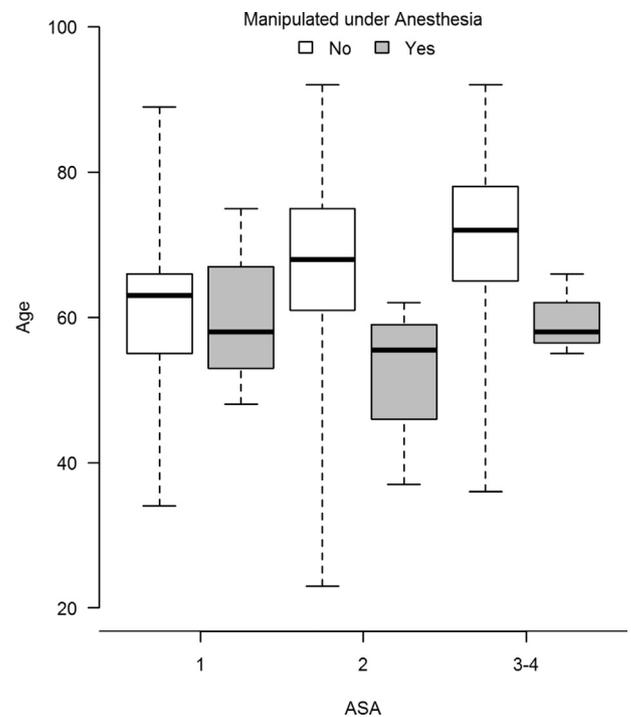
Adjusted odds ratio with 95% confidence intervals for manipulation under anesthesia after TKA. Adjust for age, sex, diabetes mellitus (DM), body mass index (BMI) and ASA score.

Multivariate logistic regression analysis			
	Odds ratio	95% CI	p-value
Age (years)	0.93	0.93–0.97	< 0.001
Sex <sup>a</sup>	0.91	0.41–2.03	0.83
BMI	1	0.91–1.07	0.83
DM <sup>b</sup>	0.76	0.16–3.60	0.73
ASA 2 <sup>c</sup>	0.11	0.04–0.31	< 0.001
ASA 3–4 <sup>c</sup>	0.18	0.07–0.52	< 0.001

<sup>a</sup> The reference value is male sex.

<sup>b</sup> The reference value is DM = 0.

<sup>c</sup> The reference value is ASA = 1



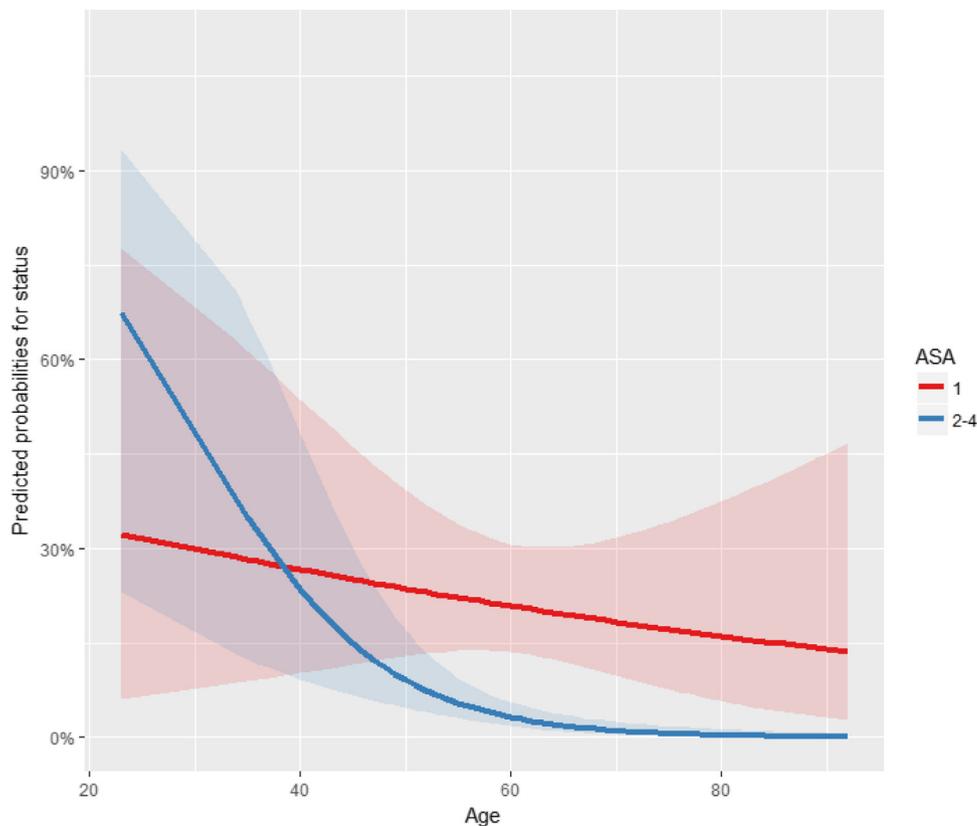
**Fig. 2.** Box-plot showing all patients mobilized under anaesthesia, the box denotes first and third quartiles and whiskers show the minimum and maximum value, respectively. The band inside the box denotes the median. This box-plot demonstrates that age distribution is similar between patients MUA and controls in the ASA I group. In the ASA II–IV group a significant age distribution is observed, patients > 65 years are less likely to be MUA.

patients (ASA I) the risk for MUA was independent of age in contrast to sicker patients (ASA  $\geq 2$ ), (Fig. 3).

### 6. Discussion

Young age is a known risk factor for prosthesis failure [17,18] and less patient-reported satisfaction [19] but age as a risk factor for MUA is controversial. The number of TKRs is overall increasing amongst younger patients and in Sweden only there was a five-fold increase of patients receiving TKR's under the age of 55 between 1998–2007 [20].

The major finding of this study was that younger and healthier patients had increased OR for MUA, a rather unknown and unexpected complication, as a result of joint stiffness after TKR. The association between post TKR joint stiffness and patient dissatisfaction has been proven [21]. The increased risk for MUA in younger patients in the present study was found independently of confounding variables such as sex, BMI and DM. Moreover, our



**Fig. 3.** This graph illustrates the interaction between age and ASA. For the healthy patients (ASA I) the risk for mobilization under anaesthesia was independent of age in contrast sicker patients (ASA  $\geq 2$ ).

cohort of young patients had not performed previous knee surgeries or presented preoperative knee stiffness to a greater extent as compared to the older patients that could explain this complication. Two earlier studies have reported young age as a risk factor for MUA after TKR [10,13] and recently Kornuijt A. et al published a review article confirming our association of higher odds of MUA in younger and healthier patients [22]. Springer et al. (2012) found a two-fold increase in the odds for MUA after TKR in patients less than 45 years compared to older. Correspondingly, Issa et al. (2015) showed fewer MUAs in those over 65 years compared to younger patients.

However, in our analysis we found an interaction between age and ASA and consequently we could not draw any further conclusions regarding the main cause of MUA. The explanation could hitherto be biological or secondary to selection bias. However, at our institution we follow predefined protocols regarding indication for surgery, implants, rehabilitation and also indication for MUA. Moreover, a third independent observer such as a resident or a physiotherapist often follows up our patients.

In an attempt to further assess the cause of increased MUA in young and healthy patients we performed a post-hoc analysis of preoperative X-rays according to the Ahlback OA classification. Contrary to the expected we found that the majority of those who underwent MUA had a low grade of OA (Ahlback I and II) in both age groups and independently of health status. As far as we know, the association between a low-grade OA and MUA has not been reported earlier and the mechanism behind this finding remains unknown. Unfortunately we could not analyze the OA stage of the control group of 669 patients and therefore this theory should be confirmed and further investigated in future studies.

We found a prevalence of MUA after TKR similar to others [1,2] and the net gain in ROM was also consistent with earlier reports [1,13,23–25]. Several earlier studies reported a lower ROM after

TKR in patients with DM [9,13,26]. In accordance with some others [27–29], we could not confirm this finding by studying the OR for MUA in patients with DM. Contrary to our findings, other studies reported that BMI > 30 and female sex increased the risk for MUA [30]. This contradictory finding further enlightens the existing controversy and difficulty to identify patients at risk for MUA as an indicator for limited ROM after TKR.

A restricted ROM after TKR remains a clinical challenge and still there is no consensus regarding several aspects such as a clear definition, causes, conservative versus interventional treatment, optimal time for MUA and rehabilitation regime after MUA. It is acknowledged that walking requires 65 degrees of flexion, lifting an object from the floor 75 degrees, climbing stairs 85 degrees, sitting 95 degrees and tying shoelaces 105 degrees [31]. Subsequently, flexion below this limit warrants treatment in order to accomplish activities of daily living. Our mean net gain in ROM after MUA was 27 degrees, regardless if patients were manipulated early or late. Others have reported similar good results independently if the manipulation was performed on an early (< 12 weeks) or late stage [21,24]. Hence we believe that an effort to manipulate knee under anesthesia should be performed regardless of time elapsed after TKR in order to shorten rehabilitation and enhance function and quality of life.

Manipulation under anesthesia is a fairly easy, non-invasive and reasonably rapid procedure to perform. Complications are relatively uncommon according to the literature, however pulmonary embolism and rupture of the extensor apparatus has been reported [32]. We did not encounter any of these complications but an undisplaced periprosthetic femoral fracture that healed without complications.

There are several limitations to this study; one is the design with inherent low accuracy and completeness of clinical data. Another is that single-institution study is less generalizable to all patients i.

e. other physicians might have different indications for MUA. Only one comorbidity, diabetes mellitus, a known risk factor was compared between the cohorts. Other comorbidities could have been different between groups and contributed to stiffness and outcome. Finally, the lack of radiographic classification of the OA stage in those who did not undergo MUA limited further analyses. A larger prospective study should be carried out to further assess the relationship between young healthy patient and early stages OA in order to further identify predictors for MUA after TKR. The strength of the study was the control group of 669 patients with no missing data regarding BMI, ASA grade and the diagnosis diabetes mellitus. Another strength is the radiographic evaluation of the patients who underwent MUA as well as the minimum follow-up with of one year.

## 7. Conclusions

Previously non-identified subgroups, healthy and young patients were particularly at risk for undergoing MUA following TKR. MUA was an effective treatment of postoperative knee stiffness regardless of patient age, and time of to manipulation.

## Disclosure of interest

The authors declare that they have no competing interest.

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## Contribution of authors

N.M.-C.: study design, data analyses, writing manuscript, A.P.: study design, collection of data, writing part of the manuscript, D.R.: data collection, writing part of the manuscript, E.B.: data analysis, writing part of the manuscript, M.H.: study design, data analyses, writing manuscript. All authors: review of the manuscript.

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