



Spinal Nerve Block and Recovery after Spinal Anesthesia in Frail Patients: A Prospective Cohort Study

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Objective: Surgical frailty is associated with a significantly higher incidence of perioperative mortality and complications. Although neuraxial anesthesia is a preferable alternative to general anesthesia in frail patients, it remains unclear whether the pharmacodynamic profiles of local anesthetics used in intrathecal spinal nerve blocks are different in this population.

Methods: This prospective observational cohort study recruited 62 patients scheduled for operations that could be performed under spinal anesthesia between April 22 and June 30, 2020, in our hospitals. The levels of dermatome blockage after spinal anesthesia and recovery of spinal nerve sensory and motor functions were recorded.

Results: The prevalence of frailty in patients receiving spinal anesthesia was 25.8%. Compared with non-frail patients, frail patients were significantly older, had a higher proportion of females, and tolerated less intense metabolic equivalent activities. The presurgical incision sensory blockage levels were not different between frail and non-frail patients following intrathecal administration of a similar dose of bupivacaine. The time intervals to pain sensation at surgical sites (sensory recovery) and voluntary knee flexion (motor recovery) were also similar between the frail and non-frail groups. However, frail patients experienced more episodes of hypotension and required more vasopressors during surgery.

Conclusions: Our study illustrates that frailty did not significantly affect bupivacaine sensitivity in spinal nerve blocks. However, special attention should be paid to correct intraoperative hypotension after spinal anesthesia in frail patients.

Key words: frailty, local anesthetics, neuraxial anesthesia, pharmacodynamics

Introduction

Frailty is a multi-dimensional state of decreased physiologic reserve that results

in diminished resiliency, loss of adaptive capacity, skeletal muscle weakness, and increased vulnerability to stressors.¹ The prevalence of frailty in general surgical patients ranges from 2% to 13%. Frailty in surgical

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patients is associated with significantly higher incidences of 30-day mortality, surgery-related complications, prolonged hospital stays, cognitive disorders, and postoperative pain, particularly after general anesthesia.^{2,3} Deficits in multiple organ systems seen in frailty can result in alterations to anesthetic pharmacokinetics and pharmacodynamics.⁴ Changes in receptor numbers at target sites, signal transduction after receptor binding, and dysregulation of homeostatic processes can all significantly affect anesthetic pharmacodynamics in elderly or frail patients, leading to increased or decreased drug sensitivity.⁵ Since regional anesthesia reduces the need for perioperative airway manipulation and neuraxial anesthesia has been shown to be associated with improved survival and wound outcomes in frail patients,⁶ regional and neuraxial anesthesia may be a preferable alternative to general anesthesia for clinical anesthesiologists.⁴ However, it remains unclear whether the pharmacodynamic profiles of local anesthetics used in intrathecal spinal nerve blocks are altered in patients with frailty and whether the therapeutic dose of local anesthetics should be adjusted and the post-anesthesia care period extended in this population. Therefore, this study aimed to compare spinal nerve blocking responses following intrathecal administration of bupivacaine in frail and non-frail patients.

Materials and Methods

Study design and protocol

This prospective observational cohort study was conducted on patients who received elective surgery under spinal anesthesia in E-Da Hospital, Taiwan, between April 22 and June 30, 2020, in accordance with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of E-Da Hospital, Taiwan (approval number EMRP-108130). This study excluded patients receiving emergency or after-hours operations

and those admitted to intensive care units after surgery (Fig. 1).

Patient frailty was assessed using Fried's 5-point frailty assessment (frail, 3 – 5 criteria; pre-frail, 1 – 2 criteria; non-frail, no positive criteria) before operation.⁷ Anesthetic staff responsible for clinical care were blinded to the frailty status of the patients. Bupivacaine dose and the techniques used to achieve the anticipated levels of spinal nerve blockage were decided by the anesthesiologist-in-charge based on clinical practice recommendations and their personal experience. Motor and sensory blockage levels after anesthesia were recorded by clinical nurse anesthetists. Patients were transferred to the post-anesthesia care unit (PACU) for postoperative care and close monitoring of their neuromuscular recovery before being discharged to the original ward. Sensory and motor blockage regression was assessed by nurses in the PACU and wards. Sensory recovery was defined as pain sensation at surgical sites, and the motor recovery period was defined as the time interval to voluntary knee flexion. Incidence rates of perioperative adverse events were also noted.

Statistical analysis

Matched controls were randomly selected from the non-frail population and propensity-

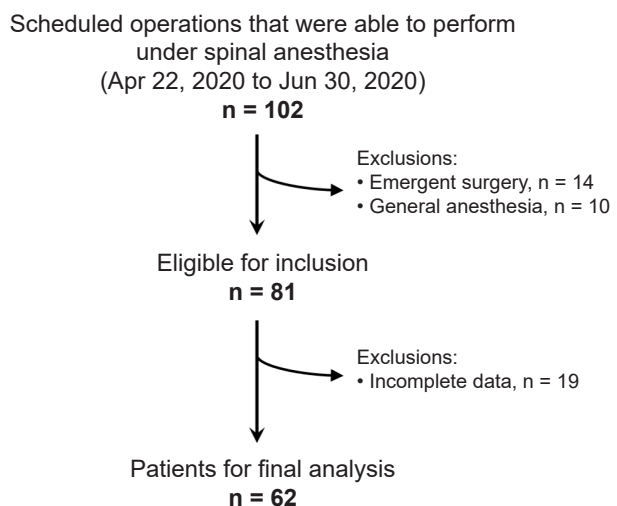


Fig. 1 Study flow chart.

matched with the basic patients' characteristics and types of operation in the frail group. The values of continuous and categorical variables were compared using a Wilcoxon rank-sum test and Fisher's exact test, respectively (SPSS software, version 24.0; IBM, Armonk, NY). Statistical significance was set at $p < 0.05$.

Results

During the study period, 102 patients were scheduled for operations that could be performed under spinal anesthesia. Twenty-four patients were excluded because the operation they underwent was an emergency operation or was performed under general anesthesia. Therefore, 81 patients were recruited,

and 19 patients were excluded from the final analysis because of incomplete clinical data (Fig. 1). Of the remaining 62 patients used in the final analysis, 16 (25.8%) were considered frail (Fried's score ≥ 3) (Table 1).

Compared with non-frail patients, frail patients were significantly older, had a higher proportion of females, tolerated less intense metabolic equivalent (MET) activities, and had lower levels of education (Table 1). The American Society of Anesthesiologists (ASA) physical classifications were similar between the two groups. Most of the participants underwent orthopedic or urological surgery (Table 1). After propensity matching, 12 patients were selected from the non-frail patients and served as the matched control group (Table 1). There

Table 1. Patient characteristics and types of operation.*

	Frail (n = 16)	Non-frail (n = 46)	Matched non-frail (n = 12)
Gender (M:F)	6:10	32:14 [†]	4:8
Age (years)	71.6 ± 7.1	59.0 ± 15.3 [†]	70.6 ± 12.9
BMI (kg/m ²)	26.6 ± 4.2	26.1 ± 3.9	25.8 ± 3.8
Independence in daily living	13 (81.3)	44 (95.7) [†]	11 (91.7)
Educational level		($p = 0.026$) [†]	($p = 0.183$)
Illiteracy	4 (25.0)	5 (10.9)	4 (33.3)
< College or high school	12 (75.0)	32 (69.6)	7 (58.3)
≥ University	0 (0)	9 (19.5)	1 (8.4)
Active smoker (yes)	0 (0)	10 (21.7) [†]	0 (0)
Dietary habit			
Non-vegetarian	15 (93.8)	46 (100)	12 (100)
Vegetarian	1 (6.3)	0 (0)	0 (0)
Metabolic equivalent (MET) activity		($p < 0.001$) [†]	($p < 0.001$) [†]
Light (< 3 MET)	16 (100)	15 (32.6)	3 (25.0)
Moderate (3 – 6 MET)	0 (0)	24 (52.2)	9 (75.0)
Vigorous (> 6 MET)	0 (0)	7 (15.2)	0 (0)
ASA physical classification			
1 and 2	11 (68.8)	38 (82.6)	9 (75.0)
> 3	5 (31.3)	8 (17.4)	3 (25.0)
Type of operation			
Orthopedic	11 (68.8)	19 (41.3)	5 (41.6)
Urology	5 (31.3)	22 (47.8)	5 (41.6)
Colorectal	0 (0)	4 (8.7)	2 (16.8)
Plastic	0 (0)	1 (2.2)	0 (0)

* A total of 81 patients were eligible to be recruited during the study period, and 19 patients were excluded from final analysis due to incomplete clinical data.

[†] $p < 0.05$ vs. frail. Results are presented as n (%) or mean ± SD.

Continuous data were analyzed by the Wilcoxon Whitney U test and categorical data were analyzed by the Fisher's exact test.

ASA: American Society of Anesthesiologists; BMI: body mass index; F: female; M: male.

were no differences in bupivacaine doses administered into the intrathecal space and pre-surgical incision sensory blockage levels were similar between frail and non-frail or matched non-frail patients (Table 2). However, frail patients experienced more episodes of hypotension and required more vasopressors during operations (Table 2). Time intervals to pain sensation at surgical sites (sensory recovery) and voluntary knee flexion (motor recovery) were similar between the frail and non-frail patients (Table 2). No in-hospital mortality or other major postoperative events occurred in this study.

Discussion

Consistent with other observational studies,² our cohort found that frailty was more commonly diagnosed in older (mean age of 71.6 years) and female patients, and they had more limitations in their daily physical performance. Since functional frailty status is not a routine consideration used in pre-anesthesia clinics for perioperative outcome predictions,⁸ this study did not find differences in the ASA

physical classifications between the frail and non-frail surgical patients.

The prevalence of frailty in patients receiving spinal anesthesia in this study population was 25.8%, which is comparable with the findings of a previous larger-scale study (21.5%).⁶ The higher prevalence rates of frailty in surgical patients receiving neuraxial anesthesia over general anesthesia could simply imply that anesthesiologists generally consider regional blocks a safer option, associated with fewer perioperative complications in sicker and elderly patients.^{4,9} In a recent cohort study, the Mayo Clinic study group found that knee arthroplasties done under neuraxial blocks on frail patients were associated with significantly lower mortality (hazard ratio 0.49; 95% confidence interval [CI] 0.27 – 0.89) and wound complication rates (hazard ratio 0.71; 95% CI 0.55 – 0.90) than those performed under general anesthesia.⁶ With neuraxial anesthesia, it is important to consider whether frail patients are more sensitive to local anesthetics during spinal nerve blocks.⁴ However, it remains unclear whether the pharmacodynamic profiles of local anesthetics used in intrathecal spinal

Table 2. Study outcomes.

	Frail (n = 16)	Non-frail (n = 46)	Matched non-frail (n = 12)	p value [§]
Dose of bupivacaine (mg)*	10 (9 – 13)	11 (7 – 14)	10 (7 – 14)	0.250/0.175
Level of sensory block*	T9 (T5 – T10)	T9 (T6 – L1)	T9 (T6 – L1)	0.236/0.823
Intraoperative hypotension [†] (yes)	11 (68.8)	17 (37.0)	4 (33.3)	0.028/0.063
Vasopressor [‡] (yes)	5 (31.3)	5 (10.9)	3 (25.0)	0.070/1.000
Time (min) to request for analgesics				0.646/1.000
< 60 min	2 (12.5)	4 (8.7)	1 (8.3)	
60 – 120 min	0 (0)	2 (4.3)	0 (0)	
> 120 min	14 (87.5)	40 (87.0)	11 (91.7)	
Time (min) to knee flexion	144.7 ± 38.4	139.5 ± 37.9	135.6 ± 45.0	0.640/0.740
Total operation time (min)	79.4 ± 34.6	64.3 ± 34.6	53.8 ± 23.6	0.138/0.043
Intraoperative fluid (mL)				0.355/0.550
0 – 600	12 (75.0)	36 (78.3)	10 (83.3)	
601 – 800	3 (18.8)	8 (17.4)	2 (16.7)	
> 801	1 (6.2)	2 (4.3)	0 (0)	

[†] Intraoperative hypotension was defined as a reduction of systolic blood pressure below 25% of the baseline level before anesthesia induction. [‡] Vasopressors included bolus of ephedrine or norepinephrine to correct intraoperative hypotension. Continuous data were analyzed by the Wilcoxon Whitney U test and categorical data were analyzed by the Fisher's exact test. Results are presented as n (%) or mean ± SD, and * are shown as median (range). [§] p values represent as frail vs. non-frail / frail vs. matched non-frail.

nerve blocks are different in patients with and without frailty.

Our study showed that sensory dermatome blockage levels achieved by similar doses of intrathecal bupivacaine were not different between frail and non-frail patients, as the anesthesiologists were blinded to patients' frailty status. Most importantly, we found that time intervals to pain sensation at the surgical site (sensory recovery) and voluntary movement of lower limbs (motor recovery) also showed no significant difference between the frail and non-frail groups, highlighting that bupivacaine sensitivity for spinal nerve blocks was not significantly affected by frailty and that clinical doses of bupivacaine for spinal anesthesia in frail patients might not have to be adjusted. However, we observed more hypotensive events in frail patients and that these patients required more vasopressor therapy after spinal anesthesia. It is known that autonomic dysregulation is the main cause of developing intraoperative hypotension in the frail.¹⁰

Several limitations should be considered when interpreting the findings of this study. Although this was a prospective study, patients in the frail groups were older and consisted of significantly more female, which might have confounded the clinical outcomes observed during spinal anesthesia. After propensity matching, 12 non-frail patients with more identical characteristics (similar in sex, age, educational levels, and smoking habit) were selected from the non-frail patients for matched comparison of the outcome assessments. Our results suggested that the pharmacodynamics of local anesthetics used in spinal nerve blocks are not significantly altered in frail patients even when compared with younger, predominantly male non-frail individuals. Furthermore, we do not expect elderly and frail patients to require higher doses of local anesthetics than younger patients to achieve similar levels of spinal anesthesia. Secondly, we used Fried's phenotypic criteria to assess frailty, where the

frailty index has been recognized as a more comprehensive tool for multiple-domain assessment of frailty.¹ Clinically, measurements using frailty phenotypes require less geriatric expertise and have a shorter assessment time. Nevertheless, Fried's criteria employ quantitative evaluation, making it a valid subjective clinical instrument for preoperative frailty assessment.^{1,7} Thirdly, time to pain sensation at the surgical site was used as a surrogate indicator for sensory recovery after spinal anesthesia instead of precise measurement of spinal dermatomes. However, as patients were cared for in the PACU and on the wards after surgery, surgical pain may be considered more subjective than dermatome measurement as spinal dermatome measurements will be done by different medical staff in the two units, leading to inconsistent interrater reliability among anesthetic, PACU, and ward personnel. Fourth, this study included a relatively small sample size in each group, which might confine the statistical power in detecting subtle clinical differences in the study endpoints. Lastly, this study focused on the effects of bupivacaine and may not be generalizable to other local anesthetics.

Conclusions

This study illustrates that bupivacaine sensitivity in spinal nerve blocks is not significantly affected by frailty, even when compared with younger, male non-frail patients. However, special attention should be paid to correct intraoperative hypotension after spinal anesthesia in frail patients.

Author Contributions

Study Design, Tzu-Ling Lee and Yi-Kai Su; Data Collection, Tzu-Ling Lee; Statistical Analysis, Tzu-Shan Chen; Data Interpretation, Tzu-Ling Lee, Yi-Kai Su, Tzu-Shan Chen and Shih-Chieh Chung; Manuscript Preparation, Tzu-Ling Lee and Shih-Chieh Chung; Litera-

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the E-Da Hospital, Taiwan (IRB approval number EMRP-108130).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

Not applicable.

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Conflicts of Interest

The authors declare no conflict of interest.

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