

阿司匹林预防膝关节置换术后静脉血栓形成的研究进展

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摘 要

接受膝关节置换术的患者发生静脉血栓栓塞(VTE, venous thromboembolism)的风险很高, 发病率约为0.6%~1.5%。考虑到这些手术的数量很大, 在美国每年大约有100万例手术, 静脉血栓栓塞的发生是一个很大的数量。尽管膝关节置换术后深静脉血栓形成(DVT, deep venous thrombosis)的发生率略有下降, 但肺栓塞(PE, pulmonary embolism)的发生率没有下降。在这段时间里, 人们已经对个体患者的药物预防VTE的最佳选择进行了大量研究, 目的是降低静脉血栓栓塞的发生率, 同时将出血等副作用降至最低。最近, 阿司匹林因其与其他药物相似的疗效和良好的安全性而成为关节置换术患者的一种很有前途的预防性药物。然而, 到目前为止, 还没有证据清楚地表明任何给定的预防性药物的优越性。因此, 本综述讨论: 1) 膝关节置换术后VTE的发生率和趋势; 2) 提供有关使用阿司匹林药物预防VTE的最新进展。

关键词

关节置换, 静脉血栓栓塞, 深静脉血栓, 肺栓塞, 外科并发症

Research Progress of Aspirin in Preventing Venous Thrombosis after Knee Arthroplasty

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Abstract

Patients undergoing knee arthroplasty have a high risk of venous thromboembolism, with an incidence of about 0.6%~1.5%. Considering the large number of these operations, there are about 1

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million operations in the United States each year, and the incidence of venous thromboembolism is a large number. Although the incidence of deep venous thrombosis decreased slightly after knee arthroplasty, the incidence of pulmonary embolism did not decrease. During this period, a large number of studies have been carried out on the best drug for the prevention of venous thromboembolism for individual patients, in order to reduce the occurrence of venous thromboembolism and minimize side effects such as bleeding. Recently, aspirin has become a promising prophylactic drug for patients undergoing joint replacement because of its similar efficacy and safety to other drugs. So far, however, there is no clear evidence of the superiority of any given prophylactic drug. Therefore, this review discusses: 1) the incidence and trend of VTE after knee arthroplasty, and 2) provide the latest progress in the use of aspirin in the prevention of VTE.

Keywords

Joint Replacement, Venous Thromboembolism, Deep Venous Thrombosis, Pulmonary Embolism, Surgical Complications

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1. 引言

全膝关节置换术(TKA, total knee arthroplasty)是治疗终末期骨性关节炎的常见和有效的手术,在美国,每年大约有 100 万例手术,超过 700 多万人接受关节置换[1] [2] [3] [4] [5]。这些择期手术的并发症发生率很低,但主要并发症,如静脉血栓栓塞(VTE, venous thromboembolism),由于住院时间延长,病情加重或死亡,以及每次 15,000~30,000 美元的额外费用,可能会使人非常虚弱[6] [7] [8] [9]。与其他大手术相比,膝关节置换术中 VTE 的发生率较高,因此在这些手术中很大程度上被认为有必要对 VTE 进行药物预防[10]。鉴于 VTE 在膝关节置换术中的巨大风险,已在预防方面作出相当大的努力,我们预期 VTE 的发生率应会随着时间的推移而下降。了解静脉血栓栓塞的发生率和趋势对于临床医生评估最近干预措施的整体成功和指导该领域的未来研究非常重要。此外,考虑到现在有很多多模式预防和药物预防 VTE 的手段,所以对这一领域的当代研究有一个简明的指南是很重要的。这篇综述评估了膝关节置换术后静脉血栓栓塞的发生率,并提供了药物预防 VTE 的最新进展,重点是阿司匹林的使用。

2. 静脉血栓栓塞症概述

静脉血栓栓塞包括深静脉血栓形成(DVT)和肺栓塞(PE)。深静脉血栓的典型表现为患肢疼痛、肿胀、发热或红斑,最常发生在下肢,但也可发生在上肢[11] [12]。深静脉血栓可进展为肺栓塞,若静脉血栓从起始处分离并滞留在肺血管系统中,可能是致命的。

关节置换术中静脉血栓栓塞的病理生理学: VTE 的危险因素由 Virchow 三联症描述: 静脉淤滞、血管内皮损伤和血液高凝状态。VTE 的发展通常需要两个或两个以上的因素[13] [14]。静脉停滞发生在手术期间,因为使用止血带(在 TKA 中经常使用)和术中制动,以及手术后,当患者在术后阶段活动较少时都会发生静脉停滞。这尤其可能发生在膝关节置换术后,此时承重关节已经重建。长时间不动是 VTE 发生的危险因素[15]。通过加强四肢的血液流动,比如应用弹力袜,可将膝关节置换术后 DVT 的发生率降低约 57% [16],并且继续在家使用时可进一步降低风险[17]。也有证据表明,术前压迫髂总静脉会增加膝关节置换术后静脉血栓栓塞的风险,而且麻醉方式的选择可能会因为各种原因影响静脉血栓栓塞的发生

率[18] [19]。快速恢复计划和早期动员可缩短膝关节置换术(TKA)后的固定期。

在外科手术中,由于组织解剖和手术操作,内皮损伤是不可避免的,静脉损伤的程度与静脉血栓栓塞率之间存在相关性[20]。虽然不可避免,但通过适当的手术技术或微创技术可以将内皮损伤降至最低。

高凝状态。最后,手术中组织损伤引起的局部和全身炎症反应导致高凝状态。术后观察到血栓形成分子如 IL-6、C-反应蛋白(CRP)和肿瘤坏死因子- α (TNF- α)的升高[21] [22]。细胞损伤导致核酸和组蛋白的释放[23]。这些分子可共同触发组织因子(TF)和凝血酶的表达、形成中性粒细胞细胞外陷阱和激活血小板,随后启动凝血级联反应和血栓形成[23] [24] [25]。此外,一些患者可能容易发生血小板高反应性,进一步增加他们的风险[26]。血流淤滞可以通过增加损伤部位促血栓形成因子的浓度来促进高凝状态[27]。聚甲基丙烯酸甲酯(PMMA, polymethyl methacrylate)水泥的使用进一步加剧了骨科手术后的高凝状态,因为未反应的聚甲基丙烯酸甲酯单体可能会激活凝血[23]。因此,通过抑制凝血级联反应来预防静脉血栓栓塞的多模式预防和药物预防 VTE 的重要性是显而易见的。事实上,在没有药物预防的情况下,膝关节置换术后 DVT 的发生率被报道高达 50% [28]。

3. 膝关节置换术后静脉血栓栓塞率

3.1. 背景

人们很早就认识到,接受手术的患者 VTE 的风险很高,但直到 20 世纪 60 年代至 70 年代,药物预防 VTE 才被采用。当时,在接受大手术的患者中,死于静脉血栓栓塞的患者约占 1%,深静脉血栓发生率约为 20% [29] [30]。采用肝素预防 VTE 后,死亡率降至 1%以下,DVT 发生率降至 3.6% [29] [30]。

在膝关节置换术中,利用药物预防静脉血栓栓塞的措施与在其他大手术中同样有效。Morris 等人在膝关节置换术后使用肝素进行了一项随机试验,发现静脉造影筛查 DVT 的比率从 50%下降到 11% [28]。Pellegrini 等人回顾了 1984~1992 年间接受膝关节置换的患者,当时华法林或肝素是主要化学预防药物,发现 6 个月内有症状的 DVT 发生率为 1.2%,有症状的 PE 发生率为 0.4% [31]。Fender 等人在 1990 年发现,在接受膝关节置换术的患者中,因 PE 导致的死亡率为 0.19% [32]。从那时起,关节置换术后静脉血栓栓塞率的变化更加微妙,这使得将其变化与个体干预措施相关联变得更加困难。重要的是,随着静脉血栓栓塞率的下降,平衡各种预防性药物的益处和不良事件的风险已经成为一个越来越受关注的话题。已经有无数关于静脉血栓栓塞率和预防性药物的研究,从回顾性的分析到大型随机对照试验,方法各异。因此,我们将讨论最近评估 TKA 后的静脉血栓栓塞的发生率和化疗预防方法的文献,重点放在前瞻性、大型数据库或荟萃分析研究设计上,因为它们比回顾性综述相比具有更好的概括性。

3.2. 研究 VTE 的方法学差异

报告的静脉血栓栓塞发生率主要取决于如何定义、记录和研究结果。常规的术后 DVT 筛查会发现大量无症状病例,与有症状的比率相比,静脉血栓栓塞发生率被夸大了[31]。各项研究对术后不同时间发生静脉血栓栓塞进行了调查,通常报告院内、30 天或 90 天的比率。大的地区注册中心和医院数据库之间的静脉血栓栓塞率也存在不一致[33]。根据环境的不同,一些医院管理数据库检测 VTE 的敏感性较差[34] [35]。最后,研究可能存在差异,具体取决于它们是否由行业资助[36]。在比较关节置换术后不同地区甚至同一地区研究之间的静脉血栓栓塞发生率时,必须始终考虑这些因素。

3.3. 最近的文献

3.3.1. 初次髋关节置换术

全髋关节置换术(THA, total hip arthroplasty)的 VTE 发生率在过去二十年中保持相对稳定,尽管有证

据表明,在2011年之前,DVT率有所下降,但PE率却没有下降,Dua等人使用美国国家住院患者样本(NIS, National Inpatient Sample)显示,院内深静脉血栓形成的发生率从2001年的0.55%下降到2011年的0.24% [37]。Shahi等人研究了2002~2011年的同一数据库,发现THA后的院内静脉血栓栓塞率为0.59% (DVT 0.4%, PE 0.23%),并得出结论,在此期间,DVT的发生率有所下降,而不是PE [6]。Lieberman等人对1997年至2013年的随机对照试验进行了meta分析,发现THA后的PE发生率稳定在0.21% [38]。

2011年之前关于静脉血栓栓塞发病率的进一步研究在很大程度上证实了这些数字,尽管静脉血栓栓塞发病率存在区域差异,但还是能部分解释。Pedersen等人研究了1997~2011年间丹麦髋关节置换术的记录,发现90天静脉血栓栓塞率为1.3%,在此期间没有显著变化[39]。Lee等人在2010年使用韩国国民健康保险(NHI, National Health Insurance)索赔数据库,发现90天的静脉血栓栓塞率为3.9% (DVT 2.7%, PE 1.5%),高于其他研究,可能是因为化学预防率仅为37.3% [40]。Januel等人研究了2006~2010年间5个不同国家(加拿大、法国、新西兰、瑞士、美国加利福尼亚州)出院前的VTE发生率(取决于国家),发现该比率在0.16%~1.41% (DVT 0.07%~1.15%, PE 0.08%~0.46%)之间,差异很大[41]。这种差异可以部分地解释为各国住院时间的差异和超声波筛查率的不同。

其他研究报告了最近在2016年进行的手术的VTE率,但没有明确的证据表明其发生率有所下降。Warren等人(2020)在2008年至2016年期间研究了美国外科医师学会国家外科质量改进计划(NSQIP, National Surgical Quality Improvement Program)数据库,发现平均30天静脉血栓栓塞率为0.6% (DVT 0.4%, PE 0.3%) [9]。2008年的VTE率为0.7% (DVT 0.6%, PE 0.2%),2016年为0.6% (DVT 0.4%, PE 0.3%),但经多因素Logistic回归分析,随时间变化没有显著差异。Grosso等人也研究了NSQIP数据库,发现2006~2016年间的DVT率为0.41%,在此期间没有变化[42]。Fuji等人使用了2008年至2013年间日本患者的数据库,发现总体静脉血栓栓塞率为0.9% (DVT 0.9%, PE 0.2%) [43]。Zeng等人研究了2013~2016年间亚洲的78家医院,发现院内DVT发生率为0.21% [44]。

3.3.2. 髋关节翻修术

与初次THA相比,接受翻修手术的患者通常具有更高的静脉血栓栓塞风险。Warren等人于2019年研究了2008~2016年间在NSQIP数据库中接受THA翻修的患者,发现总体VTE率为1.0% (DVT 0.7%, PE 0.4%),在研究期间无显著变化[8]。这与同一时间段内同一数据库中初次THA的VTE率为0.6%进行了比较[9]。Courtney等人在2011~2014年间查询了NSQIP数据库,发现翻修手术的DVT未调整为风险略高(翻修为0.6%,而初次置换为0.4%),但在控制干扰因素后没有差异[45]。Shahi等人研究了2002~2011年的NIS,发现THA翻修后的院内静脉血栓栓塞率为1.36% (DVT 1.06%, PE 0.37%),在此期间没有显著下降[6]。

3.3.3. 初次膝关节置换术

TKA的血栓形成率比THA高,通常VTE的发生率略高[46]。然而,有证据表明,在过去二十年中,美国TKA后的DVT率有所下降,但PE率似乎保持稳定,Dua等人使用NIS表明,TKA后的DVT发生率在2011年从0.86%下降到0.45% [37]。Shahi等人研究了2002~2011年的NIS,发现院内静脉血栓栓塞率为1.03% (DVT 0.62%, PE 0.46%),并得出结论,在此期间,DVT的发生率有所下降,而不是PE [6]。

截至2016年对TKA的研究在很大程度上表明DVT发病率进一步下降。Sarpong等人使用2006~2016年间的NSQIP数据库显示,TKA后的30天DVT率为0.87%,从2006~2009年的1.5%下降到2014~2016年的0.79% [47]。Warren等人在2020年也使用了2008年至2016年的NSQIP数据库,他们发现30天VTE的总体率为1.4% (DVT率为0.9%, PE率为0.6%) [9]。VTE发生率从2008年的3.0% (DVT 2.2%, PE 1.0%)下降到2016年的1.4% (DVT 0.9%, PE 0.6%),这是一个显著的时间变化。这项研究的一个局限性是,

与 2016 年相比, 2008 年的 TKA 病例较少(26,681:58,978), 这可能是一个选择偏倚。

在美国, 尽管进行 TKA 治疗后, DVT 的发病率有所下降, 但 PE 的发病率似乎保持稳定。Cote 等人对 1995~2016 年间 TKA 后 PE 发生率的研究进行了荟萃分析, 结果显示, 在此期间, 平均发生率为 0.37%, 且无显著降低[48]。

在美国以外的地区, 报告的静脉血栓栓塞发病率变化更大, 没有明确的证据表明随着时间的推移而变化。Pedersen 等人研究了 1997~2011 年间丹麦膝关节置换术记录, 发现 90 天静脉血栓栓塞率为 1.5%, 在此期间没有显著变化[39]。Fuji 等人使用了 2008 年至 2013 年间日本患者的数据库, 发现总体静脉血栓栓塞率为 1.4% (DVT 1.3%, PE 0.2%), 与丹麦的研究一致[43]。Lee 等人在 2010 年使用韩国国民健康保险(NHI)索赔数据库显示, 90 天静脉血栓栓塞率为 3.8% (DVT 3.2%, PE 0.7%), 这可能显著高于其他研究, 因为化学预防率仅为 48.4% [40]。Zeng 等人研究了 2013~2016 年间亚洲的 78 家医院, 发现院内 DVT 发生率为 0.36%, 远低于其他研究的发病率[44]。

同时双侧 TKA 已被推荐作为双侧膝关节骨关节炎的治疗选择, 但由于并发症的风险高于单侧 TKA, 人们对此表示很担忧[49] [50]。事实上, Masrouha 等人发现, 2008~2015 年 NSQIP 数据库中同时进行双侧 TKA 后的 30 天静脉血栓栓塞发生率大于单侧 TKA (2.72% vs 1.45%), 但死亡率无显著差异[51]。

3.3.4. 膝关节翻修术

膝关节翻修术后的深静脉血栓形成率最近两年可能有所下降, 几乎没有证据表明与初次 TKA 相比, 静脉血栓栓塞发生率存在差异。Shahi 等人研究了 2002~2011 年的 NIS, 发现院内静脉血栓栓塞率为 1.17% (DVT 0.88%, PE 0.34%), 发现在此期间 DVT 的发生率有所下降, 但 PE 率没有下降[6]。在同一项研究中, 初次 TKA 的 VTE 率为 1.03%。Boylan 等人使用 2003~2012 年间的纽约州规划和研究合作系统数据库, 发现 TKA 翻修的 90 天静脉血栓栓塞率为 2.13% (DVT 1.66%, PE 0.63%), 与初次 TKA 相比, 比值为 0.87, 这表明 TKA 翻修实际上可以降低患者的风险[52]。Warren 等人于 2019 年研究了 2008~2016 年间在 NSQIP 数据库中接受 TKA 翻修的患者, 发现总体静脉血栓栓塞率为 1.2% (DVT 0.9%, PE 0.4%), 研究期间无显著变化[8]。而在同一数据库中, 同一时间段内 TKA 的 VTE 率为 1.4% [9]。

3.4. 膝关节和髌关节置换术的出血和死亡

迄今为止的证据表明, 在过去一到二十年中, 关节置换术后深静脉血栓形成的发生率略有下降。许多因素可能解释了这种下降, 但关键是要将 VTE 的发生率与出血率进行比较, 以确定我们是否只是简单地用当前的静脉血栓栓塞预防策略来权衡并发症的发生。一项随机对照试验的系统评价比较了 THA 或 TKA 术后使用低分子量肝素(LMWH, low molecular weight heparin)预防 VTE 和出血率与使用磺达肝癸钠、利伐沙班、达比加群或阿哌沙班在 THA 或 TKA 后 VTE 及出血的发生率[53]。这项研究发现 VTE 的总体发病率为 0.99%, 这与本研究中回顾性的研究报告的比率相似。术后出血率为 3.44%, 是静脉血栓栓塞出血率的三倍以上, 这表明预防静脉血栓栓塞和出血之间存在权衡的问题。骨科医生提出, 积极使用抗凝治疗预防静脉血栓栓塞可能会增加出血, 这可能导致伤口愈合延迟和感染风险增加。总体而言, 必须权衡出血风险增加与抗凝治疗静脉血栓栓塞的益处。

虽然静脉血栓栓塞在患者中有显著的发病率, 但重要的是要了解随着时间的推移, VTE 的减少是否与死亡率的降低相关。Xu 等人对 1950~2016 年报告的术后死亡率的研究进行了 THA 和 TKA 的汇总 meta 分析[54]。他们表明, 在 1980 年之前, 死亡率为 1.15%, 在 1996 年至 2000 年期间降至 0.67%。从 2001~2005 年、2006~2010 年和 2011 年之后, 死亡率继续分别下降到 0.44%、0.40%和 0.24%。他们进一步表明, 接受每种常见 VTE 预防药物的患者亚群以及未接受化学预防的患者的死亡率下降, 这表明这些药物以外的

因素在降低死亡率方面发挥作用。

与初次关节置换术相比,由于手术次数增加,翻修关节置换术的死亡率可能更高。利用 NSQIP 数据库,Warren 等人(2020 年)发现初次 THA 的总死亡率为 0.2%,初次 TKA 的总死亡率为 0.1% [9]。在同一数据库中,THA 翻修的死亡率为 0.7%,TKA 翻修的死亡率为 0.5%,高于初次手术死亡率,尽管尚未对这些数字进行统计学比较[8]。

4. 药物性静脉血栓栓塞预防

4.1. 指南

关节置换术后最常用的静脉血栓栓塞预防指南是美国胸科医师学会(ACCP, The American College of Chest Physicians)指南(2012 年) [55]和美国骨科医师学会(AAOS, American Academy of Orthopaedic Surgeons)指南(2011 年) [56]。ACCP 建议对 THA 和 TKA 进行药物预防,1B 级建议为对低分子量肝素、磺达肝癸钠、达比加群、阿哌沙班、利伐沙班、普通肝素、维生素 K 拮抗剂和阿司匹林至少使用 10~14 天,最多 35 天。他们建议使用低分子量肝素而不是其他药物(2C/2B 级推荐)。AAOS 建议对 THA 和 TKA 均使用药物预防,只要患者出血风险不高,但不推荐任何特定药物。总体而言,骨科医生必须平衡更强的药物制剂带来的不良事件风险增加与预防的益处,因为每个患者的静脉血栓栓塞的风险因素不同。

对现行指南的一个不足是,他们无法在个体患者层面提供建议。在全球范围内,医疗机构对指南的遵守情况相对较差,但一直在改善;有人认为,如果指南能够提供个体患者水平的建议,依从性可能进一步提高[57] [58]。

4.2. 药物预防模式

在 VTE 预防方面,阿司匹林的使用有增加的趋势。在 2014~2016 年的美国数据库中,48%的 THA 病例和 43%的 TKA 病例接受了由阿司匹林和/或间歇式气动压力系统联合使用在内的静脉血栓栓塞预防治疗,其余患者接受了其他一种药物[59]。在澳大利亚的一项调查中,阿司匹林以外的药物使用率从 2012 年的约 75%降至 2017 年的 40% [60]。在 2008~2012 年的韩国数据库中,THA 最常用的处方药物是 LMWH (34%),肝素(23%),阿司匹林(19%),华法林(14%)和新型口服抗凝剂(NOAC) (13%),TKA 是 LMWH (28%),NOAC (22%),阿司匹林(17%),华法林(10%)和肝素(9%) [61]。在 2012~2013 年的韩国人群中,仅有约 66%~75%的 THA 或 TKA 病例接受了药物预防[61] [62] [63]。尽管许多患者受益于化学预防治疗,但有限的证据表明,适当选择的亚洲患者在 TKA 后未经预防的 VTE 发生率可能较低[64] [65]。

4.3. 阿司匹林预防静脉血栓栓塞

阿司匹林在静脉血栓栓塞预防中的使用越来越多,越来越多的证据表明其有效性和安全性。Matharu 等人对 13 项阿司匹林预防静脉血栓栓塞的随机对照试验进行了 meta 分析,发现与其他药物治疗方案相比,相对风险为 1.12 (95%可信区间 0.79~1.62) [66]。与其他药物相比,阿司匹林的 DVT 或 PE 个体风险没有统计学意义差异。接受阿司匹林治疗的患者出现瘀伤和下肢水肿的风险较低,并且在出血、感染或死亡率方面没有差异。该 meta 分析中最大的试验由 Anderson 等人进行,在所有患者使用利伐沙班 5 天后使用阿司匹林[67]。另一项 meta 分析比较了阿司匹林和低分子量肝素,也发现 VTE、出血事件或死亡率没有统计学意义差异,但指出证据不足,需要进行更好的随机对照试验[68]。其他研究发现,使用阿司匹林预防静脉血栓栓塞与心脏相关病因而导致的死亡率降低相关[69]。回顾性研究表明,即使在高危静脉血栓栓塞病例中,例如同时进行双侧 TKA 或高危患者组,阿司匹林的效果也与其他药物相同或更有效[70] [71]。

适当剂量的阿司匹林是优化其使用的重要考虑因素。一项系统评价构建了一个广义线性混合模型，用于比较低剂量(<162 mg/d)与高剂量(>162 mg/d)阿司匹林，发现两种剂量在深静脉血栓形成、PE、90 天死亡率或大出血发生率方面无统计学意义差异[72]。近期大型回顾性综述支持这一发现，显示低剂量(81 mg)阿司匹林和高剂量(325 mg)阿司匹林在 THA 和 TKA 中具有相似的结局[73] [74]。

最后，已经对阿司匹林使用的变体和阿司匹林的其他益处进行了研究。一项关于阿司匹林联合鱼油的随机试验发现，该方案与利伐沙班在预防静脉血栓栓塞方面没有统计学意义差异，但出血事件发生率较低[75]。阿司匹林还可降低 THA 后异位骨化发生率[76]。

如前所述，迄今为止，阿司匹林的随机对照试验很少，并且进行的试验尚未使用阿司匹林作为独立的化学预防剂。目前正在进行一项试验来解决这些缺陷，包括一项在澳大利亚人群中进行的随机交叉试验，比较阿司匹林与低分子量肝素[77]，以及在美国进行的一项比较阿司匹林、华法林和利伐沙班的试验[78]。

4.4. 患者对用药方案的依从性

任何药物的疗效在很大程度上取决于患者出院后的依从性。尽管患者对关节置换术后服用抗血栓药物这件事很信任，但每天一次的药物，无论是口服还是注射，都比每天两次的药物具有更好的依从性[79] [80]。即便如此，患者对治疗方案的依从性普遍较差，因此有机会制定改善患者依从性的策略[81] [82] [83]，来提高患者的依从性。从这个角度来看，阿司匹林是一种理想的药物，因为它是一种口服药物，可以每天给药一次。

5. 讨论

在过去 20 年中，关节置换术后静脉血栓栓塞的发生率相对稳定，深静脉血栓形成的发生率可能略有下降。鉴于这些事件已经变得相对罕见，研究 VTE 的最常见方法是使用大型登记表或管理数据库。虽然这些数据源具有固有的缺点，但最重要的是它们对记录 VTE 很敏感。不同数据源之间 VTE 率的巨大差异可能代表区域差异，但也可能代表不同来源的不同敏感性。无论如何，似乎有共识认为，关节置换术后 VTE 的绝对发生率目前很低。

尽管对最佳药物预防以及减少静脉血栓栓塞的其他方法仍在继续研究，但静脉血栓栓塞的发生率已经很低，而且最近也没有明显的变化，这就提出了一个问题，即如何在不增加不良事件(如出血)风险的情况下，找到进一步降低静脉血栓栓塞发生率的最成功策略。鉴于术后出血率大约是静脉血栓栓塞出血率的三倍，我们必须谨慎使用抗凝剂进行静脉血栓栓塞预防。我们已经确定了两个主要领域：1) 开发更强的个性化预测模型，这可能有助于检测 VTE 风险较高的患者，并使临床医生能够构建一个最佳权衡个人风险和收益的预防性方案[84]；2) 如果我们能够得出结论，我们已经找到了一种有效和安全的药物，可以与其他 VTE 预防手段协同工作，那么进一步降低静脉血栓栓塞发病率的最高效策略是优化医疗机构和患者对这些方案的依从性。事实上，静脉血栓栓塞的根本病因分析表明，如果更好地遵守药物预防指南，是有一些 VTE 事件是可以避免的[85]。旨在提高依从性的干预措施将需要对个体患者和医疗工作者进行更多工作，但有可能将关节置换术后已经很低的静脉血栓栓塞发生率降到最低。

总体而言，对于接受关节置换治疗的低风险患者来说，阿司匹林可能是一种合适的一线预防药物，因为目前为止，有证据表明阿司匹林是安全有效的，并且是一种低成本药物。在过去十年中，使用阿司匹林预防静脉血栓栓塞已有丰富的经验，迄今为止的证据显示，在选择合适的患者中，其疗效与其他药物相似。重要的是，阿司匹林有可能成为一种更安全的药物，大出血事件更少。鉴于关节置换术后的静脉血栓栓塞发生率相对较低，在评估不同化学预防药物的适当性时，安全性是一个越来越重要的指标。最

近一项关于 THA 和 TKA 后使用阿司匹林的综述也得出结论, 对于选择合适的低风险患者, 在利伐沙班之后使用阿司匹林(如最近的一项随机试验[67]所示)可能是安全有效的[86]。

6. 结论

静脉血栓栓塞已成为关节置换术的相对较少见的并发症, 目前正在对最佳的化学预防药物和方案进行大量研究。最近, 关节置换术后的静脉血栓栓塞发生率基本保持稳定, 在过去一到二十年中, 关节置换术后深静脉血栓形成的发生率仅轻微下降, 但 PE 没有下降。与此同时, 随着越来越多的证据支持阿司匹林的安全性和有效性, 阿司匹林作为预防药物的使用有所增加。在特定患者中使用阿司匹林与较低的并发症发生率低有关, 并可能带来额外的益处, 例如降低心肌梗死的发生率。鉴于术后出血率超过静脉血栓栓塞, 因此找到一种有效的多模式方法(包括药物)以最大限度地降低出血风险非常重要。尽管迄今为止对阿司匹林的研究表明, 在特定患者中, 阿司匹林与更有效的抗凝血剂一样有效, 但仍需要通过随机对照试验严格确定其疗效和安全性。作为多模式预防策略的一部分, 仍有必要根据每个患者的个体需求选择静脉血栓栓塞预防措施, 而预测性决策工具可能会为这一过程提供价值。最后, 仍有机会提高患者对药物治疗方案的依从性和医疗工作者对静脉血栓栓塞预防指南的依从性。

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