

ANESTHESIOLOGY

Mepivacaine versus Bupivacaine Spinal Anesthesia for Early Postoperative Ambulation

A Randomized Controlled Trial

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ANESTHESIOLOGY 2020; 133:801–11

EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Early ambulation after total hip arthroplasty is key to achieving readiness for discharge
- The spinal anesthetic for total hip arthroplasty that balances pain control with timely resolution of motor block has not been identified

What This Article Tells Us That Is New

- In this randomized, three-arm study involving 154 patients, more individuals in the mepivacaine spinal group ambulated 3 to 3.5 h after injection than did individuals in either the isobaric or hyperbaric bupivacaine group
- Likewise, more patients in the mepivacaine group achieved same-day discharge than patients in the other experimental groups

The annual volume of total hip arthroplasties in the United States could increase to 572,000 by the year 2030.¹ Over the past decade, orthopedic surgeons have focused on programs that enable patients to recover from surgery not only safely and rapidly but also increasingly

ABSTRACT

Background: Early ambulation after total hip arthroplasty predicts early discharge. Spinal anesthesia is preferred by many practices but can delay ambulation, especially with bupivacaine. Mepivacaine, an intermediate-acting local anesthetic, could enable earlier ambulation than bupivacaine. This study was designed to test the hypothesis that patients who received mepivacaine would ambulate earlier than those who received hyperbaric or isobaric bupivacaine for primary total hip arthroplasty.

Methods: This randomized controlled trial included American Society of Anesthesiologists Physical Status I to III patients undergoing primary total hip arthroplasty. The patients were randomized 1:1:1 to 52.5 mg of mepivacaine, 11.25 mg of hyperbaric bupivacaine, or 12.5 mg of isobaric bupivacaine for spinal anesthesia. The primary outcome was ambulation between 3 and 3.5 h. Secondary outcomes included return of motor and sensory function, postoperative pain, opioid consumption, transient neurologic symptoms, urinary retention, intraoperative hypotension, intraoperative muscle tension, same-day discharge, length of stay, and 30-day readmissions.

Results: Of 154 patients, 50 received mepivacaine, 53 received hyperbaric bupivacaine, and 51 received isobaric bupivacaine. Patient characteristics were similar among groups. For ambulation at 3 to 3.5 h, 35 of 50 (70.0%) of patients met this endpoint in the mepivacaine group, followed by 20 of 53 (37.7%) in the hyperbaric bupivacaine group, and 9 of 51 (17.6%) in the isobaric bupivacaine group ($P < 0.001$). Return of motor function occurred earlier with mepivacaine. Pain and opioid consumption were higher for mepivacaine patients in the early postoperative period only. For ambulatory status, 23 of 50 (46.0%) of mepivacaine, 13 of 53 (24.5%) of hyperbaric bupivacaine, and 11 of 51 (21.5%) of isobaric bupivacaine patients had same-day discharge ($P = 0.014$). Length of stay was shortest in mepivacaine patients. There were no differences in transient neurologic symptoms, urinary retention, hypotension, muscle tension, or dizziness.

Conclusions: Mepivacaine patients ambulated earlier and were more likely to be discharged the same day than both hyperbaric bupivacaine and isobaric bupivacaine patients. Mepivacaine could be beneficial for outpatient total hip arthroplasty candidates if spinal is the preferred anesthesia type.

(ANESTHESIOLOGY 2020; 133:801–11)

as outpatients.^{2,3} Hip arthroplasty is typically performed under general anesthesia or spinal anesthesia. Compared with general anesthesia, spinal anesthesia reduces operative time, complications, and blood transfusions.⁴ Furthermore, neuraxial anesthesia is strongly recommended by a recent international consensus group.⁵

Despite these benefits, spinal anesthesia can potentially be a drawback for outpatient total hip arthroplasty, with

This article is featured in "This Month in Anesthesiology," page 1A. This article has a visual abstract available in the online version. A portion of this work was accepted for presentation at the Spring 2020 meeting of the American Society of Regional Anesthesia and Pain Medicine, which was postponed due to the COVID-19 pandemic.

Submitted for publication February 10, 2020. Accepted for publication June 30, 2020. Published online first on July 23, 2020. From the Department of Anesthesiology, Sidney Kimmel Medical College (E.S.S., J.D.S., M.S.A., S.A.B., W.J.H., A.J.C., J.J.L., C.S.W., J.L.B., M.C.T.) and the Department of Physical Therapy (A.C.N.), Thomas Jefferson University (A.M.M.), Philadelphia, Pennsylvania; United Anesthesia Services, Plymouth Meeting, Pennsylvania (V.P.K.); Rothman Orthopaedics, Philadelphia, Pennsylvania (M.S.A., S.A.B., W.J.H.); and the Department of Physical Therapy, Rothman Orthopedic Specialty Hospital, Bensalem, Pennsylvania (E.E.C.).

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weakness and sensory impairment that delay ambulation and discharge. This is especially true of bupivacaine, one of the most common medications for spinal anesthesia. Bupivacaine is a long-acting amide local anesthetic that comes in several forms, including hyperbaric and isobaric. Both forms produce partial motor blockade that can last 2.5 to 3 h with even longer sensory blockade.^{6,7} Alternatively, mepivacaine, an intermediate-acting amide local anesthetic, may also be used for spinal anesthesia; it produces reliable surgical anesthesia for 1.5 to 2 h,⁸ and evidence suggests that it allows for earlier ambulation after total knee arthroplasty compared with bupivacaine.⁹

The primary outcome measure of this randomized, double-blind trial of total hip arthroplasty patients was to determine the percentage of patients achieving early ambulation with isobaric mepivacaine, hyperbaric bupivacaine, and isobaric bupivacaine. We hypothesized that patients would ambulate earlier with mepivacaine followed by hyperbaric bupivacaine, and finally isobaric bupivacaine.

Materials and Methods

General Procedures

This study was approved by the Institutional Review Board of Thomas Jefferson University, took place at two locations (Thomas Jefferson University Hospital and Rothman Orthopedic Specialty Hospital) from May to November 2019, and was registered at ClinicalTrials.gov before patient enrollment (NCT03948386; Eric Schwenk, principal investigator) on May 8, 2019. The full trial protocol is available by request. All participants provided written informed consent before participation. This study was conducted according to the Consolidated Standards of Reporting Trials statement.¹⁰ Retrospective institutional performance improvement data demonstrated that the three participating surgeons routinely completed primary total hip arthroplasty in approximately 60 min, thus ensuring that a short-acting spinal would be adequate for surgery. There were 10 participating anesthesiologists. Inclusion criteria included American Society of Anesthesiologists (ASA; Schaumburg, Illinois) Physical Status I to III patients under the age of 85 yr undergoing primary elective total hip arthroplasty with a participating surgeon. All patients could walk 10 feet independently without human assistance. Exclusion criteria included contraindication to spinal anesthesia, neuropathy in buttocks or posterior thighs, taking more than oxycodone 30 mg by mouth daily or the equivalent, and intolerance to a study drug. The unadjusted Charlson Comorbidity Index¹¹ was determined based on medical history. In this parallel-arm, double-blind (patients and assessors) study, the study statistician initiated and distributed a computer-generated sequence using simple 1:1:1 randomization, and patients were assigned in parallel to one of the following: mepivacaine 1.5% (3.5 ml, 52.5 mg), hyperbaric bupivacaine 0.75% (1.5 ml, 11.25 mg) or isobaric bupivacaine 0.5% (2.5 ml,

12.5 mg). These doses were the lowest that the staff anesthesiologists would use for total hip arthroplasty and represent a reduction from the most common bupivacaine dose used for spinal anesthesia in one review.⁷ Patients with height of 74 inches or greater or with body mass index of 35 kg/m² or greater were given an extra 0.5 ml of local anesthetic. The group assignment was given to the intraoperative anesthesia team verbally by a study team member who did not participate in postoperative assessments. Patient assignments were posted online and were only accessible by study team members. The intraoperative anesthesia team was not blinded to the group assignment, but patients, surgeons, and assessors were blinded. All patients received standard preoperative multimodal analgesia, consisting of gabapentin/pregabalin and acetaminophen and either preoperative celecoxib or intraoperative ketorolac.

Intraoperative Management

After application of blood pressure and pulse oximetry, patients received premedication with midazolam. Spinals were performed in the sitting position under sterile conditions in the lumbar region, and patients were placed in supine position after approximately 1 min for mepivacaine and hyperbaric bupivacaine groups and 3 to 4 min for isobaric bupivacaine. Sensation was tested every 2 to 3 min using a blunt-tip needle, and adequate anesthesia was confirmed when a T10 dermatomal level was achieved. If T10 was not achieved or patients had significant motor function after 15 min, general anesthesia was induced. Standard ASA monitors were used intraoperatively. For intraoperative sedation, patients were given a propofol infusion, titrated to effect by the team. Tranexamic acid (1 g) was given intravenously to all patients prophylactically, and dexamethasone (4 to 8 mg) was given for analgesia and postoperative nausea and vomiting prophylaxis. Blood pressure was managed at the discretion of the intraoperative anesthesia team. All surgeries were performed by three board-certified, fellowship-trained joint-replacement surgeons with extensive experience in performing total hip arthroplasty; two surgeons used the direct anterior approach (W.J.H. and S.A.B.), whereas the other used the direct lateral approach (M.S.A.) Both surgical approaches were performed with the patient in the supine position.

All patients were ordered intravenous fentanyl as needed in the postanesthesia care unit (PACU). Oxycodone or hydrocodone/acetaminophen was provided as needed once liquids were tolerated by mouth. PACU nurses were blinded.

Primary Outcome and Physical Therapist Assessment

The primary outcome was the percentage of patients who could ambulate between 3 and 3.5 h after spinal placement. This time was chosen because of a previous study that reported mean time to ambulation after mepivacaine

spinal anesthesia at 212 min.⁸ Physical therapists, who were blinded to group assignments, were informed of the time of spinal placement by an investigator and then assessed patients for ambulation between 3 and 3.5 h later and then every 2 h after that if ambulation did not occur at the previous assessment. Assessments occurred in the PACU or on general medical/surgical floors. Physical therapists recorded the initial Tinetti score at the time of first ambulation and total distance ambulated. The Tinetti test is a validated instrument to predict fall risk in elderly adults¹²; both the gait and ambulation components were used, with a maximum score of 28. All patients were given a walker to assist with ambulation.

Secondary Outcomes

Secondary outcomes included the following: motor function return, sensory level at time of motor function return, initial distance ambulated, Tinetti score¹² at first ambulation, urinary retention, transient neurologic symptoms, lowest intraoperative blood pressure, dizziness, length of stay, pain, surgeon intraoperative muscle tension rating, opioid consumption up to 48 h, and 30-day readmissions. Because the weak opioid tramadol was not included in the opioid calculations; opioids were converted to oral morphine equivalents using a conversion table.¹³ Sources of data included patient interviews and the electronic medical record. For pain, opioid, transient neurologic symptoms, and patient satisfaction data collected on postoperative days 1 and 2, phone interviews were conducted if the patient was discharged.

The muscle tension rating was a four-point Likert scale that blinded surgeons used to rate the perceived joint tightness intraoperatively. The scale was as follows: 0 = most relaxed; 1 = mildly tight; 2 = moderately tight; and 3 = very tight. Time to return of motor function was defined as the time when muscle strength in all three muscle groups tested was 5 of 5 on a 0 to 5 scale, where 0 = no contraction, 1 = muscle flicker, 2 = active movement but not against gravity, 3 = active movement against gravity, 4 = movement against some resistance, and 5 = full strength against resistance. Motor functions tested included thigh flexion, knee extension, and toe dorsiflexion. The sensory dermatome level at the time of motor function return was assessed using ice. Both assessments began 30 min after PACU arrival and continued every 30 min until motor function return. Patients who still did not have 5 of 5 motor strength in all three muscle groups at 6 h received a time of 360 min for analysis purposes. Consistent with previous work,¹⁴ patients were asked the following to determine whether transient neurologic symptoms were present on postoperative days 0, 1, and 2: "Do you have any back pain that you didn't have before surgery that goes into your buttocks, thighs, hips, or lower legs?"

Urinary retention was defined as placement of a straight catheter or Foley catheter before spontaneous urination or inability to urinate for 8 h after PACU arrival, consistent

with a previous study.¹⁵ Dizziness was determined by the physical therapist at the time of first attempted ambulation if lightheadedness, nausea, or dizziness was reported by the patient.

Length of stay was determined using the difference between the anesthesia start time and the discharge order time. Standard discharge criteria included safely ambulating at least 100 feet, safely negotiating stairs specific to the home setting, ability to get in and out of bed, and ability to perform transfers to and from a chair and a toilet. A patient's baseline level of function and specific home setting were factored into discharge appropriateness. All secondary outcomes were assessed by blinded study investigators.

Statistical Analysis and Sample Size Determination

Previous studies^{4,5} as well as our clinical experience suggested that it would be reasonable to assume that between 3 and 3.5 h 70% of mepivacaine, 35% of hyperbaric bupivacaine, and 25% of isobaric bupivacaine patients would ambulate. The power analysis was performed using one-way ANOVA with a balanced design for three groups. All hypotheses were based on superiority. Using the above assumptions with α set to 0.05, power at 80%, and a SD of 70%, yielding 44 patients/group for a total required sample size of 132 patients. In anticipation of screen failures and dropouts, we requested permission from the Institutional Review Board to enroll a maximum of 20% additional patients. After testing for normality (Shapiro–Wilk test), the data were expressed as means \pm SD and nonnormally distributed data as median [interquartile range] or mean [95% CI], as appropriate. Age, body mass index, case duration, mean arterial pressure, pain and patient satisfaction ratings, Tinetti score, distance ambulated, and hospital length of stay variables were analyzed using one-way ANOVA (general linear model). Sex, ASA Physical Status, Charlson Comorbidity Index, surgical approach, surgeon muscle tension rating, return of motor function, same-day discharge, urinary retention, and dizziness were analyzed using the chi-square test or Kruskal–Wallis test, as appropriate. Binary logistic regression was used to determine whether ambulation achieved between 3 and 3.5 h postsurgery was associated with treatment. The dependent variable "ambulation achieved between 3 and 3.5 h" was coded as a binary variable in the complete model with the three treatment groups entered as the categorical independent variable with number of iterations limited to 50. We used a binary logistic regression to test for the potential effect that surgeons may have had on the primary outcome and reported the *P* values comparing those three surgeons. All tests were nondirectional, and protected tests were performed for *post hoc* analyses after confirming significant main effects. The *P* value was set at 0.05 for statistical significance. Statistical analyses were performed using Systat version 13, SPSS version 25, and GraphPad Prism version 6.

Results

Patient Characteristics, Intraoperative Outcomes, and Ambulation-related Outcomes

A total of 159 randomization assignments were allocated, but because of miscommunication 1 was never assigned to a patient, leaving 158 patients randomized. Of these, 4 were excluded for various reasons (fig. 1), leaving 154 for primary analysis: 50 patients in the mepivacaine group, 53 in the hyperbaric bupivacaine group, and 51 in the isobaric bupivacaine group. Enrollment was stopped when initial sample size plus an additional 4 patients per group was achieved for balance. However, it was later discovered that 3 patients were given a study drug not originally assigned because of miscommunication. In-hospital data only were analyzed for patients lost to follow-up (fig. 1). The following data were reported for all patients: age, sex, body mass index, ASA Physical Status, case duration, surgical approach, lowest intraoperative blood pressure, ambulation between 3 and 3.5 h, and initial distance ambulated. For other outcomes, the number of patients with available data can be seen in tables 1 to 3. Demographic data are shown in table 1. There were no differences in age, body mass index, sex, ASA Physical Status, or Charlson Comorbidity Index between the three groups. There were also no statistically significant differences in surgical approach or lowest intraoperative mean arterial pressure.

The median surgeon muscle tension ratings (0 to 3 scale) for hyperbaric bupivacaine, isobaric bupivacaine, and mepivacaine were 1 (interquartile range, 1 to 2), 1 (interquartile range, 0 to 2), and 1 (interquartile range, 1 to 2), respectively, with more patients receiving a rating of 3 in the mepivacaine group (8 of 14, 57.1%) versus 3/14 (21.4%) in the hyperbaric and isobaric bupivacaine groups. There were more patients with a rating of 0 in the isobaric bupivacaine group (13 of 29 [44.8%] versus 9 of 29 [31.0%] in the hyperbaric bupivacaine group and 7 of 29 [24.1%] in the mepivacaine group), but these differences were not statistically significant overall (table 1; fig. 2; $P = 0.354$). The surgical duration was slightly shorter with mepivacaine compared with hyperbaric and isobaric bupivacaine, but the difference between the latter two was not statistically significant (table 1). Two patients (one given mepivacaine and one given hyperbaric bupivacaine) were converted to general anesthesia before surgical incision because of inadequate spinal level but remained in the study for analysis. Five patients (four hyperbaric bupivacaine and one isobaric bupivacaine) received intraoperative opioids, ranging from 25 to 75 μg of intravenous fentanyl, for hypertension or tachycardia.

For the primary outcome of ambulation between 3 and 3.5 h, 70.0% of patients met this endpoint with mepivacaine, followed by 37.7% with hyperbaric bupivacaine and then 17.6% with isobaric bupivacaine ($P < 0.001$; fig. 3). Patients who received mepivacaine were more likely to ambulate at 3.5 h than those who received hyperbaric bupivacaine

(odds ratio, 3.85; 95% CI, 1.69 to 8.8; $P = 0.001$) or isobaric bupivacaine (odds ratio, 10.8; 95% CI, 4.2 to 27.8; $P < 0.001$). Patients who received hyperbaric bupivacaine were more likely to walk between 3 and 3.5 h than patients who received isobaric bupivacaine (odds ratio, 2.83; 95% CI, 1.14 to 7.0; $P = 0.025$). Using a binary logistic regression, we confirmed that there were no statistically significant differences in the primary outcome attributable to a specific surgeon noted by the P values comparing the three surgeons (1 vs. 2: $P = 0.113$; 1 vs. 3: $P = 0.721$; and 2 vs. 3: $P = 0.142$). The mean ratio of patients ambulating between 3 and 3.5 h among the three surgeons was 0.35 (95% CI, 0.18 to 0.52). Overall, patients in the mepivacaine group were more likely to be discharged home on the day of surgery than either bupivacaine group and had a shorter length of stay than both hyperbaric and isobaric bupivacaine patients (table 2; fig. 4).

There were no statistically significant differences between groups regarding distance ambulated and initial Tinetti score (table 2), but return of motor function occurred earlier in mepivacaine patients followed by hyperbaric bupivacaine and then isobaric bupivacaine (109 min [74 to 156] vs. 123 min [88 to 188] vs. 148 min [120 to 205], respectively; $P = 0.049$; fig. 5). The most common dermatomal sensory level was L4 in mepivacaine and hyperbaric bupivacaine groups (33.3% and 23.6%, respectively) at the time of motor function return, whereas 34.3% of isobaric bupivacaine patients had a level of L3 at that time. However, the difference in distribution of sensory levels was not statistically significant ($P = 0.422$).

Pain Outcomes

There were no statistically significant differences in opioid consumption at any time point between the groups except in the PACU, where mepivacaine patients used a greater amount of opioids than the hyperbaric and isobaric bupivacaine groups (table 3). At the final PACU pain assessment just before PACU discharge, mepivacaine patients reported the highest pain levels of the three groups, but the difference was only statistically greater than the isobaric bupivacaine group (table 3). Transient neurologic symptoms occurred in 10.0% of mepivacaine, 11.3% of hyperbaric bupivacaine, and 3.9% of isobaric bupivacaine patients (table 3; $P = 0.355$).

Additional Secondary Outcomes

There were no statistically significant differences in urinary retention or dizziness among the three groups (table 2). One patient in the hyperbaric bupivacaine group had a Foley catheter placed, but no patients were discharged home with a Foley catheter. The other 18 patients with urinary retention either received a straight catheterization or did not urinate until after 8 h as per the predetermined definition. There were no differences in patient satisfaction

CONSORT

TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram

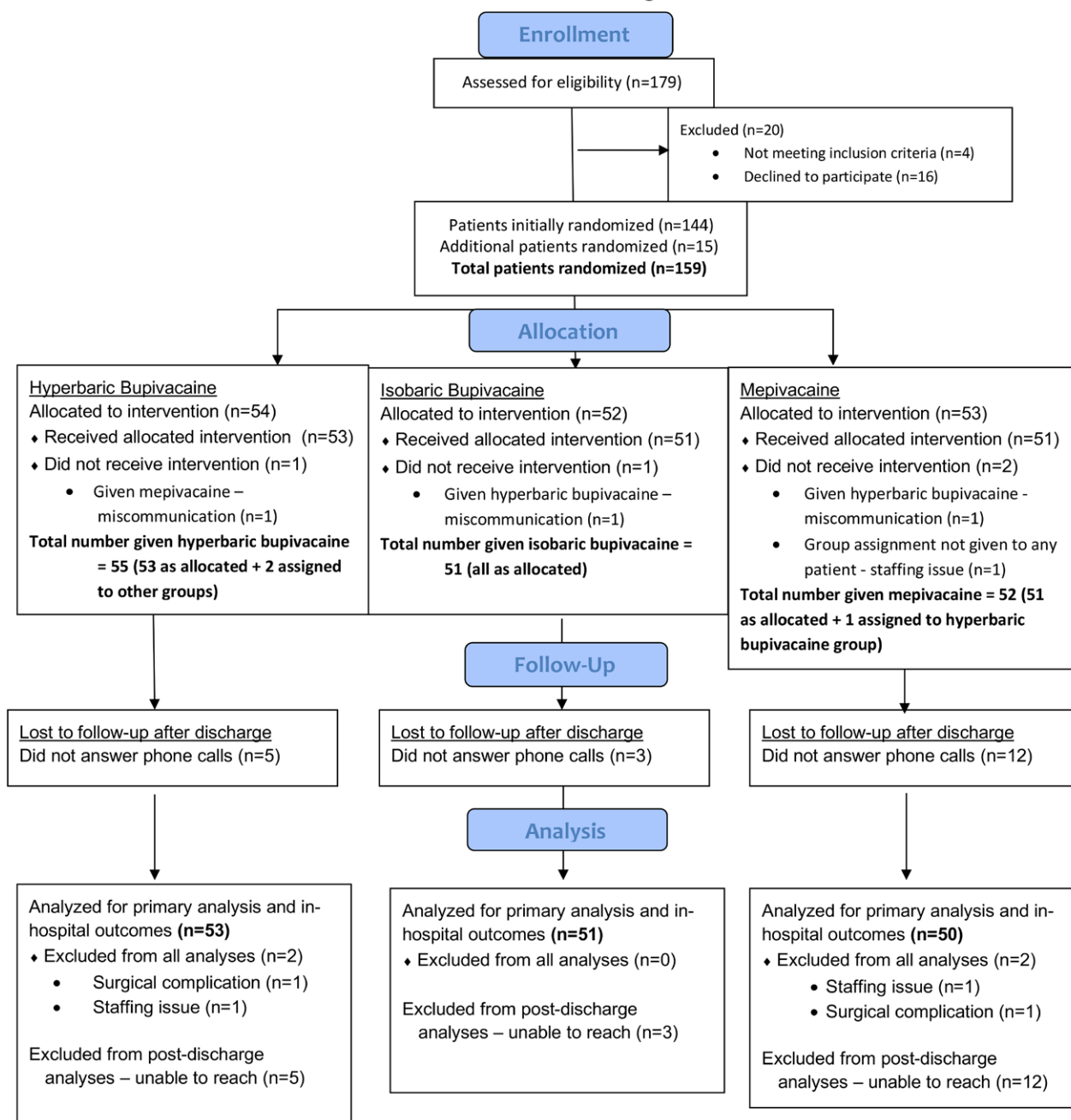


Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

ratings, which were high for all patients (table 2). Analysis of patient records revealed that one patient in the mepivacaine group was readmitted within 30 days of surgery.

This patient was an 80-yr-old male who was admitted 26 days postoperatively for a urinary tract infection that was possibly related to difficult attempted Foley catheter

Table 1. Patient Characteristics and Intraoperative Details

	Mepivacaine (N = 50)	Hyperbaric Bupivacaine (N = 53)	Isobaric Bupivacaine (N = 51)	P Value
Male sex, N (%)	28/50 (56.0)	25/53 (47.1)	23/51 (45.0)	0.508
Age (yr), mean ± SD	67 ± 8	67 ± 8	66 ± 9	0.703
Body mass index (kg/m ²), mean ± SD	28.2 ± 5.4	29.5 ± 5.1	29.7 ± 5.2	0.331
ASA Physical Status, N (%)				
I	0	0	0	
II	37 (74.0)	39 (73.5)	33 (64.7)	0.506
III	13 (26.0)	14 (26.4)	18 (35.2)	
Charlson Comorbidity Index (unadjusted), mean [95% CI]	0 [0–1] (N = 45)	0 [0–0] (N = 44)	0 [0–0] (N = 40)	0.679
Case duration (min), mean ± SD	54 ± 13	61 ± 16	64 ± 18	0.014
Surgical approach (anterior or lateral), N (%)	Anterior: 34/50 (68.0)	Anterior: 32/53 (60.3)	Anterior: 37/51 (72.5)	0.411
Lowest intraoperative MAP (mm Hg), mean ± SD	65 ± 7	65 ± 7	65 ± 11	0.967
Surgeon muscle tension rating (0 to 3), N (%) [*]				
0	7/44 (15.9)	9/51 (17.6)	13/50 (26.0)	0.354
1	16/44 (36.3)	23/51 (45.0)	16/50 (32.0)	
2	13/44 (29.5)	16/51 (31.3)	18/50 (36.0)	
3	8/44 (18.1)	3/51 (5.8)	3/50 (6.0)	

^{*}Rating scale was 0 to 3, where 0 = most relaxed, 1 = mildly tight, 2 = moderately tight, and 3 = very tight.

ASA, American Society of Anesthesiologists; MAP, mean arterial pressure.

placement in the postoperative period. No other readmissions occurred.

Discussion

This study demonstrates that spinal mepivacaine allows for earlier ambulation and discharge after total hip arthroplasty than either hyperbaric or isobaric bupivacaine. This is encouraging for outpatient programs that prefer spinal anesthesia for its outcome benefits.¹⁶ Earlier ambulation comes with more pain in the PACU. However, overall pain was low. Because pain and opioid consumption were not different at any other time, this pain may not have affected functional outcomes. Mepivacaine patients experienced a wider range of pain ratings and opioid consumption in the early postoperative period, but on average both were very low and have questionable clinical significance. The routine use of both nonsteroidal anti-inflammatory drugs and dexamethasone for all patients may have partially mitigated overall pain, leading to a statistically significant but clinically not important difference. Early ambulation predicts successful same-day discharge,⁶ which is consistent with our results. The earlier return of motor function likely allowed patients who received mepivacaine to meet physical therapy milestones sooner, contributing to a faster discharge. Our study improves upon previous work⁵ because we attempted early ambulation at a time when mepivacaine would be expected to wear off, in contrast to that study where routine ambulation assessment occurred, which is typically several hours later.

As the push for earlier discharge after total joint arthroplasty increases, those involved in their perioperative care, including anesthesiologists, are searching for the optimal combination of elements that maximize same-day

discharge chances. Although mepivacaine is not new and has been used since the 1960s,¹⁷ it has been avoided at many institutions. It is possible that early reports of an association between mepivacaine and transient neurologic symptoms^{18,19} led to hesitance by some anesthesiologists to use the drug. We observed that 5 out of 50 mepivacaine patients developed transient neurologic symptoms, which is slightly higher than others who have reported an incidence of 6.4%¹⁴ and 7.5%¹⁹ with mepivacaine in orthopedic surgery. However, patients in all three groups experienced transient neurologic symptoms, and the differences between groups were not significant.

Operative conditions were not adversely affected by mepivacaine as suggested by the overall lack of difference in muscle tension ratings and the very small difference in case duration, which was actually slightly shorter with mepivacaine. For many surgeons, this difference of 10 min is insignificant. It was notable, however, that surgeons perceived that more mepivacaine patients had “tight” joints, indicated by the number of patients with a rating of 3 (0 to 3 scale). Our study was not powered to address this outcome. This topic deserves further exploration because others who have studied spinal mepivacaine have not addressed this.^{9,14,20} Previous studies found that the incidence of hypotension does not vary between hyperbaric bupivacaine and isobaric bupivacaine,⁷ and our results suggest that substitution of mepivacaine for bupivacaine does not change this. Our results are generalizable to other joint programs in which early ambulation is desirable even without same-day discharge. However, we advise caution in applying our results to surgeons with significantly longer operative times. Pawlowski *et al.*⁸ previously demonstrated that 4 ml of mepivacaine (1.5%; 60 mg) will regress

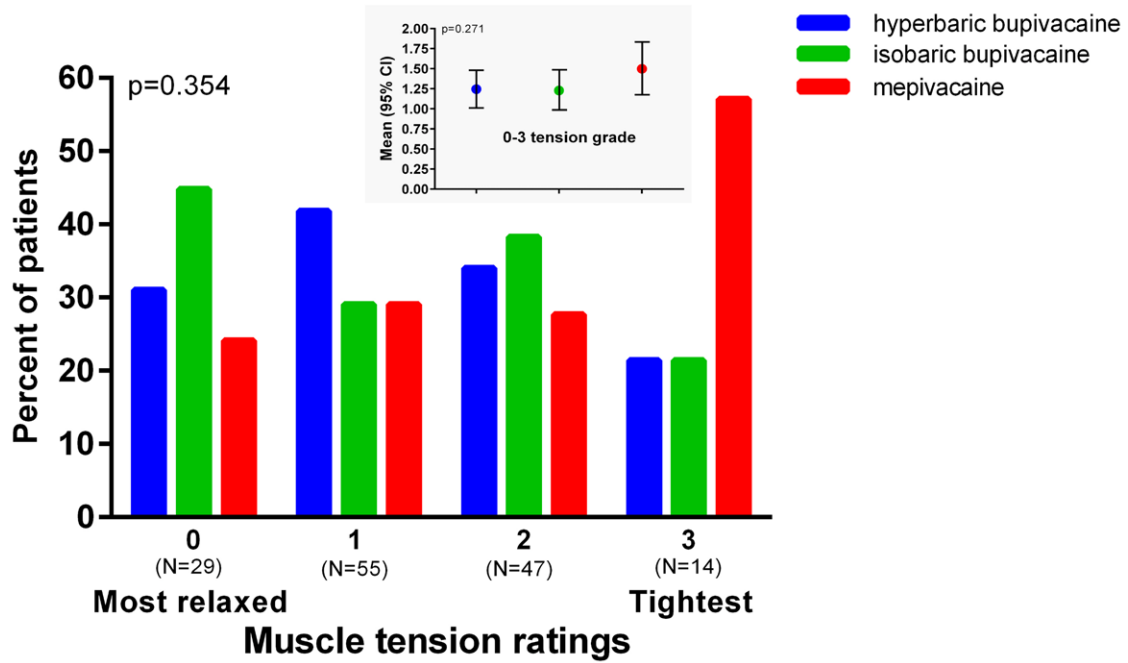


Fig. 2. Distribution of surgeon's intraoperative muscle tension ratings using a 0 to 3 scale, where 0 = most relaxed, 1 = mildly tight, 2 = moderately tight, and 3 = very tight. Superimposed on the graph is a smaller graph showing the mean tension rating for each group with 95% CI.

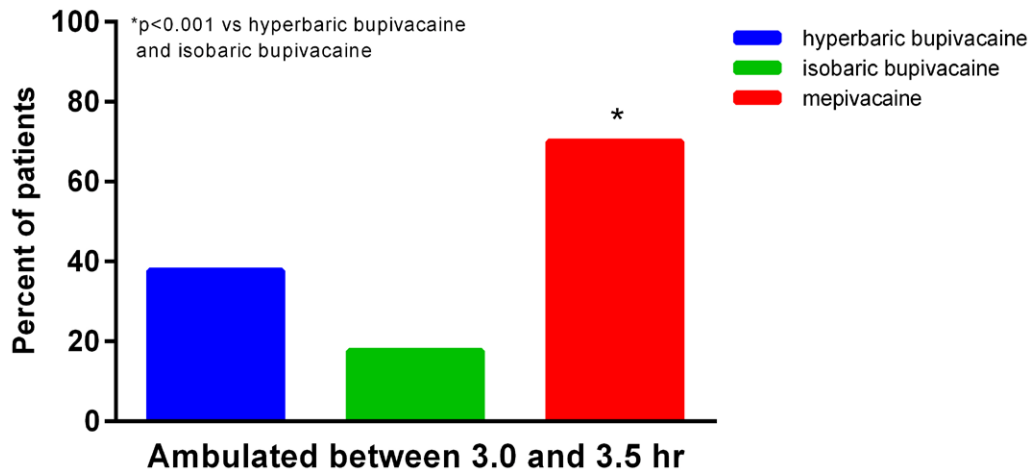


Fig. 3. Percentage of total hip arthroplasty patients ambulating between 3 and 3.5 h after spinal anesthesia with mepivacaine, hyperbaric bupivacaine, or isobaric bupivacaine.

below T10 dermatome after 120 min, putting patients at risk for inadequate anesthesia and conversion to general anesthesia. Although our study dose was slightly lower and we did not measure the time when the sensory level regressed below T10, the fact that no patient required conversion to general anesthesia during surgery (and only

two before incision) suggests adequate spinal anesthesia throughout.

Anesthetic choice is only one component of a successful outpatient program. Appropriate patient selection is critical to achieve favorable outcomes. One study found that women, patients ≤ 40 yr, patients ≥ 60 yr,

Table 2. Secondary Outcomes

	Mepivacaine (N = 50)	Hyperbaric Bupivacaine (N = 53)	Isobaric Bupivacaine (N = 51)	P Value
Return of motor function (min), median [interquartile range]	109 [74–156]	123 [88–188]	148 [120–205]	0.049
Initial distance ambulated (feet), median [interquartile range]	85 [30–200]	50 [20–150]	70 [20–225]	0.231
Initial Tinetti score (0 to 28), median [interquartile range]	19 [17–21]	18 [16–21]	18 [15–21]	0.354
Same-day discharge, N (%)	23/50 (46.0)	13/53 (24.5)	11/51 (21.5)	0.014
Length of stay (h), median [interquartile range]	22 [9–26]	26 [23–29]	26 [21–28]	0.001
Urinary retention, N (%)	5/50 (10.0)	8/52 (15.3)	6/49 (12.2)	0.712
Dizziness, N (%)	9/49 (18.3)	7/52 (13.4)	11/51 (21.5)	0.555
Patient satisfaction (0 to 10), mean ± SD*	9.5 ± 1.2	9.3 ± 1.6	9.4 ± 1.3	0.778

*Patients were asked to rate their overall anesthesia experience using a scale in which 0 represented the worst possible experience and 10 represented the best possible experience.

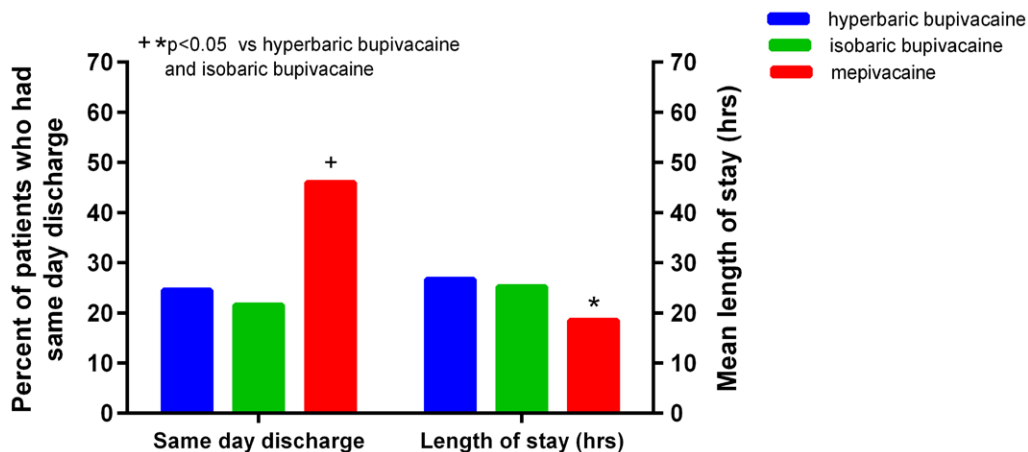


Fig. 4. Percentage of patients discharged on the day of surgery (*left*) and length of stay (*right*) after total hip arthroplasty with spinal mepivacaine, hyperbaric bupivacaine, or isobaric bupivacaine.

those with body mass index $\leq 26 \text{ kg/m}^2$, and those with higher ASA Physical Status were all associated with higher failure rates of same-day discharge.²¹ One review of outpatient total joint arthroplasty concluded that about 95% of included patients were discharged on the same day as planned but pain, hypotension, and nausea were the main reasons patients did not meet criteria.²² Although beyond the scope of our study, there are clearly patient and surgical factors that affect same-day discharge.

One of the strengths of the study includes the early and consistent time point chosen for the primary outcome assessment. Although Mahan *et al.*⁹ found no difference in ambulation time between mepivacaine and hyperbaric bupivacaine, their retrospective study design significantly impacted their ability to detect a difference between drugs, and furthermore, they did not specify nor standardize the time of first attempted ambulation. Another

strength of our study is the clinically relevant primary outcome of ambulation rather than sensory or motor function alone or pain. Because ambulation is predictive of discharge,² this makes our results applicable to those desiring to implement spinal anesthesia into an outpatient total hip arthroplasty program. The shorter length of stay and greater percentage of same-day discharges further support our choice of primary outcome as clinically meaningful. Finally, we chose to include both hyperbaric bupivacaine and isobaric bupivacaine in the study because of the diverse practice patterns that occur around the world. Although this required a larger sample size, we believe the results are even more clinically applicable because of the inclusion of both drugs.

Our study has limitations. First, a specific, early time window as the primary outcome introduces the possibility that some differences between the groups were missed because the sensory level is continuously regressing in the

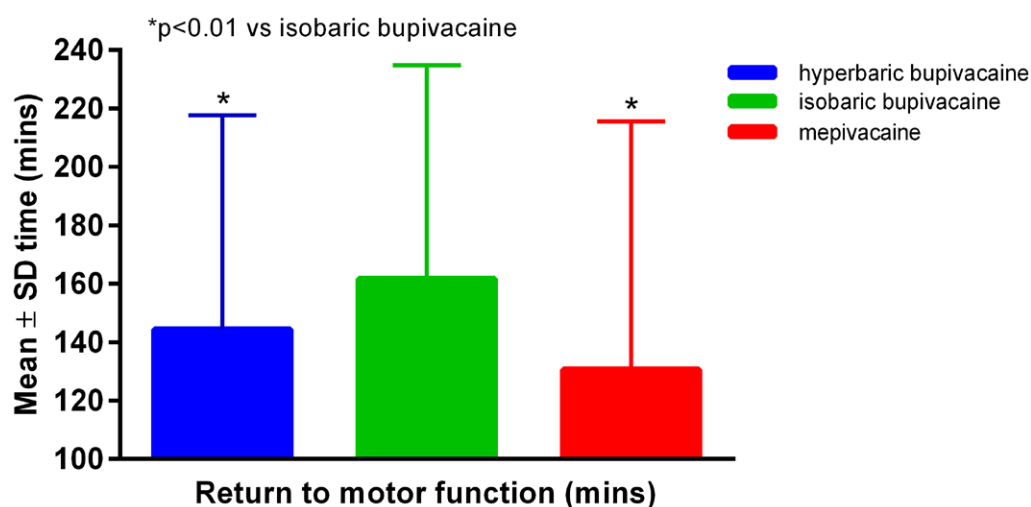


Fig. 5. Return of motor function after total hip arthroplasty under spinal anesthesia with mepivacaine, hyperbaric bupivacaine, and isobaric bupivacaine.

Table 3. Pain Outcomes

	Mepivacaine (N = 50)	Hyperbaric Bupivacaine (N = 53)	Isobaric Bupivacaine (N = 51)	P Value
Opioid consumption (mg), mean [95% CI]*				
PACU	11.3 [6.0–16.5]	2.0 [0.0–4.1]	0.8 [0.0–1.7]	< 0.001
Postoperative day 0 after PACU	21.8 [14.7–28.8]	23.8 [16.4–31.1]	18.8 [11.7–26.0]	0.423
Postoperative day 1	22.6 [14.8–30.4] (N = 43)	24.8 [15.4–34.2] (N = 52)	23.7 [13.3–34.1] (N = 47)	0.850
Postoperative day 2	17.6 [10.5–24.7] (N = 38)	16.8 [9.8–23.7] (N = 49)	13.9 [7.0–20.9] (N = 45)	0.331
Pain ratings (0 to 10), mean [95% CI]†				
Initial PACU	1 [0.1–1.1]	0 [0.0–0.9]	0	0.078
Final PACU	2 [1.0–2.3]	1 [0.4–1.4]	1 [0.3–1.1]	0.020
Postoperative day 1	4 [3.3–4.8] (N = 43)	4 [3.1–4.4] (N = 51)	4 [3.1–4.5] (N = 48)	0.778
Postoperative day 2	4 [3.3–4.9] (N = 38)	4 [3.4–4.6] (N = 49)	4 [3.0–4.6] (N = 46)	0.750
Number of patients experiencing transient neurologic symptoms at any time, %	5/50 (10)	6/53 (11.3)	2/51 (3.9)	0.355

*Opioid consumption reported in oral morphine milligram equivalents. †Pain ratings reported using a numeric rating scale. PACU, postanesthesia care unit.

postoperative period, and it is also possible that a later time point for assessment of primary outcome could have resulted in a smaller or no difference between groups. However, no continuous motor function monitor exists, and at best, very frequent assessments can approximate the time a patient is able to ambulate. The desire for accurate ambulation time had to be balanced with the practical concerns of study staff availability and the associated inconvenience of ambulation in the PACU. We believe that the pharmacokinetics of the three drugs and practical concerns were best balanced with a 30-min window of 3 to 3.5 h, which was also supported by the predicted time of first ambulation with spinal mepivacaine reported by Pawlowski *et al.*⁸ Second,

only some aspects of the intraoperative anesthetic were standardized, including premedication, spinal technique, and the use of propofol for sedation. Adjustment of sedation and treatment of blood pressure were at the discretion of the anesthesia team. However, this reflects clinical practice. Third, the shorter surgical duration for mepivacaine could have influenced our primary outcome. It is not clear what the cause of this difference was. However, a study of isobaric bupivacaine that showed that the mean time to regress two dermatomal levels was 61 min,²³ suggesting that for patients unable to ambulate between 3 and 3.5 h, a difference of less than 10 min in surgery would not greatly affect the primary outcome. Fourth, although standard

discharge criteria were applied to all patients, postoperative hypotension was not tracked, and physical therapists used discretion in recommending same-day discharge based on safety. Finally, a few outcomes are imprecise. Some patients had motor function assessment gaps in PACU for staffing reasons. Motor function data should be interpreted with caution because there were several missing data points, and some patients may have regained motor function earlier than what was reported. This limitation did not affect our primary outcome nor any other secondary outcome, but it does make this outcome measurement less reliable than others. Urinary retention measurements relied on patient recollection in some cases, which could have led to event misclassification.

In conclusion, spinal mepivacaine allowed for earlier postoperative ambulation and shorter length of stay than both hyperbaric and isobaric bupivacaine. However, between 20 and 30% of both hyperbaric and isobaric bupivacaine patients were still discharged home the same day and patient satisfaction was high in all groups. Mepivacaine might be beneficial for outpatient total hip arthroplasty if spinal anesthesia is the desired anesthetic.

Acknowledgments

The authors acknowledge Megan Walsh, B.S., Rothman Orthopaedics, Philadelphia, Pennsylvania, for assisting with patient enrollment, data collection, and follow-up phone calls; Jennifer Lessin, B.S., Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, Pennsylvania, for assisting with data collection, institutional review board submission, and follow-up phone calls; and James Filer, P.T., and Lianne Previti, P.T., Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, for performing postoperative assessments and ambulation tests.

Research Support

Support was provided solely from institutional and/or departmental sources.

Competing Interests

Dr. Schwenk has received consulting fees from Avenue Therapeutics (New York, New York) in 2017; his institution has received funding from Attune Medical (Chicago, Illinois) from 2018 to 2019. Dr. Kasper has received consulting fees from Avanos (Alpharetta, Georgia) and B. Braun (Bethlehem, Pennsylvania), and Philips (Cambridge, Massachusetts). Dr. Austin has received consulting fees from Link (Hamburg, Germany) and Corin (Tampa, Florida) and research support from Zimmer Biomet (Warsaw, Indiana); is the deputy editor of the *Journal of the American Academy of Orthopaedic Surgeons*; and is the chair of the American Association of Hip and Knee Surgeons Evidence-based Medicine Committee. Dr. Hozack has received consulting fees from Stryker

(Kalamazoo, Michigan), has received royalties from Stryker on products sold, and is on the editorial board of the *Journal of Arthroplasty*; he also reports a financial relationship as Value Health Medical Director (Leawood, Kansas). Dr. Torjman's institution has received funding from Capillary Medical (Irvine, California), National Institutes of Health (Bethesda, Maryland), and RTM Vital Signs LLC (Philadelphia, Pennsylvania). The other authors declare no competing interests.

Reproducible Science

Full protocol available at: Eric.Schwenk@jefferson.edu. Raw data available at: Eric.Schwenk@jefferson.edu.

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References

1. Kurtz S, Ong K, Lau E, Mowat F, Halpern M: Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; 89:780–5
2. Pollock M, Somerville L, Firth A, Lanting B: Outpatient total hip arthroplasty, total knee arthroplasty, and unicompartmental knee arthroplasty: A systematic review of the literature. *JBJS Rev* 2016; 4
3. Nelson SJ, Webb ML, Lukasiewicz AM, Varthi AG, Samuel AM, Grauer JN: Is outpatient total hip arthroplasty safe? *J Arthroplasty* 2017; 32:1439–42
4. Basques BA, Toy JO, Bohl DD, Golinvaux NS, Grauer JN: General compared with spinal anesthesia for total hip arthroplasty. *J Bone Joint Surg Am* 2015; 97:455–61
5. Memtsoudis SG, Cozowicz C, Bekeris J, Bekere D, Liu J, Soffin EM, Mariano ER, Johnson RL, Hargett MJ, Lee BH, Wendel P, Brouillette M, Go G, Kim SJ, Baaklini L, Wetmore D, Hong G, Goto R, Jivanelli B, Argyra E, Barrington MJ, Borgeat A, De Andres J, Elkassabany NM, Gautier PE, Gerner P, Gonzalez Della Valle A, Goytizolo E, Kessler P, Kopp SL, Lavand'Homme P, MacLean CH, Mantilla CB, MacIsaac D, McLawhorn A, Neal JM, Parks M, Parvizi J, Pichler L, Poeran J, Poultsides LA, Sites BD, Stundner O, Sun EC, Viscusi ER, Votta-Velis EG, Wu CL, Ya Deau JT, Sharrock NE: Anaesthetic care of patients undergoing primary hip and knee arthroplasty: Consensus recommendations from the International Consensus on Anaesthesia-Related Outcomes after Surgery group (ICAROS)

- based on a systematic review and meta-analysis. *Br J Anaesth* 2019; 123:269–87
6. Alston RP: Spinal anaesthesia with 0.5% bupivacaine 3 ml: Comparison of plain and hyperbaric solutions administered to seated patients. *Br J Anaesth* 1988; 61:385–9
 7. Uppal V, Retter S, Shanthanna H, Prabhakar C, McKeen DM: Hyperbaric *versus* isobaric bupivacaine for spinal anesthesia: Systematic review and meta-analysis for adult patients undergoing noncesarean delivery surgery. *Anesth Analg* 2017; 125:1627–37
 8. Pawlowski J, Orr K, Kim KM, Pappas AL, Sukhani R, Jellish WS: Anesthetic and recovery profiles of lidocaine *versus* mepivacaine for spinal anesthesia in patients undergoing outpatient orthopedic arthroscopic procedures. *J Clin Anesth* 2012; 24:109–15
 9. Mahan MC, Jildeh TR, Tenbrunsel TN, Davis JJ: Mepivacaine spinal anesthesia facilitates rapid recovery in total knee arthroplasty compared to bupivacaine. *J Arthroplasty* 2018; 33:1699–704
 10. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, Pitkin R, Rennie D, Schulz KF, Simel D, Stroup DF: Improving the quality of reporting of randomized controlled trials: The CONSORT statement. *JAMA* 1996; 276:637–9
 11. Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987; 40:373–83
 12. Tinetti ME, Williams TF, Mayewski R: Fall risk index for elderly patients based on number of chronic disabilities. *Am J Med* 1986; 80:429–34
 13. Sinatra RS: Oral and parenteral opioid analgesics for acute pain management, *Acute Pain Management*. Edited by Sinatra RS, de Leon-Casasola OA, Ginsberg B, Viscusi ER. New York, Cambridge University Press, 2009, pp 188–203
 14. YaDeau JT, Liguori GA, Zayas VM: The incidence of transient neurologic symptoms after spinal anesthesia with mepivacaine. *Anesth Analg* 2005; 101:661–5
 15. Altschul D, Kobets A, Nakhla J, Jada A, Nasser R, Kinon MD, Yassari R, Houten J: Postoperative urinary retention in patients undergoing elective spinal surgery. *J Neurosurg Spine* 2017; 26:229–34
 16. Weinstein SM, Baaklini LR, Liu J, Poultsides L, Cozowicz C, Poeran J, Saleh JN, Memtsoudis SG: Neuraxial anaesthesia techniques and postoperative outcomes among joint arthroplasty patients: Is spinal anaesthesia the best option? *Br J Anaesth* 2018; 121:842–9
 17. Luduena FP, Hoppe JO, Coulston F, Drobeck HP: The pharmacology and toxicology of mepivacaine, a new local anesthetic. *Toxicol Appl Pharmacol* 1960; 2:295–315
 18. Hiller A, Rosenberg PH: Transient neurological symptoms after spinal anaesthesia with 4% mepivacaine and 0.5% bupivacaine. *Br J Anaesth* 1997; 79:301–5
 19. Salazar F, Bogdanovich A, Adalia R, Chabás E, Gomar C: Transient neurologic symptoms after spinal anaesthesia using isobaric 2% mepivacaine and isobaric 2% lidocaine. *Acta Anaesthesiol Scand* 2001; 45:240–5
 20. Liguori GA, Zayas VM, Chisholm MF: Transient neurologic symptoms after spinal anesthesia with mepivacaine and lidocaine. *ANESTHESIOLOGY* 1998; 88:619–23
 21. Kim KY, Anoushiravani AA, Elbuluk A, Chen K, Davidovitch R, Schwarzkopf R: Primary total hip arthroplasty with same-day discharge: Who failed and why. *Orthopedics* 2018; 41:35–42
 22. Hoffmann JD, Kusnezov NA, Dunn JC, Zarkadis NJ, Goodman GP, Berger RA: The shift to same-day outpatient joint arthroplasty: A systematic review. *J Arthroplasty* 2018; 33:1265–74
 23. Stienstra R, Gielen M, van Poorten F, Kroon JW: Spinal anesthesia with plain bupivacaine 0.5%: Regression of sensory and motor blockade with different temperatures of the anesthetic solution. *Anesth Analg* 1989; 69:593–7