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## Review Article

# ERAS-Based Anesthetic Management of Patients Undergoing Abdominal-Based Free Flap Breast Reconstruction: A Narrative Review

Chenyue Guo<sup>a,#</sup>, Feifei Lou<sup>a,#</sup>, Jiong Wu<sup>b,c</sup>, Jun Zhang<sup>a,c,\*</sup>

- <sup>a</sup> Department of Anesthesiology, Fudan University Shanghai Cancer Center, Shanghai, 200032, China
- <sup>b</sup> Department of Breast Surgery, Fudan University Shanghai Cancer Center, Shanghai, 200032, China
- <sup>c</sup> Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, 200032, China

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#### ABSTRACT

Microsurgical breast reconstruction after mastectomy is emerging as the standard of care for patients with breast cancer. The enhanced recovery after surgery (ERAS) pathway in abdominal-based free flap breast reconstruction is in its early stage of development and lacks established consensus or guidelines. In the multidisciplinary ERAS team, the anesthesia sub-team is responsible for the provision of several core elements in the ERAS pathway including anesthetic protocol optimization, perioperative fluid management and homeostasis regulation, normothermia maintenance, perioperative analgesia, and postoperative nausea and vomiting prophylaxis. Here, we summarized the state-of-the-art in anesthetic practice for the patients undergoing abdominal-based free flap breast reconstruction within an ERAS framework, and also introduced the perioperative strategy for this surgical population based on the ERAS pathway in our center, aiming to improve free flap outcome and patient satisfaction, and accelerating their recovery following surgery.

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<sup>\*</sup> Corresponding author: Jun Zhang, MD, PhD, Department of Anesthesiology, Fudan University Shanghai Cancer Center, and Department of Oncology, Shanghai Medical College, Fudan University, Address: No.270, DongAn Road, Xuhui District, Shanghai 200032, China

E-mail addresses: 18161230006@fudan.edu.cn (C. Guo), loufeifei@sina.com (F. Lou), wujiong1122@vip.sina.com (J. Wu), snapzhang@aliyun.com (J. Zhang).

<sup>#</sup> These authors contributed equally to this work

The concept of enhanced recovery after surgery (ERAS) was initially proposed by Wilmore and Kehlet in 2001. Currently, the ERAS strategy is widely implemented during the perioperative period, facilitating fast recovery from surgical trauma in surgical patients. It is evident that a reduction in postoperative complications, length of hospital stay, and overall medical costs can be realized by alleviating perioperative stress. Although it has been implemented extensively in various surgical procedures, the application of ERAS strategy in abdominal-based free flap breast reconstruction remains at an early stage. Currently, ERAS protocols involved in free flap breast reconstruction may vary across different medical centers. Accordingly, there is a lack of consensus or guidelines to promote the implementation of the ERAS strategy.

The multidisciplinary nature of the ERAS strategy for abdominal-based free flap breast reconstruction requires the involvement of elements from anesthesiology, surgery, nursing, radiology, and other disciplines.<sup>3</sup> However, using these elements independently may fail to achieve the goals of ERAS. Therefore, it is imperative to integrate various elements through multidisciplinary collaborations while leveraging their respective advantages to achieve the optimal outcomes that benefit the patients. Within the multidisciplinary team outlined above, the responsibility of the anesthesia subteam encompasses perioperative components such as anesthetic protocol optimization, perioperative fluid management and homeostasis regulation, hypothermia prevention, perioperative analgesia, and postoperative nausea and vomiting (PONV) prophylaxis.<sup>4</sup> Nevertheless, current ERAS protocol for free flap breast reconstruction in various institutions often provide insufficient information or solid evidence in terms of anesthetic management. This discrepancy does not align with the important role and extensive work carried out by the anesthesia sub-team in the ERAS team for free flap breast reconstruction. The absence of guidance from the anesthesia sub-team in clinical and scientific research related to this strategy creates a gap despite the rapidly growing surgical specialty.

Microsurgical breast reconstruction after mastectomy is emerging as the standard of care for patients with breast cancer. Fudan University Shanghai Cancer Center is one of earliest cancer centers to perform free flap breast reconstruction in China. The sub-teams of anesthesia, breast surgery, nursing, and radiology in our center have implemented the ERAS protocol for these patients for several years, and it has been shown to improve postoperative recovery. Currently, our center boasts a success rate >98% for breast reconstruction using autologous flap surgery. The incidence of flap compromise after autologous free flap breast reconstruction is approximately 5%, and the success rate for salvaging is up to 70%. These data place our center at the leading position in China. This review aimed to summarize the anesthetic protocol of ERAS strategy for free flap breast reconstruction in our center, and included the latest clinical practices in other institutions that were selected to be incorporated into our protocol. By providing important information for the multidisciplinary team involved in free flap breast reconstruction, not only in medical science but also in other nonmedical specialties, we established and improved anesthetic management based on this protocol. To further strengthen the ERAS pathway implementation for free flap breast reconstruction, we reviewed the latest evidence and current practices in this field, aimed at ultimately benefiting the patients with breast cancer.

# Optimization of anesthetic regimen

## Anesthesia protocols

Compared to implant-based reconstruction, abdominal-based free flap breast reconstruction is a complex and delicate surgical procedure with longer operative duration than routine breast cancer surgery. It involves 2 surgical areas, the chest and abdomen, resulting in extensive trauma. Initially, general anesthesia (GA) alone was predominantly used for free flap breast reconstruction, and currently, epidural block or ultrasound-guided nerve block are being applied to this procedure.<sup>5-7</sup> Notably, the severity of trauma may differ between the chest and abdomen, postoperative pain is mainly derived from the abdominal donor site compared to the recipient site in the chest.<sup>8</sup> Given these characteristics, GA combined with regional anesthesia (RA) is preferred, which eliminates intraoperative opioid consumption and significantly alleviates perioperative stress.<sup>6</sup> Therefore, GA + RA has become an indispensable anesthetic regimen for free flap breast reconstruction. Different combinations of anesthesia technique are used in ERAS strategy for abdominal-based free flap breast reconstruction.<sup>9,10</sup>

Three types of RA techniques are commonly employed: epidural anesthesia (EA), transversus abdominis plane (TAP) block, and paravertebral nerve block (PVB).

**GA + epidural anesthesia** EA can provide exceptional analgesic effect, which significantly improves perioperative pain control during this procedure. In addition, EA can provide muscle relaxation that is absent in other RA techniques. During the dissection of the perforators and vascular pedicle in abdominal free flap based breast reconstruction, each perforator needs to be traced, identified, and exposed. The loupe used in microsurgery offers a limited surgical field of vision; however, muscle twitching caused by electrocautery device used within this field significantly interferes with the delicate surgical procedure.<sup>5</sup> Therefore, control of excessive muscle twitching is necessary during the procedure. EA combined with muscle relaxants can greatly prevent muscle twitching during vessel dissection, thus providing ideal working conditions for the surgeons.<sup>5</sup> Additionally, local anesthetic can be administered at any time through a catheter during the entire surgical procedure without being limited by effect of the local anesthetic.<sup>5</sup> Although widely used in several institutions, TAP block provides analgesia after rectus sheath repair and before abdominal skin closure, it cannot fully cover the total surgical procedure owing to possible overlap with surgical areas in abdominal surgeries.<sup>6,8</sup> EA potentially causes a decrease in blood pressure due to a sympathetic blockade, triggering a controversy regarding its impact on flap perfusion.<sup>5</sup> Our study demonstrated that GA + EA significantly improves postoperative pain and reduces PONV incidence in patients undergoing free flap breast reconstruction, without any adverse effects on flap outcomes.5

**GA** + **TAP block** TAP block has become a widely used RA technique for free flap breast reconstruction in recent years.<sup>3,6,8</sup> When TAP block was initially used, anesthesiologists were responsible for the fascial plane identification and transfascial injection. Currently, the surgeons can directly perform TAP block based on anatomical landmarks and tactile feedback within the fully exposed surgical area during the procedure, ultrasound-guided technology has allowed them to take over this role.<sup>3</sup> Bupivacaine is the most commonly used local anesthetic for TAP block; however, a single shot of bupivacaine may not provide long-acting analgesia in patients undergoing free flap breast reconstruction. Continuous TAP block administration may be affected by catheter displacement or dislodgement. With the introduction of liposomal bupivacaine in clinical practice, TAP block has become a viable alternative for analgesia in free flap breast reconstruction.<sup>3,6</sup>

**GA** + **paravertebral block** In addition to the 2 RA techniques mentioned above, PVB is also widely used in free flap breast reconstruction.<sup>7</sup> The operating site of PVB is far from the surgical area, a characteristic distinct from that of EA. Therefore, PVB and paravertebral catheterization will not interfere with the surgical procedure. However, the local anesthetic solution can spread rostrally and caudally in the paravertebral spaces, spread laterally into the intercostal space, or spread medially into the epidural space. However, if the local anesthetic solution spreads into the epidural space, the analgesic effects could be similar to that from EA, with side effects including sympathetic block.<sup>2</sup> Nevertheless, PVB cannot provide significant muscle relaxation.

These RA techniques can significantly reduce the use of perioperative opioids and improve the postoperative pain control. However, there is no consensus on which combination is safer and more effective for free flap breast reconstruction. A large-size sample study aimed at formulating a reasonable and optimal perioperative anesthesia protocol is needed to compare their safety and efficiency.

## Perioperative fluid therapy

**Perioperative fluid infusion** Blood loss is usually low in breast reconstruction (100 to 250 mL); therefore, blood transfusion is mostly unnecessary. A key goal of fluid management in free flap breast reconstruction is to optimize flap blood perfusion and improve the flap microcirculation.<sup>11</sup> There is a close relationship between perioperative fluid management and the free flap outcome. A survey initiated by microsurgeons showed that fluid management during free flap reconstruction is one of the most frequently discussed topics between microsurgeons and anesthesiologists.<sup>12</sup> Therefore, optimization of intraoperative fluid management is helpful in improving the free flap outcome and enhancing the postoperative recovery of patients.

The ideal fluid management for free flap breast reconstruction should maintain an appropriate circulating blood volume, ensure normal cardiac output, optimize flap perfusion while preventing flap

edema.<sup>11</sup> In a retrospective study involving 354 patients who underwent free flap breast reconstruction, Zhong et al. indicated that crystalloid infusion rate in the 24-hour perioperative period was an important predictor of postoperative complications following microsurgical breast reconstruction.<sup>11</sup> A study by Nelson et al. involving 682 patients who underwent autologous breast reconstruction showed that intraoperative fluid under resuscitation may lead to an increased risk of flap thrombosis and loss.<sup>13</sup> Another study with 104 patients who underwent free flap breast reconstruction showed that excessive fluid infusion increased the risk of flap thrombosis.<sup>14</sup> Interestingly, from the perspective of anesthesiologists, the primary goal of fluid therapy is to maintain optimal hemodynamics; however, from the perspective of microsurgeons, the primary goal of fluid therapy is to maintain adequate perfusion of the free flap. Therefore, the fluid management protocol should be optimized to meet the needs of anesthesiologists and microsurgeons.<sup>11</sup>

In 2015, Motakef et al. published a review on perioperative management for free tissue transfer based on evidence-based medicine, <sup>15</sup> in which recommendations for fluid management included: during the perioperative period, the infusion rate of crystalloids should be maintained at 3.5-6.0 mL/kg/h, while infusion rate of crystalloids >5.4 mL/kg/h may be associated with major operative complications, and intraoperative infusion volume of crystalloids >7 L within 24 h should be avoided. However, the target fluid infusion rate established based on these data continues to be inaccurate. Moreover, these recommendations do not clearly indicate how anesthesiologists should regulate the fluid infusion rate intraoperatively. In addition, there are differences in blood loss and invisible fluid loss between breast microsurgery and major free flap head and neck reconstruction. <sup>11</sup> Therefore, it is essential to develop an individualized fluid management protocol for this surgical population.

Although numerous studies have shown that inappropriate fluid infusion may increase the incidence of flap compromise and other perioperative complications, particularly, insufficient fluid infusion may lead to insufficient perfusion of free flaps. However, excessive fluid infusion may cause fluid retention leading to free flap edema and congestive heart failure. In addition, studies have indicated that in addition to the volume and rate of fluid infusion, the type of fluid may affect the outcome of free flaps. Owing to the prolonged surgical duration, extensive surgical trauma, and large amount of fluid transfer, investigators recommend crystalloid fluid infusion for the replacement of insensible losses and colloid fluid infusion for intraoperative blood loss. In

**Goal-directed fluid therapy (GDFT)** In 2015, a survey of free flap reconstruction showed that some of the responders believed that urine volume should be used as an indicator for fluid management, However, several researchers believed that urine volume, mean arterial pressure, central venous pressure, and other clinical indicators should be used as the monitoring bundles for fluid management strategy.<sup>12</sup> At present, GDFT has not been a routine strategy for fluid management in free flap breast reconstruction. However, GDFT strategy can significantly reduce postoperative morbidity and mortality in moderate and high-risk surgical patients. 16,17 The implementation of GDFT strategy in microvascular surgery can significantly shorten the length of hospital stay and decrease the incidence of postoperative complications, 16, 18 whereas the application of GDFT strategy in free flap reconstruction can significantly improve the outcomes of these patients. 19 A study conducted by Polanco et al. on the application of GDFT strategy in autologous flap breast reconstruction showed that the GDFT group had a significantly lower fluid infusion rate and median total fluid volume; consequently, the GDFT group had a significantly lower median intraoperative mean arterial pressure, higher proportion of patients using vasopressors, and significantly shorter median length of hospital stay.<sup>20</sup> However, the use of vasopressors for hypotension in microsurgery has been found to be controversial. Several previous studies have recommended against the use of vasoactive drugs in this clinical setting, Polanco et al. believed that despite the lower volume of fluid infusion and higher proportion of vasopressors used in the GDFT group, the incidence of postoperative complications did not increase. The integrated GDFT strategy with the modulation of perioperative hemodynamics should be adopted in patients undergoing autologous breast reconstruction.

In 2017, Temple-Oberle et al. published a consensus on perioperative care based on ERAS protocol in breast reconstruction.<sup>4</sup> The recommendations of fluid management include the following: applying GDFT strategy to achieve an individualized goal, maintaining water/electrolyte balance, preference for balanced crystalloids, and rational use of vasopressors supports, which may avoid over-resuscitation or under-resuscitation of fluids. In our center, we included the GDFT strategy in the routine perioperative

fluid management as an important ERAS element during free flap breast reconstruction. Furthermore, cardiac output and stroke volume variation (SVV) are routinely monitored during the surgery. As a functional hemodynamic index, SVV is more sensitive and accurate than the static index central venous pressure in predicting fluid responsiveness. SVV >13% is considered as hypovolemic and fluid supplementation should be initiated; in contrast, SVV <13% indicates sufficient circulating volume with the need for further fluid replacement.<sup>20</sup>

#### Homeostasis regulation

Adaptable changes occur during surgical/anesthesia stress, however, harmful and excessive stress can induce imbalance of homeostasis, which affects the outcome of free flap reconstruction.<sup>21-24</sup> As mentioned previously, owing to the prolonged duration and extensive surgical trauma, fluid transfer and electrolyte/acid-base imbalance are prone to occur during free flap reconstruction. Therefore, continuous monitoring and timely correction dysregulated homeostasis are essential. Arterial blood gas (ABG) analysis is an effective method for homeostasis monitoring. In patients undergoing free flap reconstruction of the head and neck, Trivedi et al. found that the PH, base excess, and serum bicarbonate (HCO<sub>3</sub><sup>-</sup>) showed a trend of shifting toward imbalance at anastomosis and surgery completion compared with the baseline.<sup>21</sup> This may be attributed to 2 factors: 1) insufficient blood volume caused by restricted fluid replacement; 2) low mean arterial pressure and organ hypoperfusion, resulting in the accumulation of intravascular acidic metabolites, such as lactate, and eventually leading to metabolic acidosis.<sup>25</sup> Hyperglycemia is significantly associated with postoperative mastectomy skin necrosis after microsurgical breast reconstruction.<sup>26</sup> Therefore, control of blood glucose level based on perioperative blood glucose monitoring is also critical for survival of transplanted flaps. Consequently, perioperative intermittent ABG and glycemic analysis should be served as routine elements in the ERAS protocol. Specially, before induction, ABG analysis and blood glucose measurement should be performed as baseline control. Several ABG and glycemic analysis can be conducted at the key surgical manipulation stages, such as 15 min after vascular anastomosis completion, and at the end of the surgery. Therefore, ABG and glycemic analysis is commonly conducted at least 3 times during the intraoperative period, and extra analysis can be conducted if necessary. Before discharge from the postanesthesia care unit, another ABG analysis can be conducted to confirm that the homeostasis is well maintained before returning the patients to the ward.

## Prevention of perioperative hypothermia

**Influence of hypothermia on free flap outcome** Studies have shown that perioperative hypothermia can impair flap healing, prolong the length of stay, and increase the risk of wound infection.<sup>4</sup> Patients undergoing free flap breast reconstruction are particularly susceptible to intraoperative hypothermia. Hypothermia may promote platelet aggregation and then decrease blood viscosity. However, hypothermia may increase peripheral vascular tone and reduce blood flow to the flap.<sup>12</sup> In their study of head and neck reconstruction, Sumer et al. found that intraoperative central body temperature <35°C was correlated with perioperative complications.<sup>27</sup> A retrospective study showed that the incidence of postoperative recipient site infection was significantly increased when the minimum central body temperature of the patient was <34.5°C during free flap reconstruction.<sup>28</sup> Although most investigators believe that hypothermia is closely related to perioperative complications, several researchers hold the opposite opinion. A retrospective study by Liu et al. showed that maintaining moderate intraoperative hypothermia could reduce the incidence of free flap thrombosis.<sup>29</sup> The influence of hypothermia on the outcomes of free flaps was inconsistent; however, numerous evidences indicate that maintaining the central body temperature >36°C during breast reconstruction can effectively avoid hypothermia-associated perioperative complications.<sup>15</sup>

**Prevention of intraoperative hypothermia** The guideline for breast reconstruction recommends continuous intraoperative body temperature monitoring and application of various methods for perioperative heat preservation. In recent years, as body temperature monitoring and active warming therapy have become routine, very few patients undergoing free flap breast reconstruction in our center experienced hypothermia during the surgery. The commonly used intraoperative warming strate-

gies for patients undergoing free flap breast reconstruction include force-air warming, thermal mattresses, and warmed intravenous fluids. A single warming therapy is commonly insufficient to prevent intraoperative hypothermia during the whole surgical procedure. Therefore, we recommend the combination of different thermal therapies to maintain perioperative normothermia and potentially improve the outcome of the flap.

## Perioperative analgesia

Adequate perioperative analgesia can accelerate early mobilization in patients receiving free flap breast reconstruction, which is conducive to reduce the length of hospital stay and costs.<sup>9</sup> Thus, GA combined with RA is recommended. However, some patients require anticoagulant administration to prevent thrombosis and patient-controlled intravenous analgesia (PCIA) is used for these patients to avoid potential epidural hematoma. An appropriate bridging between intraoperative analgesia and postoperative PCIA is recommended to avoid inadequate analgesia because inadequate analgesia may increase vascular tone and affect the perfusion of the flap,<sup>30</sup>

The main challenge from PCIA is the adverse effects, such as nausea, vomiting, constipation and pruritus, caused by opioids. Therefore, to reduce opioid use, multimodal analgesia strategy is recommended for postoperative analgesia in patients undergoing breast reconstruction according to the guidelines.<sup>4</sup> For patients undergoing free flap breast reconstruction, nonsteroidal anti-inflammatory drugs, such as selective cyclooxygenase-2 (COX-2) inhibitors, are recommended before surgery for prophylactic analgesia.

It has been demonstrated that patients treated under ERAS protocol were administered less opioids from operation with significantly fewer reconstructive failures.<sup>31</sup> Patients in our center receiving multimodal analgesia strategy had a low postoperative pain score, low incidence of adverse effects, and high patient satisfaction. Therefore, perioperative multimodal analgesia aimed at reducing opioid consumption is recommended in this surgical population.

## PONV prophylaxis

PONV can increase the subjective discomfort feeling after surgery, affect postoperative activity, prolong the length of hospital stay, and increase the medical costs.<sup>32</sup> As abdominal-based free flap breast reconstruction requires the transfer of abdominal skin and adipose tissue to the chest for breast reconstruction, lack of abdominal tissues would result in weakness of the abdominal wall. Consequently, the PONV-induced increase in abdominal pressure could cause wound dehiscence, bleeding, and other severe complications. Therefore, PONV prophylaxis is an important element in ERAS protocol in this surgical population.<sup>32</sup> Most patients undergoing abdominal-based free flap breast reconstruction are at high risk of PONV.<sup>33</sup> The overall incidence of PONV is 30% in patients undergoing breast surgery, whereas the incidence in high-risk populations may be as high as 70%.<sup>32</sup> A retrospective study by Manahan et al. showed that 76% of patients experienced PONV and 66% of patients suffered from severe PONV among the patients undergoing free flap breast reconstruction.<sup>34</sup> Therefore, PONV prophylaxis is strongly recommended in these surgical patients.

The Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting recommends at least 2 interventions for PONV prophylaxis, and combined-medication therapy was found to be superior to a single medication (evidence level A1).<sup>35</sup> For patients who underwent free flap breast reconstruction in our center, opioids consumption was greatly decreased during the perioperative period owing to the application of combined anesthetic regimen and implementation of multimodal analgesia strategy. The findings from our previous study on PONV is consistent with the consensus, that is, compared to inhaled anesthetics, propofol-based anesthesia can reduce PONV incidence in patients undergoing free flap breast reconstruction.<sup>32</sup> The prophylactic strategy includes administration of dexamethasone 5-8 mg before surgery, haloperidol 0.625-2 mg intraoperatively, and 5-hydroxytryptamine 3 receptor antagonists at the end of surgery. These interventions can significantly decrease PONV incidence in the patients undergoing free flap breast reconstruction in our center. A clinical trial with nonpharmacological intervention (transcutaneous acupointelectrical stimulation) is ongoing, which can be added into our strategy for multimodal PONV prophylaxis.

#### Patient selection

At present, most bilateral reconstructions are performed after prophylactic excision of the healthy side; however, prophylactic excision and reconstruction is not recommended by domestic surgeons as a treatment option for patients with high-risk breast cancer, as there is no consensus so far on the prophylactic excision in China, As expected, bilateral mastectomy and reconstruction take longer times, cause greater surgical trauma, and may result in longer postoperative recovery and more complications in the flap donor site compared to unilateral mastectomy and reconstruction. Beugels et al. reported that patients receiving bilateral free flap reconstruction were more likely to experience partial flap loss.<sup>36</sup> Further, Chang et al. showed that prolonged surgical time was a risk factor for overall complications in free flap breast reconstruction.<sup>37</sup> Furthermore, in a retrospective study, Wu et al. found that the risk of overall complications increased by 16% for each additional hour of surgical time, and longer operative time was significantly associated with bilateral immediate reconstructions. 38 In patients with risk factors, reducing the surgical time may decrease the incidence of postoperative complications.<sup>38</sup> Therefore, the implementation of ERAS pathway in the patients undergoing bilateral reconstruction may be more difficult and the quality of postoperative recovery may be poorer. However, no significant differences in flap donor site morbidity and recipient site complications were found between bilateral and unilateral free flap reconstruction after adjusting for operative time.<sup>39</sup>

## Anticoagulation therapy

The total incidence of venous thromboembolism (VTE) in surgical patients with breast cancer was 2.2%.<sup>40</sup> A meta-analysis showed that old age, high body mass index, and long surgical duration are risk factors for postoperative VTE. 40 Therefore, free flap breast reconstruction is at high risk of VTE. Further, immediate breast reconstruction is associated with a significantly higher incidence of VTE when compared with delayed breast reconstruction.<sup>40</sup> Interestingly, smoking history, length of hospital stay, and Caprini score were not associated with increased incidence of postoperative VTE. 40 Currently, there is no consensus on chemoprophylaxis regimens for VTE in patients undergoing free flap breast reconstruction. Krystle's study on implementation of a 2-week VTE chemoprophylaxis protocol in deep inferior epigastric perforator (DIEP) flap breast reconstruction patients successfully reduced the incidence of VTE, without affecting the incidence of hemorrhagic complications. 41 Our center does not routinely provide anticoagulation therapy to the patients. Specifically, for patients who are at high risk of VTE, a low molecular weight heparin nadroparin is administrated as prophylactic anticoagulation to prevent VTE. Furthermore, given the high risk of bleeding in plastic surgery, except for aspirin, preoperative antithrombotic therapy should be held back in patients with atrial fibrillation, mechanical heart valves, coronary artery disease, or peripheral arterial disease.<sup>42</sup> The decision to bridge with low molecular weight heparin is dependent on thromboembolic risk, Additionally, physical therapy combined with chemoprophylaxis has lower incidence of VTE than chemoprophylaxis alone.<sup>43</sup> Patients in our center used graduated compression stockings with 15-21 mmHg pressure to prevent VTE perioperatively.

## Postoperative flap monitoring

It is crucial to reduce the incidence of flap-related complications; therefore, postoperative flap monitoring is a core element of the ERAS pathway for the patients undergoing free flap breast reconstruction. Currently, our center uses a Doppler ultrasound device to monitor the flap blood supply after surgery. Typically, flap blood flow monitoring is conducted every 1 h within the 1st and 3rd day after surgery; every 4 h within the 3rd and 5th day after surgery. Notably, the monitoring frequency affects the patients' rest and causes sleep deprivation. Consequently, it may affect the patient's recovery as well. Currently, implantable anastomotic venous flow coupler are available that can be used to remotely monitor the veins in the flaps using laser Doppler flowmetry and near-infrared spectroscopy (NIRS) monitors, which can greatly reduce sleep deprivation. Our center has used NIRS to monitor patients who underwent free flap breast reconstruction, and the results showed that NIRS has advantages such as high sensitivity and early warning.<sup>44</sup> Nevertheless, remote monitoring devices for

flap blood supply have lower accuracy than Doppler ultrasound monitoring.<sup>44</sup> Therefore, flap safety remains the top priority in the ERAS pathway.

#### Nonmedical factors

**Economic factor** The ERAS pathway requires more human and material resources to implement. The imaging technology plays an important role in preoperative assessment, and the combination of angiography techniques with traditional imaging methods is an innovation. Based on the color Doppler blood flow pattern, ultrasound angiography can be used to obtain information on the diameter, direction, and anatomy of the perforator vessels, which has been proved to be the best method of perforator vessel ultrasound angiography in current clinical applications. 45 Using 3-dimensional volumetric probes to reconstruct the perforator vessels and their main branches, while using a contrast agent can provide clearer and more intuitive display of the relationship between the perforator and main vessel, as well as the branching and distribution of the perforator within the flap. Using indocvanine green laser-assisted vascular mapping can precisely identify the location of epigastric perforator vessels. 46 Dragu's study on the blood supply to each region of the free flap using Tc-99m SPECT/CT and PET/CT imaging techniques provided new insights into the free flap breast reconstruction procedure.<sup>47</sup> Preoperative assessment using imaging techniques mentioned earlier can help reduce intraoperative and postoperative complications, and improve clinical outcomes.<sup>48</sup> Hansson's study revealed that DIEP and transverse rectus abdominis myocutaneous (TRAM) flaps had similar lengths of hospital stay, whereas latissimus dorsi (LD) flaps typically had shorter length of hospital stay. The total charges to costs using the cost-to-charge ratio were also comparable between the DIEP and TRAM flaps, whereas LD flaps were significantly less expensive.<sup>49</sup> The DIEP flap was found to be costeffective compared to implant-based breast reconstruction. Our study also compared the effects of different anesthesia regimens on economic costs, and the results showed that the length of hospital stay were similar between inhalation and intravenous anesthesia; however, inhalation anesthesia was significantly cheaper than intravenous anesthesia,<sup>32</sup> From these perspectives, reducing economic inputs may be achieved through precise preoperative examination, anesthesia selection, intraoperative procedures, and postoperative monitoring.

**Cultural factors** Unlike western medicine, traditional Chinese medicine emphasizes the harmonious unity of humans with nature and society, and balancing the body, mind, and environment. The Chinese are also committed to dietary regimen, daily schedule adjustment, emotional regulation, and adherence to seasonal changes, with a recommendation for more rest and less activity after surgery. Therefore, some patients may not fully accept the concept of ERAS in the initial stages. In contrast, western patients may exhibit higher compliance to the ERAS pathway; therefore, they will be more inclined to accept the idea of early ambulation and eating after surgery.

Our multidisciplinary team for free flap breast reconstruction has helped almost all of patients accept the ERAS-based concept via physician-patient communication and planned health education. Consequently, the ERAS team have established a standardized process through PDCA (plan, do, check, and action) method. After years of our efforts, patients undergoing free flap breast reconstruction have gradually accepted the idea of ERAS, which greatly promotes implementation of the ERAS pathway and fast recovery from surgical stress.

**Emotional factor** In 2020, a survey of the preoperative anxiety status among 5018 patients indicated that the preoperative anxiety prevalence rate of adult patients in China was 16.9%.<sup>50</sup> Preoperative anxiety increases the amount of anesthetics used, aggravates postoperative pain, and increases the incidence of other postoperative adverse events including PONV.<sup>51</sup> Although breast reconstruction is related to improvements in psychological outcomes, younger patients and those choosing immediate breast reconstruction after total mastectomy reported worse symptoms of depression and anxiety.<sup>52</sup> A recent study showed that ketamine/es-ketamine may play a role in reducing postoperative depression in patients with breast cancer.<sup>53</sup> This information should be validated in future large-size clinical trials. Further, Fertsch et al. indicated that the DIEP group had higher satisfaction with the breasts, social and psychological well-being, outcome, and sexual well-being according to the Q-breast score.<sup>54</sup> Similarly, Retrouvey et al. found that mastectomy with immediate breast reconstruction can provide patients with a higher degree of satisfaction and psychosocial well-being compared to mas-

tectomy alone at 1 year after surgery.<sup>55</sup> Furthermore, psychiatric assessment in 10,114 patients who underwent bilateral breast reconstruction using the HCUP-NIS database from 2016 to 2018 showed that pre-existing psychiatric disorders were strong predictors of prolonged hospital stay and increased postoperative complications.<sup>56</sup> Psychiatric diagnosis displayed significant association with morbidity of breast reconstruction.<sup>56</sup> Therefore, these patients could be provided additional perioperative supports. A meta-analysis found that preoperative, intraoperative, and postoperative psychosocial interventions can relieve pain and anxiety, and improve clinical outcomes in surgical patients.<sup>57</sup> Early interventions aimed at reducing surgery-related psychological stress through the ERAS pathway, including psychological education, relaxation therapy, and cognitive behavioral therapy, can be helpful in alleviating perioperative stress response, reducing postoperative complications, and shortening the length of hospital stay.

#### Conclusion

With the continuous development of surgical techniques, the focus of abdominal-based free flap breast reconstruction has gradually evolved from the single goal of improving surgical techniques to the multiple goals of enhancing postoperative recovery. The close collaboration and communication between anesthesia sub-team and other multidisciplinary sub-teams are the basis for achieving these goals and ultimately benefiting the patients. Here, we summarized the anesthetic elements of ERAS strategy including medical and nonmedical factors for free flap breast reconstruction in institutes worldwide including ours. As an important element of the multidisciplinary team, the anesthesia team should quickly adapt to surgical needs, meet the patient's expectations, and play a leading role in the ERAS multidisciplinary team, to make abdominal-based free flap breast reconstruction better for patients with breast cancer.

#### Conflict of Interest

The authors declare no competing interests.

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#### **Ethical Approval**

Not required.

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