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· 临床研究 ·

口腔颌面恶性肿瘤患者术后发生便秘风险预测模型构建

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【摘要】 目的 了解口腔颌面恶性肿瘤患者术后便秘发生情况与便秘影响因素, 构建便秘风险预测模型, 为防治术后便秘提供参考。**方法** 回顾性分析2019年6月至2020年6月在中山大学附属口腔医院行口腔颌面恶性肿瘤手术的191例患者资料, 采用单因素分析和Logistic多因素回归分析筛选出独立影响因素, 建立风险预测列线图, 采用ROC曲线下面积对预测模型进行评价。内部和外部均采用C指数验证该模型的准确度。**结果** 191例患者中有52例(27.23%)术后出现便秘症状。单因素分析显示, 术前便秘史、进食能全素、气管切开、吸烟、喝酒、手术时长、出血量、卧床时间、进食匀浆膳、性别、手术修补方式、使用益生菌、癌症T分期、进食量均可能是口腔颌面恶性肿瘤患者术后便秘的影响因素($P < 0.05$)。多因素分析结果显示, 修补方式、卧床时间、性别是口腔颌面恶性肿瘤患者术后便秘的独立危险因素($P < 0.05$), 修补方式为腓骨瓣、卧床时间长、男性患者术后易出现便秘。将修补方式、卧床时间、性别纳入预测模型中, 训练组和验证组的C指数值分别为0.882和0.953; 训练组的ROC曲线下面积为0.909(95%CI: 0.850 ~ 0.968), 验证组的ROC曲线下面积为0.893(95%CI: 0.787 ~ 0.999), 列线图显示出良好的鉴别能力。**结论** 修补方式、卧床时间、性别是口腔颌面恶性肿瘤患者术后便秘的独立危险因素, 构建的风险预测模型有较好的判别能力。

【关键词】 便秘; 术后; 口腔颌面部; 外科; 恶性肿瘤; 风险预测; 模型; 危险因素

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Establishment of a risk prediction model for postoperative constipation in patients with oral and maxillofacial malignant tumors ZHU Huixuan, HE Xingfang, HUANG Qiuyu, LIU Manfeng, LIN Yantong. Stomatological Guanghua School of Stomatology, Hospital of Stomatology, Sun Yat-sen University, Guangdong Provincial Key Laboratory of Stomatology, Guangzhou 510055, China

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【Abstract】 Objective To understand the incidence and influencing factors of postoperative constipation in patients with malignant tumors who undergo oral and maxillofacial surgery and construct a constipation risk prediction model to provide a reference for the prevention and treatment of postoperative constipation. **Methods** The data of 191 patients who underwent oral and maxillofacial malignant tumor surgery at the Affiliated Stomatological Hospital of Sun Yat sen University from June 2019 to June 2020 were analyzed retrospectively. The independent influencing factors were selected via univariate analysis and logistic multivariate regression analysis, a risk prediction nomogram was established, and the prediction model was evaluated by the area under the ROC curve. Both internal and external use the C index to verify the accuracy of the model. **Results** Among 191 patients, 52 (27.23%) had postoperative constipation. Univariate

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analysis showed that a preoperative secret history of defecation, total energy intake, tracheotomy, smoking, drinking, operation duration, bleeding volume, bed time, eating homogenate diet, sex, surgical repair method, use of probiotics, T-stage of cancer and food intake may be the influencing factors of postoperative constipation in patients with oral and maxillofacial malignant tumors ($P < 0.05$). Multivariate analysis showed that repair method, bed time and sex were independent risk factors for postoperative constipation in patients with oral and maxillofacial malignant tumors ($P < 0.05$). The repair method was a fibular myocutaneous flap with a long bed time, and male patients were prone to constipation after surgery. The c-index values in the training group and the verification group were 0.882 and 0.953, respectively. The area under the ROC curve of the training group was 0.909 (95% CI: 0.850–0.968), and the area under the ROC curve of the verification group was 0.893 (95% CI: 0.787–0.999). The nomogram showed good discrimination ability.

Conclusion The repair method, bed time and sex are independent risk factors for postoperative constipation in patients with oral and maxillofacial malignant tumors. The risk prediction model has good discrimination ability.

【Key words】 constipation; postoperative; oral and maxillofacial; surgical; malignant tumors; risk prediction; model; risk factor

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口腔颌面恶性肿瘤发病率呈逐年上升之势,有研究显示2018年全球唇癌和口腔癌估计有354 864例^[1]。目前临床的治疗方法以手术为主,辅以放化疗及生物治疗,口腔颌面恶性肿瘤术后易引起各种并发症,其中术后便秘是常见的并发症之一。便秘可使人体吸收大量肠内毒素,引起代谢紊乱,增加肠道负担,长时间的便秘导致患者腹胀、食欲不振、情绪焦虑,甚至胃肠功能紊乱,对患者的心理造成负担,不利于患者术后康复,严重者可诱发心脑血管疾病^[2]。目前国内外关于术后便秘的研究主要集中于胃肠手术及骨折手术患者^[3-4],而关于口腔颌面恶性肿瘤术后患者的便秘研究较少。因此,本研究通过回顾性分析191例行口腔颌面恶性肿瘤手术患者的资料,探讨引起患者术后发生便秘的影响因素,拟建立口腔颌面恶性肿瘤患者术后发生便秘的风险预测模型。

1 资料和方法

1.1 研究对象

选取2019年6月至2020年6月在中山大学附属口腔医院进行口腔颌面恶性肿瘤手术的191例患者的临床资料。纳入标准:①病理结果诊断为口腔颌面恶性肿瘤且无远处转移;②经历全麻手术。排除标准:①全麻下行活检手术者;②有严重的胃肠道器质性疾病患者;③合并系统性疾病如神经系统疾病、结缔组织病等患者;④急危重症患者。本研究选取191例患者,术前无便秘史,根据

术后是否便秘将患者分为便秘组(52例)与无便秘组(139例)。

1.2 方法

参考相关文献^[5-6],制定《便秘临床特点及相关因素调查问卷》,问卷内容包括:①一般资料:性别、年龄、体重指数(body mass index, BMI)、婚姻状况、文化程度、高血压、糖尿病、吸烟、喝酒、嚼槟榔、病理类型、TMN分期、修补方式;②术前情况:有无便秘史、入院前体重变化、饮食是否规律;③术中情况:手术时长、术中出血情况;④术后情况:术后一周BMI、术前术后体重下降、便秘时长、质子泵抑制剂的使用、益生菌的使用、气管切开、卧床时长、进食匀浆膳的量、进食能全素、一天进食的次数、饮水量。

1.3 诊断标准及观察

便秘诊断以术后患者1周排便次数少于3次,在不用通便剂的情况下未排便,无便意感或有排便困难,大便干结^[7]。观察:①每天统计患者从前一天12:00至当天12:00的大便次数,及有无便意感、排便困难、大便干结有肛门阻塞感,或便后不尽等症状;②观察从手术当天到术后第一次排便时间。

1.4 样本量计算

根据文献提到的Logistics回归样本量估算的经验方法^[8-9],本研究估计有意义的自变量为14个,样本量取自变量的5~10倍。因此,病例样本量140人,为保证出现无效问卷时仍能有足够的样本量进行数据分析,决定扩大样本量为191人。

1.5 统计学分析

数据均采用SPSS 23.0统计软件和R语言进行处理。计数资料采用频数描述,计量资料用 $\bar{x} \pm s$ 描述;单因素分析中分类变量采用卡方检验,计量资料采用 t 检验;多因素分析采用二元logistic回归分析;采用ROC曲线进行模型分析及验证,将所有数据按7:3的比例分为训练组和验证组。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 患者一般情况

口腔颌面恶性肿瘤患者191例,其中便秘人数

52例,发生率为27.23%。连续不排便时间平均为(6.69 ± 1.65)d。

2.2 术后便秘的影响因素

以性别、吸烟、喝酒、术前便秘、进食能全素、气管切开、手术时长(h)、出血量(mL)、卧床时间(d)、进食匀浆膳(次/d)、进食量(mL)、手术修补方式、使用益生菌、癌症T分期为自变量,对便秘组和无便秘组进行比较。两组在术前便秘史、进食能全素、气管切开、吸烟、喝酒、手术时长、出血量、卧床时间、进食匀浆膳、性别、手术修补方式、使用益生菌、癌症T分期、进食量比较差异均有统计学意义($P < 0.05$),详见表1。

表1 口腔颌面恶性肿瘤患者术后便秘影响因素的单因素分析

Table 1 Univariate analysis of the factors influencing postoperative constipation in patients with oral and maxillofacial malignancies

| | No constipation group(n=139) | Constipation group(n=52) | χ^2/t | P |
|--------------------------------|------------------------------|--------------------------|------------|---------|
| Sex | | | | |
| Male | 72 | 40 | 9.949 | 0.002 |
| Female | 67 | 12 | | |
| Smoke | | | | |
| No | 103 | 28 | 7.206 | 0.007 |
| Yes | 36 | 24 | | |
| Drink | | | | |
| No | 117 | 37 | 4.107 | 0.043 |
| Yes | 22 | 15 | | |
| Constipation before surgery | | | | |
| No | 133 | 45 | 4.989 | 0.026 |
| Yes | 6 | 7 | | |
| Intake of total nutrients | | | | |
| No | 38 | 2 | 11.235 | 0.001 |
| Yes | 101 | 50 | | |
| Tracheotomy | | | | |
| No | 116 | 16 | 49.202 | < 0.001 |
| Yes | 23 | 36 | | |
| Operation duration/h | 3.17 ± 2.81 | 6.75 ± 3.18 | -7.555 | < 0.001 |
| Amount of bleeding/mL | 193.60 ± 273.00 | 472.02 ± 404.19 | -4.591 | < 0.001 |
| Time in bed/day | 2.34 ± 2.39 | 7.31 ± 3.13 | -11.648 | < 0.001 |
| Eat homogenate meals/(sub/day) | 3.04 ± 0.48 | 2.65 ± 0.62 | 4.079 | < 0.001 |
| Food-intake/mL | 1 471.94 ± 267.58 | 1 694.12 ± 214.86 | -5.895 | < 0.001 |
| Surgical repair method | | | | |
| Anterolateral thigh flap | 8 | 17 | 54.685 | < 0.001 |
| Fibula flap | 1 | 8 | | |
| Forearm flap | 13 | 10 | | |
| Other flap | 12 | 4 | | |
| No | 105 | 13 | | |
| Use of probiotics | | | | |
| No | 95 | 11 | 34.124 | < 0.001 |
| Yes | 44 | 41 | | |
| The T stage of cancer pain | | | | |
| 1-2 | 119 | 21 | 39.550 | < 0.001 |
| 3-4 | 20 | 31 | | |

将单因素分析中有统计学意义的因素进行二元 logistic 回归分析,以是否便秘为因变量,吸烟、喝酒、术前便秘史、进食能全素、气管切开、手术时长、出血量、卧床时间、进食匀浆膳、进食量、性别、

手术修补方式、使用益生菌、癌症T分期作为自变量。结果显示,修补方式(腓骨瓣)、卧床时间及性别与术后便秘显著相关($P < 0.05$),见表2。

表2 口腔颌面恶性肿瘤患者术后便秘影响因素的二元 logistic 回归分析

Table 2 Binary logistic regression analysis of influencing factors of postoperative constipation in patients with oral and maxillofacial malignant tumors

| Variable | β | SE | Wald | P | OR | 95%CI |
|--------------------------|---------|------------|--------|---------|--------|-----------------|
| Sex | -1.595 | 0.643 | 6.162 | 0.013 | 0.203 | 0.058-0.715 |
| Time in bed | 0.608 | 0.153 | 15.822 | < 0.001 | 1.837 | 1.361-2.479 |
| Surgical repair method | | | 8.297 | 0.081 | | |
| Anterolateral thigh flap | 1.128 | 1.296 | 0.757 | 0.384 | 3.090 | 0.243-39.210 |
| Fibula flap | 4.263 | 1.646 | 6.709 | 0.010 | 71.011 | 2.821-1 787.267 |
| Forearm flap | 0.430 | 1.284 | 0.112 | 0.738 | 1.537 | 0.124-19.038 |
| Other flap | 0.607 | 1.482 | 0.168 | 0.682 | 1.835 | 0.101-33.502 |
| Constants | -18.967 | 13 820.377 | 0.000 | 0.999 | 0.000 | |

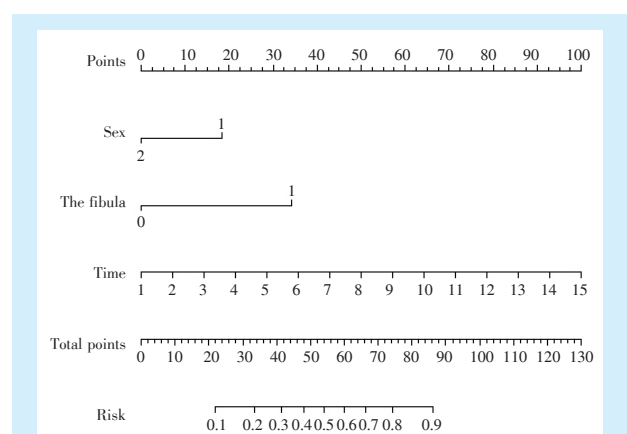
2.3 口腔颌面恶性肿瘤患者术后发生便秘的风险预测模型

基于训练组中口腔颌面恶性肿瘤患者术后发生便秘的特征数据建立风险预测模型的列线图,将性别、卧床时间和腓骨瓣修补方式作为独立风险因素纳入预测模型中,以便秘为临床结局事件,构建预测口腔颌面恶性肿瘤患者术后发生便秘的风险列线图,见图1,其中列线图各分值表示,性别(1=男性,2=女性),腓骨瓣(0=非腓骨瓣,1=腓骨瓣),卧床时间按天数(1~15 d)。

2.4 对口腔颌面恶性肿瘤患者术后发生便秘风险预测模型预测效果的验证

在训练组中通过校准曲线检验列线图的预测

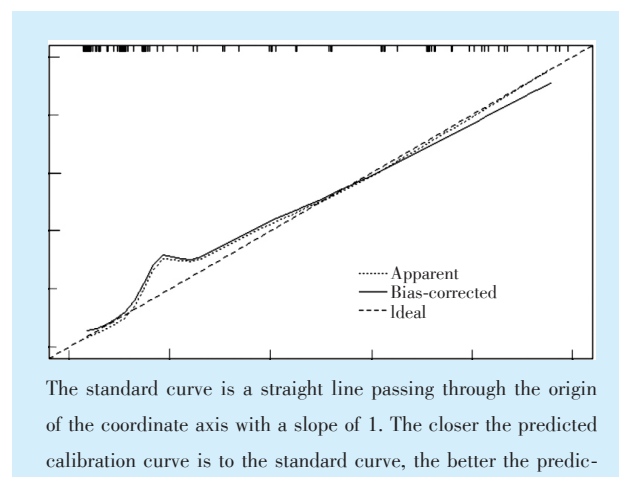
效能,可见校准后的曲线较接近对角线,即预测值与真实值之间差距较小,模型的预测性能较好,随后分别计算训练组与验证组中预测模型的C指数,结果提示,列线图在训练组中的C指数为0.882(95%CI: 0.814~0.950),验证组中的C指数为0.953(95%CI: 0.902~1.004),见图2、图3。进一步对训练组中基于性别、卧床时间与腓骨瓣修复方式变量的多元预测模型进行ROC的曲线分析,测得训练组的ROC曲线下面积为0.909(95%CI: 0.850~0.968),验证组的ROC曲线下面积为0.893(95%CI: 0.787~0.999),见图4、图5。



Gender (1= male, 2= female), fibula flap (0= nonfibula flap, 1= fibula flap), time in bed by days (1 to 15 days)

Figure 1 Nomogram for predicting constipation

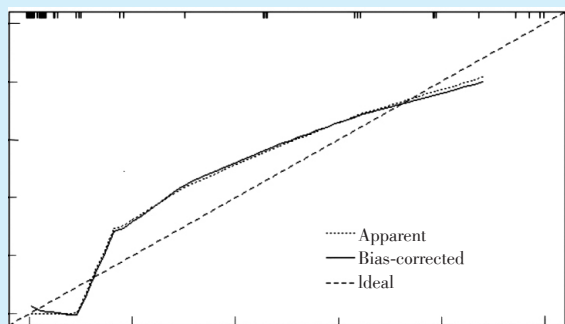
图1 预测便秘的列线图



The standard curve is a straight line passing through the origin of the coordinate axis with a slope of 1. The closer the predicted calibration curve is to the standard curve, the better the predictive power of the nomogram

Figure 2 Calibration curve for the nomogram training group

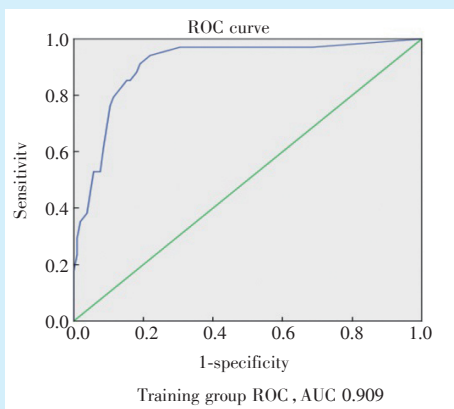
图2 训练组的列线图校准曲线



The calibrated curve is close to the diagonal, that is, the gap between the predicted value and the real value is small, and the prediction performance of the model is good

Figure 3 Calibration curve of the nomogram validation group

图3 验证组的列线图校准曲线



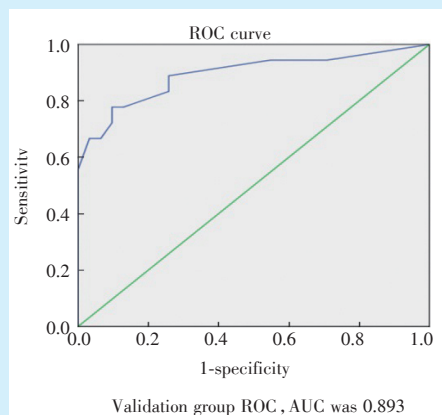
On the ROC curve, the point near the upper left of the coordinate map is the high cutoff value for both sensitivity and specificity. The sensitivity is drawn as the vertical coordinates and (1-specificity) as the horizontal coordinates, and the larger the area under the curve is, the higher the diagnostic accuracy.

Figure 4 ROC curve of predicting the risk of postoperative constipation in patients with oral and maxillofacial malignant tumors in the training group

图4 训练组口腔颌面恶性肿瘤患者术后便秘风险预测的ROC曲线

3 讨论

本研究中口腔颌面恶性肿瘤患者术后较易发生便秘,是因为口腔颌面恶性肿瘤在临床上以手术治疗为主,手术方式多为原发灶切除,若缺损范围大,无法直接拉拢缝合者还需移植皮瓣进行修复重建,如前臂瓣、股前外侧皮瓣、腓骨瓣等。以上手术患者具有创口部位多、范围大、麻醉时间及术后卧床时间长等特点。患者饮食结构也随之改



On the ROC curve, the point near the top left of the coordinate map has high cutoff values for both sensitivity and specificity, showing the excellent discrimination effect of this model for patients with constipation

Figure 5 ROC curve of predicting the risk of postoperative constipation in patients with oral and maxillofacial malignant tumors in the validation group

图5 验证组口腔颌面恶性肿瘤患者术后便秘风险预测的ROC曲线

变,术后饮食多以流质为主。由于流质缺乏粗膳食纤维,肠道黏膜缺少应有的刺激,吸水性降低,容易发生便秘^[10]。本研究结果显示卧床时间及行腓骨修复重建术是术后发生便秘的影响因素(OR值为71.011、1.837, $P < 0.05$),为维持颌面部移植皮瓣血运,术后需要头部制动^[11],卧床5~7 d。其中,老年患者、术后病情不稳定患者卧床时间更长,便秘组中术后卧床时间最长可达12 d。正常排便时结肠远端的直肠纵行肌收缩,加上腹壁肌用力收缩,腹内压力增大,同时配合重力以达到顺利排便。Li等^[12]研究表明卧床时间久的患者容易引起功能性便秘。卧床患者在床上排便时只能依靠深吸气增加腹压,腹内压力不足,而且用力时可能会牵扯伤口导致疼痛,影响排便。此外,卧床时间长可导致胃肠蠕动功能减弱,粪便在肠道内滞留时间越长,大便越干结,排便时用力不当增加术后便秘风险。因此,对于术后卧床时间长的患者除了术前训练床上大小便外,术后指导患者尽早床上活动,卧床期间多顺时针按摩腹部,促进肠蠕动功能,刺激直肠神经,在病情许可的情况下尽早下床活动以减少便秘。

Feuvrier等^[13]研究表明,血管化游离腓骨瓣术后存在疼痛、行走能力限制、步态调整等并发症。

血管化游离腓骨瓣患者由于腿部伤口卧床时间相对更长,且排便时腿部伤口疼痛可影响排便时的用力情况,导致排便困难。同时为减轻术后创口疼痛,术后常规使用阿片类药物的镇痛泵,阿片类药物与胃肠道和中枢神经系统中的特异性受体结合,抑制胃肠动力的推进及肠液分泌,阻碍胃排空及减慢肠蠕动,易致便秘^[14]。为减少术后便秘的发生,使用疼痛评分表及时评估患者疼痛强度及耐受性,尽早停用阿片类止痛药物,教会患者分散注意力来缓解疼痛。Yurtdaş等^[15]研究调查显示适当身体运动能保护胃肠道,改善胃肠道相关疾病。因此,可鼓励患者围手术期进行锻炼,卧床期间指导及协助患者在床上行腿部运动,促进创口愈合并有效改善床上排便困难。此外,口腔颌面恶性肿瘤患者全麻手术由于禁食时间长、使用麻醉药物等原因导致胃肠蠕动减少,术后恶心呕吐引起胃肠道紊乱,增加便秘风险。本研究单因素分析显示进食匀浆膳、使用益生菌、进食能全素对便秘可能有影响。因此,术后加强患者饮食管理也是改善便秘的方法,给予热量充足、营养均衡饮食,建议食用富含可溶性纤维的营养配方,适量增加水果汁和蔬菜泥,每日饮水量保持在1 500~2 000 mL^[16]。术后常规给予金双歧杆菌,调节胃肠道微生态平衡,保证肠道机能的正常。术后伴腹胀、排便困难者可适当口服乳果糖溶液辅助治疗,一天2次,每次15 mL。

性别是便秘影响因素之一,其中男性患者发生便秘风险较高。调查发现,排便时隐私的不足容易影响患者正常排便^[17]。临床上护理工作者以女性居多,在床上排便时需要暴露隐私部位,且排便时需要护理人员协助,男性患者容易有羞耻感,导致心理负担,从而影响正常排便,形成习惯性便秘。因此,术前做好男性患者的解释沟通工作,减轻患者的心理负担,术后需要与家属共同协作,尊重和患者个人隐私。便秘组中男性患者吸烟、喝酒占比较高,但未进入到回归方程,然而有研究分析认为^[18]吸烟患者的便秘风险严重高于非吸烟患者;以及长期高浓度的酒精刺激,会直接破坏小肠黏膜,导致小肠消化吸收功能障碍,对大肠上皮细胞也有显著的毒性作用,增加胃肠道相关疾病的风险^[19]。本研究主要研究术后患者便秘风险因素,与其相关吸烟、喝酒研究文献的人群、数量、研究方向不同,但可以作为风险因素指导。因此术前留意吸烟喝酒男性患者,做好戒烟戒酒宣

教指导,减少术后发生便秘的风险。

根据列线图可预测口腔颌面恶性肿瘤患者术后发生便秘的风险系数,假设患者男性,术中行腓骨瓣修复,卧床时间为5 d,则其相对应的分数分别为17.5, 32.5和30,将3个分数相加得到总分 $17.5+32.5+30=80$ 分,其总分相对应的风险值为80%~90%,即男性术中行腓骨瓣修复患者卧床时间越长,其便秘风险越高。本研究模型显示每个变量集中一起可加强便秘风险预测,对某些因素进行尽早干预,可降低便秘发生风险。

便秘预测模型预测效果分析以ROC曲线进行拟合度检验。当曲线下面积为0.5~0.7时,表示诊断价值低;当曲线下面积为0.7~0.9时,表示预测效果中等,预测效果可接受;当面积>0.9时,表示预测效果极好^[20]。本模型训练组的ROC曲线下面积为0.909(95%CI: 0.850~0.968),表明本模型可以较好地预测口腔颌面恶性肿瘤患者术后发生便秘的风险。本研究模型中显示每个变量集中一起可以加强便秘风险预测,尽早进行干预,降低便秘发生率。

综上所述,口腔颌面恶性肿瘤修复重建术后患者发生便秘风险高,术后便秘时间长,患者排便困难、腹胀、腹痛不适,加重患者的痛苦,严重影响患者的生活质量,不利于患者康复。因此,临床上应重视便秘的预防。本风险模型能对便秘风险作出判断,及早制定预防措施,提高护理管理质量,促进患者早日康复。

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