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· 论著 ·

个体化预测心脏瓣膜置换术后压力性损伤发生风险的列线图模型构建

陈慧慧, 陆真

【摘要】 背景 目前, 心脏瓣膜置换术后压力性损伤的危险因素尚未完全明确, 个体化预测压力性损伤高风险人群的方法仍需进一步探索。目的 构建个体化预测心脏瓣膜置换术后压力性损伤发生风险的列线图模型。方法 选取 2018 年 5 月至 2020 年 4 月在江苏省人民医院行心脏瓣膜置换术的患者 350 作为研究对象, 随机将其分为训练集 ($n=175$) 和验证集 ($n=175$)。收集患者的临床资料, 心脏瓣膜置换术后压力性损伤的影响因素分析采用多因素 Logistic 回归分析, 采用 R (R 3.5.3) 软件包和 rms 程序包构建列线图模型, 并通过训练集和验证集进行内外部验证, 采用一致性指数 (CI)、校准曲线、ROC 曲线和决策曲线评估列线图模型的预测效能。结果 350 例患者中 87 例发生压力性损伤, 压力性损伤发生率为 24.86%。根据是否发生压力性损伤将训练集患者分为压力性损伤组 ($n=46$) 和非压力性损伤组 ($n=129$)。压力性损伤组和非压力性损伤组患者糖尿病发生率、术前血清白蛋白 (Alb)、体外循环时间、手术时间、术中输血量及术中使用血管活性药物者所占比例比较, 差异有统计学意义 ($P < 0.05$)。多因素 Logistic 回归分析结果显示, 糖尿病、术前血清 Alb、体外循环时间、手术时间、术中输血量及术中使用血管活性药物是心脏瓣膜置换术后患者发生压力性损伤的独立影响因素 ($P < 0.05$)。基于上述影响因素构建心脏瓣膜置换术后压力性损伤发生风险的列线图模型。模型验证结果显示, 训练集和验证集的 CI 分别为 0.827 和 0.745, 列线图模型预测训练集和验证集患者心脏瓣膜置换术后压力性损伤发生风险的校正曲线均趋近于理想曲线, 表明该列线图模型的预测准确率较高; ROC 曲线分析结果显示, 列线图模型预测训练集和验证集患者心脏瓣膜置换术后压力性损伤发生风险的 ROC 曲线下面积分别为 0.840 [95% CI (0.802, 0.876)]、0.751 [95% CI (0.718, 0.785)], 表明该列线图模型的区分度良好; 决策曲线分析结果显示, 在 8%~95% 范围内, 该列线图模型预测的净获益值较高, 表明该列线图模型的临床预测效能良好。结论 基于糖尿病、术前血清 Alb、体外循环时间、手术时间、术中输血量及术中使用血管活性药物构建的心脏瓣膜置换术后患者压力性损伤发生风险的列线图模型, 能够有效预测心脏瓣膜置换术后压力性损伤发生风险, 有利于临床筛查心脏瓣膜置换术后压力性损伤高风险患者。

【关键词】 心脏瓣膜置换术; 压力性损伤; 影响因素分析; 列线图

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【Abstract】 **Background** At present, the risk factors of pressure injury after heart valve replacement have not been fully defined, and the method of individualized prediction of high-risk population of pressure injury still needs to be further explored. **Objective** To construct the nomogram model for individualized prediction of pressure injury risk after cardiac valve replacement. **Methods** A total of 350 patients who underwent heart valve replacement in Jiangsu Provincial People's Hospital from May 2018 to April 2020 were selected and randomly divided into training set ($n=175$) and verification set ($n=175$). The clinical data of patients were collected, and the influencing factors of pressure injury after heart valve replacement were analyzed by multivariate

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Logistic regression analysis, R (R 3.5.3) software package and rms program package were used to construct the nomogram model, and internal and external verification was carried out through training set and verification set. C-index (CI), calibration curve, ROC curve and decision curve were used to evaluate the prediction efficiency of nomogram model. **Results** Of the 350 patients, 87 patients had pressure injury, and the incidence of pressure injury was 24.86%. According to the occurrence of pressure injury, the patients in the training set were divided into pressure injury group ($n=46$) and non pressure injury group ($n=129$). There were significant differences in the incidence of diabetes, preoperative serum albumin (Alb), cardiopulmonary bypass time, operative time, amount of blood infusion during operation and proportion of patients using vasoactive drugs during operation between the pressure injury group and the non pressure injury group ($P < 0.05$). Multivariate Logistic regression analysis showed that diabetes, preoperative serum Alb, cardiopulmonary bypass time, operative time, amount of blood infusion during operation and using vasoactive drugs during operation were independent factors of pressure injury after cardiac valve replacement ($P < 0.05$). Based on the above independent factors, a nomogram model for predicting the risk of independent factors after heart valve replacement was constructed. The model validation results show that the CI of the training set and the validation set were 0.827 and 0.745, respectively; the calibration curve of the nomogram model for predicting the risk of pressure injury after cardiac valve replacement in training set and verification set were both close to the ideal curve, indicating that the nomogram model had good prediction accuracy; the ROC curve analysis results showed that the area under the ROC curve of the nomogram model for predicting the risk of pressure injury after cardiac valve replacement in training set and verification set were 0.840 [95%CI (0.802, 0.876)] and 0.751 [95%CI (0.718, 0.785)], respectively, indicating that the nomogram model had good discrimination; the decision curve analysis results showed that, in the range of 8%–95%, the net benefit predicted by the nomogram model was high, indicating that the nomogram model had good clinical prediction efficiency. **Conclusion** The nomogram model for predicting the risk of pressure injury after cardiac valve replacement based on diabetes, preoperative serum Alb, cardiopulmonary bypass time, operative time, amount of blood infusion during operation and using vasoactive drugs during operation can effectively predict the risk of pressure injury after heart valve replacement, which is conducive to clinical screening of patients with high risk of pressure injury after heart valve replacement.

【Key words】 Heart valve replacement; Pressure injury; Root cause analysis; Nomogram

心脏瓣膜置换术是治疗心脏瓣膜病的重要术式,其可有效改善心脏瓣膜狭窄或关闭不全患者的临床症状,治愈率较高^[1]。但心脏瓣膜置换术为有创术式,且需要在体外循环下进行,术中会对机体产生不良刺激,术后易引起一系列并发症^[2]。压力性损伤是心脏外科手术的常见并发症。据报道,全球范围内压力性损伤患病率高达4.5%~32.9%,常见临床表现为骨隆突部位的皮肤和软组织局限性损伤^[3-4]。压力性损伤不但会影响患者术后康复,加重原发疾病病情,还会增加医疗负担,延长住院时间。既往研究表明,压力性损伤会使患者住院时间平均延长10 d,预计增加治疗费用1.4~4.0万美元^[5],故预防压力性损伤对改善心脏外科手术患者预后具有重要的临床意义。目前,国内外均有研究提出,列线图可预测压力性损伤发生风险^[6-7],但尚无研究构建个体化预测心脏瓣膜置换术患者压力性损伤风险的列线图模型。基于此,本研究拟通过筛查心脏瓣膜置换术后压力性损伤的影响因素并构建列线图模型,以期临床规范管理和预防压力性损伤提供参考。

1 对象与方法

1.1 研究对象 选取2018年5月至2020年4月在江苏省人民医院行心脏瓣膜置换术的患者350作为研究对象,随机将其分为训练集($n=175$)和验证集($n=175$)。

纳入标准:(1)年龄 ≥ 18 岁,符合心脏瓣膜置换手术指征^[8];(2)临床资料完整。排除标准:(1)术前存在皮肤破损者;(2)心绞痛无法缓解者;(3)有心脏手术史者;(4)有精神病史、阿尔茨海默病史者;(5)合并皮肤病、恶性肿瘤、心力衰竭、严重肝肾功能不全、感染及免疫系统疾病者;(6)合并严重心、肝、肾功能不全者。本研究经江苏省人民医院伦理委员会审批通过〔苏医伦审(2018)第(007)号〕,所有患者对本研究知情并签署知情同意书。

1.2 心脏瓣膜置换术 所有患者在全身麻醉、气管插管、体外循环下行心内直视瓣膜置换术,具体如下:正中或经右侧开胸,经主动脉或上、下腔静脉建立体外循环,阻断升主动脉,经主动脉根部灌注冷心停搏液,同时进行心表降温。待心脏停搏后将病变的瓣膜切除并换上人工瓣膜,瓣膜缝合完毕后缝合心脏切口,恢复心脏与血液供应,辅助循环,适时撤出体外循环机,关胸。术毕患者返回重症监护室。

1.3 皮肤观察 由重症监护室及巡视医护人员共同判断患者是否发生压力性损伤,根据2016年美国国家压疮咨询委员会(National Pressure Ulcer Advisory Panel, NPUAP)压力性损伤分期标准,其中1期:指压时红斑不会消失(非苍白性发红);2期:部分真皮层损失;3期:

全层皮肤缺损; 4期: 全层皮肤和组织损失; 不明确分期: 掩盖了全层组织和组织缺损; 深部组织损伤: 持久性非苍白性发红、褐红色或紫色^[9]。

1.4 资料收集 通过自制的临床数据收集表收集患者的临床资料, 包括一般资料〔性别、年龄、病程、吸烟情况、糖尿病发生情况、高血压发生情况、心房颤动发生情况、基础心脏病、瓣膜置换部位、术前血红蛋白(hemoglobin, Hb)和术前血清白蛋白(albumin, Alb)〕和手术资料(体外循环时间、主动脉阻断时间、手术时间、术中输血量、术中血管活性药物使用情况)。

1.5 统计学方法 采用SPSS 22.0统计学软件进行数据处理。计数资料以相对数表示, 组间比较采用 χ^2 检验; 心脏瓣膜置换术后压力性损伤的影响因素分析采用多因素 Logistic 回归分析。以 $P < 0.05$ 为差异有统计学意义。采用R(R 3.5.3)软件包和rms程序包构建列线图模型, 并通过训练集和验证集进行内外部验证, 采用一致性指数(C-index, CI)、校准曲线、ROC曲线和决策曲线评估列线图模型对心脏瓣膜置换术后压力性损伤的预测效能。

2 结果

2.1 压力性损伤发生率 350例患者中87例发生压力性损伤, 压力性损伤发生率为24.86%, 其中1期81例、2期4例、深部组织损伤2例; 损伤部位: 骶尾部38例, 足跟处31例, 手肘部11例, 其他部位7例。

2.2 单因素分析 根据是否发生压力性损伤将训练集患者分为压力性损伤组($n=46$)和非压力性损伤组($n=129$)。压力性损伤组和非压力性损伤组患者性别、年龄、病程、吸烟率、高血压发生率、心房颤动发生率、基础心脏病、瓣膜置换部位、术前Hb和主动脉阻断时间比较, 差异无统计学意义($P > 0.05$); 压力性损伤组和非压力性损伤组患者糖尿病发生率、术前血清Alb、体外循环时间、手术时间、术中输血量及术中使用血管活性药物者所占比例比较, 差异有统计学意义($P < 0.05$), 见表1。

2.3 多因素 Logistic 回归分析 将压力性损伤发生情况作为因变量(赋值: 未发生=0, 发生=1), 将单因素分析中有统计学差异的指标作为自变量, 进行多因素 Logistic 回归分析, 结果显示, 糖尿病、术前血清Alb、体外循环时间、手术时间、术中输血量及术中使用血管活性药物是心脏瓣膜置换术后患者发生压力性损伤的独立影响因素($P < 0.05$), 见表2。

2.4 列线图模型的构建及验证 基于上述影响因素构建心脏瓣膜置换术后压力性损伤发生风险的列线图模型, 见图1。模型验证结果显示, 训练集和验证集的CI分别为0.827和0.745, 列线图模型预测训练集和验证集患者心脏瓣膜置换术后压力性损伤发生风险的校正曲

表1 心脏瓣膜置换术后患者发生压力性损伤影响因素的单因素分析〔 n (%)〕

Table 1 Univariate analysis on influencing factors of pressure injury in patients after heart valve replacement

组别	压力性损伤组($n=46$)	非压力性损伤组($n=129$)	χ^2 值	P 值
性别			0.338	0.561
男	29 (63.0)	75 (58.1)		
女	17 (37.0)	54 (41.9)		
年龄(岁)			0.106	0.745
< 60	28 (60.9)	82 (63.6)		
≥ 60	18 (39.1)	47 (36.4)		
病程(年)			0.603	0.438
< 10	27 (58.7)	84 (65.1)		
≥ 10	19 (41.3)	45 (34.9)		
吸烟	11 (23.9)	2 (1.6)	0.597	0.440
糖尿病	16 (34.8)	19 (14.7)	8.523	0.004
高血压	13 (28.3)	34 (26.4)	0.063	0.802
心房颤动	9 (19.6)	17 (13.2)	1.093	0.296
基础心脏病			4.000	0.262
风湿性瓣膜病	17 (37.0)	56 (43.4)		
先天性瓣膜病	10 (21.7)	39 (30.2)		
退行性瓣膜病	8 (17.4)	12 (9.3)		
感染性心内膜炎	11 (23.9)	22 (17.1)		
瓣膜置换部位			1.027	0.795
主动脉瓣	11 (23.9)	41 (31.8)		
二尖瓣	21 (45.7)	54 (41.9)		
二尖瓣和主动脉瓣	9 (19.6)	22 (17.1)		
三尖瓣	5 (10.9)	12 (9.3)		
术前Hb(g/L)			0.725	0.696
< 90	3 (6.5)	14 (10.9)		
90~120	12 (26.1)	32 (24.8)		
> 120	31 (67.4)	83 (64.3)		
术前血清Alb(g/L)			8.129	0.017
< 30	7 (15.2)	9 (7.0)		
30~35	13 (28.3)	19 (14.7)		
> 35	26 (56.5)	101 (78.3)		
体外循环时间(min)			10.309	0.001
< 120	26 (56.5)	104 (80.6)		
≥ 120	20 (43.5)	25 (19.4)		
主动脉阻断时间(min)			1.157	0.282
< 90	20 (43.5)	68 (52.7)		
≥ 90	26 (56.5)	61 (47.3)		
手术时间(min)			11.636	0.009
< 180	0	2 (1.6)		
180~239	8 (17.4)	56 (43.4)		
240~299	28 (60.9)	48 (37.2)		
≥ 300	10 (21.7)	23 (17.8)		
术中输血量(ml)			15.053	0.001
< 500	7 (15.2)	24 (18.6)		
500~1 000	23 (50.0)	92 (71.3)		
> 1 000	16 (34.8)	13 (10.1)		
术中使用血管活性药物	42 (91.3)	93 (72.1)	7.098	0.008

注: Hb= 血红蛋白, Alb= 白蛋白

表2 心脏瓣膜置换术后患者发生压力性损伤影响因素的多因素 Logistic 回归分析

Table 2 Multivariate Logistic regression analysis on influencing factors of pressure injury in patients after heart valve replacement

变量	赋值	β	SE	Wald χ^2 值	P 值	OR 值	95%CI
糖尿病	无=0, 有=1	1.055	0.458	5.311	0.021	2.871	(1.171, 7.040)
术前血清 Alb	> 35 g/L=0, 30~35 g/L=1, < 30 g/L=2	0.884	0.299	8.760	0.003	2.420	(1.348, 4.345)
体外循环时间	< 120 min=0, $\geq$ 120 min=1	0.915	0.424	4.664	0.031	2.497	(1.088, 5.728)
手术时间	< 180 min=0, 180~239 min=1, 240~299 min=2, $\geq$ 300 min=3	0.740	0.278	7.074	0.008	2.096	(1.215, 3.615)
术中输血量	> 1 000 ml=0, 500~1 000 ml=1, < 500 ml=2	0.745	0.351	4.500	0.034	2.107	(1.058, 4.193)
术中使用血管活性物质	否=0, 是=1	1.733	0.652	7.069	0.008	5.657	(1.577, 20.292)
常量	-	-5.558	1.025	29.379	< 0.001	0.004	-

注: - 表示无相关数据

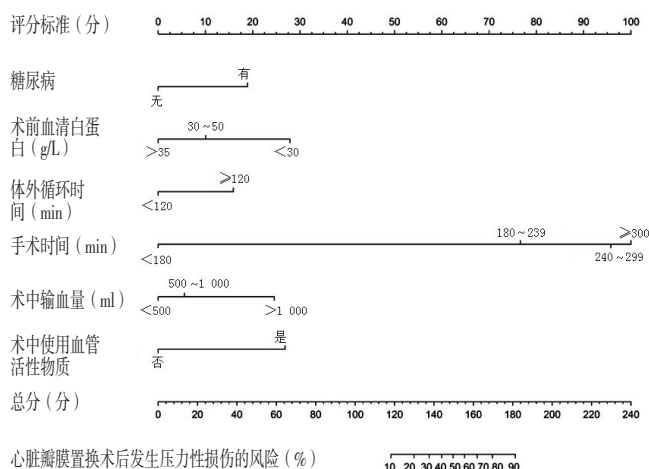


图1 心脏瓣膜置换术后压力性损伤风险预测的列线图模型
Figure 1 Nomogram model for predicting the risk of pressure injury after heart valve replacement

线均趋近于理想曲线, 见图2、3, 表明该列线图模型的预测准确率较高; ROC 曲线分析结果显示, 列线图模型预测训练集和验证集患者心脏瓣膜置换术后压力性损伤发生风险的 ROC 曲线下面积分别为 0.840 [95%CI (0.802, 0.876)]、0.751 [95%CI (0.718, 0.785)], 见图4、5, 表明该列线图模型的区分度良好; 决策曲线分析结果显示, 在8%~95% 范围内, 该列线图模型预测的净获益值较高, 见图6, 表明该列线图模型的临床预测效能良好。

3 讨论

压力性损伤是评价患者预后和护理质量的重要指标。本组患者心脏瓣膜置换术后压力性损伤发生率为24.86%, 与国内报道的心脏手术后压力性损伤发生率(14.3%~51.0%)相符^[10], 但略低于国外系统综述报道的心血管手术患者压力性损伤发生率(29.5%)^[11], 表明心脏瓣膜置换术是压力性损伤发生的高危手术类型。

本研究结果显示, 糖尿病、术前血清 Alb、体外循环时间、手术时间、术中输血量及术中使用血管活性药

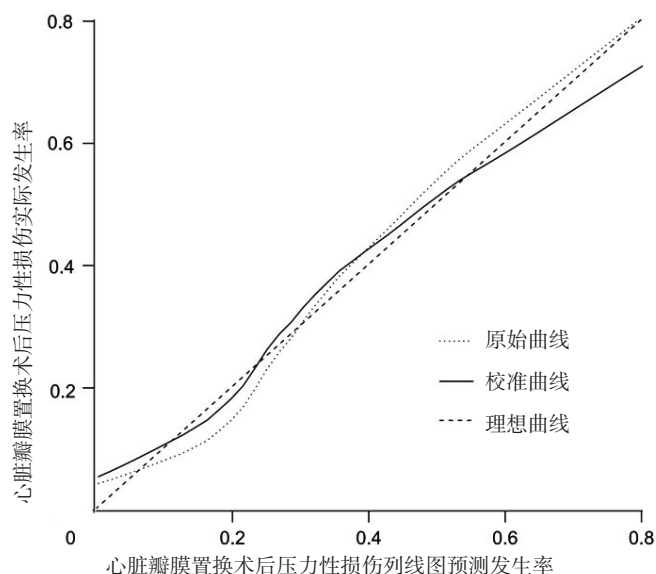


图2 列线图模型预测训练集患者心脏瓣膜置换术后压力性损伤发生风险的校准曲线

Figure 2 Calibration curve of nomogram model for predicting the risk of pressure injury after cardiac valve replacement in training set

物是心脏瓣膜置换术后患者发生压力性损伤的独立影响因素。LIANG 等^[12]研究表明, 糖尿病可使手术获得性压力性损伤的发生风险增加 1.77 倍, 本研究结果与之相似。糖尿病是微血管病变的重要原因, 微血管病变会影响周围血管灌注, 引起局部皮肤血供减少, 从而导致术后卧床患者压力性损伤发生风险增加。KIM 等^[13]研究发现, 低蛋白血症是预测术后压力性损伤的危险因素, 本研究结果亦支持该观点。既往研究表明, 体外循环是压力性损伤的危险因素, 其原因可能是体外循环装置与血液持续接触后破坏红细胞生物结构, 使其携氧能力下降, 并激活大量促炎递质的释放, 导致组织微循环缺氧和全身炎症反应, 从而引起受压部位损伤^[14-15]。HUANG 等^[16]进行的队列研究发现, 手术时间是术后患者发生压力性损伤的预测因子, 本研究结果与之相似。手术时间会因体外循环时间延长而延长, 故手术时间与

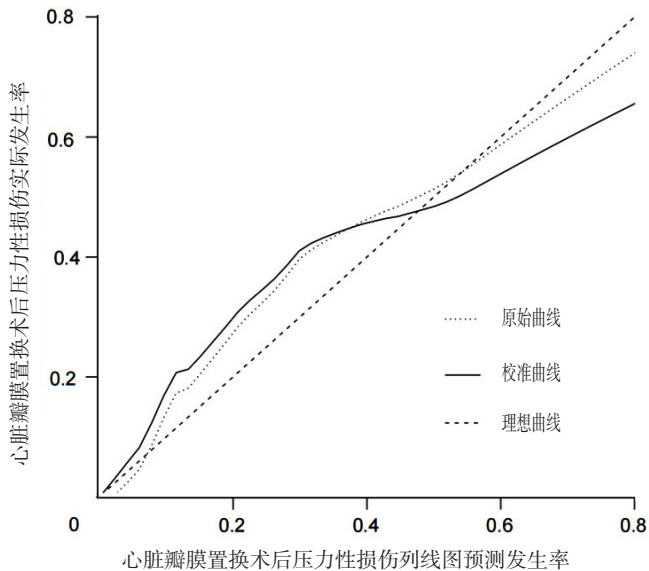


图3 列线图模型预测验证集患者心脏瓣膜置换术后压力性损伤发生风险的校准曲线

Figure 3 Calibration curve of nomogram model for predicting the risk of pressure injury after cardiac valve replacement in validation set

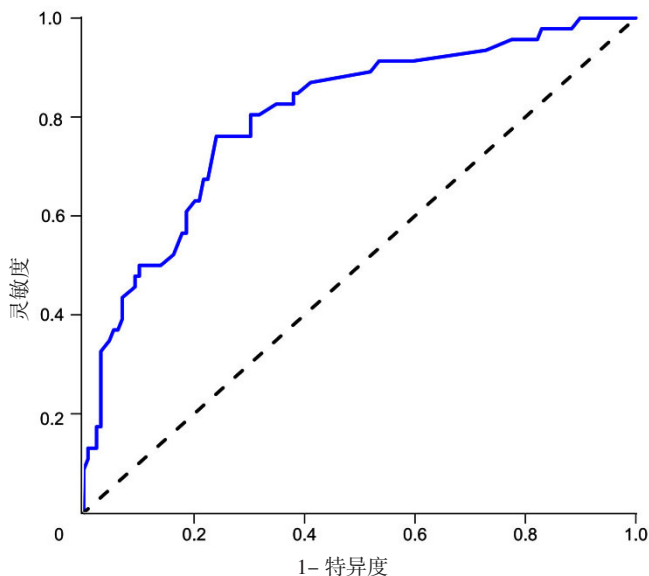


图4 列线图模型预测训练集患者心脏瓣膜置换术后压力性损伤发生风险的ROC曲线

Figure 4 ROC curve of nomogram model for predicting the risk of pressure injury after cardiac valve replacement in training set

压力性损伤的相关机制可能与体外循环时间有关。同时,术申长时间的局部组织受压也可引起组织缺血、缺氧,从而诱发术后压力性损伤^[17]。王亚婷等^[18]研究报道,术中输血量与压力性损伤相关,心脏瓣膜置换术中输血可能会造成补体激活和血小板变形,导致机体炎性损伤或缺血-再灌注损伤。ALDERDEN等^[19]研究报道,使用血管活性药物是术后发生压力性损伤的危险因素,本研究结果与之相似。心脏瓣膜置换术中常需要使用血

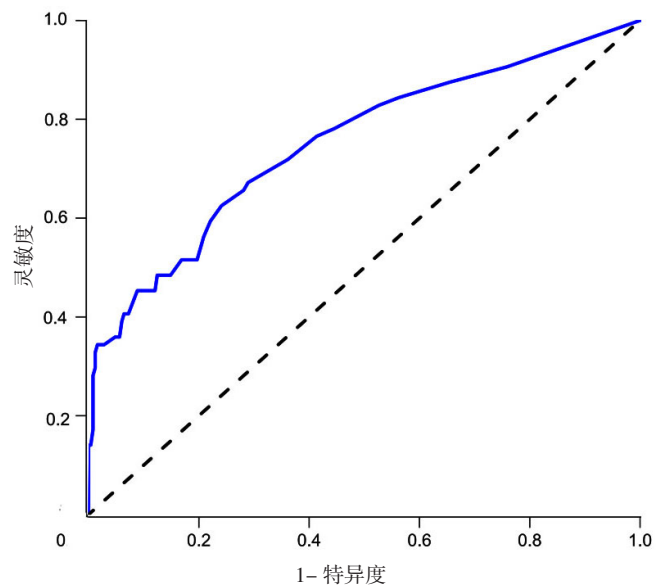


图5 列线图模型预测验证集患者心脏瓣膜置换术后压力性损伤发生风险的ROC曲线

Figure 5 ROC curve of nomogram model for predicting the risk of pressure injury after cardiac valve replacement in validation set

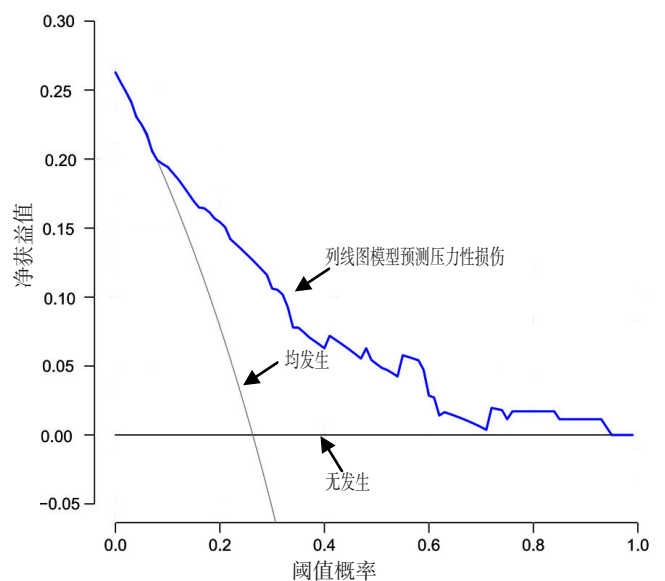


图6 心脏瓣膜置换术后压力性损伤风险预测列线图模型的决策曲线

Figure 6 Decision curve of nomogram model for predicting the risk of pressure injury after heart valve replacement

管活性药物以增加血管张力,预防组织、器官发生缺血性损伤。本研究结果显示,术申使用血管活性药物的患者发生压力性损伤的风险是术中未使用血管活性药物患者的5.657倍,其原因可能是血管收缩加重周围受压皮肤缺血、缺氧所致。

目前,Braden量表、Norton量表和Waterlow量表是评估压力性损伤发生风险使用最广泛的工具^[20-21],但上述量表均由评分条目组成,完成复杂,不适用于危

重症患者,也不利于临床制定有针对性的干预策略。列线图不仅可视、简便,易于使用,还可用于危重症患者,且模型中的各项指标也可为制定预防性措施提供参考依据。邓小红等^[22]构建了预测压力性损伤的分类回归树模型,虽然具有直观、简洁的优势,但该模型未进行内部验证,可能存在模型过度拟合现象。本研究基于影响因素构建心脏瓣膜置换术后压力性损伤风险预测的列线图模型,并进行了内外部验证,结果显示,训练集和验证集的 *CI* 分别为 0.827 和 0.745,列线图模型预测训练集和验证集患者心脏瓣膜置换术后压力性损伤发生风险的校正曲线均趋近于理想曲线,表明该列线图模型的预测准确率较高;ROC 曲线分析结果显示,列线图模型预测训练集和验证集患者心脏瓣膜置换术后压力性损伤发生风险的 ROC 曲线下面积分别为 0.840 [95%*CI* (0.802, 0.876)]、0.751 [95%*CI* (0.718, 0.785)],表明该列线图模型的区分度良好;决策曲线分析结果显示,在 8%~95% 范围内,该列线图模型预测的净获益值较高,表明该列线图模型的临床预测效能良好。

综上所述,基于糖尿病、术前血清 Alb、体外循环时间、手术时间、术中输血量及术中应用血管活性药物构建的心脏瓣膜置换术患者压力性损伤发生风险的列线图模型,能够有效预测心脏瓣膜置换术后压力性损伤发生风险,有利于临床筛查压力性损伤高风险患者。但本研究为单中心研究,且样本量较小,故所得结论仍有待今后联合多中心、扩大样本量进一步验证。

作者贡献:陈慧慧进行文章的构思与设计,数据收集、整理、分析,结果分析与解释,负责撰写、修订论文;陆真进行研究的实施与可行性分析,负责文章的质量控制及审校,并对文章整体负责、监督管理。

本文无利益冲突。

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