

## The Influence of the Analgesic Model on Postoperative Pain in Major Knee Surgery

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### Rezumat

#### *Influența modelului analgetic asupra durerii postoperatorii în chirurgia ortopedică majoră a genunchiului*

Artroplastia primară de genunchi reprezintă un model de durere severă în chirurgia ortopedică majoră. Un bun control al durerii postoperatorii este important atât pentru pacient cât și pentru obținerea unui rezultat funcțional bun al intervenției, mobilizarea precoce a genunchiului fiind limitată de durere. Studiul de față își propune trecerea în revistă a principalelor modele analgetice folosite în artroplastia primară de genunchi și influența acestora asupra durerii și a recuperării funcționale a genunchiului. Analiza comparativă a modelelor analgetice arată avantajele și efectele secundare ale fiecărei metode, evoluția în timp a acestora și ne ghidează cum să folosim medicina bazată pe dovezi. Alegerea modelului analgetic cel mai potrivit aparține însă echipei formate din ortoped-medical anestezist și kinetoterapeut, care pot stabili individual, pentru fiecare pacient obiectivele unui bun rezultat funcțional al articulației genunchiului.

**Cuvinte cheie:** artroplastia de genunchi, durere, rezultat funcțional

### Abstract

Total primary knee arthroplasty represents a model of severe pain for major orthopedic surgery. A good management of postoperative pain is important both for the patient and for a good functional surgery outcome because early knee mobilisation is pain limited. This study is a review of the main analgesic methods used in total primary knee arthroplasty and their influence on pain and on the functional recovery of the knee. The comparative analysis of the analgesic models shows the advantages and the adverse effects of each one, the evolution in time of analgesia techniques and guides us in the use of evidence-based-medicine. Which is the most appropriate analgesic model is a choice of the orthopedic surgeon-anesthesiologist and kinetotherapist team who are able to individualize for each patient good functional outcome parameters of the new knee joint.

**Key words:** total knee arthroplasty, pain, functional outcome

### Background

Total knee arthroplasty (TKA) is a part of major knee orthopedic surgery and represents a model of severe pain. According to Bonica 60% of operated patients report severe pain while 30% report moderate pain (1). Inefficiently treated postoperative pain may lead to complications related to immobility, longer hospital stay, and may interfere with knee functional outcome (1). For these reasons, the efficient treatment of postoperative pain continues to be a challenge because it

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influences the secondary surgical outcome (2) and good postoperative pain control has an important impact on the knee functional outcome both in the early and the late postoperative period (3). Otherwise, the major factor for an efficient postoperative knee flexion is good kinetotherapy and this is possible only with efficient analgesia (4).

All the TKA studies regarding the immediate or long-term outcome have pain as a common parameter. Since 1999, pain is the fifth monitored vital sign in hospitals in the US (5).

The aim of this review of the main known and used methods of postoperative analgesia is not to find any ideal technique of pain treatment, but rather to make a presentation of these techniques describing their evolution in practice and evidence-based medicine.

### ***Patient-controlled analgesia***

One modern and also elegant method for 1988 was the intravenous (IV) patient-controlled analgesia (PCA) using continuous infusion of morphine or meperidine (6). The Ferrante study compared pain control and postoperative morphine consumption between 2 groups, one of the groups receiving morphine by IV - PCA and the other group receiving morphine intramuscularly (IM). Although the IV continuous morphine administration assured a plateau with fairly constant blood concentrations of opioid and therefore without pain spikes, the results showed no difference in efficacy of pain relief between PCA and IM treatment groups, neither as morphine consumption nor as pain score on a visual analogue scale (VAS). A possible explanation for this lack of statistical differences (based purely on pharmacokinetic considerations, PCA should be more effective than IM injection) may lie in the chronicity of pain in the population under study and the small number of enrolled patients, 20 for each group.

### ***Epidural analgesia***

From the PCA opioid administration the next step in evolution was epidural analgesia. Besides its benefit on postoperative pain, epidural analgesia had another post-operative advantage for high-risk patients, emphasized by many studies. Epidural analgesia may reduce the myocardial ischemia risk and tachyarrhythmia in high-risk patients, proposed for elective major abdominal surgery, thoracic and cardiac surgery (7,8,9). Ballantyne's meta-analysis highlights the positive effect of postoperative epidural analgesia on pulmonary function and a decreasing incidence of postoperative pulmonary morbidity (10).

Epidural analgesia for postoperative pain in TKA has been used since earlier times. Mahoney administered in 1990 bupivacaine and morphine continuously on an epidural catheter and reported a good-to-excellent analgesia, but with a high incidence of adverse effects related to epidural catheter and opioids (11). The author recognizes the necessity for other solutions with a lower incidence of opioid-associated side effects.

In 1993, Kehlet reviewed and reconsidered combined analgesic regimens (balanced analgesia or a multimodal approach to the treatment of postoperative pain), because they

offered adequate analgesia due to additive or synergistic effects of different analgesics, with concomitant reduction of side effects, due to resulting lower doses of analgesics and differences in side-effect profiles (4,12). At that time, several analgesic techniques were available: 1. at peripheral level use of local anesthetics, non-steroidal anti-inflammatory drugs (NSAID), opioids, or other analgesics; 2. peripheral nerve blocks with local anesthetics and  $\alpha$ 2-adrenergic agonists; 3. at the spinal cord level using spinal or epidural local anesthetics opioids,  $\alpha$ 2-agonists or other analgesics; 4. a combination of these techniques.

Moiniche studies the effect of pain relief with balanced analgesia on postoperative convalescence parameters in major orthopedic surgery and included 20 patients scheduled for TKA (13). The study compares continuous epidural bupivacaine/morphine for 48 h postoperatively plus oral piroxicam with general anaesthesia followed by a conventional intramuscular opioid and acetaminophen regimen. Although the epidural analgesia group had significantly lower pain scores, no important differences were observed between groups related to ambulation, daily patient activity or hospital stay.

### ***Non-steroidal anti-inflammatory drugs associations***

NSAID associated to opioids represents another analgesic model. Ketorolac administered as an intravenous bolus followed by a continuous infusion determines less morphine consumption compared to placebo after total hip or knee arthroplasty, with no difference in blood loss (14). Buvanendran also used AINS and described another analgesic model with rofecoxib, a selective inhibitor of cyclooxygenase 2 administered preoperatively and postoperatively associated with epidural analgesia compared to placebo associated to epidural analgesia (15). He concluded that the perioperative use of an inhibitor of cyclooxygenase 2 is an effective component of multimodal analgesia and reduces opioid consumption, pain, vomiting, and sleep disturbance with improved knee range of motion after TKA.

Multimodal analgesia had benefits also for other types of major surgery, like thoraco-abdominal neoplastic surgery as it decreases the inflammatory response to the surgical stress and allows a faster recovery (16).

### ***The relationship between anesthetic techniques and outcome in TKA***

The relationship between anesthetic techniques and outcome in TKA was also studied by Williams-Russo (17). His study was prospective randomised and included 262 patients who received epidural anesthesia or general anesthesia and the conclusion was promising for the epidural analgesia adepts: the epidural anesthesia was associated with earlier achievement of postoperative rehabilitation objectives such as walking distance and climbing of stairs.

Evidence - based medicine regarding epidural analgesia tried to answer the question: „Is lumbar epidural analgesia more efficient than systemic analgesia or spinal analgesia for pain relief after elective total primary hip or knee arthroplasty?“. The Cochrane Data Base in 2003 shows that epidural analgesia may

be useful for postoperative pain relief following major lower limb joint replacements but the benefits may be limited to the early (four to six hours) postoperative period and an epidural infusion of local anesthetic or local anesthetic-narcotic mixture may be better than epidural narcotic alone; concerning only TKA, the pain scores measured on VAS were lower up to 48 hours compared to patients receiving systemic analgesia. The data evidence is insufficient to draw conclusions on the frequency of rare complications from epidural analgesia, postoperative morbidity or mortality, functional outcomes, or length of hospital stay (18).

Opioid consumption in pain management decreases continuously and their adverse effects remain a challenge. Because of the adverse events specific to epidural analgesia, clinicians' tendency was to provide post-TKA analgesia with other techniques moving from neuraxis to periphery: peripheral nerve blocks and even intraarticular injection of different drugs.

### ***Peripheral nerve blocks***

The lumbar plexus block offers advantages over epidural analgesia for TKA patients. These patients have an increased risk of profound venous thrombosis and the anticoagulant prophylaxis association to epidural catheter raises problems related to catheter removal.

Ganapathy used the femoral three-in-one block, described originally by Winnie et al. (20) and studied the continuous "modified" femoral three-in-one block for postoperative pain after TKA (19). The catheters were inserted under the fascia iliaca using a "double pop" technique and advanced 15–20 cm cranially, so that the catheter be located superior to the upper third of the sacroiliac joint to block 3 nerves: femoral, obturator, and lateral femoral cutaneous nerve. His conclusion is that continuous fascia iliaca block with 0.2% bupivacaine reduces opioid requirements and improves range of knee motion in the immediate postoperative period. In the same period, Capdevilla (21) studied the effects of perioperative analgesic technique on the surgical outcome, hospital duration and rehabilitation 3 months after the surgery. 56 patients were enrolled and randomly assigned to one of three groups, each to receive a different postoperative analgesic technique: continuous epidural infusion, continuous femoral block, or intravenous PCA morphine. The conclusion was that regional analgesic techniques improve early rehabilitation after TKA by effectively controlling pain during continuous passive motion and side effects were encountered more frequently in the continuous epidural infusion group than in the continuous femoral block group.

This is very close to Singelyn's conclusion (22), who studied 45 patients and assessed the influence of three analgesic techniques on postoperative knee rehabilitation after TKA, namely IV PCA with morphine, continuous 3-in-1, and epidural analgesia: the continuous 3-in-1 block is the technique of choice because it assures better pain relief, faster postoperative knee rehabilitation with fewer side effects, nearly 4 times fewer than epidural analgesia, and there were no differences at 3 month outcome between groups.

Chelly administered continuously local anesthetic over the femoral nerve catheter and considered this way to be a better analgesia alternative than PCA or epidural analgesia both for pain control and immediate knee rehabilitation. Therefore, patients who received femoral nerve block analgesia experienced also a better pain relief also a better cardiovascular stability, less nausea and vomiting compared to patients with epidural analgesia, besides a better pain relief (23).

The femoral nerve block analgesia doesn't cover the painful area associated to sciatic nerve innervation and so, one of the problems continuously challenging is the necessity of adding the sciatic nerve block or not. Study results are very variable: Allen (24) didn't find further benefit from a single shot sciatic nerve block addition to femoral nerve block, unlike Weber (25) who affirmed that 67% of the patients with femoral nerve block also needed a sciatic nerve block post-operatively.

Anatomically, the femoral, obturator and sciatic nerves from the lumbosacral plexus innervate the knee. There are also some cutaneous areas of the incision in the territory innervated by the lateral femoral cutaneous nerve.

Femoral nerve block analgesia even with a higher local anesthetic volume or more cranial spread cannot consistently produce anesthesia of the obturator nerve (26,27).

The logical conclusion is to add obturator nerve block analgesia to the femoral/sciatic nerve blocks combination. Macalou's study supports this conclusion and finds that the addition of an obturator nerve block to femoral nerve block improves postoperative analgesia after TKA (28).

McNamee reported an improved post-operative analgesia following the addition of an obturator nerve block to the femoral and sciatic blockade (29). The psoas compartment block actually blocks 3 of the 4 nerves that innervate the knee joint: femoral, obturator and lateral femoral cutaneous nerve. At least theoretically, psoas compartment block analgesia may be superior to femoral nerve block analgesia in TKA. Paradoxically, in the Morin's study the femoral/sciatic block analgesia is superior to femoral and psoas block analgesia with respect to reduced analgesic opioids requirements after TKA (30). One meta-analysis from 2008 undertook a systematic review of all randomized trials comparing epidural analgesia with peripheral nerves blocks (PNB) for TKA. Eight studies were identified with 464 patients. There was an evaluation of morphine consumption, epidural and PNB side effects and also, patient satisfaction (31). The results are: 1) there was no significant difference in pain VAS scores between epidural and PNB for the first 24 hours; 2) patient satisfaction was higher with PNB in only two studies (32,33); 3) the addition of sciatic nerve block improves the quality of analgesia by reducing posterior knee and calf pain, corresponding to the area innervated by the nerve (25,30,34,35,36). However, Fowler's analysis failed to demonstrate inferior analgesia for patients without sciatic block between 0 and 24 h after operation; 4) neurological complications referred to sphincteric disturbance in approximately 250 patients who received an epidural analgesia and no neurological complications were reported in the PNB group. Hypotension associated with epidural analgesia occurred more frequently among

these patients and may contribute to end organ ischemia or infarction if left untreated. This is the reason why epidural analgesia is not appropriate in the ward setting in every institution. If general anaesthesia is not indicated, spinal anaesthesia combined with PNB provides a good analgesia with a lower incidence of neurological complications than epidural analgesia in this risk patients group (older age, degenerative spinal disorders, chronic anticoagulation) (31,37,38).

Salinas pays attention to the continuous FNB versus single-injection technique; the study observed improved analgesia after TKA with continuous FNB versus single FNB, but the continuous technique may also pose risks for nerve injury and infection related to continuous administration (39). There was no improvement in overall outcome (39).

What is really advantageous for FNB is pain reduction related to significant reduction of quadriceps spasm, which occurs secondary after to TKA and therefore improves toleration of passive motion (20). On the other side, FNB critics reproach quadriceps weakness on the operative side compared to the contralateral side, but in Fowler's analysis this is unclear from the studies included (31).

Ultrasound FNB is relatively easy to perform, with rapid onset and 100% success rate for experimented hands (40). The idea of using ultrasound technique in regional anaesthesia for femoral nerve identification is not quiet new (41,42).

FNB analgesia presents a good balance between analgesia and side-effects, because of an almost negligible risk of injury to the neuraxis, secondary to the distance from it (31). The question to be asked is: Is PNB analgesia superior to systemic opioid administration, regardless of the surgery type? The Richmann's et al. meta-analysis tried to answer this question, with 603 patients enrolled: continuous PNB analgesia provided superior postoperative analgesia, regardless of catheter localisation and had fewer opioid-related side effects when compared with opioid analgesia (43).

Another meta-analysis dedicated exclusively to TKA from the analgesia and outcome point of view is Paul's et al. This meta-analysis with 1016 patients from 23 studies compares FNB analgesia combined with/without sciatic nerve block to epidural and opioid PCA analgesia. The conclusion is that single-shot FNB or continuous FNB (plus PCA) was superior to PCA alone for postoperative analgesia for patients having TKA; there is no evidence of a superiority of continuous FNB versus single-shot FNB and the impact of adding a sciatic block or continuous FNB to a single-shot FNB needs to be further studied (44).

The sciatic nerve block contribution was also investigated by Cappelleri (45) and Abdallah (46). The conclusion is that continuous sciatic nerve block improves analgesia, decreases morphine request, and improves early rehabilitation compared with single-injection sciatic nerve block (45), in contrast with Abdallah's et al. review, who cannot define the effect of adding sciatic nerve block to FNB on acute pain (46).

If the majority of the studies were conducted in the hospital, the multicenter, randomized, American Ilfeld's et al. study from 2010 introduces the concept of continuous ambulatory FNB for 4 days after a TKA discharge (47).

In 2012, Beaupre's et al. study brings back the idea of a

preemptive multimodal analgesia plus FNB protocol on rehabilitation, hospital length of stay, and postoperative analgesia after TKA (48). In the study a combination of Oxycodone controlled release and Celecoxib is used as a preemptive analgesia before the surgery and Celecoxib after the surgery; even though the study was not randomised, it reflects the FNB efficacy in standard clinical conditions, as it happens in current practice. The only significant difference between groups was more quadriceps motor blocks reported in the FNB group; however, no patient experienced any falls, and there were no delays reported in rehabilitation program secondary to FNB. Also, there were no significant differences between groups in terms of pain scores, knee flexion or hospital stay. In fact, the only restriction to use FNB widely is the accidental fall secondary to quadriceps weakness limiting an aggressive postoperative rehabilitation (49).

### *Periarticular and intraarticular analgesia infiltration*

Another analgesic model used in TKA is periarticular and intraarticular multimodal analgesia infiltration, consisting of a local anaesthetic, morphine, NSAIDs and epinephrine. In this analgesic model, the mixture may be injected intraoperatively periarticularly or intraarticularly at the end of the surgery or also postoperatively over an intraarticular catheter with an hourly rate. The idea of injecting intraarticular analgesics isn't new. Heard injected bupivacaine with epinephrine or morphine intraoperatively to provide analgesia after arthroscopic knee surgery; the results indicate that intraarticular injection of bupivacaine after arthroscopic knee surgery provides prolonged analgesia, but that there is no significant difference compared to intraarticular morphine (50). Klasen tried to compare intraarticular application of morphine and epidural analgesia plus "on-demand" IV analgesia to "on-demand" IV analgesia alone for TKA, but intraarticular morphine application does not reduce analgesic requirements in major knee surgery (51). The knee incision wound infiltration with a mixture of local anaesthetic, NSAID and epinephrine causes many discussions. One of them is related to the theoretical risk of local anaesthetic toxicity if it reaches the blood circulation. Busch injected large volumes of local anaesthetic with no observed signs of cardiac or central nervous system toxicity, and intraoperative periarticular injection with ropivacaine, ketorolac and epinephrine produced a superior analgesia compared to IV opioids PCA with a higher patient satisfaction (52). Regarding the risk of local anaesthetic toxicity, Gill investigated the drain fluid concentration of ropivacaine to quantify the toxicity risk related to autologous retransfusion drains after multimodal periarticular analgesia. The study included only 10 patients, but there were no cardiac toxic effects reported, only a few minor neurological disturbances and the ropivacaine concentration in autologous transfused blood in patients who have received periarticular infiltration is negligible (53). The Wallace et al. study explored the safety of periarticular local anaesthetic injection for patients with autologous blood transfusion of fluid from the patient's surgical drain in order to compare the concentration of local anaesthetic in the blood and in the fluid collected in the knee drain in 46 patients randomised to have either a periarticular

injection or a FNB (54). The evidence from this study suggests the same as the Gill study: It is safe to use periarticular injection in combination with auto-transfusion of blood from periarticular drains during TKA.

Andersen (55) designed a study inspired by the local infiltration analgesia technique developed by Kerr and Kohan (56) and assessed the efficacy of wound infiltration combined with intraarticular regional analgesia with epidural infusion in TKA. The study is a prospective, randomized, controlled trial and used a large volume of multimodal analgesia both for wound infiltration (150 ml) and intraarticular (190 ml) plus an infusion rate of 4 ml/hour. The results confirmed the hypothesis that peri- and intraarticular analgesia with multimodal drugs provided superior pain relief and reduced morphine consumption compared with continuous epidural infusion.

## Conclusions

Each one of these analgesic models has its own adepts, who acquired clinical experience with one model or another and have developed a clinical routine procedure.

All these presented studies were not able to prove which of the combinations is ideal, that means: to assure a good analgesia with a reduced opioid requirement, to have no unpleasant or toxic side effects for patients and to allow an early mobilisation. Choosing the analgesic model must be done by the team represented by the orthopedic surgeon-anesthesiologist-physical therapist, taking into account the surgical technique, analgesic model and rehabilitation program in order to permit a rapid knee flexion and walking with a lower chronic pain risk.

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