Efficacy and Side Effect Profile of Intrathecal Morphine versus Distal Femoral Triangle Nerve Block for Analgesia Following Total Knee Arthroplasty: A Randomized Trial

Marek Janiak 1,*, Rafal Kowalczyk 1, Grzegorz Gorniewski 2, Kinga Olczyk-Miiller 1, Marcin Kowalski 3, Piotr Nowakowski 4 and Janusz Trzebicki 1

1 1st Department of Anesthesiology and Intensive Care, Medical University of Warsaw, 02-091 Warszawa, Poland
2 Department of Anesthesiology and Intensive Care Education, Medical University of Warsaw, 02-091 Warszawa, Poland
3 Department of Orthopedics and Traumatology, Medical University of Warsaw, 02-091 Warszawa, Poland
4 Department of Anesthesiology and Intensive Care, Gruca Orthopaedic and Trauma Teaching Hospital, 05-400 Otwock, Poland
* Correspondence: mjaniak8@gmail.com; Tel.: +48-22-502-1724

Abstract: (1) Background: The management of postoperative pain after knee replacement is an important clinical problem. The best results in the treatment of postoperative pain are obtained using multimodal therapy principles. Intrathecal morphine (ITM) and single-shot femoral nerve block (SSFNB) are practiced in the treatment of postoperative pain after knee replacement, with the most optimal methods still under debate. The aim of this study was to compare the analgesic efficacy with special consideration of selected side effects of both methods. (2) Materials and methods: Fifty-two consecutive patients undergoing knee arthroplasty surgery at the Department of Orthopedics and Traumatology of the Medical University of Warsaw were included in the study. Patients were randomly allocated to one of two groups. In the ITM group, 100 micrograms of intrathecal morphine were used, and in the SSFNB group, a femoral nerve block in the distal femoral triangle was used as postoperative analgesia. The other elements of anesthesia and surgery did not differ between the groups. (3) Results: The total dose of morphine administered in the postoperative period and the effectiveness of pain management did not differ significantly between the groups (cumulative median morphine dose in 24 h in the ITM group 31 mg vs. SSFNB group 29 mg). The incidence of nausea and pruritus in the postoperative period differed significantly in favor of patients treated with a femoral nerve block. (4) Conclusions: Although intrathecal administration of morphine is similarly effective in the treatment of pain after knee replacement surgery as a single femoral triangle nerve block, it is associated with a higher incidence of cumbersome side effects, primarily nausea and pruritus.

Keywords: knee arthroplasty; intrathecal morphine; femoral triangle nerve block

1. Introduction

Total knee arthroplasty is a common surgical procedure with an expected increase in the number of cases due to the aging of populations and the increase in obesity [1]. Over 33,000 procedures were performed in Poland in 2019, and the number has been rising since the year 2005, as seen in data from the Polish Central Endoprostheses Database of the National Health Fund [2].

Postoperative pain following total knee arthroplasty is described as moderate to very severe by most patients [3]. It is well documented that postoperative multimodal analgesic therapy using combinations of regional analgesic techniques provides the most optimal postoperative pain control [4], but direct comparisons of different regional blocks...
do not provide a definitive answer to which technique is most preferred. To date, no one regional anesthetic technique is recommended above all others for postoperative pain control following total knee arthroplasty [5,6]. Among methods used to combat severe postoperative pain, both intrathecal morphine and femoral nerve blocks have been used. Both methods are simple to perform and have been shown to be effective in pain control but have a differing profile of side effects and reported patient satisfaction [4]. The aim of this study was to compare the analgesic efficacy of intrathecal morphine versus a single-shot distal femoral triangle nerve block with a special focus on the incidence of side effects related to morphine use.

2. Materials and Methods

In line with the Helsinki Declaration, the Bioethical Committee of the Medical University of Warsaw approved the study (number KB/107/2016, Chairperson Prof. Zbigniew Wierzbicki). Consecutive patients scheduled for primary total knee arthroplasty in the Orthopedic Department of the Medical University of Warsaw were included in the trial. All patients meeting the inclusion criteria received information materials prior and were asked for formal consent to participate in the trial. The exclusion criteria were: lack of consent for inclusion in the trial, lack of consent or a contraindication to performing the regional block techniques employed in the trial, American Association of Anesthesiology score (ASA) of IV or V, chronic opioid use, allergy or contraindications to the drugs used in the trial such as paracetamol, metamizole or ketoprofen.

The trial participants were anesthetized in a block room using a standardized procedure, as per the routine used for knee arthroplasty in our clinical center. Mandatory basic parameters, including an electrocardiogram trace, pulse-oximetry and noninvasive blood pressure, were monitored throughout from the time of admission to the surgical theater area to discharge from the postoperative recovery unit. Allocation to either the intrathecal morphine or distal femoral triangle nerve block was performed using a randomized list known to only one trial coordinator that was not performing the blocks. Due to obvious reasons, double-blinding of the procedure was not fully possible. All the procedures were performed under direct supervision of experienced anesthesiologists. Prior to the anesthetic block, all patients received an intravenous premedication with 0.1 mg of fentanyl (Fentanyl WZF, Polpha, Warszawa, Poland) and 2 mg of midazolam (Midanium WZF, Polpha, Warszawa, Poland). Participants randomized to the intrathecal morphine group (ITM) had a spinal block in the sitting position with 15 mg of 0.5% hyperbaric bupivacaine (Marcaine 0.5% Heavy Spinal, Aspen Pharma Trading Ltd., Dublin, Ireland) and 100 micrograms of intrathecal morphine (Morphini Sulfas WZF 0.1% Spinal, Polfa, Warszawa, Poland). An aseptic technique was used for the intrathecal block in the L3/L4 vertebral interspace using a 26 G atraumatic spinal needle (Atraucan, B. Braun Melsungen AG, Melsungen, Germany). Participants in the single-shot femoral nerve block group (SSFNB) had a distal femoral nerve block within the femoral triangle performed using an aseptic technique under ultrasound guidance with a high linear frequency (12–15 MHz) probe and an 80 mm echogenic block needle (Stimuplex Ultra 360, B. Braun Melsungen AG, Melsungen, Germany). A dose of 20 mL of 0.25% bupivacaine with adrenaline (original solution Marcaine Adrenaline 0.5%, Aspen Pharma Trading Ltd., Dublin, Ireland) was administered on confirmation of sub-sartorial spread lateral to the femoral artery, just as it dives under the sartorius muscle. On confirmation of sensory block with a decrease in sensation to cold in the front peripatellar thigh region, an intrathecal block was performed in the same way as the ITM group, but no intrathecal morphine was administered. Participants in both groups had their spinal block assessed using the Bromage scale and, on confirmation of spinal block effectiveness, were transferred to the operating theater.

The surgical procedure was performed by the same surgical team comprising two orthopedic specialists, with a standardized surgical procedure using a medial peripatellar approach, sacrificing the cruciate ligaments and using bone cement for prosthesis fixation. In all cases, a tourniquet was used to optimize surgical conditions and reduce intraoperative
blood loss which was deflated prior to wound closure. Antimicrobial perioperative prophylaxis and thromboprophylaxis with low molecular weight heparins were implemented in all participants of the study as per hospital protocol.

Monitoring of vital parameters was continued throughout the surgical procedure with intravenous fluid therapy given at the discretion of the anesthesiologist, and in individual cases of patient discomfort, moderate sedation with propofol was used. Following the surgical procedure, all patients were transferred to the postoperative care unit (PACU), where they were monitored for a 24 h period, after which they were discharged to the orthopedic ward. Postoperative analgesia was standardized, with regular intravenous paracetamol 1 g every 6 h and ketoprofen 100 mg every 12 h. All patients had rescue morphine at 0.1 mg/kg administered intravenously on demand under nurse-controlled analgesia every 6 h whenever the Numerical Rating Score (NRS) was more than 4. Vital parameters were recorded every hour. Additionally, trial participants were asked to assess their pain and side effects, such as nausea, vomiting, and pruritus, at 1, 6, 24, 48, and 72 h following surgery. At these time points, the nurse also recorded vital parameters and sedation levels. If required, additional doses of morphine and intravenous ondansetron 4 mg were administered. Pain was assessed at all time points using the Numerical Rating Score (NRS) from 0 (no pain) to 10 (worst possible pain) both at rest and with active knee flexion of the operated side. Urinary retention was not assessed as study participants had urinary catheterization.

Statistical analysis of the obtained data was performed using Statistica 13.1 (StatSoft Inc., Tulsa, OK, USA). The data is described using mean values and standard deviations as a measure of dispersion in the case of continuous values or cumulative values for non-continuous data. Comparison of measured variables between groups was performed using the student t-test for the parametrical data and the U Mann–Whitney test for the non-parametric data. A normality test by Kolmogorov–Smirnov was performed. For non-continuous data sets, the Chi2 test was used to compare variables. A statistically significant value of $p < 0.05$ was used. A post-hoc power analysis showed the power to be >90% for most variables, such as nausea or pruritus, when considering the sample size.

3. Results

A total of 52 participants were enrolled in the study, with 26 per group. The two groups did not differ in their basic characteristics such as sex, age, anthropometry, ASA classification or duration of surgery, as can be seen in Table 1.

Table 1. Patient characteristics.

|                          | ITM Group | SSFNB Group | $p$ Value |
|--------------------------|-----------|-------------|-----------|
| Sex Female/Male (%)      | 23/3 (88.5%/11.5%) | 23/3 (88.5%/11.5%) | $p = 1$ (Chi2) |
| Age (years)              | 68 +/− 11.9 | 67.5 +/− 9.7 | $p = 0.86$ (t test) |
| Height (cm)              | 161.2 +/− 6.4 | 161.5 +/− 6.4 | $p = 0.85$ (t test) |
| Weight (kg)              | 82.2 +/− 15.1 | 81 +/− 16.6 | $p = 0.78$ (t test) |
| Surgical procedure time (min) | 87.6 +/− 17.7 | 92.9 +/− 29.4 | $p = 0.43$ (t test) |
| Tourniquet time (min)    | 72.5 +/− 11.9 | 73.1 +/− 21.9 | $p = 0.9$ (t test) |
| ASA 1/2/3 (%)            | 1/25/0 | 0/24/2 | $p = 0.36$ (Chi2) |

Values are presented as mean +/− SD or as number/percentage. ASA—American Society of Anesthesiology physical status scale. ITM = intrathecal morphine, SSFNB = single-shot femoral triangle nerve block.

Table 2 shows the results of the assessed variables between the ITM and SSFNB groups. The cumulative morphine dose did not differ between the two groups in the 72 h observation period. A statistically and clinically relevant reduction in nausea and pruritus could be seen in the postoperative period in the femoral triangle nerve group. Both pruritus and nausea occurred in at least half of the group that received the intrathecal morphine but were a rare occurrence in the femoral nerve block group. More patients required the
administration of ondansetron in the postoperative period in the ITM group, and this was statistically significant. The effectiveness of the analgesic regimen did not differ between the two groups in terms of the NRS results (Tables 3 and 4). A benefit of the femoral nerve block was noted at some time points, such as at six postoperative hours at rest ($p = 0.0361$) and on discharge from the PACU when NRS was assessed on knee flexion ($p = 0.0138$).

Table 2. Treatment results.

|                        | ITM Group | SSFNB Group | $p$ Value (Statistical Test) |
|------------------------|-----------|-------------|------------------------------|
| Cumulative morphine dose (mg) | 31 [23–37] | 29 [23–31] | $p = 0.26$ (U Mann–Whitney) |
| Nausea N (%)           | 13 (50%)  | 2 (7.7%)    | $p = 0.0008$ (Chi2)         |
| Vomiting N (%)         | 7 (26.9%) | 1 (3.8%)    | $p = 0.211$ (Chi2)          |
| Pruritus N (%)         | 14 (53.8%)| 1 (3.8%)    | $p = 0.0001$ (Chi2)         |
| Somnolence N (%)       | 15 (57.7%)| 9 (34.6%)   | $p = 0.09$ (Chi2)           |
| Maximum NRS at rest    | 4 [2–5]   | 2 [0–6]     | $p = 0.18$ (U Mann–Whitney) |
| Maximum NRS on motion  | 4 [3–7]   | 3.5 [2–7]   | $p = 0.22$ (U Mann–Whitney) |
| Number of patients requiring ondansetron N (%) | 13 (50%) | 3 (11.6%) | $p = 0.0271$ (Chi2) |
| Number of patients requiring naloxone N (%) | 2 (7.7%) | 0 (0%) | $p = 0.1649$ (Chi2) |

ITM = intrathecal morphine. SSFNB = single-shot femoral triangle nerve block. Values x[y-z] signify median[interquartile range].

Table 3. Postoperative pain levels at rest.

| NRS at Rest          | ITM Group | SSFNB Group | $p$ Value (U Mann–Whitney) |
|----------------------|-----------|-------------|---------------------------|
| On admission to PACU | 0 [0–0]   | 0 [0–0]     | $p = 1$                   |
| At 3 h               | 0 [0–0]   | 0 [0–0]     | $p = 0.7418$              |
| At 6 h               | 3 [0–4]   | 0 [0–2]     | $p = 0.0361$              |
| At 9 h               | 0 [0–2]   | 1 [0–3]     | $p = 0.602$               |
| At 12 h              | 1 [0–2]   | 0 [0–2]     | $p = 0.3554$              |
| At 18 h              | 0.5 [0–2] | 0 [0–0]     | $p = 0.07$                |
| On discharge from PACU | 0 [0–1]   | 0 [0–0]     | $p = 0.1938$              |

NRS = numerical Rating Score, ITM = intrathecal morphine, SSFNB = single-shot femoral triangle nerve block.

Table 4. Postoperative pain levels on motion.

| NRS on Motion        | ITM Group | SSFNB Group | $p$ Value (U Mann–Whitney) |
|----------------------|-----------|-------------|---------------------------|
| On admission to PACU | 0 [0–0]   | 0 [0–0]     | $p = 0.819$               |
| At 3 h               | 0 [0–0]   | 0 [0–0]     | $p = 0.7007$              |
| At 6 h               | 3.5 [0–5] | 0 [0–3]     | $p = 0.0582$              |
| At 9 h               | 3 [0–4]   | 2 [0–4]     | $p = 0.7143$              |
| At 12 h              | 2.5 [1–3] | 1 [0–4]     | $p = 0.1176$              |
| At 18 h              | 1.5 [1–4] | 1 [0–2]     | $p = 0.1242$              |
| On discharge from PACU | 1 [1–4]   | 0 [0–2]     | $p = 0.0138$              |

NRS = numerical Rating Score, ITM = intrathecal morphine, SSFNB = single-shot femoral triangle nerve block.

No relevant complications of the spinal block or the femoral nerve block were noted among the study participants, but two patients required the administration of a small dose of naloxone due to bradypnea with overt sedation in the ITM group.

Intra- and postoperative hemodynamic values of blood pressure, heart rate or oxygen saturation did not differ between the two groups. With the exception of two cases requiring naloxone administration, no desaturations relevant to the study were noted, but it must be
stated that the measurements were recorded at specific time points, and any reduced value of oxygen saturation was treated with oxygen supplementation, which was not recorded.

4. Discussion

We assessed the efficacy of a 100 mcg intrathecal morphine in comparison to a single-shot femoral nerve block performed in the femoral triangle with a sub-sartorial spread just lateral to the femoral artery for postoperative analgesia following total knee arthroplasty. Our study shows that both these methods are equianalgesic and can be used alternatively. However, the undesirable side effect profile of intrathecal morphine must be taken into account, with a potential for a rare but dangerous respiratory depression.

Total knee arthroplasty is an orthopedic procedure commonly performed for gonarthrosis. Although the aim of the surgery is to reduce chronic pain related to knee degeneration [7], pain intensity can be very severe directly after the surgery. Effective analgesia with the use of regional blocks is optimal for fast-track patient mobilization and achievement of good functional recovery of the knee joint [8,9]. It is possible that the use of regional anesthetic techniques could help reduce hospital stay time and the incidence of side effects related to long-term opioid use [10].

A single-shot femoral nerve block is one of the accessible methods of pain management following knee arthroplasty [11]. It does not provide prolonged analgesia with the added flexibility that a continuous femoral triangle nerve block can [12,13], especially when combined with a sciatic nerve block [14], but in comparison to the continuous nerve block, it carries a reduced risk of falls in the postoperative recovery time [15,16]. A study by Wyatt et al. [17] showed no major advantage of a continuous femoral nerve block over a single-shot technique when used in combination with ITM. For these reasons, a single-shot technique with a more distant block area and no sciatic nerve blocking was chosen in our trial to reduce the risk of a fall due to quadriceps muscle weakness in early mobilization. However, we do note that the most recent PROSPECT guidelines on total knee arthroplasty do not recommend any femoral nerve block due to the potential negative impact on functional, fast-track recovery [18], but the study was designed in the time before the focus was placed on the higher risk of falls following total knee arthroplasty and this may still be debatable. No study participant experienced a fall, and femoral nerve block is still used as an analgesic option as local infiltration analgesia (LIA) is not practiced by our orthopedic surgeons.

Single-shot femoral nerve block following total knee arthroplasty is more effective compared to simple local wound infiltration [19]. It has a similar or less effective profile when compared to an adductor canal block which, on the other hand, helps preserve more motor function of the quadriceps muscle of the thigh [20,21]. A shift toward finding more optimal distal motor-sparing blocks is observed in the literature. A novel parasartorial compartment (PASC) block is one such promising alternative [22]. The study by Lee et al. [12] found a comparable analgesic result when a continuous catheter was placed in the femoral triangle in comparison to a proximal and distal adductor canal catheter position.

Morphine administered intrathecally (ITM) has a proven efficacy in the treatment of postoperative pain following large joint arthroplasties [23]. The benefit of ITM is the ease of administration and no additional complications related to the injection itself as compared to the more invasive nerve block procedure. The major drawback of ITM is the high incidence of side effects that are not well tolerated by patients, such as nausea, pruritis and sedation [24]. A potential complication remains late apnea related to post-opioid respiratory center depression [25]. In our study, 2 participants in the ITM group experienced respiratory depression with bradypnea and overt sedation after 15 h and required administration of naloxone with full recovery. No evident drop in saturation was noted as oxygen was being administered, but the apnea triggered a monitor alarm. This is not statistically significant as the study groups are small, but it remains clinically relevant. As the cumulative systemic morphine dose did not differ between the groups, it should be noted that ITM may have caused respiratory depression. No additional factors, such as obstructive sleep apnea, were found to contribute to these cases. The patients remained
in the PACU for the 24 h postoperative period and were discharged to the ward with no further action required.

In both our study groups, undesirable side effects were observed secondary to the implemented analgesia. The incidence of nausea and pruritis was significantly higher in the ITM group, even though the overall opioid consumption was similar in both groups. Our trial results remain in line with a metaanalysis which showed an associated increased pruritis and a decreased patient satisfaction [26,27], although no difference in side effect profile was observed in one study [28].

Recommendations pertaining to analgesia for total knee arthroplasty combine paracetamol, non-steroidal anti-inflammatory drugs and opioid therapy [6,9,18]. The used multimodal analgesic regimen in the trial provided good pain management in both study groups.

Our study has several limitations. Firstly, the study was not blinded—both the anesthesiologist performing the block and the patient were aware of the group allocation. However, the personnel assessing the outcomes, including pain scores and side effects, were unaware of the group allocation of the participants. Secondly, our study investigates a femoral triangle nerve block which may be related to quadriceps muscle weakness affecting early mobilization. We did not assess patient satisfaction in the perioperative period.

5. Conclusions

In our randomized trial, the results show a similar overall efficacy of intrathecal morphine at a dose of 100 micrograms to a single-shot femoral triangle nerve block but with a higher incidence of undesirable side effects among patients receiving intrathecal morphine, especially nausea and pruritus. The risk of respiratory depression, which occurred in our study in the intrathecal morphine group, confirms the need for respiratory monitoring and limits its possible safe use in day-case surgery.

Author Contributions: Conceptualization, M.J., R.K. and G.G.; methodology, M.J., R.K. and G.G.; validation, M.K., P.N. and J.T.; formal analysis, M.J. and G.G.; investigation, M.J., G.G., R.K. and K.O.-M.; resources, M.K. and J.T.; data curation, M.J. and G.G.; writing—original draft preparation, M.J. and G.G.; writing—review and editing, M.K., P.N. and J.T.; visualization, M.J. and G.G.; supervision, P.N. and J.T.; project administration, P.N. and J.T.; funding acquisition, M.J., R.K. and J.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Medical University of Warsaw, Poland (number KB/107/2016, Zbigniew Wierzbicki, on 10 May 2016).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study may be available on request made to the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Kurtz, S.M.; Ong, K.L.; Lau, E.; Widmer, M.; Maravic, M.; Gómez-Barrena, E.; de Pina, M.; Manno, V.; Torre, M.; Walter, W.L.; et al. International survey of primary and revision total knee replacement. Int. Orthop. 2011, 35, 1783–1789. [CrossRef] [PubMed]
2. Polish National Health Fund Central Database on Endoprostheses. Available online: https://www.nfz.gov.pl/download/gfx/nfz/pl/defaultstronaopisowa/349/47/1/realizacja_swiadczen_endoprotezoplastyki_stawowej_w_2019r.docx (accessed on 18 September 2022).
3. Wylde, V.; Rooker, J.; Halliday, L.; Blom, A. Acute postoperative pain at rest after hip and knee arthroplasty: Severity, sensory qualities and impact on sleep. Orthop. Traumatol. Surg. Res. OTSR 2011, 97, 139–144. [CrossRef] [PubMed]
4. Li, X.M.; Huang, C.M.; Zhong, C.F. Intrathecal morphine versus femoral nerve block for pain control in total knee arthroplasty: A meta-analysis from randomized control trials. Int. J. Surg. 2016, 32, 89–98. [CrossRef]
5. Burch, J.; Ahn, J. For people post knee replacement surgery, how does femoral nerve block (FNB) compare with opioids, epidural, or local infiltration analgesia? Cochrane Clin. Answr. 2020. [CrossRef]
6. Misiolek, H.; Zajączkowska, R.; Daszkiewicz, A.; Woroń, J.; Dobrogowski, J.; Wordliczek, J.; Owczuk, R. Postępowanie w bólu pooperacyjnym 2018: Stanowisko Sekcji Znieczulenia Regionalnego i Terapii Bólu Polskiego Towarzystwa Anestezjologii i Intensywnej Terapii, Polskiego Towarzystwa Znieczulenia Regionalnego i Leczenia Bólu, Polskiego Towarzystwa Badania Bólu oraz Konsultanta Krajowego w dziedzinie anestezjologii i intensywnej terapii. Anesthesiol. Intensive 2018, 50, 175–203.

7. Sayah, S.M.; Karunaratne, S.; Beckenkamp, P.R.; Horsley, M.; Hancock, M.J.; Hunter, D.J.; Herbert, R.D.; de Campos, T.F.; Steffens, D. Clinical Course of Pain and Function Following Total Knee Arthroplasty: A Systematic Review and Meta-Regression. J. Arthroplast. 2021, 36, 3993–4002.e37. [CrossRef] [PubMed]

8. Capdevila, X.; Barthelet, Y.; Biboulet, P.; Ryckwaert, Y.; Rubenovitch, J.; d’Athis, F. Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. Anesthesiology 1999, 91, 8–15. [CrossRef] [PubMed]

9. You, D.; Qin, L.; Li, K.; Li, D.; Zhao, G.; Li, L. A meta-analysis on advantages of peripheral nerve block post-total knee arthroplasty. Korean J. Pain 2021, 34, 271–287. [CrossRef]

10. Freys, S.M.; Pogatzki-Zahn, E. Pain therapy to reduce perioperative complications. Innov. Surg. Sci. 2019, 4, 158–166. [CrossRef] [PubMed]

11. Kopp, S.L.; Berglum, J.; Buyanovdaran, A.; Horlocker, T.T.; Ilfeld, B.M.; Memtsoudis, S.G.; Neal, J.M.; Rawal, N.; Wegener, J.T. Anesthesia and Analgesia Practice Pathway Options for Total Knee Arthroplasty: An Evidence-Based Review by the American and European Societies of Regional Anesthesia and Pain Medicine. Reg. Anesth. Pain Med. 2017, 42, 683–697. [CrossRef] [PubMed]

12. Lee, B.; Park, S.J.; Park, K.K.; Kim, H.J.; Lee, Y.S.; Choi, Y.S. Optimal location for continuous catheter analgesia among the femoral triangle, proximal, or distal adductor canal after total knee arthroplasty: A randomized double-blind controlled trial. Reg. Anesth. Pain Med. 2022, 47, 353–358. [CrossRef] [PubMed]

13. Chan, E.Y.; Fransen, M.; Parker, D.A.; Assam, P.N.; Chua, N. Femoral nerve blocks for acute postoperative pain after knee replacement surgery. Cochrane Database Syst. Rev. 2014, 5, CD009941. [CrossRef] [PubMed]

14. Abdallah, F.W.; Madjdpour, C.; Brull, R. Is sciatic nerve block advantageous when combined with femoral nerve block for postoperative analgesia following total knee arthroplasty? A meta-analysis. Can. J. Anaesth. = Can. D’anesthesie 2016, 63, 552–568. [CrossRef] [PubMed]

15. Ilfeld, B.M.; Duke, K.B.; Donohue, M.C. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. Anesth. Analg. 2010, 111, 1552–1554. [CrossRef] [PubMed]

16. Johnson, R.L.; Kopp, S.L.; Hebl, J.R.; Erwin, P.J.; Mantilla, C.B. Falls and major orthopaedic surgery with peripheral nerve blockade: A systematic review and meta-analysis. Br. J. Anaesth. 2013, 110, 518–528. [CrossRef]

17. Wyatt, M.C.; Wright, T.; Locker, J.; Stout, K.; Chapple, C.; Theis, J.C. Femoral nerve infusion after primary total knee arthroplasty: A prospective, double-blind, randomised and placebo-controlled trial. Bone Jt. Res. 2015, 4, 11–16. [CrossRef]

18. Lavand’homme, P.M.; Kehlet, H.; Rawal, N.; Joshi, G.P.; PROSPECT Working Group of the European Society of Regional Anaesthesia and Pain Therapy (ESRA). Pain management after total knee arthroplasty: PROCeDure SPEcific Postoperative Pain Management recommendations. Eur. J. Anaesthesiol. 2022, 39, 743–757. [CrossRef] [PubMed]

19. Mei, S.; Jin, S.; Chen, Z.; Ding, X.; Zhao, X.; Li, Q. Analgesia for total knee arthroplasty: A meta-analysis comparing local infiltration and femoral nerve blocks. Clinics 2015, 70, 648–653. [CrossRef]

20. Karkhur, Y.; Mahajan, R.; Kakralia, A.; Pandey, A.P.; Kapoor, M.C. A comparative analysis of femoral nerve block with adductor canal block following total knee arthroplasty: A systematic literature review. J. Anaesthesiol. Clin. Pharmacol. 2018, 34, 433–438. [CrossRef] [PubMed]

21. Gao, F.; Ma, J.; Sun, W.; Guo, W.; Li, Z.; Wang, W. Adductor Canal Block Versus Femoral Nerve Block for Analgesia After Total Knee Arthroplasty: A Systematic Review and Meta-analysis. Clin. J. Pain 2017, 33, 356–368. [CrossRef]

22. Pascarella, G.; Costa, F.; Del Buono, R.; Strumia, A.; Cataldo, R.; Agrò, F.; Carassiti, M. The para-sartorial compartments (PASC) block: A new approach to the femoral triangle block for complete analgesia of the anterior knee. Anesthesia 2022, 10, e12165. [CrossRef] [PubMed]

23. Rathmell, J.P.; Pino, C.A.; Taylor, R.; Patrin, T.; Viani, B.A. Intrathecal morphine for postoperative analgesia: A randomized, controlled, dose-ranging study after hip and knee arthroplasty. Anesth. Analg. 2003, 97, 1452–1457. [CrossRef] [PubMed]

24. Gehling, M.H.; Luesebrink, T.; Kulka, P.J.; Tryba, M. The effective duration of analgesia after intrathecal morphine in patients without additional opioid analgesia: A randomized double-blind multicentre study on orthopaedic patients. Eur. J. Anaesthesiol. 2009, 26, 683–688. [CrossRef]

25. Koning, M.V.; Reussien, E.; Vermeulen, B.; Zonneveld, S.; Westerman, E.M.; de Graaff, J.C.; Houweling, B.M. Serious Adverse Events after a Single Shot of Intrathecal Morphine: A Case Series and Systematic Review. Pain Res. Manag. 2022, 2022, 4567192. [CrossRef]

26. Qi, B.C.; Yu, J.; Qiao, W.S. Comparison of intrathecal morphine versus local infiltration analgesia for pain control in total knee and hip arthroplasty: A meta-analysis. Medicine 2020, 99, e2971. [CrossRef] [PubMed]

27. Sites, B.D.; Beach, M.; Gallagher, J.D.; Jarrett, R.A.; Sparks, M.B.; Lundberg, C. A single injection ultrasound-assisted femoral nerve block provides side effect-sparing analgesia when compared with intrathecal morphine in patients undergoing total knee arthroplasty. Anesth. Analg. 2004, 99, 1539–1543. [CrossRef]

28. Frassanito, L.; Vergari, A.; Zanghi, F.; Messina, A.; Bitondo, M.; Antonelli, M. Post-operative analgesia following total knee arthroplasty: Comparison of low-dose intrathecal morphine and single-shot ultrasound-guided femoral nerve block: A randomized, single blinded, controlled study. Eur. Rev. Med. Pharmacol. Sci. 2010, 14, 589–596. [PubMed]