Arthroplasty Today 5 (2019) 515-520



Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/



Efficacy of manipulation under anesthesia beyond three months following total knee arthroplasty

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ARTICLE INFO

Article history: Received 21 May 2019 Received in revised form 5 August 2019 Accepted 8 August 2019 Available online 10 October 2019

Keywords: Total knee arthroplasty Manipulation under anesthesia Stiffness Range of motion

ABSTRACT

Background: Stiffness after total knee arthroplasty (TKA) is often treated with manipulation under anesthesia (MUA) to improve range of motion (ROM). However, many authors recommend against MUA beyond 3 months after TKA. This study investigates the timing of MUA for stiffness after TKA, focusing on MUA performed at >12 weeks.

Methods: In total, 142 MUAs were retrospectively reviewed. "Early" MUAs were at <12 weeks after TKA; "Late" MUAs were >12 weeks. MUAs were further subdivided into 4 groups: 83 "Group I" cases at <12 weeks, 34 "Group II" between 12 and 26 weeks, 12 "Group III" between 26 and 52 weeks, and 13 "Group IV" at >52 weeks. Gains in ROM were compared between groups.

Results: Gains in flexion and overall ROM were statistically equivalent in Early vs Late MUA when controlling for pre-MUA ROM. ROM gains between the early Group I and the later Groups II-IV were also statistically comparable. Overall ROM gain in Group I was 24.1°, 17.9° in Group II, 20.8° in Group III, and 11.1° in Group IV. There were no significant complications.

Conclusions: Early and late MUA resulted in statistically equivalent gains in ROM, regardless of timing after TKA. All groups showed an average improvement in ROM of $\geq 11^{\circ}$. MUA performed beyond 3 months, and even beyond 1 year, appears to be safe and may improve ROM and allow select patients to avoid revision surgery.

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Introduction

Total knee arthroplasty (TKA) is highly effective and reliable at relieving debilitating pain and dysfunction from end-stage degenerative joint disease of the knee [1]. However, up to 20%-60% of patients have been reported to develop postoperative knee stiffness of unclear etiology that can drastically reduce range of motion

(ROM) and compromise functional outcomes [2-7]. Soft tissue balance and bony resection during surgery, the design and placement of arthroplasty implants, postoperative rehabilitation protocols, and multimodal pain management can all contribute to postoperative ROM. The role and effect of each of these factors continues to be debated in the literature.

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Treatment options for knee stiffness following TKA include physical therapy, arthroscopic vs open resection of scar tissue. revision of TKA components, and manipulation under anesthesia (MUA). Additionally, in a systematic review, Fitzsimmons et al [8] found that multiple authors recommend arthroscopic lysis of adhesions along with MUA to improve ROM. Several studies have shown MUA to be a safe and effective method to improve long-term ROM and prevent additional surgery [9,10]. Nevertheless, there is ongoing debate in the literature concerning the indications, timing, and expected outcomes for MUA. Some studies have found MUA to be most effective when performed "early" (<3 months after TKA),

https://doi.org/10.1016/j.artd.2019.08.002

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to https://doi.org/10.1016/j.artd.2019.08.002.

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while others have shown no difference in outcome whether MUA is performed "early" or "late" (>3 months following TKA) [7,8,11,12].

Most discussion of "late" manipulation in the literature is during the time frame of 3-6 months post-TKA, but there are very little data concerning MUA performed beyond 6 months after TKA. This uncertainty and deficiency in the literature makes it difficult for surgeons to develop a reliable algorithm for how to best treat a patient with a stiff TKA, particularly if they are greater than 6 months after TKA. In practice, this could mean unnecessarily subjecting patients to the morbidity and risks of additional surgery, or withholding potentially effective treatment like MUA while patients suffer with limited ROM and functional disability. As such, further investigation is needed to elucidate the outcomes of MUA performed in a time period later than is generally considered plausible.

In this context, we investigated the ROM and clinical outcomes of MUA for stiff TKA performed at our institution. We hypothesized that (1) distant MUA (performed >52 weeks status post index primary TKA) significantly improves knee ROM (defined as >10°) and (2) late MUA (performed >12 weeks post-TKA) is as effective as early MUA (performed \leq 12 weeks post-TKA).

Material and methods

After obtaining Institutional Review Board approval, we retrospectively identified all patients who underwent MUA of their primary TKA performed by one of the 6 fellowship-trained adult reconstruction specialists at a high-volume orthopaedics-only institution from January 2004 to April 2016. Of the 271 manipulations identified in our database, 142 were eligible for inclusion in this study. The inclusion criteria were cases with complete followup data recorded a minimum of 12 weeks after manipulation. The remaining 129 cases were excluded due to lack of adequate followup data. Of the 142 MUA cases included, 46 were performed in men and 96 in women, with a mean age of 63.4 years (range 46-84). All 142 patients had undergone primary TKA via standard medial parapatellar approach. One patient had rheumatoid arthritis, while the remaining 141 patients had end-stage osteoarthritis. See Table 1 for complete demographic data.

Overall average follow-up time post-MUA was 52.0 weeks (range 12-262). Of note, 35 of the 142 cases analyzed underwent a second manipulation within 12 weeks after their original manipulation due to insufficient improvement in ROM after their first MUA. These 35 cases were included in the study as they are indicators of poor outcomes after MUA, and excluding them would have biased our results toward a more favorable outcome. For

Table 1

Demographic characteristics of early vs late MUA groups.

Demographics	Early MUA group ^a	Late MUA group ^a	P value
No. of cases	83	59	
Mean age (y)	62.9	64.2	.32
Gender (%)			.36
Male	35.7	27.1	
Female	64.3	72.9	
Height (cm)	166	165	.19
Weight (kg)	84.6	83.8	.9
BMI	31.5	30.8	.54
Side (%)			
Right	52.4	64.4	
Left	47.6	35.6	
Mean pre-TKA total ROM (°)	89.4	104.1	<.0001
Mean pre-MUA total ROM (°)	71.5	89.8	<.0001

MUA, manipulation under anesthesia; BMI, body mass index; TKA, total knee arthroplasty; ROM, range of motion.

Bolded values represent the significant P values.

^a Early Group is defined as MUA within 12 wk post-TKA; Late Group as MUA >12 wk post-TKA.

patients who had multiple MUAs, data for only their first MUA were included, and subsequent manipulations were excluded. For patients who had manipulations performed on both the left and right knee, each manipulation was recorded as a separate case.

All available medical records were reviewed, including admission history and physical examinations, operative reports, discharge reports, and outpatient clinic notes. The primary outcomes measured were (1) knee ROM (extension, flexion, and total, at preoperative, intraoperative, and postoperative time points) and (2) the timing post-TKA of the MUA. Secondary outcome measures analyzed included age, sex, height, weight, body mass index (BMI), and primary diagnosis.

Data on other perioperative variables were also gathered; however, these were not felt to be significant contributors and were not included in the final analysis. These variables included operative side, history of knee surgery prior to TKA, history of infection or trauma, history of chronic pain or opioid use, prosthesis type, surgeon, and complications such as wound issues, infection, venous thromboembolism, or medical issues (such as postoperative intensive care unit stay, myocardial infarction, stroke, etc.).

Knee stiffness can be the result of myriad causes, with some being more easily remedied than others. It is imperative that the surgeon fully evaluate the stiff knee and properly identify the cause so that appropriate treatment can be administered. Differentiating the stiff painful knee from the stiff painless knee can be particularly helpful. Causes of stiffness include infection, disorders of the hip, spine, or central nervous system, reflex sympathetic dystrophy, heterotopic ossification, arthrofibrosis, posterior cruciate ligament tightness, and technical causes such as incomplete removal of posterior femoral osteophytes [13,14]. The decision to proceed with MUA was made through shared decision-making with the patient when they were not satisfied with their ROM or they were losing ROM despite appropriate trial of physical therapy. Contraindications for MUA included any active wound or skin problems, active infection, component malalignment or failure, or being a poor medical candidate to undergo anesthesia. Manipulations were performed under anesthesia with full muscle relaxation following standard technique described by Fox and Poss in 1981 [15]. Alternatively, the leg may be allowed to fall from full extension into flexion. This maneuver is repeated several times: the weight of the limb itself is used to disrupt adhesions [14,16]. The variation in technique was based on surgeon preference; there was no observed difference in outcomes between the 2 techniques. All patients followed a routine post-manipulation rehabilitation protocol that included ice, analgesia, full weight bearing, and aggressive physical therapy.

Manipulations were categorized according to when they were performed after their index arthroplasty procedure. In keeping with prior studies, all MUAs performed within 12 weeks were considered "Early" and those performed after 12 weeks were considered "Late." We further substratified all patients into the following 4 groups for analysis: "Group I" manipulations were performed within 12 weeks, "Group II" between 12 and 26 weeks, "Group III" between 26 and 52 weeks, and "Group IV" performed at greater than 52 weeks (ie, distant MUA). Final ROM and net gain in ROM were compared between these 4 groups.

Post-MUA flexion and extension were measured during followup office visits, at least 12 weeks out from the MUA. A negative value for extension ROM indicates that the knee had a flexion contracture and was not able to fully extend. Total ROM was calculated by adding the flexion and extension ROM. Gain in flexion was calculated by subtracting the pre-MUA flexion from the post-MUA flexion. Similarly, gain in total ROM was calculated by subtracting the pre-MUA total ROM.

Patients were generally seen in follow-up clinic at 4 weeks, 6 months, 1 year, and then yearly afterward. The clinical data from the

1-year follow-up were most frequently used for analysis in this study, as this time point was felt to provide an accurate assessment of the success of the MUA based on the patient's ROM and functional status [7]. When the 1-year follow-up data were not available, we used the data closest to the 1-year time point, again with a minimum of 12 weeks out from the MUA.

Statistical analysis was performed by a biostatistician using SAS software. In all analyses, a *P*-value of <.05 was considered significant. To assess the significance in differences between Early and Late groups, we used *t*-test for normally distributed continuous variables, Wilcoxon signed-rank test using the NPAR1WAY procedure for abnormally distributed continuous variables, and chi-squared and Fisher's exact tests for categorical variables. To evaluate changes in ROM between the Early vs Late groups, as well as between the substratified groups I-IV, we used a multivariable regression model via the REG procedure, with the Early group (or Group 1) as our reference group. This model adjusted for age, gender, height, weight, BMI, mean pre-TKA total ROM, and mean pre-MUA total ROM via both individual prediction and backward selection.

An initial power analysis was performed based on prior literature, and a sample size of 50 patients was likely to be adequate (25 patients having an MUA at <12 weeks and 25 at >12 weeks). This was performed using ClinCalc.com (http://clincalc.com/Stats/ SampleSize.aspx). This was calculated under an assumption from prior literature that post-MUA mean ROM can be expected to be ~120° \pm 15°, with an anticipated 10% difference in the late MUA group, as well as enrollment ratio of 1, alpha level 0.05, beta 0.2, and power 0.8. We also performed additional a priori retrospective power analyses to see if we could find differences between the 2 groups based on timing of their MUA. Although the utility of a retrospective power analysis is often regarded as uncertain, we used 2-sample *t*-test to compare the 2 group model (Early vs Late), and *F*test for one-way analysis of variance to compare the 4 group model (Groups I-IV), and found a power of 0.471 and 0.415, respectively.

Results

Of the 142 MUA cases eligible for our study, 83 were performed Early (mean 7.1 weeks, range 0.9-11.7) and 59 were performed Late (mean 38.1 weeks, range 12.1-278.1). The substratified groupings yielded 83 Group I manipulations, 34 Group II manipulations, 12 Group III manipulations, and 13 Group IV manipulations. All patients in the Early and Late manipulation groups had similar premanipulation demographics with respect to age, sex, height, weight, BMI, and primary diagnosis. However, the Late group had significantly higher total ROM both prior to their index arthroplasty (pre-TKA total ROM) and prior to their manipulation (pre-MUA total ROM) as compared to the early group (P < .0001). Table 1 summarizes the patient demographic characteristics.

The mean gain in total ROM among all patients from all MUA time points was 21.2° (range -80° to 80° , where a negative value represents a loss of ROM). The mean gain in total ROM within the 83 Early group patients was 24.1° (range -80° to 80°) compared to 17.0° (range -15° to 45°) within the 59 Late group patients (P = .93). The mean gain in flexion within the Early group patients was 22.1°, compared to 15.4° within the late group patients (P = .99). When controlling for all variables in our regression model, including pre-MUA ROM, no significant difference was found in mean gain in total ROM (P = .93) and mean gain in flexion (P = .99) between the Early vs Late groups. This indicates that Early vs Late MUA resulted in comparable gains in flexion and total ROM, and that both groups showed significant improvement in ROM of at least 11° (Table 2).

Further analysis of the 4 substratified groups demonstrated a gain in total ROM of 24.1° in Group I (range -80° to 80°), 17.9° in

Table	2
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Ear	ly	vs	late	MU	A	resul	ts.

Measurements	Early MUA group ^a	Late MUA group ^a
No. of cases	83	59
Mean time to MUA (wk)	7.1	38.1
Mean pre-MUA flexion (°)	75.6	88.5
Mean pre-MUA extension (°)	-4.1	-2.8
Mean pre-MUA total ROM (°)	71.5	85.6
Mean time to follow-up (wk)	44.6	56.3
Mean post-MUA flexion (°)	97.7	103.9
Mean post-MUA extension (°)	-2.0	-1.2
Mean post-MUA total ROM (°)	95.6	102.6
Mean gain in flexion (°) + $(P)^{b}$	22.1	15.4 (0.99)
Mean gain in extension (°)	2.0	1.6
Mean gain in total ROM (°) + $(P)^{b}$	24.1	17.0 (0.93)

MUA, manipulation under anesthesia; BMI, body mass index; TKA, total knee arthroplasty; ROM, range of motion.

 $^{\rm a}\,$ Early Group is defined as MUA within 12 wk post-TKA; Late Group as MUA >12 wk post-TKA.

^b *P*-value as compared to the Early MUA group. *P*-value calculated using regression analysis, adjusted for age at the time of MUA, gender, height, weight, BMI, and pre-MUA total ROM.

Group II (range -15° to 40° , P = .88), 20.8° in Group III (range $0^{\circ}-40^{\circ}$, P = .54), and 11.1° in Group IV (range -7° to 25° , P = .57) (Table 3). Mean gain in flexion was 22.1° in Group I (range -100° to 80°), 16.2° in Group II (range -20° to 45° , P = .92), 20.8° in Group III (range $0^{\circ}-40^{\circ}$, P = .58), and 10.7° in the distant group, Group IV (range -7° to 25° , P = .69). This again shows that early vs later MUA resulted in comparable gains in ROM, no matter how distant the late MUA was performed, and that all groups showed significant improvement in ROM of at least 11° (Table 3).

Twenty-six of 83 Early group (31.0%) and 9 of 59 Late group patients (15.3%) went on to have multiple MUAs. The recommendation for repeat MUA is reserved for patients who gained

Table 3	
MUA subgroupings I-IV results.	

Measurements	Group I (early) ^a	Group II (intermediate) ^a	Group III (late) ^a	Group IV (distant) ^a
No. of cases	83	34	12	13
Mean time to MUA (wk)	7.1	15.5	34.8	100.2
Mean pre-MUA flexion (°)	75.6	86.1	90.2	93.0
Mean pre-MUA extension (°)	-4.1	-3.4	-3.3	-0.8
Mean pre-MUA total ROM (°)	71.5	82.7	86.8	92.2
Mean time to follow-up (wk)	44.6	36.7	59.1	104.9
Mean post-MUA flexion (°)	97.7	102.3	108.5	103.7
Mean post-MUA extension (°)	-2.0	-1.7	-0.8	-0.4
Mean post-MUA total ROM (°)	95.6	100.6	107.7	103.3
Mean gain in flexion $(^{\circ}) + (P)^{b}$	22.1	16.2 (0.92)	18.3 (0.58)	10.7 (0.69)
Mean gain in extension (°)	2.0	1.7	2.5	0.4
Mean gain in total ROM (°) + $(P)^{b}$	24.1	17.9 (0.88)	20.8 (0.54)	11.1 (0.57)

MUA, manipulation under anesthesia; BMI, body mass index; TKA, total knee arthroplasty; ROM, range of motion.

^a Early Group is defined as MUA within 12 wk post-TKA; intermediate as within 13-26 wk; Late as within 27-52 wk; distant as 53 wk or more.

^b *P*-value as compared to the Early MUA group. *P*-value calculated using regression analysis, adjusted for age at time of MUA, gender, height, weight, BMI, and pre-MUA total ROM.

518 **Table 4**

Characteristics of multiple MUA patients.

Measurements	Early MUA ^a	Late MUA ^a	P-value
No. of multiple MUA cases	26	9	.03
% of all cases that were multiple MUA cases	31.0%	15.3%	.03
Mean time to first MUA (d) ^b	50.8	177.1	
Mean pre-MUA flexion (°) ^c	77.2	87.2	
Mean pre-MUA extension (°) ^c	-5.6	-4.2	
Mean pre-MUA total ROM (°) ^c	71.4	83.0	.09
Mean time to follow-up (d)	130.0	175.1	
Mean post-MUA flexion (°) ^c	74.9	88.6	
Mean post-MUA extension (°) ^c	-5.1	-2.8	
Mean post-MUA total ROM (°) ^c	69.8	85.8	.17
% of multiple MUA cases that required ≥3 MUA	11.5%	0%	

MUA, manipulation under anesthesia; TKA, total knee arthroplasty; ROM, range of motion.

Bolded values represent the significant P values.

^a Early vs Late MUA groups were defined based on when these patients had their first manipulation.

^b Mean number of days from date of TKA to date of first MUA.

^c Refers to the preop and postop characteristics of the patient's first MUA only. The postop outcomes of the second and/or subsequent MUA are not recorded.

motion from prior MUA with subsequent loss, and is not intended to attempt increased ROM beyond what was achieved from prior MUA. Only data related to their first manipulation were included in our analysis; the post-MUA outcomes for the second and/or subsequent MUAs were not included in our statistical analysis. Table 4 summarizes the demographics and outcomes for these repeat MUA patients.

The complications in the 83 Early group patients were the following: 1 partial wound dehiscence during the MUA that healed without further issue, 1 revision TKA 8 months after MUA, 1 deep vein thrombosis 10 months after MUA, and 1 deep infection 3 years after TKA. Complications among the 59 Late group patients were the following: 2 deep infections at 7 and 11 months after MUA, 1 arthroscopic lysis of adhesions 14 months after MUA, and 1 revision TKA 3 years after MUA. There were no other complications in either groups, including periprosthetic fracture, ligament damage, or rupture of the extensor mechanism.

To assist in the interpretation and clinical application of our findings, we have presented in a bar graph the percentage of patients in each MUA analysis group according to the degree of their overall change in ROM: no change or worsening of their total ROM ($\leq 0^{\circ}$), improved ROM $\geq 10^{\circ}$, improved ROM $\geq 20^{\circ}$, or improved ROM $\geq 30^{\circ}$ (Fig. 1). Furthermore, we graphed the data of overall gain in ROM according to the timing of MUA with a scatter plot and logarithmic regression line (Fig. 2).



Figure 1. Percentage of patients in each MUA analysis grouping who experienced no change or worse ROM ($\leq 0^{\circ}$), improved ROM $\geq 10^{\circ}$, improved ROM $\geq 20^{\circ}$, or improved ROM $\geq 30^{\circ}$.

Discussion

TKA remains a tremendously effective intervention to alleviate pain and improve function in patients with end-stage degenerative joint disease of the knee [1]. However, the potential adverse outcome of arthrofibrosis continues to challenge and frustrate both patients and surgeons. Several factors may play a role in developing unsatisfactory ROM after TKA, including design of the prosthetic implants, surgical techniques and soft tissue balance, patient factors including preoperative ROM or prior surgery, patient motivation and effort in postoperative rehabilitation, or postoperative complications such as hematoma or infection [2,17-22]. It is well accepted that a minimum ROM of ~90° must be attained to perform basic activities of daily living, with 1 study reporting that knee flexion of 83°, 93°, and 106° is necessary for climbing stairs, sitting, and tying a shoelace, respectively [23]. As such we believe that all nonoperative treatments to attain these baseline ROM goals should be considered before proceeding with more invasive revision surgery where the benefits may be modest and the risks of complication substantial [24-28].

When conservative measures fail to improve stiffness following TKA, MUA is the next noninvasive treatment option generally considered [8,9,28-30]. Although MUA is generally very safe, it is not completely benign, with potential risks of the procedure including periprosthetic fracture, wound complications, hemarthrosis, avulsion of the patella tendon, myositis ossificans, supracondylar femur fracture, or medical complications [8,15,29,31].

Optimal timing for MUA has been debated in the literature for years. It is frequently presumed that MUA is most successful only when performed within 3 months of index TKA and should not be performed beyond then [5,7,8,28,29,31]. Issa et al [7] reviewed 144 MUAs and reported that early manipulations had significantly higher gain in flexion (36.5° vs 17°), final ROM (119° vs 95°), and Knee Society objective and function scores than late manipulations. They also reported that 15 patients who underwent MUA after 26 weeks post-TKA had unsatisfactory clinical outcomes with gain in ROM of 12° (range 5°-20°). This is similar to our findings with 13 patients who underwent much later "distant" manipulation (Group IV, >52 weeks) and had an overall increased ROM of 11.1° (range -7° to 25°). However, our 12 patients who underwent "late" MUA at 26-52 weeks had better overall gains in ROM of 20.8° (range 0°-40°), as compared to Issa et al.

Three systematic reviews by Ghani et al [28], Fitzsimmons et al [8], and Pivec et al [29] reported similar results to Issa et al [7], with mean gain in flexion of nearly 30° (range $22^{\circ}-42^{\circ}$, P > .01), and better results with early manipulation. In a more recent systematic review, Gu et al [32] found that the best results following MUA



Figure 2. Logarithmic regression of total ROM gained after MUA (in degrees) as a function of time since primary TKA (in weeks).

occurred between 4 and 12 weeks postoperatively. Yercan et al [5] reported mean gain in flexion arc of 47°, and early MUA produced significantly better final ROM than MUA after 3 months ($121^{\circ} \pm 11^{\circ}$ vs $112^{\circ} \pm 16^{\circ}$; P = .021). This contrasts with our study in that our gain of flexion in our early group was comparatively modest at 22.1° (range -80° to 80°). Moreover, the final flexion and overall ROM in our 83 Early group patients (97.7° and 95.6°, respectively) was less than our composite 59 Late group patients (103.9° and 102.6°, respectively). This held true for all the subgroups, with the early Group I MUA patients having lower final flexion and ROM than the later Groups II-IV. Although the early MUA Group I showed higher gains in ROM compared to each of the 3 later Groups II-IV, when pre-MUA ROM was controlled for, there were no significant difference in gains in ROM. This may be expected because Group I had lower ROM before their index TKA as well as before their MUA than the later subgroups, giving Group I a greater range for potential gains in ROM. However, it should be noted that there could be clinical significance for the final ROM achieved by the early group as it did not achieve that expected to be adequate for all basic activities of daily living [23].

Our encouraging findings for patients who underwent MUA greater than 3 months after TKA, or even greater than 1 year from TKA, are consistent with several other studies that also reported equivalent results when MUA was performed after 3 months from index TKA [4,10-12,33]. As shown, after controlling for pre-MUA ROM and the other variables per our regression model, we found no significant difference in either flexion gains or total ROM gains when comparing each of the 3 late groups to the early Group I. Total ROM gain *P*-values were .88 for Group II. .54 for Group III. and .57 for Group IV. Flexion gain P-values were .92 for Group II, .58 for Group III, and .69 for Group IV. This shows that Early vs Late MUA resulted in comparable gains in ROM, no matter how distant the late MUA was performed, and that all groups showed significant improvement in ROM of at least 10° (Table 3). The results of this study suggest that late MUA is a safe and effective treatment option without additional interventions such as open or arthroscopic lysis of adhesions; this is important because open or arthroscopic lysis of adhesions can potentially create additional scar tissue as a result of further trauma to the joint, resulting in even more stiffness.

We have presented these data in a unique format in Figure 1 to aid in clinical decision-making and patient counseling. For example, using the data demonstrated in Figure 1 a provider can surmise that 69% of patients who underwent MUA at greater than a year (Group IV, greater than 52 weeks) after TKA achieved an improvement in their overall ROM of 10°-20°, or that 92% of patients who underwent MUA in the range of 6-12 months (Group III, 26-52 weeks) achieved an improvement in their overall ROM of 10°-20°. Interestingly, there was a small percentage of patients in each grouping who experienced no change or worse ROM ($<0^{\circ}$) following MUA. It is important to understand that ROM after TKA is multifactorial, and is influenced by surgical technique, patient motivation, and the biology of healing. The surgeon has control over surgical technique. The patient has control over his or her motivation to participate in physical therapy. Neither the surgeon nor the patient has control over the biology of healing and the degree to which scar tissue forms. The variability in patient motivation and biology of healing confounds interpretation of these data. Decision-making remains individualized and results are unpredictable, that is, a bell shaped curve. Such interpretation of our data, and similar interpretation of future studies with larger sample size, may guide surgeons in their clinical decision-making.

There are several limitations to this study, including those inherent to being a retrospective review from a single institution. Additionally, given that our study aggregated the data of 6 surgeons

with different practice patterns, we acknowledge that the incidence of and timing of MUA is influenced by the individual surgeon's threshold for recommending and performing MUA. Our sample size is larger than most reports in the literature and seemed adequate from our power analysis; however, a larger sample size might find associations with the variables we excluded from our final analysis. As noted previously, these data that were gathered but not included in the analysis were operative side, history of knee surgery prior to TKA, history of infection or trauma, history of chronic pain or opioid use, prosthesis type, surgeon, and any complications including wound issues, infection, venous thromboembolism, or medical issues (such as postoperative intensive care unit stay, myocardial infarction, stroke, etc.). Moreover, a larger sample size, particularly with MUAs performed greater than 6 months and greater than 1 year following TKA, may better delineate the overarching effect of timing of MUA on overall ROM gained. Our logarithmic regression in Figure 2 suggests that there may be an initial decrease in efficacy after the first 2 months, but there may be a relatively modest but still clinically relevant and worthwhile improvement when MUA is performed at times very distant from a TKA. We also did not include Knee Society Score or other patientreported outcome measures, as these were not consistently available in the medical record.

Future prospective studies with larger sample size, particularly including patients who undergo MUA at time points later than typically considered to be effective, may further elucidate the efficacy of MUA of stiff TKA performed greater than 6 months or even greater than 1 year after TKA.

Conclusions

Stiffness after TKA remains a challenging problem for surgeons and patients. MUA is a relatively safe and reliable option to improve ROM and potentially avoid more invasive revision surgery. However, the optimal and acceptable timing to attempt manipulation has continued to be uncertain in the literature. Although we subjectively agree with many authors that feel early manipulation within 3 months after TKA may provide better results than later manipulation, the results of this paper demonstrate that MUA performed beyond 3 months, and even beyond 1 year, may still be safe and effective. As such, we recommend surgeons consider employing MUA in select patients who present with inadequate ROM beyond 3 months or longer after their index TKA, as this may improve ROM to within an acceptable clinical range and avoid the risks and morbidity of revision surgery.

References

- Consensus NIH, Statements S. NIH Consensus Statement on total knee replacement. NIH Consens State Sci Statements 2003;20(1):1.
- [2] Daluga D, Lombardi AV, Mallory TH, Vaughn BK. Knee manipulation following total knee arthroplasty. Analysis of prognostic variables. J Arthroplasty 1991;6(2):119.
- [3] Mauerhan DR, Mokris JG, Ly A, Kiebzak GM. Relationship between length of stay and manipulation rate after total knee arthroplasty. J Arthroplasty 1998;13(8):896.
- [4] Scranton PE. Management of knee pain and stiffness after total knee arthroplasty. J Arthroplasty 2001;16(4):428.
- [5] Yercan HS, Sugun TS, Bussiere C, Ait Si Selmi T, Davies A, Neyret P. Stiffness after total knee arthroplasty: prevalence, management and outcomes. Knee 2006;13(2):111.
- [6] Rubinstein RA, DeHaan A. The incidence and results of manipulation after primary total knee arthroplasty. Knee 2010;17(1):29.
- [7] Issa K, Banerjee S, Kester MA, Khanuja HS, Delanois RE, Mont MA. The effect of timing of manipulation under anesthesia to improve range of motion and functional outcomes following total knee arthroplasty. J Bone Joint Surg Am 2014;96(16):1349.
- [8] Fitzsimmons SE, Vazquez EA, Bronson MJ. How to treat the stiff total knee arthroplasty?: a systematic review. Clin Orthop Relat Res 2010;468(4):1096.

- [9] Issa K, Kapadia BH, Kester M, Khanuja HS, Delanois RE, Mont MA. Clinical, objective, and functional outcomes of manipulation under anesthesia to treat knee stiffness following total knee arthroplasty. J Arthroplasty 2014;29(3):548.
- [10] Yeoh D, Nicolaou N, Goddard R, et al. Manipulation under anaesthesia post total knee replacement: long term follow up. Knee 2012;19(4):329.
- [11] Keating EM, Ritter MA, Harty LD, et al. Manipulation after total knee arthroplasty. J Bone Joint Surg Am 2007;89(2):282.
- [12] Namba RS, Inacio M. Early and late manipulation improve flexion after total knee arthroplasty. J Arthroplasty 2007;22(6 Suppl):58. [13] Stamos V, Bono JV. The stiff knee. In: Scuderi G, Tria A, editors. Surgical
- techniques in total knee arthroplasty. New York, NY: Springer-Verlag: 2002. p. 687.
- [14] Stamos VP, Borchard KS, Bono JV. Management of the stiff total knee arthroplasty. In: Bono IV. Scott RD. editors. Revision total knee arthroplasty. New York, NY: Springer-Verlag; 2018. p. 357.
- [15] Fox JL, Poss R. The role of manipulation following total knee replacement. | Bone Joint Surg Am 1981;63(3):357.
- [16] Smith E, Banerjee S, Bono JV. Supracondylar femur fracture after knee manipulation: a report of 3 cases. Orthopedics 2009;32:1.
- [17] Ritter MA, Lutgring JD, Davis KE, Berend ME. The effect of postoperative range of motion on functional activities after posterior cruciate-retaining total knee arthroplasty. J Bone Joint Surg Am 2008;90(4):777.
- [18] Gatha NM, Clarke HD, Fuchs R, Scuderi GR, Insall JN. Factors affecting postoperative range of motion after total knee arthroplasty. J Knee Surg 2004:17(4):196.
- [19] Kotani A, Yonekura A, Bourne RB. Factors influencing range of motion after contemporary total knee arthroplasty. J Arthroplasty 2005;20(7):850.
- [20] Parsley BS, Engh GA, Dwyer KA. Preoperative flexion. Does it influence postoperative flexion after posterior-cruciate-retaining total knee arthroplasty? Clin Orthop Relat Res 1992;(275):204.

- [21] Schurman DJ, Parker JN, Ornstein D. Total condylar knee replacement. A study of factors influencing range of motion as late as two years after arthroplasty. | Bone Joint Surg Am 1985;67(7):1006.
- [22] Dennis DA, Komistek RD, Scuderi GR, Zingde S. Factors affecting flexion after total knee arthroplasty. Clin Orthop Relat Res 2007;464:53.
- [23] Laubenthal KN, Smidt GL, Kettelkamp DB, Anonymous. A quantitative analysis of knee motion during activities of daily living. Phys Ther 1972;52(1):34.
- [24] Kim GK, Mortazavi SMJ, Parvizi J, Purtill JJ. Revision for stiffness following TKA: a predictable procedure? Knee 2012:19(4):332.
- [25] Kim J, Nelson CL, Lotke PA. Stiffness after total knee arthroplasty. Prevalence of the complication and outcomes of revision. J Bone Joint Surg Am 2004;86-A(7):1479.
- [26] Nelson CL, Kim J, Lotke PA. Stiffness after total knee arthroplasty. J Bone Joint Surg Am 2005:87(Pt 2):264
- [27] Hartman CW, Ting NT, Moric M, Berger RA, Rosenberg AG, Della Valle CJ. Revision total knee arthroplasty for stiffness. J Arthroplasty 2010;25(Suppl. 6):62.
- [28] Ghani H, Maffulli N, Khanduja V. Management of stiffness following total knee arthroplasty: a systematic review. Knee 2012;19(6):751.
- [29] Pivec R, Issa K, Kester M, Harwin SF, Mont MA. Long-term outcomes of MUA for stiffness in primary TKA. J Knee Surg 2013;26(6):405.
- Mohammed R, Syed S, Ahmed N. Manipulation under anaesthesia for stiffness [30] [30] Montallined K, Syed S, Allined N, Manpulation under anacosta for statistics of following knee arthroplasty. Ann R Coll Surg Engl 2009;91(3):220.
 [31] Esler CN, Lock K, Harper WM, Gregg PJ. Manipulation of total knee replacements. Is the flexion gained retained? J Bone Joint Surg Br 1999;81(1):27.
- [32] Gu A, Michalak AJ, Cohen JS, Almeida ND, McLawhorn AS, Sculco PK. Efficacy of manipulation under anesthesia for stiffness following total knee arthroplasty: a systemic review. J Arthroplasty 2018;33:1598.
- [33] Ipach I, Mittag F, Lahrmann J, Kunze B, Kluba T. Arthrofibrosis after TKA influence factors on the absolute flexion and gain in flexion after manipulation under anaesthesia. BMC Musculoskelet Disord 2011;12:184.