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Perioperative Factors Associated With Unplanned Re-exploration Following Free Flap Reconstruction for Oral and Maxillofacial Malignancies: A Retrospective Case-Control Study

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TITLE PAGE

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Perioperative Factors Associated With Unplanned Re-exploration Following Free Flap Reconstruction for Oral and Maxillofacial Malignancies: A Retrospective Case-Control Study

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Disclosures

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Author Contributions

Xiang Dong: manuscript drafting and critical revision.

Xinmeng Wang: data collection and data curation.

Ren Zhou: statistical analysis and interpretation of the results.

Jie Chen: study conception and design, data interpretation, and manuscript revision.

All authors reviewed and approved the final manuscript.

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None.

Abstract

Background:

Free flap reconstruction is the standard approach for restoring complex defects following oral and maxillofacial malignancy resection. However, unplanned re-exploration due to postoperative flap vascular compromise remains a major challenge and may adversely affect reconstructive outcomes. This study aimed to evaluate perioperative factors associated with unplanned re-exploration after free flap reconstruction.

Methods:

A retrospective case-control study was conducted among patients who underwent oral and maxillofacial malignancy resection followed by free flap reconstruction. The study included 139 patients who underwent unplanned re-exploration for postoperative flap vascular compromise as cases and 285 randomly selected patients without unplanned re-exploration from the same eligible study population as controls. Demographic characteristics, treatment history, perioperative hemodynamic variables, laboratory findings, and surgical variables were collected. Variables showing significant associations in univariate logistic regression analyses were further evaluated using covariate-adjusted multivariable logistic

regression models. Exploratory subgroup analyses were performed to assess the consistency of these associations.

Results:

In univariate analyses, prior radiotherapy (OR = 2.29, *P* = 0.001), preoperative diastolic blood pressure (DBP) (OR = 1.33 per 10-mmHg increase, *P* = 0.006), preoperative mean arterial pressure (MAP) (OR = 1.27 per 10-mmHg increase, *P* = 0.014), postoperative DBP (OR = 1.46 per 10-mmHg increase, *P* = 0.004), postoperative MAP (OR = 1.35 per 10-mmHg increase, *P* = 0.019), and the number of previous surgical procedures (OR = 1.26 per additional procedure, *P* = 0.018) were associated with unplanned re-exploration.

After adjustment for age, sex, and intraoperative vasoactive drug use, prior radiotherapy (adjusted odds ratio [aOR] = 2.22, *P* = 0.002), preoperative DBP (aOR = 1.32 per 10-mmHg increase, *P* = 0.008), preoperative MAP (aOR = 1.28 per 10-mmHg increase, *P* = 0.013), postoperative DBP (aOR = 1.46 per 10-mmHg increase, *P* = 0.004), postoperative MAP (aOR = 1.40 per 10-mmHg increase, *P* = 0.012), and the number of previous surgical procedures (aOR = 1.26 per additional procedure, *P* = 0.022) remained independently associated with unplanned re-exploration. Intraoperative vasoactive drug use was not independently associated with the outcome (aOR = 1.40, *P* = 0.106).

Conclusions:

Prior radiotherapy, multiple previous surgical procedures, and elevated perioperative DBP and MAP were independently associated with unplanned re-exploration following oral and maxillofacial free flap reconstruction. These findings provide additional evidence to inform perioperative risk assessment and may help optimize perioperative management strategies in patients undergoing oral and maxillofacial free flap reconstruction.

Keywords:

Oral and maxillofacial malignancy; Free flap reconstruction; Flap vascular compromise; Unplanned re-exploration; Radiotherapy; Mean arterial pressure; Diastolic blood pressure.

Background

Oral and maxillofacial malignancies exhibit aggressive biological behaviors and may involve multiple adjacent anatomical structures, including the tongue, buccal mucosa, the mandible and maxilla, and pharyngeal spaces(1). Radical ablative resection followed by free vascularized tissue transfer remains a standard approach for reconstructing extensive defects caused by oral and maxillofacial malignancies[2]. By strategically utilizing free tissue transfers，such as the radial forearm free flap (RFFF), anterolateral thigh (ALT) free flap, and fibular osteocutaneous free flap (FFF), clinicians can achieve not only precise anatomical reconstruction but also functional recovery of mastication and speech, thereby significantly improving postoperative quality of life(2, 3). However, these microsurgical procedures remain inherently complex and technically demanding, with postoperative vascular compromise representing a major cause of flap failure. The occurrence of such vascular compromise may require unplanned re-exploration, which not only imposes additional physiological insult and raises healthcare expenditures, but also elevates the risk of secondary complications, potentially undermining patients' long-term reconstructive outcomes(4, 5).

Although previous studies have primarily focused on advances in free flap reconstruction techniques and refinements in microsurgical

procedures, the perioperative factors associated with unplanned re-exploration remain incompletely characterized. Existing clinical studies have been limited by relatively small sample sizes and heterogeneous outcome definitions, leaving the associations between patient characteristics, treatment history, perioperative hemodynamic parameters, and unplanned re-exploration insufficiently understood(6, 7). Accordingly, we conducted a single-center retrospective case-control study to investigate perioperative factors associated with unplanned re-exploration following free flap reconstruction in patients undergoing resection of oral and maxillofacial malignancies.

Methods

This retrospective case-control study investigated perioperative factors associated with unplanned surgical re-exploration secondary to postoperative free flap vascular compromise following radical ablative resection of oral and maxillofacial malignancies. The retrospective study protocol was reviewed and approved by the Institutional Review Board and Medical Ethics Committee of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine (Approval No.SH9H-2025-T444-1). The requirement for individual informed consent was waived because of the retrospective nature of the study.

Medical records of patients who underwent radical ablative resection of oral and maxillofacial malignancies combined with free flap reconstruction at the Department of Oral and Maxillofacial Surgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, from June 2020 to June 2025, were retrospectively reviewed. The primary objective was to identify perioperative variables associated with unplanned surgical re-exploration following postoperative flap vascular compromise. Eligible patients were classified as cases or controls according to the occurrence of unplanned surgical re-exploration for postoperative flap vascular compromise.

Case group (Re-exploration cases): Patients who developed definitive clinical signs of postoperative flap vascular compromise, including dusky discoloration, decreased skin temperature, abnormal capillary refill, venous congestion, or diminished tissue turgor, who failed initial conservative management, such as systemic warming, antispasmodics, or anticoagulation therapy, and ultimately required unplanned surgical re-exploration, including vascular exploration, microvascular re-anastomosis, or partial flap debridement.

Control group (non-re-exploration controls): Contemporaneous patients who underwent comparable microvascular reconstructive procedures during the same study period and achieved uncomplicated flap

survival without clinical evidence of postoperative vascular compromise. Control participants were randomly selected from the same eligible study population at an approximate 2:1 control-to-case ratio.

Inclusion criteria:

1. Pathologically confirmed oral and maxillofacial malignancies (e.g., tongue carcinoma, buccal carcinoma and gingival carcinoma) treated with radical ablative resection.
2. Primary single-stage microvascular reconstruction with free flaps, including radial forearm free flap (RFFF), anterolateral thigh free flap (ALT), and fibular osteocutaneous free flap.
3. Availability of sufficient perioperative medical, surgical, and anesthetic records for study inclusion and analysis.

Exclusion criteria:

1. Severe concomitant organ dysfunction or failure (e.g., advanced cardiac, hepatic, or renal failure) or inadequately controlled systemic diseases (e.g., uncontrolled diabetes mellitus) that could impair wound healing or jeopardize free flap viability.
2. Patients who underwent secondary operations because of early tumor recurrence, distant metastasis, or other conditions unrelated to postoperative vascular compromise.

3. Incomplete medical records lacking essential perioperative variables required for analysis.
4. For patients experiencing recurrent or multiple vascular compromise events, only data from the initial episode and corresponding surgical re-exploration were included in the analysis.

The primary clinical outcome was unplanned re-exploration, defined as unplanned return to the operating room for flap exploration because of postoperative vascular compromise. Within the analytic dataset, outcome = 1 denoted the occurrence of an unplanned return to the operating room, whereas outcome = 0 represented the absence of such an event. Elective secondary revision procedures, scheduled delayed debridement, and staged reconstructive procedures were excluded from this outcome definition.

Data extraction was independently performed by two investigators using the electronic medical record (EMR) system and entered into a standardized Microsoft Excel database. Following duplicate data entry, cross-validation, data cleaning, and logical consistency checks, the final dataset was prepared for subsequent statistical analysis. The assessed perioperative variables were categorized into four domains:

- Demographic and baseline characteristics: Sex, age, body mass index (BMI), as well as histories of tobacco smoking and alcohol consumption.
- Preoperative clinical characteristics: Coexisting comorbidities, including hypertension, diabetes mellitus, coronary artery disease, and other chronic diseases; primary tumor subsite (tongue, buccal mucosa, gingiva, floor of the mouth, etc.); maximum tumor diameter; AJCC 8th-edition TNM stage; number of previous head and neck surgical procedures; prior radiotherapy or chemotherapy; and anticoagulant therapy use.
- Intraoperative and anesthetic variables: duration of anesthesia, operative time, flap type and geometric dimensions (flap length and width), estimated intraoperative blood loss, perioperative fluid management (including allogeneic blood transfusion volume and crystalloid/colloid infusion volume), and intraoperative continuous infusion of vasoactive agents.

- Perioperative monitoring variables: Pre- and postoperative laboratory parameters, including hemoglobin, platelet count, fibrinogen, D-dimer, albumin, and fasting plasma glucose levels; pre- and postoperative hemodynamic parameters, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP); absolute change in SBP (ΔSBP) within

the initial 24 hours after surgery (defined as a significant fluctuation when ΔSBP ≥ 30 mmHg); postoperative surgical drainage volume within 24 hours; postoperative infection within 48 hours (defined as core temperature > 38.5°C, white blood cell count > 10×10^9/L, or positive bacterial culture); postoperative 24-hour fasting plasma glucose level; postoperative serum potassium level; and arterial partial pressure of oxygen (PaO_2).

Statistics

The statistical analysis plan was developed after access to the study data and before the final statistical analyses were performed. Continuous variables were presented as medians with interquartile ranges (IQRs), whereas categorical variables were reported as frequencies and percentages. Intergroup differences were compared using the Mann-Whitney U test, chi-square test, or Fisher's exact test, as appropriate. Univariate logistic regression analyses were performed to identify variables associated with unplanned surgical re-exploration. To mitigate the risk of statistical overfitting given the moderate sample size and the large number of candidate variables, a predefined covariate-adjustment strategy was adopted for multivariable analyses. Specifically, each variable showing a significant association in univariate logistic regression analysis ($P < 0.05$) was subsequently evaluated in an independent multivariable logistic

regression model adjusted for age, sex, vasoactive drug use, and the variable of interest. Exploratory subgroup analyses were subsequently conducted for variables that remained statistical significance following covariate adjustment. Prespecified stratification factors included age (<60 years vs. ≥60 years), sex, prior radiotherapy, number of previous surgical procedures, intraoperative vasoactive agent use, intraoperative transfusion, and flap length (dichotomized according to the median value). Stratification was omitted when the target variable was identical to or highly correlated with the stratifying factor. Potential interaction effects were evaluated by incorporating multiplicative interaction terms into logistic regression models. Continuous variables were modeled using clinically meaningful increments, including age per 10 years, blood pressure per 10 mmHg, anesthesia duration per 60 minutes, blood loss per 100 mL, and albumin per 5 g/L increase. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

A total of 424 patients were included in the analytic sample, comprising 139 re-exploration cases and 285 randomly selected controls without re-exploration. Among them, 139 patients developed postoperative vascular compromise refractory to conservative management and consequently required urgent surgical re-exploration, forming the re-

exploration group. The remaining 285 patients achieved uncomplicated flap survival and comprised the non-re-exploration group. The flow chart of the research process is presented in Figure 1.

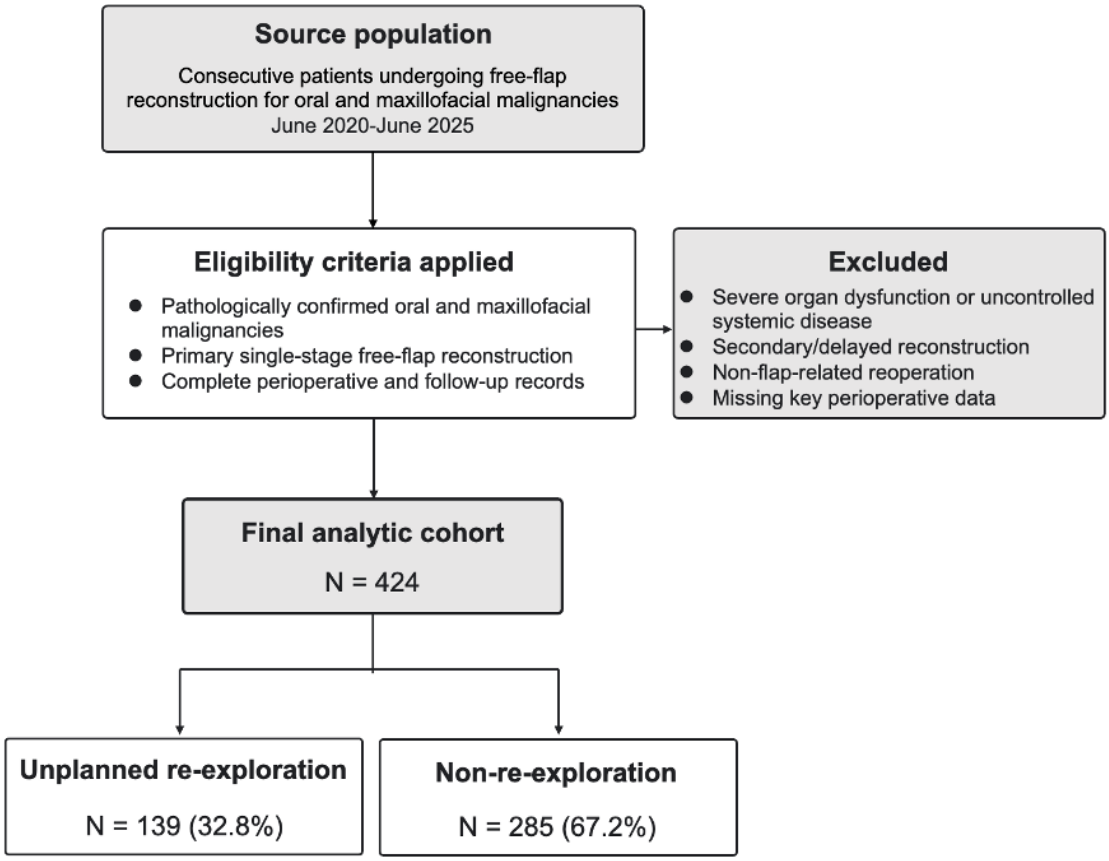


Fig.1 Flow diagram of patient selection and study design.

Baseline demographic, clinical, and perioperative characteristics are summarized in Table 1. Compared with patients who did not undergo re-exploration, those in the re-exploration group had a significantly higher prevalence of prior radiotherapy (26.6% vs. 13.7%, P = 0.001). Several hemodynamic parameters also differed significantly between cases and controls: preoperative DBP (80.0 [74.0-86.0] vs. 78.0 [72.0-84.0]

mmHg, P = 0.016), preoperative MAP (95.0 [90.5-103.2] vs. 93.0 [88.0-101.3] mmHg, P = 0.028), postoperative DBP (75.0 [70.0-80.5] vs. 74.0 [69.0-78.0] mmHg, P = 0.011), and postoperative MAP (93.3 [88.3-98.0] vs. 91.0 [87.3-95.7] mmHg, P = 0.025) were all elevated in the re-exploration cases. The number of previous surgical procedures and flap length also differed significantly between the two groups.

No statistically significant differences were observed in age, sex, BMI, preoperative diabetes mellitus, intraoperative blood loss, transfusion status, use of vasoactive agents (norepinephrine), postoperative infection, albumin, hemoglobin, or the majority of routine laboratory indices. The postoperative day 1 fasting plasma glucose level was elevated in the re-exploration group compared with the control group (8.9 [7.3-9.9] mmol/L vs 8.6 [7.7-10.9] mmol/L, P = 0.034). Detailed baseline characteristics are provided in Supplementary Table S1.

The results of the univariate logistic regression analyses are presented in Table 2. Prior radiotherapy was significantly associated with unplanned surgical re-exploration (OR = 2.29, 95% CI: 1.38–3.79, P = 0.001). Among the hemodynamic variables, preoperative DBP (OR = 1.33 per 10-mmHg increase, 95% CI: 1.08–1.63, P = 0.006), preoperative MAP (OR = 1.27 per 10-mmHg increase, 95% CI: 1.05–1.53, P=0.014), postoperative DBP (OR = 1.46 per 10-mmHg increase, 95% CI: 1.13–

1.88, P = 0.004), and postoperative MAP (OR = 1.35 per 10-mmHg increase, 95% CI: 1.05–1.74, P = 0.019) were significantly associated with unplanned re-exploration. In addition, an increase in the number of previous surgical procedures (OR = 1.26 per additional procedure, 95% CI: 1.04–1.53, P = 0.018), longer flap length (OR = 1.05 per 1-cm increase, 95% CI: 1.00–1.09, P = 0.030), and greater intraoperative blood loss (OR = 1.09 per 100-mL increase, 95% CI: 1.01–1.18, P = 0.036) were also significantly associated with re-exploration. The complete univariate regression results are shown in Supplementary Table S2.

The results of covariate-adjusted multivariable logistic regression analyses are presented in Table 3. After adjustment for the predefined covariates (age, sex, and vasoactive medication use), prior radiotherapy remained independently associated with unplanned re-exploration (adjusted OR [aOR] = 2.22, 95% CI: 1.33–3.69, P = 0.002). Preoperative DBP (aOR = 1.32 per 10-mmHg increase, 95% CI: 1.08–1.63, P = 0.008), preoperative MAP (aOR = 1.28 per 10-mmHg increase, 95% CI: 1.05–1.54, P = 0.013), postoperative DBP (aOR = 1.46 per 10-mmHg increase, 95% CI: 1.13–1.90, P = 0.004), and postoperative MAP (aOR = 1.40 per 10-mmHg increase, 95% CI: 1.08–1.82, P = 0.012) all remained independently associated with unplanned re-exploration. Similarly, a greater number of previous surgical procedures remained independently associated with re-exploration (aOR = 1.26 per additional procedure, 95% CI: 1.03–

1.53, P = 0.022). In contrast, the associations for flap length and intraoperative blood loss were attenuated after adjustment and remained only of borderline statistical significance. Intraoperative vasoactive agent use was not independently associated with unplanned re-exploration.

Exploratory subgroup and interaction analyses for variables that remained independently associated with unplanned re-exploration are summarized in Figure 2 and Supplementary Table S3. The association between prior radiotherapy and unplanned re-exploration remained directionally consistent across most predefined subgroups, with no evidence of significant interaction (all P for interaction > 0.05). Significant interactions were observed between age and the preoperative hemodynamic variables (DBP and MAP). The associations of higher preoperative DBP and MAP with unplanned re-exploration were stronger among patients younger than 60 years (P for interaction = 0.033 and 0.040, respectively). Although higher postoperative DBP and MAP were significantly associated with higher odds of re-exploration in patients with no prior radiotherapy, no previous surgical procedures, and longer flap length, the corresponding interaction tests were not statistically significant.

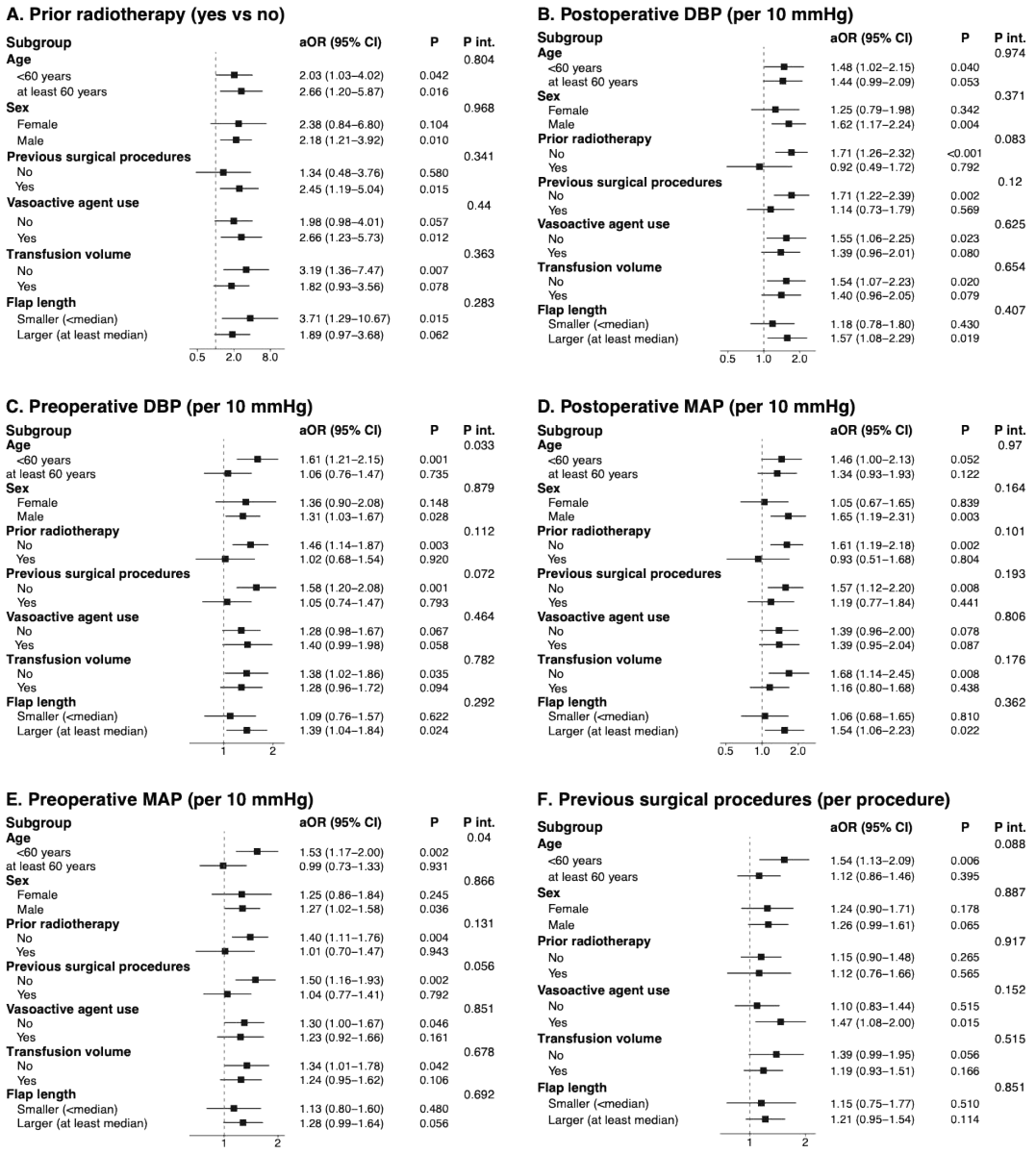


Figure 2. Exploratory subgroup analyses for variables independently associated with unplanned surgical re-exploration.

(A) Prior radiotherapy

(B) Postoperative diastolic blood pressure

(C) Preoperative diastolic blood pressure

(D) Postoperative mean arterial pressure

(E) Preoperative mean arterial pressure

(F) Number of previous surgical procedures

Note: Squares represent adjusted odds ratios (aORs), and horizontal lines indicate 95% confidence intervals (CIs). The vertical dashed line denotes the null value (aOR = 1.0). Odds ratios were estimated using covariate-adjusted multivariable logistic regression models. *P* values for interaction are displayed at the corresponding subgroup-variable row. Detailed numerical results are shown in Supplementary Table S3.

Discussion

In this retrospective case-control study of 424 patients undergoing resection of oral and maxillofacial malignancies followed by free tissue reconstruction, we identified several perioperative factors that were independently associated with unplanned re-exploration following postoperative flap vascular compromise. Prior radiotherapy showed a consistent association with unplanned re-exploration across the analyses performed. Among the hemodynamic variables examined, preoperative and postoperative DBP and MAP showed consistent associations with unplanned re-exploration, whereas SBP did not demonstrate a statistically significant association. A greater number of prior surgical procedures was also independently associated with the outcome, potentially reflecting the influence of previous surgical manipulation on local tissue characteristics or recipient vessel conditions, although these mechanisms could not be

directly evaluated in the present study. In contrast, the associations observed for intraoperative blood loss and flap length in univariate analyses did not remain statistically significant after multivariable adjustment, suggesting that these associations may be influenced by other patient or perioperative characteristics.

In our study, prior radiotherapy was independently associated with an increased likelihood of unplanned re-exploration (aOR = 2.22, 95% CI: 1.33–3.69, $P = 0.002$), consistent with findings from previous studies(8, 9). Radiotherapy is an important component of multimodal treatment for many head and neck malignancies, but radiation exposure can cause endothelial injury, vascular fibrosis, and obliterative endarteritis, potentially impairing vascular integrity and tissue perfusion. Prior radiotherapy may also induce extensive soft-tissue fibrosis and cicatricial contracture, leading to altered tissue architecture and reduced tissue compliance around the reconstructed flap. Such changes may increase the susceptibility of the vascular pedicle to mechanical compression or distortion, potentially increasing susceptibility to impaired venous outflow and contributing to venous congestion and subsequent flap vascular compromise. In addition, radiation-induced vascular injury may impair endothelial integrity and microvascular homeostasis. Chronic radiation-associated tissue changes may establish a locally pro- thrombotic microenvironment and compromise microvascular autoregulation, thereby increasing

susceptibility to thrombosis, microcirculatory disturbances, and vasospasm during the perioperative period(10, 11). From a microsurgical perspective, radiation-associated vascular and tissue changes may complicate recipient vessel preparation and anastomosis and could increase susceptibility to thrombosis or vasospasm(12). The consistent direction of the association across univariate, covariate-adjusted, and exploratory subgroup analyses suggests that the observed relationship between prior radiotherapy and unplanned re-exploration was relatively consistent across the analyses performed in this study. However, the underlying mechanisms and the extent to which prior radiotherapy may serve as a marker of treatment complexity cannot be determined from the present observational data. For patients with prior radiotherapy, clinicians should maintain extreme vigilance during preoperative recipient vessel mapping, intraoperative anastomotic planning, and postoperative flap monitoring, alongside the judicious initiation of prophylactic anticoagulants and antispasmodics.

Traditionally, perioperative hemodynamic management for free flap reconstruction has often emphasized maintaining adequate systemic blood pressure to support flap perfusion. This strategy is based on the assumption that maintaining adequate systemic blood pressure may support perfusion across newly established anastomoses, thereby optimizing flap microcirculation and improving flap viability(13). However, our multivariable logistic regression models demonstrated that elevated

perioperative DBP and MAP were independently associated with an increased likelihood of unplanned re-exploration, whereas SBP did not demonstrate a consistent independent association across covariate-adjusted models. These findings suggest that routine augmentation of systemic blood pressure solely to optimize flap perfusion should be approached with caution and raise the possibility that higher DBP and MAP may not necessarily confer additional protection against flap-related complications.

From a pathophysiological perspective, persistently elevated DBP and MAP may reflect heightened peripheral vascular resistance and microvascular vasospasms. One possible explanation is that higher transmural vascular pressure may increase bleeding from microvessels that were not ligated across the surgical bed, potentially increasing the risk of postoperative hematoma formation. A postoperative hematoma may mechanically compress the thin-walled, low-pressure venous pedicle, impair venous outflow, and contribute to acute venous congestion and subsequent flap compromise(14, 15). Elevated DBP may increase hydrostatic pressure within the flap microcirculation, potentially promoting interstitial fluid extravasation, which precipitates severe tissue edema and further compromises venous drainage(16). The summation of these pathways markedly increases the probability of postoperative flap re-exploration. Additionally, alterations in endothelial shear stress and fluid mechanics triggered by persistently elevated DBP and MAP constitute

another critical mechanism underlying vascular compromise(17). High systemic pressure directly inflicts mechanical injury upon the fragile endothelial monolayer at the anastomotic site, exposing the highly prothrombotic subendothelial collagen fibers. Simultaneously, mild size-mismatch of the matching vessels can generate pathological turbulence and localized vortices at the anastomosis. This aberrant hemodynamic environment activates the local coagulation cascade, promoting rapid platelet adhesion and aggregation near the anastomosis, alongside the release of pro-thrombotic factors (such as thromboxane A2), ultimately culminating in localized microthrombus formation(18). Together, these mechanisms provide a plausible explanation for how altered perioperative hemodynamics might contribute to arterial or mixed vascular compromise, although this mechanistic pathway could not be directly evaluated in the present study. Our findings challenge the assumption that higher systemic blood pressure is uniformly beneficial for flap perfusion. Excessively high DBP and MAP, rather than protecting the flap, foster a hazardous hemodynamic environment characterized by increased hematoma formation, microvascular endothelial disruption, and anastomotic thrombosis. Consequently, meticulous perioperative blood pressure titration to maintain a stable, normotensive target range—specifically avoiding pathological elevations in DBP and MAP—is a vital clinical

strategy to minimize vascular compromise and lower unplanned re-exploration rates.

The number of prior surgical interventions remained independently associated with unplanned re-exploration (aOR = 1.26, 95% CI: 1.03–1.53, $P = 0.022$). Repeated surgical dissections may disrupt normal tissue planes, yielding dense localized scarring and distorted anatomy within the head and neck region. These structural changes may increase the technical complexity of vascular dissection and recipient vessel preparation, thereby increasing susceptibility to inadvertent vascular injury or compromised flap perfusion(19). This mechanism may partially explain the observed association between prior surgery and postoperative vascular complications in the present study. For patients undergoing salvage reconstruction after tumor recurrence or with prior radiotherapy exposure, enhanced preoperative vascular assessment, including computed tomography angiography (CTA) or ultrasonography when appropriate, may facilitate surgical planning and risk stratification.

Traditionally, the intraoperative administration of vasoactive agents, particularly norepinephrine, has been approached cautiously because of concerns regarding potential anastomotic vasoconstriction and flap perfusion impairment(13). However, our multivariable logistic regression model demonstrated that, after adjustment for relevant

confounders, the use of intraoperative vasoactive agent was not independently associated with unplanned re-exploration (aOR = 1.40, 95% CI: 0.93–2.11, *P* = 0.106). This finding is consistent with several recent large-scale, multicenter cohort studies, suggesting that the rational application of vasoactive drugs does not independently increase the risk of flap vascular complications(20-22). From a pathophysiological perspective, persistently elevated DBP and MAP may reflect increased systemic vascular tone and impaired microvascular regulation, which could compromise flap perfusion through increased vascular resistance and microcirculatory disturbances. Conversely, the clinical objective of targeted intraoperative norepinephrine administration is not intended to deliberately induce excessive hypertension, but rather to counteract anesthesia-induced vasodilation, thereby stabilizing systemic blood pressure within a tight, normotensive range. Furthermore, free tissue flaps undergo substantial denervation during harvest, which may attenuate the local microvascular responsiveness to systemic α-adrenergic stimulation(23). Under conditions of optimal volume resuscitation, the controlled administration of norepinephrine may maintain adequate arterial pressure and systemic perfusion, thereby supporting perfusion pressure across the reconstructed microvascular circulation without necessarily causing clinically significant pedicle vasospasm. Collectively, our

findings support a goal-directed approach to hemodynamic management during head and neck microvascular reconstructions, emphasizing the importance of maintaining adequate perfusion while avoiding excessive elevations in blood pressure that may compromise microvascular circulation.

Notably, flap length (multivariable $P = 0.058$) and intraoperative blood loss (multivariable $P = 0.093$), which were significant in univariate analyses, showed attenuated associations after multivariable adjustment and did not reach conventional statistical significance. This shift indicates that the independent impact of these two parameters may be partially confounded by crucial covariates such as surgical duration, tumor subsite, or the patient's baseline systemic status. Although their independent associations were attenuated after adjustment, substantial blood loss may still contribute to perioperative hemodynamic instability and coagulation disturbances, while extensive tissue flaps remain technically demanding because of complex microvascular anastomotic requirements. Therefore, these factors warrant continued clinical attention during perioperative management.

This study did not identify independent associations between unplanned re-exploration and flap type, TNM staging, cardiovascular diseases, diabetes mellitus, D-dimer, or albumin levels. Although these findings differ from some previous reports, the lack of independent

associations with traditional metabolic and tumor-burden-related factors may reflect the impact of contemporary multidisciplinary perioperative management strategies, including nutritional optimization and standardized clinical pathways. This observation is consistent with the effectiveness of established perioperative protocols in our specialized head and neck oncology center, although further prospective studies are needed to clarify the contribution of specific interventions. In contrast, our analyses consistently demonstrated that potentially modifiable perioperative hemodynamic disturbances (elevated DBP and MAP) and historical treatment-related factors (prior radiotherapy and repeated surgical interventions) remain important independent factors associated with flap complications. Collectively, these findings provide additional insights into flap risk stratification. As perioperative protocols become increasingly standardized, individualized hemodynamic management and careful preoperative assessment of patients with prior radiotherapy exposure or repeated surgical history may represent important targets for further improving outcomes in head and neck free flap reconstruction.

Research Strengths and Novelty

The major strength of this study lies in the inclusion of all 139 patients requiring unplanned re-exploration and the inclusion of 285 randomly selected controls, allowing comprehensive evaluation of factors

associated with postoperative vascular complications after head and neck free flap reconstruction. Distinct from previous studies that have primarily focused on complete flap loss as the ultimate outcome, this study investigated unplanned secondary re-exploration, a clinically relevant endpoint associated with early flap salvage decision-making and healthcare resource utilization. Furthermore, our findings highlight the potential clinical importance of perioperative DBP and MAP beyond baseline blood pressure measurements alone, providing additional insights into hemodynamic assessment during microvascular reconstruction.

Limitations

Despite these insights, several limitations must be acknowledged. First, as an inherent limitation of the retrospective design, this study relies on clinical information extracted from electronic medical records, which introduces potential information bias. Several potentially relevant variables, including smoking/alcohol exposure, surgeons' learning curves, and detailed microsurgical parameters such as vessel mismatch ratios, were not completely available for analysis. Second, all patients were recruited from a single specialized head and neck oncology center, which may limit the generalizability of our findings to institutions with different surgical volumes or perioperative resources. Finally, the clinical diagnosis of vascular compromise relied primarily on subjective bedside clinical

signs, lacking real-time support from objective, quantitative modalities such as laser Doppler flowmetry or oxygen saturation monitoring. In addition, dynamic coagulation profiles were unavailable because thromboelastography (TEG) was not routinely performed. Future prospective studies incorporating objective perfusion monitoring and coagulation assessment may further clarify the temporal relationship between microvascular dysfunction and flap compromise.

Conclusion

In conclusion, prior radiotherapy, repeated surgical interventions, and elevated perioperative DBP and MAP were independently associated with unplanned re-exploration after head and neck free flap reconstruction. These findings suggest that individualized risk assessment incorporating treatment history and perioperative hemodynamic parameters may facilitate early identification of patients at increased risk of flap-related complications. For patients with prior radiotherapy exposure or multiple surgical interventions, careful preoperative vascular evaluation and tailored surgical planning may be beneficial. Furthermore, perioperative hemodynamic management should avoid the indiscriminate pursuit of aggressive hypertensive targets; instead, individualized titration of DBP and MAP within an appropriate physiological range may be important for maintaining microvascular

perfusion and potentially reducing the likelihood of flap vascular complications.

Declarations

Ethics approval and consent to participate

This retrospective study was reviewed and approved by the Institutional Review Board and Medical Ethics Committee of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine (Approval No. SH9H-2025-T444-1). The study was conducted in accordance with the Declaration of Helsinki.

The requirement for written informed consent was waived by the Ethics Committee due to the retrospective nature of the study. All patient data were anonymized prior to analysis.

Consent for publication

Not applicable. This manuscript does not contain any individual person’s data in any form (including individual details, images, or videos).

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to patient privacy and institutional data protection policies, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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No specific funding was received for this study.

Authors' contributions

Xiang Dong: manuscript drafting and critical revision.

Xinmeng Wang: data collection and data curation.

Ren Zhou: statistical analysis and interpretation of the results.

Jie Chen: study conception and design, data interpretation, and manuscript revision.

All authors reviewed and approved the final manuscript.

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667 Microsurgery. 2013;33(4):275–81.

668 **Table 1. Baseline demographic, clinical, and perioperative**

669 **characteristics according to unplanned re-exploration.**

Variable	Missing, n	Overall	Non-re-exploration (n=285)	Re-exploration (n=139)	*P* value
Male sex	0	298 (70.3)	197 (69.1)	101 (72.7)	0.454
Age, years	0	59.0 [49.8, 68.0]	61.0 [50.0, 68.0]	57.0 [48.0, 68.0]	0.296
Body mass index, kg/m²	8	22.8 [20.8, 24.8]	22.9 [20.8, 24.8]	22.6 [20.3, 25.0]	0.295
Duration of anesthesia, min	0	427.5 [375.0, 510.0]	435.0 [375.0, 495.0]	420.0 [360.0, 525.0]	0.916
Intraoperative blood loss, mL	0	500.0 [400.0, 600.0]	500.0 [400.0, 600.0]	500.0 [400.0, 700.0]	0.150
Number of previous surgical procedures	0	0.0 [0.0, 1.0]	0.0 [0.0, 1.0]	0.0 [0.0, 1.0]	0.021
Preoperative systolic blood pressure, mmHg	0	128.0 [119.0, 138.0]	127.0 [119.0, 137.0]	130.0 [120.0, 138.0]	0.118
Preoperative diastolic blood pressure, mmHg	0	79.0 [72.0, 85.0]	78.0 [72.0, 84.0]	80.0 [74.0, 86.0]	0.016
Preoperative mean arterial pressure, mmHg	0	95.0 [89.0, 102.0]	94.0 [88.0, 101.3]	96.7 [90.5, 103.2]	0.028
Postoperative systolic blood pressure, mmHg	2	128.0 [121.0, 135.0]	127.0 [121.0, 135.0]	130.0 [122.0, 135.0]	0.270
Postoperative diastolic blood pressure,	2	75.0 [69.0, 79.0]	74.0 [69.0, 78.0]	75.0 [70.0, 80.5]	0.011

Variable	Missing, n	Overall	Non-re-exploration (n=285)	Re-exploration (n=139)	*P* value
mmHg					
Postoperative mean arterial pressure, mmHg	2	91.7 [87.3, 96.7]	91.0 [87.3, 95.7]	93.3 [88.3, 98.0]	0.025
Absolute change in systolic blood pressure (ΔSBP), mmHg	2	12.0 [5.0, 21.0]	12.0 [5.0, 21.0]	11.0 [6.0, 19.5]	0.769
Flap length, cm	56	12.0 [7.5, 15.0]	11.5 [7.0, 15.0]	12.0 [9.0, 15.0]	0.038
Flap width, cm	91	6.0 [5.0, 6.5]	6.0 [5.0, 6.0]	6.0 [5.0, 7.0]	0.124
Preoperative hemoglobin level, g/L	1	136.0 [124.0, 147.0]	136.0 [124.8, 146.0]	137.0 [122.0, 150.5]	0.616
Preoperative D-dimer level, mg/L	10	0.3 [0.2, 0.6]	0.3 [0.2, 0.6]	0.3 [0.2, 0.5]	0.064
Preoperative albumin level, g/L	10	43.0 [40.0, 46.0]	43.0 [40.0, 46.0]	43.0 [40.0, 45.0]	0.989
Postoperative day 1 albumin level, g/L	13	32.0 [29.0, 34.0]	32.0 [29.0, 34.0]	32.0 [30.0, 34.0]	0.165
Postoperative day 1 glucose level, mmol/L	13	8.7 [7.4, 10.2]	8.6 [7.3, 9.9]	8.9 [7.7, 10.9]	0.034
Intraoperative blood transfusion	0	188 (44.3)	122 (42.8)	66 (47.5)	0.363
Intraoperative vasoactive agent use	0	181 (42.7)	114 (40.0)	67 (48.2)	0.109
Prior radiotherapy	0	76 (17.9)	39 (13.7)	37 (26.6)	0.001

Variable	Missing, n	Overall	Non-re-exploration (n=285)	Re-exploration (n=139)	*P* value
Prior chemotherapy	0	122 (28.8)	76 (26.7)	46 (33.1)	0.170
History of hypertension	0	161 (38.0)	108 (37.9)	53 (38.1)	0.963
History of diabetes mellitus	0	60 (14.2)	43 (15.1)	17 (12.2)	0.428
History of cardiac disease	0	25 (5.9)	18 (6.3)	7 (5.0)	0.599
Anticoagulant or antiplatelet therapy	0	19 (4.5)	15 (5.3)	4 (2.9)	0.265
Smoking history	0	115 (27.1)	81 (28.4)	34 (24.5)	0.389
Alcohol consumption history	0	76 (17.9)	46 (16.1)	30 (21.6)	0.170
Postoperative infection	0	115 (27.1)	74 (26.0)	41 (29.5)	0.443
Blood pressure fluctuation	2	50 (11.8)	30 (10.6)	20 (14.4)	0.258

Note: Continuous variables are presented as median [interquartile range], and categorical variables as number (percentage). *P* values were obtained using the Mann-Whitney U test, chi-square test, or Fisher exact test as appropriate.

674 **Table 2. Univariate logistic regression analysis of variables associated**

675 **with unplanned re-exploration.**

Variable	Unit/comparison	OR (95% CI)	*P* value
Prior radiotherapy	Yes vs no	2.29 (1.38-3.79)	0.001
Postoperative diastolic blood pressure, mmHg	Per 10 mmHg	1.46 (1.13-1.88)	0.004
Preoperative diastolic blood pressure, mmHg	Per 10 mmHg	1.33 (1.08-1.63)	0.006
Preoperative mean arterial pressure, mmHg	Per 10 mmHg	1.27 (1.05-1.53)	0.014
Number of previous surgical procedures	Per additional procedure	1.26 (1.04-1.53)	0.018
Postoperative mean arterial pressure, mmHg	Per 10 mmHg	1.35 (1.05-1.74)	0.019
Flap length, cm	Per 1 cm	1.05 (1.00-1.09)	0.030
Intraoperative blood loss, mL	Per 100 mL	1.09 (1.01-1.18)	0.036
Postoperative day 1 albumin level, g/L	Per 5 g/L	0.77 (0.59-1.02)	0.066
Intraoperative transfusion volume, units	Per 1 unit	1.12 (0.99-1.28)	0.076
Postoperative day 1 platelet count, $\times 10^9$/L	Per 50×10^9/L	0.86 (0.73-1.02)	0.076
Postoperative day 1 fibrinogen level, g/L	Per 1 g/L	0.80 (0.62-1.04)	0.091
Intraoperative vasoactive agent use	Yes vs no	1.40 (0.93-2.10)	0.110
Preoperative systolic blood pressure, mmHg	Per 10 mmHg	1.11 (0.98-1.26)	0.112
Body mass index, kg/m²	Per 1 kg/m²	0.96 (0.90-1.02)	0.165
Age, years	Per 10 years	0.93 (0.80-1.08)	0.338
Intraoperative blood transfusion	Yes vs no	1.21 (0.80-1.82)	0.363
Postoperative systolic blood pressure, mmHg	Per 10 mmHg	1.07 (0.91-1.27)	0.414
Postoperative infection	Yes vs no	1.19 (0.76-1.87)	0.443

Variable	Unit/comparison	OR (95% CI)	*P* value
Male sex	Yes vs no	1.19 (0.76-1.86)	0.454
Duration of anesthesia, min	Per 60 min	1.03 (0.93-1.14)	0.577
History of hypertension	Yes vs no	1.01 (0.67-1.53)	0.963

Note: Odds ratios are scaled according to the unit/comparison column. Binary variables are expressed as yes versus no. This table includes variables with $P < 0.10$ and selected clinically relevant variables; complete results are provided in Supplementary Table S2.

Table 3. Covariate-adjusted multivariable logistic regression analyses for factors associated with unplanned surgical re-exploration

Variable	Unit/comparison	aOR (95% CI)	*P* value
Prior radiotherapy	Yes vs no	2.22 (1.33-3.69)	0.002
Postoperative diastolic blood pressure, mmHg	Per 10 mmHg	1.46 (1.13-1.90)	0.004
Preoperative diastolic blood pressure, mmHg	Per 10 mmHg	1.32 (1.08-1.63)	0.008
Postoperative mean arterial pressure, mmHg	Per 10 mmHg	1.40 (1.08-1.82)	0.012
Preoperative mean arterial pressure, mmHg	Per 10 mmHg	1.28 (1.05-1.54)	0.013
Number of previous surgical procedures	Per additional procedure	1.26 (1.03-1.53)	0.022
Flap length, cm	Per 1 cm	1.04 (1.00-1.09)	0.058
Intraoperative blood loss, mL	Per 100 mL	1.08 (0.99-1.17)	0.093
Intraoperative vasoactive agent use	Yes vs no	1.40 (0.93-2.11)	0.106

Note: Each model was adjusted for age, sex, intraoperative vasoactive agent use, and the variable of interest. aOR indicates adjusted odds ratio.

Supplementary Tables

Supplementary Table S1. Complete baseline and perioperative characteristics

Variable	Missing, n	Overall	Non-re-exploration (n=285)	Re-exploration (n=139)	*P* value
Male sex	0	298 (70.3)	197 (69.1)	101 (72.7)	0.454
Age, years	0	59.0 [49.8, 68.0]	61.0 [50.0, 68.0]	57.0 [48.0, 68.0]	0.296
Body mass index, kg/m²	8	22.8 [20.8, 24.8]	22.9 [20.8, 24.8]	22.6 [20.3, 25.0]	0.295

Variable	Missing, n	Overall	Non-re-exploration (n=285)	Re-exploration (n=139)	*P* value
Duration of anesthesia, min	0	427.5 [375.0, 510.0]	435.0 [375.0, 495.0]	420.0 [360.0, 525.0]	0.916
Intraoperative blood loss, mL	0	500.0 [400.0, 600.0]	500.0 [400.0, 600.0]	500.0 [400.0, 700.0]	0.150
Number of previous surgical procedures	0	0.0 [0.0, 1.0]	0.0 [0.0, 1.0]	0.0 [0.0, 1.0]	0.021
Drainage volume during postoperative days 0-2, mL	176	120.0 [80.0, 170.0]	120.0 [80.0, 165.0]	120.0 [80.0, 180.0]	0.585
Preoperative systolic blood pressure, mmHg	0	128.0 [119.0, 138.0]	127.0 [119.0, 137.0]	130.0 [120.0, 138.0]	0.118
Preoperative diastolic blood pressure, mmHg	0	79.0 [72.0, 85.0]	78.0 [72.0, 84.0]	80.0 [74.0, 86.0]	0.016
Preoperative mean arterial pressure, mmHg	0	95.0 [89.0, 102.0]	94.0 [88.0, 101.3]	96.7 [90.5, 103.2]	0.028
Postoperative systolic blood pressure, mmHg	2	128.0 [121.0, 135.0]	127.0 [121.0, 135.0]	130.0 [122.0, 135.0]	0.270
Postoperative diastolic blood pressure, mmHg	2	75.0 [69.0, 79.0]	74.0 [69.0, 78.0]	75.0 [70.0, 80.5]	0.011
Postoperative mean arterial pressure, mmHg	2	91.7 [87.3, 96.7]	91.0 [87.3, 95.7]	93.3 [88.3, 98.0]	0.025
Absolute change in systolic blood pressure（△SBP）, mmHg	2	12.0 [5.0, 21.0]	12.0 [5.0, 21.0]	11.0 [6.0, 19.5]	0.769
T-stage	221	3.0 [2.0, 3.0]	3.0 [2.0, 3.0]	3.0 [2.0, 3.0]	0.212
N-stage	222	0.5 [0.0, 2.0]	0.0 [0.0, 2.0]	1.0 [0.0, 2.0]	0.564
M-stage	228	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.154
Tumor length, cm	45	3.1 [2.5, 4.0]	3.2 [2.5, 4.0]	3.0 [2.5, 4.1]	0.439

Variable	Missing, n	Overall	Non-re-exploration (n=285)	Re-exploration (n=139)	*P* value
Tumor width, cm	45	2.3 [1.8, 3.2]	2.5 [2.0, 3.0]	2.0 [1.8, 3.5]	0.442
Tumor depth, cm	45	1.4 [1.0, 2.0]	1.5 [1.0, 2.0]	1.3 [0.8, 2.4]	0.883
Flap length, cm	56	12.0 [7.5, 15.0]	11.5 [7.0, 15.0]	12.0 [9.0, 15.0]	0.038
Flap width, cm	91	6.0 [5.0, 6.5]	6.0 [5.0, 6.0]	6.0 [5.0, 7.0]	0.124
Preoperative hemoglobin level, g/L	1	136.0 [124.0, 147.0]	136.0 [124.8, 146.0]	137.0 [122.0, 150.5]	0.616
Preoperative platelet count, $\times 10^9$/L	1	227.0 [181.0, 273.5]	230.5 [184.0, 276.0]	216.0 [177.0, 272.0]	0.210
Preoperative fibrinogen level, g/L	5	3.4 [2.7, 4.1]	3.4 [2.7, 4.1]	3.4 [2.7, 4.1]	0.835
Preoperative D-dimer level, mg/L	10	0.3 [0.2, 0.6]	0.3 [0.2, 0.6]	0.3 [0.2, 0.5]	0.064
Preoperative albumin level, g/L	10	43.0 [40.0, 46.0]	43.0 [40.0, 46.0]	43.0 [40.0, 45.0]	0.989
Preoperative glucose level, mmol/L	6	5.3 [4.7, 6.1]	5.3 [4.7, 6.1]	5.3 [4.8, 6.1]	0.446
Postoperative day 1 hemoglobin level, g/L	1	116.0 [107.0, 125.0]	116.5 [108.0, 124.2]	115.0 [103.5, 127.5]	0.518
Postoperative day 1 platelet count, $\times 10^9$/L	2	182.5 [146.0, 224.8]	186.0 [149.0, 227.0]	173.0 [140.0, 216.5]	0.058
Postoperative day 1 fibrinogen level, g/L	6	3.1 [2.6, 3.8]	3.2 [2.7, 3.8]	3.1 [2.5, 3.8]	0.165
Postoperative day 1 D-dimer level, mg/L	29	1.2 [0.7, 2.5]	1.2 [0.7, 3.0]	1.1 [0.6, 2.2]	0.108
Postoperative day 1 potassium level, mmol/L	2	3.9 [3.6, 4.1]	3.9 [3.6, 4.1]	3.9 [3.6, 4.1]	0.732
Postoperative day	13	32.0 [29.0,	32.0 [29.0, 34.0]	32.0 [30.0, 34.0]	0.165

Variable	Missing, n	Overall	Non-re-exploration (n=285)	Re-exploration (n=139)	*P* value
1 albumin level, g/L		34.0]			
Postoperative day 1 glucose level, mmol/L	13	8.7 [7.4, 10.2]	8.6 [7.3, 9.9]	8.9 [7.7, 10.9]	0.034
Postoperative day 1 PaO2, mmHg	12	150.0 [125.0, 175.2]	151.0 [126.0, 173.0]	149.0 [124.5, 179.5]	0.858
Intraoperative transfusion volume	0	188 (44.3)	122 (42.8)	66 (47.5)	0.363
Intraoperative vasoactive agent use	0	181 (42.7)	114 (40.0)	67 (48.2)	0.109
Prior radiotherapy	0	76 (17.9)	39 (13.7)	37 (26.6)	0.001
Prior chemotherapy	0	122 (28.8)	76 (26.7)	46 (33.1)	0.170
History of hypertension	0	161 (38.0)	108 (37.9)	53 (38.1)	0.963
History of diabetes mellitus	0	60 (14.2)	43 (15.1)	17 (12.2)	0.428
History of COPD	0	1 (0.2)	1 (0.4)	0 (0.0)	1.000
History of cardiovascular disease	0	25 (5.9)	18 (6.3)	7 (5.0)	0.599
Anticoagulant or antiplatelet therapy	0	19 (4.5)	15 (5.3)	4 (2.9)	0.265
Smoking history	0	115 (27.1)	81 (28.4)	34 (24.5)	0.389
Alcohol consumption	0	76 (17.9)	46 (16.1)	30 (21.6)	0.170
Postoperative infection	0	115 (27.1)	74 (26.0)	41 (29.5)	0.443
Blood pressure fluctuation	2	50 (11.8)	30 (10.6)	20 (14.4)	0.258

688 Note: Continuous variables are presented as median [interquartile range],

and categorical variables as number (percentage).

Supplementary Table S2. Complete univariable logistic regression results

Variable	Unit/comparison	OR (95% CI)	P value
Prior radiotherapy	Yes vs no	2.29 (1.38-3.79)	0.001
Postoperative diastolic blood pressure, mmHg	Per 10 mmHg	1.46 (1.13-1.88)	0.004
Preoperative diastolic blood pressure, mmHg	Per 10 mmHg	1.33 (1.08-1.63)	0.006
Preoperative mean arterial pressure, mmHg	Per 10 mmHg	1.27 (1.05-1.53)	0.014
Number of previous surgical procedures	Per additional procedure	1.26 (1.04-1.53)	0.018
Postoperative mean arterial pressure, mmHg	Per 10 mmHg	1.35 (1.05-1.74)	0.019
Flap length, cm	Per 1 cm	1.05 (1.00-1.09)	0.030
Intraoperative blood loss, mL	Per 100 mL	1.09 (1.01-1.18)	0.036
Postoperative day 1 albumin, g/L	Per 5 g/L	0.77 (0.59-1.02)	0.066
Intraoperative transfusion volume, units	Per 1 unit	1.12 (0.99-1.28)	0.076
Postoperative day 1 platelet count, $\times 10^9$/L	Per 50×10^9/L	0.86 (0.73-1.02)	0.076
Postoperative day 1 fibrinogen level, g/L	Per 1 g/L	0.80 (0.62-1.04)	0.091
Intraoperative vasoactive agent use	Yes vs no	1.40 (0.93-2.10)	0.110
Preoperative systolic blood pressure, mmHg	Per 10 mmHg	1.11 (0.98-1.26)	0.112
Flap width, cm	Per 1 cm	1.13 (0.96-1.33)	0.137
Postoperative day 1 glucose level, mmol/L	Per 1 mmol/L	1.05 (0.98-1.13)	0.148
Body mass index, kg/m²	Per 1 kg/m²	0.96 (0.90-1.02)	0.165
Prior chemotherapy	Yes vs no	1.36 (0.88-2.11)	0.171

Variable	Unit/comparison	OR (95% CI)	P value
Alcohol consumption history	Yes vs no	1.43 (0.86-2.39)	0.172
Blood pressure fluctuation	Yes vs no	1.42 (0.77-2.60)	0.259
Anticoagulant or antiplatelet therapy	Yes vs no	0.53 (0.17-1.64)	0.272
Drainage volume during postoperative days 0-2, mL	Per 100 mL	1.22 (0.85-1.76)	0.273
T-stage	Per 1-point increase	0.82 (0.56-1.18)	0.284
Postoperative day 1 hemoglobin level, g/L	Per 10 g/L	0.94 (0.83-1.06)	0.309
Age, years	Per 10 years	0.93 (0.80-1.08)	0.338
Tumor depth, cm	Per 1 cm	1.10 (0.90-1.35)	0.355
Intraoperative transfusion volume	Yes vs no	1.21 (0.80-1.82)	0.363
Preoperative platelet count, $\times 10^9$/L	Per 50×10^9/L	0.94 (0.81-1.08)	0.371
Smoking history	Yes vs no	0.82 (0.51-1.30)	0.390
Postoperative systolic blood pressure, mmHg	Per 10 mmHg	1.07 (0.91-1.27)	0.414
History of diabetes mellitus	Yes vs no	0.78 (0.43-1.43)	0.429
Postoperative infection	Yes vs no	1.19 (0.76-1.87)	0.443
Male sex	Yes vs no	1.19 (0.76-1.86)	0.454
Postoperative day 1 D-dimer level, mg/L	Per 1 mg/L	0.97 (0.91-1.04)	0.463
Preoperative glucose level, mmol/L	Per 1 mmol/L	1.04 (0.92-1.17)	0.513
Duration of anesthesia, min	Per 60 min	1.03 (0.93-1.14)	0.577
Preoperative hemoglobin level, g/L	Per 10 g/L	1.03 (0.93-1.14)	0.585
History of cardiac disease	Yes vs no	0.79 (0.32-1.93)	0.600
Postoperative day 1 potassium level, mmol/L	Per 0.5 mmol/L	1.07 (0.84-1.36)	0.603
Absolute change in	Per 10 mmHg	1.04 (0.88-1.23)	0.634

Variable	Unit/comparison	OR (95% CI)	P value
systolic blood pressure, mmHg			
N-stage	Per 1-point increase	1.06 (0.81-1.40)	0.656
Postoperative day 1 PaO2, mmHg	Per 20 mmHg	0.99 (0.89-1.09)	0.773
Preoperative albumin level, g/L	Per 5 g/L	0.98 (0.79-1.21)	0.846
Tumor length, cm	Per 1 cm	0.99 (0.85-1.14)	0.857
Preoperative D-dimer level, mg/L	Per 1 mg/L	0.98 (0.76-1.26)	0.867
History of hypertension	Yes vs no	1.01 (0.67-1.53)	0.963
Tumor width, cm	Per 1 cm	1.00 (0.84-1.18)	0.981
Preoperative fibrinogen level, g/L	Per 1 g/L	1.00 (0.83-1.20)	0.988
History of COPD	Yes vs no		1.000
M-stage	M1 vs M0		1.000

692 Note: Odds ratios are scaled according to the unit/comparison column.
693 Binary variables are expressed as yes versus no.

694 **Supplementary Table S3. Complete exploratory subgroup and**
695 **interaction analyses for the main positive variables**

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
Prior radiotherapy	Yes vs no	Age	<60 years	2.03 (1.03-4.02)	0.042	0.804
Prior radiotherapy	Yes vs no	Age	≥60 years	2.66 (1.20-5.87)	0.016	
Prior radiotherapy	Yes vs no	Sex	Female	2.38 (0.84-6.80)	0.104	0.968
Prior radiotherapy	Yes vs no	Sex	Male	2.18 (1.21-	0.010	

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
				3.92)		
Prior radiotherapy	Yes vs no	Number of previous surgical procedures	No	1.34 (0.48-3.76)	0.580	0.341
Prior radiotherapy	Yes vs no	Number of previous surgical procedures	Yes	2.45 (1.19-5.04)	0.015	
Prior radiotherapy	Yes vs no	Intraoperative vasoactive agent use	No	1.98 (0.98-4.01)	0.057	0.440
Prior radiotherapy	Yes vs no	Intraoperative vasoactive agent use	Yes	2.66 (1.23-5.73)	0.012	
Prior radiotherapy	Yes vs no	Intraoperative transfusion volume	No	3.19 (1.36-7.47)	0.007	0.363
Prior radiotherapy	Yes vs no	Intraoperative transfusion volume	Yes	1.82 (0.93-3.56)	0.078	
Prior radiotherapy	Yes vs no	Flap length	Smaller (<median)	3.71 (1.29-10.67)	0.015	0.283
Prior radiotherapy	Yes vs no	Flap length	Larger (≥median)	1.89 (0.97-3.68)	0.062	
Postoperative diastolic blood pressure	Per 10 mmHg	Age	<60 years	1.48 (1.02-2.15)	0.040	0.974
Postoperative diastolic blood pressure	Per 10 mmHg	Age	≥60 years	1.44 (0.99-2.09)	0.053	
Postoperative diastolic blood pressure	Per 10 mmHg	Sex	Female	1.25 (0.79-1.98)	0.342	0.371
Postoperative diastolic blood	Per 10 mmHg	Sex	Male	1.62 (1.17-	0.004	

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
pressure				2.24)		
Postoperative diastolic blood pressure	Per 10 mmHg	Prior radiotherapy	No	1.71 (1.26-2.32)	<0.001	0.083
Postoperative diastolic blood pressure	Per 10 mmHg	Prior radiotherapy	Yes	0.92 (0.49-1.72)	0.792	
Postoperative diastolic blood pressure	Per 10 mmHg	Number of previous surgical procedures	No	1.71 (1.22-2.39)	0.002	0.120
Postoperative diastolic blood pressure	Per 10 mmHg	Number of previous surgical procedures	Yes	1.14 (0.73-1.79)	0.569	
Postoperative diastolic blood pressure	Per 10 mmHg	Intraoperative vasoactive agent use	No	1.55 (1.06-2.25)	0.023	0.625
Postoperative diastolic blood pressure	Per 10 mmHg	Intraoperative vasoactive agent use	Yes	1.39 (0.96-2.01)	0.080	
Postoperative diastolic blood pressure	Per 10 mmHg	Intraoperative transfusion volume	No	1.54 (1.07-2.23)	0.020	0.654
Postoperative diastolic blood pressure	Per 10 mmHg	Intraoperative transfusion volume	Yes	1.40 (0.96-2.05)	0.079	
Postoperative diastolic blood pressure	Per 10 mmHg	Flap length	Smaller (<median)	1.18 (0.78-1.80)	0.430	0.407
Postoperative diastolic blood pressure	Per 10 mmHg	Flap length	Larger (≥median)	1.57 (1.08-2.29)	0.019	
Preoperative diastolic blood pressure	Per 10 mmHg	Age	<60 years	1.61 (1.21-2.15)	0.001	0.033
Preoperative diastolic blood	Per 10 mmHg	Age	≥60 years	1.06 (0.76-	0.735	

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
pressure				1.47)		
Preoperative diastolic blood pressure	Per 10 mmHg	Sex	Female	1.36 (0.90-2.08)	0.148	0.879
Preoperative diastolic blood pressure	Per 10 mmHg	Sex	Male	1.31 (1.03-1.67)	0.028	
Preoperative diastolic blood pressure	Per 10 mmHg	Prior radiotherapy	No	1.46 (1.14-1.87)	0.003	0.112
Preoperative diastolic blood pressure	Per 10 mmHg	Prior radiotherapy	Yes	1.02 (0.68-1.54)	0.920	
Preoperative diastolic blood pressure	Per 10 mmHg	Number of previous surgical procedures	No	1.58 (1.20-2.08)	0.001	0.072
Preoperative diastolic blood pressure	Per 10 mmHg	Number of previous surgical procedures	Yes	1.05 (0.74-1.47)	0.793	
Preoperative diastolic blood pressure	Per 10 mmHg	Intraoperative vasoactive agent use	No	1.28 (0.98-1.67)	0.067	0.464
Preoperative diastolic blood pressure	Per 10 mmHg	Intraoperative vasoactive agent use	Yes	1.40 (0.99-1.98)	0.058	
Preoperative diastolic blood pressure	Per 10 mmHg	Intraoperative transfusion volume	No	1.38 (1.02-1.86)	0.035	0.782
Preoperative diastolic blood pressure	Per 10 mmHg	Intraoperative transfusion volume	Yes	1.28 (0.96-1.72)	0.094	
Preoperative diastolic blood pressure	Per 10 mmHg	Flap length	Smaller (<median)	1.09 (0.76-1.57)	0.622	0.292
Preoperative diastolic blood	Per 10 mmHg	Flap length	Larger (≥median)	1.39 (1.04-	0.024	

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
pressure				1.84)		
Postoperative mean arterial pressure	Per 10 mmHg	Age	<60 years	1.46 (1.00-2.13)	0.052	0.970
Postoperative mean arterial pressure	Per 10 mmHg	Age	≥60 years	1.34 (0.93-1.93)	0.122	
Postoperative mean arterial pressure	Per 10 mmHg	Sex	Female	1.05 (0.67-1.65)	0.839	0.164
Postoperative mean arterial pressure	Per 10 mmHg	Sex	Male	1.65 (1.19-2.31)	0.003	
Postoperative mean arterial pressure	Per 10 mmHg	Prior radiotherapy	No	1.61 (1.19-2.18)	0.002	0.101
Postoperative mean arterial pressure	Per 10 mmHg	Prior radiotherapy	Yes	0.93 (0.51-1.68)	0.804	
Postoperative mean arterial pressure	Per 10 mmHg	Number of previous surgical procedures	No	1.57 (1.12-2.20)	0.008	0.193
Postoperative mean arterial pressure	Per 10 mmHg	Number of previous surgical procedures	Yes	1.19 (0.77-1.84)	0.441	
Postoperative mean arterial pressure	Per 10 mmHg	Intraoperative vasoactive agent use	No	1.39 (0.96-2.00)	0.078	0.806
Postoperative mean arterial pressure	Per 10 mmHg	Intraoperative vasoactive agent use	Yes	1.39 (0.95-2.04)	0.087	
Postoperative mean arterial pressure	Per 10 mmHg	Intraoperative transfusion volume	No	1.68 (1.14-2.45)	0.008	0.176
Postoperative mean arterial	Per 10 mmHg	Intraoperative transfusion	Yes	1.16 (0.80-	0.438	

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
pressure		volume		1.68)		
Postoperative mean arterial pressure	Per 10 mmHg	Flap length	Smaller (<median)	1.06 (0.68-1.65)	0.810	0.362
Postoperative mean arterial pressure	Per 10 mmHg	Flap length	Larger (≥median)	1.54 (1.06-2.23)	0.022	
Preoperative mean arterial pressure	Per 10 mmHg	Age	<60 years	1.53 (1.17-2.00)	0.002	0.040
Preoperative mean arterial pressure	Per 10 mmHg	Age	≥60 years	0.99 (0.73-1.33)	0.931	
Preoperative mean arterial pressure	Per 10 mmHg	Sex	Female	1.25 (0.86-1.84)	0.245	0.866
Preoperative mean arterial pressure	Per 10 mmHg	Sex	Male	1.27 (1.02-1.58)	0.036	
Preoperative mean arterial pressure	Per 10 mmHg	Prior radiotherapy	No	1.40 (1.11-1.76)	0.004	0.131
Preoperative mean arterial pressure	Per 10 mmHg	Prior radiotherapy	Yes	1.01 (0.70-1.47)	0.943	
Preoperative mean arterial pressure	Per 10 mmHg	Number of previous surgical procedures	No	1.50 (1.16-1.93)	0.002	0.056
Preoperative mean arterial pressure	Per 10 mmHg	Number of previous surgical procedures	Yes	1.04 (0.77-1.41)	0.792	
Preoperative mean arterial pressure	Per 10 mmHg	Intraoperative vasoactive agent use	No	1.30 (1.00-1.67)	0.046	0.851
Preoperative mean arterial	Per 10 mmHg	Intraoperative vasoactive	Yes	1.23 (0.92-	0.161	

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
pressure		agent use		1.66)		
Preoperative mean arterial pressure	Per 10 mmHg	Intraoperative transfusion volume	No	1.34 (1.01-1.78)	0.042	0.678
Preoperative mean arterial pressure	Per 10 mmHg	Intraoperative transfusion volume	Yes	1.24 (0.95-1.62)	0.106	
Preoperative mean arterial pressure	Per 10 mmHg	Flap length	Smaller (<median)	1.13 (0.80-1.60)	0.480	0.692
Preoperative mean arterial pressure	Per 10 mmHg	Flap length	Larger (≥median)	1.28 (0.99-1.64)	0.056	
Number of previous surgical procedures	Per additional procedure	Age	<60 years	1.54 (1.13-2.09)	0.006	0.088
Number of previous surgical procedures	Per additional procedure	Age	≥60 years	1.12 (0.86-1.46)	0.395	
Number of previous surgical procedures	Per additional procedure	Sex	Female	1.24 (0.90-1.71)	0.178	0.887
Number of previous surgical procedures	Per additional procedure	Sex	Male	1.26 (0.99-1.61)	0.065	
Number of previous surgical procedures	Per additional procedure	Prior radiotherapy	No	1.15 (0.90-1.48)	0.265	0.917
Number of previous surgical procedures	Per additional procedure	Prior radiotherapy	Yes	1.12 (0.76-1.66)	0.565	
Number of	Per additional	Intraoperative	No	1.10	0.515	0.152

Exposure	Unit/comparison	Subgroup variable	Subgroup	aOR (95% CI)	*P* value	*P* for interaction
previous surgical procedures	procedure	vasoactive agent use		(0.83-1.44)		
Number of previous surgical procedures	Per additional procedure	Intraoperative vasoactive agent use	Yes	1.47 (1.08-2.00)	0.015	
Number of previous surgical procedures	Per additional procedure	Intraoperative transfusion volume	No	1.39 (0.99-1.95)	0.056	0.515
Number of previous surgical procedures	Per additional procedure	Intraoperative transfusion volume	Yes	1.19 (0.93-1.51)	0.166	
Number of previous surgical procedures	Per additional procedure	Flap length	Smaller (<median)	1.15 (0.75-1.77)	0.510	0.851
Number of previous surgical procedures	Per additional procedure	Flap length	Larger (≥median)	1.21 (0.95-1.54)	0.114	

Note: Adjusted odds ratios were estimated within each subgroup. *P* values for interaction were obtained from exposure-by-subgroup interaction terms.

Supplementary Table S4. Missing data summary

Variable	Missing, n	Missing, %
M-stage	228	53.8
N-stage	222	52.4
T-stage	221	52.1
Drainage volume during postoperative days 0-2, mL	176	41.5
Flap width, cm	91	21.5
Flap length, cm	56	13.2

Variable	Missing, n	Missing, %
Tumor depth, cm	45	10.6
Tumor width, cm	45	10.6
Tumor length, cm	45	10.6
Postoperative day 1 D-dimer level, mg/L	29	6.8
Postoperative day 1 albumin level, g/L	13	3.1
Postoperative day 1 glucose level, mmol/L	13	3.1
Postoperative day 1 PaO2, mmHg	12	2.8
Preoperative albumin level, g/L	10	2.4
Preoperative D-dimer level, mg/L	10	2.4
Body mass index, kg/m²	8	1.9
Preoperative glucose level, mmol/L	6	1.4
Postoperative day 1 fibrinogen level, g/L	6	1.4
Preoperative fibrinogen level, g/L	5	1.2
Postoperative day 1 platelet count, $\times 10^9$/L	2	0.5
Postoperative day 1 potassium level, mmol/L	2	0.5
Absolute change in systolic blood pressure, mmHg	2	0.5
Postoperative systolic blood pressure, mmHg	2	0.5
Postoperative diastolic blood pressure, mmHg	2	0.5
Postoperative mean arterial pressure, mmHg	2	0.5
Blood pressure fluctuation	2	0.5
Postoperative day 1 hemoglobin level, g/L	1	0.2
Preoperative hemoglobin level, g/L	1	0.2
Preoperative platelet count, $\times 10^9$/L	1	0.2

Note: Variables with substantial missingness should not be directly

included in multivariable models without an appropriate missing-data strategy, such as multiple imputation or a prespecified restricted analysis.