ANESTHESIOLOGY

Long-term Outcomes with Spinal *versus* General Anesthesia for Hip Fracture Surgery: A Randomized Trial

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ABSTRACT

Background: The effects of spinal *versus* general anesthesia on long-term outcomes have not been well studied. This study tested the hypothesis that spinal anesthesia is associated with better long-term survival and functional recovery than general anesthesia.

Methods: A prespecified analysis was conducted of long-term outcomes of a completed randomized superiority trial that compared spinal anesthesia *versus* general anesthesia for hip fracture repair. Participants included previously ambulatory patients 50 yr of age or older at 46 U.S. and Canadian hospitals. Patients were randomized 1:1 to spinal or general anesthesia, stratified by sex, fracture type, and study site. Outcome assessors and investigators involved in the data analysis were masked to the treatment arm. Outcomes included survival at up to 365 days after randomization (primary); recovery of ambulation among 365-day survivors; and composite endpoints for death or new inability to ambulate and death or new nursing home residence at 365 days. Patients were included in the analysis as randomized.

Results: A total of 1,600 patients were enrolled between February 12, 2016, and February 18, 2021; 795 were assigned to spinal anesthesia, and 805 were assigned to general anesthesia. Among 1,599 patients who underwent surgery, vital status information at or beyond the final study interview (conducted at approximately 365 days after randomization) was available for 1,427 (89.2%). Survival did not differ by treatment arm; at 365 days after randomization, there were 98 deaths in patients assigned to spinal anesthesia *versus* 92 deaths in patients assigned to general anesthesia (hazard ratio, 1.08; 95% CI, 0.81 to 1.44, $P = 0.59$). Recovery of ambulation among patients who survived a year did not differ by type of anesthesia (adjusted odds ratio for spinal *vs.* general, 0.87; 95% CI, 0.67 to 1.14; $P = 0.31$). Other outcomes did not differ by treatment arm.

Conclusions: Long-term outcomes were similar with spinal *versus* general anesthesia.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Hip fractures are associated with substantial mortality and disability
- The Regional versus General Anesthesia for Promoting Independence after Hip Fracture (REGAIN) trial showed that spinal and general anesthesia for hip fracture surgery resulted in similar rates of recovery of ambulation, survival, and return to prefracture residence at 60 days of follow-up
- Few data are available comparing spinal and general anesthesia with respect to long-term mortality and other patient outcomes

What This Article Tells Us That Is New

- In this prespecified secondary analysis of this large, pragmatic, rigorously conducted, multicenter randomized controlled clinical trial, there was no meaningful difference in rates of survival at 1 yr with spinal anesthesia *versus* general anesthesia for hip fracture repair
- Other outcomes assessed, including recovery of ambulation over the first year after surgery and death or new transition to nursing home residence at 365 days, were also similar with spinal *versus* general anesthesia

Spinal and general anesthesia are the most common options for individuals undergoing surgery on the lower extremities.[1] While spinal anesthesia has been theorized to improve survival after surgery through reductions in short-term complications, particularly among older adults, long-term differences in outcomes by anesthesia technique remain poorly characterized.[2,3]

This article is featured in "This Month in ANESTHESIOLOGY," page A1. This article is accompanied by an editorial on p. 352. This article has a related Infographic on p. A17. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). This article has an audio podcast. This article has a visual abstract available in the online version.

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Each year, 1.5 million older adults worldwide undergo surgery to repair a fractured hip,[4] and most patients receive either spinal or general anesthesia.[5] While one randomized trial found differences in 1-yr mortality according to anesthesia technique,[6] others have found no differences in survival beyond the immediate perioperative period.[7,8] Hip fractures are associated with marked decreases in long-term survival and functional independence,[9–11] but past trials have not evaluated recovery of ambulation or the need for new nursing home care after spinal *versus* general anesthesia. Recently, the Regional versus General Anesthesia for Promoting Independence after Hip Fracture (REGAIN) multicenter trial found similar rates of recovery of ambulation, survival, and return to prefracture residence at 60 days with either spinal or general anesthesia.[12] Outcomes related to long-term survival, recovery of ambulation, and need for new nursing home placement have not yet been reported.

We conducted a preplanned analysis of long-term outcomes of a multicenter pragmatic randomized trial comparing spinal *versus* general anesthesia for hip fracture surgery.[12,13] This study aimed to examine 1-yr survival, recovery of ambulation over the first year after surgery, and new nursing home residence at 1 yr among those living independently before fracture. Specifically, we tested the hypothesis that spinal anesthesia improves long-term outcomes compared to general anesthesia.

Materials and Methods

Study Design

The REGAIN trial was a randomized superiority trial conducted in 46 hospitals in the United States and Canada (Clinicaltrials.gov identifier NCT02507505, Principal Investigator Mark D. Neuman, registered July 24, 2015). The study design and primary outcome analyses have been described previously.[12,13] We worked with patients and stakeholders to select outcomes of importance to patients.[14] The trial protocol was published in advance of patient enrollment.[13] The Institutional Review Board (IRB) of the University of Pennsylvania (Philadelphia, Pennsylvania) approved the protocol and was the IRB of record for 11 sites; approval at other sites was *via* local IRB review.[15]

Participants

At each study hospital, staff reviewed emergency department registration and hospital admission lists, and surgical case schedules to identify adults aged 50 yr or older who were scheduled to undergo surgical repair of a clinically or radiographically diagnosed femoral neck, intertrochanteric, or subtrochanteric hip fracture.

Major exclusions were the inability to walk approximately 10 feet (3 m) or across a room without human assistance before fracture; the need for a concurrent procedure

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not amenable to spinal anesthesia; periprosthetic fracture; and contraindications to spinal anesthesia (coagulopathy; anticoagulant medications;[16,17] critical or severe aortic stenosis; infection at the injection site; or elevated intracranial pressure). Patients were also excluded if they had previously participated in the trial or were determined to be unsuitable for randomization by the surgeon or anesthesiologist. Written informed consent was obtained from the participant or, for individuals who could not provide consent, from their healthcare proxy.

Randomization and Masking

Consenting patients were assigned to receive spinal anesthesia or general anesthesia in a 1:1 ratio using permuted block randomization with variable block sizes.[18,19] Randomization was stratified by hospital, sex, and fracture location (femoral neck *vs.* intertrochanteric or subtrochanteric fracture) using a central online data management system. Site staff obtained the randomization assignment from the data management system web portal and communicated it to the treating anesthesia team 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 study principal investigator or a designated staff member. Participants, treating clinicians, and data and safety monitoring board members were not masked to treatment assignment. The principal investigator, coinvestigators, clinical coordinating center staff, and statisticians remained masked to treatment assignment until the database was locked for analysis.

Procedures

Treatments were delivered by clinical anesthesia staff at each site. For patients assigned to spinal anesthesia, providers were instructed to perform single-injection spinal anesthetics with sedation as needed for patient comfort. Conversion to general anesthesia was permitted based on clinical circumstances or patient request. For patients assigned to general anesthesia, providers were instructed to use an inhaled anesthetic agent for maintenance and an endotracheal tube, supraglottic airway, or other device for airway management. All other aspects of care, including pre-, intra-, and postoperative analgesic medications and use of peripheral nerve blocks for pain management, were determined by the clinical team. Follow-up was performed by phone interviews with participants or proxy informants at approximately 60, 180, and 365 days after randomization.

Outcomes

The primary outcome for this analysis was the number of days from randomization to death, censored at the time of the final study interview (conducted approximately 365 days after randomization) or postrandomization day 365, whichever came first. Survival status and date of death information were ascertained from site staff reports and *via* telephone interviews with participants or appropriate proxy informants conducted by central coordinating center staff who were masked to treatment assignment. Telephone interviews were recorded and randomly audited for quality control. For U.S. patients whose vital status could not be otherwise ascertained, we searched the National Death Index through 2022 (the most recent year available). For subjects with partial date-of-death data (*i.e.*, month and year only), the date of death was imputed as the 15th day of the month in which they died.

We evaluated three secondary outcomes: (1) recovery of ambulation as assessed at 60, 180, and 365 days among individuals surviving to day 365; (2) a composite of death or new inability to ambulate without human assistance at 1 yr; and (3) a composite of death or residence in a nursing home or other institution at 1 yr among individuals who were community-dwelling at the time of fracture. For composite endpoints, death was included to account for potential survivor bias. Ambulatory status and location of residence were ascertained *via* masked telephone interview as above. For the ambulatory status assessment, patients were queried regarding their ability to walk 10 feet (3 m) or across a room independently or with a walker or cane but without the assistance of another person. As an exploratory outcome, we also report overall functional status at approximately 60, 180, and 365 days after randomization as collected *via* telephone interview using the 12-item World Health Organization Disability Schedule 2.0, which assesses disability in six functional domains (cognition, mobility, self-care, social interaction, life activities, and community participation).[20] Adverse events were assessed at each follow-up interview.

Statistical Analysis

Sample size planning for REGAIN was based on the overall study primary outcome, which was a composite of death or new inability to walk approximately 10 feet without human assistance at 60 days. We estimated that 1,600 participants would provide 80% power to detect a 0.78 relative risk for this outcome among patients assigned to spinal *versus* general anesthesia at a two-sided significance level of 0.05, assuming a 34.2% rate of this outcome in the general anesthesia arm.[21] We did not conduct separate power analyses for the long-term outcomes presented here. Our main analysis included all patients in the modified intention-to-treat population with available outcome data. 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 compared survival time between treatment arms using Kaplan–Meier curves and a Cox proportional hazards regression model, adjusted for sex, fracture type, and country of enrollment. We assessed the proportional

hazards assumption using failure-time graphs and statistical tests of zero slopes in the Schoenfeld residuals; additional models incorporating time-varying effects were considered when the proportional hazards assumption was not met. Recovery of ambulation over the first year after randomization was compared by group *via* logistic mixed effects regression model (generalized linear mixed model approach) using data from the 60-, 180-, and 365-day interviews. This model included all participants with at least one valid postrandomization ambulation assessment and was adjusted for sex, fracture type, country, and days since randomization at assessment. To account for within-subject correlation, we included a random intercept term per individual with an unstructured variance–covariance matrix. For binary outcomes (death or new inability to ambulate; death or new transition to a nursing home residence), we used the Mantel–Haenszel test for differences in proportions, stratified by sex, fracture type, and country.

For our primary survival outcome, we considered the possibility of heterogeneity of treatment effects by exploring treatment-covariate interactions for six prespecified patient characteristics: age (85 yr or older *vs.* less than 85 yr), sex, country of enrollment, location of residence before fracture (nursing home *vs.* community residence), reliance on assistive devices to ambulate before fracture, and fracture type. We conducted exploratory subgroup analyses for interactions with P values of 0.20 or lower using Cox models adjusted as above. Our survival analysis included all patients in the modified intention-to-treat population; to assess whether our findings may have been influenced by patterns of censoring before the end of the study, we compared characteristics of patients in each study arm who were censored before the final study interview due to withdrawal or loss to follow-up. Additionally, we carried out a supplementary analysis *via* a Cox model that imputed censored failure times.[22] For censored subjects, failure times were imputed based on a model including patient age, sex, fracture type, country of enrollment, assigned arm, and comorbidities. Finally, to assess the potential impact of nonadherence to the assigned treatment on the study outcomes, we used a structural Cox model to estimate the per-protocol effect of spinal anesthesia on survival time with the assigned treatment as an instrumental variable.[23]

Analyses were performed using SAS 9.4 (SAS Institute, USA). All hypotheses were tested at a two-sided significance level of 0.05. The data were reviewed at prespecified intervals by an independent data and safety monitoring board. Analyses followed a prespecified statistical analysis plan; this plan plus all modifications made after initiation of analysis appear in the supplemental digital content (https://links.lww.com/ALN/D351).

Table 1. Patient Characteristics by Treatment Assignment

Characteristic	Randomized to Spinal Anesthesia (N = 795)	Randomized to General Anesthesia (N = 804)
Age at randomization, n/N (%)		
Less than 65 yr	116/795 (14.6%)	96/803 (12.0%)
65 to 74 yr	191/795 (24.0%)	193/803 (24.0%)
75 to 84 yr	262/795 (33.0%)	266/803 (33.1%)
85 yr or older	226/795 (28.4%)	248/803 (30.9%)
Male sex, n/N (%)	258/795 (32.5%)	269/804 (33.5%)
Race, n/N (%)		
White	683/762 (89.6%)	690/773 (89.3%)
Black	55/762 (7.2%)	67/773 (8.7%)
Other or more than one race	24/762 (3.1%)	16/773 (2.1%)
Hispanic ethnic group, n/N (%)	15/750 (2.0%)	12/762 (1.6%)
Enrolled at a Canadian site, n/N (%)	210/795 (26.4%)	211/804 (26.2%)
Number of coexisting medical conditions,* median (interquartile range)	1 (0 – 2)	1 (0 – 1)
American Society of Anesthesiologists Physical Status classification, n/N (%)		
I or II, no or mild systemic disease	251/782 (32.1%)	288/793 (36.3%)
III or IV, moderate or severe systemic disease	531/782 (67.9%)	505/793 (63.7%)
Do Not Resuscitate status documented, n/N (%)	125/795 (15.7%)	121/803 (15.1%)
Use of assistive walking device when ambulating 10 feet (3 m) or across a room 2 weeks before fracture, n/N (%)	249/779 (32.0%)	248/792 (31.3%)
3D-CAM assessment positive for delirium before randomization, n/N (%)	96/746 (12.9%)	104/752 (13.8%)
Preadmission residence, n/N (%)		
Home or retirement home	688/748 (92.0%)	689/762 (90.4%)
Nursing home or other location	60/748 (8.0%)	73/762 (9.6%)
WHODAS 2.0 summary score,† median (interquartile range)	9.1 (2.1 – 22.9)	8.3 (2.1 – 25.0)

*Coexisting conditions included chronic pulmonary disease, diabetes mellitus, disseminated cancer, coronary artery disease, congestive heart failure, cerebrovascular disease, dementia, and serum creatinine greater than 2 mg/dl or current dialysis. †WHODAS scores range from 0 to 100, with lower scores indicating lower degrees of disability.

3D-CAM, 3-minute Diagnostic Interview for Confusion Assessment Method; WHODAS 2.0, World Health Organization Disability Schedule 2.0.

Role of the Funding Source

The funder had no role in the design or conduct of the study; the collection, management, analysis, or interpretation of data; the preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Results

Between February 12, 2016, and February 18, 2021, we screened 22,022 patients (supplemental fig. 1, https://links.lww.com/ALN/D349). A total of 12,915 patients were excluded based on eligibility criteria; 3,565 declined consent; 2,660 were not enrolled because of staff unavailability, and 1,282 were excluded for other reasons. Of 1,600 patients who underwent randomization, 795 were assigned to spinal anesthesia, and 805 were assigned to general anesthesia. One patient in the general anesthesia group died before receiving either treatment; this patient was not included in any study analyses.

Prerandomization characteristics were similar across treatment arms (table 1). Among 1,599 patients randomized, 527 (33%) were male, with mean age of 78 yr (± SD 10.7). A total of 1,377 (91%) were admitted from home or a retirement home (*vs.* a nursing home, rehabilitation facility, or another acute care hospital), and 497 (32%) used an assistive device when ambulating more than 10 feet (3 m) 2 weeks before fracture. As reported previously,[12] 666 of 795 patients assigned to spinal anesthesia (84%) received spinal anesthesia only. Of the remaining patients in the spinal anesthesia arm, 119 (15%) received general anesthesia, with or without an initial attempt to place a spinal block. Eight patients (1%) withdrew before surgery, and anesthesia type was not recorded. Of the 804 patients assigned to general anesthesia who were included in intention-to-treat analysis, 769 (96%) received general anesthesia, and 28 (3%) received spinal anesthesia; 7 patients (0.9%) withdrew before surgery or did not have a recorded anesthesia type.

Among all patients, median follow-up was 365 days (interquartile range, 354 to 365); there was no difference in the duration of follow-up between patients randomized to spinal *versus* general anesthesia. During the study period, 190 deaths occurred: 98 in the spinal anesthesia group and 92 in the general anesthesia group. Deaths were identified *via* U.S. National Death Index search in 39 patients; for the remaining 151 patients, deaths were ascertained *via* telephone follow-up or site report. Vital status information at or beyond the final study interview (conducted at approximately 365 days) was available for 1,427 (89.2%) of the overall study population, including 714 of 795 (89.8%) patients allocated to spinal anesthesia and 713 of 804 (88.7%) patients allocated to general anesthesia (supplemental table

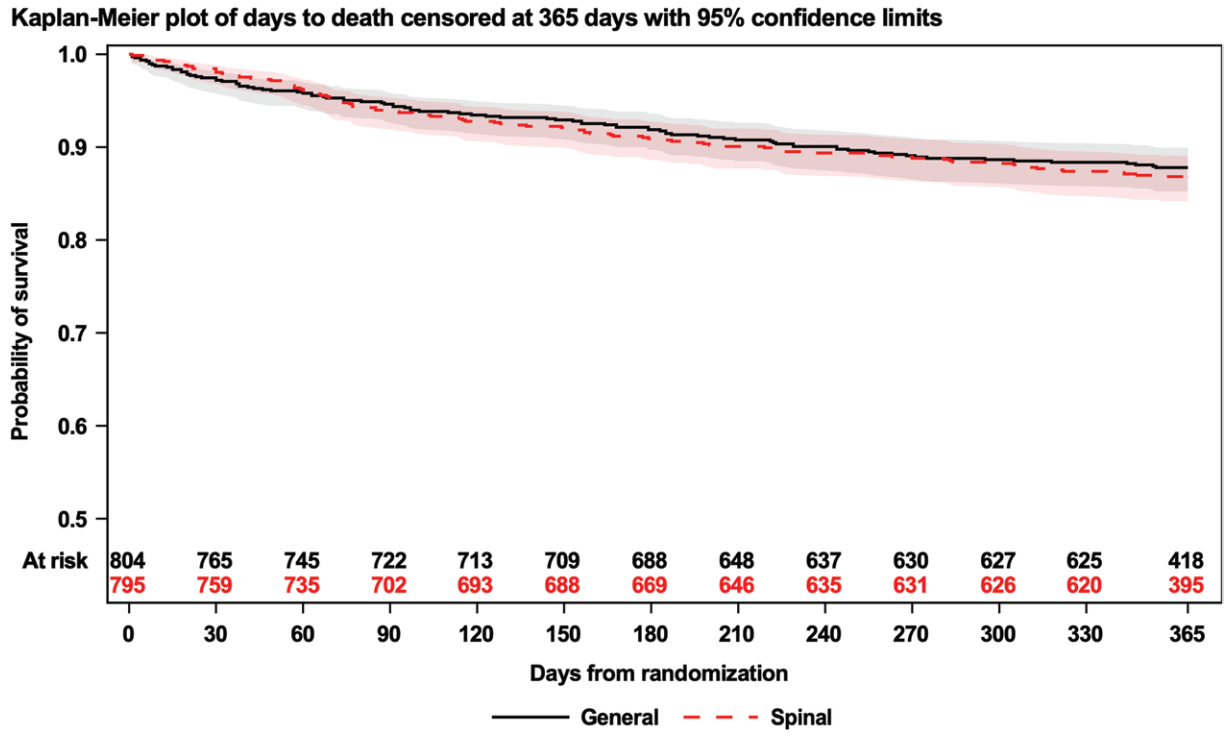

Fig. 1. Kaplan–Meier plot of days to death censored at 365 days. *Shading* represents 95% confidence limit (log-rank $P = 0.59$). The hazard ratio from the Cox model adjusting for age group, fracture type, and country of randomization is 1.08 (95% CI, 0.81 to 1.44; $P = 0.59$).

1, https://links.lww.com/ALN/D349). Among these patients, 1-yr mortality was 13.7% for patients in the spinal anesthesia arm and 12.9% for patients in the general anesthesia arm. Survival at up to 365 days after randomization did not differ by treatment arm (fig. 1; table 2; hazard ratio, spinal *vs*. general anesthesia: 1.08; 95% CI, 0.81 to 1.44; $P = 0.59$). Of six prespecified interaction analyses, we observed a *P* value for interaction of 0.2 or less for two patient characteristics: age less than 85 yr *versus* 85 yr or older and country of randomization. Adjusted hazards of death were not significantly different among these subgroups. In the model including patients 85 yr or older, failure-time graphs and diagnostic tests did not verify the proportional hazards assumption; we subsequently confirmed the findings from this model by estimating the hazard ratio for death at 365 days in a Cox model that incorporated a time-varying effect (supplemental table 2, https://links.lww.com/ALN/D349). Diagnostic testing of other Cox models did not indicate violations of the proportional hazards assumption.

Recovery of independence in ambulation over the first year after surgery did not differ among patients assigned to spinal anesthesia *versus* general anesthesia (adjusted odds ratio for spinal *vs*. general, 0.87; 95% CI, 0.67 to 1.14; $P = 0.31$; supplemental table 3, https://links.lww.com/ALN/D349). At the 60-, 180-, and 365-day interviews, death or new inability to walk occurred in 18.5% (132 of 712), 19.6% (136 of 694), and 24.1% (165 of 684) of patients assigned to receive spinal anesthesia and 18.0% (132 of 732), 18.7% (132 of 707), and 21.6% (146 of 676) of patients assigned to receive general anesthesia, respectively (fig. 2).

Table 2. Effect of Spinal Anesthesia *versus* General Anesthesia on Survival at up to 365 Days after Randomization

	Hazard Ratio, Spinal *versus* General Anesthesia (95% CI)	*P* Value
Overall study sample	1.08 (0.81 – 1.44)*	0.59
Subgroup analyses†		
Age		
Less than 85 yr	0.91 (0.61 – 1.36)*	
85 yr or older	1.35 (0.90 – 2.01)‡	
Country of enrollment		
United States	0.98 (0.71 – 1.34)§	
Canada	1.63 (0.85 – 3.12)§	

*Cox proportional hazards model for death over the study period adjusted for sex, fracture type, and country. Proportional hazards assumption confirmed *via* examination of failure time graph and $P > 0.05$ in test for zero slope in Schoenfeld residuals. †We tested for interactions between treatment assignment and the following prespecified patient characteristics on the primary outcome: age 85 yr or older *versus* younger than 85 yr; sex; country of enrollment; the need for assistive devices to ambulate before fracture; location of residence before fracture; and fracture type. Subgroup analyses were carried out only when the *P* value for the interaction term was 0.20 or less. ‡Cox proportional hazards model for death at 365 days after enrollment adjusted for sex, fracture type, and country. Failure time graphs and test for zero slope in Schoenfeld residuals did not confirm proportional hazards assumption ($P = 0.02$); additional analyses are shown in supplemental table 1 (https://links.lww.com/ALN/D349). §Cox proportional hazards model adjusted for sex and fracture type. Proportional hazards assumption confirmed *via* examination of failure time graph and $P > 0.05$ in test for zero slope in Schoenfeld residuals.

The incidence of death or new inability to walk across study visits did not vary between treatment arms by visual inspection. The adjusted odds of dying or being newly unable to ambulate at 365 days did not differ by treatment arm (table 3). Among patients not living in a nursing home before fracture, death or new transition to nursing home residence occurred in 119 of 584 patients assigned to spinal anesthesia (20.4%) *versus* 116 of 572 patients assigned to general anesthesia (20.3%; adjusted odds ratio for spinal *vs*. general, 1.01; 95% CI, 0.76 to 1.35). Median World Health Organization Disability Schedule 2.0 scores were similar by treatment assignment across study visits (supplemental table 4, https://links.lww.com/ALN/D349). Adverse events reported at up to 365 days were similar across treatment arms (supplemental table 5, https://links.lww.com/ALN/D349).

Supplemental table 6 (https://links.lww.com/ALN/D349) shows characteristics of patients without available vital status information at or beyond the 365-day interview due to loss to follow-up or study withdrawal. Sensitivity analyses imputing survival status for these patients returned results comparable to those from our main models (hazard ratio for spinal *vs*. general anesthesia, 1.08; 95% CI, 0.81 to 1.44; $P = 0.59$). Analyses that accounted for treatment nonadherence did not differ from our main results (hazard ratio for spinal *vs*. general anesthesia 1.10; 95% CI, 0.78 to 1.56; $P = 0.59$).

Discussion

In this prespecified secondary analysis of a pragmatic randomized trial of 1,600 adults aged 50 yr and older, assignment to spinal anesthesia *versus* general anesthesia did not affect survival at up to 1 yr after hip fracture surgery. Secondary outcomes, including recovery of ambulation over the first year after surgery, death or inability to walk without human assistance at 365 days, and death or new transition to nursing home residence at 365 days did not differ by anesthesia type.

Among older adults undergoing surgical procedures for which spinal or general anesthesia may be suitable, information on how anesthesia choices may influence survival and functional recovery over the first year after surgery can inform treatment choices by patients and clinicians. Most recent randomized trial data have not suggested major differences in short-term outcomes by anesthesia type.[12,24] However, some differences have been noted that could plausibly affect longer-term outcomes. A recent meta-analysis found lower rates of acute kidney injury among patients randomized to spinal *versus* general anesthesia,[3] which could potentially affect long-term survival. A previous analysis of data from REGAIN suggested potential differences in pain and opioid use in the early postoperative period among patients who received spinal anesthesia,[25] which could possibly influence rehabilitation and recovery of ambulation.

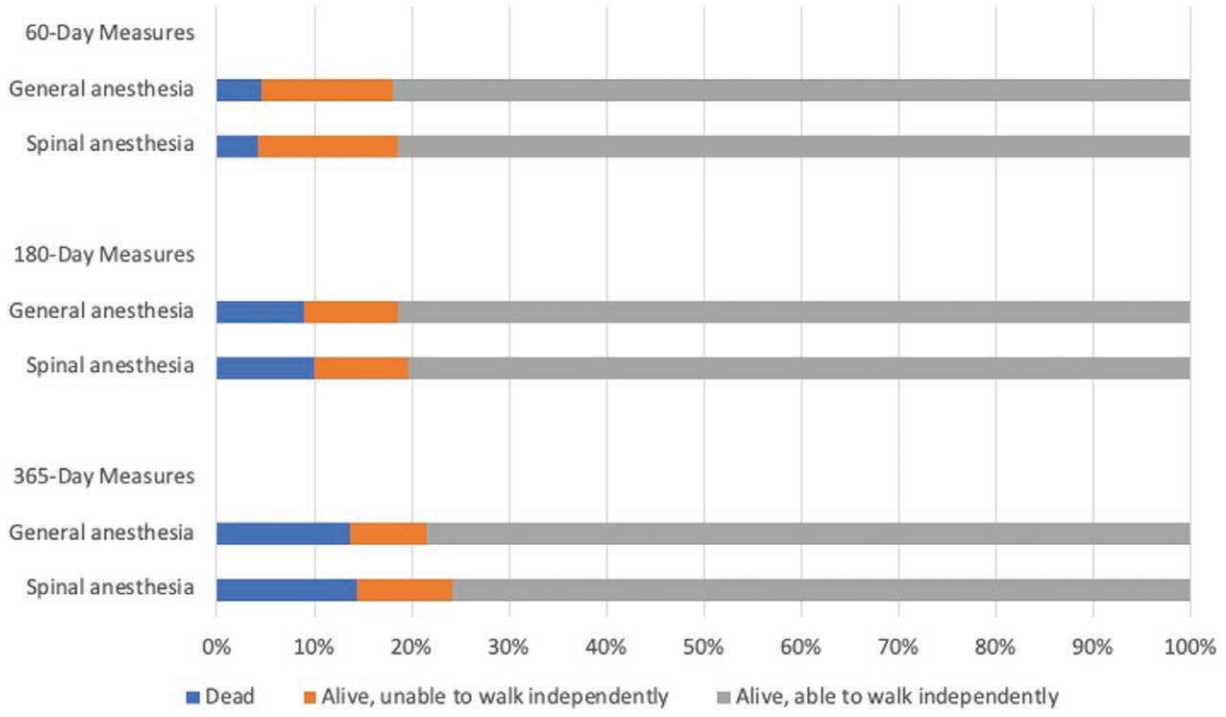

Fig. 2. Unadjusted ambulation and survival outcomes at approximately 60, 180, and 365 days after randomization, stratified by treatment group. Data from 60-day interviews were available for 712 patients in the spinal anesthesia group and 732 patients in the general anesthesia group; data from 180-day interviews were available for 694 patients in the spinal anesthesia group and 707 patients in the general anesthesia group; and data from 365-day interviews were available for 684 patients in the spinal anesthesia group and 676 patients in the general anesthesia group.

Table 3. Effect of Spinal Anesthesia *versus* General Anesthesia on Composite Secondary Outcomes

	Spinal Anesthesia		General Anesthesia		
	No. of Patients	No. (%)	No. of Patients	No. (%)	Odds Ratio (95% CI)
Death or inability to walk without human assistance at 365 days	684	165 (24.1)	676	146 (21.6)	1.16 (0.90 – 1.50)*
Death or new nursing home admission at 365 days†	584	119 (20.4)	572	116 (20.3)	1.01 (0.76 – 1.35)*

*Mantel–Haenszel test adjusted for sex and fracture type. †Among community-dwelling patients at randomization.

To date, few studies have compared 1-yr outcomes with spinal *versus* general anesthesia. A 2017 meta-analysis by Guay *et al.*[2] identified two single-center trials from the 1980s that evaluated survival at 1 yr among patients assigned to spinal *versus* general anesthesia for hip fracture surgery and found no difference in survival by anesthesia type among a total of 726 patients enrolled across both studies.[7,8] More recently, Parker and Griffiths[6] reported mortality at 1 yr to be 20.2% with spinal anesthesia *versus* 12.1% with general anesthesia in a single-center randomized trial enrolling 322 hip fracture patients.

The current study provides important new insights that add to and extend beyond past work in this area. Studies conducted in the 1980s predated the introduction of modern anesthesia medications and monitoring standards; the current study employed pragmatic treatment protocols to represent current standards of practice across the diverse U.S. and Canadian hospitals in our network. We did not confirm findings from Parker and Griffith's previous trial of differences in survival at 1 yr by anesthesia type[6]; this may have been due to differences in the characteristics of the patients enrolled in each study, in anesthesia techniques employed, or in postoperative care delivery across studies. In contrast to previous studies of long-term anesthesia outcomes, we evaluated outcomes of major importance to patients and families beyond survival alone, including

recovery of ambulation and the need for new nursing home care 1 yr after surgery. The large sample recruited for the current study also permitted additional analyses to examine for heterogeneity of treatment effects on survival outcome according to patient age and country of enrollment. These subgroup analyses did not identify significant differences in these groups according to anesthesia type.

Our study has limitations. Some patients were censored before completing the final study visit due to withdrawal or loss to follow-up. Sensitivity analyses conducted to address missing data produced results similar to those of primary analyses; however, since these analyses rely on assumptions we cannot fully verify, we cannot rule out bias due to missing data. As previously reported, some patients in each group failed to receive the assigned treatment.[12] Nonetheless, our findings regarding survival remained unchanged in supplemental analyses that accounted for crossover between spinal and general anesthesia using instrumental variable analyses. As we did not obtain cause-of-death information for most decedents in our analysis, we are unable to compare differences in the cause of death between groups. One-yr mortality in our sample was lower than has been reported in unselected populations of hip fracture patients,[11] which may have been due to study eligibility criteria or differences in enrollment rates between sicker *versus* healthier patients. While the CI reported here argue against large effects of anesthesia type on long-term outcomes, the available sample does not permit us to fully exclude the potential for more subtle effects. Finally, based on resources available for the current study, we chose to conduct ambulation and location of residence assessments by telephone at three time points over the first year after surgery; it is possible that more frequent assessments or in-person evaluations may have produced different results.

Use of spinal anesthesia has increased over time,[5] potentially reflecting beliefs regarding potential outcome benefits.[26] Our finding of similar outcomes at 365 days with either technique in hip fracture patients suggests that, for older surgical patients who may be candidates for either spinal or general anesthesia, treatment choices can be based on operative planning and patient preference rather than on anticipated differences in clinical outcomes.

Conclusions

In a large multicenter randomized trial of spinal *versus* general anesthesia for hip fracture surgery in older adults, mortality, ambulation, or other patient-centered outcomes at 1 yr after surgery did not vary by anesthesia type.

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Competing Interests

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Reproducible Science

Full protocol available at: neumanm@pennmedicine.upenn.edu. Raw data available at: neumanm@pennmedicine.upenn.edu. IRB approval and a completed data use agreement are required for data sharing.

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Supplemental Digital Content

Supplemental appendix, https://links.lww.com/ALN/D349

Study protocol, https://links.lww.com/ALN/D350
Statistical analysis plan, https://links.lww.com/ALN/D351

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