



硬膜外镇痛在微创食管切除术中的应用: 证据与实践*

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【摘要】 食管切除术作为治疗食管癌的有效手段,其术后疼痛管理的重要性日益受到关注,硬膜外镇痛是开放食管切除术首选的镇痛方式。随着外科技术的发展,微创食管切除术(minimally invasive esophagectomy, MIE)已成为主流手术方式,硬膜外镇痛是否仍是MIE的首选镇痛方式,目前尚无定论。本综述通过分析近年来的相关文献,发现硬膜外镇痛仍然是MIE的重要镇痛方式,镇痛效果最佳,可以减少肺部并发症,改善生活质量,减少应激反应。通过准确选择穿刺节段、个体化用药和多模式镇痛可以减少不良反应。未来可以使用大数据和人工智能达到精准多模式镇痛。

【关键词】 镇痛, 硬膜外 微创外科手术 食管切除术 手术后并发症 综述

Epidural Analgesia in Minimally Invasive Esophagectomy: Evidence and Practice

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【Abstract】 Esophagectomy is an effective treatment for esophageal cancer, and there has been growing attention on the importance of postoperative pain management in patients undergoing the surgery. Epidural analgesia is the preferred analgesic approach for open esophagectomy. With the development of surgical technology, minimally invasive esophagectomy (MIE) has become the mainstream surgical approach. However, no conclusion has been reached concerning whether epidural analgesia is still the preferred analgesic approach for MIE. Herein, we analyzed the relevant literature published in recent years and found that epidural analgesia continued to be an important analgesic approach for MIE, offering the best analgesic effect. Epidural analgesia can reduce postoperative pulmonary complications, improve the quality of life, and reduce the stress response. Adverse effects can be minimized through accurate selection of epidural puncture segments, individualized medication, and multimodal analgesia strategies. In the future, precision-based multimodal analgesia can be achieved using emerging technologies such as big data analytics and artificial intelligence.

【Key words】 Analgesia, epidural Minimally invasive surgical procedures Esophagectomy Complications Review

中国是食管癌高发国家。2020年中国癌症负担报告显示,食管癌是中国排位第六的癌症,是癌症相关死亡的第四大原因^[1]。食管癌根治术是早中期食管癌的主要治疗手段,传统的手术方式包括开胸开腹胸内吻合(Ivor Lewis)、开胸开腹颈部吻合(MecKeown)或开腹经食管裂孔颈部吻合。自1992年第一次报道胸腔镜食管切除术以来,微创术式不断演变,包括胸腔镜胸内吻合、胸腔镜颈部吻合或纵隔镜联合腹腔镜颈部吻合,3种微创手术的腹部部分

又分为全腹腔镜和手辅助腹腔镜(上腹部小切口),目前以手辅助腹腔镜为主。微创食管切除术(minimally invasive esophagectomy, MIE)可以减少手术创伤及术后疼痛,降低肺部并发症发生率^[2]。MIE在全球范围内约占食管癌根治术的50%^[3],已成为食管癌根治的主要手术方式。

硬膜外镇痛是开放食管切除术的首选镇痛方式,食管切除术快速康复指南建议首选硬膜外镇痛^[4-5]。2024年发表的一篇关于食管切除术后镇痛策略的网状meta分析比较了9种不同的镇痛方式,结果显示硬膜外镇痛效果确切,可明显降低术后疼痛评分和阿片类药物消耗^[6]。硬膜外镇痛效果毋庸置疑,但硬膜外镇痛对技术要求高,且有低血压、穿刺出血等风险。相较于开放手术,MIE创伤更小,疼

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痛更轻。有研究者仍然推荐MIE中使用硬膜外镇痛,并指出即使在切口较小的MIE中,硬膜外镇痛良好的疼痛控制将允许早期活动和康复^[7-9]。但临床医生也在积极探索其他镇痛方式来替代硬膜外镇痛^[10]。MIE是否首选硬膜外镇痛存在争议。故本综述拟从硬膜外镇痛的优势、穿刺节段、用药以及不良反应等方面探讨其在MIE中的研究进展。

笔者在PubMed、Web of Science数据库检索到一些探讨硬膜外镇痛在MIE中应用的研究,研究主题主要包括镇痛效果、肺部并发症、生活质量、应激反应、住院时长等(图1)。

1 硬膜外镇痛的优势

1.1 镇痛效果

在多模式镇痛背景下,临床医生们一直努力探索其他镇痛方式在MIE中的使用,包括鞘内镇痛、椎旁阻滞、腹横肌平面阻滞、肋间神经阻滞、竖脊肌阻滞、前锯肌平面阻滞、切口浸润、静脉阿片类药物镇痛、非甾体抗炎药等^[11-16],希望能替代硬膜外镇痛。目前研究最多的是椎旁阻滞,包括单次阻滞与持续阻滞(图2)。随机对照试验发

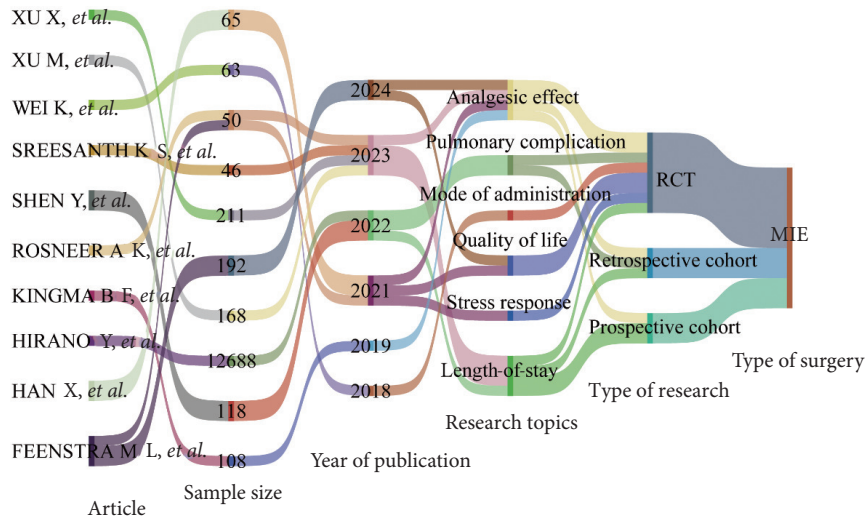


图 1 硬膜外镇痛在MIE术中应用相关文献桑基图

Fig 1 Application of epidural analgesia in minimally invasive esophagectomy in Sankey diagram visualization

RCT: randomized controlled trial; MIE: minimally invasive esophagectomy.

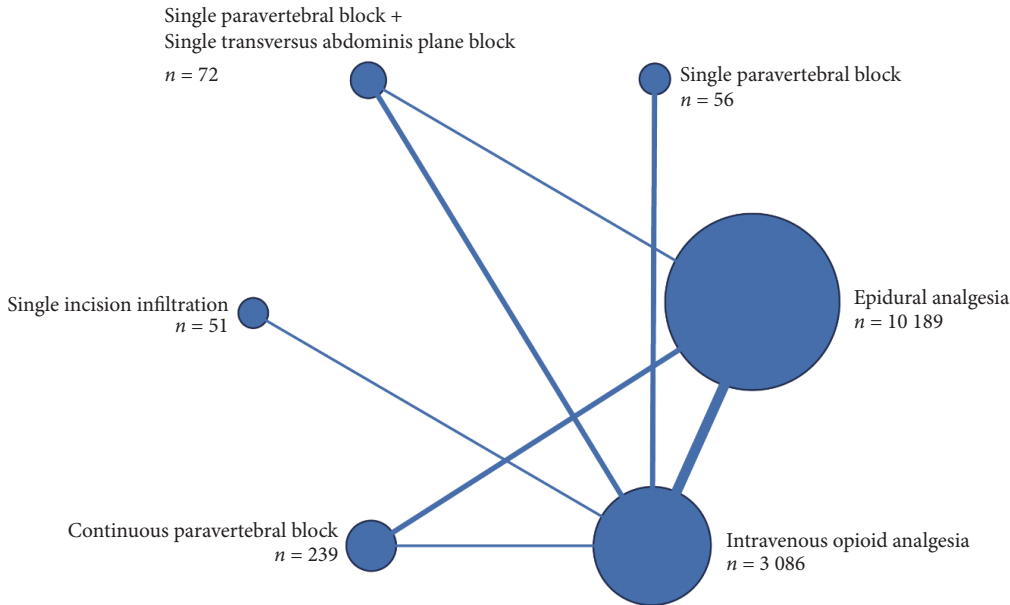


图 2 不同镇痛方式在MIE术后镇痛的对照研究

Fig 2 A comparative study of different analgesic methods in MIE

The size of the nodes corresponds to the sample size of the study. The lines linking the nodes represent the comparison of the two analgesic methods. The thicker the line, the more published reports comparing the two analgesic methods.

现单次椎旁阻滞镇痛效果仅能维持约24 h, 之后疼痛明显加重^[16]。单次椎旁阻滞无法满足MIE术后持续数天的疼痛。随后一项包含233例MIE患者的回顾性队列研究发现, 持续椎旁阻滞在术后48 h内镇痛效果均优于静脉镇痛^[17]。尽管持续椎旁阻滞较单纯静脉镇痛可提供更好的镇痛效果, 但一项比较持续椎旁阻滞与硬膜外镇痛的队列研究发现, 持续椎旁阻滞组患者术后最高疼痛评分仍然高于硬膜外镇痛^[18]。2024年一项包含192例MIE患者的随机对照试验亦证明, 术后2 d硬膜外镇痛效果明显优于持续椎旁阻滞^[19]。MIE其他镇痛方式研究相对较少, 包括鞘内镇痛、腹横肌平面阻滞、切口浸润、非甾体抗炎药、竖脊肌阻滞^[20]等。由于食管手术涉及切口范围广, 术后疼痛持续时间长, 除了硬膜外镇痛, 单用一种镇痛方式通常镇痛不足, 多与椎旁阻滞联用, 作为多模式镇痛的一部分^[16]。

因此, 基于上述研究结果, 笔者推断硬膜外镇痛仍是MIE的重要镇痛方式, 持续椎旁阻滞未来可能替代硬膜外镇痛, 但仍需临床研究和实践验证。

1.2 肺部并发症

肺部并发症是食管切除术后最常见的并发症, 不仅增加住院费用, 延长住院时间, 也是住院期间死亡的主要原因。硬膜外镇痛有助于早期拔管, 降低无效咳嗽与肺部并发症发生率^[21]。日本的一项大型回顾性研究显示, 与无硬膜外镇痛组相比, MIE后硬膜外镇痛与住院死亡率、肺部并发症〔比值比(odds ratio, OR)=0.74, 95%置信区间(confidence interval, CI): 0.66~0.84〕和吻合口漏发生率的降低显著相关^[9]。根据2023年的一项随机对照试验报道, 相较于静脉镇痛, 硬膜外镇痛患者肺部并发症发生率从30.4%降至8.9%^[16], 2024年的一篇meta分析也证实与静脉镇痛相比, 硬膜外镇痛显著降低肺部并发症风险〔相对危险度(relative risk, RR)=3.88, 95%CI: 1.98~7.61〕^[22]。因此, 即使手术微创化, 硬膜外镇痛对食管切除术后肺部并发症的减少仍然有重要作用^[23]。

1.3 生活质量

目前关于食管切除术后生活质量的相关研究较少。已有研究常用的量表包括简短健康调查量表-8(Short Form-8 Health Survey, SF-8)、简短健康调查量表-36(Short Form-36 Health Survey, SF-36)、生命质量核心量表-30(Quality of Life Questionnaire-Core 30, QLQ-C30)、食管癌生命质量量表-18(Quality of Life Questionnaire-Oesophageal Cancer Module 18, QLQ-oes18)和恢复质量量表-40(Quality of Recovery-40, QoR-40)。与持续椎旁阻滞相比, 硬膜外镇痛患者术后第1、2天的QoR-40评分更

高(术后第1天: 168.8 vs. 161.3, 术后第2天: 168.8 vs. 161.5)^[19]。硬膜外镇痛患者术后24 h的SF-8和术后1周的SF-36健康调查的身心评分均显著优于静脉镇痛患者^[24]。从术中就开始使用硬膜外镇痛的患者术后7 d与1个月生活质量(QLQ-C30)评分更高, 特别是在社交、情感和整体健康领域^[25]。在与持续椎旁阻滞比较的研究中, 虽然术后前2 d硬膜外镇痛患者的QoR-40评分优于持续椎旁阻滞, 但术后第3天两组没有明显差异^[19]。因此, 硬膜外镇痛对于MIE患者的生活质量是否优于基于神经阻滞的多模式镇痛仍需要进一步研究。

1.4 应激反应

手术创伤激活交感神经系统, 会引起激素和免疫反应以及凝血系统的明显变化。硬膜外镇痛的节段性交感神经阻滞作用可以减少应激反应, 这在硬膜外镇痛中起着重要作用。目前硬膜外镇痛减少应激反应的研究主要在开放食管切除术中开展, 表明硬膜外镇痛可以显著降低术后血浆中皮质醇、促肾上腺皮质激素、肾上腺素、去甲肾上腺素、白细胞介素(interleukin, IL)-6、IL-8和C反应蛋白水平, 减少应激反应及炎症介质的释放^[26]。一项针对65~75岁老年MIE的研究表明, 术中开始使用硬膜外镇痛相比术后开始使用更能减少MIE患者术后S100 β (一种蛋白质, 提示急性脑损伤, 与神经炎症相关)的释放, 减少神经炎症反应^[25]。

1.5 住院时长

硬膜外镇痛对食管切除术患者住院时长的研究结果不一致。有研究认为硬膜外镇痛可以缩短住院时长^[27-28], 但这些研究包含其他快速康复的措施, 不能简单认定为硬膜外镇痛对住院时长的影响。单独研究硬膜外镇痛对住院时长影响的研究发现, 硬膜外镇痛可以缩短住院时长^[29], 但另一些研究表明硬膜外镇痛对住院时长没有明显影响^[23, 30]。由于住院时长多作为次要结局指标, 因此, 硬膜外镇痛对MIE患者住院时长的影响还需要进一步研究。

1.6 远期生存率

目前暂无硬膜外镇痛与MIE患者远期生存率相关性的研究。既往少量关于开放食管切除术的研究, 结果不太一致。有研究(倾向评分匹配后每组178例)表明硬膜外镇痛与静脉镇痛患者的3年总生存率无差别, 分别为70.8%和67.6%^[30]。一项包含153例(硬膜外镇痛118例, 静脉镇痛35例)开放食管切除术患者的回顾性队列研究显示, 硬膜外镇痛与静脉镇痛患者在癌症复发率(27% vs. 23%)、1年死亡率(11% vs. 14%)以及5年生存率(28% vs. 29%)方面没有明显差异^[31]。但一项包含1921例(硬膜外

镇痛1169例,非硬膜外镇痛752例)患者的回顾性研究显示,硬膜外镇痛与5年生存率的提高相关[33.5% vs. 26.5%, $RR=0.81(95\%CI: 0.70 \sim 0.93)$],在亚组分析中,这种优势仍然存在[$RR=0.81(95\%CI: 0.67 \sim 0.96)$]^[32]。但前两个研究样本量相对较小,所有研究均为回顾性队列研究,因此,硬膜外镇痛对MIE患者的远期生存率的影响还需要前瞻性研究进一步证实。

2 硬膜外穿刺间隙的选择

MIE通常包括胸腔镜和腹腔镜甚至颈部三部分切口,胸腔部分一般涉及第4~9肋间隙,腹腔部分涉及第6~10肋间神经支配区域。因此,胸4~10(T4~T10)的阻滞平面可以覆盖MIE疼痛。MIE术后硬膜外置管的穿刺点从T4~T10不等,大多获得了良好的镇痛效果^[16, 19, 25, 29],只有一项包含108例机器人辅助(McKeown)MIE患者的研究提出在T4~T9硬膜外置管(55%的患者接受T6~T7硬膜外置管)患者中近50%出现阻滞不全(未达到双侧T4~T9平面阻滞)^[33]。但该研究只记录了部分患者硬膜外阻滞平面[术后第1~4天分别记录了65例(66%)、72例(78%)、69例(84%)和46例(81%)]。尽管有50%的患者硬膜外阻滞平面未完全达到T4~T9,但与无硬膜外镇痛组相比,术后吗啡用量明显减少。一项关于63例McKeown食管切除术患者硬膜外置管位置对术后镇痛效果影响的回顾性研究^[34],患者硬膜外置管位置为T4~T10,将置管位置分为T6/T7以上、T7/T8、T8/T9以下。结果发现T7/T8硬膜外置管术后镇痛效果更好,胸腔镜/腹腔镜辅助亚组分析中,T8/T9以下硬膜外置管术后疼痛明显增加。但该研究样本量较小,包括4种手术方式,混杂因素较多。由于低位胸段硬膜外给药后药液更多地向头端扩散,加上硬膜外向上置管3~5 cm,且胸段神经根是从对应椎体的下缘穿出,因此硬膜外穿刺点需要比目标阻滞区域的中心低才能达到理想的阻滞平面。有研究表明以T10/T11为主要穿刺间隙,置管深度3~5 cm,导管尖端大多在T9~T10之间,头端扩散平面约5个节段,尾端扩散平面约2.6个节段^[35]。笔者团队术后随访发现,对于MIE后静脉镇痛患者,无论是微创Ivor Lewis、McKeown或者纵隔镜联合腹腔镜,大部分患者术后咳嗽时最痛部位是上腹部切口,约T6~T8神经支配区域,建议微创食管切除术硬膜外穿刺水平为T8~T10。

3 硬膜外镇痛药物的选择

目前硬膜外使用的镇痛药物主要为局麻药和阿片类药物。硬膜外阿片类药物通过减少脊髓背角神经元的神

经递质释放和超极化膜来发挥镇痛效果。硬膜外局麻药通过阻断神经细胞膜上的钠通道,抑制神经冲动的传递而发挥镇痛作用。临床研究表明,单次硬膜外吗啡的镇痛效果较硬膜外罗哌卡因联合舒芬太尼效果差^[36]。当局麻药与阿片类药物合用时,镇痛效果更好,还可以减少两种药物的用量及相关不良反应。因此临床上最常用的硬膜外镇痛药为局麻药联合脂溶性阿片类药物(如舒芬太尼、芬太尼)。常用0.15%~0.2%罗哌卡因或0.125%~0.25%布比卡因,联合舒芬太尼0.3~0.5 $\mu\text{g/mL}$ 或芬太尼2~5 $\mu\text{g/mL}$,给药速度2~8 mL/h^[19, 25, 29]。

4 硬膜外镇痛的不良反应

4.1 低血压

2024年的一项随机对照试验(RCT)发现,MIE硬膜外镇痛患者术后第1天血管加压药的使用率是38.3%,而持续椎旁阻滞组为13.3%^[19]。但不同研究可能由于低血压定义不同或硬膜外穿刺点及用药不同而呈现出差异。2023年一项RCT发现硬膜外镇痛与椎旁阻滞患者术后低血压发生率无差异(5.4% vs. 3.6%)^[16]。日本一项大样本回顾性研究显示,硬膜外镇痛与非硬膜外镇痛患者术后3 d内血管加压药使用率有差异,但差异较小(44.1% vs. 41.8%)^[9]。也有小样本研究未检测到差异^[18]。硬膜外镇痛后低血压的发生可能与局麻药的交感神经阻滞作用相关:外周血管扩张,外周阻力下降,回心血量减少。加上围术期限制性补液策略,术后容量相对不足,机体需要一定时间的调节与代偿,这与文献报道术后低血压主要发生在术后第1天相吻合^[37]。有预测模型指出术后低血压的危险因素包括年龄、ASA分级、术前使用血管紧张素转换酶抑制剂或血管紧张素II受体拮抗剂、慢性动脉高血压和夜间非下降型血压^[38]。因此,对于术后低血压高危患者(如年龄>75岁),可选择其他对血压影响较小的镇痛方式,避免低血压相关并发症。

目前术后低血压的处理包括补液与血管加压药的使用,但最重要的是预防低血压发生。低血压的严重程度与交感神经阻滞范围有关。硬膜外穿刺点越高,越容易阻滞心脏交感神经(T1~T4),抑制反射性心率增快,减少心输出量,增加低血压发生率。因此临床中选择穿刺点应平衡镇痛效果与低血压。低血压除了与穿刺点相关,还与局麻药的容量及浓度、注药速度、年龄等相关。因此老年患者硬膜外药物浓度、速度、剂量均应降低。

4.2 吻合口瘘

食管吻合口漏是食管切除术后的严重并发症,硬膜外镇痛对于吻合口瘘的发生具有两面性。一方面,硬膜

外镇痛可减少吻合口瘘^[7,9],这可能与管状胃微循环改善相关^[39]。但另一方面,硬膜外镇痛后低血压亦会减少管状胃灌注。目前,血管加压药对吻合口灌注的影响尚不明确。有研究表明血管加压药可以改善硬膜外镇痛后低血压导致的吻合口灌注减少^[40]。在临床实践中,推荐术中目标导向液体治疗和术后“近乎零”的液体平衡液体管理策略^[41],并使用血管加压药来维持低血压患者术中和术后吻合口的灌注^[3],这可能比低血压或容量超负荷更有利,能减少吻合口瘘的发生率。

4.3 其他

硬膜外镇痛会增加瘙痒、尿潴留、运动阻滞。瘙痒主要与硬膜外使用阿片类药物有关,硬膜外单独使用阿片类药物比静脉注射阿片类药物的瘙痒发生率更高,但大部分瘙痒无须特殊处理。尿潴留增加和运动阻滞主要发生在腰段硬膜外阻滞,胸段硬膜外阻滞很少引起运动阻滞和尿潴留。硬膜外穿刺置管对麻醉医生技术要求高,有硬脊膜穿破、脊髓神经损伤、硬膜外感染等风险,但发生率很低,随着超声技术在临床的广泛应用^[42],胸段硬膜外穿刺的成功率明显提高。硬膜外镇痛的术后管理相对更繁琐,需要更加关注术后血压和神经系统并发症,消耗更多的人力资源。

5 总结与展望

本综述系统回顾了硬膜外镇痛在MIE中的应用现状。现有证据表明,相较于其他镇痛方式,硬膜外镇痛在提供更优镇痛效果的同时,还能有效减轻患者的应激反应,降低肺部并发症的发生率,促进患者早期下床及快速康复,进而提高患者生活质量,并减少术后急性肾损伤的风险^[43]。然而,当前的研究仍存在一定的局限性,如研究数量相对较少,且多为单中心小样本研究,对于术后康复质量、应激反应、住院时长及远期生存率等方面的证据尚不充分。

尽管硬膜外镇痛在术后展现出了确切的镇痛效果,但术后低血压和穿刺失败仍然是需要高度重视的问题。为了降低低血压的发生率,选择满足镇痛需求的最低硬膜外穿刺节段、最低药物浓度和剂量、降低给药流速^[44]显得尤为重要。因此,未来应致力于开展临床研究,探索针对MIE术后镇痛的最佳硬膜外穿刺节段、药物浓度剂量、给药流速,为临床广泛应用提供科学依据。

人工智能在麻醉学领域的研究已较为广泛^[45],未来有望建立术后疼痛及低血压预测模型。对患者进行分层管理:对术后疼痛严重且非低血压高风险的人群,实施硬膜外镇痛;对预计术后疼痛轻微或低血压高风险的人群,

采用联合神经阻滞的多模式镇痛方案,实现更加个体化的镇痛治疗。此外,将患者的疼痛、不良反应、血压等数据导入智能镇痛管理系统,也是未来发展的一个重要方向。该系统能够根据患者的实时数据自动调整镇痛泵的用量,不仅节约了人力成本,更实现了精准术后镇痛,有望显著改善患者的预后。另外,胸段硬膜外穿刺失败率高是影响硬膜外镇痛应用的另一个难题,其失败率甚至高达30%。超声引导技术有望提高穿刺成功率,但目前相关研究和报道仍较少。因此,未来应进一步加强这方面的研究,探索影响穿刺成功率的因素,并优化穿刺技术,以降低穿刺失败率。

* * *

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