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· 临床研究 ·

游离组织瓣修复口腔颌面部肿瘤术后缺损血管危象的影响因素配对logistic回归分析

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【摘要】 目的 探讨口腔颌面部肿瘤切除游离组织瓣移植术后发生血管危象的影响因素。**方法** 对2015—2020年某三甲专科医院头颈肿瘤外科病房完成游离组织瓣移植术且发生血管危象的所有患者进行回顾性分析。从同时期该病房未发生血管危象的患者中,根据手术医生、手术时间、患者性别和年龄进行1:1配对,收集46个可能的影响因素,采用SPSS 26.0统计软件对数据进行单因素和多因素logistic回归分析。**结果** 共纳入158例患者,其中危象组和配对组各79例,先对各变量进行单因素分析,将单因素分析 $P < 0.2$ 的变量进行配对logistic回归分析,仅术后血钾($P = 0.048$, $OR = 3.118$, 95% CI : 1.008 ~ 9.641)和术前术后红细胞计数差值($P = 0.004$, $OR = 4.53$, 95% CI : 1.609 ~ 12.750)有统计学意义。**结论** 术后血钾水平高及手术前后红细胞计数差值大是血管危象的危险因素。

【关键词】 口腔颌面部; 口腔癌; 游离组织瓣; 移植术; 血管危象; 动脉危象; 静脉危象; 影响因素; 血钾; 红细胞计数

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Paired logistic regression analysis of influencing factors for vascular crisis after repair of oral and maxillofacial tumors with free tissue flaps ZHENG Ying¹, BI Xiaoqin². 1. West China School of Nursing, Sichuan University & West China Hospital of Stomatology, Sichuan University, Chengdu 610041, China; 2. State Key Laboratory of Oral Diseases & National Clinical Research Center for Oral Diseases & West China Hospital of Stomatology, Sichuan University, Chengdu 610041, China

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【Abstract】 Objective To investigate the influencing factors of vascular crisis after oral and maxillofacial tumor free tissue flap transplantation. **Methods** A retrospective analysis was performed on all patients who underwent free tissue flap transplantation and developed vascular crisis in the surgical ward of head and neck cancer in a grade A specialized hospital. Forty-six possible influencing factors were collected using 1:1 matching according to surgeons, operation time, sex and age of patients from patients without vascular crisis from 2015-2020 in this ward during the same period. SPSS 26.0 statistical software was used for univariate and multivariate logistic regression analyses of the data. **Results** A total of 158 patients were enrolled, including 79 in the crisis group and 79 in the pairing group. Univariate analysis was performed for each variable. Paired logistic regression analysis showed that only postoperative blood potassium ($P = 0.048$, $OR = 3.118$, 95% CI : 1.008-9.641) and preoperative and postoperative red blood cell count differences ($P = 0.004$, $OR = 4.53$, 95% CI : 1.609-12.750) were statistically significant. **Conclusion** High blood potassium levels and red blood cell count differences before and after surgery were risk factors for vascular crisis.

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【Key words】 oral maxillofacial; oral cancer; free tissue flap; transplantation; vascular crisis; arterial crisis; vein crisis; influencing factors; blood potassium; red blood cell count

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游离组织瓣移植已成为修复口腔颌面部肿瘤软组织缺损的重要方式,并随着显微吻合等技术日臻成熟,已具有较高的成功率^[1-3]。然而,血管危象这一威胁移植皮瓣存活的重要因素在临床上仍时有发生,相关文献显示,血管危象的危险因素包括高血压病史、糖尿病史和脑血管事件等^[4-6],另有研究认为高血压病史^[7]、吸烟^[8]与血管危象之间并无联系。本文基于对单一中心既往临床病例信息的回顾性分析对口腔肿瘤游离组织瓣移植术后血管危象的影响因素进行了相关研究与探讨。

1 资料和方法

1.1 一般资料

选择某三甲专科医院头颈肿瘤病房2015年1月1日至2020年12月31日期间完成游离组织瓣修复缺损且发生血管危象的患者共82例。从同时期该病房未发生血管危象的患者中,根据手术医生、手术时间、患者性别和年龄进行1:1配对,1例患者因病情危重转院治疗予以排除,2例患者因配对失败予以排除,79例患者配对成功。共纳入本研究158例患者。

1.2 方法

1.2.1 样本量计算 本研究为配对病例对照研究,配对logistic回归样本量应至少为纳入变量个数的20倍^[9],本文纳入回归分析的变量为7个,即样本量应至少为140例,本文共纳入158例患者。

1.2.2 选择变量方法 根据文献报道^[1-8],患者吸烟饮酒史、合并其他疾病、血生化、血常规、凝血、手术时长等因素均可能与游离组织瓣移植术后血管危象的发生相关,本研究收集该158例患者的术前资料:吸烟史、饮酒史、放疗史、化疗史、糖尿病史、高血压史、是否合并其他共病、肿瘤是否多发、是否肿瘤晚期、总胆固醇值、甘油三酯、低密度脂蛋白(low-density lipoprotein, LDL)、高密度脂蛋白(high density lipoprotein, HDL)、术前白蛋白值、术

前白细胞计数(white blood cell count, WBC)、术前血钾、术前血钙、术前血钠、术前血氯、术前血红蛋白值、术前红细胞计数(red blood cell count, RBC)、术前活化部分凝血酶原时间(activated partially prothrombin time, APPT)、术前凝血酶时间(thrombin time, TT)、术前国际标准化比值(international normalized ratio, INR)、术前凝血酶原时间(prothrombin time, PT)、术前纤维蛋白原浓度(fibrinogen concentration, FBG-C)、术前等待时长;术中资料:手术时长、失血量、补液量、尿量、总出入量、是否颈清、是否切骨;术后资料:平均住院日、术后血钾、术后红细胞计数、术后血氯、术后白细胞计数、术后血钠、是否感染,并分别计算两组患者术前术后血钾差值(difference of blood potassium before and after operation)、红细胞计数差值(difference of red blood cell count before and after operation, dRBC)、血氯差值(difference of blood chlorine before and after operation)、血钠差值(difference of blood sodium before and after operation)、白细胞计数差值(difference of leukocyte count before and after operation),共46项资料进行统计分析。

1.2.3 收集数据方法 使用该院电子病历信息系统,根据入院评估表收集患者吸烟饮酒史、放化疗史、既往史等。根据手术及麻醉记录收集患者手术时长、术中失血量、补液量、尿量、是否切骨等;根据该院HIS系统收集术前及术后各项实验室指标,术前指标均为入院第2日的检测值,术后指标均为术后24h内的检测值,危象组术后指标为术后至发生血管危象之前的值;根据出院记录收集平均住院日;是否发生血管危象则是根据电子病历信息系统的手术记录中是否对吻合动静脉进行了探查,结合护士移动工作站的护理记录进行收集。

1.3 评价指标界定

1.3.1 血管危象 根据朱家恺《外科学辞典》^[10]及

张志愿《口腔颌面外科学》^[11]中的相关定义,血管危象包括静脉危象、动脉危象和复合动静脉危象。静脉危象表现为组织瓣发紫、肿胀、组织瓣缝合处渗血、针刺试验血液为暗红色或黑色;动脉危象表现为组织瓣苍白或灰白、萎缩、缺乏弹性、针刺试验无出血;动静脉危象则是在临床表现基础上,手术探查时在吻合动脉及静脉中均发现血栓。

1.3.2 手术部位感染诊断 参照2001年卫生部《医院感染诊断标准(试行)》^[12]。

1.3.3 吸烟、饮酒、是否发生转移 戒烟 ≥ 5 年为不吸烟,戒烟 < 5 年及偶尔吸烟、经常吸烟界定为吸烟;戒酒 ≥ 3 个月为不饮酒,戒酒 < 3 个月及偶尔饮酒、经常饮酒界定为饮酒;本文是否发生转移均为局部淋巴转移。

1.4 统计学处理

采用SPSS26.0统计学软件对数据进行处理。首先对数据进行单因素分析,对符合正态分布和

近似正态分布的定量数据进行独立样本 t 检验,对偏态数据进行两独立样本非参数检验,对二分类数据进行卡方检验。纳入所有 $P < 0.2$ ^[13]且无明显交互作用的影响因素进行配对logistic回归分析,计算OR值及95%置信区间, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 血管危象发生情况

2组临床资料情况见表1所示。危象组共采用7种皮瓣:股前外侧皮瓣、前臂皮瓣、背阔肌皮瓣、腓骨肌皮瓣、腹壁下动脉穿支皮瓣、上臂皮瓣、股前内侧皮瓣;配对组采用6种皮瓣:股前外侧皮瓣、前臂皮瓣、背阔肌皮瓣、腓骨肌皮瓣、上臂皮瓣、股前内侧皮瓣。79例危象组患者中,动脉危象24例(30.4%),静脉危象52例(65.8%),复合动静脉危象3例(3.8%),其中45例(57.0%)组织瓣发生坏死。

表1 158例口腔颌面部游离组织瓣移植术患者一般资料

Table 1 General information of 158 patients undergoing oral and maxillofacial free tissue flap transplantation		n (%)	
Variables		Pairing group(n = 79)	Crisis group(n = 79)
Age[Year, Median (P ₂₅ , P ₇₅)]		61(48.66)	60(48.66)
Gender	Male	53(67.10)	53(67.10)
	Female	26(32.90)	26(32.90)
Defect site	Cheek	37(46.80)	30(38.00)
	Tongue	18(22.80)	22(27.80)
	Floor of mouth	12(15.20)	10(12.70)
	Other	12(15.20)	17(21.50)
Type of flap	Latissimus dorsi flap	1(1.30)	8(10.00)
	Deep inferior epigastric perforator flap	0(0.00)	1(1.25)
	Upper flap	1(1.30)	1(1.25)
	Anterolateral thigh flap	67(84.80)	55(68.75)
	Anteromedial thigh flap	1(1.30)	1(1.25)
	Fibula free flap	1(1.30)	3(3.75)
	Forearm flap	8(10.10)	11(13.75)
	Other	6(7.70)	9(12.50)
Pathological diagnosis	Squamous cell carcinoma	63(79.70)	66(82.50)
	Sarcoma	3(3.80)	3(3.75)
	Basal cell carcinoma	2(2.50)	1(1.25)
	Mucoepidermoid carcinoma	3(3.80)	0(0.00)
	Adenoid cystic carcinoma	2(2.50)	0(0.00)
	Other	6(7.70)	9(12.50)

One of the 79 patients in the crisis group was repaired with fibula free flap and forearm flap at the same time

2.2 血管危象影响因素的筛选分析结果

对所有血管危象的影响因素进行单因素分析(表2、表3),共10个变量满足 $P < 0.2$,但结合临床实际情况,有无“其他共病”在临床无统一界定标准,总住院日被认为是血管危象的结果而非原因,

予以筛选。经筛选,纳入所有符合要求的变量——总胆固醇、术后血钾、dRBC、HDL、有无术前放疗、术前化疗、是否颈清及有无感染共8个影响因素进行配对logistic回归分析(表4)。结果仅术后血钾($P = 0.048$, $OR = 3.118$, $95\%CI: 1.008 \sim 9.641$)和术

表2 定量变量单因素分析
Table 2 Single-factor analysis of quantitative variables

Variables	Crisis group	Pairing group	$\bar{x} \pm s$ /Median (P ₂₅ , P ₇₅)	t/z	P
Total cholesterol/(mmol/L)	4.788 ± 1.075	4.581 ± 0.909		1.298	0.196
LDL/(mmol/L)	2.909 ± 1.095	2.727 ± 0.726		1.208	0.229
Value of preoperative albumin/(g/L)	42.524 ± 3.604	42.583 ± 3.023		-0.111	0.912
Preoperative serum potassium/(mmol/L)	4.036 ± 0.383	4.023 ± 0.371		0.216	0.829
Preoperative blood calcium/(mmol/L)	2.346 ± 0.211	2.315 ± 0.103		1.147	0.253
Preoperative serum sodium/(mmol/L)	139.840 ± 2.381	139.740 ± 2.381		0.264	0.792
Preoperative RBC/(×10 ¹² /L)	4.648 ± 0.570	4.539 ± 0.586		1.190	0.236
Operative time/(min)	349.190 ± 138.145	339.180 ± 123.136		0.481	0.631
Volume of intraoperative infusion/(mL)	3 275.320 ± 1 218.471	3 216.460 ± 1166.787		0.310	0.757
Total in and out/(mL)	1 977.420 ± 990.309	1 979.100 ± 894.351		-0.010	0.992
Postoperative blood potassium/(mmol/L)	3.728 ± 0.375	3.614 ± 0.371		1.918	0.057*
Postoperative RBC/(×10 ¹² /L)	3.665 ± 0.594	3.712 ± 0.537		-0.518	0.605
Postoperative blood chlorine/(mmol/L)	104.277 ± 3.535	104.428 ± 3.004		-0.288	0.773
Postoperative WBC/(×10 ⁹ /L)	14.385 ± 3.890	13.822 ± 4.402		0.849	0.397
APPT/s	25.981 ± 3.842	26.742 ± 3.669		-1.266	0.207
TT/s	18.113 ± 1.192	18.128 ± 1.339		-0.076	0.940
Difference of blood potassium before and after operation/(mmol/L)	0.308 ± 0.415	0.409 ± 0.409		-1.538	0.126
Difference of blood sodium before and after operation/(mmol/L)	2.691 ± 3.364	2.299 ± 3.255		0.742	0.459
Difference of blood chlorine before and after operation/(mmol/L)	0.532 ± 3.907	0.906 ± 2.835		-0.688	0.493
DRBC/(×10 ¹² /L)	0.983 ± 0.512	0.827 ± 0.418		2.098	0.038**
Difference of leukocyte count before and after operation/(×10 ⁹ /L)	-8.150 ± 3.568	-7.639 ± 4.193		-0.823	0.412
Triglyceride/(mmol/L)	1.255(0.880,1.720)	1.305(0.870,1.780)		-0.048	0.962
HDL/(mmol/L)	1.230(1.040,1.460)	1.180(1.030,1.340)		-1.464	0.143*
Preoperative WBC/(×10 ⁹ /L)	5.830(4.790,7.300)	6.060(4.620,7.100)		-0.402	0.688
Preoperative blood chlorine/(mmol/L)	105.050(103.330,106.830)	105.800(104.500,106.700)		-1.041	0.298
Preoperative hemoglobin/(g/L)	143.000(133.000,152.250)	140.000(130.000,149.000)		-0.980	0.327
Waiting time for surgery/d	6(4,7)	6(4,7)		-0.304	0.761
Intraoperative blood loss/mL	400(300,600)	400(300,500)		-0.803	0.422
Urine volume/mL	775(500,1025)	700(500,1200)		-0.042	0.966
Postoperative blood sodium/(mmol/L)	137.400(135.810,139.050)	137.400(135.570,139.600)		-0.411	0.681
PT/s	10.950(10.400,11.630)	11.35(10.400,12.100)		-1.119	0.263
INR	0.950(0.900,1.013)	0.98(0.900,1.040)		-1.066	0.286
FBG-C/(g/L)	3.100(2.580,3.600)	3.24(2.550,3.700)		-0.666	0.505
Average length of stay/d	20(16,24)	16(14,20)		-4.227	<0.001***

*: $P < 0.2$; **: $P < 0.05$; ***: $P < 0.01$. LDL: low density lipoprotein; RBC: red blood cell count; WBC: white blood cell count; APTT: activated partially prothrombin time; TT: thrombin time; dRBC: difference of red blood cell count before and after operation; HDL: high density lipoprotein; PT: prothrombin time; INR: international normalized ratio; FBG-C: fibrinogen concentration

前术后红细胞计数差值($P = 0.004$, $OR = 4.53$, 95% $CI: 1.609 \sim 12.75$)有统计学意义。

2.3 共线性诊断

通过共线性诊断(表5),方差膨胀因子均未超过5,容忍度均接近1,可认为各影响因素间相互独立,不存在明显共线性^[14]。

3 讨论

3.1 术后血钾水平

本研究结果显示,术后血钾水平与血管危象

呈正相关($P = 0.048$, $OR = 3.118$, 95% $CI: 1.008 \sim 9.641$),提示术后血钾每增加1 mmol/L,发生血管危象的危险增加约2.118倍。这可能与钾离子可通过多种途径发挥降低血压的作用^[15]相关。血钾浓度升高可直接调节肾素-血管紧张素-醛固酮系统中醛固酮的释放,促进肾脏远曲小管与集合管上皮细胞对水钠的重吸收和对钾离子的排泄,促进血容量下降,从而降低血压,相应的,血钾浓度降低,其利尿钠作用相应减弱,血压升高;钾浓度升高也可使交感神经系统的活性降低,从而松弛

血管平滑肌降低血压;另外,钾离子浓度升高也可激活钠/钾泵和刺激质膜钾通道,导致血管内皮超极化和胞质平滑肌钙减少或通过改善血管内皮功能和一氧化氮的释放来降低血压。低钾血症与血压升高的直接关系在由淑萍等^[16]的报道中也得到了证实。头颈肿瘤患者术后维持血钾在正常范围的低水平可维持血压保持在较高水平,保持血管

壁的扩张,减少血管内血栓形成,这与一项 meta 分析^[17]结果吻合——使用血管加压素可减少吻合血管血栓发生及组织瓣坏死的发生,提示在临床工作中应重点观察患者术后血钾水平及血压的变化而不仅限于高血压病史,这也一定程度上解释了有的学者认为高血压病史是血管危象的危险因素^[4],而有的学者认为高血压病史是血管危象的保

表3 二分类数据单因素分析

Table 3 Single factor analysis of binary data

n (%)

Variables	Group	Pairing group	Crisis Group	χ^2	P
Chemotherapy	0	76(97.4)	72(91.1)	1.832	0.176*
	1	2(2.6)	7(8.9)		
Neck dissection	0	18(22.8)	26(32.9)	2.016	0.156*
	1	61(77.2)	53(67.1)		
Radiotherapy	0	78(98.7)	71(89.9)	4.242	0.039**
	1	1(1.3)	8(10.1)		
Smoking	0	47(59.5)	45(57.0)	0.104	0.747
	1	32(40.5)	34(43.0)		
Drinking	0	44(55.7)	51(64.6)	1.294	0.255
	1	35(44.3)	28(35.4)		
Osteotomy	0	19(24.1)	20(25.3)	0.034	0.854
	1	60(75.9)	59(74.7)		
Diabetes	0	68(86.1)	68(86.1)	0.000	1.000
	1	11(13.9)	11(13.9)		
Hypertension	0	61(77.2)	65(82.3)	0.627	0.428
	1	18(22.8)	14(17.7)		
Multi-site	0	73(92.4)	71(89.9)	0.313	1.000
	1	6(7.6)	8(10.1)		
Terminal tumor	0	41(51.9)	44(55.7)	0.229	0.632
	1	38(48.1)	35(44.3)		
Other comorbidities	0	65(82.3)	56(70.9)	2.859	0.091*
	1	14(17.7)	23(29.1)		
Infection	0	51(76.1)	42(64.6)	2.098	0.148*
	1	16(23.9)	23(35.4)		

*: $P < 0.2$; **: $P < 0.05$

表4 配对 logistic 回归多因素分析

Table 4 Multivariate analysis of paired logistic regression

Variables	β	SE	Wald	P	OR (95%CI)
Radiotherapy	1.144	1.262	0.821	0.365	3.138(0.265~37.223)
Postoperative blood potassium	1.137	0.576	3.897	0.048	3.118(1.008~9.641)
dRBC	1.511	0.528	8.185	0.004	4.530(1.609~12.750)
Neck dissection	-1.001	0.582	2.958	0.085	0.368(0.118~1.150)
Chemotherapy	1.267	1.453	0.761	0.383	3.552(0.206~61.302)
Total cholesterol	0.283	0.227	1.554	0.213	1.327(0.850~2.071)
HDL	-0.003	0.697	0.000	0.996	0.997(0.254~3.906)
Infection	0.254	0.483	0.276	0.599	1.289(0.500~3.325)

dRBC: difference of red blood cell count before and after operation; HDL: high density lipoprotein

表5 共线性诊断
Table 5 Collinearity diagnostics

Variables	TOL	VIF
Neck dissection	0.901	1.109
Chemotherapy	0.559	1.789
Radiotherapy	0.554	1.804
Total cholesterol	0.817	1.224
HDL	0.793	1.261
Postoperative blood potassium	0.878	1.139
dRBC	0.909	1.100
Infection	0.916	1.092

TOL: tolerance; VIF: variance inflation factor. HDL: high density lipoprotein; dRBC: difference of red blood cell count before and after operation

护因素^[1]这一矛盾。

3.2 手术前后红细胞计数差值

手术前后红细胞计数差值与血管危象呈正相关($P = 0.004$, $OR = 4.53$, $95\%CI: 1.609 \sim 12.75$),提示术后红细胞计数比术前红细胞计数每减少 $1 \times 10^9/L$,发生血管危象的危险增加约 3.53 倍。这可能与红细胞计数显著波动改变了血流动力学,也可能与红细胞中的血红蛋白值变化和携氧能力有关。来自不同海拔、不同民族、不同性别的患者,其红细胞计数、血红蛋白值基线水平均不相同,对术前红细胞计数偏高的患者来说,其血流存在较高的粘滞度,阻力较大,舒张末期血流明显降低,微循环本身存在供血不足的风险^[18],Jiang 等^[19]的研究证实了红细胞增多会导致纤溶系统发生显著改变,而术后单位面积红细胞波动较大,致使血红蛋白携氧能力减弱,缺氧环境下无氧代谢产物增多,也可能对微循环造成影响^[20]。对术前红细胞计数偏高的患者,建议进行术前急性等容血液稀释,有研究表明其具有明显的血液保护效应^[21],治疗性红细胞提取术^[22]也被认为是有效的治疗措施。

本研究未见糖尿病史对血管危象的影响具有统计学意义,与已有研究^[4]结论不符,可能与患者围手术期血糖已被调整至接近正常水平有关,建议临床常规纳入糖化血红蛋白的检验,可反映患者较长期的血糖平均水平;本研究未见凝血因素对血管危象的影响具有统计学意义,与已有研究^[6]研究结果不一致,可能数据跨越年度较大,电子病历信息系统中凝血相关指标存在较多的缺失值相关,在未来前瞻性研究中可进一步分析;本研究也未见吸烟对血管危象的影响,与已有研究^[8]相符,

但也可能与笔者对吸烟的划分有关——笔者在搜集资料过程中,发现存在部分已戒烟的患者,因戒烟时间长短不一,为便于数据分析,本文将戒烟 5 年(含)以上认定为不吸烟,戒烟 5 年以内认定为吸烟,在以后的分析中,应将吸烟类型列为吸烟、未吸烟、已戒烟多分类数据,且“已戒烟”一项还可以根据戒烟时间再进行细分后进行探讨,以探索何时戒烟对术后并发症的减少是最佳的。本文主要对非手术层面的影响因素进行了分析,对手术因素的探讨较少,在以后的研究中会对手术技术层面的影响因素再进行深入探讨。

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