Int. J. Oral Maxillofac. Surg. 2019; 48: 447–451
https://doi.org/10.1016/j.ijom.2018.08.009, available online at https://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Reconstructive Surgery

Intraoperative factors associated with free flap failure in the head and neck region: a four-year retrospective study of 216 patients and review of the literature

Y. Lin[1], J.-f. He[1], X. Zhang[2], H.-m. Wang[1]
[1]Department of Oral and Maxillofacial Surgery, the First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zheijang, China; [2]Department of VIP, the First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zheijang, China

Y. Lin, J.-f. He, X. Zhang, H.-m. Wang: Intraoperative factors associated with free flap failure in the head and neck region: a four-year retrospective study of 216 patients and review of the literature. Int. J. Oral Maxillofac. Surg. 2019; 48: 447–451. © 2018 Published by Elsevier Ltd on behalf of International Association of Oral and Maxillofacial Surgeons.

Abstract. The aim of this study was to identify intraoperative factors associated with free flap failure. The outcomes of 216 patients (220 flaps) were analyzed retrospectively. A statistical analysis was performed to determine the association of flap failure with the intraoperative factors of prolonged operation time, flap type, vascular pedicle at the recipient site, and use of vasoactive medication. A review of the recent literature was also conducted to identify other intraoperative risk factors. Univariate regression analysis revealed that a prolonged operative time ($P = 0.013$) and the vascular pedicle at the recipient site ($P = 0.027$) were primary risk factors for flap failure. Furthermore, the intraoperative use of papaverine improved the success rate of free flap transfer ($P = 0.015$). Multivariate regression analysis showed that only the application of papaverine remained statistically significant ($P = 0.011$). The results confirmed that the choice of flap type had no influence on free flap survival ($P = 0.583$). In addition, the literature review showed that excessive intraoperative fluid administration is a risk factor for free flap failure. These conclusions may provide microvascular surgeons with information to reduce the failure rate. Also, microvascular surgeons should always consider the details of intraoperative fluid management.

Key words: free flap failure; papaverine; microsurgery.

Accepted for publication
Available online 6 September 2018

0901-5027/040447 + 05

Since Seidenberg et al. first described free flap transfer in 1959, head and neck reconstruction surgery has largely relied on microvascular free flap techniques.[1] It is well known that surgeon experience is the most important factor associated with flap survival, and the free flap success rate of one surgeon reportedly improved from about 70% in early cases to more than 96% in later cases.[2] Although the success rate of free flap techniques is reported to range from 91% to 99%,[3] failure always leads to additional surgery, increased costs, prolonged hospitalization, and inferior results, with corresponding functional, cosmetic, and psychosocial consequences. Previous studies have identified a number of risk factors that influence the outcome of microsurgery and free flap failure, which include older age, diabetes mellitus, cigarette smoking, body mass index, preoperative radiotherapy, and chemotherapy.

Obviously, most of these risk factors are related to the patient's general condition and cannot be changed by the surgeon. Although the majority of studies have demonstrated a significant correlation between patient-related risk factors and free flap failure, few studies have identified intraoperative factors that can actually be controlled by the surgeon during the intervention. Thus, it appears important to identify intraoperative factors associated with an increased risk of flap failure.

The aim of this 4-year retrospective study of 216 patients (220 flaps) and review of the literature was to assess the influence of specific intraoperative factors (i.e., prolonged operative time, flap type, vascular pedicle at the recipient site, and intraoperative use of vasoactive medication) on free flap failure.

Materials and methods

A retrospective chart review of patients who had undergone free flap transfers in the head and neck region during the 4-year period 2013–2017 was conducted. This study included 220 free flap transfers in 216 patients. The primary outcome was the occurrence of free flap failure, which was classified as flap necrosis, reoperation because of vascular crisis, or intraoperative revision of the anastomosis. Of note, only one patient underwent flap repair after radiotherapy (radial forearm flap, RFF) and the flap survived.

Patients were categorized into groups on the basis of intraoperative factors, which included the operative time, flap type, vascular pedicle at the recipient site, and intraoperative use of vasoactive medication. Free flaps included the RFF, anterolateral thigh flap (ALTF), medial sural artery perforator flap (MSAPF), fibula free flap, and iliac crest flap. The operative time was categorized as <480 min, 480–640 min, or >640 min.

Papaverine is regarded as the 'gold standard' prophylactic topical treatment for intraoperative vasospasm. Of the 220 flaps, 138 (62.7%) that required vascular anastomosis were treated with papaverine, which was dripped onto the vascular anastomosis (3 mg every 5–10 min). The vascular pedicles at the recipient sites were divided into two groups. The first group included the preferred vessels, i.e. the facial artery, superior thyroid artery, common facial vein, and internal jugular vein branches, which are the recipient vessels most commonly used by maxillofacial surgeons. The second group included other vessels, such as the transverse cervical artery, lingual artery, superficial temporal artery, internal jugular vein, external jugular vein, superficial temporal vein, superior thyroid vein, and innominate vessels. At the study institution, the choice of recipient vessels is largely based on the diameter of the donor vessels, location of the recipient site, and specific intraoperative vascular conditions.

The statistical analysis of free flap failure was performed using SPSS version 16.0 software (SPSS, Inc., Chicago, IL, USA). A probability (P) value of <0.05 was considered statistically significant.

An extensive search of the PubMed database (https://www.ncbi.nlm.nih.gov/pubmed/) was performed to identify relevant articles published in the English language, using combinations of the search terms ''free flap failure'', ''flap loss'', ''free tissue transfer'', ''risk factors'', ''head and neck'', and ''intraoperative''. Articles from medical centres in different countries were selected to avoid duplication of data, and each publication was carefully examined to identify other intraoperative factors associated with free flap failure.

Results

A total of 216 patients (154 (71.3%) male and 62 (28.7%) female; mean age 52.9 years, age range 17–79 years) received 220 free flaps for reconstruction during the study period (2013–2017). The overall flap survival rate was 92.3%. The 220 free flaps consisted of 131 (59.5%) RFFs, 45 (20.5%) fibula free flaps, 21 (9.5%) ALTFs, 20 (9.1%) MSAPFs, and three (1.4%) iliac crest flaps. One patient simultaneously received two free flaps.

Free flap failure occurred in 17 (7.7%) cases. Three RFFs were performed as secondary repairs and four cases were successfully rescued from vascular crisis. When examining the free flap failure rate based on the flap type, all iliac crest flaps were excluded because of the small sample size (Table 1). The results confirmed that the choice of flap type had no influence on free flap survival ($P = 0.583$).

On univariate analysis, the local application of papaverine improved the success rate of vascular anastomosis ($P = 0.015$). A longer operative time was associated with a higher free flap failure rate ($P = 0.013$). Also, on analysis of the vascular pedicles at the recipient sites, the group in which the preferred vessels were used had a significantly lower failure rate than the group in which other vessels were used ($P = 0.027$) (Table 2).

The use of papaverine remained significant on multivariate regression analysis ($P = 0.011$) (Table 3). However, the data showed that the operative time and recipient vessels were confounding factors and these were not independent risk factors for flap failure. This may be because the sample size was not sufficiently large. In this study, the flap failure rate increased significantly when a longer operation time and use of non-preferred vessels were both present.

Discussion

Improvements in techniques, surgical equipment, and postoperative management have dramatically improved the quality of life and survival rates of patients undergoing free flap reconstruction for complex defects. The average free flap survival rate is now 95%,[4] with even higher success rates of 99% commonly

Table 1. Statistical analysis of flap failure according to the flap type.

Flap type	No. of cases	Flap failure	Failure rate	*P*-value
Total	220	17	7.7%	0.583
RFF	131	8	6.1%	
Fibula free flap	45	4	8.9%	
ALTF	21	3	14.3%	
MSAPF	20	2	10.0%	
Iliac free flap	3	0	0	

RFF, radial forearm flap; ALTF, anterolateral thigh flap; MSAPF, medial sural artery perforator flap.

Table 2. Identification of intraoperative risk factors for flap failure; univariate regression analysis.

Intraoperative factors	No. of cases	Flap failure	*P*-value
Use of papaverine			0.015
Yes	138	6	
No	82	11	
Duration of surgery			0.013
<640 min	114	5	
640–800 min	62	4	
>800 min	44	8	
Vascular pedicle at the recipient site			0.027
Preferred vessels	133	6	
Other vessels	87	11	

Table 3. Multivariate regression analysis of risk factors for flap failure.

Intraoperative factors	Adjusted OR	95% CI	*P*-value
Papaverine	0.244	0.082–0.728	0.011
Operative time			0.081
640–800 min	3.807	1.089–13.312	0.036
>800 min	2.809	0.759–10.391	0.122
Use of non-preferred vessels	2.763	0.900–8.481	0.076

CI, confidence interval; OR, odds ratio.

reported.[5] Surgical experience is often described as a critical factor for free flap success. Although previous reports have identified patient-related risk factors, the aim of the present study was to identify surgeon-related and intraoperative factors associated with free flap failure.

A prolonged operative time has been identified as an independent risk factor for failure of head and neck free flaps. Ishimaru et al. conducted a retrospective national database study in Japan; they identified 2846 patients and found that a longer operative time was associated with a significant increase in free flap failure.[6] Also, Sanati-Mehrizy et al. found an association between flap failure and the operative time ($P = 0.002$) on univariate analysis in a study of 2013 patients from the American College National Surgical Quality Improvement Program database in 2015.[7] Serletti et al. reported that an operative time longer than 10 h was associated with an increased risk of postoperative complications, such as flap failure, thrombosis, bleeding, and haematoma.[8] A prolonged operative time often indicates a longer ischemic period and tissue damage due to anoxic injuries. Furthermore, the risk of reperfusion injury and the incidence of the no-flow phenomenon increase with longer ischemia times.[9] The flap ischemia time is likely a better predictor of flap outcome. Unfortunately, the ischemia time for each flap in this study was not available, so it was not possible to differentiate between the total operative time and the free flap ischemia time with regard to free flap failure. In addition, as suggested by the present study findings, there is some confounding between a prolonged operative time and other factors; for example, if the preferred vessels are not available, the surgeon will need more time to complete the operation.

Despite improvements in surgical techniques and methods, there remains a risk of thrombotic occlusion of small anastomosed vessels.[10] Many studies have reported that aspirin, low molecular weight heparin, and dextran are the most common forms of postoperative prophylaxis against thrombosis after free flap transfer. A meta-analysis by Pan et al. found that prophylaxis with heparin and aspirin is associated with similar flap loss rates after free flap transfer, and that high-dose heparin therapy is associated with a greater flap failure rate than low-dose therapy.[11] However, few reports have suggested pharmacological regimens to improve the success rate of anastomosis in head and neck free flap transfer. It is well known that peripheral vasospasm is a severe complication that leads to a reduction in flap perfusion, thrombosis, and flap failure,[12] as well as increased difficulty of anastomosis and a prolonged operative time.

The application of papaverine during anastomosis has been found to increase carotid artery blood flow in humans[13] and in rabbits.[14] Similarly, it was found in the present study that the local application of papaverine could sustain anastomotic dilatation and contribute to the implementation of the vascular anastomosis. In a systematic review including 20 articles, Vargas et al. concluded that papaverine could produce a significant increase in vessel diameter (a 66% increase) and that it had a vasodilatory effect on non-spastic vessels.[15] Papaverine acts directly on calcium channels causing a direct increase in cyclic adenosine monophosphate. The subsequent increase in secondary messengers leads to protein kinase activation and non-selective smooth muscle relaxation.[16] In a rat femoral artery model, papaverine showed longer sustained vasodilation as compared to lidocaine.[17]

In the present study, the application of papaverine decreased the flap failure rate to 4.3% (6/138 flaps failed), as compared to 13.4% for the untreated group (11/82 flaps failed). The half-life of papaverine is 0.5–2.0 hours. Taking this into consideration, papaverine was dripped directly onto the vascular anastomosis (3 mg every 5–10 min) to maintain the vascular anastomosis in a dilated state. This was found to be helpful for the success of free flaps. However, papaverine also has some drawbacks, as it has been shown to impair endothelial function and trigger apoptosis of both human endothelial cells and smooth muscle cells.[18] Hence, further research is warranted to find new alternatives.

The choice of the recipient vessel was found to be a factor contributing to flap failure. In the authors' experience, the facial artery, superior thyroid artery, common facial vein, and internal jugular vein branches are the most suitable for anastomosis. A study conducted in Shanghai covering a 34-year period and including 4640 flaps showed that the facial artery and superior thyroid artery were most often selected, as these arteries are in close proximity to oral and maxillofacial defects and the diameters of these vessels are similar to those of the donor vessels.[19]

Venous failure can occur due to extrinsic compression on the vein or thrombosis within the venous anastomosis, whereas arterial failure occurs much less frequently; hence the choice of vein is far more important than the choice of artery. The diameter of the recipient vein should be relatively larger than the donor vein to guarantee blood backflow.[20] The present authors prefer to create a venous end-to-side anastomosis to the internal jugular vein over the external jugular vein, because the long path and superficial location of the external jugular vein may lead to torsion and frequent compression of the pedicle. A recent retrospective analysis of 1530 free flaps in the Netherlands cautions

that anastomosis to the lingual vein or superficial temporal artery should be avoided. Anastomosis to the lingual vein may be rather difficult because of its cranial position under the mandible, while the diameter of the superficial temporal artery may be insufficient and vasospasm may easily develop.[20]

The flap type is mainly chosen according to the type and size of the defect. The RFF is the most widely used in the head and neck region because it is easy to harvest, the anatomy of the vessels tends to be constant, a long vascular pedicle can be constructed, and the size of the pedicle vessels are comparable to those at the recipient site. The disadvantage of the RFF is that there is not enough tissue to restore large defects.

The ALTF and MSAPF are both typical perforator flaps and can provide some subcutaneous fat and muscle tissue according to the size of the defect. Also, the skin can be used to create multiple perforator flaps, so the skin paddle can be divided into several islands. The ALTF has been used successfully at Chang Gung Hospital (Taipei, Taiwan) since 2002[21] and its use has subsequently become more widespread. In a retrospective study, Kao et al. reviewed the cases of 47 patients who underwent head and neck reconstruction with 29 RFFs and 18 MSAPFs. The study found no significant difference in flap harvest time, but significantly better functional and cosmetic outcomes in the MSAPF group as compared with the RFF group.[22] In a study conducted in Finland, ALTF and RFF were found to have failure rates similar to the average.[23] The fibula free flap is the most widely used osteocutaneous flap, as it is suitable for the restoration of subtotal and total mandibular defects because a large length of bone can be harvested.

Investigations into the flap failure rate according to the type of flap have found no significant differences in regard to the flap type (Table 4[6,24–26]). Kwok and Agarwal examined the overall flap failure rate based on the flap type (muscle, fascial, skin, bone, and bowel flap) in 1187 cases and concluded that there were no significant associations between known risk factors and the flap type ($P = 0.464$)[27]. In contrast, the failure rate was greater with ALTFs in the present study, but this difference was not statistically significant. Other studies have also arrived at different conclusions. In a series of 548 free flaps for head and neck reconstruction, which were divided into an RFF group and non-RFF group, Las et al. showed a significantly better survival rate for the RFF ($P = 0.015$)[20]. However, the frequencies of the flap types have varied greatly and the outcomes have differed slightly among centres, reflecting obvious differences in surgical experience.

A review of the literature found that excessive intraoperative fluid administration may be another risk factor influencing the success of free flaps. Haughey et al. hypothesized that oedema of the flap or recipient site can result from increased volumes of crystalloids, and a cut-off value of >7 litres of crystalloids during surgery was found to result in major flap complications[28]. Ruttmann et al. suggested that the use of crystalloids, as compared to colloids, can cause a hypercoagulable state, especially when administered rapidly[29]. On the basis of a literature review on perioperative fluid management summarizing 84 articles, Brinkman et al. recommended that basic fluid maintenance should not exceed 6 ml/kg/h and that normovolaemic haemodilution should be preferred, because blood with a reduced haematocrit has a better flow profile than blood with a normal hematocrit[30]. Namdar et al. concluded through a clinical data analysis that saline administration was associated with flap loss (4534 ml vs. 6125 ml for those without flap loss vs. those with flap loss; $P = 0.048$)[31]. Hence, favourable intraoperative fluid administration is considered to be critical in microsurgical flap procedures.

Table 4. Flap loss in relation to flap type, as reported in the literature.

Flap type	Total/flap loss			
	Mücke et al.[24]	Joo et al.[25]	Kim et al.[26]	Ishimaru et al.[6]
RFF	230/7	187/8	25/1	
ALTF	110/3	34/8	77/7	
Fibula flap	76/7	8/0		
Iliac crest flap	13/0			
Myocutaneous flap				1462/51
Osteocutaneous flap				1384/43
P-value	0.185	0.351	0.309	0.601

RFF, radial forearm flap; ALTF, anterolateral thigh flap.

Conclusions

This study identified some intraoperative factors associated with flap failure, which included a prolonged operative time and the vascular pedicle at the recipient site. The intraoperative use of a vasoactive medication, such as papaverine, can improve the success rate of free flap transfer. There is no available evidence to show that the choice of flap type influences the survival of free flaps. However, excessive intraoperative fluid administration is a risk factor that is often ignored by surgeons. Therefore, it is important to continually reinforce that hydration should be administered judiciously.

Funding

This work was supported by grants from the Medical Science and Technology Project of Zhejiang Province (No. 2015KYB160).

Competing interests

None declared.

Ethical approval

Approved by the First Affiliated Hospital, College of Medicine, Zhejiang University.

Patient consent

Not required.

References

1. Seidenberg B, Rosenak SS, Hurwitt ES, Som ML. Immediate reconstruction of the cervical esophagus by a revascularized isolated jejunal segment. *Ann Surg* 1959;**149**:162–71.
2. Khouri RK. Avoiding free flap failure. *Clin Plast Surg* 1992;**19**:773–81.
3. Suh JD, Sercarz JA, Abemayor E, Calcaterra TC, Rawnsley JD, Alam D, Blackwell KE. Analysis of outcome and complications in 400 cases of microvascular head and neck reconstruction. *Arch Otolaryngol Head Neck Surg* 2004;**130**:962–6.
4. Wax MK. The role of the implantable Doppler probe in free flap surgery. *Laryngoscope* 2014;**124**(Suppl 1):S1–2.
5. Cervenka B, Bewley AF. Free flap monitoring: a review of the recent literature. *Curr Opin Otolaryngol Head Neck Surg* 2015;**23**:393–8.
6. Ishimaru M, Ono S, Suzuki S, Matsui H, Fushimi K, Yasunaga H. Risk factors for free flap failure in 2,846 patients with head and neck cancer: a national database study in

Japan. *J Oral Maxillofac Surg* 2016;**74**:1260–70.
7. Sanati-Mehrizy P, Massenburg BB, Rozehnal JM, Ingargiola MJ, Hernandez Rosa J, Taub PJ. Risk factors leading to free flap failure: analysis from the national surgical quality improvement program database. *J Craniofac Surg* 2016;**27**:1956–64.
8. Serletti JM, Higgins JP, Moran S, Orlando GS. Factors affecting outcome in free-tissue transfer in the elderly. *Plast Reconstr Surg* 2000;**106**:66–70.
9. Pattani KM, Byrne P, Boahene K, Richmon J. What makes a good flap go bad? A critical analysis of the literature of intraoperative factors related to free flap failure. *Laryngoscope* 2010;**120**:717–23.
10. Froemel D, Fitzsimons SJ, Frank J, Sauerbier M, Meurer A, Barker JH. A review of thrombosis and antithrombotic therapy in microvascular surgery. *Eur Surg Res* 2013;**59**:32–43.
11. Pan XL, Chen GX, Shao HW, Han CM, Zhang LP, Zhi LZ. Effect of heparin on prevention of flap loss in microsurgical free flap transfer: a meta-analysis. *PLoS One* 2014;**9**:e95111.
12. Quinlan J. Anaesthesia for reconstructive surgery. *Anaesth Intensive Care Med* 2006;**7**:31–5.
13. Dillon PF, Aksoy MO, Driska SP, Murphy RA. Myosin phosphorylation and the cross-bridge cycle in arterial smooth muscle. *Science* 1981;**211**:495–7.
14. Gao YJ, Stead S, Lee RM. Papaverine induces apoptosis in vascular endothelial and smooth muscle cells. *Life Sci* 2002;**70**:2675–85.
15. Vargas CR, Iorio ML, Lee BT. A systematic review of topical vasodilators for the treatment of intraoperative vasospasm in reconstructive microsurgery. *Plast Reconstr Surg* 2015;**136**:411–22.
16. Dregelid E, Heldal K, Resch F, Stangeland L, Breivik K, Svendsen E. Dilation of the internal mammary artery by external and intraluminal papaverine application. *Eur J Thorac Cardiovasc Surg* 1995;**110**:41–8.
17. Kerschner JE, Futran ND. The effect of topical vasodilating agents on microvascular vessel diameter in the rat model. *Laryngoscope* 1996;**106**:1429–33.
18. Wang XL, Liu LB, Song FM, Wang QY. Meta-analysis of the safety and factors contributing to complications of MS-TRAM, DIEP, and SIEA flaps for breast reconstruction. *Aesthetic Plast Surg* 2014;**38**:681–91.
19. Zhang C, Sun J, Zhu H, Xu L, Ji T, He Y, Yang W, Hu Y, Yang X, Zhang Z. Microsurgical free flap reconstructions of the head and neck region: Shanghai experience of 34 years and 4640 flaps. *Int J Oral Maxillofac Surg* 2015;**44**:675–84.
20. Las DE, de Jong T, Zuidam JM, Verweij NM, Hovius SE, Mureau MA. Identification of independent risk factors for flap failure: a retrospective analysis of 1530 free flaps for breast, head and neck and extremity reconstruction. *J Plast Reconstr Aesthet Surg* 2016;**69**:894–906.
21. Wei FC, Jain V, Celik N, Chen HC, Chuang DC, Lin CH. Have we found an ideal soft-tissue flap? An experience with 672 anterior lateral thigh flaps. *Plast Reconstr Surg* 2002;**109**:2219–26.
22. Kao HK, Chang KP, Wei FC, Cheng MH. Comparison of the medial sural artery perforator flap with the radial forearm flap for head and neck reconstructions. *Plast Reconstr Surg* 2009;**124**:1125–32.
23. Husso A, Mäkitie AA, Vuola J, Suominen S, Bäck L, Lassus P. Evolution of head and neck microvascular reconstructive strategy, at an academic centre: an 18-year review. *J Reconstr Microsurg* 2016;**32**:294–300.
24. Mücke T, Ritschl LM, Roth M, Güll FD, Rau A, Grill S, Kesting MR, Wolff KD, Loeffelbein DJ. Predictors of free flap loss in the head and neck region: a four-year retrospective study with 451 microvascular transplants at a single centre. *J Craniomaxillofac Surg* 2016;**44**:1292–8.
25. Joo YH, Sun DI, Park JO, Cho KJ, Kim MS. Risk factors of free flap compromise in 247 cases of microvascular head and neck reconstruction: a single surgeon's experience. *Eur Arch Otorhinolaryngol* 2010;**267**:1629–33.
26. Kim H, Jeong WJ, Ahn SH. Results of free flap reconstruction after ablative surgery in the head and neck. *Clin Exp Otorhinolaryngol* 2015;**8**:167–73.
27. Kwok AC, Agarwal JP. An analysis of free flap failure using the ACS NSQIP database Does flap site and flap type matter? *Microsurgery* 2017;**37**:531–8.
28. Haughey BH, Wilson E, Kluwe L, Piccirillo J, Fredrickson J, Sessions D, Spector G. Free flap reconstruction of the head and neck: analysis of 241 cases. *Otolaryngol Head Neck Surg* 2001;**125**:10–7.
29. Ruttmann T, James MF, Finlayson J. Effects on coagulation of intravenous crystalloid or colloid in patients undergoing peripheral vascular surgery. *Br J Anaesth* 2002;**89**:226–30.
30. Brinkman JN, Derks LH, Klimek M, Mureau MA. Perioperative fluid management and use of vasoactive and antithrombotic agents in free flap surgery: a literature review and clinical recommendations. *J Reconstr Microsurg* 2013;**29**:357–66.
31. Namdar T, Bartscher T, Stollwerck PL, Mailänder P, Lange T. Complete free flap loss due to extensive hemodilution. *Microsurgery* 2010;**30**:214–7.

Address:
Hui-ming Wang
Department of Oral and Maxillofacial Surgery
The First Affiliated Hospital
College of Medicine
Zhejiang University
#79 Qingchun Road
Hangzhou 310003
Zhejiang
China
Tel.: +86 571 8723689; Fax: +86 571 87236395
E-mail: whmwhm@zju.edu.cn