

全膝关节置换术后镇痛治疗进展

曾昭荣¹, 李吉辉¹, 徐忠世^{2*}

¹暨南大学第二临床医学院, 深圳市人民医院骨关节外科, 广东 深圳

²深圳市人民医院(南方科技大学第一附属医院, 暨南大学第二临床医学院)骨关节外科, 广东 深圳

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摘要

全膝关节置换术(TKA)目前已取得显著进步, 但其术后疼痛的控制仍是一个较大的挑战。常见的阿片类药物并不总是能有效缓解疼痛且常伴不良反应。随着手术技术和药理学的进步, 运用药物镇痛、局部浸润麻醉、外周神经阻滞以及非药物手段的联合镇痛模式才是TKA后疼痛的有效管理方案。本文就总结目前全膝关节置换手术围手术期疼痛控制的研究, 介绍相关镇痛方式以减少或替代阿片类药物的使用并评估其有效性。

关键词

全膝关节置换术, 术后镇痛, 局部浸润麻醉, 外周神经阻滞

Advances in Analgesic Therapy after Total Knee Arthroplasty

Zhaorong Zeng¹, Jihui Li¹, Zhongshi Xu^{2*}

¹The Second Clinical Medical College of Jinan University, Department of Orthopedics, Shenzhen People's Hospital, Shenzhen Guangdong

²Department of Orthopedics, Shenzhen People's Hospital (The First Affiliated Hospital of Southern University of Science and Technology, The Second Clinical Medical College of Jinan University), Shenzhen Guangdong

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Abstract

Total knee arthroplasty (TKA) has made significant progress, but the control of postoperative pain remains a major challenge. Common opioid drugs do not always effectively relieve pain and are often accompanied by adverse reactions. With the advancement of surgical techniques and pharmacology,

*通讯作者。

a combined analgesic mode using drug analgesia, local infiltration anesthesia, peripheral nerve block, and non-drug methods is the effective management plan for pain after TKA. This article summarizes the current research on pain control during the perioperative period of total knee arthroplasty, introduces relevant analgesic methods to reduce or replace the use of opioid drugs, and evaluates their effectiveness.

Keywords

Total Knee Arthroplasty, Postoperative Analgesia, Local Infiltration Anesthesia, Peripheral Nerve Block

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1. 背景

相关流行病学显示,随着全球人口老龄化加剧,全膝关节置换术(TKA)预计将在未来25年内大幅增加[1][2]。相关研究报告显示,超过60%接受TKA的患者在手术后会出现中度至重度疼痛[3]。TKA患者的术后疼痛导致了康复延迟、增加阿片类药物消耗量以及不良反应事件风险增高[4]同时也降低了患者的满意度[5]。近期一项大型荟萃分析显示,与无阿片类药物镇痛相比,阿片类药物处方并不能减轻出院后第一天的疼痛且会增加不良事件的发生风险[6]。因此我们应当应用其他非阿片类药物或者非药物手段来减少阿片类药物在TKA患者术后镇痛使用频率。

2. 材料与方

在中文数据库中国知网、以“全膝关节置换”“术后镇痛”“局部浸润麻醉”“外周神经阻滞”为关键词进行检索,在PubMed数据库中以“TKA”“Postoperative analgesia”“Local infiltration anesthesia”“peripheral nerve block”为关键词进行检索,检索时间为各数据库建立至2026年3月1日,优先选择具有高证据等级的近15年发表的文献。稿件标题和摘要由一位作者根据下述纳入和排除标准进行独立筛选,讨论所有纳入冲突,并就是否应纳入该文章达成共识。通过初步标题和摘要筛选的文章在全文筛选中遵循相同的审稿流程。全文筛选中纳入冲突的解决方式与标题和摘要筛选相同。文献纳入标准:① 随机对照试验;系统评价;② 术后镇痛、局部浸润麻醉、外周神经阻滞的文献;③ 相似研究内容,优先选择研究证据等级更高的文献。文献排除标准:① 重复发表、无法获取全文的文献;② 英文、中文以外语种的文献。

3. 全膝关节置换术后疼痛的潜在机制

TKA的术后疼痛来源于中枢和外周机制。外周来源包含骨与膝关节的软组织损伤、手术后的局部组织缺血、创口部位神经的直接损伤以及炎症介质的释放、对伤害感受器的刺激。中枢来源包括脊髓中N-甲基-D-天冬氨酸(NMDA)受体的激活,其激活后在皮质水平起作用以启动或调节疼痛通路[7]。全膝关节置换术后疼痛是一个复杂的过程。其术后疼痛与各种机械等损伤有关。这些损伤使得炎症介质(如缓激肽、5-羟色胺、肾上腺素、细胞因子)从受损组织中释放出来,一方面,它们可以直接刺激伤害感受器。另一方面它们还可以降低伤害感受器的激活阈值,从而减少引起激活所需的刺激[8]。这就使得原本无痛的机械刺激(如术后轻微活动)即可诱发剧烈疼痛。

4. 系统性药物

4.1. 对乙酰氨基酚

乙酰氨基酚是一种广泛应用于围手术期疼痛控制的镇痛药。它具有疗效可靠、副作用小以及经济负担小的特点而得到广泛应用[9]。其作用于中枢并抑制大脑环氧合酶,但具体机制目前不详。对乙酰氨基酚的通常使用形式分为口服和静脉注射。Politi 等发现,静脉注射和口服对乙酰氨基酚的镇痛效果无显著差异且口服相较于静脉注射的价格更为低廉[10]。目前的临床建议主要是对不能耐受口服制剂的患者静脉注射对乙酰氨基酚。同时对于对乙酰氨基酚在术前镇痛的应用,目前仍需进一步探索。在 Wang 等的随机对照试验中,其并未减少术后吗啡使用量或改善镇痛效果[11]。

4.2. 非甾体类抗炎药

非甾体抗炎药(如布洛芬、酮咯酸)通过抑制环氧合酶的活性减少前列腺素生成,从而降低伤害性感受器的激活与敏化程度,进而缓解炎性疼痛。非选择性甾体抗炎药的重要不良反应包括血小板功能异常与出血、胃溃疡、肾功能损伤,以及在过敏体质哮喘患者中诱发支气管痉挛。而选择性环氧合酶(cox)-2 抑制剂(如帕瑞昔布,美洛昔康,塞来昔布)靶向作用于该酶的诱导型亚型,使得胃肠道出血的发生风险更低[8]。在 Fillingham 等发现,口服非选择性甾体抗炎药或经静脉注射(如酮咯酸)可减轻 TKA 术后疼痛、降低术后阿片类药物使用量,并且术前静脉注射酮咯酸减少阿片类药物用量优于术后[12]。

在 TKA 术后的多模式镇痛中,非甾体类抗炎药已成为基石。而选择性环氧合酶(cox)-2 抑制剂(如帕瑞昔布,美洛昔康,塞来昔布)常因其副作用更少而作为首选药。一些研究表明 TKA 术后早期使用选择性 cox-2 抑制剂比安慰剂更有效,其降低了术后患者的疼痛评分、吗啡使用量且术后前 48 小时的出血风险更小[13] [14]。另一项大样本荟萃分析显示选择性 cox-2 抑制剂可显著降低静息或卧床时的疼痛评分,减少 TKA 术后 3 天内吗啡使用量,减少恶心、呕吐和发热的发生率[15]。在常见的选择性环氧合酶(cox)-2 抑制剂中,相较于塞来昔布,美洛昔康对于抑制 cox-2 途径的选择性更低且高剂量时还会部分抑制 cox-1。然而,在最近的研究中,在 TKA 术后,相较于塞来昔布,高剂量(15 mg/d)美洛昔康用于全膝关节置换术多模式镇痛时,因 COX-1 抑制导致的胃肠道和伤口并发症风险未显著增加,且成本更低[16]。

4.3. 神经调节类药物(加巴喷丁,普瑞巴林,度洛西汀)

抗抑郁类药物(如加巴喷丁,普瑞巴林,度洛西汀)主要用于抗抑郁,癫痫发作。近期的一些研究表明,其也可用于 TKA 的术后镇痛使用。加巴喷丁类的药物(加巴喷丁、普瑞巴林)通过与电压门控钙通道的 $\alpha_2\text{-}\delta$ 亚单位结合,从而抑制兴奋性神经递质的释放,进而抑制疼痛传递[8]。关于加巴喷丁类药物用于 TKA 术后镇痛目前尚有争议。既往一些研究表明,术前应用加巴喷丁可以改善 TKA 患者的术后疼痛,减少阿片类药物的使用量,改善患者的心理状况,降低术后恶心发生率[17] [18]。然而,近期的一些研究发现,围手术期使用加巴喷丁类药物无明显的 TKA 术后镇痛作用,并且未能减少阿片类药物的使用[18] [19]。且增加了术后不良事件的发生率,主要包括术后镇静作用[18]、术后肺部并发症(如呼吸抑制) [20]等。这可能与患者人群的差异或用药时机等有关。尽管加巴喷丁类药物存在上述的使用风险,但它仍可使部分患者受益;同时,对于一些高风险人群(如老年人),其使用应当慎重。度洛西汀是一种 5-羟色胺-去甲肾上腺素再摄取抑制剂[21]。5-羟色胺和去甲肾上腺素可调节中枢神经系统,影响下行抑制性疼痛通路。YaDeau 等的随机对照试验表明,度洛西汀可以减少全膝关节置换术后患者的阿片类药物使用量,提高患者的满意度[21]。但值得注意的是, Pinsornsak 等的研究表明,低剂量的度洛西汀可以减少 TKA 术后阿片类药物的使用量,但并不能明显减轻休息或行走时的疼痛[22]。度洛西汀的最佳治疗剂量目前还需大规

模的对照实验进一步研究。

4.4. 糖皮质激素

糖皮质激素因其有效的抗炎特性而得到广泛使用。它可以降低关节纤维化风险[23]，减轻 TKA 术后的疼痛，改善恶心呕吐，减少阿片类药物的用量[24]。尽管糖皮质激素有着这些益处，其也伴随着一些潜在的风险(如增加术后感染风险、提高术后血糖管理难度等)。Yang 等的荟萃分析表明，在 TKA 术前 3 个月向关节腔内注射糖皮质激素会增加术后的感染风险[25]。然而，Jørgensen 等的涉及 3972 例初次接受关节置换术患者的大型前瞻性队列研究发现，术前接受全身性甲泼尼龙治疗的患者与未接受甲泼尼龙治疗的患者之间的感染率并无显著差异[26]。同时，另外一项回顾性研究也表明，TKA 术前使用糖皮质激素并未对其血糖水平、血糖波动情况及感染发生率产生明显不良影响且可以缩短住院时间[27]。这些表明，尽管糖皮质激素存在潜在的风险，但在适当情况下使用并不会增加感染风险和术后血糖管理难度。目前文献上常见的糖皮质激素给药方式分为静脉给药和关节局部给药。这两种方式均可促进患者 TKA 术后的康复[28] [29]。相较于关节局部给药，静脉给药的术后呕吐发生率更低[28]，抗炎抗血栓栓塞效果更优[29]。而关节局部给药的术后镇痛效果更佳[29]。

4.5. N-甲基-D-天冬氨酸受体拮抗剂(NMDA 受体拮抗剂)

NMDA 受体拮抗剂(如氯胺酮、S-氯胺酮)通过抑制伤害性感受通路的致敏化，并阻止与阿片类药物相关的促伤害性感受系统激活，从而缓解 TKA 术后的疼痛并减少阿片类药物耐受的产生[30]。近期的一些研究表明，NMDA 受体拮抗剂可以减少阿片类药物的使用，有效减轻患者的术后疼痛，降低恶心呕吐的发生率[30] [31]。同时，Li 等的随机对照实验表明氯胺酮可有效降低全膝关节置换术后反跳性疼痛发生的风险，并延迟其发作[32]。Weinstein 等对 TKA 术中使用氯胺酮所引起的术后谵妄风险进行了评估。有学者回顾性研究了 41,766 例 TKA 患者，发现术中和术后输注氯胺酮会导致术后谵妄的风险增高[33]。然而，Zhu 等的随机对照实验表明，氯胺酮可以降低术后谵妄的发生率，但会提高幻觉、头晕和噩梦的发生率[34]。因此，氯胺酮虽具有镇痛效果，且能降低阿片类药物引起恶心呕吐的发生率。但其使用时间，最佳剂量仍需进一步的研究来确定。

5. 局部浸润麻醉

得益于其操作简便、性价比高、镇痛效果可靠且副作用轻微的特点，膝关节周围局部浸润麻醉广泛用于 TKA 术后的镇痛。其能够有效的减轻术后的疼痛与阿片类药物的使用[35]。局部麻醉药(如布比卡因、罗哌卡因)的作用机制是通过与神经元上的钠通道发生可逆性结合，阻止去极化过程中钠离子内流，从而抑制伤害性感受器上动作电位的传导[8]。但这些局部麻醉药的镇痛持续时间通常不超过 12~18 h [36]。往往需要添加佐剂以加强镇痛效果或者进一步减少阿片类药物的用量。目前较为常见的佐剂有糖皮质激素(如地塞米松，曲安奈德) [29] [37]、非甾体抗炎药(如酮咯酸) [38]、阿片类药物(如吗啡) [39]、肾上腺素 [40]等。同时，应用佐剂时应当考虑患者的情况。一项回顾性研究表明，对患有慢性肾脏疾病的患者而言，在膝关节周围局部浸润麻醉中添加酮咯酸会增加其急性肾损伤的风险[41]。Zhao 的一项研究尝试将硫酸镁用于局部浸润麻醉镇痛中，发现其可延长局部浸润麻醉的术后镇痛时间、减少阿片类药物的消耗[36]。Zhao 等的研究表明，将右美托咪定作为佐剂用于局部浸润麻醉可增强和延长 TKA 术后早期的镇痛效果、减少阿片类药物的使用并降低术后炎症标志物水平[42]。此外，布比卡因脂质体作为一种能够长时间缓慢释放布比卡因的新型制剂，其 DepoFoam 多囊脂质体递送系统能延长药物作用时间[43]。虽然 Mont 等的研究中发现布比卡因脂质体可以减轻患者术后疼痛及术后阿片类药物的使用[44]，但 Danoff 等的研究却

表现出相反的结果[45],因此布比卡因脂质体仍需进一步研究目前关于如何延长局部浸润麻醉的镇痛时间、加强术后镇痛效果的研究仍在探索中。同时,目前学界对于局部浸润镇痛的最佳制剂配方、注射部位及用药剂量还未形成统一共识,上述的局麻药及佐剂的使用更多依赖于外科医生的经验决定。因此,临床上急需标准化的指南来优化局部浸润麻醉镇痛的临床方案。

6. 外周神经阻滞

6.1. 股神经阻滞(Femoral Nerve Block, FNB)

股神经阻滞(Femoral Nerve Block, FNB)作为TKA术后的常见镇痛方法。该技术通过将局麻药注射至股神经附近从而阻断相应的感觉分支。尽管大多数研究证实股神经阻滞可以有效缓解TKA术后的疼痛[46],但其阻断股神经也同时减少股四头肌的收缩,从而削弱股四头肌的力量,影响早期的康复锻炼[47]。相较于单次注射的股神经阻滞,通过导管的持续性股神经阻滞有着更好的镇痛效果[48]。但持续性股神经阻滞可能会导致长时间的运动障碍,从而对股四头肌的力量产生负面影响并延长康复过程。

6.2. 内收肌管阻滞(Adductor Canal Block, ACB)

内收肌管阻滞的目标主要是股神经的远端分支(即隐神经和股内侧神经),从而在镇痛的同时保留股四头肌的运动功能。近期的研究表明,ACB可以提供FNB相似的镇痛效果且患者可获得更好的股四头肌力量,进而加快术后功能恢复,减少住院时间[49][50]。同时,一项荟萃分析表明,相较于单次内收肌管阻滞,持续性内收肌管阻滞的镇痛效果更优,但并未发现其在较少呕吐和恶心并发症以及住院时间方面优于单次内收肌管阻滞[51]。

6.3. 腘动脉与膝关节后囊间隙阻滞(Infiltration between the Popliteal Artery and Capsule of the Knee, IPACK)

由于ACB不阻断后方及外侧的感觉神经,许多TKA术后的患者在接受ACB治疗后仍会出现严重的膝关节后方的疼痛,而腘动脉与膝关节后囊间隙阻滞(IPACK)能够可以选择性阻滞膝关节后方的末梢感觉神经为膝后部提供有效的镇痛。近期研究表明,在TKA术后的镇痛方案中,相较于单纯ACB,ACB与IPACK联合使用在减轻疼痛、减少吗啡消耗量、改善功能能力方面效果更优[52][53]。此外,一些研究表明,在TKA术后,相较于单独应用局部浸润麻醉,联合应用局部浸润麻醉和IPACK的镇痛效果更优且术后使用吗啡类药物消耗量更少[54]。

7. 非药物治疗(冷疗, 针灸, 止血带管理)

除药物治疗外,越来越多的非药物治疗方法(如:神经射频消融、经皮神经电刺激、冷敷疗法、止血带管理等)开始用于TKA的镇痛当中。例如:膝神经射频消融术(GNRFA)通过将疼痛信号从膝盖传输到大脑的膝神经的热凝固从而达到镇痛的效果。Stake等研究发现,术前GNRFA可以降低接受TKA的患者术后长时间使用阿片类药物的比例且不会增加术后并发症的风险[55]。经皮神经电刺激(TENS)通过在皮肤表面施加脉冲电流,激活深部神经上阿片受体的内源性抑制通路。一项荟萃分析表明在TKA后的急性期(48小时内),TENS降低了术后的疼痛评分(VAS评分)和总体疼痛。而另外一项随机对照试验表明,与假TENS相比,TENS对TKA后住院期间的疼痛缓解效果没有差别[56]。这表明TENS对于缓解TKA后的急性期疼痛有着良好的效果,但对于慢性期的疼痛缓解效果较差。冷敷疗法通过收缩血管减轻局部炎症和肿胀从而达到减轻疼痛的效果。一项对照实验发现,冷敷疗法能够在TKA术后第一周内有效减轻疼痛和减少阿片类药物的消耗[57]。除此之外,相关研究表明,减少手术期间的止血带使用时长可以有效

降低 TKA 后的疼痛、加快术后的功能恢复[58]。

8. 总结和展望

TKA 的发生率在全球人口老龄化的背景下预计逐渐增加。高效的疼痛管理是 TKA 中的关键一环，它与病人术后的功能恢复与病人满意度息息相关。以药物为基础的多模式镇痛模式正成为当前 TKA 术后的理想镇痛模式，它不仅可以减少阿片类药物的使用，同时也能加速病人的术后恢复，提高病人满意度。通过术前和术后联合使用非甾体类抗炎药、对乙酰氨基酚、抗抑郁类药物(如：加巴喷丁)、糖皮质激素、NMDA 受体拮抗剂(如氯胺酮)等药可以有效地控制术后疼痛。除此之外，神经阻滞、局部浸润麻醉、冷疗等非药物治疗也同样在术后疼痛管理中占据重要地位，相较于神经阻滞，局部浸润麻醉操作更加简单且成本更低可能是 TKA 术后镇痛的更优选择，但标准化方案的缺失，是当前局部浸润麻醉镇痛所面临的困境。尽管多模式镇痛模式已广泛应用于 TKA 术后，但目前仍未形成统一的规范，各医疗机构间实践过程中差异巨大。未来仍需进一步的研究来探索多模式镇痛的标准化方案，例如针对特定人群(如高疼痛敏感性患者)优化镇痛方案的研究。

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