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Impact of regional anesthesia on outcomes of geriatric patients undergoing lower extremity revascularization

A propensity score-matched cohort study

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Abstract

Lower extremity revascularization (LER) for peripheral artery disease in elderly patients is associated with a high risk of perioperative morbidity and mortality. This study aimed to a conduct retrospective review and propensity score matching analysis to determine whether the use of regional anesthesia (RA) instead of general anesthesia (GA) in geriatric patients undergoing LER for peripheral artery disease results in improved short-term mortality and health outcomes. We reviewed medical records of 1271 patients aged >65 years who underwent LER at our center between May 1998 and February 2016. According to the anesthesia method, patients were grouped in the GA and RA groups. The primary outcome was short-term mortality (7-day and 30-day). The secondary outcomes were 5-year survival rate, intraoperative events, postoperative morbidity, and postoperative length of stay. A propensity score-matched cohort design was used to control for potentially confounding factors including patient demographics, comorbidities, American Society of Anesthesiologists physical status, and preoperative medications. After propensity score matching, 722 patients that received LER under GA (n = 269) or RA (n = 453) were identified. Patients from the GA group showed significantly higher 7-day mortality than those from the RA group (5.6% vs 2.7% $P = .048$); however, there was no significant difference in 30-day mortality between the groups (GA vs RA: 6.3% vs 3.6%, $P = .083$). The 5-year survival rate and incidence of arterial and central venous catheter placement or intraoperative dopamine and epinephrine use were significantly higher in the GA group than in the RA group ($P < .05$). In addition, the frequency of immediate postoperative oxygen therapy or mechanical ventilation support was higher in the GA group ($P < .05$). However, there was no difference in the postoperative cardiopulmonary and cerebral complications between the 2 groups. These results suggest that RA can reduce intraoperative hemodynamic support and provide immediate postoperative respiratory intensive care. In addition, the use of RA may be associated with better short-term and 5-year survival rates in geriatric patients undergoing LER.

Abbreviations: aPTT = activated partial thromboplastin time, GA = general anesthesia, LER = lower extremity revascularization, PAD = peripheral artery disease, PT = prothrombin time, RA = regional anesthesia.

Keywords: peripheral arterial disease; regional anesthesia; mortality; survival rate

1. Introduction

Peripheral artery disease (PAD) is a progressive disease that affects 12% to 20% of general population aged >65 years.[1] It is well known that critical limb threatening ischemia occurs when PAD progresses to advanced stage resulting in more severe symptoms such as pain at rest or tissue loss, and is associated with worse outcomes.[2] Lower extremity revascularization (LER) is performed based on the anatomy and severity of the disease. Treatment options are broadly categorized as either open surgery or endovascular treatment. Advanced age is a known risk factor for PAD and is often accompanied by systemic diseases, such as diabetes mellitus, hypertension, coronary artery disease, and cerebrovascular disease.[3] Elderly patients with PAD belong to the high-risk surgical group when undergoing LER; therefore, it is important to provide patient-specialized and appropriate anesthesia and intraoperative management for each patient.

PAD is associated with decreased functional capacity and increased risk of mortality.[4] Cardiac complications are a major

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cause of perioperative morbidity and mortality.[5] In addition, failure to wean from mechanical ventilation, pneumonia, urinary tract infection, renal insufficiency, cardiac arrest, and systemic sepsis have been reported to affect long-term survival after vascular surgery.[6] Therefore, it is also important to identify factors that reduce the risk of adverse outcomes in short-term and long-term follow-up.

Previous studies have investigated the effect of anesthesia type on patients by comparing regional anesthesia (RA) and general anesthesia (GA) during LER.[7–9] They reported the benefits of RA through short-term comparative factors, such as postoperative complications, length of stay, reoperation, and amputation. However, there are no definite results on the effect of anesthesia type on short-term and long-term mortality during LER surgery, especially in elderly patients with PAD. This retrospective propensity score-matched cohort study aimed to analyze the effect of anesthesia on postoperative outcomes in elderly patients receiving LER for PAD.

2. Materials and methods

This was a retrospective analysis of all patients who received a LER under GA or RA at Daegu Catholic University Medical Center (DCUMC) from May 1998 and February 2016 after obtaining the Institutional Review Board approval (CR-22-142-L) and registered at Clinical Research Information Service (KCT0007886). The electronic medical records of a total 1956 patients who underwent LER for PAD under GA or RA were reviewed. Among them, 607 patients under 65 years of age were excluded because the purpose of this study was to investigate geriatric patients. Thirty-nine patients operated on the contralateral leg, 22 patients operated on a site other than the lower extremity, and 17 patients with insufficient data were excluded. The remaining subjects divided into 2 groups based on the type of anesthesia: the GA and RA groups. GA consisted of endotracheal intubation or use of a laryngeal mask airway with a combination of inhalational anesthetics and intravenous narcotics for the maintenance of anesthesia. RA was defined as spinal or epidural anesthesia or peripheral nerve block with or without sedation.

2.1. Patient demographics and preoperative variables

Standard demographic data, including surgery type (elective or emergency operation), age, sex, and American Society of Anesthesiologists physical status (ASA PS) classification, were obtained for all patients. Data on comorbidities, including history of diabetes mellitus, hypertension, coronary artery disease, valvular heart disease, history of tuberculosis, chronic obstructive pulmonary disease, pulmonary hypertension, cerebrovascular accident, chronic kidney disease, liver disease, history of coronary bypass surgery, drug allergy history, and preoperative tests, such as pulmonary function testing or echocardiography, were also collected. Preoperative use of antithrombotic drugs such as clopidogrel, cilostazol, warfarin, and low molecular weight heparin, preoperative abnormalities of the prothrombin time (PT) or activated partial thromboplastin time (aPTT), and abnormal electrocardiography findings were also recorded.

2.2. Outcomes

The primary study outcome was short-term mortality (7-day and 30-day). Secondary outcomes included: longer-term mortality (5-year survival rate); major adverse cardiovascular events (cardiovascular death, stroke, myocardial infarction, or cardiac consultation); postoperative pulmonary complications (oxygen therapy, unplanned or prolonged mechanical ventilation, pneumonia, acute respiratory distress syndrome, or pulmonary consultation); major adverse limb events (reoperation, acute limb ischemia, or amputation); neuraxial or RA-related adverse events (epidural hematoma, spinal cord injury, or peripheral nerve injury); length of hospital stay; and intraoperative events (arterial line, central venous line, or the use of a vasoactive drug (i.e., dopamine, epinephrine, norepinephrine, or amiodarone).

2.3. Study design and statistical analysis

We used a propensity score-matched cohort design to control for potential confounding factors. All demographic and preoperative variables were considered confounding factors. We then matched each case of GA to a case of RA that had a similar propensity score. In this study, the dependent variable was the anesthesia type. The independent variables were the primary and secondary outcomes.

Statistical analyses were performed using the IBM SPSS software version 25.0 (IBM Corp., Armonk, NY). Cross analysis or Fisher's exact test was used for ordinal data and independent sample *t* test was used for average comparison of scale data. Descriptive data are presented as numbers (%) or means ± standard errors of mean. Statistical significance was set at P value < .01. The 5-year overall survival rates were calculated using the Kaplan-Meier method in both groups. Deaths from any cause observed during the 5-year postoperative period were counted as events in survival analysis. Survival curves drawn using the Kaplan-Meier method were compared using the log-rank test. P values were calculated using the log-rank test.

3. Results

A flowchart of this study is shown in Figure 1. In total, 1271 patients over 65 years of age underwent LER under GA or RA at Daegu Catholic Hospital between May 1998 and February 2016. Of them, 392 and 879 patients were included in the GA and RA groups, respectively. After propensity score matching, 269 and 453 patients were included in the GA and RA groups, respectively. Patient demographic data, preoperative comorbidities, preoperative medications, and test results are presented in Tables 1 and 2. After propensity score matching, no statistically significant differences were observed between the 2 groups. Table 3 shows the types of surgery and anesthesia. No difference was found between the 2 groups in terms of the type of surgery. In the RA group, 441 patients received epidural anesthesia, 10 received spinal anesthesia, and 2 received peripheral nerve block. Table 4 presents the preoperative echocardiography and pulmonary function tests parameters. There were no significant differences between the 2 groups.

The 7-day mortality rate was significantly lower in the RA group than in the GA group (2.7% vs 5.6%; $P = .045$). However, there was no significant difference in the 30-day mortality rate between the groups (3.6% in RA vs 6.3% in GA; $P = .083$) (Table 5). As shown in Figure 2, the 5-year survival rate was significantly lower in the RA group than in the GA group. Intraoperative catheterization and vasoactive medication use are shown in Table 6. Arterial or central venous line placement was significantly higher in the GA group than in the RA group. Furthermore, the frequency of intraoperative dopamine or epinephrine use in the GA group was significantly higher than that in the RA group.

Table 7 shows the cardiopulmonary or cerebral complications, postoperative surgical complications, and nerve injury. The incidence of postoperative oxygen therapy or mechanical ventilation support was higher in the GA group. However, there was no difference between the 2 groups in terms of cardiac or pulmonary complications, medical consultation, incidence of postoperative acute myocardial infarction or stroke within 1 month, and hospital stay. Additionally, there was no significant difference in the postoperative incidence of amputation or reoperation between the 2 groups ($P > .05$).

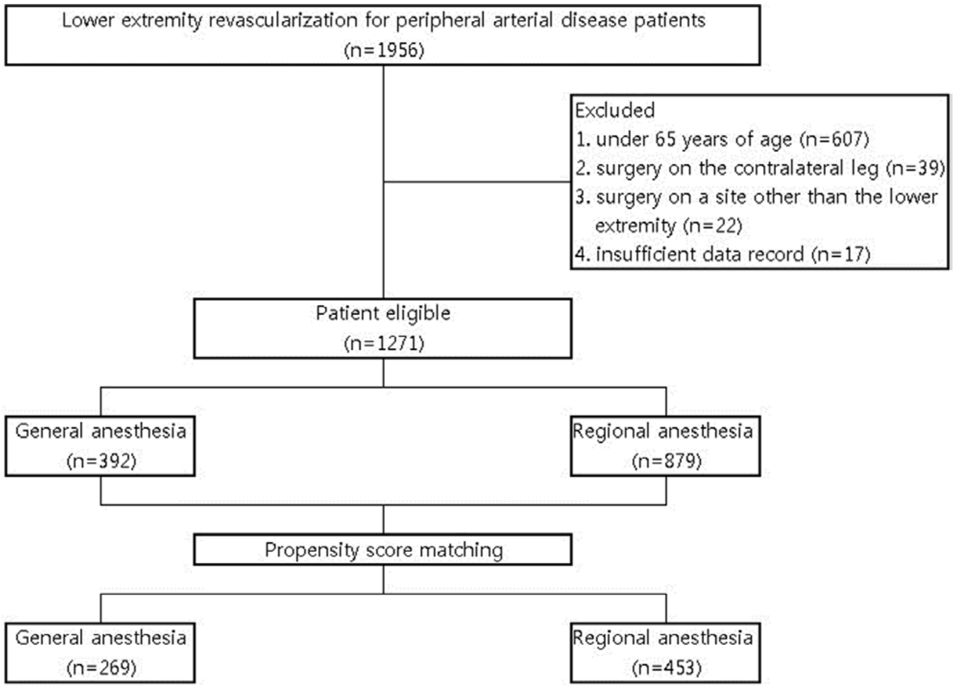

Figure 1. Study flow chart.

Table 1

Patient demographic data.

	Raw data			Matched data		
Variable	**Regional (n = 879)**	**General (n = 392)**	***P* value**	**Regional (n = 453)**	**General (n = 269)**	***P* value**
Surgery			.000			.067
Elective	600 (68.3)	223 (56.9)		305 (67.3)	163 (60.6)	
Emergency	279 (31.7)	169 (43.1)		148 (32.7)	106 (39.4)	
ASA PS			.000			.662
I or II	802 (91.2)	388 (99.0)		447 (98.7)	267 (99.3)	.662
III	34 (3.9)	3 (0.8)		5 (1.1)	2 (0.7)	
IV	43 (4.9)	1 (0.2)		1 (0.2)	0 (0)	
Sex			.119			.922
Male	686 (78.0)	321 (81.9)		359 (79.3)	214 (79.6)	
Female	193 (22.0)	71 (18.1)		94 (20.7)	55 (20.4)	
Age	74.5 ± 6.3	73.7 ± 5.7	.030	73.6 ± 6.1	73.8 ± 6.0	.574
Weight	57.0 ± 10.0	58.4 ± 9.6	.017	57.2 ± 9.3	57.3 ± 9.4	.840
Height	161.9 ± 7.9	163.2 ± 8.6	.007	162.1 ± 7.5	162.6 ± 7.9	.373

Data was expressed as mean ± SD or the number of patients. Parentheses indicate percentage.
ASA PS = American society of anesthesiologists physical status.

4. Discussion

In this retrospective propensity-matched cohort study of 722 patients undergoing LER for PAD, we found that the use of RA was associated with decreased short-term (7-day) and long-term (5-year) mortality rates. The secondary outcome analysis suggests that decreased mortality after RA might have been related to reduced perioperative cardiopulmonary complications among patients who received RA.

Patients undergoing LER are at high risk of developing postoperative complications. They are well known to be older, cigarette smokers, and have multiple comorbidities, including diabetes mellitus and hypertension, coronary artery, pulmonary, cerebral, and chronic kidney disease.[3] The findings presented in Table 2 also show that included geriatric patients receiving LER had a high number of comorbidities. Diabetes mellitus was present in approximately 35% of all patients, hypertension in 61% to 62%, ischemic heart disease in 15% to 20%, pulmonary disease in 11% to 12%, cerebrovascular disease in 20%, and kidney disease in 3.4% to 4%. Generally, intraoperative hemodynamic changes during GA are associated with cardiovascular suppression and peripheral vasodilation by inhalation or intravenous anesthetic agents. Geriatric patients with high comorbidities may be more vulnerable to systemic effects of GA during surgery. In patients undergoing LER, especially geriatric patients, RA can avoid hemodynamic instability associated with GA. The use of drugs such as epinephrine to sustain intraoperative stability was lower in the RA group. Compared with GA, RA has another advantage in addition to hemodynamic stability. RA can avoid endotracheal intubation and mechanical ventilation during surgery, which may be related to the reduction of postoperative pulmonary complications, such as oxygen therapy, pneumonia, postoperative intubation, or mechanical ventilation. Our results showed that patients who underwent RA were significantly less likely to receive immediate

Table 2

Medical comorbidities and preoperative medications and test.

	Raw data			Matched data		
Variable	**Regional (n = 879)**	**General (n = 392)**	***P* value**	**Regional (n = 453)**	**General (n = 269)**	***P* value**
Diabetes mellitus	332 (37.8)	127 (32.4)	.066	162 (35.8)	95 (35.3)	.904
Hypertension	545 (62.0)	242 (61.7)	.928	281 (62.0)	164 (61.0)	.776
Ischemic heart disease	156 (17.8)	88 (22.5)	.049	72 (15.9)	55 (20.5)	.120
Valvular heart disease	229 (26.1)	86 (22.0)	.117	104 (23.0)	58 (21.6)	.664
Tuberculosis	68 (7.7)	32 (8.2)	.794	40 (8.8)	20 (7.4)	.511
Pulmonary disease	103 (11.7)	43 (11.0)	.699	55 (12.1)	31 (11.5)	.805
Pulmonary hypertension	39 (4.4)	12 (3.1)	.248	17 (3.8)	10 (3.7)	.981
Cerebrovascular disease	185 (21.1)	80 (20.4)	.796	93 (20.5)	56 (20.8)	.926
Chronic renal failure	50 (5.7)	16 (4.1)	.233	18 (4.0)	9 (3.4)	.667
Liver disease	20 (2.3)	3 (0.8)	.062	7 (1.6)	3 (1.1)	.633
CABG	14 (1.6)	5 (1.3)	.667	5 (1.1)	3 (1.1)	.989
Drug allergy history	3 (0.3)	0 (0)	.247	1 (0.2)	0 (0)	.441
Antithrombotics						
Clopidogrel	64 (7.3)	30 (7.6)	.815	23 (5.1)	17 (6.3)	.480
Cilostazol	32 (3.6)	21 (5.4)	.157	20 (4.4)	14 (5.2)	.628
Warfarin	35 (4.0)	23 (5.9)	.137	19 (4.2)	18 (6.7)	.141
LMWH	20 (2.3)	6 (1.53)	.386	13 (2.9)	3 (1.1)	.122
Abnormal PT/aPTT	143 (16.3)	108 (27.6)	.000	65 (14.4)	53 (19.7)	.060
Abnormal ECG	531 (60.4)	243 (62.0)	.594	255 (56.3)	166 (61.7)	.153
PFT	563 (64.1)	218 (55.6)	.004	280 (61.8)	154 (57.3)	.226
Echocardiography	685 (77.9)	275 (70.2)	.003	337 (74.4)	192 (71.4)	.376

Data was expressed as mean ± standard deviation or the number of patients. Parentheses indicate percentage.

CABG = coronary artery bypass graft, ECG = electrocardiography, LMWH = low molecular weight heparin, PFT = pulmonary function test, PT/aPTT = prothrombin time/activated partial thromboplastin time.

Table 3

Surgery type and anesthesia type.

Variable	**Regional (n = 453)**	**General (n = 269)**	***P* value**
Surgery type			.060
Open surgery	385 (85.0)	214 (79.6)	
Endovascular intervention	67 (15.0)	55 (20.4)	
Anesthesia type		269 (100)	.000
General anesthesia	441 (97.3)		
Epidural anesthesia	10 (2.2)		
Spinal anesthesia	2 (0.5)		
Peripheral nerve block			

Data was expressed as the number of patients. Parentheses indicate percentage.

Table 4

Comparison of preoperative cardiopulmonary function test findings between 2 groups.

Variable	**Regional (n = 261)**	**General (n = 87)**	***P* value**
Echocardiography			
Ejection fraction	62.3 ± 9.4	62.7 ± 9.7	.702
Presence of RWMA	51 (15.1)	31 (16.2)	.746
Valvular heart disease grade			.493
Mild	71 (65.7)	39 (64.0)	
Moderate	34 (31.5)	18 (29.5)	
Severe	3 (2.8)	4 (6.6)	
Pulmonary function test			
FEV1	91.8 ± 24.4	96.3 ± 26.5	.070
Degree of obstructive disease			.071
None	186 (66.4)	94 (61.0)	
Mild	50 (17.9)	43 (27.9)	
Moderate	33 (11.8)	14 (9.1)	
Severe	11 (4.0)	3 (2.0)	

Data was expressed as the number of patients. Parentheses indicate percentage.

RWMA = regional wall motion abnormality, FEV1 = forced expiratory volume 1 second.

postoperative oxygen therapy and mechanical ventilation support after surgery. Taken together, these findings suggest that the lower 7-day mortality of RA can be explained by the greater likelihood of intraoperative hemodynamic stability and lower need for intensive respiratory care after surgery.

Previous studies have reported the effect of anesthetic type on perioperative morbidity and mortality but with different results. Sgroi et al[10] presented data from 15,997 patients undergoing infra-inguinal bypass surgery between 2011 and 2016, and reported a reduced length of stay, lower frequency of both postoperative congestive heart failure and acute kidney injury, and a trend toward lower perioperative mortality in patients with RA (1.1 vs 2.2%, $P = .07$). In addition, a cohort study by Ghanami et al[11] including 5462 patients who underwent elective infra-inguinal bypass procedures found no difference in length of stay, morbidity, or mortality after RA versus GA. However, the results of a retrospective study Roberts et al on 20,998 patients who underwent LER[12] showed that RA was associated with decreased 30-day mortality (adjusted odds ratio 0.72, 95%, confidence interval 0.58 to 0.89; $P < .001$) and hospital length of stay compared with GA and suggested that RA use was associated with decreased in-hospital cardiopulmonary and renal complications. Bisgaard et al[7] in their propensity score-matched nationwide cohort study of 17,359 procedures also reported that the 30-day mortality (2.4% vs 3.1%), length of hospital stay, and perioperative complications were significantly lower in RA, suggesting that RA may be associated with a better outcome. In the present study, 7-day mortality was 2.7% in the RA group as compared with 5.6% in the GA group ($P = .045$), but there was no difference in 30-day mortality (RA vs GA: 3.6% vs 6.3%, $P = .083$). These results are similar to those of previous studies; however, there seem to be some obvious differences. In the present study, the short-term (7-day and 30-day) mortality rates were slightly higher than those reported in other studies. This difference is presumed to be due to the fact that this study was conducted in geriatric patients.

Studies on the effect of RA on long-term survival in surgical patients have been conducted in patients with cancer,[13–15] but there are few studies in patients with other pathologies. Although the mechanism underlying the association between

Table 5

One-week and 1-month mortality rates.

Variable	Regional (n = 453)	General (n = 269)	*P* value
Postoperative mortality within 1 wk	12 (2.7)	15 (5.6)	.045
Postoperative mortality within 1 mo	16 (3.6)	17 (6.3)	.083

Data was expressed as the number of patients. Parentheses indicate percentage.

difference in the 1- and 3-year mortality rates between the RA and GA groups; however, the 5-year survival rate was higher in patients receiving RA. Further, the proportion of patients that survived to 14 years postoperatively in those receiving RA was higher than in those undergoing GA (57% vs 58%, *P* = .009). However, Brox et al[17] reported that 30-, 90-, and 365-day mortality rates in elderly patients with hip fracture were not significantly different between neuroaxial anesthesia and GA groups. These results suggest that no specific anesthetic method affects long-term survival in hip fracture surgery, rather than age, sex,

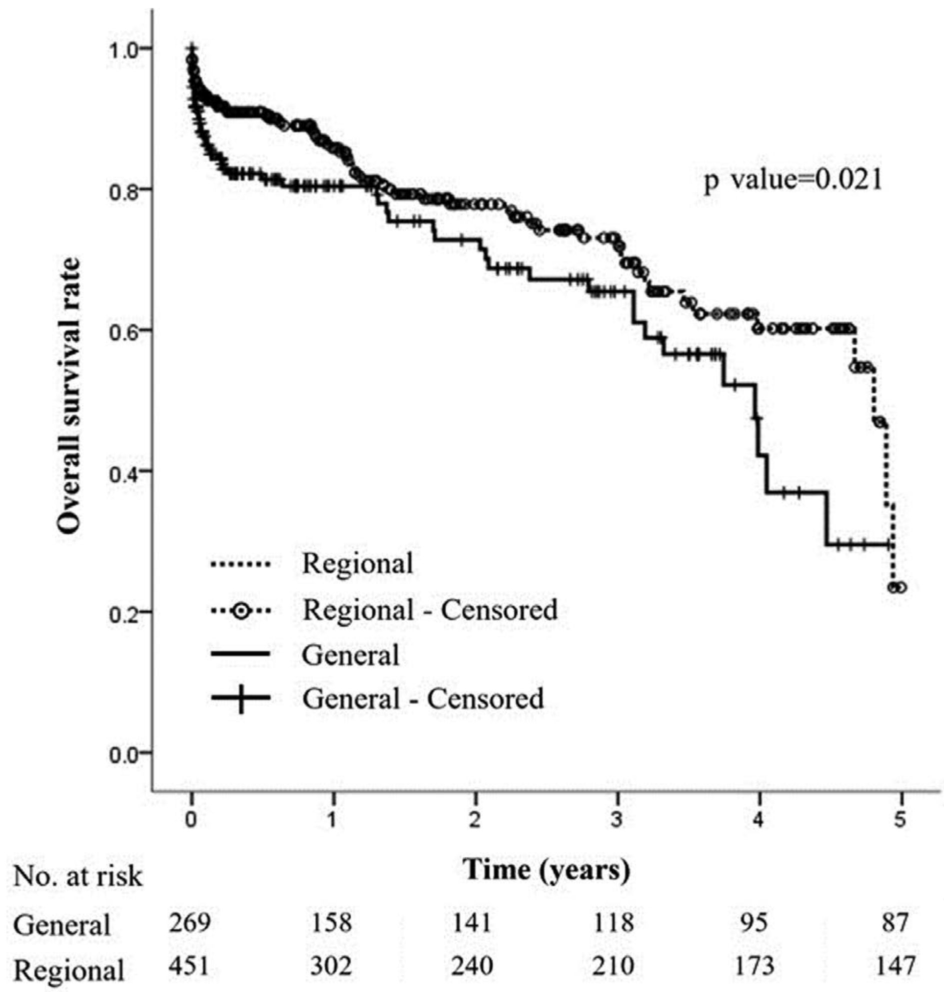

Figure 2. Kaplan-Meier 5-year survival curve. The cumulative survival rate in patients undergoing lower extremity revascularization under general anesthesia (line) or regional anesthesia (dot). *P* values were obtained by log-rank test.

Table 6

Intraoperative catheterization and vasoactive medications.

Variable	Regional (n = 453)	General (n = 269)	*P* value
Intraoperative catheterization			
Arterial line	408 (90.1)	262 (97.4)	.000
Central venous line	211 (46.6)	203 (75.5)	.000
Vasoactive medications			
Dopamine	212 (46.8)	193 (72.0)	.000
Epinephrine	5 (1.1)	10 (3.7)	.017
Norepinephrine	5 (1.1)	8 (3.0)	.068
Amiodarone	0 (0)	1 (0.4)	.194

Data was expressed as the number of patients. Parentheses indicate percentage.

neuraxial anesthesia and long-term survival after total hip or knee joint replacement is unknown, Chen et al[16] reported no

and comorbidities. A surprising result of the present study was that the 5-year survival rate of patients with RA was higher than that of patients with GA. To the best of our knowledge, this is the first study on the effect of anesthesia type on the long-term survival of patients with LER. The reason why the RA group had a high 5-year survival rate is not well explained. According to several studies on anesthetic factors affecting the long-term survival (1-year mortality) of patients undergoing non-cardiac surgery, the degree of hypnosis and presence of intraoperative hypotension have been reported as outcome predictors.[18,19] These results are similar to those of the present study in that the frequency of use of vasoactive drugs during RA was lower than that during GA, suggesting that fewer hemodynamic changes during RA are advantageous not only for short-term survival, but also from a long-term perspective. To date, there is no evidence that GA or anesthetics themselves have a clear negative effect on long-term

Table 7

Postoperative cardiopulmonary complications and hospital stay.

Variable	Regional (n = 453)	General (n = 269)	*P* value
Oxygen therapy	55 (12.1)	56 (20.8)	.002
Mechanical ventilatory support	8 (1.8)	17 (6.3)	.001
Pulmonary complications	17 (3.8)	13 (4.8)	.486
Pulmonary consultation	16 (3.5)	13 (4.8)	.389
Cardiology consultation	11 (2.4)	10 (3.7)	.315
Postoperative stroke within 1 mo	3 (0.7)	2 (0.7)	.899
Postoperative AMI within 1 mo	7 (1.6)	5 (1.9)	.750
Length of hospital stay (d)	18.7 ± 21.7	25.0 ± 97.3	.193
Toe or leg amputation	16 (3.5)	13 (4.8)	.393
Reoperation	78 (17.2)	32 (11.9)	.054

Data was expressed as the number of patients. Parentheses indicate percentage.
AMI = acute myocardial infarction.

survival in surgical patients. However, looking at the patient distribution in the unmatched data of this study, the number of patients who underwent RA was higher than that of those who underwent GA (RA vs GA: 69.2% vs 30.8%). This is quite different from other previous studies because our hospital has a clear preference for RA in patients undergoing LER. Absolute or relative contraindications to RA include emergency surgery and PT/aPTT abnormalities. In this study, the GA group in the unmatched data had a significantly higher percentage of emergency surgery and preoperative PT/aPTT abnormalities than the RA group. In addition, the GA group in the unmatched data had a significantly higher percentage of concurrent coronary artery disease than the RA group. After propensity score matching, although these variables lost their statistical significance, since the frequency of these variables in the GA group was still higher than that in the RA group, they may have contributed to the 5-year survival rate. This is because PAD and coronary artery disease share the mechanism of atherosclerosis,[5] and patients with coronary artery disease may have limitations in performing RA due to antithrombotic drugs use. In addition, results similar to those of a previous study showed that an increase in cardiac biomarkers levels after surgery can lead to an increase in myocardial injury and thus affect long-term survival.[20] From this point of view, further studies with different designs and statistical analyses should be conducted.

This study had several limitations. First, it was a retrospective review of a large database, which has inherent limitations. Second, although propensity score matching was used to exclude the effects of variables other than anesthesia modality as far as possible, the operating and anesthesia times and surgical complications such as blood loss or wound infection were not controlled; however, any differences were unlikely to be clinically significant. Third, as mentioned above, the fact that this center has a preference for RA should not be overlooked when interpreting the results of our study.

Despite these limitations, our present findings suggest that RA may positively affect short-term mortality and health outcomes in geriatric patients undergoing LER for PAD. Therefore, the choice of RA should not be limited to the selection of anesthesia for these patients until further prospective randomized controlled studies have been performed.

Author contributions

Conceptualization: Jae Hoon Lee, Ki Hyuk Park, Woon Seok Roh.
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