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Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults

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Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults

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ABSTRACT

BACKGROUND

The effects of spinal anesthesia as compared with general anesthesia on the ability to walk in older adults undergoing surgery for hip fracture have not been well studied.

METHODS

We conducted a pragmatic, randomized superiority trial to evaluate spinal anesthesia as compared with general anesthesia in previously ambulatory patients 50 years of age or older who were undergoing surgery for hip fracture at 46 U.S. and Canadian hospitals. Patients were randomly assigned in a 1:1 ratio to receive spinal or general anesthesia. The primary outcome was a composite of death or an inability to walk approximately 10 ft (3 m) independently or with a walker or cane at 60 days after randomization. Secondary outcomes included death within 60 days, delirium, time to discharge, and ambulation at 60 days.

RESULTS

A total of 1600 patients were enrolled; 795 were assigned to receive spinal anesthesia and 805 to receive general anesthesia. The mean age was 78 years, and 67.0% of the patients were women. A total of 666 patients (83.8%) assigned to spinal anesthesia and 769 patients (95.5%) assigned to general anesthesia received their assigned anesthesia. Among patients in the modified intention-to-treat population for whom data were available, the composite primary outcome occurred in 132 of 712 patients (18.5%) in the spinal anesthesia group and 132 of 733 (18.0%) in the general anesthesia group (relative risk, 1.03; 95% confidence interval [CI], 0.84 to 1.27; $P=0.83$). An inability to walk independently at 60 days was reported in 104 of 684 patients (15.2%) and 101 of 702 patients (14.4%), respectively (relative risk, 1.06; 95% CI, 0.82 to 1.36), and death within 60 days occurred in 30 of 768 (3.9%) and 32 of 784 (4.1%), respectively (relative risk, 0.97; 95% CI, 0.59 to 1.57). Delirium occurred in 130 of 633 patients (20.5%) in the spinal anesthesia group and in 124 of 629 (19.7%) in the general anesthesia group (relative risk, 1.04; 95% CI, 0.84 to 1.30).

CONCLUSIONS

Spinal anesthesia for hip-fracture surgery in older adults was not superior to general anesthesia with respect to survival and recovery of ambulation at 60 days. The incidence of postoperative delirium was similar with the two types of anesthesia. (Funded by the Patient-Centered Outcomes Research Institute; REGAIN Clinical-Trials.gov number, NCT02507505.)

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*The REGAIN investigators are listed in the Supplementary Appendix, available at NEJM.org.

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NEARLY ALL PATIENTS WITH HIP FRACTURE undergo surgery,¹ most commonly with spinal anesthesia or general anesthesia.² Observational studies have suggested that spinal anesthesia may be associated with lower risks of death,³ delirium,^{4,5} and major medical complications⁶ and with shorter lengths of stay in the hospital than general anesthesia.⁷ Randomized trials have shown conflicting results regarding differences in outcomes according to anesthesia type, but most of these trials were conducted more than 30 years ago and do not reflect current practice, had small numbers of participants, or were not designed to assess outcomes beyond the hospital stay.⁸ Patients may view recovery of independence in walking after hip fracture as a priority,⁹ but studies evaluating the effect of anesthesia technique on this outcome are lacking.⁸

We conducted a trial to evaluate the recovery of walking ability after receipt of spinal as compared with general anesthesia for hip-fracture surgery in older adults who could walk independently before the fracture. We hypothesized that patients assigned to receive spinal anesthesia would be more likely to be alive and walking independently at 60 days than those assigned to receive general anesthesia.

METHODS

TRIAL DESIGN AND OVERSIGHT

We conducted the Regional versus General Anesthesia for Promoting Independence after Hip Fracture (REGAIN) trial, a multicenter, pragmatic, randomized superiority trial funded by the Patient-Centered Outcomes Research Institute. The trial design has been described previously.¹⁰ The trial was investigator-initiated and was planned and conducted with the participation of patients and stakeholder organizations (the Center for Advocacy for the Rights and Interests of the Elderly and the Gerontological Society of America).¹¹ There was no commercial participation in the trial. The institutional review board of the University of Pennsylvania, the institution that oversaw the conduct of the trial, approved the protocol (available with the full text of this article at NEJM.org) and was the institutional review board of record for 11 sites; approval at other sites was obtained through local institutional review boards.¹² Written informed consent was obtained

from the patients or, for patients who could not provide consent, from their health care proxy. The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

TRIAL POPULATION

Trial staff at 46 hospitals in the United States and Canada reviewed emergency department registration lists, hospital admission lists, and surgical case schedules to identify adults who were 50 years of age or older and were scheduled to undergo surgical repair of a clinically or radiographically diagnosed femoral neck, intertrochanteric, or subtrochanteric hip fracture. Inclusion and exclusion criteria were evaluated by means of in-person interview and medical record review. Patients were excluded if they had not been able to walk approximately 10 ft (3 m) or across a room without the assistance of another person before the fracture, as reported by the patient or by a proxy who knew the patient; if a concurrent procedure that was not amenable to spinal anesthesia was planned; if the fracture was periprosthetic; if the patient was at risk for malignant hyperthermia; or if the patient had contraindications to spinal anesthesia (coagulopathy, use of anticoagulant or antiplatelet medications,^{13,14} critical or severe aortic stenosis, a high risk of infection at the spinal needle insertion site, or elevated intracranial pressure). Patients were also excluded if they had previously participated in the trial or if they were considered to be unsuitable for randomization by the surgeon or anesthesiologist on the basis of the physician's clinical assessment. Patients who were judged to have delirium before surgery were not excluded if consent would be obtained from a proxy or the patient.

Patients were randomly assigned in a 1:1 ratio, with the use of permuted block randomization with variable block sizes, to receive either spinal anesthesia or general anesthesia.^{15,16} Randomization was stratified according to hospital, sex, and fracture location (femoral neck vs. intertrochanteric or subtrochanteric fracture) and was performed centrally through an online data-management system. Site staff obtained each randomization assignment from the data-management system Web portal and communicated it to

the treating anesthesia team. Site staff were instructed to obtain and communicate the assignment on the day of surgery, immediately before the start of anesthesia care. When site personnel could not access the online system, the randomization assignment was communicated by telephone to site staff by the principal investigator or the lead project manager.

TRIAL TREATMENT

Anesthesia was administered by the usual clinical anesthesia staff at each site. For patients assigned to receive spinal anesthesia, providers received instructions to administer a single-injection spinal anesthetic with sedation as needed for patient comfort; sedation was adjusted to ensure an Observer's Assessment of Alertness/Sedation (OAAS) scale¹⁷ score between 5 ("Responds readily to name spoken in normal tone") and 2 ("Responds only after mild shaking or prodding").¹⁸ Crossover to general anesthesia was permitted on the basis of clinical circumstances or patient request. For patients assigned to general anesthesia, providers were instructed to use an inhaled anesthetic agent for maintenance, with the choice of agent conforming to their usual practice, and to use an endotracheal tube, supraglottic airway, or another device for airway management in accordance with local practice. All other aspects of care were determined by the clinical team. Trial participants and treating clinicians were aware of the treatment assignments.

OUTCOMES

The primary outcome was a composite of death or an inability to walk 10 feet (3 m) or across a room independently or with a walker or cane but without the assistance of another person at approximately 60 days after randomization. Death was included in the primary outcome to account for potential survivorship bias.^{19,20} Data on the primary outcome were obtained through telephone interviews performed by trial staff who were unaware of the treatment assignments; data collection from caregivers or other proxies was permitted when participants were unable to complete the outcome interview. Interviews were recorded and randomly audited. For patients who could not be contacted by telephone for the 60-day interview, we ascertained vital status from subsequent interviews; for U.S. patients for whom vital status could not be ascertained, we

searched the National Death Index through 2019, the most recent year available.

Secondary outcomes included the two components of the primary outcome (death by 60 days after randomization and new inability to walk at 60 days among survivors); new-onset delirium, with delirium assessed as present or absent on the basis of the 3-Minute Diagnostic Interview for CAM (Confusion Assessment Method)-defined Delirium (3D-CAM²¹; measurements were conducted before randomization and once daily over each of the first 3 days after surgery by trained site staff); and time from randomization to hospital discharge. Exploratory outcomes included medical complications during hospitalization, ascertained by site trial staff on the basis of medical record review using standardized definitions; time to first ambulation; discharge disposition (i.e., discharge to home or retirement home, nursing home or skilled nursing facility, rehabilitation or acute care hospital, or hospice or other location); residential location at 60 days; and functional status at 60 days, as measured with the 12-item World Health Organization Disability Assessment Schedule 2.0.²² Data on serious adverse events were reviewed by an internal monitoring committee for severity, expectedness, and relatedness to treatment.

Data were reviewed at prespecified intervals by an independent data and safety monitoring board, the members of which were aware of the treatment assignments. Additional details of the trial monitoring plan are provided in the Supplementary Appendix, available at NEJM.org. The principal investigator, statisticians, coordinating center staff, and coinvestigators remained unaware of the treatment assignments until the database was locked for analysis.

STATISTICAL ANALYSIS

We estimated that a sample of 1600 patients would provide 80% power to detect a 0.78 relative risk of the primary outcome among patients assigned to spinal anesthesia as compared with those assigned to general anesthesia, at a two-sided significance level of 0.05. The calculation was performed under the assumption that the primary outcome would occur in 34.2% of the patients in the general anesthesia group,²³ loss to follow-up would be 5%, and 5% of the patients assigned to spinal anesthesia would crossover to general anesthesia.^{24,25} The primary analy-

sis and analyses of all secondary and exploratory outcomes included patients in the modified intention-to-treat population for whom complete data were available for the relevant outcomes. The modified intention-to-treat population included all patients who underwent randomization and did not die before receiving treatment. Patients were included in the analysis according to their original treatment assignment. We performed a Mantel–Haenszel test, stratified according to fracture location (femoral neck fracture vs. intertrochanteric or subtrochanteric fracture), sex, and country (United States vs. Canada), to compare the risks of the primary outcome in each group. Although randomization was stratified according to fracture location, sex, and hospital, recruitment at many sites was too low to permit stratification of the analysis according to hospital. Superiority testing was based on a two-sided significance level of 0.05.

Secondary outcomes were analyzed with the use of approaches similar to those used in our primary analysis for binary data. For time-to-event data, we used competing-risk Cox regression and confirmed the proportional hazards assumption with log–log survival plots and Schoenfeld residuals. Patients who were assessed as having delirium before randomization on the basis of 3D-CAM were eligible for enrollment if proxy consent could be obtained, and these patients were excluded from the analysis of incident delirium but were included in analyses of other outcomes. There was no plan for adjustment of the width of confidence intervals for multiple comparisons in analyses of secondary outcomes, and no definite conclusions can be drawn from these results.

To assess the effect of missing data on the findings for the primary outcome, we performed an inverse-probability–weighted analysis²⁶ that weighted each patient according to the inverse probability of being a “complete case,” as estimated on the basis of 10 prerandomization factors (age, sex, enrollment country, fracture location, and status with respect to pulmonary disease, cancer, diabetes, coronary artery disease, cerebrovascular disease, and dementia). We performed an instrumental variable analysis to estimate the per-protocol effect²⁷ of spinal anesthesia as compared with general anesthesia on the primary outcome (see the Supplementary Appendix).²⁸ For the primary outcome, we explored prespeci-

fied patient characteristics (sex, fracture type, country of enrollment, reliance on assistive devices to ambulate before fracture, age [≥ 85 years vs. < 85 years], location of residence before fracture, and status with respect to dementia, chronic pulmonary disease, and coronary artery disease or heart failure). We conducted exploratory subgroup analyses for interactions with P values of 0.20 or lower. Data are current as of June 17, 2021. Analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

PATIENTS AND TREATMENT

Between February 12, 2016, and February 18, 2021, we screened 22,022 patients for eligibility; 1848 provided informed consent, and 248 withdrew consent before randomization. A total of 7.4% of screened patients (1621 of 22,022) were excluded on the basis of physician decision or surgeon nonparticipation. Of the 1600 patients who were randomly assigned to a treatment group, 795 were assigned to receive spinal anesthesia and 805 were assigned to receive general anesthesia (Fig. 1). The characteristics of the patients were similar in the two treatment groups (Table 1). The mean age of the patients was approximately 78 years, 33.0% were men, and 7.6% were Black.

Of the 795 patients who were assigned to the spinal anesthesia group, 119 (15.0%) instead received general anesthesia. Reasons for administration of general anesthesia were an inability to place a spinal block (52 patients), clinician selection of general anesthesia (29 patients), patient or proxy request (18 patients), crossover to general anesthesia after spinal block placement (e.g., due to block failure or intraoperative events; 12 patients), and communication issues (e.g., due to case rescheduling or shift changes; 7 patients); no reason was provided in 1 instance. Ten patients who had been assigned to receive spinal anesthesia (1.3%) withdrew consent before surgery; data collection for these patients stopped at withdrawal. Of the 502 patients with available data on the maximum depth of sedation during spinal anesthesia, 431 (85.9%) had an OAAS score between 5 (lighter sedation) and 2 (deeper sedation), and 71 (14.1%) had a deeper level of sedation.

Of the 805 patients assigned to receive gen-

Figure 1. Screening, Enrollment, Randomization, and Follow-up.

The other reasons for patients not meeting the eligibility criteria included no surgery planned, history of malignant hyperthermia, previous participation in the trial, elevated intracranial pressure, active skin infection at the needle insertion site, and incarceration. In addition to the 1600 randomization codes generated for enrolled patients, 7 codes were unintentionally generated because of technical errors in operating the screening log for patients who had been excluded from participation at screening; these patients had no data collected and were not included in the trial sample.

eral anesthesia, 28 (3.5%) instead received spinal anesthesia; reasons for administration of spinal anesthesia were clinician selection of spinal anesthesia (15 patients), patient or proxy request (7 patients), and communication issues (i.e., as a result of case rescheduling or shift changes; 4 patients); in 2 cases, no reason was provided. Seven patients who had been assigned to general anesthesia (0.9%) withdrew consent before surgery; no outcome data were collected for these 7 patients after withdrawal. The median total anesthesia time was 132 minutes (interquartile range, 102 to 165) in the spinal anesthesia group and 131 minutes (interquartile range, 103 to 165) in the general anesthesia group (Table S1 in the Supplementary Appendix).

One patient in the general anesthesia group died after randomization but before the start of anesthesia; data from this patient were not included in the outcome analyses. Data on the primary outcome were available for 1445 of the 1599 remaining patients (90.4%) in the modified intention-to-treat analysis (Tables 2 and S2). For patients assigned to spinal anesthesia, the median time from randomization to the primary outcome interview was 59 days (interquartile range, 55 to 65); for patients assigned to general anesthesia, it was 60 days (interquartile range, 54 to 66).

OUTCOMES

The composite primary outcome of death or a new inability to walk independently occurred in 132 of 712 patients (18.5%) who received spinal anesthesia and in 132 of 733 patients (18.0%) who received general anesthesia (complete case analysis: relative risk, 1.03; 95% confidence interval [CI], 0.83 to 1.28; inverse-probability-weighted analysis: relative risk, 1.03; 95% CI,

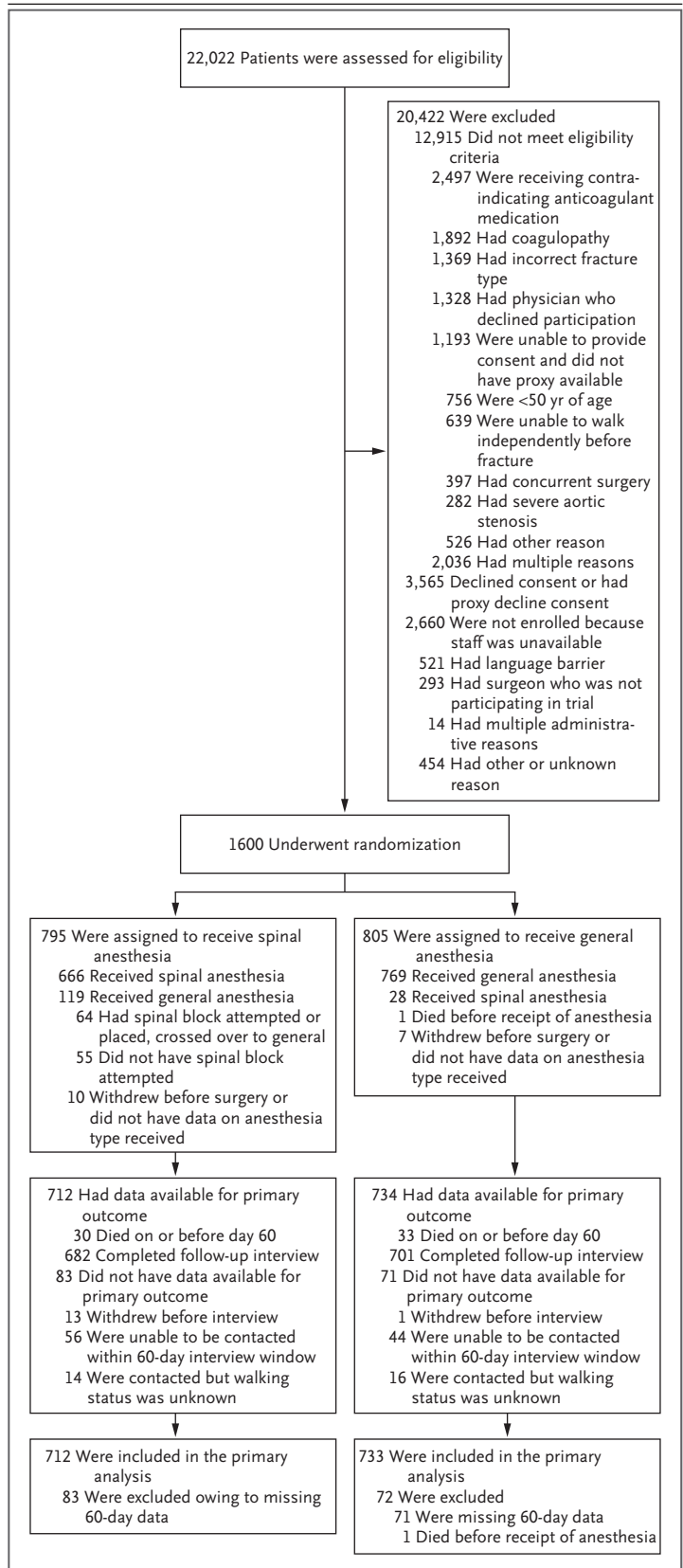


Table 1. Characteristics of the Patients Who Underwent Randomization.*

| Characteristic | Spinal Anesthesia (N=795) | General Anesthesia (N=805) |
|--|------------------------------|-------------------------------|
| Age at randomization — yr† | 77.7±10.7 | 78.4±10.6 |
| Male sex — no. (%) | 258 (32.5) | 270 (33.5) |
| Race — no./total no. (%)‡ | | |
| White | 683/762 (89.6) | 691/774 (89.3) |
| Black | 55/762 (7.2) | 67/774 (8.7) |
| Other or more than one race | 24/762 (3.1) | 16/774 (2.1) |
| Hispanic ethnic group — no./total no. (%)‡ | 15/750 (2.0) | 12/763 (1.6) |
| Enrolled at a non-U.S. site — no. (%) | 210 (26.4) | 212 (26.3) |
| Coexisting conditions — no./total no. (%) | | |
| Chronic pulmonary disease | 124/795 (15.6) | 100/804 (12.4) |
| Diabetes mellitus | 155/795 (19.5) | 142/804 (17.7) |
| Disseminated cancer | 60/795 (7.5) | 50/804 (6.2) |
| Coronary artery disease | 118/795 (14.8) | 119/804 (14.8) |
| Cerebrovascular disease | 80/795 (10.1) | 66/804 (8.2) |
| Dementia | 109/795 (13.7) | 94/804 (11.7) |
| Creatinine level >2 mg/dl or current dialysis | 47/790 (5.9) | 41/797 (5.1) |
| American Society of Anesthesiologists Physical Status Classification — no./total no. (%) | | |
| I, no systemic disease | 22/782 (2.8) | 18/793 (2.3) |
| II, mild systemic disease | 229/782 (29.3) | 270/793 (34.0) |
| III, severe systemic disease | 486/782 (62.1) | 463/793 (58.4) |
| IV, severe systemic disease that is a constant threat to life | 45/782 (5.8) | 42/793 (5.3) |
| Final confirmed fracture type — no./total no. (%)§ | | |
| Femoral neck | 406/795 (51.1) | 409/804 (50.9) |
| Intertrochanteric | 355/795 (44.7) | 350/804 (43.5) |
| Subtrochanteric or multiple locations | 34/795 (4.3) | 45/804 (5.6) |
| 3D-CAM assessment positive for delirium before randomization — no./total no. (%) | 96/746 (12.9) | 104/753 (13.8) |
| Used assistive device to ambulate before fracture — no./total no. (%) | 249/779 (32.0) | 248/793 (31.3) |
| Preadmission residence — no./total no. (%) | | |
| Home or retirement home | 688/748 (92.0) | 690/763 (90.4) |
| Nursing home or other location | 60/748 (8.0) | 73/763 (9.6) |

* Plus-minus values are means ±SD. To convert the values for creatinine to micromoles per liter, multiply by 88.4. 3D-CAM denotes 3-Minute Diagnostic Interview for CAM (Confusion Assessment Method)—Defined Delirium.

† Data on age were missing for 1 patient in the general anesthesia group.

‡ Race and ethnic group were reported by the patients or their proxies.

§ Randomization was stratified on the basis of provisional fracture-type data that were subsequently confirmed by medical record review; final confirmed fracture-type data were not available for 1 patient who had been assigned to the femoral neck fracture stratification group for randomization.

0.84 to 1.27; $P=0.83$) (Table 2). We obtained similar findings in sensitivity analyses that accounted for nonadherence to the anesthesia assignment (Table S3). The percentages of patients with each component of the primary outcome at 60 days were also similar in the two treatment

Table 2. Primary Outcome and Prespecified Secondary Outcomes (Modified Intention-to-Treat Population).*

| Outcome | Spinal Anesthesia (N = 795) | General Anesthesia (N = 804) | Relative Risk (95% CI)† | P Value‡ |
|--|-----------------------------|------------------------------|-------------------------|----------|
| Primary outcome | | | | |
| Death or inability to walk without human assistance at 60 days — no./total no. (%) | 132/712 (18.5) | 132/733 (18.0) | 1.03 (0.84–1.27) | 0.83 |
| Secondary outcomes‡ | | | | |
| Death by 60 days — no./total no. (%)§ | 30/768 (3.9) | 32/784 (4.1) | 0.97 (0.59–1.57) | |
| Inability to walk without human assistance at 60 days among survivors — no./total no. (%) | 104/684 (15.2) | 101/702 (14.4) | 1.06 (0.82–1.36) | |
| 3D-CAM assessment positive for new-onset delirium — no./total no. (%)¶ | 130/633 (20.5) | 124/629 (19.7) | 1.04 (0.84–1.30) | |
| Hazard Ratio (95% CI) | | | | |
| Median time from randomization to discharge, according to enrollment location (IQR) — days** | | | | |
| Canada | 6 (4–9) | 6 (5–10) | 0.92 (0.76–1.10) | |
| United States | 3 (2–5) | 3 (3–5) | 1.06 (0.96–1.16) | |

* The modified intention-to-treat population included all patients who underwent randomization with the exception of 1 patient who died before receiving treatment. Patients were included in the analysis according to their original treatment assignment. Results shown for the primary outcome comparison reflect inverse-probability weighting to account for missing outcome data; the variables included in the inverse-probability-weighting model were age, sex, country, fracture type, pulmonary disease, cancer, diabetes, coronary artery disease, cerebrovascular disease, and dementia. All other comparisons were performed by complete case analysis. IQR denotes interquartile range.

† Relative risks and P values were calculated with a Mantel–Haenszel test with adjustment for sex, fracture type, and country of enrollment.

‡ The widths of confidence intervals for secondary outcomes have not been adjusted for multiple comparisons.

§ For patients who could not be contacted for the 60-day interview, vital status at 60 days was ascertained from subsequent planned trial interviews and from the U.S. National Death Index.

¶ This outcome was assessed only among patients who had a negative 3D-CAM assessment for delirium before randomization.

|| Hazard ratios were calculated with a Cox proportional hazards model with adjustment for sex and fracture type.

** Differences between the United States and Canada reflect differences in practice. For patients enrolled in Canada, data were available for 210 patients in the spinal anesthesia group and 211 in the general anesthesia group; for patients enrolled in the United States, the corresponding numbers were 585 and 593.

groups. The percentages of patients with the primary outcome in each treatment group were similar across participating sites (Table S4).

New-onset postoperative delirium occurred in 130 of 633 patients (20.5%) assigned to spinal anesthesia and in 124 of 629 patients (19.7%) assigned to general anesthesia (relative risk, 1.04; 95% CI, 0.84 to 1.30); other secondary outcomes were also similar in the two treatment groups (Table 2). The primary outcome was similar across subgroups as judged by visual inspection of descriptive numerical data (Table 3). Death during hospitalization occurred in 5 of 782 patients assigned to spinal anesthesia (0.6%) and in 13 of 790 patients assigned to general anesthesia (1.6%). Acute kidney injury occurred

in 32 of 709 patients (4.5%) assigned to spinal anesthesia, and admission to a critical care unit occurred in 18 of 783 (2.3%); the corresponding numbers among the patients assigned to general anesthesia were 55 of 726 (7.6%) and 29 of 793 (3.7%) (Table 4). Table S5 lists the serious adverse events according to treatment group; the incidence of adverse events was similar in the two groups.

DISCUSSION

In this pragmatic randomized trial involving 1600 older adults undergoing hip-fracture surgery, the incidence of death or a new inability to walk 60 days after randomization did not differ signifi-

Table 3. Subgroup Analyses for the Primary Outcome (Modified Intention-to-Treat Population).

| Subgroup* | Spinal Anesthesia (N = 795) | General Anesthesia (N = 804) | Relative Risk (95% CI)† |
|--|--------------------------------|---------------------------------|----------------------------|
| | <i>no. of patients (%)</i> | | |
| Age | | | |
| <85 yr | 63/509 (12.4) | 67/499 (13.4) | 0.93 (0.67–1.27) |
| ≥85 yr | 69/203 (34.0) | 65/234 (27.8) | 1.25 (0.94–1.66) |
| History of chronic pulmonary disease | | | |
| Present | 17/109 (15.6) | 22/88 (25.0) | 0.64 (0.35–1.17) |
| Absent | 115/603 (19.1) | 110/645 (17.1) | 1.11 (0.88–1.41) |
| History of congestive heart failure or coronary artery disease | | | |
| Present | 21/103 (20.4) | 31/110 (28.2) | 0.76 (0.47–1.23) |
| Absent | 111/609 (18.2) | 101/623 (16.2) | 1.12 (0.88–1.44) |

* Selected subgroups of interest are shown.

† Relative risks were calculated with a Mantel–Haenszel test with adjustment for sex, fracture type, and country.

cantly between patients assigned to receive spinal anesthesia and those assigned to receive general anesthesia. Secondary outcomes, including death within 60 days, new inability to walk at 60 days among survivors, incident delirium, and time from randomization to discharge, did not differ substantially according to anesthesia type. The incidences of death during hospitalization, acute kidney injury, and postoperative critical care admission were low but differed between the treatment groups.

Trials evaluating spinal anesthesia as compared with general anesthesia for hip-fracture surgery have primarily assessed differences in intraoperative events^{29,30} and in-hospital complications^{31–33} and have not been powered to test for differences in outcomes beyond hospital discharge. We evaluated recovery of the ability to walk 10 ft or across a room without the assistance of another person, an outcome that is of importance to patients and families,⁹ and delirium, an outcome that our patient partners identified as a priority.¹¹ We recruited patients from diverse academic and community hospitals. Fewer than 4% of all patients with hip fractures in the United States are Black,³⁴ and Black patients made up approximately 8% of our trial population.

Limitations of our trial include a considerable amount of missing outcome data; however, the results of sensitivity analyses that accounted for

missing data were similar to those in the primary analysis. The primary outcome occurred in a lower percentage of patients than had been anticipated when the trial was planned. This reduced power and may have occurred as a result of enrollment of patients into the trial who were healthier than anticipated. Although approximately 15% of the patients who had been randomly assigned to receive spinal anesthesia crossed over to general anesthesia, our main findings persisted in an instrumental variable analysis that accounted for nonadherence to the assigned treatment. Nevertheless, the rate of nonadherence may have reduced the power to detect differences between the groups. An inability to place a spinal block was the most common reason for nonadherence, followed by clinician selection of the anesthesia type and patient or proxy request for one anesthesia type. Since we aimed to compare anesthetic regimens as they are used in typical practice,¹⁸ we allowed sedation regimens to be given to patients receiving spinal anesthesia in order to follow usual practices, and therefore these practices varied across sites. This heterogeneity may have limited our ability to detect differences in outcomes between the groups. A previous trial showed similar clinical outcomes with deeper as compared with lighter sedation regimens during spinal anesthesia.^{35,36} Finally, one component of the composite primary outcome (walking independently) was con-

Table 4. Exploratory Outcomes (Modified Intention-to-Treat Population).

| Outcome | Spinal Anesthesia (N = 795) | General Anesthesia (N = 804) |
|---|--------------------------------|---------------------------------|
| Outcomes in the hospital | | |
| Complications — no./total no. (%) | | |
| Death | 5/782 (0.6) | 13/790 (1.6) |
| Myocardial infarction* | 6/783 (0.8) | 9/793 (1.1) |
| Nonfatal cardiac arrest | 2/780 (0.3) | 0/784 |
| Stroke* | 5/783 (0.6) | 7/793 (0.9) |
| Pneumonia* | 8/783 (1.0) | 16/793 (2.0) |
| Pulmonary edema* | 9/783 (1.1) | 8/793 (1.0) |
| Pulmonary embolism* | 4/783 (0.5) | 5/793 (0.6) |
| Unplanned postoperative intubation | 4/783 (0.5) | 7/793 (0.9) |
| Acute kidney injury* | 32/709 (4.5) | 55/726 (7.6) |
| Surgical-site infection† | 2/783 (0.3) | 0/793 |
| Urinary tract infection* | 35/783 (4.5) | 28/793 (3.5) |
| Postoperative transfusion | 130/782 (16.6) | 146/793 (18.4) |
| Any return to the operating room | 10/783 (1.3) | 14/793 (1.8) |
| Critical care admission | 18/783 (2.3) | 29/793 (3.7) |
| Fall within 12 hr after administration of anesthesia | 1/783 (0.1) | 1/793 (0.1) |
| Median time to first ambulation after surgery (IQR) — days‡ | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) |
| Discharge disposition — no./total no. (%) | | |
| Home or retirement home | 201/777 (25.9) | 191/777 (24.6) |
| Nursing home or skilled nursing facility | 347/777 (44.7) | 349/777 (44.9) |
| Rehabilitation or acute care hospital | 221/777 (28.4) | 229/777 (29.5) |
| Hospice or other location | 8/777 (1.0) | 8/777 (1.0) |
| Outcomes within 60 days after randomization | | |
| Median time to death up to day 60 (IQR) — days§ | 32.5 (16.0–53.0) | 20.0 (7.0–37.0) |
| Median 12-item WHODAS 2.0 score (IQR)¶ | 22.7 (8.3–43.2) | 18.2 (6.3–31.8) |
| Worsened walking ability — no./total no. (%) | 403/672 (60.0) | 397/694 (57.2) |
| Death or transition to new institutional residence — no./total no. (%)** | 108/613 (17.6) | 114/625 (18.2) |

* Events were classified by site staff as mild, moderate, or severe on the basis of standardized definitions in the manual of procedures for the trial; data shown indicate all events reported across severity categories.

† Surgical-site infections were classified by site staff as superficial, deep, or joint-space infections on the basis of standardized definitions in the manual of procedures for the trial; data shown indicate all events reported across infection types.

‡ Data were available for 731 patients in the spinal anesthesia group and 729 patients in the general anesthesia group.

§ Data on time to death were available for 30 patients in the spinal anesthesia group and 31 patients in the general anesthesia group.

¶ The 12-item World Health Organization Disability Schedule 2.0 (WHODAS 2.0) measures disability in six functional domains (cognition, mobility, self-care, social interaction, life activities, and community participation). Scores range from 0 to 100, with lower scores indicating lower degrees of disability. Data were available for 225 patients in the spinal anesthesia group and 242 patients in the general anesthesia group.

|| Worsened walking ability was defined as death, inability to walk without human assistance, or new use of an assistive device (e.g., cane or walker) at 60 days. Data were available for 672 patients in the spinal anesthesia group and 694 patients in the general anesthesia group.

** This outcome was assessed among patients who were not admitted from a nursing home, rehabilitation facility, or acute care hospital (613 in the spinal anesthesia group and 625 in the general anesthesia group). Institutional residence at 60 days was defined as the reported location of residence (nursing home, acute rehabilitation facility, acute care hospital, hospice, or other location).

ditional on the other component (vital status), but we did not conduct a joint modeling analysis because these separate secondary outcomes did not differ between the groups.

In the United States, the use of spinal anesthesia for hip-fracture surgery increased by 50% between 2007 and 2017,² potentially reflecting a belief that spinal anesthesia is superior to general anesthesia. Our finding of similar outcomes at 60 days with either technique suggests that anesthesia choices for hip-fracture surgery may be based on patient preference rather than on anticipated differences in clinical outcomes.

In this pragmatic randomized trial involving older patients undergoing hip-fracture surgery, spinal anesthesia was not superior to general anesthesia with respect to the risk of death or new inability to walk independently at 60 days.

The incidence of new-onset delirium and hospital lengths of stay were similar with the two types of anesthesia.

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APPENDIX

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