

doi: 10.13241/j.cnki.pmb.2020.02.016

胸外科手术后神经病理性疼痛的发生情况及相关因素分析*

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摘要 目的:探讨胸外科手术后神经病理性疼痛的发生情况及相关危险因素。**方法:**回顾性分析 2015 年至 2016 年就诊于我院行胸外科手术的患者的临床资料,包括患者的年龄、性别、吸烟史、BMI、术前是否使用催眠药物、术前诊断、手术侧别、手术方式、是否为微创、硬膜外自控镇痛泵使用情况、术中失血量、手术持续时间、引流管引流时间及是否发生神经病理性疼痛,对比分析是否发生神经病理性疼痛患者的临床资料,对有差异的临床资料进行多因素 Logistic 回归分析探讨发生神经病理性疼痛的危险因素。**结果:**共有 123 例患者纳入研究,33 例(26.8%)患者的患者术后出现神经病理性疼痛,6 例(4.9%)患者在术后一年仍有持续性神经病理性疼痛,术后出现神经病理性疼痛的平均时间为术后第 7 天,平均持续时间为 75 天,发生神经病理性疼痛的患者吸烟比例(81.8%)、术前使用催眠药比例(57.6%)、开胸手术比例(81.8%)、术中失血量(185 mL)、手术时间(196 分钟)、术后引流时间(2.5 天)均高于没有发生神经病理性疼痛的患者。多因素分析显示术前使用催眠药 ($OR=2.322, P<0.001$)、手术时间延长 ($OR=3.703, P<0.001$)和术后引流时间延长($OR=2.675, P=0.002$)均是神经病理性疼痛发生的危险因素,电视辅助胸腔镜手术方式是保护性因素($OR=0.453, P=0.002$)。**结论:**术前使用催眠药物、延长的手术时间及术后引流时间增加了神经病理性疼痛发生的风险,电视辅助胸腔镜技术可减少其发生率。

关键词:神经病理性疼痛;胸外科手术;危险因素

中图分类号:R655 **文献标识码:**A **文章编号:**1673-6273(2020)02-281-04

Analysis of the Occurrence and Related Factors of Neuropathic Pain after Thoracic Surgery*

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ABSTRACT Objective: To investigate the occurrence of neuropathic pain and related risk factors after thoracic surgery. **Method(s):** The clinical data of patients who underwent thoracic surgery in our hospital from 2015 to 2016, including patients' age, gender, smoking history, BMI, preoperative use of hypnotics, preoperative diagnosis, surgical side, surgical approach, whether it was minimally invasive, the use of epidural analgesia pump, intraoperative blood loss, duration of surgery, tube drainage time and whether neuropathic pain occurred were retrospectively collected. The clinical data of patients with neuropathic pain and without were comparably analyzed. Multivariate logistic regression analysis was performed on the differential clinical data to explore the risk factors of neuropathic pain. **Result (s):** A total of 123 patients were enrolled in the study. 33 patients (26.8%) had postoperative neuropathic pain. 6 patients (4.9%) had persistent neuropathic pain for one year after surgery. The time for postoperative neuropathic pain was on the 7th day after surgery and the duration was 75 days. The smoking proportion (81.8%), the proportion of hypnotics before surgery (57.6%), the proportion of thoracotomy (81.8%), and the amount of intraoperative blood loss (185 mL), operative time (196 minutes), and postoperative drainage time (2.5 days) of patients with neuropathic pain were higher than those without neuropathic pain. Multivariate analysis showed that preoperative use of hypnotics ($OR=2.322, P<0.001$), prolonged operative time ($OR=3.703, P<0.001$), and prolonged postoperative drainage time ($OR=2.675, P=0.002$) were the risk factors of neuropathic pain. Conversely, Video-assisted thoracoscopic surgery is a protective factor ($OR=0.453, P=0.002$). **Conclusion (s):** Preoperative use of hypnotics, and prolonged operative time and postoperative drainage time increase the risk of neuropathic pain. Video-assisted thoracoscopic techniques can reduce the incidence.

Key words: Neuropathic pain; Thoracic surgery; Risk factors

Chinese Library Classification (CLC): R655 **Document code:** A

Article ID:1673-6273(2020)02-281-04

* 基金项目:国家自然科学基金项目(81572252)

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(收稿日期:2019-08-08 接受日期:2019-08-31)

前言

胸外科术后发生神经病理性疼痛(Neuropathic pain, NP)较为常见且严重影响患者术后生活质量,特点为自发性、疼痛过敏即轻微碰触即可引起剧烈疼痛、疼痛性质多样及感觉异常^[1],疼痛性质可为烧灼样、电击样、撕裂样、针刺样、牵扯样等^[2],长期慢性疼痛可导致失眠和食欲不振,并可能使患者丧失日常生活能力^[3]。虽然目前研究认为胸外科术后 NP 的发生有许多机制,但大多数学者认为 NP 与肋间神经的损伤和继发性功能障碍关系最为密切。NP 术后的镇痛方案较多,研究显示电视辅助胸腔镜手术(Video-assisted thoracoscopic surgery, VATS)可有效减少术后疼痛程度^[4]。我院较早开展 VATS,与开胸手术相比,术后患者恢复较快住院时间缩短,但有些患者入院时没有主诉疼痛但术后诉长时间疼痛,且有些患者表述的症状为 NP 的症状,提示即使 VATS 明显减少手术创伤但术后仍有 NP 发生。因此,本研究主要研究了胸外科术后 NP 的发生情况及相关危险因素,以期临床的治疗及预防提供参考。

1 资料与方法

1.1 一般资料

收集 2015 年 1 月至 2016 年 12 月份就诊于我科因肺部疾病或纵膈肿瘤行 VATS 或者开胸手术的患者,排除标准为:①有胸外科手术史;②术前考虑已发生 NP 的患者;③年龄小于 18 岁;④患有其他系统的严重疾病。NP 的定义为"由躯体感觉系统的病变或疾病引起的疼痛"^[5]。采用已验证的 NP 筛查工具,Leeds 评估量表评估患者是否术后发生 NP^[6]。慢性疼痛定义为手术后持续超过三个月的疼痛。所有的手术均是由我科同一医疗组完成,术后镇痛方案由我院麻醉科医师制定。该研究取得我院伦理委员会同意。

1.2 临床资料

收集患者的基本临床资料,包括年龄、性别、吸烟史、BMI、术前是否使用催眠药物、术前诊断、手术侧别(左侧或者右侧)、手术方式、是否为微创(VATS 或者开胸手术)、术后是否使用硬膜外自控镇痛泵、术中失血量、手术持续时间、引流管引流时间及是否发生 NP。术前的诊断包括原发性肺癌、转移性肺癌、纵膈肿瘤、其他肺部疾病。手术方式包括肺部分切除、肺段切除、肺叶切除、纵膈肿瘤切除及其他手术。

1.3 统计学分析

采用 SPSS 20.0 软件进行统计学分析,计量资料的差异采用 t 检验分析,计数资料的差异采用卡方检验或者 Fisher 精确检验分析,影响因素采用多因素 Logistic 回归分析,以 $P < 0.05$ 为差异有统计学意义。

2 结果

根据纳入排除标准,从 2015 年 1 月至 2016 年 12 月共有 123 例患者纳入研究,所有患者均完成了 12 个月随访,共有 33 例患者术后发生 NP,有 6 例患者 NP 持续至术后一年,从手术结束至 NP 发生的平均时间为第 7 天,术后一年内 NP 平均持续时间为 75 天,所有的患者均诉疼痛部位为手术切口周围,发生 NP 的患者术后因急性疼痛需镇痛干预有 26 例(78.8%)高于

没有发生 NP 的 32 例(35.6%)($P < 0.001$),术后住院时间(14.8 ± 3.5 天)高于没有发生 NP 的患者(8.7 ± 2.1 天)($P < 0.001$)。

2.1 患者的基本临床资料

123 例患者的基本资料(见表 1),平均年龄为 65.7 ± 13.2 天,男性有 84 例(68.3%)患者,65 例(52.8%)患者有吸烟史,平均 BMI 为 22.7 ± 4.7 ,术前有 35 例(28.5%)患者使用催眠药,有 57 例(46.3%)患者接受 VATS,术中平均失血量为 125 ± 34 mL,平均手术时间为 168 ± 51 分钟,术后平均引流时间为 2.3 ± 0.3 天。

表 1 123 例患者基本资料

Table 1 Basic information of 123 patients

Parameter	
Age (Year)	65.7 ± 13.2
Sex (Male, %)	84, 68.3%
History of smoking (n, %)	65, 52.8%
BMI	22.7 ± 4.7
Preoperative use of hypnotics (n, %)	35, 28.5%
Diagnosis (n, %)	
Primary lung cancer	67, 54.5%
Secondary lung cancer	12, 9.8%
Other lung diseases	18, 14.6%
Mediastinal tumor	26, 21.1%
Surgical side (right, %)	72, 58.5%
Surgical method (n, %)	
Partial resection	20, 16.3%
Segmentectomy	21, 17.1%
Lobectomy	50, 40.1%
Mediastinal tumor resection	26, 21.2%
Other	6, 4.9%
VATS(n, %)	57, 46.3%
Epidural controlled analgesia (n, %)	92, 74.8%
Intraoperative blood loss (mL)	125 ± 34
Surgery time (minutes)	168 ± 51
Drainage time (days)	2.3 ± 0.3

2.2 是否发生 NP 患者的临床资料比较

123 例患者中,33 例患者术后发生 NP,发生 NP 的患者吸烟比例(81.8%)、术前使用催眠药比例(57.6%)、开胸手术比例(81.8%)、术中失血量(185 ± 42 mL)、手术时间(196 ± 53 分钟)、术后引流时间(2.5 ± 0.4 天)均高于没有发生 NP 的患者的吸烟比例(42.2%)、术前使用催眠药比例(17.8%)、开胸手术比例(43.3%)、术中失血量(103 ± 33 mL)、手术时间(157 ± 47 分钟)、术后引流时间(2.2 ± 0.2 天)($P < 0.05$)。两组患者在年龄、性别比例、BMI、术前诊断、手术侧别、手术方式及术后硬膜外自控镇痛泵的使用方面均没有统计学差异(见表 2)。

2.3 NP 发生的相关因素分析

我们将手术时间是否高于手术时间平均值分为手术时间是否延长两组,将术后引流时间是否长于平均引流时间分为引流时间是否延长两组,将术中失血量是否高于平均值分为失血量是否增多两组。以表2中有差异的因素(是否吸烟、术前是否使用催眠药、是否为VATS、术中失血量是否增多、手术时间是否延长、术后引流时间是否延长)为自变量,以是否发

生NP为因变量进行多因素Logistic回归分析。多因素分析显示术前使用催眠药($OR=2.322, P<0.001$)、手术时间延长($OR=3.703, P<0.001$)和术后引流时间延长($OR=2.675, P=0.002$)均是NP发生的危险因素,VATS是保护性因素($OR=0.453, P=0.002$) (见表3)。

表2 是否发生神经性疼痛的患者临床资料对比

Table 2 Comparison of the clinical data of patients with and without neuropathic pain

Parameter	Yes (n=33)	No (n=90)	t/χ^2	P value
Age (Year)	67.8± 12.3	64.9± 11.7	1.201	0.232
Sex (Male, %)	24, 72.7%	60, 66.7%	0.410	0.522
History of smoking (n, %)	27, 81.8%	38, 42.2%	15.19	<0.001
BMI	22.5± 4.9	22.7± 5.2	0.192	0.848
Preoperative use of hypnotics (n, %)	19, 57.6%	16, 17.8%	18.786	<0.001
Diagnosis (n, %)				
Primary lung cancer	17, 51.5%	50, 55.6%	0.339	0.952
Secondary lung cancer	4, 12.1%	8, 8.9%		
Other lung diseases	5, 15.2%	13, 14.4%		
Mediastinal tumor	7, 21.2%	19, 21.1%		
Surgical side (right, %)	20, 66.7%	52, 57.8%	0.080	0.778
Surgical method (n, %)				
Partial resection	5, 15.2%	15, 16.7%	3.782	
Segmentectomy	7, 21.2%	14, 15.6%		
Lobectomy	10, 30.3%	40, 44.4%		
Mediastinal tumor resection	10, 30.3%	16, 17.7%		
Other	1, 3.0%	5, 5.6%		
VATS(n, %)	6, 18.2%	51, 56.7%	14.382	<0.001
Epidural controlled analgesia (n, %)	26, 78.8%	66, 73.3%	0.381	0.537
Intraoperative blood loss (mL)	185± 42	103± 33	11.320	<0.001
Surgery time (minutes)	196± 53	157± 47	3.938	<0.001
Drainage time (days)	2.5± 0.4	2.2± 0.2	5.504	<0.001

表3 是否发生神经性疼痛的多因素分析结果

Table 3 Results of multivariate analysis of neuropathic pain

Parameter	OR	95% confidence interval	P value
VATS	0.453	0.026-0.045	<0.001
Preoperative use of hypnotics	2.322	1.590-3.393	<0.001
Surgery time	3.703	1.971-6.956	<0.001
Drainage time	2.675	1.436-4.982	0.002

3 讨论

术后疼痛直接影响患者就医体验,是术后关注的重点,关

于胸外科术后镇痛方案也制定了相应指南^[7]。胸外术后NP发生概率较高^[8],即便是VATS在临床上应用越来越广泛^[9],术后NP仍然较常见,临床医师需要了解术后NP发生的危险因素。

本研究结果显示四分之一的患者术后发生 NP, 疼痛部位均位于手术切口周围, 发生 NP 的患者术后住院时间明显延长, 仍有少量患者在术后 1 年仍遭受 NP 困扰, 术前使用催眠药物、手术时间和引流管放置时间延长均增加术后 NP 的发生, VATS 可降低术后 NP 的发生风险。

术后 NP 可导致住院时间延长和医疗花费增加, 为减轻疼痛症状, 大多数患者应用非阿片类药物镇痛^[10], 阿片类药物可控制术后中至重度疼痛^[11-13], 长时间应用阿片类药物增加了心血管事件发生的风险^[14,15], 且研究表明胸外科术后 NP 患者应用阿片类药物增多^[16], 更好的理解 NP 发生的危险因素对于临床医师及患者制定医疗决策至关重要。之前有研究报道了胸外科术后 NP 的发生情况^[17], 但是没有研究关注 NP 发生的时间、持续时间及发生部位, 且 VATS 与开胸手术对术后 NP 的影响仍不清楚。有报道称胸外科术后三个月 NP 发生率高达 80%, 术后一年高达 61%^[18], 但是我们的研究发现术后 NP 发生率低于之前的报道, 我们认为是 VATS 降低了术后 NP 的发生, VATS 手术创伤较小^[19-22], NP 的发生部位为手术切口的前缘, 该区域受到肋间神经的前皮支支配^[3]。在本研究中, 没有发现由其他分支支配区域的疼痛; 因此, 这些发现可以帮助临床医师区分 NP 和非 NP。

除了微创手术方式外, 我们发现术前使用催眠药物和延长的手术时间和引流管引流时间增加术后 NP 发生。社会心理状态包括焦虑、抑郁、缺乏社会支持和较低的社会地位是公认的影响认知和慢性 NP 的因素^[23-25], 术前的恐惧焦虑和术后出现急性疼痛及镇痛药物使用量密切相关, 是术后持续性疼痛的危险因素^[26-28], 焦虑和抑郁的患者术前使用催眠药物概率大, 同样地, 我们也发现术前使用催眠药物与 NP 密切相关, 术前使用催眠药物往往预示着术后发生 NP 风险高。此外, 手术时间和术后引流时间的延长也是术后 NP 发生的危险因素, 胸外科手术术中的暴露伤口通常会持续牵拉压迫肋间神经, 特别是在肋骨尾侧暴露神经的地方^[3]。肋间神经损伤可能随着手术时间和术后引流管放置时间的延长而成比例增加, 而 VATS 由于减少了对肋间神经的损伤故可以减少 NP 发生。因此, 在手术结束时, 对利用局麻药物对肋间神经进行麻醉可减轻术后疼痛^[29,30]。

本研究存在一些缺陷, 首先, 该研究的研究样本有限, 是单中心研究结果。其次, 手术方式的选择可能存在选择偏倚, 比如术者可能会部分根据自己的手术习惯选择 VATS 和开胸手术。但是不可否认的是术后 NP 是胸外科术后某些高危患者不可避免的并发症, 对于大多数患者, 避免术后 NP 发生可以产生更好的术后体验、减少术后住院时间和医疗花费。近年来, 研究表明普瑞巴林是治疗 NP 的有效药物, 但是仍需要大样本、多中心的前瞻性研究证明普瑞巴林对预防胸外科术后 NP 发生的作用。

总之, 术前使用催眠药物、延长的手术时间及术后引流时间增加了胸外科术后 NP 发生的风险, VATS 可减少术后 NP 的发生, 术前制定治疗方案时为获得满意的临床疗效充分考虑上述因素。

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