Am J Transl Res 2025;17(5):4054-4061
www.ajtr.org /ISSN:1943-8141/AJTR0163096

Original Article

Prospective study of continuous low-dose norepinephrine infusion during induction of anesthesia: effects on the stability of blood pressure and recovery quality in elderly patients undergoing robotic radical prostatectomy

Aini Maimaitiming[1], Bing Zhang[1], Jie Chen[2], Xiaohai Wang[3]

[1]Department of Anesthesiology, The Affiliated Cancer Hospital of Xinjiang Medical University, Urumqi, Xinjiang, The People's Republic of China; [2]Department of Anesthesiology, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, The People's Republic of China; [3]Department of Anesthesiology, Taikang Xianlin Drum Tower Hospital, Nanjing, Jiangsu, The People's Republic of China

Received January 4, 2025; Accepted May 13, 2025; Epub May 15, 2025; Published May 30, 2025

Abstract: Objective: To assess the effect of low-dose norepinephrine infusion on hemodynamic changes during anesthesia induction and its correlation with postoperative recovery in elderly patients undergoing robot-assisted radical prostatectomy. Methods: A prospective observational study was conducted on 63 elderly patients divided into two groups: the norepinephrine group (NE group) receiving 2-5 μg/kg·h norepinephrine by injection pump during anesthesia induction, and the control group (C group) with regular anesthesia. Heart rate (HR) and invasive blood pressure (BP) were recorded at four time points: before induction, pre-intubation lowest value (T1), post-intubation (T2), and lowest BP between intubation and skin incision (T3). Postoperative recovery (QoR-15) was evaluated on Days 1 and 3. Results: Statistically significant differences in systolic (SBP) and diastolic blood pressure (DBP) were observed between groups at T1 and T3 ($P<0.05$), but no significant differences in HR were found at any time point ($P>0.05$). The NE group had significantly higher SBP, DBP, and HR at T1 and T3 compared to the C group ($P<0.05$). Hemodynamic stability was significantly better in the NE group ($P<0.05$). No significant differences were seen in QoR-15 scores or postoperative hospital stay between groups ($P>0.05$), but the Barthel Index increased significantly in the NE group ($P<0.05$). Conclusions: Continuous low-dose norepinephrine infusion effectively reduced blood pressure and heart rate fluctuations during anesthesia induction. However, the study showed only a weak correlation between intraoperative hemodynamic changes and postoperative recovery.

Keywords: Hemodynamic stability, anesthesia induction, norepinephrine, postoperative recovery

Introduction

As the general population lives longer [1] and health care is enhanced, anesthesiologists are more likely to encounter more geriatric surgical patients, many of whom are frail or suffer from multiple diseases. According to the United Nations, by 2050, there will be 400 million Chinese citizens aged 65 and older [2]. In addition, approximately 45 million surgeries are performed annually in China, and 40% of patients are older than 65 years of age (data obtained from the National Bureau of Statistics of China). Because of the increasing proportion of the elderly population, anesthesiologists have been searching for good techniques to optimize the perioperative safety and experience of patients [3, 4].

It is well known that general anesthetics have a strong effect on hemodynamic stability, especially during the anesthesia induction period [5], and hemodynamic changes throughout a surgery even affect the patient's postoperative recovery [6, 7]. Previous studies have shown that increased blood pressure and heart rate (HR) may increase the risk of arrhythmia, myocardial infarction, and cerebral hemorrhage [5,

https://doi.org/10.62347/HWWN6029

8]; however, dramatically decreased blood pressure may also result in cerebral ischemia, myocardial injury and kidney dysfunction among susceptible individuals, especially those with advanced age or those suffering from coronary artery disease, hypertension or cerebrovascular disorders [7, 9, 10]. Many drugs can be used to minimize hemodynamic fluctuation during the anesthesia induction period. However, some studies have presented diverse results regarding this issue and used different techniques to minimize hemodynamic changes [11, 12]. Furthermore, the optimal management for decreasing hemodynamic alterations in patients and the best drug dosage choice are not yet clear [13-15]. In the clinical setting, we infused low-dose norepinephrine through the general anesthesia induction period to soften the hemodynamic effects of anesthetics in elderly individuals.

Therefore, the purpose of this study was to evaluate the effects of a continuous infusion of low-dose norepinephrine on the hemodynamic changes during the induction of anesthesia and postoperative recovery in elderly patients through collection and analysis of the patient's hemodynamic data, the Mandarin version of the Quality of Recovery-15 (QoR-15) score, [16-18] and the Barthel Index [19].

Patients and methods

Study patients and study design

After approval by the Ethics Committee of Drum Tower Hospital, Medical College of Nanjing University (2020-124-02), and provision of written informed consent, 63 elderly patients aged between 65 and 85 years old, with American Society of Anesthesiologists (ASA) physical status II-III and scheduled for robot-assisted radical prostatectomy for prostate cancer, were included in this prospective observational study. The exclusion criteria included patients who refused to participate in the study, patients with cardiac implanted pacemakers, patients who presented with interference from any of the techniques or drugs used in the present study, patients who were obese if their body mass index (BMI) was ≥30 kg/m^2, and patients with preexisting severe heart, liver, or kidney dysfunction.

After arrival in the operating room and routine monitoring, including electrocardiogram, pulse oximetry, nasopharyngeal temperature, and noninvasive arterial pressure, the radial artery was cannulated to constantly monitor hemodynamic changes through the general anesthesia induction period. The researchers responsible for the follow-up postoperative recovery scoring were blinded to the study hypothesis regarding the effects of low-dose norepinephrine on hemodynamic changes during the induction of anesthesia and the relationship between hemodynamic stability and postoperative recovery. According to the habits of different anesthesiologists, general anesthesia was induced with intravenous injection of midazolam, etomidate and/or propofol, fentanyl, and rocuronium with or without injection of norepinephrine by an injection pump (2-5 μg/kg*h) through the induction period (Supplementary Table 1). Before induction, hemodynamic data such as heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice in awake patients without any medication, and their average values were taken as the preoperative baseline value (T0). The extreme points of hemodynamic fluctuations at the following three time points were recorded: before endotracheal intubation (T1), immediately after intubation (T2), and the lowest value of blood pressure between intubation and skin incision (T3). After surgery, patients were delivered to the recovery room or AICU for recovery and then returned to the ward the next morning. Postoperative recoveries and physical function were evaluated by the QoR-15 at postoperative Day 1 and Day 3 and by the Barthel Index at postoperative Day 1. The total score on the QoR-15 ranges from 0 (the poorest quality of recovery) to 150 (the best quality of recovery), and the Barthel Index ranges from 0 (the poorest physical function) to 100 (the best physical function).

Definition of the extreme points of blood pressure fluctuation

Fluctuations in a patient's blood pressure during the anesthesia induction period were quantified by calculating the variance of the patient's extreme point blood pressure record (T1, T2, and T3) during induction. Variance is a measure of the data spread. Therefore, a patient whose blood pressure fluctuates more during the induction period, commonly known as blood pressure lability, will have greater variance than a patient whose blood pressure remains rela-

Table 1. Patient characteristics in the two groups

Characteristic	NE group (n = 33)	C group (n = 30)	t/z/χ^2	*P*
Age (yr)[a]	71.0 (66.0-76.0)	71.5 (68.9-75.0)	0.596	0.507
BMI (kg/m^2)[b]	24.6 (21.5-26.8)	25.1 (22.9-27.3)	1.108	0.349
ASA class II/III	13 (39%)/20 (61%)	14 (47%)/16 (53%)	0.339	0.560
Hypertension	24 (72.4%)	21 (70%)	0.057	0.811
Diabetes	1 (3%)	2 (6.7%)	0.458	0.498
Coronary artery disease	4 (12.1%)	4 (13.3%)	0.021	0.885

Data are expressed as the median (interquartile range) or number of patients (%) as appropriate. [a]Mann-Whitney U test. [b]Student's t test. NE group = low-dose norepinephrine group; C group = regular anesthesia induction group. ASA = American Society of Anesthesiologists; BMI = body mass index.

Table 2. Hemodynamic data at the different time points

	NE group (n = 33)	C group (n = 30)	t/z	*P*
SBP (mmHg)				
T0	164.2±13.9	169.9±13.9	1.557	0.125[b]
T1	129.1±14.3	116.8±21.6*	2.650	0.011[b]
T2	167.3±22.2	171.8±25.6	0.751	0.455[b]
T3	128.5±15.4	113.6±17.4*	3.625	0.000[a]
HR (bpm)				
T0	73.7±10.1	70.2±10.6	0.896	0.412[a]
T1	65.6±10.0	60.9±10.6	1.803	0.076[b]
T2	79.9±15.4	86.0±13.4	1.676	0.099[b]
T3	59.6±8.9	59.5±11.9	0.054	0.957[b]
DBP (mmHg)				
T0	78.9±8.5	75.3±12.1	1.404	0.165[b]
T1	71.4±12.1	56.5±11.0*	5.074	0.000[a]
T2	84.3±11.6	82.1±15.4	0.654	0.515[b]
T3	67.3±7.2	59.6±9.6*	3.618	0.001[b]

Data are expressed as the mean ± SD. [a]Mann-Whitney U test. [b]Student's t test. *Denotes significance in different states between groups (P<0.05). NE group = low-dose norepinephrine group; C group = regular anesthesia induction group.

tively constant. Blood pressure fluctuations at each time point were calculated according to the formula $T_x \text{ variance} = \frac{T_x - T_{x-1}}{T_{x-1}} \times 100\%$, where T_x is a patient's blood pressure at a particular time point and T_{x-1} is the patient's blood pressure before that time point. Hemodynamic stability was defined as variance at any time point of less than 30%.

Statistical analysis

The primary outcome was hemodynamic changes in the general anesthesia induction period. The secondary outcome was the quality of postoperative recoveries. According to the primary outcome, the power was 91% (calculated by PASS version 11.0) with a sample size of 63.

For statistical analysis, the SPSS package (version 26.0, SPSS, Chicago, IL) was used. All quantitative variables were tested for normal distribution by means of the Kolmogorov-Smirnov test and were presented as the median (interquartile range) or the mean ± SD. For comparisons of quantitative variables between the groups, Student's t test was used for normal data, and for nonnormal data, the Mann-Whitney test was used. Categorical variables and proportions were compared between the groups using the chi-square test or Fisher's exact test as needed. A *P* value <0.05 was considered significant.

Results

Between September 2, 2020 and December 5, 2020, a total of 63 eligible patients undergoing robot-assisted radical prostatectomy were enrolled in the study. Chi-square tests and Student's t tests showed no significant differences regarding age, BMI, background history, or ASA classification between the groups (**Table 1**).

Primary outcomes

The hemodynamic data at the different timepoints are presented in **Table 2**. There were no significant differences between the two groups in baseline SBP, HR or DBP (P = 0.125, 0.415 and 0.165, respectively). Significant differences in SBP and DBP were observed between the two groups at T1 (P = 0.011 and 0.000 for SBP and DBP, respectively) and T3 (P<0.001 and = 0.001 for SBP and DBP, respectively). The HR showed no significant differences at any time

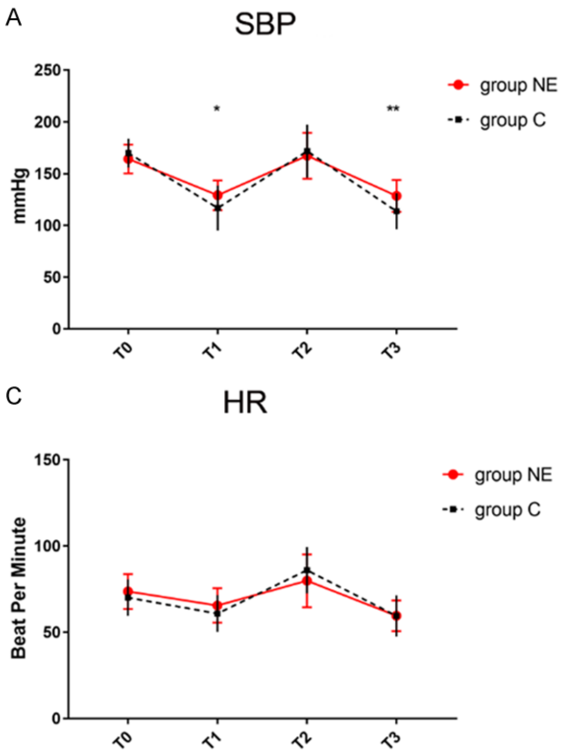

Figure 1. Effect of norepinephrine on hemodynamic changes in the anesthesia induction period (A: Systolic blood pressure; B: Diastolic blood pressure; C: Heart rate). The hemodynamic data were taken before induction (T0), before endotracheal intubation (T1), immediately after intubation (T2), and before skin incision (T3). The data are presented as the mean ± standard deviation; NE group - low-dose norepinephrine group; C group - regular anesthesia induction group.

point, and SBP and DBP presented no significant differences at T2 (**Figure 1**). There were significant differences in SBP, DBP, and HR variances between the two groups at T1, T2, and T3. The SBP variance was higher in the C group than in the NE group at T1 ($P<0.05$) (**Table 3**). The induction time, i.e., the time between the start of injection of anesthetic, and skin incision showed no significant differences between the two groups. The hemodynamic data stability was significantly higher in the NE group than in the C group (P = 0.018, 0.021 and 0.001 for SBP, HR and DBP, respectively) (**Table 3**). There were no significant differences in the dosage of anesthetics for induction between the two groups (Supplementary Table 1).

Secondary outcomes

The effect of norepinephrine usage on postoperative recovery is presented in **Table 4**. The QoR-15 score showed no statistical significance at postoperative Days 1 and 3 between the groups (120.0 vs. 120.0 and 126.0 vs. 128.5, respectively). Postoperative nausea or vomiting (PONV), flatus time, and hospital stay duration after surgery also showed no significant differences between groups ($P>0.05$). The Barthel Index at postoperative Day 1 was significantly higher in the NE group than in the C group ($P<0.05$). The first ambulation times in the C group were longer than those of the NE group (P = 0.029, 23.1 vs. 20.5 in the C group vs. the NE group).

The relationships between postoperative recovery and hemodynamic stability at the induction period are introduced in **Table 5**. The QoR-15 at postoperative Day 1 and Day 3 and the Barthel Index showed no significant differences between the hemodynamically stable group and the unstable group. First ambulation time, hospital stay duration after surgery, and PONV also showed insignificant differences between the groups. Furthermore, flatus time decreased significantly in the hemodynamically stable group (P = 0.039 13.2 vs. 24.0 in the stable group vs. the nonstable group).

Discussion

It is essential for anesthesiologists to improve intraoperative safety and to enhance the quality of postoperative recovery. Dramatic hemodynamic changes may increase cardiac and important organ dysfunction. The present study demonstrated that low-dose induction of norepinephrine (2-5 μg/kg*h) improved the stabil-

Table 3. Blood pressure and HR variance between the groups

	NE group (n = 33)	C group (n = 30)	t/z/x^2	*P*
Induction time (min)	30.0 (22.5-35.0)	30 (23.75-40.0)	0.588	0.557
SBP variance (%)				
T1	-21.2±8.0	-31.4±10.3*	4.400	0.000[b]
T2	30.3±17.3	50.9±30.4*	2.711	0.007[a]
T3	-22.2±11.6	-32.7±13.1*	3.377	0.001[b]
Stability of SBP	16 (48.5%)	6 (20%)*	5.610	0.018
HR variance (%)				
T1	-10.7±10.0	-12.7±11.9	0.702	0.485[b]
T2	22.6±20.4	42.4±23.0*	3.798	0.000[b]
T3	-23.8±13.3	-30.4±12.3*	2.052	0.046[b]
Stability of HR	17 (51.5%)	7 (23.3%)*	5.292	0.021
DBP variance (%)				
T1	-9.4±12.9	-23.9±14.2	3.861	0.000[a]
T2	19.4±15.2	49.2±34.8*	3.688	0.000[b]
T3	-19.2±10.5	-25.7±14.6*	1.898	0.047[b]
Stability of DBP	23 (69.7%)	8 (26.7%)*	11.642	0.001

Data are expressed as the mean ± SD or number of patients (%) as appropriate. [a]Mann-Whitney U test. [b]Student's t test. *Denotes significance in different states between the groups ($P<0.05$). - Indicates that the hemodynamic value decreased at this time point. NE group = low-dose norepinephrine group; C group = regular anesthesia induction group.

ity of hemodynamic changes at the anesthesia induction stage in elderly people. In addition, we observed that there were no or only weak associations between hemodynamic stability and the quality of postoperative recovery (**Tables 4**, **5**).

Clinically, fluctuations in blood pressure induced by standardized anesthesia remain a common and expected response and are considered in principle to be compensated for by vasoactive drugs and intravenous fluids or anesthetics [20, 21]. Usually, because of decreased cardiovascular tension and increased body fat proportion, elderly individuals are more vulnerable to drug-induced adverse effects, and certain drugs may have more profound and prolonged effects [22, 23]. Studies have implicated several anesthetics to have a stabilizing effect on hemodynamic changes during the anesthesia induction period [24, 25]. Receiving a preoperative fluid bolus decreased the incidence of significant blood pressure drops and the need for vasoactive drugs during anesthesia induction [26]. Theoretically, concomitant use of vasoactive drugs and preoperative fluids may be a superior approach to prevent a drop in blood pressure during the induction of anesthesia. Solitary use of α1-agonists may lead to abundant vasoconstriction and poor perfusion; thus, these drugs should not be used as primary drugs before ruling out or normalizing a low level of venous return with intravenous fluids [27, 28]. However, rapid rehydration and fluid overload may lead to myocardial edema and compromised cardiovascular function [29]. The benefits of the use of vasopressors instead of conventional fluid loading during induction were not verified in the studies; thus, more studies are needed regarding hemodynamic stability and postoperative outcomes. It has been suggested that being proactive in minimizing perioperative insufficiency and fluctuations in blood pressure is beneficial in reducing the incidence of complications [7, 10]. It is necessary to begin this work before surgery during induction of anesthesia [30, 31]. The aim of the study was to demonstrate that norepinephrine is effective in minimizing BP fluctuation during general anesthesia induction without complications. Indeed, the induction of anesthesia should be considered one of the most critical stages in general anesthesia, since it presents challenges for patient safety. Anesthesia-inducing drugs can inhibit the hyperexcitability of the sympathetic nerve associated with endotracheal intubation and easily lead to vasodilation and intraoperative hypotension. If the dose of anesthesia-inducing drugs is reduced to prevent hypotension during induction, it may lead to serious cardiovascular side effects of endotracheal intubation. This paradox was more pronounced among the elderly [32]. In those studies, no drugs had been provided to prevent sympathetic hyperactivation following intubation, yet hemodynamic fluctuations were significantly observed in comparison with the pre-injection values [12]. Attenuation of such changes in cardiovascular responses is vital in the prevention of perioperative mortality and morbidity [12, 33]. Studi-

Table 4. Postoperative data comparisons between the two groups

	NE group (n = 33)	C group (n = 30)	t/z/x^2	*P*
Post-Day 1 QoR-15	120.0 (115.5-123.0)	120.0 (117.0-123.5)	0.540	0.589[a]
Post-Day 3 QoR-15	126.0 (120.0-133.0)	128.5 (122.8-140.0)	1.012	0.311[a]
Post-Day 1 Barthel Index	66.1±9.8	58.7±15.0*	2.338	0.023[b]
Postoperative nausea or vomiting	7 (21.2%)	4 (13.3%)	0.677	0.411
Flatus time (h)	24.0 (18.0-26.4)	26.4 (21.0-36.0)	1.275	0.202[a]
First ambulation time (h)	20.5±5.3	23.1±5.0*	2.180	0.029[a]
Hospital stay duration after surgery (days)	6.0 (4.5-8.0)	7.0 (5.0-10.0)	1.628	0.104[a]

Data are expressed as the M (IQR), mean ± SD or number of patients (%) as appropriate. [a]Mann-Whitney U test. [b]Student's t test. *Denotes significance in different states between the groups (P<0.05). NE group = low-dose norepinephrine group; C group = regular anesthesia induction group.

Table 5. Relationships between postoperative recovery and hemodynamic data stability during the induction period

	Stable (n = 12)	Not stable (n = 51)	t/z/x^2	*P*
Post-Day 1 QoR-15	120.0 (115.8-124.5)	120.0 (117.0-123.0)	0.079	0.937[a]
Post-Day 3 QoR-15	131.0 (124.3-143.4)	127.0 (119.0-135.0)	1.244	0.214[a]
Post-Day 1 Barthel Index	61.3±12.8	62.8±13.1	0.380	0.705[b]
Postoperative nausea or vomiting	0 (0.0%)	11 (21.6%)	1.818	0.178
Flatus time (h)	13.2 (9.6-28.2)	24.0 (21.6-33.6)	2.062	0.039[a]
First ambulation time (h)	21.6 (21.6-24.0)	21.6 (19.2-24.0)	0.893	0.372[a]
Hospital stay duration after surgery (days)	6.0 (5.0-8.75)	6.0 (5.0-9.0)	0.265	0.791[a]

Data are expressed as the M (IQR), mean ± SD or number of patients (%) as appropriate. [a]Mann-Whitney U test. [b]Student's t test. Stable = SBP, HR and DBP variance at T1, T2 and T3 below 30%; Not stable = SBP, HR or DBP variance at T1, T2 or T3 over 30%.

es have shown that during and after noncardiac surgery, hyperactivation of the sympathetic nervous system occurs, which could lead to a mismatch between the supply of and demand for myocardial oxygen and to subsequent myocardial infarction [32, 34]. Our study showed that norepinephrine could dampen the blood pressure changes in the induction period; furthermore, blood pressure drops in elderly individuals at the induction time were mostly caused by anesthetics. Thus, norepinephrine may be a better option for preventing a drop in blood pressure than preinduction fluid infusion.

In terms of norepinephrine use and postoperative recovery, this study found that norepinephrine increased the Barthel Index on the first postoperative day and reduced the time to first ambulation. At the same time, in our study, stable blood pressure had no effect on PONV, which was contradictory to other studies [35]. Elderly patients tend to exhibit exaggerated hypoactivity after surgery [22]. In our study, the use of norepinephrine reduced the postoperative immobility time, which has not been previously reported. Hirsch [7] et al. reported that decreases in blood pressure during surgery were not associated with a significant increase in the risk of postoperative delirium. Rather, fluctuations in blood pressure during surgery were associated with early postoperative delirium. Our findings suggested that blood pressure stability in the anesthesia induction period was not related to the QoR-15 scale after surgery, and its relationship with postoperative delirium needs to be further examined.

Limitations

Our findings may be somewhat limited by several factors, such as the low number of subjects (n = 63), which may have contributed to a reduced statistical power of the secondary outcome results. Another potential concern of our study was the anesthesia induction period, where hemodynamic measurements changed dramatically compared to any other perioperative period, which may have been the result of the hemodynamic changes in our study being more prominent than in other studies [10, 23]. Furthermore, we observed hemodynamic changes with or without norepinephrine only in the anesthesia induction period and not throughout the operation process, which may not have had a profound influence on postoperative recovery. The changes in electrical heart function and the depth of anesthesia were not assessed. Finally, since this was a single-center study, our results may not be applicable to other settings.

Conclusion

The results of this study showed that continuous infusion of low-dose norepinephrine (2-5 μg/kg*h) could effectively reduce BP and HR fluctuations during the induction of anesthesia. Also, there was only a weak association between blood pressure fluctuations in the induction period and postoperative recovery.

Disclosure of conflict of interest

None.

Address correspondence to: Bing Zhang, Department of Anesthesiology, The Affiliated Cancer Hospital of Xinjiang Medical University, Urumqi, Xinjiang, The People's Republic of China. E-mail: drzhangbing@xjmu.edu.cn; Jie Chen, Department of Anesthesiology, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, The People's Republic of China. E-mail: 4364683@qq.com

References

[1] Partridge L, Deelen J and Slagboom PE. Facing up to the global challenges of ageing. Nature 2018; 561: 45-56.
[2] Fang EF, Scheibye-Knudsen M, Jahn HJ, Li J, Ling L, Guo H, Zhu X, Preedy V, Lu H, Bohr VA, Chan WY, Liu Y and Ng TB. A research agenda for aging in China in the 21st century. Ageing Res Rev 2015; 24: 197-205.
[3] Murphy GS, Szokol JW, Greenberg SB, Avram MJ, Vender JS, Nisman M and Vaughn J. Preoperative dexamethasone enhances quality of recovery after laparoscopic cholecystectomy: effect on in-hospital and postdischarge recovery outcomes. Anesthesiology 2011; 114: 882-890.
[4] Alizadeh R and Fard ZA. Renal effects of general anesthesia from old to recent studies. J Cell Physiol 2019; 234: 16944-16952.
[5] Choi BH and Lee YC. Effective bolus dose of sufentanil to attenuate cardiovascular responses in laryngoscopic double-lumen endobronchial intubation. Anesth Pain Med 2016; 6: e33640.
[6] Futier E, Lefrant JY, Guinot PG, Godet T, Lorne E, Cuvillon P, Bertran S, Leone M, Pastene B, Piriou V, Molliex S, Albanese J, Julia JM, Tavernier B, Imhoff E, Bazin JE, Constantin JM, Pereira B and Jaber S; INPRESS Study Group. Effect of individualized vs standard blood pressure management strategies on postoperative organ dysfunction among high-risk patients undergoing major surgery: a randomized clinical trial. JAMA 2017; 318: 1346-1357.
[7] Hirsch J, DePalma G, Tsai TT, Sands LP and Leung JM. Impact of intraoperative hypotension and blood pressure fluctuations on early postoperative delirium after non-cardiac surgery. Br J Anaesth 2015; 115: 418-426.
[8] Simpson GD, Ross MJ, McKeown DW and Ray DC. Tracheal intubation in the critically ill: a multi-centre national study of practice and complications. Br J Anaesth 2012; 108: 792-799.
[9] Sun LY, Wijeysundera DN, Tait GA and Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology 2015; 123: 515-523.
[10] Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, Cywinski J, Thabane L and Sessler DI. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. Anesthesiology 2013; 119: 507-515.
[11] Kim WY, Lee YS, Ok SJ, Chang MS, Kim JH, Park YC and Lim HJ. Lidocaine does not prevent bispectral index increases in response to endotracheal intubation. Anesth Analg 2006; 102: 156-159.
[12] Sameenakousar, Mahesh and Srinivasan KV. Comparison of fentanyl and clonidine for attenuation of the haemodynamic response to laryngocopy and endotracheal intubation. J Clin Diagn Res 2013; 7: 106-111.
[13] Ugur B, Ogurlu M, Gezer E, Nuri Aydin O and Gürsoy F. Effects of esmolol, lidocaine and fentanyl on haemodynamic responses to endotracheal intubation: a comparative study. Clin Drug Investig 2007; 27: 269-277.
[14] Ko SH, Kim DC, Han YJ and Song HS. Small-dose fentanyl: optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesth Analg 1998; 86: 658-661.
[15] Ahn E, Kang H, Choi GJ, Park YH, Yang SY, Kim BG and Choi SW. Intravenous lidocaine for effective pain relief after a laparoscopic colecto-

my: a prospective, randomized, double-blind, placebo-controlled study. Int Surg 2015; 100: 394-401.

[16] Lee L, Tran T, Mayo NE, Carli F and Feldman LS. What does it really mean to "recover" from an operation? Surgery 2014; 155: 211-216.

[17] Royse CF, Newman S, Chung F, Stygall J, McKay RE, Boldt J, Servin FS, Hurtado I, Hannallah R, Yu B and Wilkinson DJ. Development and feasibility of a scale to assess postoperative recovery: the post-operative quality recovery scale. Anesthesiology 2010; 113: 892-905.

[18] Ni J, El-Ansary D, Heiberg J, Shen G, You Q, Gao Y, Liu K, Ke H and Royse CF. Validation of a revised Mandarin Chinese language version of the Postoperative Quality of Recovery Scale. Anaesth Intensive Care 2018; 46: 278-289.

[19] Leung SO, Chan CC and Shah S. Development of a Chinese version of the Modified Barthel Index-validity and reliability. Clin Rehabil 2007; 21: 912-922.

[20] Hahn RG and Lyons G. The half-life of infusion fluids: an educational review. Eur J Anaesthesiol 2016; 33: 475-482.

[21] Navarro LH, Bloomstone JA, Auler JO Jr, Cannesson M, Rocca GD, Gan TJ, Kinsky M, Magder S, Miller TE, Mythen M, Perel A, Reuter DA, Pinsky MR and Kramer GC. Perioperative fluid therapy: a statement from the international Fluid Optimization Group. Perioper Med (Lond) 2015; 4: 3.

[22] Garcia PS, Duggan EW, McCullough IL, Lee SC and Fishman D. Postanesthesia care for the elderly patient. Clin Ther 2015; 37: 2651-2665.

[23] Aurini L and White PF. Anesthesia for the elderly outpatient. Curr Opin Anaesthesiol 2014; 27: 563-575.

[24] Hosseinzadeh H, Eidy M, Golzari SE and Vasebi M. Hemodynamic stability during induction of anesthesia in elderlypatients: Propofol + Ketamine versus Propofol + Etomidate. J Cardiovasc Thorac Res 2013; 5: 51-54.

[25] Doi M, Hirata N, Suzuki T, Morisaki H, Morimatsu H and Sakamoto A. Safety and efficacy of remimazolam in induction and maintenance of general anesthesia in high-risk surgical patients (ASA Class III): results of a multicenter, randomized, double-blind, parallel-group comparative trial. J Anesth 2020; 34: 491-501.

[26] Myrberg T, Lindelöf L and Hultin M. Effect of preoperative fluid therapy on hemodynamic stability during anesthesia induction, a randomized study. Acta Anaesthesiol Scand 2019; 63: 1129-1136.

[27] Levy B, Fritz C, Tahon E, Jacquot A, Auchet T and Kimmoun A. Vasoplegia treatments: the past, the present, and the future. Crit Care 2018; 22: 52.

[28] Myburgh JA and Mythen MG. Resuscitation fluids. N Engl J Med 2013; 369: 1243-1251.

[29] O'Connor ME and Prowle JR. Fluid overload. Crit Care Clin 2015; 31: 803-821.

[30] Muller L, Brière M, Bastide S, Roger C, Zoric L, Seni G, de La Coussaye JE, Ripart J and Lefrant JY. Preoperative fasting does not affect haemodynamic status: a prospective, non-inferiority, echocardiography study. Br J Anaesth 2014; 112: 835-841.

[31] Kratz T, Hinterobermaier J, Timmesfeld N, Kratz C, Wulf H, Steinfeldt T, Zoremba M and Aust H. Pre-operative fluid bolus for improved haemodynamic stability during minor surgery: a prospectively randomized clinical trial. Acta Anaesthesiol Scand 2018; 62: 1215-1222.

[32] Udelsman R, Norton JA, Jelenich SE, Goldstein DS, Linehan WM, Loriaux DL and Chrousos GP. Responses of the hypothalamic-pituitary-adrenal and renin-angiotensin axes and the sympathetic system during controlled surgical and anesthetic stress. J Clin Endocrinol Metab 1987; 64: 986-994.

[33] Chraemmer-Jørgensen B, Hertel S, Strøm J, Høilund-Carlsen PF and Bjerre-Jepsen K. Catecholamine response to laryngoscopy and intubation. The influence of three different drug combinations commonly used for induction of anaesthesia. Anaesthesia 1992; 47: 750-756.

[34] Landesberg G, Beattie WS, Mosseri M, Jaffe AS and Alpert JS. Perioperative myocardial infarction. Circulation 2009; 119: 2936-2944.

[35] Yang L, Xu YJ, Shen J, Lou FF, Zhang J and Wu J. Propofol-based total intravenous anesthesia decreases the incidence of postoperative nausea and vomiting without affecting flap survival in free flap breast reconstruction. Gland Surg 2020; 9: 1406-1414.

Supplementary Table 1. Comparison of anesthetics in the induction period

	Group NE	Group C	t/z	*P*
Midazolam (mg/kg)	0.029 (0.026-0.031)	0.029 (0.025-0.035)	0.014	0.989[a]
Etomidate (mg/kg)	0.208 (0.170-0.250)	0.206 (0.149-0.260)	0.296	0.767[a]
Propofol (mg/kg)	0.036 (0.000-0.048)	0.013 (0.000-0.083)	0.825	0.409[a]
Fentanyl (ug/kg)	3.677 (3.290-3.914)	3.280 (20857-3.930)	1.714	0.086[a]
Rocuronium	0.114 (0.103-0.126)	0.108 (0.101-0.118)	1.655	0.103[b]

Data are expressed as median (interquartile range). [a]Mann-Whitney U test. [b]Student's t test. Group NE = low dosage norepinephrine group; Group C = regular anesthesia induction group.