

Low manipulation prevalence following fast-track total knee arthroplasty

A multicenter cohort study involving 3,145 consecutive unselected patients

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Background and purpose — Postoperative joint stiffness following total knee arthroplasty (TKA) may compromise the outcome and necessitate manipulation. Previous studies have not been in a fast-track setting with optimized pain treatment, early mobilization, and short length of stay (LOS), which may have influenced the prevalence of joint stiffness and subsequent manipulation. We investigated the prevalence of manipulation following fast-track TKA and identified patients at risk of needing manipulation.

Patients and methods — 3,145 consecutive unselected elective primary unilateral TKA patients operated in 6 departments with well-defined fast-track settings were included in the study. Demographic data, prevalence, type and timing of manipulation, and preoperative and postoperative ROM were recorded prospectively, ensuring complete 1-year follow-up.

Results — 70 manipulations were performed within 1 year (2.2%) at a mean of 4 months after index surgery. Younger age and not using walking aids preoperatively were associated with a higher risk of manipulation. LOS ≤ 4 days (as opposed to a longer LOS) was not associated with an increased risk of manipulation.

Interpretation — The prevalence of manipulation was lower or comparable to that in most published studies following more conventional pathways. Inherent patient demographics were identified as risk factors for manipulation whereas LOS ≤ 4 days was not. Thus, fast-track TKA does not result in increased risk of manipulation—despite a shorter LOS. Optimized pain treatment and early mobilization may contribute to these favorable results that support the use of fast-track.

Stiffness of the knee after total knee arthroplasty (TKA) can follow in the postoperative weeks or months, compromise the result, and necessitate manipulation under anesthesia (MUA). Stiffness is not well-defined in the literature, making comparison between studies difficult. One study defined stiffness as a knee having a flexion contracture of ≥15 degrees and/or < 75 degrees of flexion (Kim et al. 2004). With various definitions, prevalence of some stiffness has been reported to range from 1.3% to 60% of patients (Kim et al. 2004, Fitzsimmons et al. 2010). Stiffness may be multifactorial: reduced preoperative range of motion (ROM), previous multiple surgery, arthrofibrosis, component malposition, psychological reasons (discrepancy between perceived pain and ability to overcome this in flexion), and more rare conditions such as heterotopic ossification and hemophilia. Also, stiffness may be influenced by the pain treatment given, the timing of first mobilization, and the length of stay (LOS)—as these factors may influence the ability to flex the knee, the (avoidance of) scar formation, and the amount of physiotherapy-guided flexion, respectively. These issues are all addressed in fast-track TKA, where short-acting regional analgesia and standardized opioid-sparing analgesia are applied in order to facilitate early mobilization and flexion of the operated knee—thus with a potentially positive effect, lowering the prevalence of stiffness necessitating MUA (Husted et al. 2010a, 2012). On the other hand a shorter hospital stay, resulting in less inpatient physiotherapy-guided exercises, may result in a higher prevalence of MUA, as proposed in an earlier study (Mauerhan et al. 1998).

As all the published studies on prevalence of MUA following TKA have not been on well-defined fast-track TKA during hospital stays, and as fast-track is gaining increasing interest worldwide (Kehlet 2013), the present study was performed to determine the prevalence of MUA following fast-track TKA in a standardized multicenter setting involving 6 departments. Specifically, we wanted to: (1) identify the prevalence of MUA in a large cohort of unselected consecutive patients operated with primary unilateral TKA; (2) determine the timing and the results thereof; and (3) identify the underlying risk factors for MUA. Thus, is it safe to do fast-track TKA with short LOS regarding the specific risk of MUA?

Patients and methods

From the database established under “the Lundbeck Foundation Center for Fast-track Hip and Knee Replacement” comprising 6 Danish departments with a well-described standardized fast-track setting (Jørgensen et al. 2013a), preoperative comorbidity data were collected prospectively on consecutive unselected patients operated with primary unilateral TKA from January 10, 2010 to May 31, 2012. The fast-track setup has been described earlier in detail (Husted et al. 2008, 2010b, 2012) and includes the use of regional analgesia (spinal), no or limited use of drains, the use of tranexamic acid to reduce blood loss, the standardized use of local infiltration analgesia (LIA), the use of multimodal opioid-sparing analgesia, early mobilization on the day of surgery when the spinal anesthesia has worn off, and early discharge to own home upon fulfillment of identical functional discharge criteria for all patients, followed by outpatient physiotherapy. The intention is that LOS should be 1–3 days. The choice of prosthesis and surgical technique was at the surgeon’s discretion, as was the indication for MUA (Table 1). Also, the intensity and method of postoperative physiotherapy may have varied between departments, as there was no attempt at standardization before the study period.

Mean age was 68 years (SD 10; range: 24–94), mean BMI was 30 (SD 5, range 14–53), 34% were living alone, 13% smoked, 6% drank ≥ 2 units of alcohol a day, 22% used some form of walking aid before the operation, 13% had cardiac disease, 7% had pulmonary disease, 14% had diabetes, and 8% had psychiatric disease. Median LOS was 3 days (interquartile range (IQR): 2–3; range: 1–33). 91% had a LOS of less than 4 days, with all patients discharged to their own homes. 5.0% of patients were re-admitted for reasons other than manipulation at ≤ 30 days; this number increased to 6.0% at ≤ 90 days.

3,145 unselected consecutive patients (61% women) had unilateral TKA performed at one of the 6 departments during the inclusion period.

The primary outcome was patients who had any form of MUA (closed, open, or arthroscopic) within 1 year of index surgery. Also, any revision operation (soft tissue, exchange of components) on the operated knee was registered. The data

collected included: age, sex, BMI, smoking, comorbidities, diagnosis for index surgery, time of surgery, hospital of surgery, total number of primary TKAs performed in the study period (in order to determine incidence of MUA), LOS following TKA, time of manipulation, type of manipulation, pre-manipulation ROM, and ROM achieved at MUA. LOS was defined as number of postoperative nights in hospital (including transferral to other departments) until discharge to the patient’s own home. All admissions with LOS > 4 days and re-admissions within 90 days were checked against the Danish National Patient Registry (DNPR), followed by review of patient records in order to identify cause of LOS > 4 days or re-admission (Jørgensen et al. 2013a). The DNPR registers all hospitalizations (including transferrals, diagnoses, and surgical procedures) at Danish hospitals, allowing information on LOS and re-admissions regardless of localization. As reporting is mandatory for receipt of reimbursement, complete follow-up is ensured (Andersen et al. 1999).

Statistics

Comparisons of continuous data were done using Mann-Whitney U-test and t-test, and for categorical data, the χ^2 -test (Pearson). Events (incident cases) are reported as actual number and percentage with 95% confidence intervals (CIs). Multivariate logistic regression analysis was used to evaluate possible association between preoperative patient characteristics and comorbidities and MUA. Univariate risk estimates were initially obtained for the following potential risk factors for MUA: age, BMI, regular use of walking aids, smoking, alcohol use of > 2 units a day, living alone, pharmacologically treated cardiac, pulmonary, and psychiatric disease, and diabetes. These variables were chosen as they might influence postoperative outcome with regard to both somatic and psychological function. In addition, we investigated whether patients with a LOS of < 4 days and surgically-related re-admissions within 30 and 90 days for reasons other than MUA were associated with increased risk of MUA. Any variable with a significance level of less than 0.25 was then included in a backwards, stepwise multiple logistic regression model. Analyses were performed on a per-procedure basis and any 2-tailed p-value of < 0.05 was considered significant. All data analyses were done using SPSS version 20 and the STATA statistical package version 10.1.

Ethics

The regional ethics committee waived the need for informed consent. Permission was received from the Danish National Board of Health (3-3013-56/1/HKR) and the Danish Data Protection Agency (2007-58-0015) to review and store patient records.

Trial registration

The Lundbeck Foundation Center for Fast-track Hip and Knee Replacement database on preoperative patient characteristics

Table 1. The setup and outcome regarding various aspects of manipulation in the 6 fast-track departments

	Hvidovre	Farsø	Århus	Vejle	Esbjerg	Holstebro
First FU ^a	12 w	6 w	6 w	4 w	12 w	6 w
First FU by ^b	surgeon	physio	physio/surgeon	physio	physio	physio
Indication for manipulation by surgeon	surgeon	surgeon	surgeon	surgeon	surgeon	surgeon
Indication for manipulation	< 90° flexion or unsatisfactory flexion	< 90° flexion or > 5° extension defect	< 90° flexion	unsatisfactory flexion	< 90° flexion	< 90° flexion (90–110° rel)
When performed	> 12 w	> 6 w	8–20 w	pref < 12 w	> 12 w	> 6 w
MUA/scopic/open ^c	MUA + scopic	MUA + scopic	MUA	MUA + scopic	MUA	MUA + open
Admitted ^d	3 days	3 days	no/1 day	1–2 days	3 days	few days
CPM ^e	3 days	3 days	no	rarely	3 days	few days
Inpatient physiotherapy ^f	ordinary	intense	ordinary	intense	intense	intense
Outpatient physiotherapy ^g	12 w	6 w	6 w	12 w	yes, varies	individual
Follow-up after MUA	12 w	8 w	12 w	12 w	8–12 w	2 w + later
Follow-up after MUA by	surgeon	surgeon	surgeon	surgeon/physio	surgeon	physio/surgeon
Repeat MUA if needed	yes	rarely	no	yes	yes	rarely
Component exchange if no effect ^h	yes	rarely	yes	yes	rarely	no
Prevalence (%) of MUA (95% CI)	3.3 (2.2–5.0)	1.2 (1.1–3.4)	1.7 (0.8–3.3)	2.0 (1.0–4.2)	3.0 (1.9–4.6)	1.0 (0.4–2.4)
Days until MUA (median)	130	73	81	116	153	105

^a time of first follow-up after index TKA.

^b the staff seeing the patient at first follow-up.

^c indicates whether patients were manipulated closed, with arthroscopic assistance or with open surgery.

^d indicates whether or not the patient was hospitalized and if so, the number of days.

^e indicates whether or not continuous passive motion was used.

^f indicates whether standard physiotherapy (as offered following index TKA) or a more intense version was offered.

^g the number of weeks that outpatient physiotherapy was offered following MUA.

^h indicates whether or not the department would offer open surgery with exchange of components (downsizing) if one or more initial closed or arthroscopy-assisted attempts had failed.

and postoperative outcomes used in this study is registered as a trial registry at ClinicalTrials.gov (ID: NCT01515670).

Results

Criteria for type and timing of MUA differed slightly between departments (Table 1). All the departments used flexion < 90 degrees or unsatisfactory flexion (depending on the needs of specific patients) as indication, which was always decided by the surgeon. All surgeons agreed to wait at least 6 weeks post-operatively before intervention, but after that some preferred to do MUA before 12 weeks whereas others favored the period after.

70 manipulations out of 3,145 procedures were performed, resulting in a prevalence of 2.2% (45 closed MUA, 25 arthroscopic MUA, and no open MUA). The MUA prevalence values for different departments had overlapping CIs and there was no significant difference between departments (Table 1). The median time between index surgery and manipulation was 121 days (IQR: 83–161). Time until MUA varied between departments: median 73 days to median 153 days ($p = 0.001$). There was, however, no difference in the gain of ROM following MUA between early intervention (< 120 days) and late intervention (> 120 days), as both groups had a median gain of 40 degrees at MUA. At manipulation, the median extension deficit was 5 degrees (IQR: 0–10, range: 0–40) and the median

flexion was 80 degrees (IQR: 70–90, range: 30–100), similar between closed and arthroscopy-assisted MUA. The intraoperative improvement in ROM was median 38 degrees (IQR: 30–50, range: 0–90) for closed MUA and median 40 degrees (IQR: 30–50, range: 10–75) for arthroscopy-assisted MUA.

Univariate statistical analysis using a significance level of 0.25 found a potential association between age, sex, smoking, living alone, preoperative use of walking aids and the risk of manipulation: patients with MUA were younger (mean 59 years) than patients who did not need manipulation (mean age 68 years) ($p = 0.001$), were more likely to be male (odds ratio (OR) = 16, CI: 0.97–2.5; $p = 0.07$) and to smoke (OR = 1.8, CI: 1.0–3.2; $p = 0.05$). Patients living alone (OR = 0.7, CI: 0.4–1.3) or using walking aids before surgery (OR = 0.3, CI: 0.1–0.7) were less likely to have MUA than patients living with a spouse ($p = 0.3$) or not using walking aids preoperatively ($p = 0.005$). There was no association between MUA and BMI ($p = 0.19$) or diabetes ($p = 0.66$). Nor did we find any association between alcohol use of ≥ 2 units per day, cardiac or pulmonary or psychiatric disease, and the risk of MUA. Importantly LOS, categorized as LOS < 4 days and LOS > 4 days, was not associated with the risk of manipulation ($p = 0.6$); nor was re-admission within 30 or 90 days for reasons other than manipulation ($p = 0.8$). Multiple regression analysis found only (1) younger age, and (2) no need for walking aids preoperatively, to be significant predictors of higher risk of MUA (Table 2).

Table 2. Results of the stepwise multivariate logistic regression analysis. The final model included 3,145 patients and only 2 variables: age/year and preoperative use of walking aids

Preoperative characteristic	Odds ratio (95% CI)	p-value
Age/year	0.93 (0.91–0.95)	< 0.001
Male vs. Female	1.48 (0.91–2.41)	0.1
Living alone vs. living with spouse	1.19 (0.68–2.10)	0.7
Preoperative use of walking aids	0.39 (0.15–0.97)	0.05
Smoking	1.15 (0.61–2.19)	0.7

Discussion

Some form of stiffness is common after TKA, and it has been found to occur twice as often in younger patients (< 45 years old) (Springer et al. 2012), which is in accordance with our findings. One can speculate whether it is more pronounced fibroblast proliferation or a lower pain threshold that causes stiffness in younger patients. In support of the former explanation, we found that smokers had a higher risk of MUA (although this was not statistically significant after adjustment for patient characteristics), as smoking may induce episodes of hypoxia-induced oxidative stress with formation of hypertrophic scar tissue (Mahdavian Delavary et al. 2012). Differences in pain perception may also play a part, as one study found that patients who underwent MUA had more preoperative pain than those who had not had MUA (Keating et al. 2007).

We found that more men than women tended to need MUA, in contrast to results published by Gadinsky et al. (2011). However, that study found that higher BMI also resulted in a higher risk of needing MUA, a finding that was not confirmed in the present study.

The results of our analysis of patient-related factors associated with MUA must be interpreted with caution, due to the limited number of outcomes. Also, as this was a descriptive study, we can only report associations and not causality. However, it does appear to be the younger, fitter patients (i.e. those without preoperative walking aids) who are at risk of MUA, possibly caused by a higher preoperative activity level and the expectation of returning to this level, necessitating the ability to have good flexion (confounding by indication). This is supported by the fact that smoking ceased to be associated with MUA when we adjusted for age and sex, as we have previously shown that TKA and THA patients who smoke are younger and are more often male (Jørgensen et al. 2013b). However, in this context it is reassuring that short LOS was not associated with MUA, despite the fact that the youngest patients—and those not using walking aids preoperatively—often had shorter LOS, also after fast-track TKA (Jørgensen et al. 2013a). Other patient-related factors may also influence postoperative pain, ROM, and therefore the prevalence of MUA, but our study setup did not allow for an extensive evaluation of all parameters.

Stiffness may be treated by MUA: closed manipulation under anesthesia, arthroscopy-assisted shaving and removal of scar tissue, or open removal of scar tissue (also permitting component exchange). One review found the gains in ROM after closed MUA and arthroscopy-assisted MUA to be similar, while open arthrolysis appears to give inferior gains in ROM (Fitzsimmons et al. 2010). MUA may be more successful in increasing ROM when performed early, but it is also still effective when performed late—as arthroscopy-assisted MUA has been shown to be useful up to 1 year after index TKA (Fitzsimmons et al. 2010). This may explain the variations in the preferred timing and modality of MUA between departments in our study, which also seems to be justified, as median gains of 40 degrees were found irrespective of whether MUA was performed before or after 120 days.

Various prevalences of manipulation have been reported: 1% (Husted et al. 2010a), 2% (Yeoh et al. 2012), 4% (Bawa et al. 2013), 7% (Harvie et al. 2013), and 12% (Mauerhan et al. 1998), the latter when LOS was reduced from 6.4 days to 4.4 days. This study found that the prevalence of MUA doubled when LOS was reduced as a result of implementation of a clinical pathway (an early form of fast-track) (Mauerhan et al. 1998). In contrast, we found a MUA rate of only 2% with a median LOS of 3 days in a multicenter fast-track setup, and also that LOS of < 4 days was not associated with an increase in MUA. This may have been due to the improved information, improved pain treatment, or early mobilization—or a combination of these factors, factors that have previously been shown to result in a very low prevalence of MUA in a single fast-track hospital setup (Husted et al. 2010a). However, the incidence of 1% found in that fast-track setup was with a shorter follow-up and a slightly different setting than in the present study, as we concentrated on re-admissions within 3 months (Husted et al. 2010a). Although manipulation in Mauerhan's (1998) study was reported at only 6 weeks of follow-up, most studies have reported longer follow-ups: 8 (3–14) weeks (Harvie et al. 2013) or 12 (3–48) weeks (Yeoh et al. 2012). We chose 52 weeks of follow-up to compensate for inter-departmental variations in the setting and to ensure registration of all MUA potentially related to the index operation. Also, the intensity and method of postoperative physiotherapy may have varied between departments. But as studies have so far failed to show any lasting effect of any form of physiotherapy, the potential bias from this seems negligible (Minns Lowe et al. 2007).

Component malposition (size, malrotation) may not play any significant role in the incidence of MUA; there have been cases reported, and 1 study found internal rotation of components in all 34 patients revised for stiffness (Bédard et al. 2011) but a study examining 12 parameters regarding component positioning in 281 patients failed to show any difference in any parameter between patients needing manipulation and those not (Harvie et al. 2013). We did not investigate component positioning, as there were no open manipulations, and

no component changes were found to be necessary as the surgeons did not find any gross misplacement. Also, the choice of prosthesis was at the surgeons' discretion, and could possibly influence the prevalence of MUA, as one recent study found different prevalences associated with different types of prostheses (Berend et al. 2013) whereas others did not (Barnes et al. 2013; Peters et al. 2014). Although 1 study found that warfarin prophylaxis (compared to LMWH) resulted in more arthrofibrosis, necessitating manipulation in 26% as opposed to 6% of patients (Walton et al. 2005), we did not study this aspect as none of the patients received prolonged warfarin prophylaxis (Jørgensen et al. 2013c).

We found intraoperative improvement of 38 and 40 degrees of MUA without and with arthroscopic assistance, respectively. This finding compares well with results presented by Kim et al. (2004), who found that the mean arc of motion improved from 55 degrees to 82 degrees, with findings by Bawa et al. (2013), who showed a mean increase in ROM of 34 degrees, and also a meta-analysis (involving 14 studies, 913 patients) (Pivec et al. 2013) where the gain in the range-of-motion arc at 1-, 5-, and 10-year follow-up was 30, 33, and 33 degrees compared to the pre-manipulation ROM. The authors concluded that MUA for a stiff primary TKA is an efficacious procedure to restore ROM and early gains in motion appear to be maintained at long-term follow-up (Pivec et al. 2013).

The interval between index TKA and MUA—with a cutoff of 120 days—did not correlate with the prevalence of MUA. This contrasts with an earlier study where this interval was inversely correlated with final ROM, with a decrease after 75 days (Bawa et al. 2013). Various outcomes exist, as another study found no difference in the gain in ROM between knees manipulated before or after 12 weeks (Yeoh et al. 2012). Pivec et al (2013) confirmed the gain in ROM following MUA to be 35 degrees at 5-year follow-up, with no difference between patients manipulated before or after 12 weeks. These findings are reassuring, and show that despite the postoperative setup—which also differed between the 6 departments in the present study (including slight variations in the indication for MUA—equal results can be achieved after early and late MUA.

In conclusion, fast-track TKA does not increase the prevalence of MUA, as MUA was found to have a low prevalence regardless of LOS, but depending on inherent patient characteristics. The optimized pain regimen permitting early mobilization may contribute to the favorable outcome.

HH, KG, and AT wrote the protocol; CCJ and HK revised it; CCJ and KG undertook all data gathering; CCJ, AT, and HH performed and evaluated all statistical analyses; HK supervised the work done by CCJ and helped to revise the manuscript. HH wrote the first draft, revised it, and submitted it for publication. KS implemented the study setup at Aarhus Hospital and helped revise the manuscript. TBH implemented the study setup at Holstebro Regional Hospital and helped revise the manuscript. PKA, LTH, and MBL implemented the study setup at their respective study locations and revised the manuscript. All authors approved the final version to be published. CCJ and AT had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses.

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