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CHLOROPROCAINE *VS.* PRILOCAINE FOR SPINAL ANESTHESIA IN OUTPATIENT KNEE ARTHROSCOPY: A PROSPECTIVE ECONOMIC EVALUATION USING ACTIVITY-BASED COSTING

C. FRANCESCHI[1,2], F. TASSO[1], V. SIMILI[1], G. MONTELEONE[1], F. MARTORELLI[1], A. DE ANGELIS[1], E. CIALDELLA[1], D. ESPOSITO[1], G. ANZILLOTTI[1,2], P. CONTE[1,2], B. DI MATTEO[1,2], E. KON[1,2], M. SCARDINO[1]

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[1]IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[2]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy

CORRESPONDING AUTHOR
Carlotta Franceschi, MD; e-mail: carlotta.franceschi@humanitas.it

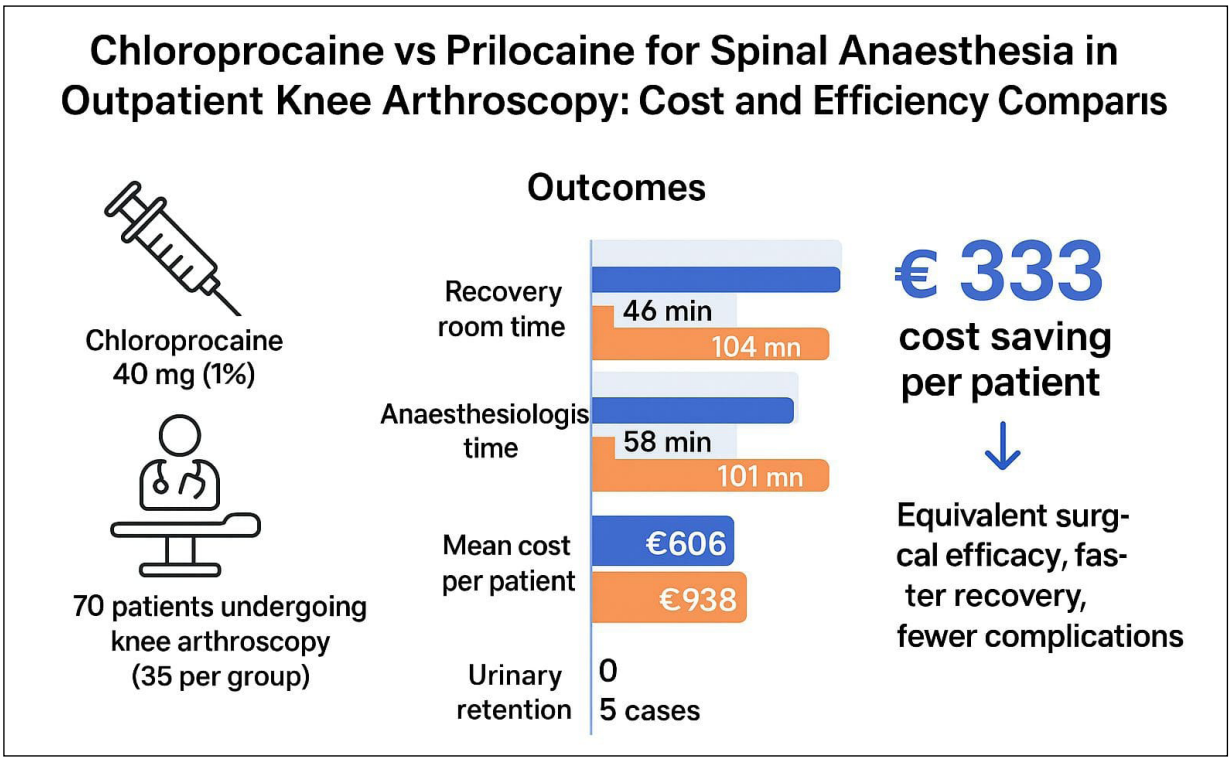
ABSTRACT – *Objective:* In orthopedic day-hospital interventions like knee arthroscopy, the choice of the short-acting local anesthetic to be used for spinal anesthesia may significantly impact both recovery times and hospital-related costs.

Materials and Methods: This prospective, two-arm cohort study included 70 adult patients undergoing an elective knee arthroscopy for meniscectomy who received either spinal chloroprocaine (40 mg, 1%) or prilocaine (40 mg, 2%). Cost analysis was performed using an activity-based costing approach, whereby resource utilization was multiplied by corresponding unit tariffs and summed across the following cost domains: operating room time, recovery room time, nurse care time, physician (anesthesiologist) care time, drug and device usage, and any unplanned overnight hospitalization. The primary outcome was the mean procedure cost per patient; secondary outcomes included perioperative time metrics and adverse events.

Results: Seventy subjects were recruited and assigned to one of the two groups, each consisting of 35 patients. The mean cost of the procedure per patient was €604.76 in the chloroprocaine group *vs.* €938.09 in the prilocaine group (difference = €333.33). Recovery room time and physician (anesthesiologist) care time were significantly shorter in the chloroprocaine group compared to the prilocaine group (45.63 *vs.* 104.00 minutes and 57.86 *vs.* 100.57 minutes, respectively, both *p*-values < 0.001). Urinary retention occurred in five patients in the prilocaine group, compared to none in the chloroprocaine group. One patient in the prilocaine group required overnight hospitalization.

Conclusions: The use of chloroprocaine for spinal anesthesia was associated with significantly shorter perioperative care times and lower hospital-related costs compared to prilocaine. Nonetheless, further high-quality, multicenter randomized controlled trials are needed to confirm the pharmacoeconomic advantages of using chloroprocaine for cost-effective spinal anesthesia.

KEYWORDS: Knee, Arthroscopy, Spinal anesthesia, Local anesthetic, Cost analysis.



Graphical Abstract. Comparison of chloroprocaine (40 mg, 1%) *vs*. prilocaine (40 mg, 2%) for spinal anesthesia in outpatient knee arthroscopy. In this prospective, two-arm cohort study (n = 70), chloroprocaine was associated with significantly shorter recovery room time and physician (anesthesiologist) care time, fewer peri-operative complications (notably, no cases of urinary retention), and lower overall hospital-related costs compared to prilocaine, accounting for a difference of €333.33 per patient for the former.

INTRODUCTION

In recent years, spinal anesthesia with local anesthetics has progressively replaced general anesthesia in various surgical settings, including orthopedic, gynecological, and urological surgery. Regarding orthopedic day-hospital interventions such as knee arthroscopy, spinal anesthesia is not only considered the current standard of care[1-4] but is also recognized as a critical determinant of clinical outcomes, patient satisfaction, and cost-effectiveness. This latter aspect is particularly relevant in today's clinical practice: indeed, as healthcare systems are transitioning towards outpatient models driven by the need to reduce hospital stays and to optimize resource utilization[5], the choice of the local anesthetic to be used for spinal anesthesia has become a central focus for clinicians and administrators alike. In this regard, activity-based costing (ABC) analysis is a highly effective and valuable tool for accurately determining the true costs of clinical activities[6,7]. It is a method of cost management that estimates the comprehensive costs of products and services by calculating the specific costs associated with the activities required to deliver them. Compared to traditional methods, which typically distribute indirect costs across support activities in an arbitrary manner[8], ABC analysis directly links indirect costs to the specific activities that generate them, thereby providing a more precise and objective strategy for cost allocation[9].

Chloroprocaine hydrochloride, an amino-benzoic acid ester, has recently gained significant attention as a local anesthetic for spinal anesthesia. Originally introduced in the 1950s for various loco-regional anesthesia techniques, chloroprocaine experienced a true resurgence after the development of preservative-free formulations specifically designed for spinal use[10,11]. In fact, its unique pharmacokinetic profile – in particular, its ultra-rapid onset and its short duration of action – makes it well suited for brief surgical procedures lasting less than one hour[12-14]. Moreover, compared to traditional amino-amide local anesthetics, chloroprocaine may offer distinct advantages in orthopedic practice, including clinical efficacy[15-26], patient satisfaction[13,14,16,18,20,22-23], and, consequently, economic impact – although there are no publications in the existing literature that directly address this issue. Thus, the aim of the present study is to compare the direct and the indirect costs associated with the use of chloroprocaine *vs.* prilocaine – which is currently considered the standard of care[27,28] – for spinal anesthesia in the perioperative management of 70 adult patients who underwent an elective knee arthroscopy for meniscectomy in an orthopedic ambulatory surgery setting.

MATERIALS AND METHODS

Study design

This is a prospective, two-arm cohort study comparing the direct and indirect costs associated with the use of chloroprocaine *vs.* prilocaine for spinal anesthesia in the perioperative management of 70 adult patients who underwent elective knee arthroscopy for meniscectomy in an orthopedic outpatient setting at IRCCS Humanitas Research Hospital of Rozzano between March 2023 and February 2024. Once eligibility was ensured, participants were recruited and assigned to one of the two groups, each consisting of 35 patients. The study protocol was approved by the Independent Ethics Committee of IRCCS Humanitas Research Hospital of Rozzano (ID: 2390) on February 23rd, 2023, ensuring that it conformed to the principles of the Declaration of Helsinki and to the pertinent national laws of the country involved. Eligible patients were individually selected by the surgical and anesthesiologic teams. Written informed consent was obtained from each participant during the preoperative visit, authorizing the use of his/her anonymized data for scientific purposes.

Participants

Inclusion criteria included adults undergoing elective knee arthroscopy for meniscectomy and classified as class I or II according to the American Society of Anesthesiologists' physical status classification system. Exclusion criteria to spinal anesthesia with either chloroprocaine or prilocaine included known allergy to local anesthetics, International Normalized Ratio > 1.3, platelet count < 75,000/µL, ongoing anticoagulant therapy, skin disorders involving the injection site, neurological disorders (e.g., spinal stenosis or neuropathies), heart or renal failure, chronic pain syndromes, history of drug or alcohol abuse, and pregnancy or breastfeeding. Patients' characteristics at baseline were comparable between the two groups and are summarized in Table I.

Intervention

Spinal anesthesia was administered using a Sprotte 25G needle with the patient lying down in a lateral decubitus position and the operative limb facing upwards. After the preparation of a sterile field with disposable drapes, chloroprocaine 10 mg/mL (40 mg, 1%) or prilocaine 20 mg/mL (40 mg, 2%) was injected in the L3-L4 intervertebral space. A dose of 40 mg typically provides a satisfactory sensory and motor blockade. A pinprick test with a hypodermic 25G needle (AnHui Hongyu Wuzhou Medical Manufacturer, China) was used to assess the sensory block, whereas the modified Bromage score (0 = no motor block, the patient is able to lift a straight leg against gravity; 1 = the patient is unable to lift a straight leg against gravity but is able to flex the knee and the ankle; 2 = the patient is unable to flex the knee but is able to flex the ankle; and 3 = complete motor block)[29] was used to test the motor block. During surgery, spinal anesthesia was considered to be effective if no further analgesia, no sedation, nor conversion to general anesthesia was required. For the majority of patients in both groups, perioperative pain management consisted of oral non-steroidal anti-inflammatory drugs, paracetamol, and, eventually, weak opioids.

Outcome measures

The primary outcome of the study was the mean cost of the procedure per patient, estimated using an ABC approach, whereby resource utilization was multiplied by corresponding unit tariffs and summed across the following cost domains: op-

Table I. Patients' characteristics at baseline stratified by type of local anesthetic used for spinal anesthesia (chloroprocaine *vs.* prilocaine). Each group consisted of 35 patients undergoing elective knee arthroscopy for meniscectomy. Data are expressed as numbers and percentages or as means, standard deviations, and ranges.

	Chloroprocaine group	Prilocaine group
Group size	35	35
Age (years)	25.91 (± 4.5; 19-34)	27.80 (± 4.5; 20-35)
Females	6 (17.14%)	8 (22.86%)
Males	29 (82.86%)	27 (77.14%)
Body mass index (kg/m^2)	24.83 (± 2.1; 20.2-27.8)	24.36 (± 2.4; 20.6-29.1)

SD: standard deviation.

erating room (OR) time, recovery room (RR) time, nurse care time, physician (anesthesiologist) care time, drug and device usage, and any unplanned overnight hospitalization. The secondary outcomes of the study included: (i) time-to-patient positioning (measured from arrival in the OR to completion of surgical positioning), (ii) OR time (measured from skin incision to wound closure), (iii) RR time, and (iv) nurse care time and physician (anesthesiologist) care time (measured from the induction of spinal anesthesia to discharge from the RR, as reported in the electronic anesthesia records and in the nurse logs). Adverse events, including urinary retention, hypotension, dizziness, post-operative nausea and vomiting, and delayed motor recovery, were all recorded until discharge.

Statistical analysis

Statistical analysis was performed using the software Statistical Package for Social Science (SPSS, Version 27.0, IBM Corp., Chicago, IL, USA). Patients' characteristics at baseline, as well as perioperative time metrics and cost-related variables, were compared through an independent samples *t*-test. A *p*-value of less than 0.05 was considered statistically significant. All numerical variables were presented as mean, standard deviation, and range. Cost analysis was conducted using the mean costs at our institution in 2024 as a reference. Specifically, the cost of the OR was set at €500/hour per patient (that is €8.33/minute), the cost of the RR was set at €200/hour per patient (that is €3.33/minute), the cost of the nurse care time was set at €50/hour per patient (that is €0.83/minute), the cost of the physician (anesthesiologist) care time was set at €100/hour per patient (that is €1.67/minute), the cost of bladder catheterization was set at €12/kit per patient, and the cost of overnight hospitalization was set at €600/night per patient.

RESULTS

A total of 70 subjects considered eligible for the study were recruited, assigned to one of the two groups, and treated at IRCCS Humanitas Research Hospital of Rozzano. The two groups were relatively homogeneous in terms of size, age, sex, and body mass index. The mean OR time was comparable between the two groups with no statistically significant differences, thereby excluding the duration of surgery as a potential source of bias. However, the mean time of onset of the motor block was significantly shorter in the chloroprocaine group compared to the prilocaine group ($p = 0.017$), which, in turn, accounted for the mean time-to-patient positioning from the induction of spinal anesthesia to also be 17 minutes shorter for the former ($p < 0.001$). The mean RR time was 45.63 (SD 11.77; range 25-70) minutes for the chloroprocaine group and 104.00 (SD 9.40; range 90-120) minutes for the prilocaine group ($p < 0.001$), accounting for a difference of €194.38 in the mean cost of the RR per patient for the latter. The mean nurse care time was 160.46 (SD 13.41; range 125-177) minutes for the chloroprocaine group and 208.57 (SD 17.60; range 180-230) minutes for the prilocaine group ($p < 0.001$), accounting for a difference of €39.93 in the mean cost of the nurse care per patient for the latter. The mean physician (anesthesiologist) care time was 57.86 (SD 7.79; range 45-75) minutes for the chloroprocaine group and 100.57 (SD 12.05; range 80-120) minutes for the prilocaine group, accounting for a difference of €70.90 in the mean cost of the physician (anesthesiologist) care per patient for the latter. No perioperative complications were recorded, and no patients required overnight hospitalization in the chloroprocaine group. In contrast, the prilocaine group reported five cases of urinary retention – three of which required bladder catheterization – four cases of dizziness, three cases of hypotension, and six cases of delayed motor recovery, and one patient required overnight hospitalization, accounting for a difference of €17.14 in the mean cost of the perioperative complications per patient for the latter. The cost per vial of the local anesthetic was €15.60 for the chloroprocaine group and €10.80 for the prilocaine group, accounting for a difference of €4.80 in the mean cost of the local anesthetic per patient for the former. By summing up all the afore-mentioned direct and indirect costs, the mean cost of the procedure per patient was calculated to be €604.76 for the chloroprocaine group and €938.09 for the prilocaine group, accounting for a difference of €333.33 per patient for the latter. The perioperative time metrics and the direct and indirect costs of the procedure are summarized for each group in Table II and Table III, respectively.

DISCUSSION

The primary finding of the present study is that, in adult patients undergoing elective knee arthroscopy for meniscectomy, the use of chloroprocaine for spinal anesthesia was associated with shorter perioperative care times and with lower hospital-related costs compared to prilocaine. Notably, the mean procedure cost per patient was €333.33 lower in the chloroprocaine group, reflecting parallel reductions in RR time and anesthesiologic team requirements. From a clinical point of view,

Table II. Summary of the perioperative time metrics stratified by type of local anesthetic used for spinal anesthesia (chloroprocaine *vs*. prilocaine). Variables include time of onset of the motor block, time-to-patient positioning, operating room time, recovery room time, nurse care time, and physician (anaesthesiologist) care time. Data are expressed as means, standard deviations, and ranges. The column "*p*-value" reports between-group comparisons.

	Chloroprocaine group	Prilocaine group	*p*-value
Time of onset of the motor block (min)	2.34 (0.48; 2-3)	2.91 (0.70; 2-4)	0.017
Time-to-patient positioning (min)	14.26 (1.65; 11-17)	31.31 (3.34; 25-38)	< 0.001
OR time (min)	24.97 (8.40; 14-45)	26.74 (7.34; 15-44)	0.336
RR time (min)	45.63 (11.77; 25-70)	104.00 (9.40; 90-120)	< 0.001
Nurse care time (min)	160.46 (13.41; 125-177)	208.57 (17.60; 180-230)	< 0.001
Physician (anaesthesiologist) care time (min)	57.86 (7.79; 45-75)	100.57 (12.05; 80-120)	< 0.001

Min: minutes; SD: standard deviation; OR: operating room; RR: recovery room.

Table III. Summary of the direct and of the indirect costs of the procedure stratified by type of local anesthetic used for spinal anesthesia (chloroprocaine vs. prilocaine). Data are reported as mean cost (€) per patient for each cost domain and for the entire procedure. The column "Difference" reports between-group cost differences.

	Chloroprocaine group	Prilocaine group	Difference
Mean cost of the OR	208.00	222.74	14.74
Mean cost of the RR	151.94	346.32	194.38
Mean cost of the nurse care	133.18	173.11	39.93
Mean cost of the physician (anaesthesiologist) care	96.04	166.95	70.90
Mean cost of the local anaesthetic	15.60	10.80	-4.80
Mean cost of bladder catheterization	0	1.03	1.03
Mean cost of overnight hospitalization	0	17.14	17.14
Mean cost of the procedure	604.76	938.09	333.33

OR: operating room; RR: recovery room.

urinary retention was observed exclusively in the prilocaine group, which was also the only arm in which one overnight hospitalization was required. Considered collectively, these results suggest that, within a standardized day-surgery pathway, the use of an ultra-short-acting local anesthetic like chloroprocaine for spinal anesthesia may enhance operational efficiency and yield measurable cost savings without compromising patient safety. In this respect, the pharmacokinetic characteristics of chloroprocaine – in particular, its ultra-rapid onset and its short duration of action – certainly play a pivotal role; they allow for a quick induction of spinal anesthesia, for a predictable recovery, and for a favorable safety profile[22,30-32]. Elucidating these aspects allows us to understand why chloroprocaine is nowadays increasingly preferred to amino-amide local anesthetics like prilocaine for short-duration surgical procedures.

Regarding onset of action, chloroprocaine is among the fastest-acting local anesthetics, typically achieving an effective sensory and motor blockade within 5 to 10 minutes of administration[13-15,17,19,23,24,26]. This ultra-rapid onset of action is particularly valuable in high-throughput surgical centers where time efficiency is of paramount importance. Indeed, by minimizing the time from the induction of spinal anesthesia to the beginning of surgery, chloroprocaine allows for the streamlining of OR workflows, thus contributing to shortening the length of hospital stays and improving resource utilization[4]. Conversely, amino-amide local anesthetics generally display longer onsets of action that delay OR start times and, consequently, prolong their idle times. For orthopedic day-hospital surgeries like knee arthroscopy, this delay becomes a true bottleneck hindering the optimization of surgical schedules.

Regarding the duration of anesthesia achieved with spinal chloroprocaine, it normally ranges from 40 to 60 minutes, making it ideally suited for brief surgical procedures lasting less than one hour[13-14,22,24]. This predictable duration of action ensures alignment of the anesthetic effect with the surgical timeline, thus preventing both premature offset of anesthesia and unnecessary prolongation of the motor and sensory block. Longer-acting local anesthetics such as prilocaine,

while effective for more extended surgeries, are associated with longer recovery times that, in turn, may delay patient discharge[18,19,25].

As it pertains to its metabolism, chloroprocaine is converted into inactive, non-toxic compounds by plasma esterases[33]. This enzymatic digestion minimizes the risk of systemic toxicity associated with the accumulation of the active drug at toxic concentrations, especially in patients with hepatic or renal failure. Therefore, even in the elderly and in patients with multiple comorbidities, chloroprocaine provides a broader safety profile than amino-amide local anesthetics, which rely solely on hepatic metabolism[34]. Of note, the recent introduction of preservative-free formulations specifically designed for spinal use has eliminated the risk of neurotoxicity associated with earlier formulations[16,35].

Having said that, the clinical utility of chloroprocaine extends far beyond its pharmacokinetic properties to encompass tangible improvements in clinical outcomes and in procedural efficiency. In this respect, one of the most notable clinical benefits of chloroprocaine is the ability to expedite recovery and to facilitate early discharge. The mean RR time of 45.63 minutes recorded in the chloroprocaine group is significantly shorter than the 104.00 minutes observed in the prilocaine group, supporting the superiority of chloroprocaine in accelerating post-anesthetic recovery. A shorter recovery, in turn, is translated into several practical benefits, including diminished patient discomfort, reduced RR congestion, and, ultimately, increased availability of surgical slots. From the patient's perspective, the possibility of returning home sooner after surgery enhances overall satisfaction and meets a growing demand for convenient, patient-centered care[36].

As previously mentioned, chloroprocaine is associated with a significantly lower risk of perioperative complications, particularly urinary retention, compared to longer-acting local anaesthetics[13,17,20,22], contributing to a smoother perioperative experience for both patients and healthcare providers. Faster recovery, fewer perioperative complications, and the possibility of resuming daily activities a few hours after surgery are key factors that improve overall patient satisfaction[36]. In a healthcare environment increasingly focused on patient-reported outcomes like today's, these benefits underscore the value of chloroprocaine in delivering high-quality care.

The economic implications associated with the use of chloroprocaine are multifaceted, encompassing direct cost savings, enhanced resource utilization, and increased revenue generation. A comprehensive analysis of these factors demonstrates that chloroprocaine is not only clinically effective but also highly cost-efficient[37]. First of all, peri-operative complications like urinary retention often require overnight hospitalization, especially in patients receiving longer-acting local anesthetics[13,17,20,22]. In our study, one patient in the prilocaine group experienced urinary retention and required overnight hospitalization, accounting for an increase of €17.14 in the mean cost of the procedure per patient. Thus, the ability of chloroprocaine to avoid urinary retention is directly translated into substantial cost savings. Secondly, its faster recovery times significantly decrease the duration of RR monitoring, reducing also nurse care requirements and accelerating discharge times. Thirdly, by decreasing turnover times, chloroprocaine may enable performing a higher number of cases within the same surgical session, potentially leading to an even greater monthly revenue increase. Even though the cost of chloroprocaine per vial is €4.80 higher than prilocaine, this marginal difference becomes negligible when weighted against the broader cost savings and the potential revenue gains associated with its use. In fact, by combining both direct and indirect costs for all 35 patients, the total economic benefit for the chloroprocaine group would be €11,666.55. This enhanced surgical efficiency emphasizes, again, the economic value of using chloroprocaine for short-duration surgical procedures, especially in high-volume tertiary surgical centers.

Despite these positive findings, the present study suffers from several limitations. To begin with, its prospective, non-randomized design introduces the risk of allocation, selection, and performance bias. Additionally, the relatively small sample size and the single-center setting may limit both the precision and the generalizability of the results. Furthermore, the economic evaluation was limited by a hospital-based perspective, since societal costs (e.g., productivity and caregiver time) and patient-reported outcomes were not assessed. Consequently, a full cost-effectiveness analysis could not be undertaken. Lastly, data from our study are limited to Italian hospitals, as comparable cost analyses from other European countries are currently not available in the literature. Nevertheless, given the similarities in spinal anesthesia guidelines across Europe, we expect that the cost-saving potential of chloroprocaine that we have herein described would likely be similar. For these reasons, although promising, these preliminary results must be validated by additional high-quality, multi-center randomized controlled trials to confirm the pharmaco-economic advantages of using chloroprocaine for cost-effective spinal anesthesia.

CONCLUSIONS

For orthopedic day-hospital interventions like knee arthroscopy, the use of chloroprocaine for spinal anesthesia demonstrated an excellent safety profile and was associated with shorter perioperative care times and with lower hospital-related costs compared to prilocaine.

Conflict of Interest
The authors have no conflicts of interest to disclose.

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Authors' Contributions
C.F. wrote the original draft of the manuscript; M.S. supervised the writing process and provided a comprehensive revision of the last version of the paper; F.T., V.S., G.M., and F.M. were responsible for data collection; G.A., P.C., B.D.M., and E.K. critically reviewed and refined the article; A.D.A., E.C., and D.E. performed the statistical analysis. All authors read and approved the present version of the manuscript.

Ethics Approval
The study protocol was approved by the Independent Ethics Committee of IRCCS Humanitas Research Hospital of Rozzano (ID: 2390) on February 23rd, 2023, ensuring that it conformed to the principles of the Declaration of Helsinki and to the pertinent national laws of the country involved.

Informed Consent
Written informed consent was obtained from each participant during the pre-operative visit, authorizing the use of his/her anonymized data for scientific purposes.

Data Availability
The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

ORCID ID
Carlotta Franceschi: 0009-0007-9247-8712
Francesco Tasso: 0009-0008-4132-5596
Federica Martorelli: 0000-0002-9690-2548
Giuseppe Anzillotti: 0000-0001-9327-5350
Pietro Conte: 0000-0001-5425-0652
Berardo Di Matteo: 0000-0002-9807-0271
Elizaveta Kon: 0000-0003-0649-2336
Marco Scardino: 0000-0001-6776-1830

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