Original Article

Effect of thoracic paravertebral block on intraoperative hypotension and postoperative pain in patients undergoing breast cancer surgery under general anesthesia: a retrospective study

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Background: To retrospectively compare the effects of general anesthesia (GA) and thoracic paravertebral block (TPVB) combined with general anesthesia on the incidence of hypotension and postoperative pain in breast cancer (BC) surgery.

Methods: We retrospectively collected the medical records of patients who underwent BC surgery under general anesthesia from January 2018 to December 2020, and divided them into 2 groups according to the patient's anesthesia management method: GA group (Group G) and TPVB combined with GA group (Group T). During the operation, the use of boosting drugs and ephedrine, amount of fluid infusion, amount of bleeding, and operation time of the 2 participant groups were recorded, as well as the pain score in the resting state.

Results: During anesthesia, the bispectral index (BIS) value of Group G was significantly lower than that of Group T, the use of sufentanil and the use rate of ephedrine were significantly higher than that of Group T, and the difference was statistically significant ($P<0.05$). At the T4 time point, the blood pressure [systolic blood pressure/diastolic blood pressure (SBP/DBP)] of Group G was higher than that of Group T; at time point T3, the blood pressure (SBP/DBP) of Group G was lower than that of Group T. At the T4 time point, the heart rate of G group was higher than that of Group T, and the heart rate of G group was lower than that of Group T at the time points T2 and T3. The difference between the 2 groups was statistically significant. The change trend of the visual analogue scale (VAS) scores of the 2 participant groups was basically the same when they were resting peacefully, and there were statistical differences in the VAS scores at 1, 2, 4, and 8 h after surgery ($P<0.05$).

Conclusions: When TPVB is combined with GA, there is a lower incidence of hypotension, more stable circulatory state, and better postoperative analgesic effect.

Keywords: Thoracic paravertebral block (TPVB); general anesthesia; breast cancer; hypotension; postoperative pain

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Introduction

Breast tumors are the most common tumors in women worldwide and one of the most common public health problems for women. Malignant breast tumors are mainly breast cancer (BC). More than 1.5 million women worldwide are diagnosed with BC each year (1), and in 2015, approximately 570,000 BC patients died worldwide. The incidence of BC in the United States in 2020 has accounted for approximately 30% of all new cancer cases in women (273,879) (2). In 2013, the prevalence of BC in China accounted for 19.5% of all female cancer reported (3). Advances in oncology have enabled patients with breast tumors to be effectively treated, and surgical removal of the tumor is the main treatment method of breast tumors. After BC surgery, more than 35% of patients will experience acute pain, and 20–30% of patients will experience chronic pain (4). Acute pain is mainly caused by recent body injury, and the duration of pain is generally no more than 2 months, while chronic pain is mainly caused by previous body injury, and the duration of pain is more than 3 months. Most BC patients experience acute pain after surgery, but it can develop into chronic pain if effective treatment is not provided in time. Therefore, for this type of surgery, it is necessary to deliver a safe, suitable, and effective anesthesia program in order to effectively control intraoperative adverse reactions and postoperative pain, reduce hospital stay, and improve the quality of life of patients after surgery.

General anesthesia (GA) is the main anesthesia for BC surgery. However, GA can only inhibit the projection system of the cortical limbic system or hypothalamic cortex, it can neither completely block the transmission of peripheral noxious stimulation to the central nervous system, nor effectively inhibit the intraoperative stress response (5,6), and the extensive use of GAs and opioid analgesics leads to extubation delay, respiratory depression, nausea, and vomiting. Intraoperative hypotension is a common adverse reaction of GA (7,8), which can increase the incidence of postoperative myocardial ischemia, renal injury, and cerebral ischemia, prolong the length of hospital stay, and even increase postoperative mortality (9,10), Therefore, it is necessary to identify the factors related to the development of intraoperative hypotension.

Thoracic paravertebral block (TPVB) was first proposed by Hugo Sellheim in 1905 and used for abdominal analgesia. In 1979, Eason and Wyatt reevaluated and created a classic anatomical method of surface marker. Later, there were gradually "pressure measurement" and neurostimulator guided positioning method for paravertebral nerve block, which greatly improved the success rate, but there was blindness of operation, which could not avoid the puncture of blood vessels. In 2009, Hara *et al.* First reported the paracsagittal approach and TPVB technology guided by out of plane ultrasound. According to the paracsagittal approach, lateral approach, in-plane and out of plane technology, there are at least nine different blocking methods (11), as well as the placement of TPVB continuous catheter under the direct vision of thoracoscope, it effectively avoids the blindness of operation and catheterization, greatly improves the success rate, reduces the complications, and ensures the effect of block. Its clinical value has been paid more and more attention, and is widely used in postoperative analgesia of breast surgery. Lönnqvist *et al.* reported in 1995 that the total failure rate of TPVB under anatomic localization was 10.1%. The incidence of complications was as follows: hypotension 4.6%, vascular injury 3.8%, pleural perforation 1.1%, pneumothorax 0.5% (12). With the development of anesthesia technology, ultrasound-guided operation can significantly improve the accuracy of puncture. In a survey of more than 1,400 cases of TPVB, the probability of complications is 0.7% (13). Pace *et al.* investigated 856 breast cancer patients. The probability of unilateral PVB complications was 0.35%, bilateral PVB was 0.88%, no perforation of pleural effusion, pneumothorax and abnormal drug diffusion were observed, 4 cases of hypotension and bradycardia, and 2 cases of local anesthetic toxicity (14). Studies have shown that TPVB combined with GA delivers better postoperative pain control, lower incidence of postoperative nausea and vomiting, shorter recovery time, and higher patient satisfaction than GA alone in BC surgery (15). The use of TPVB can prevent the frequency and intensity of chronic postoperative pain and the incidence of cancer recurrence after BC surgery (16,17). However, there is no report about the effect of TPVB combined with GA on intraoperative hypotension and postoperative pain in BC patients.

The purpose of this study was to explore the effect of TPVB combined with GA on intraoperative hypotension and postoperative analgesia in patients with BC, so as to provide a reference for the selection of anesthesia methods for BC surgery.We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1803).

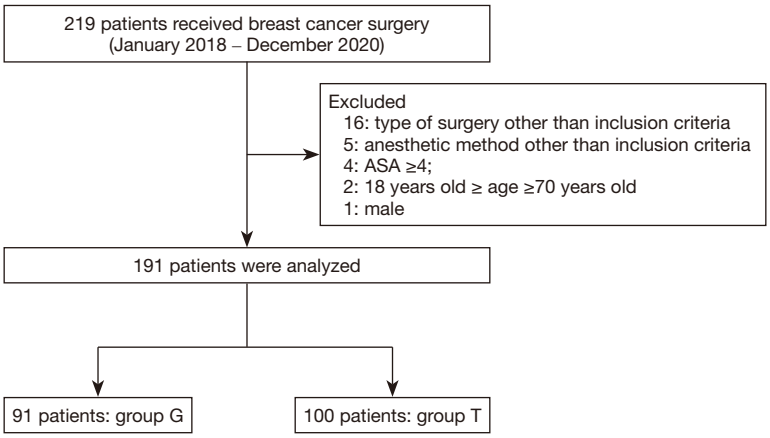

Figure 1 Flowchart of participants.

Methods

Patient selection

This study was approved by the Ethics Committee of Wuxi 9th People's Hospital Affiliated to Soochow University (No.: 2017059) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). All participants provided informed consent. We reviewed the medical records of patients who underwent modified radical mastectomy for BC at Wuxi 9th People's Hospital from January 2018 to December 2020 (*Figure 1*). The inclusion criteria were as follows: (I) modified radical mastectomy for BC for the first time; (II) 18 years ≤ age ≤70 years; (III) female gender; (IV) American Society of Anesthesiologists (ASA) physical status 1–3. The exclusion criteria were as follows: (I) missing medical records; (II) block level smaller than T3–T6; (III) receiving other nerve blocks except TPVB before operation; (IV) receiving TPVB after operation; (V) abnormal liver and kidney or heart and lung; (VII) patients experiencing neuropsychiatric or neuromuscular diseases. According to whether the patients received TPVB, they were divided into 2 groups: GA group (Group G) and TPVB combined with GA group (Group T).

Anesthesia

Participants fasted for 6 h and did not consume water for 2 h before the operation. After entering the operating room, a contralateral upper limb intravenous infusion was initiated, the patient was connected to a multi-functional monitor, and the electrocardiogram (ECG) oscilloscope, pulse-oxygen saturation (SpO_2), and electroencephalogram bispectral index (EEG BIS) were continuously monitored. Under local anesthesia, the contralateral radial artery was punctured and catheterized, and continuous invasive arterial blood pressure (CIAP) was monitored.

The GA group (Group G) received the following intravenous injection: midazolam 2 mg, flurbiprofenaxetil 50 mg, sufentanil 0.4–0.6 μg/kg, plasma target concentration 2–4 μg/mL, and a target-controlled infusion of propofol induction. After the patient had fallen asleep, they were intravenously injected with atracuriumcisbesilate 0.15 mg/kg. After muscle relaxation was deemed satisfactory, a laryngeal mask was placed in the airway. Auscultation was used to confirm that there was no leakage, no flatulence, and the airway resistance during mechanical ventilation was appropriate. The airway of the laryngeal mask was fixed, followed by connection of the anesthesia machine. For intraoperative intermittent positive pressure ventilation (IPPV), the positive end-expiratory pressure was 5 cm H_2O, inhaled oxygen concentration was 60%, tidal volume (VT) was 8 mL/kg, respiratory rate (RR) was 10–12 bpm, inspiratory/expiratory ratio (I/E) 1/2, the minute ventilation (VE) was adjusted, and the end-tidal carbon dioxide partial pressure ($PetCO_2$) was maintained at 35–45 mmHg.

The TPBV combined with GA group (Group T) received the following protocol: before the vein induction, ultrasound guidance was used to administer a single time point parathoracic block. From the supine position, the patients' knee was bent and pushed toward the opposite side, to enable the chest side lying position, and the puncture site was exposed satisfactorily. The transverse process (TP) of the 4th thoracic vertebrae was identified as the puncture

point by ultrasonic probe. After the local anesthesia had been performed with lidocaine 1% at the puncture point, the sterilized ultrasonic probe was used to guide the needle to enter slowly and evenly. The needle tip pierced the upper ligament of the costal transverse process, entered the intercostal intima, and entered the parathoracic space. After the blood was able to be withdrawn without blood and gas, 1–2 mL of normal saline was injected immediately to confirm the forward displacement of pleura. After confirming the position of the needle, 0.5% ropivacaine (2.0 mg/kg) was injected slowly and the needle was removed. The block plane was measured and recorded. The plane of sensory or temperature decrease was no less than the area of T3–T6. After confirming 10 min of effective sustainment of this TPBV, the same method of GA induction was used as that in the G group.

Anesthesia maintenance was conducted as follows: both participant groups received a propofol target-controlled infusion to maintain plasma concentration at 2–4 μg/mL. When the arterial blood pressure was higher than the baseline value by more than 20%, an additional bolus of sufentanil 0.1–0.2 μg/kg was administered. The depth of anesthesia was monitored by the EEG BIS, and the BIS value was maintained at 45–60. If the BIS value was less than 45, the propofol target-controlled infusion plasma concentration was decreased to the minimum value of 2.0 μg/mL. If the BIS value was greater than 60, the propofol target-controlled infusion plasma concentration was increased (maximum 4 μg/mL). These adjustments were made to ensure the BIS value was again between 45–60. In the case of hypotension (SBP <30% of the baseline value or <90 mmHg), ephedrine was administered intravenously at 5 mg/time.

Observation index

The electronic medical record system, anesthesia record system, recovery room record system, and analgesia follow-up system were used to check the past medical records and collect relevant information, including demographic indicators [age, body mass index (BMI)]; past combined diseases (hypertension, diabetes, and coronary heart disease); intraoperativesufentanil dosage; intraoperative hypertensive drug use (ephedrine); and intraoperative blood loss and fluid infusion. A nurse recorded the patient's resting pain score at 1, 2, 4, 8, 12, 24, 36, and 48 h after surgery. The visual analogue scale (VAS) was used, which involves an unmarked 10 cm lined segment, wherein 0 cm indicates no pain, and 10 cm indicates the most severe pain imaginable. The details are as follows: 0 cm: 0 points, without any pain; 1–3 cm: 1–3 points, mild pain, does not affect work and life; 4–6 cm: 4–6 points, moderate pain, affects work, does not affect life; and 7–10 cm: 7–10 points, severe pain, affecting both work and life.

Statistical analyses

The statistical software SPSS 22.0 (SPSS Inc., Chicago, IL, USA) was used for analysis. The statistical data of normal distribution were expressed as mean ± standard deviation ($\bar{x}$ ± s). One way analysis of variance (ANOVA) was used for comparison between groups; the chi-square (χ^2) test was used to compare tcount data, and Kruskal-Wallis H test was used for rank data comparison. A P value <0.05 for the difference was statistically significant. All tests were bilateral.

Results

General information

This study included 191 patients who underwent modified radical mastectomy. A total of 91 were in Group G, and 100 were in Group T. The age of Group G was (51.3± 9) years old, BMI (22.6±2.8) kg/m^2, ASA physical status was 27/52/12, there were 4 (4.4%) patients with diabetes, 14 (15.4%) with hypertension, and 2 (2.2%) with coronary heart disease. The age of Group T was (52.0 ± 3) years old, BMI (22.2±2.5) kg/m^2, ASA physical status was 30/56/14, there were 4 (4%) patients with diabetes, 16 (16%) with hypertension. and 0 (0%) with coronary heart disease. There were no statistically significant differences in the indicators of the general data of the 2 groups (P>0.05), see *Table 1*.

Comparison of various indicators during the operation

There were no statistically significant differences in duration of surgery, duration of anesthesia, and intravenous fluid volume between the 2 groups. During anesthesia, the BIS value of Group G was significantly lower than that of Group T, and the difference was statistically significant (P<0.05). The use of sufentanil and the use rate of ephedrine in Group G were significantly higher than that of Group T, and the difference was statistically significant (P<0.05) , see *Table 2*.

Table 1 Comparison of the general data of the 2 participant groups

Characteristics	G (n=91)	T (n=100)
Age (years)	51.3±11.9	52.0±12.3
BMI (kg/m^2)	22.6±2.8	22.2±2.5
ASA physical status (1/2/3)	27/52/12	30/56/14
Comorbidity, n (%)		
Diabetes	4 (4.4)	4 (4.0)
Hypertension	14 (15.4)	16 (16.0)
Coronary heart disease	2 (2.2)	0 (0)

BMI, body mass index; ASA, American Society of Anesthesiologists; G, general anesthesia group; T, TPVB combined with GA group.

Table 2 Comparison of various indexes of the 2 participant groups during surgery

Item	G (n=91)	T (n=100)
Duration of surgery (min)	124±16	118±38
Duration of anesthesia (min)	132±17	124±21
Intravenous fluid volume (mL)	1128±165	1071±175
Blood loss (mL)	178 ±24	162±32
BIS value[a]	45± 6	56±7*
Sufentanil (μg)	33±4.1	29±4.8*
Use of ephedrine (n)	35 (38.5%)	11 (11%)

*, P<0.05 *vs.* G group. BIS, bispectral index; G, general anesthesia group; T, TPVB combined with GA group. a, average value measured every 5 minutes during anesthesia.

Comparison of hemodynamic changes during the perioperative period

At the T1, T2, and T5 time points, there was no significant difference between the blood pressure of the 2 groups (P>0.05); at the T4 time point, the blood pressure (SBP/DBP) of Group G was higher than that of Group T (P<0.05); and at the T3 time point, the blood pressure of Group G was lower than that of Group T (P<0.05). At the T1 and T5 time points, there was no significant difference between the heart rate (HR) of the 2 groups (P>0.05); at the T4 time point, the HR of Group G was higher than that of Group T (P<0.05); and at the T2 and T3 time points, the HR of Group G was lower than that of Group T (P<0.05) (see *Table 3*).

Postoperative pain score

There were significant differences in the VAS scores at 1, 2, 4, and 8 h after operation between the 2 groups (P<0.05) (see *Table 4*).

Complications

Among the postoperative analgesia-related complications of the 2 participant groups, there were 17 cases in Group G and 15 cases in Group T of nausea and vomiting. There were 9 cases in Group G and 7 cases in Group T of dizziness. There was 1 case in Group G of respiratory depression or excessive sedation. There was no statistically significant difference between the 2 participant groups (P>0.05) (see *Table 5*).

Discussion

Approximately 40% of patients experience acute severe postoperative pain after breast surgery, and TPVB is an effective measure to control such pain. The TPVB is a regional nerve block method in which local anesthetics are injected into the thoracic paravertebral space (TPVS) near the spinal nerve (18). The TPVS is located on both sides of the spine, and the anatomical structure is roughly wedge-shaped. The boundary of the space comprises the posterior lateral surface of the intervertebral body and the intervertebral foramen, parietal pleura, intercostal endometrium, the front end of the connecting rib neck, and the supracostotransverse ligament at the root of the transverse process, which mainly contains the anterior branch of spinal nerve (intercostal nerve), posterior branch of spinal nerve, sympathetic ganglion, and gray communicating branch. The local anesthetic is injected into the gap through a puncture needle to block the motor, sensory, and sympathetic nerve fibers of the corresponding segment, so as to achieve ipsilateral somatic anesthesia and the analgesia effect (19,20). The stimulus produced by breast surgery causes the body to produce a strong stress response. Suppression of the stress response to simple general anesthesia is often achieved by increasing the dosage of opioids, which not only enhances the inhibitory effect of opioids on the cardiovascular system, but can cause severe hemodynamic fluctuations, leading to an increased likelihood of intraoperative cardiovascular accidents, and can easily cause postoperative complications

Table 3 Comparison of perioperative hemodynamic changes between the 2 groups

Item	SBP (mmHg)		DBP (mmHg)		HR (bpm)	
	G (n=91)	T (n=100)	G (n=91)	T (n=100)	G (n=91)	T (n=100)
Before anesthesia (T1)	119.67±10.23	117.73±11.28	75.34±7.50	76.87±8.30	74.32±9.07	73.38±11.16
During operation (T2)	135.58±9.87	132.64±9.45	80.95±8.45	79.53±6.83	72.57±6.91	76.60±8.17*
Before skin cutting (T3)	113.21±8.76	119.21±9.88*	68.26±8.29	74.64±8.65*	71.03±7.06	74.72±8.12*
After cutting the skin (T4)	119.36±8.32	114.68±8.68*	73.67±6.89	68.14±7.33*	75.76±6.23	72.34±5.67*
At the end of the operation (T5)	115.39±8.46	112.31±8.66	70.03±8.22	68.34±6.54	80.34±7.31	78.45±7.69

*, P<0.05 *vs.* G group. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

Table 4 Comparison of postoperative VAS scores between the 2 groups

Item	Postoperative pain VAS score [range]	
	G (n=91)	T (n=100)
1 h after operation (cm)	2.8±1.1 [1–5]	1.2±0.9* [0–4]
2 h after operation (cm)	3.1±1.0 [1–5]	1.3±0.8* [0–4]
4 h after operation (cm)	3.4±1.2 [1–6]	2.1±0.9* [1–4]
8 h after operation (cm)	3.9±1.1 [1–6]	2.8±1.0* [1–5]
12 h after operation (cm)	3.5±1.2 [1–6]	3.4±1.1 [1–6]
24 h after operation (cm)	3.2±1.2 [0–6]	3.0±1.3 [1–6]
36 h after operation (cm)	2.3±1.0 [0–5]	2.2±0.9 [0–5]
48 h after operation (cm)	1.9±1.0 [0–4]	1.8±0.9 [0–4]

*, P<0.05 *vs.* G group. VAS, visual analogue scale; G, general anesthesia group; T, TPVB combined with GA group.

Table 5 Comparison of complications between the 2 groups

Item	G (n=91)	T (n=100)
Nausea and vomit	17 (18.7%)	15 (15%)
Dizziness	9 (9.9%)	7 (7%)
Respiratory depression	1 (1.1%)	0 (0%)
Itchy skin	0 (0%)	0 (0%)
Over sedation	1 (1.1%)	0 (0%)

G, general anesthesia group; T, TPVB combined with GA group.

including delayed awakening. Use of TPVB can block the transmission of noxious signals caused by surgery to the central nervous system at the periphery (19,20), and reduce the stress response caused by surgery. Patients receiving TPVB had lower incidence of postoperative nausea and vomiting, reduced use of postoperative analgesics, shorter postoperative recovery time and hospital stay, and lower hospital expenses (21). The TPVB can provide 72 h of effective analgesia, with the advantages of this pain control being more apparent in the first 24 h. The results of Fahy *et al.* (22) showed that among patients undergoing unilateral mastectomy, the use of opioids in TPVB combined with GA was less than that in GA alone. The difference was more obvious in patients who received mastectomy plus breast reconstruction. This difference was more obvious in patients undergoing mastectomy plus breast reconstruction. A study by Coopey *et al.* (23) also found that the hospital stay of breast surgery patients in a single TPVB group was significantly shortened, which was associated with effective pain control, reduced intraoperative and postoperative analgesics, and a corresponding reduction in the incidence of postoperative nausea and vomiting, and so on. The advantages of TPVB in patients with mastectomy plus breast reconstruction are more obvious, because such patients experience more severe pain than breast-conserving surgery patients, and complications from major surgery and prolonged anesthesia lead to longer hospital stays. For such patients, pain control is more necessary. At the same time, due to the increase in the proportion of pain among mastectomy plus breast reconstruction surgery in breast surgery, it is recommended to use TPVB routinely for patients with this type of surgery.

This study compared the incidence of hypotension and postoperative pain in BC surgery with GA and TPVB combined with GA. We found that the number of hypotensive episodes and circulatory status of TPVB combined with GA were more stable, and the postoperative analgesia effect was better. Compared with GA alone,

TPVB combined with GA has a better postoperative analgesic effect, which may be due to the higher BIS value maintained during anesthesia. In our scheme, we chose a deeper level of sedation to keep BIS value around 60, so that not only the operation can be carried out smoothly, but also the patients in MAC group can feel comfortable. Complete unconsciousness is the expected level of sedation in many patients, and intraoperative consciousness is one of the main causes of dissatisfaction (24,25). Hypotension is not common in hypovolemic patients receiving TPVB (26).

In this study, the VAS score of Group T within 8 h after operation was significantly reduced, indicating that TPVB has a good effect on relieving postoperative acute pain. Although the VAS score of Group T was still lower than that of Group G at 8 h after operation, the change trend of VAS score of the 2 groups was basically the same, and the difference was not statistically significant, which was consistent with the time of elimination of analgesic effect after a single administration of TPVB. In Group G, 38.5% of patients received ephedrine during anesthesia, which was consistent with the results of Kairaluoma *et al.*, who demonstrated that the total dose of ephedrine consumed in the TPVB group was significantly lower than that in the GA group during BC surgery (27). In our study, the HR of Group T was higher than that of Group G at the T2 and T3 time points, which indicated that under the same conditions, the effect of Group T on heart rate was smaller. At the T4 time point, SBP, DBP, and HR in Group T were lower than that of Group G, which was statistically significant ($P<0.05$). As skin cutting is a strong stimulation to patients, it activates their stress response. In Group T, TPVB inhibited stress response better than it did in Group G, because it blocks the conduction of injury to the central nervous system. In our study, the blood pressure and HR of 5 time points were observed. There were great fluctuation in SBP, DBP, and HR in Group G, while all 3 remained relatively stable in Group T. This showed that compared with Group G, the hemodynamics of Group T were more stable and the effect of the operation and drugs on patients was less.

Due to its retrospective design, our research had certain limitations. The participants were not prospectively randomized, therefore, selection bias cannot be ruled out. However, because there were no differences in the characteristics of the 2 participant groups before surgery, the results are unlikely to be misleading. Although the attending anesthesiologist knew which plan was implemented, the lack of blinding is unlikely to have affected the collection of cardiopulmonary variables and physiological data during anesthesia.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-1803

Data Sharing Statement: Available at https://dx.doi.org/10.21037/apm-21-1803

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1803). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Ethics Committee of Wuxi 9th People's Hospital Affiliated to Soochow University (2017059) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). All participants provided informed consent.

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