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胸神经 II 阻滞和胸椎旁神经阻滞对改良乳腺癌根治术的镇痛效果比较

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[摘要] 目的: 比较胸神经II(pectoral nerves II, Pecs II)阻滞与胸椎旁神经(thoracic paravertebral nerve, TPVN)阻滞改良乳腺癌根治术围手术期的镇痛效果及对炎性细胞因子、术后早期恢复质量的影响。方法: 选取2019年3月至2021年3月于江苏省太仓市第一人民医院择期行改良乳腺癌根治术的80例患者为研究对象, 随机分为Pecs II组与TPVN组, 每组40例, 并以同期20例健康体检者作对照组。Pecs II组采用Pecs II阻滞, TPVN组采用TPVN阻滞。比较两组术后0.5、2、4、6、12、24、48 h时疼痛视觉模拟量表(Visual Analogue Scale, VAS)及镇痛持续时间、术后24 h内舒芬太尼用量, 检测术前、术后1、3 d时血清白细胞介素-6(interleukin-6, IL-6)、肿瘤坏死因子- α (tumor necrosis factor, TNF- α)水平, 比较术后1、2、3 d时40项恢复质量评分量表(40-item Quality of Recovery Questionnaire, QoR-40)评分, 观察术后不良反应。结果: 与TPVN组相比, Pecs II组在术后2~24 h时的VAS评分均明显更低, 镇痛持续时间更长, 术后24 h内舒芬太尼用量更少($P < 0.05$)。Pecs II组在术后1、3 d时的血清IL-6、TNF- α 水平均明显低于TPVN组($P < 0.05$)。Pecs II组QoR-40评分在术后1~3 d均明显高于TPVN组($P < 0.05$)。两组术后不良反应总发生率比较无明显差异(17.50% vs 25.00%, $P > 0.05$)。结论: Pecs II阻滞相较于TPVN阻滞对改良乳腺癌根治术患者的术后镇痛效果更好, 还可有效降低炎性细胞因子水平, 提升术后早期恢复质量。

[关键词] 胸神经II阻滞; 胸椎旁神经阻滞; 镇痛; 炎性细胞因子; 术后恢复

Comparison of analgesic effect of pectoral nerve II block and thoracic paravertebral nerve block in modified radical mastectomy

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Abstract **Objective:** To compare effects of pectoral nerves II (Pecs II) block and thoracic paravertebral nerve (TPVN) block on perioperative analgesia, inflammatory cytokines and quality of early postoperative recovery after modified radical mastectomy. **Methods:** A total of 80 patients scheduled for modified radical mastectomy in our

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hospital from March 2019 to March 2021 were randomly divided into a Pecs II group and a TPVN group, 40 cases in each group, meanwhile, 20 healthy people in the same period served as the control group. Pecs II block was used in the Pecs II group and TPVN block was used in the TPVN group. The Visual Analogue Scale (VAS) at 0.5, 2, 4, 6, 12, 24, 48 h after the operation, and duration of analgesia, sufentanil dosage within 24 h after the operation were compared between the 2 groups. The serum interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) were detected before operation, 1 and 3 d after the operation, and the scores of 40-item Quality of Recovery Questionnaire (QoR-40) were compared at 1, 2 and 3 d after the operation and the adverse reactions were observed. **Results:** Compared with the TPVN group, the VAS score of the Pecs II group was significantly lower at 2–24 hours after the operation, the duration of analgesia was longer, and sufentanil dosage was less in 24 h after the operation ($P < 0.05$). The levels of IL-6 and TNF- α of the Pecs II group at 1 and 3 d after the operation were significantly lower than those of the TPVN group ($P < 0.05$). The QoR-40 score at 1–3 d in Pecs II group was significantly higher than that in the TPVN group ($P < 0.05$). There was no significant difference in the total incidence of adverse reactions between the 2 groups (17.50% vs 25.00%, $P > 0.05$). **Conclusion:** Compared with TPVN block, Pecs II block has better postoperative analgesia effect in patients with modified radical mastectomy, and can effectively reduce the level of inflammatory factors and improve the quality of early postoperative recovery.

Keywords pectoral nerve II block; thoracic paravertebral nerve block; analgesia; inflammatory cytokines; postoperative recovery

乳腺癌是因乳腺上皮细胞增殖失控、恶变而发, 其在全球女性癌症中发病率较高^[1]。手术治疗为临床乳腺癌首选治疗方案, 改良根治术可保留胸肌, 具有良好的近远期疗效和术后外观效果^[2]。但患者术后常伴发急性疼痛, 限制患者咳嗽、排痰、呼吸、肩关节活动等^[3], 手术创伤与麻醉也会显著增加患者的炎性反应, 诱发肺部感染、低血氧症等并发症, 不利于术后早期康复^[4]。因而提高围手术期的镇痛效果十分必要^[5]。胸椎旁神经(thoracic paravertebral nerve, TPVN)阻滞因可显著缓解乳腺癌根治术患者术后急性疼痛而在临床常用, 但因TPVN阻滞难以有效阻滞源自臂丛的胸长、胸背、胸内侧、胸外侧神经, 患者仍易出现上臂、腋窝不适, 使镇痛不完善^[6]。胸神经(pectoral nerves, Pecs)阻滞是通过在胸肩峰动脉旁支、胸大小肌间注射局麻药来发挥阻滞胸内外侧神经的效果, 常用于乳腺手术、心脏起搏器、胸腔闭式引流术等^[7]。Blanco等^[8]对Pecs阻滞方案改进后发现, Pecs II阻滞可弥补TPVN阻滞的缺陷, 对肋间神经($T_2 \sim T_6$)、胸长神经、胸背神经均有效, 适用于改良乳腺癌根治术。目前国内临床关于Pecs II阻滞与TPVN阻滞对乳腺癌根治术镇痛效果的对比报道尚不多见。基于此, 本研究比较Pecs II阻滞与TPVN阻滞用于改良乳腺癌根治术围手术期的镇痛效果及对炎性细胞因子、术后早期恢复质量的影

响, 旨在为临床提供一定参考。

1 对象与方法

1.1 对象

选取2019年3月至2021年3月于江苏省太仓市第一人民医院行改良乳腺癌根治术的患者为研究对象。纳入标准: 1)首次确诊为乳腺癌, 择期行改良乳腺癌根治术; 2)单侧病变; 3)年龄 ≥ 18 岁; 4)美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级为I-II级; 5)肿瘤淋巴结转移(tumor node metastasis, TNM)分期为II-III期; 6)知情同意参与研究。排除标准: 1)术前神经阻滞部位存在感染; 2)存在其他部位肿瘤; 3)存在Pecs II阻滞或TPVN阻滞禁忌; 4)合并凝血功能异常、免疫系统疾病、严重心肝肾肺疾病、神经及精神疾病、病态肥胖者; 5)对麻醉药物过敏者。本研究开始前基于统计学原理进行了实验所需样本量的估算, 参照既往研究^[9]进行样本量估算, 样本量计算公式为: $n_1 = n_2 = 2[(t_{\alpha/2} + t_{\beta})s/\delta]^2$, 样本量计算结果为: 当两组病例数相等时, 每组例数应不少于37例。实际入组80例, 随机(随机数字表法)分为Pecs II组与TPVN组, 每组40例。另选取20例同期健康体检者为对照组。本研究经江苏省太仓市第一人民医院医学伦理委员会审核批准。

1.2 麻醉方法

两组术前均禁饮禁食,入室后吸氧,常规检测血压(blood pressure, BP)、心率(heart rate, HR)、心电图(electrocardiogram, ECG)、脑电双频指数(bispectral index, BIS)、脉搏血氧饱和度(pulse oxygen saturation, SpO₂)等,建立静脉通路。采用ACUSON S2000型彩色超声多普勒超声诊断仪进行超声引导,使用25 mL罗哌卡因(10 mL:89.4 mg,江苏恩华药业股份有限公司,国药准字:H20052621)进行神经阻滞麻醉;Pecs II组采用Pecs II阻滞,患者取平卧位,外展术侧上臂,在锁骨中点下用超声探头定位腋动脉、腋静脉,后将探头移动至第3肋骨水平处,定位胸小肌、深部前锯肌,在穿刺点注入利多卡因(5 mL:0.1 g,石药银湖制药有限公司,国药准字:H14024045)2~3 mL行皮下浸润麻醉,进针使用短轴平面内技术,针尖自内向外,在超声辅助下确认针尖在胸小肌、前锯肌区域内注入15 mL罗哌卡因,退回胸大肌、胸小肌区域内注入10 mL罗哌卡因;TPVN组采用TPVN阻滞,患者取坐位,行触诊,在拟穿刺节段上下的棘突处作标记,定位T₃椎间隙,明确肋骨走向,用超声探头沿肋间扫描T₃平面旁矢状切面,定位横突、胸膜、肋横突韧带,在探头外侧缘处进针注入利多卡因2~3 mL行局部浸润麻醉,进针使用短轴平面内技术,在超声辅助下确认针尖至肋横突韧带,试推2 mL生理盐水,针尖缓慢突破肋横突韧带,确认回抽无脑脊液、无血后,注入25 mL罗哌卡因,超声影像中可见壁层胸膜下压、椎旁间隙扩张。两组均在确认神经阻滞起效后行全身麻醉,麻醉诱导:静脉输注枸橼酸舒芬太尼(2 mL:100 μg,宜昌人福药业有限责任公司,国药准字:H20054172) 0.1 μg/kg,苯磺顺阿曲库铵(5 mL:10 mg,北京泰德制药股份有限公司,国药准字:H20203696),丙泊酚(20 mL:200 mg,费森尤斯卡比医药有限公司,国药准字:H20170305)1.5~2.5 mg/kg麻醉维持:静脉输注丙泊酚100~200 μg/(kg·min),间断静注舒芬太尼0.1 μg/kg。术中对两组麻醉深度进行调整,使BP、HR波动幅度低于基础水平的20%,BIS值稳定在45~60,可酌情加用阿托品、去甲肾上腺素等。术后开启自控静脉镇痛泵(patient controlled intravenous analgesia, PCIA),转入麻醉后恢复室(post anesthesia care unit, PACU)。PCIA:舒芬太尼150 μg,生理盐水稀释至150 mL,无背景剂量,设置单次给药量为3 mL、锁定时间为15 min。

1.3 观察指标

1)围手术期镇痛效果:使用疼痛视觉模拟量表(Visual Analogue Scale, VAS)^[10]评估术后0.5、2、4、6、12、24、48 h时患者疼痛程度;记录镇痛持续时间(神经阻滞完成至首次按压PCIA)、术后24 h内舒芬太尼用量。2)炎症细胞因子:术前、术后1 d、术后3 d时血清白细胞介素-6(interleukin-6, IL-6)、肿瘤坏死因子-α(tumor necrosis factor, TNF-α)水平,均采用免疫酶联吸附法(enzyme-linked immunosorbent assay, ELISA)进行检测,血样为外周静脉血3 mL,试剂盒购自上海酶联生物科技有限公司,操作严格按照说明书进行。3)使用40项恢复质量评分量表(40-item Quality of Recovery Questionnaire, QoR-40)^[11]评估术后1、2、3 d时患者术后恢复质量,QoR-40共40个条目,每条目1~5分,总分为40~200,评分越高提示患者术后恢复质量越好。4)术后不良反应:观察术后恶心、呕吐、感染等不良反应发生情况。

1.4 统计学处理

使用SPSS 22.0统计学软件进行数据分析。计量资料[年龄、体重指数(body mass index, BMI)、查尔森合并症指数(Charlson comorbidity index, CCI)、镇痛持续时间、术后24 h内舒芬太尼用量]均符合正态分布,以均数±标准差($\bar{x} \pm s$)表示,比较行两独立样本 t 检验或配对 t 检验;对重复测量数据(VAS、IL-6、TNF-α、QoR-40)采用重复测量设计的方差分析,两两比较行LSD- t 检验;计数资料(ASA分级、新辅助化疗例数、TNM分期、术后不良反应)以频数(%)表示,比较行 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 一般资料

3组一般资料比较差异无统计学意义($P > 0.05$,表1)。

2.2 围手术期镇痛效果

对两组术后不同时刻的VAS评分进行重复测量方差分析,两组VAS评分均在术后0.5~6 h时呈明显上升趋势,在12~48 h时呈下降趋势($P < 0.05$);且与TPVN组相比,Pecs II组在术后2~24 h时的VAS评分均明显更低($P < 0.05$);两组在术后0.5、48 h时的VAS评分比较无明显差异($P > 0.05$,表2)。

Pecs II组镇痛持续时间、术后24 h内舒芬太尼用量分别为(338.59±56.84) min、(6.88±1.04) μg, TPVN组镇痛持续时间、术后24 h内舒芬太尼用量分别为(225.87±63.25) min、(10.62±2.13) μg, 组间比较差异均有统计学意义(均P<0.05, 表3)。

2.3 炎性细胞因子

术前, Pecs II组和TPVN组血清炎性细胞因子水平均明显高于对照组(P<0.05); 但Pecs II组和TPVN组血清炎性细胞因子水平比较差异均无统计学意义(P>0.05)。术后, 两组血清IL-6、TNF-α水平均表现为先上升、后下降(P<0.05); 且Pecs II组

在术后1、3 d时的血清IL-6、TNF-α水平均明显低于TPVN组(均P<0.05, 表4)。

2.4 术后早期恢复质量

两组QoR-40评分在术后1~3 d均呈明显上升趋势(P<0.05); 且Pecs II组QoR-40评分在术后1~3 d均明显高于TPVN组(均P<0.05, 表5)。

2.5 术后不良反应

两组均为发生穿刺和阻滞相关不良反应。Pecs II组术后不良反应总发生率为17.50%, TPVN组术后不良反应总发生率为25.00%, 组间比较差异无统计学意义(P>0.05, 表6)。

表1 3组一般资料比较

Table 1 Comparison of general data between the 3 groups

组别	n	年龄/岁	BMI/(kg m ⁻²)	ASA分级 (I/II)/例	新辅助化疗/[例(%)]	TNM分期 (I/II)/例	CCI/分
Pecs II组	40	47.31 ± 9.58	24.76 ± 3.45	17/23	12 (30.00)	22/18	4.21 ± 1.02
TPVN组	40	46.28 ± 10.34	24.33 ± 3.67	19/21	15 (44.44)	24/16	4.26 ± 1.05
对照组	20	45.31 ± 9.62	24.66 ± 3.58	—	—	—	—
F/χ ²		0.473	0.549	0.202	0.503	0.205	0.216
P		0.639	0.587	0.653	0.478	0.651	0.829

表2 两组术后VAS评分比较

Table 2 Comparison of postoperative VAS scores between the 2 groups

组别	n	术后0.5 h	术后2 h	术后4 h	术后6 h	术后12 h	术后24 h	术后48 h
Pecs II组	40	0.95 ± 0.19	1.04 ± 0.22	2.02 ± 0.57	3.61 ± 0.85	2.73 ± 0.68	2.15 ± 0.72	1.75 ± 0.61
TPVN组	40	1.03 ± 0.24	2.61 ± 0.76	3.67 ± 1.04	4.03 ± 0.96	3.54 ± 0.84	2.88 ± 0.91	2.03 ± 0.72
t		1.652	12.549	8.799	2.072	4.740	3.978	1.876
P		0.102	<0.001	<0.001	0.042	<0.001	<0.001	0.064

处理因素主效应, F=93.163, P<0.001; 时间因素主效应, F=113.351, P<0.001; 二者交互, F=108.492, P<0.001。

Main effect of processing factors, F=93.163, P<0.001; main effect of time factor, F=113.351, P<0.001; interaction between the two, F=108.492, P<0.001.

表3 两组镇痛持续时间、术后24 h内舒芬太尼用量比较

Table 3 Comparison of analgesic duration and sufentanil dosage within 24 hours after the operation between the 2 groups

组别	n	镇痛持续时间/min	舒芬太尼用量/μg
Pecs II组	40	338.59 ± 56.84	53.76 ± 4.89
TPVN组	40	225.87 ± 63.25	60.73 ± 7.15
t		8.383	5.089
P		<0.001	<0.001

表4 3组炎症细胞因子水平比较

Table 4 Comparison of inflammatory cytokines between the 3 groups

组别	n	IL-6/(pg·mL ⁻¹)			TNF-α/(pg·mL ⁻¹)		
		术前	术后1 d	术后3 d	术前	术后1 d	术后3 d
Pecs II组	40	84.25 ± 9.52 [△]	127.34 ± 8.73	103.56 ± 8.26	1.12 ± 0.33 [△]	3.04 ± 0.24	1.68 ± 0.35
TPVN组	40	82.68 ± 9.11 [△]	143.91 ± 7.87	121.57 ± 7.93	1.08 ± 0.37 [△]	3.43 ± 0.34	1.87 ± 0.28
对照组	20	20.39 ± 6.88	—	—	22.56 ± 7.12	—	—
t/F		2.413	8.916	9.947	2.586	5.927	2.681
P		0.005	<0.001	<0.001	0.008	<0.001	0.009

与对照组相比, [△]P<0.05; IL-6: 处理因素主效应, F=98.631, P<0.001; 时间因素主效应, F=94.051, P<0.001; 二者交互, F=101.33, P<0.001。TNF-α: 处理因素主效应, F=64.571, P<0.001; 时间因素主效应, F=78.221, P<0.001; 二者交互, F=79.543, P<0.001。

Compared with the control group, [△]P<0.05; IL-6: Main effect of processing factors, F=98.631, P<0.001; main effect of time factor, F=94.051, P<0.001; interaction between the two, F=101.33, P<0.001. TNF-α: Main effect of processing factors, F=64.571, P<0.001; main effect of time factor, F=78.221, P<0.001; interaction between the two, F=79.543, P<0.001.

表5 两组术后早期QoR-40评分比较

Table 5 Comparison of QoR-40 scores in the early postoperative period between the 2 groups

组别	n	术后1 d	术后2 d	术后3 d
Pecs II组	40	150.23 ± 8.42	156.74 ± 8.57	169.58 ± 7.84
TPVN组	40	143.56 ± 9.86	148.35 ± 10.26	161.63 ± 8.12
t		3.253	3.969	4.455
P		0.002	<0.001	<0.001

处理因素主效应, F=114.561, P<0.001; 时间因素主效应, F=124.784, P<0.001; 二者交互, F=119.233, P<0.001。

Main effect of processing factors, F=114.561, P<0.001; main effect of time factor, F=124.784, P<0.001; interaction between the two, F=119.233, P<0.001.

表6 两组术后不良反应发生情况比较

Table 6 Comparison of postoperative adverse reactions between the 2 groups

组别	n	恶心/[例(%)]	干呕/呕吐/[例(%)]	感染/[例(%)]	总发生率/%
Pecs II组	40	5 (12.50)	1 (2.50)	1 (2.50)	17.50
TPVN组	40	7 (17.50)	2 (5.00)	1 (2.50)	25.00
χ ²					0.672
P					0.412

3 讨论

改良乳腺癌根治术是乳腺癌治疗常用手段, 可在有效清除病灶组织的基础上保留胸肌, 满足患者对疗效、美观的要求。尽管术式日渐成熟,

但调查发现, 近半数患者在术后出现了中度以上的急性疼痛, 影响患者术后早期康复质量^[12]。PCIA可通过抑制大脑皮层边缘系统在一定程度上缓解术后疼痛, 却对外周伤害性刺激向中枢神经系统的传导过程无效, 因而镇痛效果略显不足。

Pecs II阻滞和TPVN阻滞均属于周围神经阻滞麻醉技术,可直接阻断外周伤害性刺激传导至中枢的过程。研究^[13]显示:其在术前应用有助于降低乳腺癌患者术后疼痛感、促进康复进展,但学者在具体神经阻滞方案选择上尚未统一观点。

TPVN阻滞虽可通过在椎间孔脊神经附近注射局麻药物来阻滞相关神经,实现麻醉、镇痛同侧躯体之效,但因其无法完全阻滞胸长、胸背、胸内侧、胸外侧神经,镇痛不全。且有研究^[14]发现:TPVN阻滞中的感觉平面阻滞范围通常不超过注药节段($T_3\sim T_5$ 、 T_2 、 T_6 较少),而Pecs II阻滞则可向两端扩散,达到 $T_2\sim T_6$ 节段,局麻药扩散范围更广。本研究结果显示:Pecs II组在术后2~24 h时的VAS评分均明显低于TPVN组,且Pecs II组镇痛持续时间更长,术后24 h内舒芬太尼用量更少,提示在改良乳腺癌根治术中应用Pecs II阻滞可取得更好的术后镇痛效果,与Kulhari等^[15]的研究结果一致。这与Pecs II阻滞对胸长、胸背、胸内侧、胸外侧神经的完善阻滞作用有关^[16]。Wahba等^[17]的研究结果也证实:Pecs II阻滞相较于TPVN阻滞可为患者提供更持久的镇痛效果,并可减少术后镇痛药物用量。但Martsiniv等^[18]的研究则显示:Pecs II阻滞与TPVN阻滞的镇痛效果相当,结论存在一定差异,这可能与样本量选择、人群素质存在差异有关。

疼痛、手术创伤均会引发机体应激反应,进而扰乱免疫状态、代谢平衡,激活免疫细胞并使其大量释放炎症细胞因子,加重炎症反应^[19]。IL-6、TNF- α 均是由淋巴细胞、巨噬细胞、成纤维细胞等免疫细胞合成分泌的促炎因子,二者血清水平可在一定程度上反映机体的炎症应激状态^[20]。既往研究^[21]指出:血清中IL-6、TNF- α 等水平越高,提示机体细胞介质爆发、炎症应激程度越严重,对其他远隔脏器造成损伤的风险越高、程度越显著。本研究发现:Pecs II组在术后1、3 d时的血清IL-6、TNF- α 水平均明显低于TPVN组,表明Pecs II阻滞相较于TPVN阻滞可更有效地减轻乳腺癌患者术后因手术创伤等引发的急性期全身炎症反应。这可能与Pecs II阻滞对手术操作区域内周围神经的阻滞作用更完全有关,Pecs II阻滞对肋间神经($T_2\sim T_6$)、胸长神经、胸背神经均有效,可避免因中枢敏化而降低疼痛阈值,明显降低患者疼痛程度,延缓疼痛发生,从而减轻机体因疼痛出现的一系列过度反应^[22]。

另外,本研究结果显示:Pecs II组QoR-40评分在术后1~3 d均明显高于TPVN组,提示Pecs II阻

滞麻醉有助于提升患者术后早期的恢复质量,这得益于Pecs II阻滞对患者术后疼痛的有效控制和炎症反应的抑制,为患者术后早期康复创造了有利条件^[23]。本研究还发现:两组术后不良反应总发生率无明显差异,均未出现严重并发症,提示两种神经阻滞方式的安全性相当,这得益于术中超声辅助技术的支持。超声可帮助术者直观、持续地观察到进针路径、周围组织结构、药物扩散状态等,进而提高神经阻滞操作的安全性^[24]。

综上所述,在改良乳腺癌根治术中使用Pecs II阻滞可取得比TPVN阻滞更好的镇痛效果,明显降低患者在术后24 h内的疼痛程度,延长镇痛时间并减少镇痛药物用量,还可显著抑制炎症反应,提高患者术后早期恢复质量。但本研究仍存在一定不足,其一是样本量较少结论具有局限性;其二是因受试条件限制并未实施盲法及分配隐藏。本研究结果仍需多中心、大样本研究进一步验证。

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