

SCIENTIFIC ARTICLE

## Comparison between subarachnoid morphine and femoral nerve block for analgesia after knee ligament reconstruction: a randomized clinical trial<sup>☆</sup>



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### KEYWORDS

Acute pain;  
Anterior cruciate  
ligament  
reconstruction;  
Femoral nerve block;  
Spinal anesthesia

### Abstract

**Background and objectives:** There are no consensus of the ideal technique to provide analgesia in knee ligament reconstructions. The aim of this study was to compare the intensity of postoperative pain in these patients under different modalities of analgesia.

**Method:** Randomized and controlled clinical trial of patients undergoing reconstruction of the Anterior Cruciate Ligament (ACL) with flexor tendons between December 2013 and 2014. All patients underwent spinal anesthesia and rescue analgesia with tramadol. The groups C, M, R0,375 and R0,25 was compared with only the previously described technique, subarachnoid morphine (100 µg), or Femoral Nerve Block (BNF) with 25 mL of 0.375% ropivacaine and 0.25%, respectively. Pain intensity at 6, 12 and 24 hours, age, sex, rescue analgesia, adverse reactions and satisfaction were evaluated.

**Results:** Among the 83 eligible patients, a predominance of males (85.7%) was observed, between 28 and 31 years. The group C requested more opioid (27.3%) than the other groups, without significance when compared. There were no significant differences in pain intensity at 6, 12 and 24 hours. There was a higher incidence of urinary retention in the M group (23.8%) than in the R0,375 (0%) and prolonged quadriceps motor block in the R0,375 group (30%) than in the M and C groups (0%), with statistical significance ( $p < 0.05$ ).

<sup>☆</sup> This study was performed at Hospital Universitário Cajuru, Curitiba, Paraná.

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**PALAVRAS-CHAVE**

Dor aguda;  
Reconstrução do  
ligamento cruzado  
anterior;  
Bloqueio do nervo  
femoral;  
Anestesia espinal

**Conclusion:** There was no difference in the intensity of postoperative pain in patients submitted to ACL reconstruction with flexor tendons under the analgesic modalities evaluated, despite the predominance of urinary retention in the M group and motor block in the R0,375 group.

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### Comparação entre morfina subaracnoidea e bloqueio do nervo femoral para analgesia após reconstrução ligamentar de joelho: estudo clínico randomizado

**Resumo**

**Justificativa e objetivos:** Não há consenso sobre qual é a técnica ideal para prover analgesia em reconstruções ligamentares de joelho. Objetivou-se comparar a intensidade da dor pós-operatória desses pacientes sob diferentes modalidades de analgesia.

**Método:** Ensaio clínico randomizado e controlado de pacientes submetidos à reconstrução do Ligamento Cruzado Anterior (LCA) com tendões flexores entre Dezembro de 2013 e 2014. Todos os pacientes foram submetidos a raqui-anestesia e analgesia de resgate com tramadol. Comparou-se os grupos C, M, R0,375 e R0,25, aos quais ofereceu-se apenas a técnica anteriormente descrita, morfina subaracnoidea (100 µg) ou Bloqueio de Nervo Femoral (BNF) com 25 mL de ropivacaína 0,375% e 0,25%, respectivamente. Avaliou-se intensidade da dor em 6, 12 e 24 horas, idade, sexo, analgesia de resgate, reações adversas e satisfação.

**Resultados:** Dentre os 83 pacientes elegíveis, observou-se predomínio do sexo masculino (85,7%), entre 28 e 31 anos. O grupo C solicitou mais opioide (27,3%) do que os demais grupos, sem significância quando comparados. Não houve diferenças significativas na intensidade da dor em 6, 12 e 24 horas. Houve maior incidência de retenção urinária no grupo M (23,8%) do que no R0,375(0%) e de bloqueio motor prolongado do quadríceps no grupo R0,375 (30%) do que nos grupos M e C (0%), com significância estatística ( $p < 0,05$ ).

**Conclusão:** Não houve diferença na intensidade da dor pós-operatória nos pacientes submetidos à reconstrução de LCA com tendões flexores sob as modalidades analgésicas avaliadas, apesar do predomínio de retenção urinária no grupo M e bloqueio motor no grupo R0,375.

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**Introduction**

Anterior Cruciate Ligament (ACL) reconstruction involves replacement of the native ligament with autograft and the most common grafts harvested for the procedure are patellar and flexors tendons.<sup>1</sup>

Although there is dispute over the issue, when comparing the patellar tendon to the flexor tendon graft, some authors have reported that using the latter was associated to lower surgical morbidity, which may contribute to lower intensity postoperative pain.<sup>1</sup>

Adding a supplementary analgesia technique is recommended based on the evidence of pain associated with the incision of the suprapatellar and meniscal capsules, the infrapatellar fat pad and the sites of graft insertion and harvesting.<sup>2</sup>

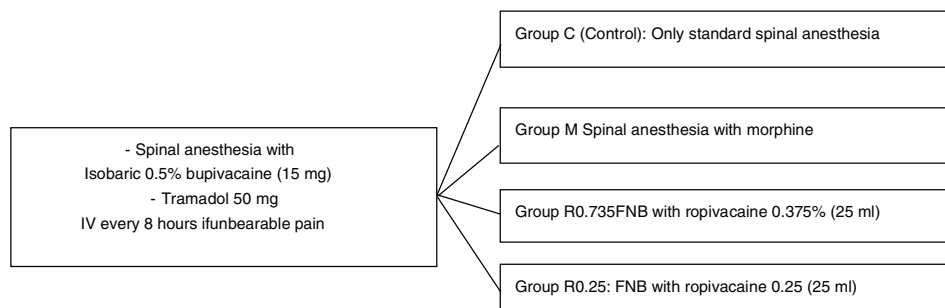
The femoral nerve block at the inguinal region is suggested to provide analgesia to the skin incision, to the graft insertion at the tibia<sup>3</sup> and, due to the possibility of local anesthetic dispersion to the obturator nerve, the femoral nerve block analgesia could be superior to that provided by using intrathecal morphine.<sup>4</sup> Despite easy execution, morphine administration is associated with undesirable side effects.<sup>4,5</sup>

There is disagreement in the literature regarding what postoperative analgesia technique would be ideal for this group of patients. Our study aimed to assess the intensity of postoperative pain in patients submitted to ACL reconstruction with flexor tendons, comparing intravenous opioid analgesia with the administration of intrathecal morphine and Femoral Nerve Block (FNB), using different concentrations of ropivacaine.

**Methods**

A randomized controlled clinical trial was carried out with the main objective of assessing the intensity of postoperative pain in patients submitted to ACL reconstruction with flexor tendon graft, at Hospital Universitário Cajuru in Curitiba/PR, between December 2013 and December 2014. The study was approved by the Research Ethics Committee of the Pontifícia Universidade Católica do Paraná – PUCPR (opinion 495,780) and registered on [ClinicalTrials.gov](http://ClinicalTrials.gov). There are no financial, personal, academic, institutional, political or religious conflicts of interest.

Postoperative pain intensity was assessed 6, 12, and 24 hours postoperatively using the visual numeric scale (VNS), ranging between 0 and 10 and according to inten-



**Figure 1** Interventions according to the study groups.

sity, classified as mild (VNS 1–2), moderate (VNS 3–6) and intense (VNS 8–10). We also assessed patient age and gender, need for postoperative rescue opioids, occurrence of adverse events, occurrence of patient falls, and patient satisfaction with the technique offered.

The study included patients between 18 and 65 years of age and physical status ASA class I and II. We excluded from the analysis patients with neurological deficit of the operated limb, diabetics, coagulopathy, infection at puncture sites and when there were changes in relation to the initially proposed surgical technique.

To calculate the minimum sample size, we used OpenEpi 3.0 software, which requires mean and standard deviation values of the analyzed variable between two separate groups. Guirro et al.<sup>6</sup> studied the intensity of pain in ACL reconstruction surgery and compared patients submitted to spinal anesthesia with FNB associated with spinal anesthesia. They found minimum values of VNS of 2 and maximum of 4, with no statistically significant difference between the groups. Based on their findings we decided to use the variables described –VNS of 2.0 and 4.0 with Standard Deviation of  $SD = 2.0$ . Adopting an alpha error of 0.05 and beta of 0.2 (80% power), we found 16 patients ( $n = 16$ ) as the minimum sample size per group.

To account for the possible loss of participants, we decided to randomize a total of 95 research protocols. The principal investigator was responsible for identifying each protocol sequentially, according to the four study groups. Subsequently, they were folded and placed in envelopes, which were sealed, mixed, and only then randomly numbered from 1 to 95. The envelope seal was only broken after the patient signed the consent form.

All groups were equally submitted to mild sedation with midazolam and fentanyl, spinal anesthesia with 15 mg of isobaric bupivacaine and adjuvant drugs in the perioperative period – ketoprofen 100 mg, dipyron 2 g, dexamethasone 4 mg and ondansetron 4 mg – and in the postoperative period – ketoprofen 100 mg every 12 hours, dipyron 1 g every 6 hours, tramadol 50 mg every 8 hours if pain was refractory to medications, and ondansetron 4 mg in the Presence of Nausea or Vomiting (PONV).

Group C (Control) was offered only the technique described above. Group M had intrathecal 100 mcg morphine added to spinal anesthesia. Groups R0.375 and R0.25 had spinal anesthesia associated to FNB using 25 mL of 0.375% and 0.25% ropivacaine, respectively (Fig. 1).

Patients belonging to groups R0.375 and R0.25 were submitted to FNB before spinal anesthesia to reduce the risk of inadvertent administration of intraneural local anesthetic. With the patient in supine position and after antisepsis, FNB was performed using the perivascular inguinal technique, aiming the femoral nerve 1 to 2 cm lateral to the palpation of the femoral artery pulse. A short bevel needle and peripheral nerve stimulator set with a stimulus intensity between 1 and 1.2 mA was used, aiming for persistent rectus femoris muscle contractions and patellar twitch, after reducing the intensity of the stimulus (0.6 to 0.3 mA), without exerting pressure on the needle, and then proceeding with the administration of local anesthetic.

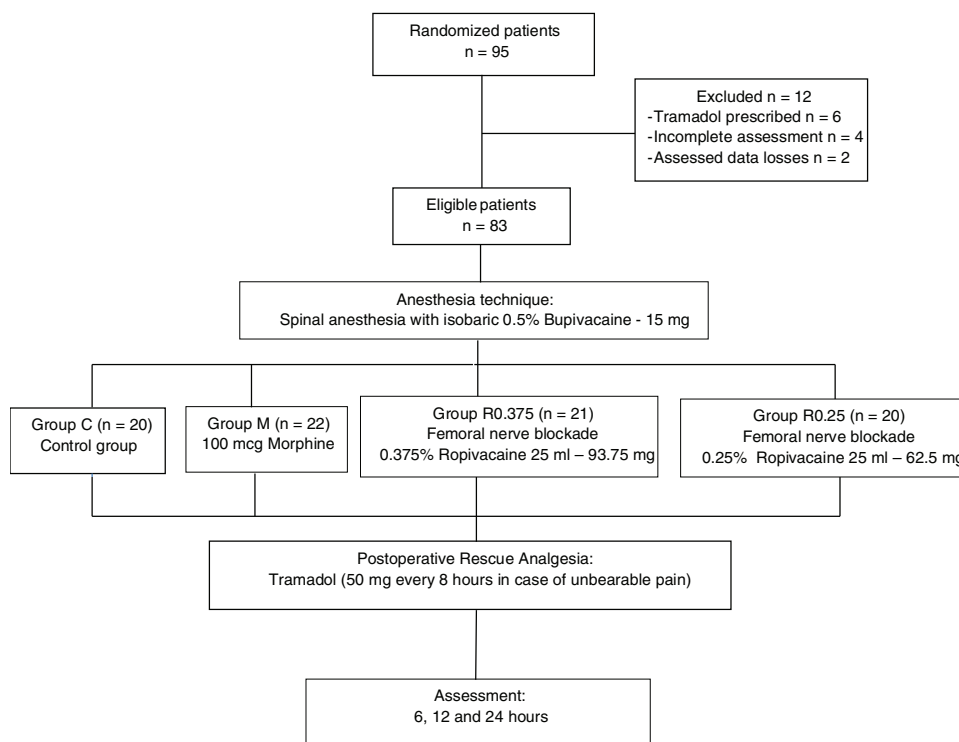
Since 2008, orthopedic knee group surgeons at our hospital have used the technique of anatomical ACL reconstruction with flexor tendon grafts, which reproduces the anatomy of the native ligament, with adequate biomechanical function and rare cases of surgical revision to date. Incisions are made in the proximal third of the tibia, 2 cm medial and inferior to the anterior tuberosity. The semitendinosus and gracilis tendons are dissected with a tendon stripper at the level of their insertion. Occasionally, debridement and/or partial meniscectomies are associated. ACL remnants are carefully identified and debrided from anatomical insertion sites, therefore minimizing the possibility of tunnel positioning mismatch, by direct visualization of insertion sites.<sup>7</sup>

Assessments were performed at 6, 12 and 24 hours post-operatively by one of the study investigators. Initially, we tried to blind the investigators, but we had to discontinue it due to incompatibility with the team's routine.

Quantitative variable results are described by means, medians, standard deviations, minimum and maximum values. Qualitative variables are described by frequencies and percentages.

VNS results from each group were compared using Kruskal-Wallis or Kolmogorov-Smirnov non-parametric tests. The Wald test was used for comparisons between groups. Chi-square tests were used to compare pain intensity and gender, and the Kolmogorov-Smirnov or ANOVA tests were used to compare medians and means.

Data were analyzed using the IBM SPSS v.20 software. Level of significance adopted was 95% ( $p < 0.05$ ).



**Figure 2** Study design.

## Results

Of the 95 patients submitted to ACL reconstruction using flexor tendon graft during the study period, 12 were excluded due to failure in any of the study phases (Fig. 2).

The mean age of the 83 patients eligible for the study ranged from 28 to 31 years, with a predominance of males (mean of 85.7%), with no difference between groups.

Group C presented higher postoperative opioid consumption when compared to groups M, R0.375 and R0.25 – 27.2% vs. 14.2%, 10% and 5%, respectively – however, there was no statistically significant difference (Table 1). In every group, tramadol was requested only once, between 8 and 14 hours postoperatively, and the dose did not surpass 50 mg. These patients were excluded from pain-related analyses, due to possible interference by the intravenous opioid on the variable, and possibly not reflecting the pain associated with the analgesic technique initially proposed. Thus, sample size of group C, M, R0.375 and R0.25 was reduced to 16, 18, 18 and 19 patients, respectively.

The assessment performed 6 hours after anesthesia showed both motor and sensorial functions were similarly reversed in the contralateral limb in all groups, demonstrating full recovery from spinal anesthesia. There was no statistically significant difference in the incidence of pain among all groups at 6, 12, and 24-hour assessments.

Pain intensity assessed by VNS varied in all groups between 0.3 to 1.2 at 6 hours, 1.5 to 2.4 at 12 hours and 2.2 to 2.7 at 24 hours from the initiation of the procedure, with no statistically significant difference among groups (Table 2). As for the classification of pain intensity as mild, moderate and severe, there was a predominance of mild

pain in all groups, with no statistically significant difference when groups were compared.

Groups C, M, R0.375 and R0.25 presented adverse events in 13.6%, 33.3%, 35% and 15% of the cases, respectively, with no statistically significant difference among groups. Among adverse events investigated, urinary retention, prolonged motor blockade of the quadriceps muscles, and nausea and vomiting were observed. No patient falls, itching, respiratory depression, local hematoma or paresthesia during the postoperative period were reported.

The incidence of urinary retention (defined as absence of diuresis in 18 to 24 hours) was 13.6%, 23.8%, 0% and 5%, in groups C, M, R0.375 and R0.25, respectively. Higher incidence of urinary retention was observed in group M when compared to group R0.375 ( $p = 0.048$ ), as described in Table 3.

Prolonged quadriceps muscle motor block (defined by decreased muscle strength 18 to 24 hours after FNB) was reported in the R0.375 group (30%), and was statistically higher than in the groups C ( $p = 0.07$ ) and M ( $p = 0.009$ ), as shown in Table 4.

Nausea or vomiting occurred only in group M (10%), with no statistical significance when groups were compared.

All patients reported being satisfied with the anesthetic and analgesia technique used.

## Discussion

In this study, the analgesia modalities offered to patients submitted to ACL reconstruction with flexor tendon graft showed similar postoperative pain control results. Nonethe-

**Table 1** Postoperative opioids consumption.

Rescue opioid	Group				Group comparison	p
	C	M	R0.37	R0.25		
No	16 72.7%	18 85.7%	18 90.0%	19 95.0%	C × M C × R0.37	0.303 0.170
Yes	6 27.3%	3 14.3%	2 10.0%	1 5.0%	C × R0.25 M × R0.37	0.083 0.676
Total	22	21	20	20	M × R0.25 R0.37 × R0.25	0.337 0.556

Chi-Square Test.

<sup>a</sup>p < 0.05.**Table 2** Pain intensity assessed 6, 12, and 24 hours using visual numeric scale.

	Group	n	Mean	Median	Minimum	Maximum	SD	p
EVN 6h	C	16	0.9	0	0	4	1.3	0.296
	M	18	0.7	0.5	0	2	0.8	
	R0.37	18	0.3	0	0	2	0.7	
	R0.25	19	1.2	0	0	6	1.9	
EVN 12h	C	16	1.8	2	0	5	1.5	0.345
	M	18	1.5	1	0	7	1.7	
	R0.37	18	2.4	2	0	7	1.9	
	R0.25	19	1.9	2	0	6	1.7	
EVN 24h	C	16	2.5	2	0	7	1.9	0.645
	M	18	2.2	2	0	6	1.6	
	R0.37	18	2.7	3	0	6	1.7	
	R0.25	19	2.6	2	0	7	1.7	

SD, Standard Deviation.

Kruskal-Wallis non-parametric Test.

<sup>a</sup>p < 0.05.**Table 3** Incidence of urinary retention.

Urinary retention	Group				Group comparison	p
	C	M	R0.37	R0.25		
Absent	19 86.4%	16 76.2%	20 100.0%	19 95.0%	C × M C × R0.37	0.457 0.233
Present	3 13.6%	5 23.8%	0 0.0%	1 5.0%	C × R0.25 M × R0.37	0.608 0.048 <sup>a</sup>
Total	22	21	20	20	M × R0.25 R0.37 × R0.25	0.184 1

Chi-Square Test.

<sup>a</sup>p < 0.05.

less, there was a higher incidence of urinary retention in group M and prolonged motor block in group R0.375.

A review that assessed 48,000 patients submitted to ACL reconstruction in the US, between 2004 and 2009, showed predominance of males (63.4%) with the majority of patients within the 10 and 29-year old age range,<sup>8</sup> similar to our results.

A study that assessed patients undergoing ACL reconstruction with patellar and flexor tendon grafts, under spinal anesthesia associated or not with FNB (20 mL of 0.5% ropivacaine), also did not report a significant difference in the mean pain intensity assessed by the VNS at 6-hour (2.1

vs. 2.5), 12-hour (3.9 vs. 3.2) and 24-hour (2.4 vs. 2.3) assessments.<sup>6</sup>

The randomized clinical trial performed by Harbell et al.<sup>9</sup> in patients submitted to ACL reconstruction under general anesthesia compared analgesia provided by FNB (20–30 mL of 0.5% ropivacaine) versus FNB associated with sciatic nerve block (20–30 mL of 0.5% ropivacaine), and found greater intensity of pain in the first group (VNS equal to 7 vs. 5;  $p = 0.002$ ), longer stay in the recovery room (128.2 vs. 103.1 minutes;  $p = 0.006$ ) and higher opioid consumption during the stay at the operating room area (31.8 vs. 19.8 mg of morphine;  $p < 0.001$ ), but with no difference in subse-

**Table 4** Incidence of prolonged quadriceps muscle motor block.

Quadriceps motor blockade	Group				Group Comparison	p
	C	M	R0.37	R0.25		
Absent	22 100.0%	21 100.0%	14 70.0%	18 90.0%	C × M C × R0.37	1 0.007 <sup>a</sup>
Present	0 0.0%	0 0.0%	6 30.0%	2 10.0%	C × R0.25 M × R0.37	0.221 0.009 <sup>a</sup>
Total	22	21	20	20	M × R0.25 R0.37 × R0.25	0.232 0.235

Chi-square Test.

<sup>a</sup>  $p < 0.05$ .

quent assessments, up to 72 hours postoperatively. In our study, spinal anesthesia duration may have concealed possible differences in analgesia in the initial postoperative hours.

Performing FNB with 40 mL of 0.5% ropivacaine has been associated with 100%, 90% and 85% success for the femoral, obturator and lateral femoral cutaneous nerves, respectively. FNB has been more effective than intrathecal morphine to provide analgesia in hip, femur and knee surgeries in evaluations performed up to 16 hours postoperatively, although the effects have been assessed as more consistent in the morphine group.<sup>4</sup>

A systematic review that compared FNB to multimodal analgesia in patients submitted to ACL reconstruction showed no significant differences between groups for the scores of pain and hospital length of stay.<sup>10</sup>

A study comparing FNB with spinal anesthesia alone found that FNB was associated with better pain control in the first 12 hours after ACL reconstruction with patellar and flexor tendon grafts, rendering FNB as an option for analgesia in this population, as long as patients are oriented on risk of falls.<sup>6</sup>

Frost et al.<sup>11</sup> compared FNB using 0.25% bupivacaine with a placebo group in patients submitted to ACL reconstruction with flexor tendon graft. The authors observed postoperative pain reduction only during the night after the surgery, with no evidence of clinical significance, and no support to the recommendation of FNB for providing ACL postoperative analgesia.

A randomized, double-blind trial that submitted patients to general anesthesia and FNB (20 mL of 0.75% ropivacaine) associated or not with infiltration of the donor-site space and the surgical incision (40 mL of 0.25% ropivacaine) showed a significant decrease in pain intensity assessed by VNS (4.2 to 2.3 in the first hour; 2.8 to 1.3 in the sixth hour) and decrease of rescue doses of fentanyl (58 to 35  $\mu$ g) and morphine (10 to 6 mg) in the first 6 hours postoperatively, without a difference after this period.<sup>12</sup>

Likewise, a reduction in opioid consumption was found postoperatively in a prospective cohort, but without reduction in pain intensity and functional difference after 6 months.<sup>13</sup> Such findings confirm studies that have suggested the graft harvesting site as responsible for the greatest pain intensity. The donor-site of the flexor tendon is innervated by the tibial and obturator nerves.<sup>3</sup>

Kristensen et al.<sup>14</sup> randomized 60 patients who underwent ACL reconstruction with flexor tendon grafts and

compared FNB versus local infiltration (20 mL of 0.2% ropivacaine), associated with intra-articular administration of local anesthetics, and showed no difference in pain intensity and opioid consumption up to 48 hours postoperatively.

We observed higher occurrence of urinary retention in group M (23.8%), similarly to the incidence reported in the literature between 17.3% to 29.9% of urinary retention related to neuraxial morphine administration, regardless of the dose administered.<sup>15</sup> However, this finding can occur in any group, as a result of autonomic block related to spinal anesthesia.<sup>16</sup>

Statistically significant prolonged quadriceps motor block was shown in the R0.375 group (30%) when compared to groups in which FNB was not performed, with no patient falls reported. A similar study of patients submitted to 0.5% bupivacaine FNB described the occurrence of quadriceps transient motor paralysis in 80.8%, leading to the fall of 2 patients while walking (7.7%).<sup>6</sup> Because it is less lipophilic, ropivacaine penetrates less into myelinated motor fibers, resulting in less motor block when compared to bupivacaine.<sup>17</sup>

Fonseca et al.<sup>4</sup> evaluated the 3-in-1 FNB technique and described that using 40 mL of 0.5% ropivacaine produced motor block that lasted  $9.9 \pm 3.54$  hours. A meta-analysis described that the quadriceps maximal voluntary isometric contraction at the first postoperative hour was reduced in 79.4% of patients undergoing FNB.<sup>3</sup>

A systematic review carried out by Swank<sup>10</sup> assessed quadriceps isokinetic and functional muscle tests of patients submitted to FNB versus multimodal anesthesia for ACL reconstruction. The review found greater motor deficit in the early postoperative period (without apparent clinical or functional relevance), however, with conflicting results at 6 months.

A cohort study that assessed children and adolescents undergoing ACL reconstruction showed a significant isokinetic deficit in knee extension and flexion strength 6 months postoperatively in the group submitted to FNB, with a four times less likely return to sports in 6 months.<sup>18</sup>

A retrospective study of adults undergoing ACL reconstruction with patellar tendon graft that compared FNB with 0.5% bupivacaine (20–30 mL), followed by 10 mL hourly infusion of 0.1% bupivacaine for 40 hours versus no FNB, showed lower strength of extension and higher functional deficit of the knee at 6 months, however, without differences regarding the return to sport.<sup>19</sup>

A study that assessed patients undergoing ACL reconstruction under general anesthesia, compared FNB versus Adductor Canal Block (ACB) guided by US with 0.5% ropivacaine (20 mL) and showed no difference in postoperative analgesia, although, in the latter, there was preservation of the quadriceps muscle strength.<sup>20</sup>

Despite the absence of analgesic superiority, one meta-analysis that compared analgesia conferred by ACB to FNB and to control group showed a reduction in the maximum voluntary isometric contraction in 26.2% of patients submitted to saphenous nerve block, possibly related to more proximal blocks (mid-thigh).<sup>3</sup>

Motor block resulting from FNB can directly influence the performance of early physiotherapy, whereas intrathecal morphine poorly controls dynamic pain,<sup>21</sup> factors that can negatively interfere with rehabilitation.

Many services still perform FNB or ACB as an isolated technique of choice to provide analgesia for knee surgeries, however, its indication in this surgical modality should be reviewed. The unavailability of ultrasound at the time of the beginning of the study made it impossible to perform purely sensory blocks.

There is no consensus in the literature regarding the ideal technique for controlling postoperative pain in ACL reconstruction with flexor tendon graft. Thus, each technique should be evaluated individually, in order to reduce pain, postoperative opioid consumption and patient morbidity.

## Final remarks

The intensity of pain related to ACL reconstruction with flexor tendon graft was similar in all groups, but higher incidence of urinary retention was observed in the intrathecal morphine group and more motor block in the FNB group with 0.375% ropivacaine.

## Conflicts of interest

The authors declare no conflicts of interest.

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