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Impact of Regional Anesthesia in Functional Recovery after Total Hip or Knee Replacement

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Impact of Regional Anesthesia in Functional Recovery after Total Hip or Knee Replacement

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DEDICATION

To my family, for all the investment, support, patience and encouragement throughout this journey, specially to my parents.

To my friends who always supported me and motivated me to make the most of this academic life.

To Instituto de Ciências Biomédicas Abel Salazar and to Centro Hospitalar do Porto, for being integral parts of my academic formation and my second home for the last 6 years.

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RESUMO

Introdução: A artroplastia total da anca e do joelho estão associadas a dor pós-operatória intensa e são dois dos procedimentos cirúrgicos mais comuns mundialmente. A analgesia pós-operatória inadequada pode conduzir a atrasos na mobilização e reabilitação, hospitalização prolongada, aumento da incidência de complicações e desenvolvimento de dor crônica. Assim, a gestão apropriada da dor pós-operatória é essencial, não só pelo seu impacto no processo de recuperação, mas também pela sua associação com maior satisfação do doente e melhores resultados perioperatórios e a longo prazo.

Historicamente, os opióides eram o *gold-standard* para o controlo da dor pós-operatória. Contudo, a atual gestão rápida de pacientes exige redução de custos e mobilização e alta hospitalar precoces. Consequentemente, tem havido um aumento do uso de técnicas de anestesia regional nas últimas décadas.

Objetivos: Esta revisão da literatura tem como objetivo reconhecer os avanços na anestesia regional ao longo da última década e evidenciar o seu impacto clínico na recuperação funcional após prótese total da anca e do joelho.

Metodologia: Foi realizada uma pesquisa estruturada no PubMed, da qual 84 artigos cumpriram todos os critérios de inclusão. Adicionalmente, 14 artigos de diversas sociedades profissionais médicas foram selecionados e considerados para avaliação de texto integral.

Resultados: Apesar dos bloqueios neuroaxiais serem frequentemente utilizados em cirurgia ortopédica, as técnicas periféricas de anestesia regional têm demonstrado ser mais vantajosas. Os bloqueios nervosos periféricos proporcionam alívio da dor semelhante à analgesia epidural, mas com recuperação funcional mais rápida e menor morbilidade.

Todavia, alguns bloqueios nervosos aumentam o risco de bloqueio motor, prejudicando a deambulação precoce. Existem vários bloqueios nervosos disponíveis para a prótese total da anca e do joelho, mas o bloqueio ou combinação de bloqueios ideal para o controlo da dor pós-operatória ainda não foi estabelecido.

A infiltração local de analgesia é uma técnica simples, menos dispendiosa e aparentemente segura que parece proporcionar uma analgesia comparável aos bloqueios nervosos, enquanto evita o bloqueio motor e o seu impacto funcional negativo. Apesar da sua eficácia após a artroplastia total do joelho ser fortemente apoiada, no que diz respeito à artroplastia total da anca, os resultados são inconsistentes.

Conclusão: Embora não exista atualmente consenso sobre um regime de analgesia perioperatória ideal, existe ampla concordância de que os protocolos analgésicos multimodais que incluem técnicas de anestesia regional melhoram a reabilitação pós-

operatória, minimizam as complicações e asseguram a satisfação do paciente após prótese total da anca ou do joelho.

Palavras-chave: “Recuperação funcional”; “Anestesia Regional”; “Prótese Total da Anca”; “Prótese Total do Joelho”.

ABSTRACT

Introduction: Total knee and hip arthroplasty are associated with intense postoperative pain and are two of the most common surgical procedures worldwide. Inadequate postoperative analgesia can lead to delayed mobilization and rehabilitation, prolonged hospitalization, increased incidence of complications and development of chronic pain. Thereby, appropriate postoperative pain management is essential, not only for its impact on the recovery process, but also for its association with improved patient satisfaction and better perioperative and long-term outcomes.

Historically, opioids were the gold-standard for postoperative pain control. However, current fast track patient management demands cost reduction and early mobilization and discharge from hospital. Consequently, there has been an increase in the use of regional anesthesia techniques in the last decades.

Objectives: This literature revision aims to acknowledge advances in regional anesthesia over the last decade and evidence its clinical impact in functional recovery following total hip and knee replacement.

Methods: A structured search was performed on PubMed, from which 84 articles met all the inclusion criteria. Additionally, 14 articles from several medical professional societies were selected and considered for full-text assessment.

Results: Even though neuraxial blocks are frequently used in orthopedic surgery, peripheral regional anesthetic techniques have demonstrated to be more advantageous. Peripheral nerve blocks provide pain relief similar to epidural analgesia, but with faster functional recovery and lower morbidity.

Nevertheless, some nerve blocks have increased risk of motor blockade, impairing early ambulation. There are several nerve blocks available for total hip and knee replacement, but the ideal block or combination of blocks for postoperative pain control has not been established yet.

Local infiltration analgesia is a simple, less expensive, and apparently safe technique that seems to provide comparable analgesia to nerve blocks while avoiding motor block and its negative functional impact. While its effectiveness following total knee arthroplasty is strongly supported, in what concerns total hip replacement the results are inconsistent.

Conclusion: Although there is no current consensus on an optimal perioperative analgesia regimen, there is wide agreement that analgesic multimodal protocols that include regional anesthesia techniques improve postoperative rehabilitation, minimize complications and ensure patient satisfaction following total hip or knee replacement.

Keywords: “Functional recovery”; “Regional Anesthesia”; Total Hip Replacement”; “Total Knee Replacement”.

LIST OF ABBREVIATIONS

ACB – Adductor Canal Block
FIB – Fascia Iliaca Block
FN – Femoral Nerve
FNB – Femoral Nerve Block
FTB – Femoral Triangle Block
IPACK – Interspace between Popliteal Artery and Posterior Capsule of the Knee
LAST - Local Anesthetic Systemic Toxicity
LFCN – Lateral Femoral Cutaneous Nerve
LIA – Local Infiltration Analgesia
LPB – Lumbar Plexus Block
ON – Obturator Nerve
ONB – Obturator Nerve Block
PNB – Peripheral Nerve Blocks
PVB – Paravertebral Block
QLB – Quadratus Lumborum Block
RCT – Randomized Controlled Trial
SNB – Sciatic Nerve Block
THA – Total Hip Arthroplasty
TKA – Total Knee Arthroplasty
TNB – Tibial Nerve Block
TUG – Timed Up and Go
USA – United States of America

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INTRODUCTION

Total knee arthroplasty (TKA) and total hip arthroplasty (THA) are two of the most common surgical procedures worldwide.^{2,3} Annually, over a million of total joint replacements are performed only in the United States of America (USA).⁴ Furthermore, thanks to the longer life expectancy in developed countries, the increase of active elderly population that wants to maintain functionality and the concomitant obesity epidemic, osteoarthritis is projected to increase dramatically in the coming decades, with a huge impact on healthcare resources, economics and patients' quality of life.⁴⁻⁶ In Portugal, this tendency is also reflected. According to Portugal Nacional Statistics Institute, population aged 65 years or more is going to increase from 17,4% in 2008 to 32,3% in 2060, with a major growth in the population over 80 years old.⁷

In this vulnerable population, most of the patients are frail with multiple comorbidities and polymedicated, which increases the risk of drug adverse effects and unpredictable interactions.⁸⁻¹⁰

Both total knee and total hip replacement are associated with intense postoperative pain, as 23% of patients refer "severe/extreme" pain after surgery and 54% indicates "severe pain at least once".¹¹⁻¹³ Inadequate postoperative analgesia can lead to delayed patients' mobilization and rehabilitation, longer length of stay in the intensive care unit, prolonged hospitalization, hospital readmission, decreased quality of life, increased incidence of surgical site infections, pulmonary and thromboembolic complications, anxiety and cognitive dysfunction and development of chronic pain, since patients with uncontrolled pain management in the first 48 hours after surgery are limited to a 50 percent chance of achieving long-term satisfactory pain relief.^{2,3,14-18}

Therefore, appropriate pain management is vital, not only for its impact on the recovery process, but also for its association with improved patient satisfaction, cost reduction and better perioperative and long-term outcomes.^{2,16,19}

Historically, opioids were the gold-standard for postoperative pain control. However, besides their addictive potential, they are associated with an increased risk of several postoperative complications and significative adverse effects like nausea, vomits, obstipation, paralytic ileus, sedation, cardiorespiratory depression and pruritus.^{2,17,20}

In the last decades, the emergence of new techniques and equipment has increased the number of analgesia and regional anesthesia modalities available.⁹ Thereby, the use of regional anesthesia techniques such as neuraxial analgesia, peripheral nerve blocks (PNB) and local infiltration analgesia (LIA) has become increasingly widespread, since they provide adequate postoperative pain relief with less side effects, decreased morbidity and reduced perioperative opioid consumption.^{11,14} Additionally, the financial pressure on health

care systems demands rapid mobilization and discharge from hospital while reducing costs, which makes regional anesthesia strategies an attractive choice for all patients without contraindications.²¹⁻²³

A critical assessment of the current literature is warranted to elucidate the advantages and drawbacks of each regional anesthesia technique with the ultimate goal of further improving postoperative pain management and functional recovery.

As such, this literature revision aims to acknowledge advances in regional anesthesia over the last decade and evidence its clinical impact following total joint replacement.

METHODS

A search was performed on PubMed during the months of September, October and November of 2019 using the following formula of MeSH words: (Recovery[Title/Abstract] OR "Recovery of Function"[Mesh]) AND ("Anesthesia, Conduction"[Mesh]) AND ("Arthroplasty, Replacement, Hip"[Mesh] OR "Arthroplasty, Replacement, Knee"[Mesh]).

The filters "human", "english", "spanish", "portuguese" and "publication date from 2009/10/19 to 2019/10/16" were used.

Inclusion criteria included studies and review articles that assessed the use of regional anesthesia in total hip or knee replacement and its impact in patient functional recovery. Articles in other languages, case reports, individual opinion articles, letters to authors, studies comparing general and epidural anesthesia, articles regarding postoperative complications, articles that were not about total arthroplasty and regional anesthesia and articles which full text wasn't available were excluded.

A total of 124 publications were screened through the structured search, of which 84 were selected based on title and abstract potential relevance and considered for full-text assessment.

Moreover, in November of 2019, a search was conducted through several medical professional societies, such as: American Society of Anesthesiologists, European Society of Anesthesiology, American Society of Regional Anesthesia and Pain Medicine, European Society of Regional Anesthesia and *Associação Portuguesa de Cirurgia Ambulatória*. A total of 14 articles about regional anesthesia and perioperative pain management were selected for full-text assessment. Figure 1 represents the article selection flowchart.

Based on the selected articles, the relevant information was collected for the review and organized according to the regional anesthesia method used and the type of joint replacement.

BODY OF THE REVIEW

1. Neuraxial Analgesia

Selection of anesthetic technique influences the effectiveness of postoperative pain relief and functional recovery.²⁴ Neuraxial anesthesia is frequently utilized in joint replacement surgery, since it provides adequate intraoperative anesthesia which may be extended to postoperative analgesia with epidural technique. Compared to general anesthesia, it is associated with decreased incidence of adverse events, lower morbidity and mortality and less costs.^{9,25-27}

Neuraxial techniques include epidural, spinal or combined spinal-epidural administration of a local anesthetic, an analgesic (opioid), or both and may be performed as a single-dose or continuous infusion to provide analgesia following total knee or hip arthroplasty.^{20,28} Combination of low concentrations of both opioid and a local anesthetic, like intrathecal morphine and bupivacaine, creates a synergistic effect, providing adequate pain relief in the early postoperative time, a reduction in intravenous opioid requirements and a decreased rate of opioid-related side-effects.^{20,29,30} Regardless of the analgesic regimen used, epidural analgesia appears to provide superior pain control with less adverse effects than systemic opioid analgesia.³¹

Despite that, epidural analgesia is non-selective for unilateral surgery and has potential side effects, such as hypotension, urinary retention, motor block limiting mobilization and risk of spinal/epidural hematoma in anticoagulated patients with epidural catheters, depending on the dose and patient population.^{9,20,32,33} This is an important limitation, as early anticoagulation is strongly recommended as a prophylactic measure to reduce the incidence of venous thrombotic events.³⁴

These complications can increase patients' morbidity and delay discharge from the post-anesthesia care unit and the hospital and have led to a search for alternative modalities to improve pain control and functional recovery following major orthopedic surgery.^{20,21}

Neuraxial blocks have no beneficial effects over peripheral regional techniques, in terms of safety, pain control, patient satisfaction, hospital length of stay and long-term functional outcomes.^{30,35} Data comparing continuous epidural analgesia to femoral nerve block (FNB) or LIA after TKA, show that both offer better pain relief and early recovery of knee flexion angle.^{26,30,35} This is clinically relevant since minimal improvements in knee flexion are needed to accomplish daily activities such as getting up from a chair and climbing stairs.³⁴

2. Peripheral Nerve Blocks

Spinal and epidural anesthesia used to be the first choice for lower limb procedures, but as fast track patient management became an increasing trend, the use of peripheral regional anesthetic techniques has been gaining popularity.^{1,36} There has been an increase in the use of PNB from 6,5% to 8,7% for THA and from 10,3% to 20,4% for TKA, between 2006 and 2012 in the USA.⁴ Despite being technically difficult and requiring training and practice, lower extremity nerve blocks allow selective unilateral peripheral block, which provides pain relief similar to epidural analgesia and intravenous opioids, but with shorter functional recovery time, fewer adverse effects, complications and costs.^{20,31,37}

Thanks to the advances in ultrasonography, needles, catheters and nerve stimulator technology, there was a significant improvement in PNB's quality, allowing better visibility of the neural structures and local anesthetic dispersion, lower administration volume, faster procedure, lower risk of vascular puncture and higher success rates.^{20,35,38}

Nevertheless, PNB have potential complications like nerve and vessel injury due to local anesthetic neurotoxicity or mechanical trauma, bleeding, heel ulcers and catheter-site infection, although these consequences are rare and less severe than those associated with neuraxial blockade.^{20,39,40} Additionally, some nerve blocks have increased risk of motor blockade, impairing physical therapy and early ambulation and predisposing patients to falls.^{37,41} Fortunately, peripheral nerve injury is rare and more than 90% of cases have a favorable outcome with complete recovery in weeks to months.^{40,42}

PNB can be administered whether as a single-dose injection or as a continuous infusion or intermittent boluses by a catheter, extending the duration of treatment.^{16,36} Even though the optimal regimen for administration of adductor canal block (ACB) and FNB remains undefined, studies suggest that in the presence of a multimodal pain management protocol, single-shot ACB or FNB alone can provide equivalent analgesia as continuous catheter after TKA.⁴³⁻⁴⁵ Furthermore, catheters may be technically difficult to insert and are associated with several complications like catheter site infection, prolonged nerve palsy, nerve injury, heel ulcers and premature displacement due to knee mobilization.^{39,46,47}

Local anesthetic doses should be adapted to the duration and level of pain of the procedure.^{1,15} Addition of adjuvants to the anesthetic solution can change the pharmacokinetic dynamics, increasing not only the duration of the block, but also complication rates.¹

Selection of regional analgesic technique depends on the surgical site.²⁰ PNB provide regional anesthesia in the distribution of the nerve blocked, so PNB techniques' practice requires appropriate knowledge of dermatomes, myotomes and osteotomes of the lower limb (figure 2).^{1,16}

2.1. Peripheral Nerve Block Techniques for Total Hip Arthroplasty

Hip joint innervation is complex with contributions from both lumbar and sacral plexus. The anterolateral region is innervated by the femoral nerve (FN), and the anteromedial portion by the obturator nerve (ON). The posterior and inferior parts of the hip joint capsule are innervated by the sacral plexus (branches of the sciatic nerve, the nerve to the quadratus femoris muscle, and superior gluteal nerve). Nociceptive fibers are predominantly located in the anterior and superolateral parts of the hip joint capsule and mechanoreceptors are mainly in the posterior region. Lateral femoral cutaneous nerve (LFCN) is also important for hip analgesia, since it is responsible for the innervation of the skin of the lateral part of the thigh, which is frequently the area of the skin incision.⁹

There are several selective nerve blocks available for hip surgery, but the ideal block or combination of blocks for postoperative management following THA has not been established yet.⁹

a) Lumbar Plexus Block

Lumbar Plexus Block (LPB), also known as Psoas Compartment Block, targets FN, LFCN and ON, which are major contributions for the innervation of the hip.⁹ As such, LPB is a well-accepted technique for regional anesthesia after THA.^{9,41}

Available data indicates that both single-shot and continuous LPB are associated with significant pain relief and reductions in postoperative opioid consumption after THA.^{9,31} Lumbar plexus catheter technique not only reduces postoperative pain ratings in the first 48 hours, but also allows early discharge from hospital.⁹

However, LPB is a deep and technically difficult block, which make it subject to the same restrictions of neuraxial blocks in anticoagulated patients because of the risk of retroperitoneal bleeding.⁴⁸ In addition, it has potential serious complications secondary to neuraxial spread, intravascular local anesthetic administration or visceral injury.⁹

Although quadriceps weakness is reported in many patients after LPB, when compared to FNB, this technique seems to provide better analgesia and mobilization following THA.^{41,48} However, the risk of falls is uncertain and should be considered, especially in high-risk patients.³¹

b) Fascia Iliaca Compartment Block

Fascia Iliaca Block (FIB), or 3-in-1 block, consists in injecting high volumes of local anesthetic in the intermuscular plane, bellow the fascia iliaca, with proximal dispersion to the psoas muscle, targeting FN, LFCN, and ON.^{9,49} It can be used for postoperative analgesia following THA as it provides an indirect proximal approach to the lumbar plexus, but it is technically easier to perform and has less risk of complications.⁴

Compared to the FNB, FIB technique is safer as it has the advantage that the puncture site is more distant from large vessels and femoral nerve, decreasing the potential of induced injury.^{9,50} Despite that, it's not possible to visualize the spread of local anesthetics around the targeted nerves and, consequently, results depend on the adequate spread of the solution in the intermuscular plane.⁵⁰ An adequate volume and correct needle placement are necessary to obtain a successful block, without simultaneously increasing the risk of local anesthetic systemic toxicity (LAST).⁵⁰

Results concerning the efficacy of FIB to treat acute postoperative pain from THA are not consistent.⁵⁰ Studies comparing FIB with LPB or FNB, indicate equivalent postoperative analgesia and opioid consumption in all groups and in a 2017 randomized controlled trial (RCT), use of continuous FIB resulted in decreased pain scores in the first 24 hours and 45% reduction in morphine requirements in the first 48 hours postoperatively, compared to intravenous analgesia alone.^{9,50} Nevertheless, other studies couldn't report clinical benefit of FIB and a RCT found spinal morphine to be superior to this nerve block in the first postoperative day.^{4,9}

In spite of these conflicting results, FIB has generally been reported to provide superior postoperative analgesia when compared to placebo, regardless of the type of hip surgery.⁹ The lack of evidence might be explained by the different approaches of the iliac fascia, since in some trials a supra-inguinal approach was used, while in other studies, they preferred an infra-inguinal approach.⁵⁰ Currently, there is not enough data to establish the efficacy and safety of FIB for THA and further search is required to determine the role of FIB as a part of a multimodal analgesia protocol after THA.^{9,50}

c) L2 Paravertebral Block

Although LPB is a reference standard PNB for THA, it can lead to motor blockade, impairing fast-track discharge. Thereby, there is a constant search to find more favorable alternatives.⁴¹

Paravertebral somatic nerve blocks allow ipsilateral segmental analgesia and have been successfully used for several thoracic, abdominal and pelvic procedures and L2 paravertebral block (PVB) in specific, has recently been reported as an adequate analgesic modality in hip arthroscopy.⁴¹

In what concerns pain management following THA, a RCT compared continuous L2 PVB with LPB and concluded that both techniques resulted in similar pain scores, motor preservation and length of stay, but LPB resulted in lower morphine consumption. Therefore, as L2 PVB doesn't seem to have any advantage in terms of rehabilitation outcomes compared to LPB and not much is known about its safety profile, it shouldn't be recommend as an alternative to LPB following THA yet.⁴¹

d) Interfascial Plane Blocks: Quadratus Lumborum Block

Quadratus lumborum block (QLB) has traditionally been used for abdominal surgery because it blocks the anterior branches of thoracoabdominal nerves. In addition, it may be extended to the superior branches of the lumbar plexus, through the spread of the anesthetic solution into the paravertebral space. Recently, QLB has been reported for hip fractures and it has been described to have an analgesic effect for more than 24 hours without being associated with muscle weakness, especially with posterior and superficial approach. Thus, QLB may have a place in multimodal pain management for hip surgery, in order to improve functional rehabilitation, but more well-designed prospective studies are needed to evidence the risks and clinical benefits of this block post-THA.⁹

e) Lateral Femoral Cutaneous Nerve Block

LFCN is a sensitive branch of the lumbar plexus, which is responsible for the innervation of the anterolateral part of the hip. Even so, there is a high individual variability in LFCN course and branches, and consequently, in its area of sensory coverage.⁹ When performed alone, effectiveness of LFCN block is limited because surgical incision normally extends beyond its innervated skin area.⁹ However, it can be useful for postoperative pain control after THA, if utilized in combination with other blocks.^{1,9}

2.2. Peripheral Nerve Block Techniques for Total Knee Arthroplasty

Knee joint is innervated anterolaterally by branches of the lumbar plexus (femoral and obturator nerves) and posteriorly by the sacral plexus (sciatic nerve).^{16,43}

Ideal PNB for analgesia of the knee should be balanced between optimizing analgesia and providing early ambulation after TKA. This is difficult to accomplish because all major nerves that contribute to knee innervation have combined sensory and motor function.^{13,51} As such, the ideal peripheral regional technique for TKA is still a matter of debate.^{12,35}

a) Femoral nerve block

FNB has been the gold-standard approach for postoperative pain management after TKA for the last 2 decades and remains a commonly used technique, as it is utilized in about 25% of patients following TKA in the USA.^{44,52} It provides superior pain control, less opioid consumption and related side-effects and greater knee flexion and patients' satisfaction when compared to intravenous patient-controlled analgesia or epidural analgesia.³⁵ As it comprises both sensory and motor innervation of the knee joint, it can cause anesthetic-induced quadriceps weakness and, consequently, increase risk of falls

and delayed ambulation.^{11,53,54} Although falls are a rare event, they may impair postoperative recovery and delay discharge.⁵⁵

This is an important concern, since modern clinical practice requires adequate analgesia with early active mobility (often on the day of surgery) and short length of stay.^{48,56} Such goals demand a reappraisal on the way FNB is used.⁵⁶ One of the techniques that has been utilized in order to reduce falls and allow early mobilization is the use of a knee immobilizer until the end of the effect of the block and the patient regain quadriceps strength.^{20,44} In combination with a front wheeled walker, it makes possible to use a FNB and still be able to ambulate in the immediate post-operative period.^{44,57}

Nevertheless, motor impairment secondary to FNB has led to a search for other alternatives, such as ACB and saphenous nerve block.^{37,54}

b) Adductor canal block

ACB provides a sensory block of the anteromedial knee and, in recent years, it has been emerging as a substitute for FNB, since most studies suggest that it offers at least equivalent analgesia with minimal effect on quadriceps strength after TKA.^{5,16,58}

The advantages of ACB over FNB in terms of motor function are due to anatomical reasons.³⁷ Adductor canal is an aponeurotic space in the thigh, extending from the apex of the femoral triangle to the adductor hiatus.^{59,60} It contains multiple afferent sensory nerves, including saphenous nerve and only a single efferent motor nerve to vastus medialis.^{36,60,61} Therefore, ACB is almost a pure sensory nerve block and infusion of local anesthetics into this space provides effective analgesia of the knee and simultaneously spares the majority of motor contributions to the lower limb.^{25,36,39}

Quadriceps strength plays an essential role for balance, gait and knee function rehabilitation, so its preservation, even if partial, is crucial for early functional recovery.^{61,62}

There are a lot of RCTs and meta-analysis comparing ACB to FNB after TKA. Although there are inconsistent results in what concerns postoperative analgesia, the majority of studies show that pain control at rest or mobilization and opioid consumption are not significantly different between ACB and FNB, at any follow up time.^{11,27,45,53,61}

Otherwise, in terms of functional outcomes, studies consistently favor ACB. It offers significantly superior or at least similar results regarding most of the functional recovery parameters evaluated such as muscle strength, assessed by quadriceps maximum voluntary isometric contraction or manual muscle strength scale, degree of knee extension, range of motion and ability to sit, stand upright and ambulate sooner.^{27,36,37,45,53,61} So, ACB seems to be associated with earlier mobility rehabilitation and faster knee function recovery at least during the first 48 postoperative hours.^{27,39,45,61} This is clinically relevant since early mobilization, even in the first 24 hours, reduces length of stay, immobility-complications like

deep vein thrombosis and overall costs and is one of the best predictors for a good outcome after TKA.^{54,62} It allows effective rehabilitation and rapid return to normal ambulatory function, which are also important measures of TKA success, currently.^{11,39} Moreover, ACB is also associated with decreased risk of falls.⁶¹

Nonetheless, the anatomical location of the adductor canal needs to be better defined as it remains unclear which is the ideal location of the continuous block and if it has impact in ACB effectiveness.^{11,51,63} A more proximal ACB may provide better pain relief, but it can result in greater motor block by targeting more afferent branches of the femoral nerve. On the other hand, a distal approach may have a lower risk of muscle weakness yet it may not offer adequate analgesia.⁶³ Optimal local anesthetic dose and concentration are also still a matter of discussion.⁶¹

Despite that, there is crescent consensus that ACB should be recommended to replace FNB as the block of choice for TKA at present.^{47,53,59} However, like other PNB, it can't provide total analgesia of the knee alone.^{17,43} Thereby, co-administration of other nerve blocks or LIA is essential to optimize postoperative pain treatment after TKA and requires further investigation.^{17,43}

c) Saphenous nerve block

Saphenous nerve passes through the adductor canal and innervates the anterior part of the knee capsule, the infrapatellar skin and the medial side of the leg. It is a terminal sensory branch of the femoral nerve and is the largest contribution from the femoral nerve to the sensory innervation of the knee.^{11,19,48}

Saphenous nerve block is a recent ultrasound-guided technique that targets the distal thigh level of the adductor canal.⁴⁸ This approach has been gaining considerable interest for TKA since it is a sensory block that enables adequate pain relief with less quadriceps motor weakness when compared to traditional FNB.⁴⁸

A RCT compared combination of intraoperative single-shot LIA with continuous saphenous block to LIA catheter alone, in order to improve LIA's duration and efficacy.⁴⁶ Combination of LIA with continuous saphenous block resulted in lower pain scores during movement and at rest on the day of surgery and superior capacity to ambulate than LIA alone, which represents a determinant milestone in the recovery process after TKA.^{46,64} Thereby, this combination appears to be a promising strategy, but further studies are needed to elucidate its effectiveness.⁴⁸

d) Sciatic Nerve Block

In general, FNB and ACB are the preferred PNB to extend pain treatment after TKA.^{27,30,47} However, none of these techniques provides complete analgesia of the joint

since the posterior aspect of the knee is innervated by the sciatic nerve and, in some patients, by a posterior branch of the obturator nerve.^{43,65} The sciatic nerve consists of the tibial and common peroneal nerves, which are responsible for the innervation of the posterior region of the leg and plantar region and anterolateral leg and dorsum of the foot, respectively.⁶⁶

Therefore, the combination of FNB with a sciatic nerve block (SNB) seems to be an adequate choice to address posterior knee pain and, consequently, optimize pain control after TKA.^{30,67} In fact, combined FNB and SNB have been shown to provide better postoperative analgesia than FNB alone.¹⁶ A 2016 meta-analysis suggest that the addition of SNB to FNB reduces morphine consumption at the first postoperative day and decreases knee pain at rest and during movement, whether a single-shot or a continuous block is used.⁶⁸ On the other hand, no differences were found regarding functional recovery outcomes.⁶⁸

In what concerns long-term outcomes, an RCT concluded that although adding SNB to continuous FNB improves short-term postoperative analgesia, it doesn't improve knee function, stiffness and pain level at rest and during mobilization at 3 and 12 months post-TKA.⁶⁹

Due to blockade of the common peroneal nerve, SNB is associated with motor inhibition of the entire lower limb below knee, increasing risk of postoperative falls, ischemic heel ulcers and foot drop that can mask surgically induced peroneal nerve injury and may delay postoperative rehabilitation.^{48,65,66}

The available data supporting the benefit of using SNB in combination with FNB following TKA is marked by significant heterogeneity, especially when combined with a multimodal analgesic regimen.^{67,68} As additional use of SNB is associated with potential risks and additional time, costs and technical skills, more prospective studies on the effectiveness of this block are needed, so it can be recommended as a standard block after TKA.^{35,67,68} Currently, its use should be considered according to the risk-to-benefit ratio of each patient individually.^{35,67}

e) Selective Tibial Nerve Block

Since it only blocks tibial nerve component of the sciatic nerve, selective tibial nerve block (TNB) could be an alternative to provide pain relief to the posterior aspect of the knee, while avoiding foot drop due to common peroneal nerve block.⁶⁶

A prospective randomized study showed that selective TNB performed in the popliteal fossa can provide the same analgesic efficacy as SNB while avoiding complete blockade of the common peroneal nerve when combined with FNB for patients undergoing TKA.⁶⁶ Other RCT showed that TNB resulted in superior pain control and better ambulation

than ONB, when combined to LIA and ACB.⁶⁵ This suggests that tibial nerve contribution to the sensory block of the posterior knee might be clinically more important than common peroneal nerve.⁶⁶ These results are difficult to compare with other studies because there is high variability in local anesthetic's preference, definition of success and assessment time.⁶⁶

f) Interspace between Popliteal Artery and Posterior Capsule of the Knee block

ACB provides analgesia to the anterior and medial aspects of the knee joint, but not to the posterior capsule, as it doesn't have effect on deep genicular nerves.^{5,70} As such, these patients have moderate to severe pain in the posterior aspect of the knee, hindering complete knee extension and early ambulation.⁷⁰

SNB used to be the first choice to block pain in the posterior region of the knee. However, it involves common peroneal nerve, resulting in complete sensorial and motor block of the calf, foot and ankle.^{5,70}

Ultrasound-guided local anesthetic infiltration of the Interspace between Popliteal Artery and Posterior Capsule of the Knee (IPACK) has been described as an alternative approach to target posterior knee pain, that appears to provide adequate posterior knee analgesia without affecting muscle strength, since it only blocks the terminal sensory branches of the tibial nerve, sparing the motor branches of the tibial and peroneal nerves.^{5,70} This results in early ambulation and, consequently, in better rehabilitation and functional recovery.⁷⁰

Patients who receive a combination of FNB+IPACK block have a significantly lower postoperative opioid consumption, compared to continuous FNB alone and a prospective control trial found that the combination of ACB and IPACK resulted in significantly better pain scores on postoperative day 0, better range of motion and ambulation distance compared to ACB alone.^{5,70} Other study showed that ACB+IPACK reduces length of stay and improves ambulation distance, although with slightly superior opioid consumption compared to FNB+IPACK block.⁷⁰ A retrospective review reported that continuous ACB+IPACK is associated with shorter hospitalization, decreased opioid requirements and opioid related adverse events, increased discharge to home, further ambulation and lower pain scores, when compared to single-shot FNB plus liposomal bupivacaine pericapsular injection.¹²

Combination of ACB and IPACK block is a promising technique due to its analgesic efficacy and muscle-sparing characteristics.^{5,70} Nevertheless, there are few published studies that assess effectiveness of IPACK block, so further large randomized studies are necessary to evaluate its utility in postoperative pain management after TKA.⁷⁰

g) Obturator Nerve Block

ON innervates the medial part of the hip and knee, which makes it potentially useful for THA and TKA.¹ Despite that, it remains unclear whether Obturator Nerve Block (ONB) alone or combined with other PNB can significantly improve pain relief after total joint replacement, or if it has possible advantages compared with other peripheral regional techniques.^{9,65}

A study described that the combination of ONB and LFCN block can be effective in acute pain management after hip fracture surgery, yet other RCTs didn't found clinical benefit in using ONB. Nonetheless, the current evidence is mostly based in indirect comparison and must be interpreted with caution.⁹

In what concerns TKA, previous studies showed that ONB added to FNB or femoral triangle block (FTB) results in better pain relief than FNB alone, but other studies didn't found additional advantages.⁶⁵ In a 2016 RCT, addition of ONB to FTB after TKA resulted in a 90% decrease in morphine consumption, reduced opioid related side effects and better pain relief compared with single FTB or LIA, without impairing mobility, as all patients in the ONB+FTB group were able to perform the Timed Up and Go (TUG) test in the first postoperative 24 hours.⁷¹ In prior studies, combined ONB and FNB seem to be inferior to SNB plus FNB.⁶⁵ However, triple block combining ONB, ACB and TNB with LIA has shown to improve immediate functional recovery in the first postoperative day following TKA.⁶⁵

3. Local infiltration analgesia

LIA consists in injecting a local anesthetic, alone or in combination with other analgesic adjuncts, directly into the operative field or around joint space before surgical wound closure, involving both capsular and soft tissues.^{9,16} Due to its simplicity, convenience and apparent safety, LIA has gained widespread acceptance over the last decade as an alternative method of providing pain control for patients undergoing hip and knee replacement.^{48,72,73}

LIA requires minimal instrumentation and technical skills as it can be administered intraoperatively by the surgeon, without the risk of neurovascular injury and the additional time and procedural cost of the administration of a PNB by a specialized anesthesiologist preoperatively.^{16,54,74} Beyond that, it blocks pain conduction directly at its origin, decreasing body's central response to pain, preventing systemic side effects and motor block of the lower limb, one of major problems of other regional anesthesia techniques.^{30,73,75,76}

The biggest disadvantage of local infiltration is its short duration of action.⁷⁷ LIA's effect is limited to a few hours, as the injected local solution is reabsorbed from the operative site.⁷² To prolong pain relief, a catheter can be placed in the periarticular space, with continuous infusion of local anesthetic solution.⁷² However, several RCTs have

demonstrated no benefit in using a catheter over single-shot technique and continuous techniques are associated with increased risk of local infection and local anesthetic toxicity by local anesthetics tissue infiltration.^{16,30,48,72}

Infiltrated solutions normally contain a local anesthetic such as bupivacaine or ropivacaine, epinephrine, a narcotic like morphine, an anti-inflammatory (usually ketorolac), with some mixtures also containing dexamethasone.¹⁶ The optimal mixture of local infiltration analgesia is not yet defined, as well as the ideal method and location.^{2,75} These variables are very difficult to control when comparing LIA studies.⁷⁵

3.1. Local Infiltration Analgesia for Total Hip Arthroplasty

From an anatomical perspective, LIA should be particularly convenient for THA as the sensory innervation of the hip is complex and may extend from T12 (subcostal nerve) to S1 (proximal sciatic branches).⁴⁸ Nevertheless, studies using LIA for analgesia after THA show mixed results and its use has not been generally recommended yet.^{9,78}

In a 2016 RCT, LIA has shown to significantly reduce pain scores in the first 24 hours after surgery, but no significant differences were found in opioid consumption, length of stay and early and long-term functional recovery outcomes, such as day to get out of bed alone and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC score).⁷³

Moreover, several RCTs found that LIA as a part of a multimodal analgesic regimen doesn't provide any additional analgesic benefit or reduction in opioid consumption, which means LIA may not be effective or required when multimodal pain management is given following THA.^{72,79,80}

These results contrast with previous RCTs that suggest that LIA reduces pain scores and opioid requirements in patients who had undergone THA, but the differences could be justified by the absence of a comprehensive multimodal regimen in those studies.^{9,48,72}

Unlike TKA, it's not consensual which structure should be infiltrated to provide pain relief after THA, yet a recent RCT found that use of LIA to block lateral cutaneous and subcostal nerves didn't show clinically relevant analgesic benefits after a straight lateral approach THA.⁷⁸

One of the main causes of postoperative pain is local tissue damage due to surgical procedure.⁷⁸ This may explain why LIA doesn't have consistent results following THA since there is high variability in the surgical approach of the hip and different combination of analgesics and methods of administration of LIA in the previous RCTs, making results difficult to interpret.^{48,78,80} Further research should focus on the ideal composition, volume and location of LIA for each THA approach separately.⁷⁸

3.2. Local Infiltration Analgesia for Total Knee Arthroplasty

In contrast to THA, efficacy of LIA for analgesia following TKA is strongly supported and has become one of the cornerstones of rapid recovery protocols in TKA.^{9,30,78}

Like PNB, the use of LIA is associated with improved pain control, inferior opioid consumption and related side-effects and decreased length of stay, when compared to systemic narcotics or epidural analgesia.^{16,30,48,76}

Contrary to previous studies, a recent RCT found that performing LIA in addition to a standardized multimodal analgesia regimen not only results in reduced resting and dynamic pain scores and decreased opioid requirements on the first postoperative day, but also in increased patient satisfaction rates in patients undergoing TKA.⁵⁴

As duration and efficacy of LIA are not sufficient to provide pain relief for TKA's postoperative period alone, adding it to nerve blocks like ACB or saphenous nerve block may provide additional benefit and warrants consideration.^{13,16,46,48}

a) Local Infiltration Analgesia versus Femoral Nerve Block with or without Sciatic Nerve Block

Compared to FNB, LIA seems to provide similar pain control while avoiding motor block and its negative functional impacts.^{16,81} Overall, studies comparing FNB to LIA, show no significant differences in pain intensity at rest or in opioid consumption.^{16,24} However, LIA results in better knee function, earlier functional recovery, easier rehabilitation and shorter hospitalization.^{33,82-84}

As SNB produces significant motor impairment, LIA can be an option to provide postoperative analgesia of the knee.⁵⁴

A prospective randomized trial that compared the combination of FNB and SNB, FNB plus posterior LIA and FNB alone within a multimodal analgesic regimen, found no differences in pain scores at rest or with movement in the first 48 hours and in the functional outcomes between the 3 groups.⁶⁷ According to this study, addition of SNB or posterior LIA to FNB appears to have no clinical benefits.⁶⁷

However, a retrospective study comparing combination of FNB with single-shot SNB or with posterior LIA revealed significant better mobilization, muscle strength and pain reduction in early postoperative period in the LIA group, although FNB+SNB resulted in no falls or short-term complications and functional recovery was comparable after 7 days among both groups.³⁰

A RCT comparing LIA with a combination FNB and single-shot SNB after TKA found that despite both pain scores and narcotic consumption were higher in the LIA group on the day of surgery, quadriceps function (assessed by quadriceps extensor lag and ability to straight-leg raise) was lower in the PNB group until the afternoon of postoperative day 2.⁷⁷

Moreover, PNB group was associated with higher rate of neurological sequelae at 6 weeks follow-up (12% versus 1% in the LIA group).⁷⁷

This earlier return of quadriceps function with LIA can be clinically important as it allows earlier intensive rehabilitation, decreases the risk of early immobilization complications such as deep venous thrombosis and results in nearly half a day less length of stay, which in some cases, can mean discharge one day sooner.^{30,77}

b) Local Infiltration Analgesia combined with Adductor Canal Block

Since ACB alone doesn't provide appropriate analgesia to the posterior knee and LIA has a short duration of action, it has been suggested that combined the two techniques could be advantageous.^{13,65,85}

In a 2018 prospective study, Sankineani *et al.* concluded that patients receiving ACB and multimodal peri-articular infiltration have demonstrated better pain scores and better range of motion in the immediate postoperative period than ACB alone, although there was no difference at the time of discharge.⁸⁵ A RCT comparing ACB with LIA or combined ACB+LIA found that patients who received ACB alone had higher immediate postoperative pain scores at rest or knee bending, followed by patients who received LIA alone. Patients with combined ACB+LIA reported the lowest pain scores, with significantly less postoperative pain on walking compared with those who received ACB or LIA only.⁸⁶ Other recent RCT concluded that addition of ACB to LIA is associated with improved analgesic profile when compared to LIA alone, despite there were no differences in TUG test on postoperative day 2 or in global functional outcomes at 3 months postoperatively.¹³

Nevertheless, this is controversial as several recent RCTs reported that ACB alone is inferior for perioperative pain control and early mobility than either LIA alone or ACB+LIA, but there were no significant differences between LIA and ACB+LIA. This suggests that these techniques have non-additive action and its combination is not superior to LIA alone.^{16,54,58,62} Moreover, this association involves the use of a high total dose of local anesthetic with increased potential for LAST.⁶⁰

Therefore, it's not clear that adding ACB to LIA has clinically relevant benefits and additional studies are needed to determine if the increased cost and risks associated with ACB are warranted.^{58,86}

4. Multimodal analgesic regimen

Pain perception is complex and mediated by multiple pathways and mechanisms.⁸ Each class of analgesic agents has a different site of action, so when classes with synergistic effects are combined, several pathways are targeted at the same time.^{8,18,20,44}

This maximizes multimodal effect and allows optimization of pain control while limiting associated adverse effects of the different treatment strategies.^{8,18,20}

In the last decade, there has been a significant improvement in postoperative pain management, focusing on the implementation of comprehensive multimodal analgesic protocols with the ultimate goal of reducing perioperative opioid use, improving clinical outcomes and functional recovery and simultaneously reducing length of hospital stay and costs.^{14,20,58,70,85,87}

These protocols vary widely between institutions, but typically incorporate a combination of preoperative oral analgesic drugs, postoperative oral or intravenous narcotics and at least one form of regional anesthesia, which is the keystone of multimodal analgesia in hip and knee replacement surgery.^{35,77} The several elements of a multimodal regimen can be chosen according to individual clinical factors, provider's preference and experience and patient's desire, after discussing the available options and its risks and benefits.^{1,18,44}

Although there is no current consensus on an optimal perioperative pain management regimen, there is wide agreement that multimodal protocols that include regional anesthesia techniques improve perioperative patient care, since they minimize postoperative pain, decrease morbidity, facilitate early mobilization and rehabilitation and maximize patient satisfaction following THA and TKA.^{12,14,49,77,88} Therefore, "enhanced recovery" or "fast-track" programs are being developed to standardize care and hasten patient's discharge without an increase in pain, complications, and readmissions, benefiting not only patients, but also surgeons and hospital systems.^{12,14} Pre-operative education and faster rehabilitation are the most important components to achieve these improvements.⁸⁸

CONCLUSION

For an intervention to be considered superior to another, it needs to result in improved pain control and at least similar, if not better, rehabilitation outcomes. Despite there is still debate of which strategy is most effective for THA and TKA currently, regional anesthesia, especially peripheral regional anesthesia techniques have been established as optimal analgesic methods for postoperative pain management in the last years. Both peripheral nerve blocks and local infiltration analgesia are associated with superior analgesia, lower morbidity, earlier hospital discharge and better functional outcomes following THA or TKA.

Multiple patient and procedure factors must be balanced when choosing the appropriate analgesic strategy. As functional recovery of the quadriceps may be affected by regional anesthesia modalities, clinicians should consider the motor involvement of each technique when establishing individual postoperative rehabilitation protocols after total hip or knee replacement.

Regardless of which regional anesthesia technique is used, a comprehensive multimodal pain management should be employed, ideally in the setting of an enhanced recovery program.

In most of the studies assessed, functional recovery aspects are infrequently reported, and when reported, they are mostly secondary outcomes of the trial and, therefore, do not have as much statistical strength as primary outcomes. Thereby, additional investigation in the form of large prospective randomized control trials is warranted to clarify the potential benefits and effect of regional anesthesia techniques on functional recovery after total joint replacement and determine the optimal multimodal postoperative analgesic strategy for these patients.

ATTACHMENT

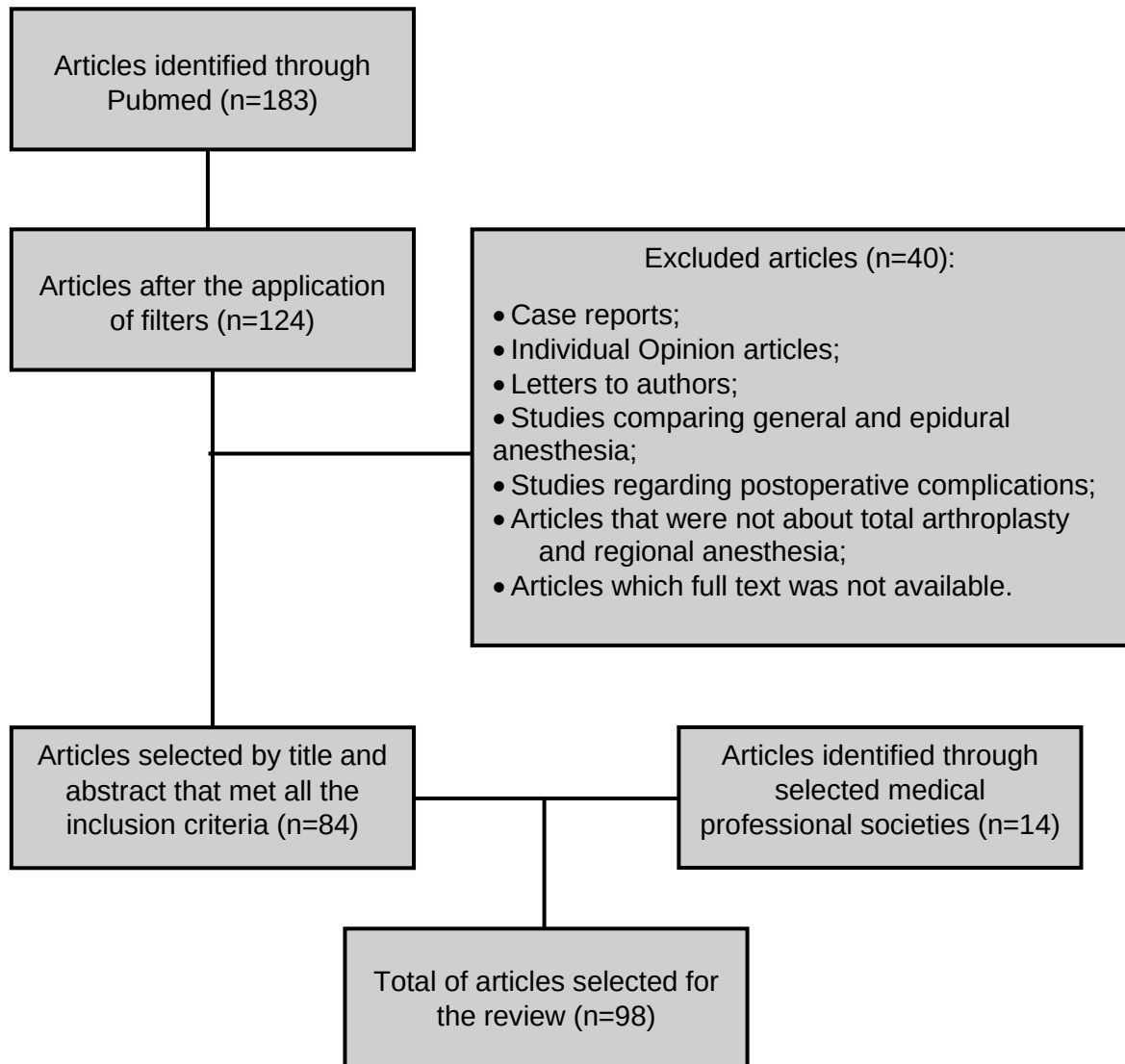


Figure 1 - Article selection flowchart

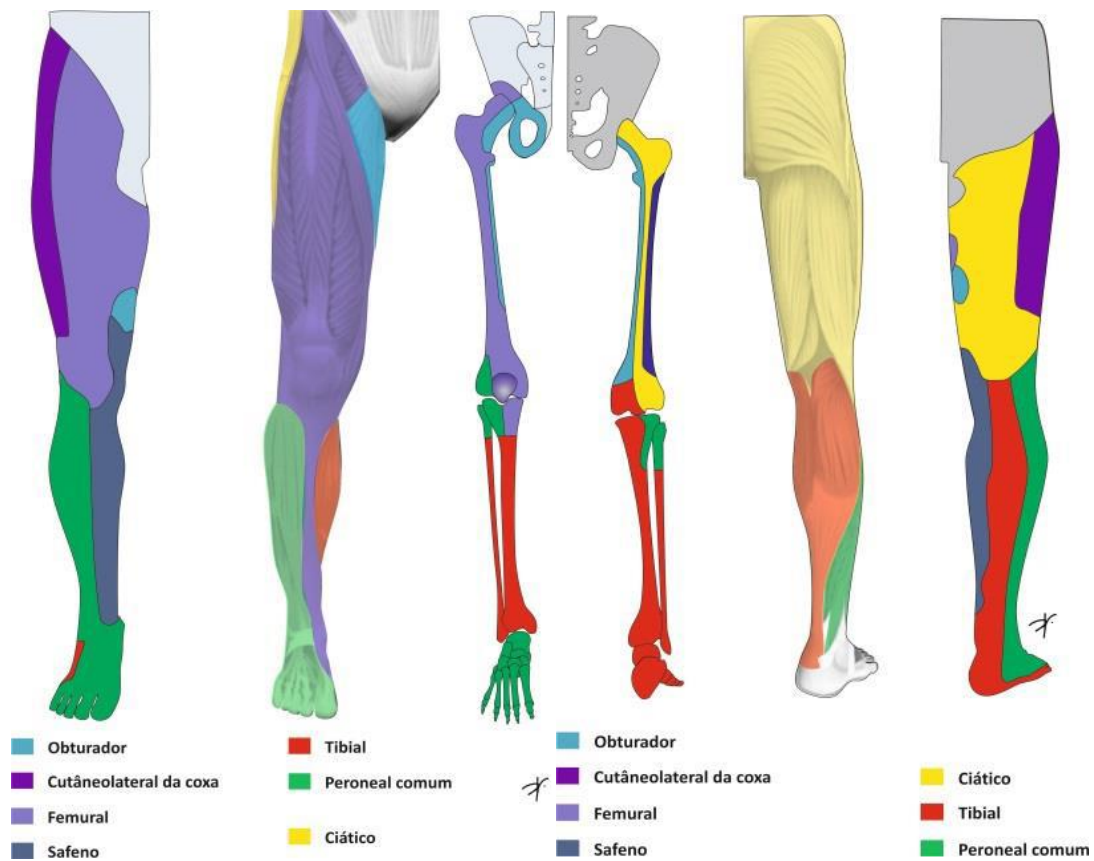


Figure 2 – Cutaneous, muscular and bone innervation of each peripheral nerve of the lumbar and sacral plexus.¹

REFERENCES

1. Recomendações para Anestesia Regional em Cirurgia Ambulatória. <http://www.apca.com.pt/ver.php?cod=0B0A0A>. Accessed 15/04/2020.
2. Zhao J, Davis SP. An integrative review of multimodal pain management on patient recovery after total hip and knee arthroplasty. *Int J Nurs Stud*. Oct 2019;98:94-106.
3. Gaffney CJ, Pelt CE, Gililand JM, Peters CL. Perioperative Pain Management in Hip and Knee Arthroplasty. *Orthop Clin North Am*. Oct 2017;48(4):407-419.
4. Elmofly DH, Buvanendran A. Regional Anesthesia in Total Joint Arthroplasty: What Is the Evidence? *J Arthroplasty*. Sep 2017;32(9s):S74-s76.
5. Kumar L, Kumar AH, Grant SA, Gadsden J. Updates in Enhanced Recovery Pathways for Total Knee Arthroplasty. *Anesthesiol Clin*. Sep 2018;36(3):375-386.
6. Gabriel RA, Kaye AD, Nagrebetsky A, Jones MR, Dutton RP, Urman RD. Utilization of Femoral Nerve Blocks for Total Knee Arthroplasty. *J Arthroplasty*. Aug 2016;31(8):1680-1685.
7. Lucas R, Monjardino M. O estado da Reumatologia em Portugal. In: Reumáticas ONdD, ed2010.
8. Milani P, Castelli P, Sola M, Invernizzi M, Massazza G, Cisari C. Multimodal Analgesia in Total Knee Arthroplasty: A Randomized, Double-Blind, Controlled Trial on Additional Efficacy of Periarticular Anesthesia. *J Arthroplasty*. Nov 2015;30(11):2038-2042.
9. Bugada D, Bellini V, Lorini LF, Mariano ER. Update on Selective Regional Analgesia for Hip Surgery Patients. *Anesthesiol Clin*. Sep 2018;36(3):403-415.
10. Liu J, Yuan W, Wang X, et al. Peripheral nerve blocks versus general anesthesia for total knee replacement in elderly patients on the postoperative quality of recovery. *Clin Interv Aging*. 2014;9:341-350.
11. Hussain N, Ferreri TG, Prusick PJ, et al. Adductor Canal Block Versus Femoral Canal Block for Total Knee Arthroplasty: A Meta-Analysis: What Does the Evidence Suggest? *Reg Anesth Pain Med*. May-Jun 2016;41(3):314-320.
12. Klement MR, Bullock WM, Nickel BT, et al. Continuous adductor canal blockade facilitates increased home discharge and decreased opioid consumption after total knee arthroplasty. *Knee*. Jun 2019;26(3):679-686.
13. Biswas A, Perlas A, Ghosh M, et al. Relative Contributions of Adductor Canal Block and Intrathecal Morphine to Analgesia and Functional Recovery After Total Knee Arthroplasty: A Randomized Controlled Trial. *Reg Anesth Pain Med*. Feb 2018;43(2):154-160.
14. Schwenk ES, Pozek JJ, Viscusi ER. Managing Prolonged Pain After Surgery: Examining the Role of Opioids. *J Arthroplasty*. Nov 2018;33(11):3389-3393.
15. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. Feb 2012;116(2):248-273.
16. Chung AS, Spangehl MJ. Peripheral Nerve Blocks vs Periarticular Injections in Total Knee Arthroplasty. *J Arthroplasty*. Nov 2018;33(11):3383-3388.
17. Hannon CP, Keating TC, Lange JK, Ricciardi BF, Waddell BS, Della Valle CJ. Anesthesia and Analgesia Practices in Total Joint Arthroplasty: A Survey of the American Association of Hip and Knee Surgeons Membership. *J Arthroplasty*. Jul 8 2019.
18. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain*. Feb 2016;17(2):131-157.
19. Kayupov E, Okroj K, Young AC, et al. Continuous Adductor Canal Blocks Provide Superior Ambulation and Pain Control Compared to Epidural Analgesia for Primary

- Knee Arthroplasty: A Randomized, Controlled Trial. *J Arthroplasty*. Apr 2018;33(4):1040-1044.e1041.
20. Horlocker TT. Pain management in total joint arthroplasty: a historical review. *Orthopedics*. Sep 2010;33(9 Suppl):14-19.
 21. Awad IT, Cheung JJ, Al-Allaq Y, Conroy PH, McCartney CJ. Low-dose spinal bupivacaine for total knee arthroplasty facilitates recovery room discharge: a randomized controlled trial. *Can J Anaesth*. Mar 2013;60(3):259-265.
 22. Wang Y, Klein MS, Mathis S, Fahim G. Adductor Canal Block With Bupivacaine Liposome Versus Ropivacaine Pain Ball for Pain Control in Total Knee Arthroplasty: A Retrospective Cohort Study. *Ann Pharmacother*. Mar 2016;50(3):194-202.
 23. Choi S, Trang A, McCartney CJ. Reporting functional outcome after knee arthroplasty and regional anesthesia: a methodological primer. *Reg Anesth Pain Med*. Jul-Aug 2013;38(4):340-349.
 24. 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 block. *Clinics (Sao Paulo)*. Sep 2015;70(9):648-653.
 25. Leung P, Dickerson DM, Denduluri SK, et al. Postoperative continuous adductor canal block for total knee arthroplasty improves pain and functional recovery: A randomized controlled clinical trial. *J Clin Anesth*. Sep 2018;49:46-52.
 26. Mahan MC, Jildeh TR, Tenbrunsel TN, Davis JJ. Mepivacaine Spinal Anesthesia Facilitates Rapid Recovery in Total Knee Arthroplasty Compared to Bupivacaine. *J Arthroplasty*. Jun 2018;33(6):1699-1704.
 27. Borys M, Domagała M, Wencław K, Jarczyńska-Domagała J, Czuczwar M. Continuous femoral nerve block is more effective than continuous adductor canal block for treating pain after total knee arthroplasty: A randomized, double-blind, controlled trial. *Medicine (Baltimore)*. Sep 2019;98(39):e17358.
 28. Practice Advisory for the Prevention, Diagnosis, and Management of Infectious Complications Associated with Neuraxial Techniques: An Updated Report by the American Society of Anesthesiologists Task Force on Infectious Complications Associated with Neuraxial Techniques and the American Society of Regional Anesthesia and Pain Medicine*. *Anesthesiology: The Journal of the American Society of Anesthesiologists*. 2017;126(4):585-601.
 29. Cheah JW, Sing DC, Hansen EN, Aleshi P, Vail TP. Does Intrathecal Morphine in Spinal Anesthesia Have a Role in Modern Multimodal Analgesia for Primary Total Joint Arthroplasty? *J Arthroplasty*. Jun 2018;33(6):1693-1698.
 30. Berninger MT, Friederichs J, Leidinger W, et al. Effect of local infiltration analgesia, peripheral nerve blocks, general and spinal anesthesia on early functional recovery and pain control in total knee arthroplasty. *BMC Musculoskelet Disord*. Jul 18 2018;19(1):232.
 31. Soffin EM, Wu CL. Regional and Multimodal Analgesia to Reduce Opioid Use After Total Joint Arthroplasty: A Narrative Review. *Hss j*. Feb 2019;15(1):57-65.
 32. 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*. Sep 3 2014;96(17):1433-1438.
 33. Reinhardt KR, Duggal S, Umunna BP, et al. Intraarticular analgesia versus epidural plus femoral nerve block after TKA: a randomized, double-blind trial. *Clin Orthop Relat Res*. May 2014;472(5):1400-1408.
 34. Nader A, Kendall MC, Wixson RL, Chung B, Polakow LM, McCarthy RJ. A randomized trial of epidural analgesia followed by continuous femoral analgesia compared with oral opioid analgesia on short- and long-term functional recovery after total knee replacement. *Pain Med*. Jul 2012;13(7):937-947.
 35. Bauer MC, Pogatzki-Zahn EM, Zahn PK. Regional analgesia techniques for total knee replacement. *Curr Opin Anaesthesiol*. Oct 2014;27(5):501-506.

36. Shah NA, Jain NP. Is continuous adductor canal block better than continuous femoral nerve block after total knee arthroplasty? Effect on ambulation ability, early functional recovery and pain control: a randomized controlled trial. *J Arthroplasty*. Nov 2014;29(11):2224-2229.
37. Zhao XQ, Jiang N, Yuan FF, Wang L, Yu B. The comparison of adductor canal block with femoral nerve block following total knee arthroplasty: a systematic review with meta-analysis. *J Anesth*. Oct 2016;30(5):745-754.
38. Neal JM, Brull R, Horn JL, et al. The Second American Society of Regional Anesthesia and Pain Medicine Evidence-Based Medicine Assessment of Ultrasound-Guided Regional Anesthesia: Executive Summary. *Reg Anesth Pain Med*. Mar-Apr 2016;41(2):181-194.
39. 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*. Apr 2017;33(4):356-368.
40. Jacob AK, Mantilla CB, Sviggum HP, Schroeder DR, Pagnano MW, Hebl JR. Perioperative nerve injury after total hip arthroplasty: regional anesthesia risk during a 20-year cohort study. *Anesthesiology*. Dec 2011;115(6):1172-1178.
41. Wardhan R, Auroux AS, Ben-David B, Chelly JE. Is L2 paravertebral block comparable to lumbar plexus block for postoperative analgesia after total hip arthroplasty? *Clin Orthop Relat Res*. May 2014;472(5):1475-1481.
42. Neal JM, Barrington MJ, Brull R, et al. The Second ASRA Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine: Executive Summary 2015. *Reg Anesth Pain Med*. Sep-Oct 2015;40(5):401-430.
43. Shah NA, Jain NP, Panchal KA. Adductor Canal Blockade Following Total Knee Arthroplasty-Continuous or Single Shot Technique? Role in Postoperative Analgesia, Ambulation Ability and Early Functional Recovery: A Randomized Controlled Trial. *J Arthroplasty*. Aug 2015;30(8):1476-1481.
44. Dixit V, Fathima S, Walsh SM, et al. Effectiveness of continuous versus single injection femoral nerve block for total knee arthroplasty: A double blinded, randomized trial. *Knee*. Aug 2018;25(4):623-630.
45. Koh HJ, Koh IJ, Kim MS, Choi KY, Jo HU, In Y. Does Patient Perception Differ Following Adductor Canal Block and Femoral Nerve Block in Total Knee Arthroplasty? A Simultaneous Bilateral Randomized Study. *J Arthroplasty*. Jun 2017;32(6):1856-1861.
46. Andersen HL, Gyrn J, Møller L, Christensen B, Zaric D. Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. *Reg Anesth Pain Med*. Mar-Apr 2013;38(2):106-111.
47. Lee S, Rooban N, Vaghadia H, Sawka AN, Tang R. A Randomized Non-Inferiority Trial of Adductor Canal Block for Analgesia After Total Knee Arthroplasty: Single Injection Versus Catheter Technique. *J Arthroplasty*. Apr 2018;33(4):1045-1051.
48. Fowler SJ, Christelis N. High volume local infiltration analgesia compared to peripheral nerve block for hip and knee arthroplasty-what is the evidence? *Anaesth Intensive Care*. Jul 2013;41(4):458-462.
49. Perry CR, Jr., Fahs AM, Kurdziel MD, Koueiter DM, Fayne RJ, Verner JJ. Intraoperative Psoas Compartment Block vs Preoperative Fascia Iliaca Block for Pain Control After Direct Anterior Total Hip Arthroplasty: A Randomized Controlled Trial. *J Arthroplasty*. Jun 2018;33(6):1770-1774.
50. Desmet M, Balocco AL, Van Belleghem V. Fascia iliaca compartment blocks: Different techniques and review of the literature. *Best Pract Res Clin Anaesthesiol*. Mar 2019;33(1):57-66.
51. Chuan A, Lansdown A, Brick KL, et al. Adductor canal versus femoral triangle anatomical locations for continuous catheter analgesia after total knee arthroplasty: a multicentre randomised controlled study. *Br J Anaesth*. Sep 2019;123(3):360-367.

52. Masaracchia MM, Herrick MD, Barrington MJ, Hartmann PR, Sites BD. Adductor canal blocks: changing practice patterns and associated quality profile. *Acta Anaesthesiol Scand*. Feb 2017;61(2):224-231.
53. Kuang MJ, Ma JX, Fu L, He WW, Zhao J, Ma XL. Is Adductor Canal Block Better Than Femoral Nerve Block in Primary Total Knee Arthroplasty? A GRADE Analysis of the Evidence Through a Systematic Review and Meta-Analysis. *J Arthroplasty*. Oct 2017;32(10):3238-3248.e3233.
54. Tziona D, Papaioannou M, Mela A, Potamianou S, Makris A. Local infiltration analgesia combined with a standardized multimodal approach including an adductor canal block in total knee arthroplasty: a prospective randomized, placebo-controlled, double-blinded clinical trial. *J Anesth*. Jun 2018;32(3):326-332.
55. Elkassabany NM, Antosh S, Ahmed M, et al. The Risk of Falls After Total Knee Arthroplasty with the Use of a Femoral Nerve Block Versus an Adductor Canal Block: A Double-Blinded Randomized Controlled Study. *Anesth Analg*. May 2016;122(5):1696-1703.
56. Albrecht E, Morfey D, Chan V, et al. Single-injection or continuous femoral nerve block for total knee arthroplasty? *Clin Orthop Relat Res*. May 2014;472(5):1384-1393.
57. Beebe MJ, Allen R, Anderson MB, Swenson JD, Peters CL. Continuous femoral nerve block using 0.125% bupivacaine does not prevent early ambulation after total knee arthroplasty. *Clin Orthop Relat Res*. May 2014;472(5):1394-1399.
58. Grosso MJ, Murtaugh T, Lakra A, et al. Adductor Canal Block Compared with Periarticular Bupivacaine Injection for Total Knee Arthroplasty: A Prospective Randomized Trial. *J Bone Joint Surg Am*. Jul 5 2018;100(13):1141-1146.
59. Li D, Yang Z, Xie X, Zhao J, Kang P. Adductor canal block provides better performance after total knee arthroplasty compared with femoral nerve block: a systematic review and meta-analysis. *Int Orthop*. May 2016;40(5):925-933.
60. Perlas A, Kirkham KR, Billing R, et al. The impact of analgesic modality on early ambulation following total knee arthroplasty. *Reg Anesth Pain Med*. Jul-Aug 2013;38(4):334-339.
61. Wang D, Yang Y, Li Q, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a meta-analysis of randomized controlled trials. *Sci Rep*. Jan 12 2017;7:40721.
62. Gudmundsdottir S, Franklin JL. Continuous adductor canal block added to local infiltration analgesia (LIA) after total knee arthroplasty has no additional benefits on pain and ambulation on postoperative day 1 and 2 compared with LIA alone. *Acta Orthop*. Oct 2017;88(5):537-542.
63. Meier AW, Auyong DB, Yuan SC, Lin SE, Flaherty JM, Hanson NA. Comparison of Continuous Proximal Versus Distal Adductor Canal Blocks for Total Knee Arthroplasty: A Randomized, Double-Blind, Noninferiority Trial. *Reg Anesth Pain Med*. Jan 2018;43(1):36-42.
64. Carli F, Clemente A, Asenjo JF, et al. Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block. *Br J Anaesth*. Aug 2010;105(2):185-195.
65. Kampitak W, Tanavalee A, Ngarmukos S, Amarase C. Opioid-Sparing Analgesia and Enhanced Recovery After Total Knee Arthroplasty Using Combined Triple Nerve Blocks With Local Infiltration Analgesia. *J Arthroplasty*. Feb 2019;34(2):295-302.
66. Sinha SK, Abrams JH, Arumugam S, et al. Femoral nerve block with selective tibial nerve block provides effective analgesia without foot drop after total knee arthroplasty: a prospective, randomized, observer-blinded study. *Anesth Analg*. Jul 2012;115(1):202-206.
67. Safa B, Gollish J, Haslam L, McCartney CJ. Comparing the effects of single shot sciatic nerve block versus posterior capsule local anesthetic infiltration on analgesia

- and functional outcome after total knee arthroplasty: a prospective, randomized, double-blinded, controlled trial. *J Arthroplasty*. Jun 2014;29(6):1149-1153.
68. Abdallah FW, 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*. May 2016;63(5):552-568.
 69. Wegener JT, van Ooij B, van Dijk CN, et al. Long-term pain and functional disability after total knee arthroplasty with and without single-injection or continuous sciatic nerve block in addition to continuous femoral nerve block: a prospective, 1-year follow-up of a randomized controlled trial. *Reg Anesth Pain Med*. Jan-Feb 2013;38(1):58-63.
 70. Sankineani SR, Reddy ARC, Eachempati KK, Jangale A, Gurava Reddy AV. Comparison of adductor canal block and IPACK block (interspace between the popliteal artery and the capsule of the posterior knee) with adductor canal block alone after total knee arthroplasty: a prospective control trial on pain and knee function in immediate postoperative period. *Eur J Orthop Surg Traumatol*. Oct 2018;28(7):1391-1395.
 71. Runge C, Borglum J, Jensen JM, et al. The Analgesic Effect of Obturator Nerve Block Added to a Femoral Triangle Block After Total Knee Arthroplasty: A Randomized Controlled Trial. *Reg Anesth Pain Med*. Jul-Aug 2016;41(4):445-451.
 72. Solovyova O, Lewis CG, Abrams JH, et al. Local infiltration analgesia followed by continuous infusion of local anesthetic solution for total hip arthroplasty: a prospective, randomized, double-blind, placebo-controlled study. *J Bone Joint Surg Am*. Nov 6 2013;95(21):1935-1941.
 73. Villatte G, Engels E, Erivan R, et al. Effect of local anaesthetic wound infiltration on acute pain and bleeding after primary total hip arthroplasty: the EDIPO randomised controlled study. *Int Orthop*. Nov 2016;40(11):2255-2260.
 74. Zhang LK, Ma JX, Kuang MJ, Ma XL. Comparison of Periarticular Local Infiltration Analgesia With Femoral Nerve Block for Total Knee Arthroplasty: a Meta-Analysis of Randomized Controlled Trials. *J Arthroplasty*. Jun 2018;33(6):1972-1978.e1974.
 75. Sporer SM, Rogers T. Postoperative Pain Management After Primary Total Knee Arthroplasty: The Value of Liposomal Bupivacaine. *J Arthroplasty*. Nov 2016;31(11):2603-2607.
 76. Song MH, Kim BH, Ahn SJ, et al. Peri-articular injections of local anaesthesia can replace patient-controlled analgesia after total knee arthroplasty: a randomised controlled study. *Int Orthop*. Feb 2016;40(2):295-299.
 77. Spangehl MJ, Clarke HD, Hentz JG, Misra L, Blocher JL, Seamans DP. The Chitranjan Ranawat Award: Periarticular injections and femoral & sciatic blocks provide similar pain relief after TKA: a randomized clinical trial. *Clin Orthop Relat Res*. Jan 2015;473(1):45-53.
 78. Bron JL, Verhart J, Sierevelt IN, De Vries D, Kingma HJ, Rademakers MV. No effect of double nerve block of the lateral cutaneous nerve and subcostal nerves in total hip arthroplasty. *Acta Orthop*. Jun 2018;89(3):272-277.
 79. Kehlet H, Andersen LO. Local infiltration analgesia in joint replacement: the evidence and recommendations for clinical practice. *Acta Anaesthesiol Scand*. Aug 2011;55(7):778-784.
 80. Hofstad JK, Winther SB, Rian T, Foss OA, Husby OS, Wik TS. Perioperative local infiltration anesthesia with ropivacaine has no effect on postoperative pain after total hip arthroplasty. *Acta Orthop*. 2015;86(6):654-658.
 81. Chaumeron A, Audy D, Drolet P, Lavigne M, Vendittoli PA. Periarticular injection in knee arthroplasty improves quadriceps function. *Clin Orthop Relat Res*. Jul 2013;471(7):2284-2295.
 82. Zinkus J, Mockute L, Gelmanas A, Tamosiunas R, Vertelis A, Macas A. Comparison of 2 Analgesia Modalities in Total Knee Replacement Surgery: Is There an Effect on Knee Function Rehabilitation? *Med Sci Monit*. Jun 20 2017;23:3019-3025.

83. Ishida K, Shibamura N, Matsumoto T, Tei K, Kuroda R, Kurosaka M. Periarticular multimodal drug injection improves post-operative pain and functional recovery after total knee arthroplasty. *J Orthop Sci.* Mar 2016;21(2):178-183.
84. Horn BJ, Cien A, Reeves NP, Pathak P, Taunt CJ, Jr. Femoral Nerve Block vs Periarticular Bupivacaine Liposome Injection After Primary Total Knee Arthroplasty: Effect on Patient Outcomes. *J Am Osteopath Assoc.* Dec 2015;115(12):714-719.
85. Sankineani SR, Reddy ARC, Ajith Kumar KS, Eachempati KK, Reddy AVG. Comparative analysis of influence of adductor canal block and multimodal periarticular infiltration versus adductor canal block alone on pain and knee range of movement after total knee arthroplasty: a prospective non-randomised study. *Musculoskelet Surg.* Aug 2018;102(2):173-177.
86. Sawhney M, Mehdian H, Kashin B, et al. Pain After Unilateral Total Knee Arthroplasty: A Prospective Randomized Controlled Trial Examining the Analgesic Effectiveness of a Combined Adductor Canal Peripheral Nerve Block with Periarticular Infiltration Versus Adductor Canal Nerve Block Alone Versus Periarticular Infiltration Alone. *Anesth Analg.* Jun 2016;122(6):2040-2046.
87. Yu S, Dundon J, Solovyova O, Bosco J, Iorio R. Can Multimodal Pain Management in TKA Eliminate Patient-controlled Analgesia and Femoral Nerve Blocks? *Clin Orthop Relat Res.* Jan 2018;476(1):101-109.
88. McDonald DA, Deakin AH, Ellis BM, et al. The technique of delivery of peri-operative analgesia does not affect the rehabilitation or outcomes following total knee arthroplasty. *Bone Joint J.* Sep 2016;98-b(9):1189-1196.