



Contents lists available at ScienceDirect

Asia-Pacific Journal of Sports Medicine, Arthroscopy, Rehabilitation and Technology

journal homepage: www.ap-smart.com

Original Article

Initiating range of motion exercises within 24 hours following total knee arthroplasty affects the reduction of postoperative pain: A randomized controlled trial

Kentaro Iwakiri ^{a,*}, Yoichi Ohta ^b, Yuuki Shibata ^a, Yukihide Minoda ^b, Akio Kobayashi ^a, Hiroaki Nakamura ^b

^a Department of Orthopaedic Surgery, Shiraniwa Hospital Joint Arthroplasty Center, 6-10-1 Shiraniwadai Ikoma-city, Nara, 630-0136, Japan

^b Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, 1-4-3 Asahi-machi Abeno-ku Osaka-city, Osaka, 545-8585, Japan

ARTICLE INFO

Article history:

Received 14 December 2019

Received in revised form

18 March 2020

Accepted 31 March 2020

ABSTRACT

Background: Postoperative limitations in the range of motion (ROM) after TKA may occur occasionally and restrict a patient's ADL. Although ROM exercise is a means of increasing the ROM after TKA, the optimal time of initiating ROM exercise is still unclear. The purpose of this study is to examine different initiation timings of postoperative ROM exercises after TKA and to compare the results in terms of postoperative pain, swelling, and ROM improvement to determine the optimal time of initiating ROM exercises following TKA.

Methods: This was a prospective, single-center, single-blinded randomized controlled trial involving 109 patients scheduled for unilateral TKA. All patients underwent the physiotherapist assisted passive and active same rehabilitation program that only differed in the starting time of ROM exercise on postoperative day 1 or day 7. Postoperative assessment was performed with all attending personnel blinded to group assignment. Visual analog scale (VAS) of pain, ROM, thigh swelling, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and adverse outcomes were compared between groups on postoperative days within 2 years after surgery.

Results: VAS scores during the postoperative period from 18 to 72 h were significantly lower in the group with starting time of ROM exercise on postoperative day 1. The ROM, laboratory data, thigh girth, WOMAC and the incidence of complications did not differ between the two groups at any postoperative time-point.

Conclusions: The results of this study suggested that ROM exercises beginning in the early postoperative stage are advantageous in reducing the postoperative pain after TKA.

© 2020 Asia Pacific Knee, Arthroscopy and Sports Medicine Society. Published by Elsevier (Singapore) Pte Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Total knee arthroplasty (TKA) is an effective procedure for alleviating pain and improving activities of daily living (ADL) in patients with end-stage osteoarthritis of the knee.¹ However, postoperative limitations in the range of motion (ROM) may occur occasionally and restrict a patient's ADL.^{1,2} The ROM after TKA is

reported to be strongly influenced by the preoperative ROM.^{3,4} It has also been reported that the postoperative ROM is influenced by nerve block, changes in ligament balance in the knee joint, accurate implant positioning and by the implant design adopted^{4–10} and the improved ROM after TKA affect the patient function and satisfaction.¹¹

Although ROM exercise is known to be a means of increasing the ROM after TKA^{1,12} and starting early rehabilitation within 24 h have benefits for the early recovery,^{13,14} the optimal time of initiating only ROM exercise has not been discussed in the literature; it still remains to be unclear and varies per institution. In particular, it has been reported that local inflammation and swelling may occur in an early stage after TKA^{15–17}; therefore, we speculated and

* Corresponding author.

E-mail addresses: kenpiecekenpiece@yahoo.co.jp (K. Iwakiri), ohta@msic.med.osaka-cu.ac.jp (Y. Ohta), nostalgie1901@gmail.com (Y. Shibata), yminoda@msic.med.osaka-cu.ac.jp (Y. Minoda), ak@med.osaka-cu.ac.jp (A. Kobayashi), hnakamura@med.osaka-cu.ac.jp (H. Nakamura).

hypothesized that ROM exercises beginning in the early postoperative stage are disadvantageous in restoring the ROM and relieving pain postoperatively, for eliciting local inflammation and swelling. However, there has been no report that denied the propriety of ROM exercise during the early postoperative stage.

In this study, we aimed to examine different initiation timings of postoperative ROM exercises after TKA and to compare the results in terms of postoperative pain, swelling, and ROM improvement to determine the optimal time of initiating ROM exercises following TKA.

Materials & methods

This study was a prospective, single-center, single-blinded randomized controlled trial. The study protocol was approved by the institutional review board. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The trial was registered as a randomized controlled trial with the University Hospital Medical Information Network (UMIN) registration number UMIN000020298.

Study population

This study focused on patients who underwent unilateral TKAs from March 2016 to August 2017. Patients with renal insufficiency, a history of cardiac disease, deep vein thrombosis, or surgery of the knee joint were excluded, and 120 patients were eligible for the study. We excluded patients who were scheduled for simultaneous or staged bilateral TKA ($n = 10$) or for revision TKA ($n = 1$). Finally, 109 patients (89 women and 20 men) were included for the study. The flowchart for patient selection for the study is presented in Fig. 1.

Interventions

Before admission, the patients were randomly divided into 2 groups using the envelope method. (1) patients who started the postoperative ROM exercises on postoperative day 1 (Day 1 group:

$n = 55$) and (2) patients who started the postoperative ROM exercises on postoperative day 7 (Day 7 group: $n = 54$). A staff member who did not participate in this study performed the envelope selection. All patients underwent the physiotherapist assisted passive and active hospital-based rehabilitation program that only differed in the starting time of ROM exercise until 3 months postoperatively. The rehabilitation program consisted of walking with a walker starting at day 1 after TKA and walking with a T-shaped cane and climbing and descending stairs starting at day 7 after TKA. Patients in Day 7 group did not have any active and passive ROM exercises until postoperative day 6. The operating surgeon, ward nursing staff, and data collectors, excluding patients and physiotherapists, remained blinded for the whole duration of the trial.

Both groups performed flexion and extension of the knee joint on the affected side (30-min training by a physiotherapist in each day, combined with permitted self-training), but with different starting time (1 or 7 days after TKA).

Perioperative medications

The following postoperative analgesic medications were administered in both groups. A nonsteroidal anti-inflammatory drug (200 mg of celecoxib; Astellas Pharma Inc., Tokyo, Japan) was taken twice a day for the first 7 days; for the remaining 14 days, the dose was decreased to 100 mg of celecoxib. The diclofenac sodium suppository (25 mg of Voltaren; Novartis, Tokyo, Japan) was used for rescue analgesia.

No thromboprophylaxis was provided except for lower-leg stocking and foot pump.

Surgery

All surgery were performed by one of the two surgeons (KI and AK) with a medial parapatellar approach under general anesthesia. A pneumatic tourniquet was treated in all patients with the pressure of 300 mmHg during surgery. The implants used were cemented cruciate-substituting devices (Physio Knee; Kyocera, Kyoto, Japan/GMK Sphere; Medacta, Switzerland) for 50/19 knees and cemented posterior-stabilized devices (Vanguard Rotating

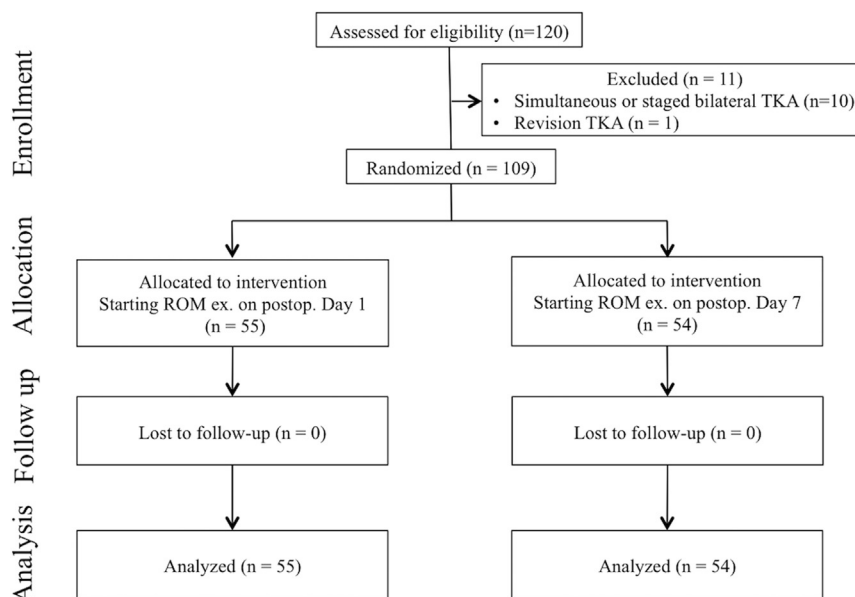


Fig. 1. CONSORT (consolidated Standards of Reporting Trials) flow diagram, showing the flow of patients through each stage of the trial.

Platform High Flex; Biomet, Warsaw, IN) for 40 knees [Table 1].

Intraoperative periarticular cocktail injection was used for the postoperative pain relief that Iwakiri et al. have previously reported.^{18,19} Tranexamic acid (Transamin; Daiichi-Sankyo, Tokyo, Japan) was used intravenously at 1 g before surgery and into the joint capsule at a dose of 2 g after the suture of the joint capsule as a prophylaxis for perioperative bleeding.^{18,19} No drainage tube was used. To alleviate postoperative swelling, cryotherapy was treated at 5 °C for 72 h immediately after surgery, and the patients were instructed to wear the cryotherapy device whenever on bed.

Outcome measurements

Primary outcomes

The primary outcomes included the visual analog pain score (VAS) at rest (preoperatively, every 3 h from 3 to 24 h from time zero immediately after surgery, every 8 h from 24 to 72 h, and on postoperative days 7 and 14).

The VAS score was shown from 0 mm (indicating no pain) to 100 mm (indicating extreme pain) in 10-mm increments. The amount of using diclofenac sodium suppository for the rescue analgesia was also measured.

Secondary outcomes

The secondary outcome measures evaluated were the laboratory data (C-reactive protein, creatinine kinase, hemoglobin level: preoperatively and on postoperative days 1, 4, 7, and 14; D-dimer: preoperatively and on postoperative days 7 and 21), the estimated blood loss, the ROM of the knee (preoperatively and on postoperative days 7, 14, 21, 28 and 3 months, and 1–2 year), and thigh swelling (two points; thigh circumference at the superior border of the patella and 5-cm proximal from the superior border of the patella: preoperatively and on postoperative days 7, 14, and 21), the WOMAC Index (preoperatively and 3 months and 1–2 year postoperatively),²⁰ and adverse complications, including wound complications, surgical site infection, peroneal nerve palsy, and deep

venous thrombosis, during this study. The estimated blood loss was calculated using the Nadler formula.²¹ The ratio of the postoperative thigh circumference divided by the preoperative thigh circumference was calculated for comparing the thigh swelling between two groups.^{18,19}

Sample size

We considered a reduction of 20 points in the VAS pain scale score to be the relevant minimal clinically important difference after TKA. We needed 43 patients per each group to detect a mean difference and standard deviation of 20 ± 33 points in the VAS pain score with a two-sided 5% significance level and 80% power.^{18,22}

Statistical analysis

To analyze the primary and secondary outcomes, the Student T test for continuous variables and the chi-square test for categorical variables were used for the comparison between two groups. The p value of less than 0.05 was considered to indicate a statistically significant difference. SPSS statistics version 22.0 (IBM Corp., US) was used for all statistical analyses.

Results

The demographic characteristics of the patients in both groups are summarized in Table 1. The mean age of all patients at operation was 75.3 ± 6.8 years. The preoperative diagnosis was osteoarthritis of the knee in 107 patients and spontaneous osteonecrosis of the knee in two patients. Between the two groups, there was no significant difference in age, sex, BMI, diagnosis, preoperative laboratory data, preoperative status (VAS score at rest, preoperative ROM, and WOMAC), Hip-Knee-Ankle angle²³ or operative status (implant, estimated blood loss, and duration of surgery).

Primary outcomes

The VAS scores at rest from 18 to 72 h postoperatively (except

Table 1
Patient Demographics and baseline characteristics.

	ROM Day1 group (55 patients, 55knees)	ROM Day 7 group (54 patients, 54knees)	p value
Demographic characteristics			
Age* (yr)	75.0 ± 7.3	75.6 ± 6.2	0.64†
Female/Male	45/10	44/10	0.71‡
Right/Left	34/21	24/30	0.26‡
Height* (cm)	154.5 ± 8.7	151.8 ± 7.1	0.06†
Weight* (kg)	59.1 ± 13.7	58.3 ± 10.8	0.88†
Body mass index* (kg/m ²)	24.5 ± 4.2	25.2 ± 3.7	0.28†
Osteoarthritis/spontaneous osteonecrosis	54/1	53/1	–
Hip-Knee-Ankle angle* (deg)	7.4 ± 5.5	9.4 ± 7.6	0.10†
Preop. Laboratory values			
Hemoglobin* (g/dl)	13.0 ± 1.4	13.1 ± 1.4	0.54†
C-reactive protein* (mg/dl)	0.30 ± 0.88	0.26 ± 0.72	0.76†
Creatinine Kinase* (mg/dl)	102.8 ± 48.1	112.2 ± 59.2	0.39†
D-dimer* (mg/ml)	1.5 ± 1.3	1.7 ± 1.6	0.75†
Preop. status			
Preoperative VAS score at rest*	15.7 ± 24.2	9.5 ± 15.7	0.11†
Preoperative flexion angle* (deg)	125.7 ± 13.1	123.7 ± 14.3	0.21†
Preoperative extension angle* (deg)	–8.6 ± 6.0	–10.3 ± 4.9	0.11†
Preoperative WOMAC score*	38.3 ± 20.9	43.7 ± 16.1	0.16†
Operative status			
CS/PS	35/20	34/20	0.99‡
Estimated blood loss* (ml)	494.6 ± 282.2	466.1 ± 305.4	0.66†
Duration of surgery* (min)	82.0 ± 21.8	78.2 ± 14.3	0.39†

* The values are given as the mean and standard deviation. † The p values were determined with the Student T-test. ‡ The p values were determined with the chi-square test.

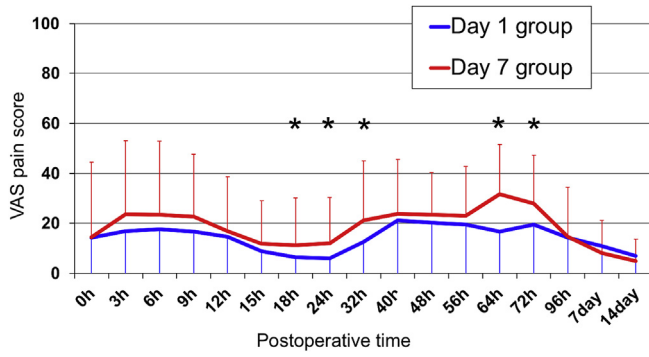


Fig. 2. Pain VAS score at rest (mean and standard deviation) following total knee arthroplasty in the two groups. Time zero is defined as the time immediately after surgery in the recovery room. **p* < 0.05.

from 40 to 56h) were significantly lower in the Day 1 group, with starting time of ROM exercise on postoperative day 1 (*p* < 0.05) (Fig. 2). There were no statistically significant differences in the other primary outcomes between the two groups (including total number of rescue analgesia by diclofenac sodium suppository in Table 2).

Secondary outcomes

There were no statistically significant differences in all secondary outcome between the two groups (including laboratory data in Table 2, and ROM and thigh swelling in Figs. 3 and 4). There were no cases with surgical site infection, peroneal nerve palsy or deep venous thrombosis in either group (Table 2).

Table 2
Primary & secondary outcomes.

	ROM Day 1 group (55 patients, 55 knees)	ROM Day 7 group (54 patients, 54 knees)	<i>p</i> value
Postop. Laboratory values: Hemoglobin (g/dl)*			
Day 1	11.8 ± 1.3	11.8 ± 1.2	0.6
Day 4	11.7 ± 1.5	11.8 ± 1.2	0.42
Day 7	11.5 ± 1.5	11.7 ± 1.4	0.3
Day 14	11.6 ± 1.4	11.6 ± 2.0	0.79
Postop. Laboratory values: C-reactive protein (mg/dl)*			
Day 1	0.68 ± 0.83	0.65 ± 0.76	0.9
Day 4	5.78 ± 3.63	5.48 ± 3.87	0.78
Day 7	1.48 ± 1.08	1.77 ± 1.78	0.32
Day 14	0.40 ± 0.41	0.50 ± 0.48	0.37
Postop. Laboratory values: Creatinine Kinase (mg/dl)*			
Day 1	107.3 ± 33.3	115.3 ± 47.3	0.36
Day 4	92.3 ± 40.7	107.2 ± 54.4	0.11
Day 7	68.1 ± 36.8	64.8 ± 30.7	0.63
Day 14	59.2 ± 24.7	56.6 ± 24.3	0.73
Postop. Laboratory values: D-dimer (mg/mL)*			
Day 7	7.1 ± 3.5	6.8 ± 3.2	0.34
Day 21	7.4 ± 3.0	8.6 ± 5.4	0.14
Total number of rescue analgesia by suppositories*			
Day 0 to Day 2	0.71 ± 1.49	1.02 ± 2.11	0.37
Postop. WOMAC score*			
3 months	19.1 ± 16.8	15.0 ± 10.3	0.35†
1 year	15.6 ± 16.3	13.4 ± 8.6	0.56†
2 years	13.3 ± 13.1	12.5 ± 12.7	0.76†
Complications			
Surgical site infection‡	0	0	–
Wound problem‡	0	0	–
Transient peroneal nerve palsy‡	0	0	–
Deep vein thrombosis‡	0	0	–

* The values are given as the mean and standard deviation. † The *p* values were determined with the Student T-test. ‡ The values are expressed as the number of patients.

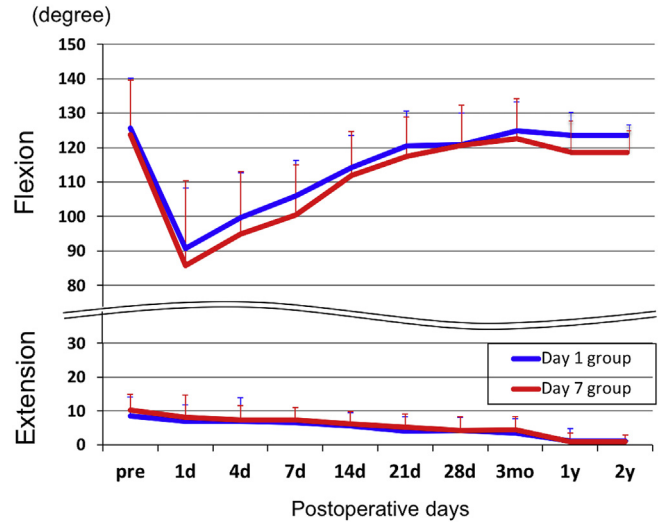


Fig. 3. Knee flexion and extension (mean and standard deviation) following total knee arthroplasty in the two groups.

Discussion

The remarkable findings of this study were that the postoperative pain was significantly reduced in patients who started the ROM exercises on postoperative day 1 (Day 1 group) than in those who started on postoperative day 7 (Day 7 group), and the initiating early ROM exercise within 24 h did not adversely affect swelling, ROM or WOMAC score after surgery.

It has been reported that limited ROM following TKA may

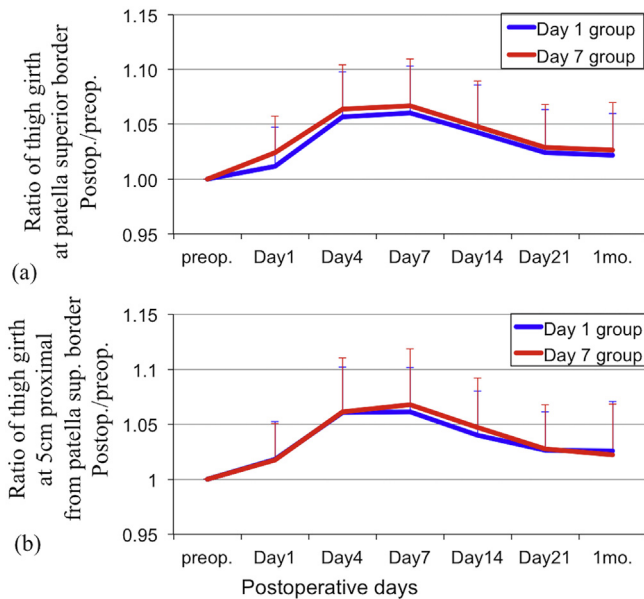


Fig. 4. (a) Ratio of the thigh circumference at the patella superior border following total knee arthroplasty. (b) Ratio of the thigh circumference at 5-cm proximal from the patella superior border following total knee arthroplasty.

restrict ADL and decrease patient satisfaction.^{1,2} Therefore, having a sufficient ROM following TKA, as well as alleviating pain, is a very important factor in increasing patient satisfaction.

The ROM after TKA is reported to be largely influenced by the preoperative ROM.^{3,4} Especially, it is considered difficult to achieve a marked improvement in ROM postoperatively in patients who have a poor ROM preoperatively. However, measures available to achieve sufficient improvement in ROM include proper implant selection, adjustment of soft tissue balance, use of navigation, removal of bone spurs, adequate implant positioning, rehabilitation methods, and continuous passive motions.^{4–10,24–27} It has also been reported that initiation of physiotherapy in an early postoperative stage leads to improvement in postoperative motor function.²⁸ However, there has been no report about the optimal time to initiate the only ROM exercise. Given that local inflammation and swelling reportedly occur during the early postoperative stage, we speculated that ROM exercise initiated during the early postoperative stage may induce further inflammation and swelling of the local tissue around the knee joint, resulting in adverse effects on the postoperative process of restoration of ROM.^{15–17} However, in this randomized controlled trial, thigh swelling, postoperative ROM and WOMAC score were not adversely affected in the group with an early start of postoperative ROM exercise (on postoperative day 1) compared with the group with ROM exercises started on postoperative day 7.

The postoperative pain was significantly decreased in the group with ROM exercise starting on postoperative day 1. Postoperative adhesions are generally known to start immediately after surgery and end on postoperative day 7.^{29,30} Surgically damaged tissue emits fibrin, macrophages, and fibroblasts in the recovery process of inflammation. Fibroblasts begin to form fibrous tissue in postoperative day 2–3, followed by the appearance of angiogenesis and neuroblasts, and fibrous tissue organize and adhere in postoperative day 5–7. Starting ROM exercise within 24 h after surgery might have prevented the occurrence of postoperative adhesion around the knee joint, contributing to amelioration of pain. All the participants in this study underwent intraoperative multimodal periarticular injection for potent analgesic effect, lasting for about

48–72 h.^{18,19,31} Therefore, early postoperative pain may be less susceptible by the early ROM exercise.

According to the results of this study, the initiating ROM exercise within 24 h after surgery is recommended for the postoperative pain relief.

Study limitations

There are several limitations to this study. First, because intraoperative multimodal periarticular injection, intra-articular and intravenous tranexamic acid, and post-operative cryotherapy were administered to prevent postoperative swelling and blood loss and to reduce the postoperative pain, the mild degree of swelling may have made it difficult to detect the effect of ROM exercise. Second, the patients were not blinded to the timing of initiating the ROM exercise because of the characteristics of this study. There might be any mental conflict existed between the groups. Third, there might be a bias in measuring the VAS score at each point by several nurses. Fourth, there is a report about Minimal Clinically Important Difference (MCID) as a clinical significance of VAS score.³² The difference in VAS score in this study may not be clinically significant from the MCID perspective. The advantage of the study was that the operating surgeons, ward nursing staff, and data collectors remained blinded to the groups' status during the whole study duration.

Conclusions

Our data show that there was no difference in swelling or postoperative range of knee motion between patients who started ROM exercises on postoperative day 1 and those who started on postoperative day 7. However, postoperative pain was significantly reduced in patients who started the ROM exercises on postoperative day 1 than in those who started on postoperative day 7, indicating the benefit of starting ROM exercises during the early postoperative stage. The ROM exercises beginning in the early postoperative stage might be advantageous in reducing the postoperative pain after TKA.

Declaration of competing interest

All authors have no conflicts of interest relevant to this article.

Acknowledgements

All authors have no conflict of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.asmart.2020.03.003>.

References

- Larsen K, Hansen TB, Søballe K, Kehlet H. Patient-reported outcome after fast-track knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc.* 2012 Jun;20(6):1128–1135.
- Becker R, Doring C, Denecke A, Brosz M. Expectation, satisfaction and clinical outcome of patients after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc.* 2011 Sep;19:1433–1441.
- 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. *J Bone Joint Surg Am.* 1985 Sep;67(7):1006–1014.
- Lampe F, Marques CJ, Fiedler F, Sufi-Siavach A, Carita AI, Matziolis G. Patient-specific and intra-operatively modifiable factors assessed by computer

- navigation predict maximal knee flexion one year after TKA. *Knee Surg Sports Traumatol Arthrosc.* 2016 Nov;24(11):3457–3465.
5. Brennan PT, Villa JM, Rossi MD, Sanchez-Gonzalez MA, Lavernia CJ. Rehabilitation outcomes for total knee arthroplasties: continuous adductor canal block versus continuous femoral nerve block. *Geriatr Orthop Surg Rehabil.* 2018 Mar 19:9.
 6. Lützner J, Hartmann A, Lützner C, Kirschner S. Is range of motion after cruciate-retaining total knee arthroplasty influenced by prosthesis design? A prospective randomized trial. *J Arthroplasty.* 2014 May;29(5):961–965.
 7. Meftah M, Ranawat AS, Ranawat CS. Safety and efficacy of a rotating-platform, high-flexion knee design three- to five-year follow-up. *J Arthroplasty.* 2012 Feb;27(2):201–206.
 8. Fritzsche H, Beyer F, Postler A, Lützner J. Different intraoperative kinematics, stability, and range of motion between cruciate-substituting ultracongruent and posterior-stabilized total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc.* 2018 May;26(5):1465–1470.
 9. Ahn JH, Back YW. Comparative study of two techniques for ligament balancing in total knee arthroplasty for severe varus knee: medial soft tissue release vs. bony resection of proximal medial tibia. *Knee Surg Relat Res.* 2013 Mar;25(1):13–18.
 10. Watanabe T, Muneta T, Sekiya I, Banks SA. Intraoperative joint gaps affect postoperative range of motion in TKAs with posterior-stabilized prostheses. *Clin Orthop Relat Res.* 2013 Apr;471(4):1326–1333.
 11. Van Onsem S, Verstraete M, Dhont S, Zwaenepoel B, Van Der Straeten C, Victor J. Improved walking distance and range of motion predict patient satisfaction after TKA. *Knee Surg Sports Traumatol Arthrosc.* 2018 Nov;26(11):3272–3279.
 12. Ibrahim MS, Khan MA, Nizam I, Haddad FS. Peri-operative interventions producing better functional outcomes and enhanced recovery following total hip and knee arthroplasty: an evidence-based review. *BMC Med.* 2013 Feb;11:37.
 13. Labraca NS, Castro-Sanchez AM, Mataran-Péñarrocha GA, Arroyo-Morales M, Sanchez-Joya Mdel M, Moreno-Lorenzo C. Benefits of starting rehabilitation within 24 hours of primary total knee arthroplasty: randomized clinical trial. *Clin Rehabil.* 2011 Jun;25(6):557–566.
 14. Munin MC, Rudy TE, Glynn NW, Crosssett LS, Rubash HE. Early inpatient rehabilitation after elective hip and knee arthroplasty. *J Am Med Assoc.* 1998 Mar;279(11):847–852.
 15. Hunt TK, Rabkin J, von Smitten K. Effects of edema and anemia on wound healing and infection. *Curr Stud Hematol Blood Transfus.* 1986;53:101–113.
 16. Abramson DI, Chu LS, Tuck Jr S, Lee SW, Richardson G, Levin M. Effect of tissue temperatures and blood flow on motor nerve conduction velocity. *J Am Med Assoc.* 1966 Dec;198:1082–1088.
 17. Matsen III FA, Questad K, Matsen AL. The effect of local cooling on postfracture swelling. A controlled study. *Clin Orthop.* 1975;109:201–206.
 18. Iwakiri K, Minami Y, Ohta Y, Kobayashi A. Effect of periarticular morphine injection for total knee arthroplasty: a randomized, double-blind trial. *J Arthroplasty.* 2017 Jun;32(6):1839–1844.
 19. Iwakiri K, Ohta Y, Kobayashi A, Minoda Y, Nakamura H. Local efficacy of periarticular morphine injection in simultaneous bilateral total knee arthroplasty: a prospective, randomized, double-blind trial. *J Arthroplasty.* 2017 Dec;32(12):3637–3642.
 20. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities osteoarthritis Index (WOMAC): a review of its utility and measurement properties. *Arthritis Rheum.* 2001 Oct;45(5):453–461.
 21. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. *Surgery.* 1962 Feb;51(2):224–232.
 22. Tsukada S, Wakui M, Hoshino A. Postoperative epidural analgesia compared with intraoperative periarticular injection for pain control following total knee arthroplasty under spinal anesthesia: a randomized controlled trial. *J Bone Joint Surg Am.* 2014 Sep;96(17):1433–1438.
 23. Sheehy L, Felson D, Zhang Y, et al. Does measurement of the anatomic axis consistently predict hip-knee-ankle angle (HKA) for knee alignment studies in osteoarthritis? Analysis of long limb radiographs from the multicenter osteoarthritis (MOST) study. *Osteoarthritis Cartilage.* 2011 Jan;19(1):58–64.
 24. Chesham RA, Shanmugam S. Does preoperative physiotherapy improve postoperative, patient-based outcomes in older adults who have undergone total knee arthroplasty? A systematic review. *Physiother Theory Pract.* 2017 Jan;33(1):9–30.
 25. Li D, Yang Z, Kang P, Xie X. Home-based compared with hospital-based rehabilitation program for patients undergoing total knee arthroplasty for osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *Am J Phys Med Rehabil.* 2017 Jun;96(6):440–447.
 26. Hiyama Y, Kamitani T, Wada O, Mizuno K, Yamada M. Effects of group-based exercise on range of motion, muscle strength, functional ability, and pain during the acute phase after total knee arthroplasty: a controlled clinical trial. *J Orthop Sports Phys Ther.* 2016 Sep;46(9):742–748.
 27. Salter RB. Continuous passive motion: from origination to research to clinical applications. *J Rheumatol.* 2004 Nov;31(11):2104–2105.
 28. Bade MJ, Struessel T, Dayton M, et al. Early high-intensity versus low-intensity rehabilitation after total knee arthroplasty: a randomized controlled trial. *Arthritis Care Res.* 2017 Sep;69(9):1360–1368.
 29. Fukui N, Tashiro T, Hiraoka H, Oda H, Nakamura K. Adhesion formation can be reduced by the suppression of transforming growth factor-beta1 activity. *J Orthop Res.* 2000 Mar;18(2):212–219.
 30. Okabayashi K, Ashrafian H, Zacharakis E, et al. Adhesions after abdominal surgery: a systematic review of the incidence, distribution and severity. *Surg Today.* 2014 Mar;44(3):405–420.
 31. Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, Ranawat CS. Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections: a prospective randomized study. *J Arthroplasty.* 2007 Sep;22(6 Suppl2):33–38.
 32. Danoff JR, Goel R, Sutton R, Maltenfort MG, Austin MS. How much pain is significant? Defining the minimal clinically important difference for the visual analog scale for pain after total joint arthroplasty. *J Arthroplasty.* 2018 Jul;33(7S):S71–S75.