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急性肺栓塞的腔内治疗研究进展

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摘　要

急性肺栓塞(pulmonary embolism, PE)是继心肌梗死和脑卒中后的第三大临床常见心血管疾病，甚至在全球也具有高临床致残率和致死率。总结过去几十年的治疗经验，PE的治疗已经取得了重大进展，尤其是血管腔内治疗方法。但是，目前关于血管腔内治疗PE的安全性和有效性缺乏I级证据支持，使得具有前景的血管腔内治疗依然存在争议。本文旨在总结归纳近些年来关于急性PE血管腔内治疗研究进展相关文献，以期进一步验证血管腔内治疗的安全性和有效性。

关键词

肺栓塞，抗凝，全身溶栓，腔内治疗

Advances in Endovascular Treatment of Acute Pulmonary Embolism

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Abstract

Acute pulmonary embolism (PE) is the third most common clinical cardiovascular disease after myocardial infarction and stroke, and has a high clinical disability and fatality rate even globally. Summarizing the treatment experience in the past decades, great progress has been made in the treatment of PE, especially the endovascular therapy. However, the lack of class I evidence for the safety and effectiveness of endovascular therapy for PE makes the promising endovascular therapy still controversial. The purpose of this paper is to summarize the literature related to the research progress of endovascular therapy for acute PE in recent years, in order to further verify the safety and effectiveness of endovascular therapy.

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Keywords

Pulmonary Embolism, Anticoagulation, Systemic Thrombolysis, Endovascular Therapy

1. 引言

PE 是一种从无症状到严重至威胁生命的异质性心血管疾病，其临床表现特异性较差，从而带来了诊断和治疗的困难。年龄是肺栓塞发病的独立因素，随着目前人口老龄化的逐年增长，肺栓塞发病率也越来越高，因此需要对肺栓塞实施安全有效的管理措施。当前指南推荐的肺栓塞治疗依然以抗凝为标准治疗方案，但一些患者可能需要更积极的治疗，包括全身溶栓治疗以及外科手术治疗等，但是需要充分考虑全身溶栓治疗带来的临床收益和出血风险[1] [2] [3]。近些年来腔内血管治疗取得了重大进展，其旨在达到与全身溶栓同样的治疗效果的同时大大减少并发症的发生。

2. PE 的危险分层

目前的 PE 管理策略，根据 PE 患者临床表现及相关辅助检查进行了危险分层，这对于指导临床决策至关重要。高危 PE：这类患者的血流动力学不稳定(收缩压 < 90mmHg 且持续时间 > 15min)或者需要依靠血管升压药维持血压稳定。临床上这些患者约占肺栓塞患者总量的 5%，但是这些患者的死亡率最高，其 30 天死亡率接近 50% [4]。中危 PE：这类患者的血流动力学稳定，但是经超声心动图或计算机断层扫描检查证实有右心室功能不全抑或是伴有肌钙蛋白等心肌标志物升高的心肌损伤证据，又根据 sPESI [5] 评分将中危 PE 进一步分为中低危组及中高危组，其中将同时伴右心室功能不全及心肌损伤的这类患者划分为中高危组，中低危组患者则右心室功能不全或心肌损伤至多伴有一个。这类患者约占总量的 35%~55% [6] [7]，这类患者接受单纯抗凝治疗其 90 天死亡率约 2%~15% [8]-[14]。低危 PE：这类患者血流动力学稳定(收缩压峰值 ≥ 90 mmHg)且不伴有右心室功能不全及心肌损伤，通常这一类患者可接受单纯抗凝治疗且预后最好。

3. PE 的治疗

3.1. 抗凝治疗

抗凝治疗是所有急性 PE 的治疗基础，排除绝对抗凝禁忌后，及时进行抗凝治疗对于患者的预后具有重要意义。Smith 等[15]研究显示患者出现症状时立即进行抗凝治疗与延迟抗凝治疗相比，前者可以降低患者死亡率。根据 PE 危险分层，低危 PE 患者接受单纯抗凝治疗即可，但是对于中危以及高危 PE 患者可能需要在抗凝治疗基础上采取进一步治疗措施，其主要包括全身溶栓治疗以及血管腔内治疗等[2] [4] [16]。

3.2. 全身溶栓

全身溶栓通常是指将溶栓药物通过外周静脉血管输入体内，其临床应用优势是易于给药，但是溶栓药物容易带来出血的风险。Meyer 等[17]的 PEITHO 试验研究结果表明全身溶栓与单纯抗凝相比可降低血

流动力学失代偿的风险，临床收益明确，但是也增加了大出血或出血性脑卒中的风险。后来 Chatterjee 以及 Marti 等[8] [18]的荟萃研究显示，全身溶栓治疗肺栓塞有着显著的临床收益并极大降低了临床恶化发生率以及全因死亡率，但是这种治疗收益并不能抵消溶栓所致致命性出血并发症风险。而出血并发症的发生限制了全身溶栓的临床应用。鉴于全身溶栓可能带来的大出血甚至是致命性颅脑出血并发症，所有进行全身溶栓治疗时需要充分考虑临床收益与出血风险或其他并发症的关系，因此越来越多的临床应用借助血管腔内设备治疗急性 PE，腔内血管治疗可以减少溶栓药剂的剂量或避免溶栓，旨在达到全身溶栓的临床治疗效果而减少或避免出血等并发症的发生，其主要包括导管溶栓以及机械血栓清除等。

3.3. 导管接触性溶栓

导管接触性溶栓(catheter-directed thrombolysis, CDT)是指通过溶栓导管定向将溶栓药物注入肺动脉循环而达到溶栓做，其优势在于减少溶栓药物剂量，此种治疗方法的目标是快速消除阻塞性血栓从而解除致命性的心脏损伤并迅速恢复肺部再灌注，并且减少出血并发症。Kuo 等[19]的 PERFECT 注册表研究肯定了 CDT 治疗急性 PE 的即刻疗效以及术后 30~90 天的临床收益，且没有致命性出血并发症的报道、未出现因治疗导致死亡患者。几项荟萃分析[20] [21] [22]结果表明大多数的患者接受 CDT 治疗后可恢复血流动力学稳定并缓解缺氧症状、出院时存活，无致命性出血并发生，但是有患者可能需要输血对照处理，而且这几项荟萃分析属于回顾性研究。3 项前瞻性研究[23] [24] [25]的结果表明 CDT 可以快速地改善患者右心室功能不全，并且不会增加死亡颅内出血的风险。与全身溶栓相比，CDT 具有减少出血并发症的潜在收益，但是目前缺少两种治疗方法的随机对照研究。仅有少数研究[24] [26]将 CDT 与单独抗凝进行比较，肯定了 CDT 的治疗效果，此种治疗方法可降低 24 h 时右心室/左心室比值。结合目前的研究结果及临床，应用导管接触性溶栓带来了较大的临床收益、效果显著，但是不能完全避免应用溶栓药物所带来的出血并发症，并且部分患者因禁忌症而不能接受导管溶栓，因此借助于导管或者其他设备来进行血栓清除的治疗方法正在逐渐开展。目前 EKOsonic 系统已经批准上市，EKOsonic 系统是超声辅助导管溶栓系统，和 CDT 相比其最大优势在于理论上可以更短时间内渗透更多溶栓药物，但是目前的研究并没有发现二者在安全性和有效性方面短期或长期差异[27] [28] [29]。

3.4. 机械清除血栓

机械血栓清除需要借助专业设备来清除血栓，通常不需要溶栓从而避免因溶栓药物可能带来的出血并发症，目前经批准应用于临床的设备有 Flowtriver 栓塞切除装置 Indigo 血栓切除系统。几项研究[7] [30] [31] [32]结果表明表明了 Flowtriver 栓塞切除装置的安全性和有效性，其主要是利用大口径(20~24 Fr)静脉入路置入导管后，利用导管产生的负压而到达清除血栓目的，患者术后的肺动脉压、右心室功能以及其他指标显著改善，患者术后平均肺动脉压和氧气需求在统计学上显着降低，仅有少数患者出现出血并发症，而没有和治疗相关的不良事件出现。两项研究[33] [34]应用 Indigo 血栓切除系统治疗急性 PE，其结果都表明患者术后肺动脉压力及右心室与左心室比值显著降低，并且未出现相关治疗不良事件。多个病例报道[35] [36]结果表明 Angiojet 血栓切除系统的治疗有效性，但是会引起心律失常、低血压等并发症而不被推荐应用，其工作原理是利用伯努利原理在工作导管尖端利用高压喷射生理盐水而产生压力梯度从而吸栓，也可局部喷射溶栓药物达到溶栓目的。AngioVac 设备的临床应用数据目前仅有案例报告以及结果各异的小样本文献[37] [38] [39]，缺少前瞻性随机对照试验来证明其优于其他设备，并且有文献报道称，该设备因体积大、灵活性差而难以通过右心房和心室进入肺动脉[40]。关于机械清除血栓设备，虽然其避免了应用溶栓药物而带来出血并发症的风险，但是目前仅有少数的设备在临床中正式应用，大多数设备还在研发中，因此关于机械清除血栓设备的安全性和有效性还需要更多的随机对照试验来进一步证实，

当前的数据还不能为临床决策提供临床指导。并且这种治疗方案一般不会单独应用，还需要与局部溶栓等治疗方法联合应用才可以达到更好的治疗方法。

4. 结论

尽管目前关于PE的病理生理学、危险分层以及治疗方式等方面已经进行了大量的研究，但是依然缺乏高质量证据也导致了目前的临床管理层策略具有局限性。截至目前为止，依赖于导管系统的血管腔内治疗还是仅限于小样本随机对照试验和单臂前瞻性研究，这些研究的安全终点和有效终点是改善患者右心室功能以及降低肺动脉收缩压。虽然目前的一些单臂研究对于血管腔内治疗设备的安全性和有效性方面具有一定的价值，但是这些研究证据质量还不足以指导临床实践。并且到迄今为止，还没有任何相关研究试验能够评估导管接触性溶栓术、导管内血栓切除术等在短期甚至中长期中死亡率或是恢复血流动力学正常的益处。因此，在进一步获得高质量证据之前，治疗决策可能还要受患者的潜在出血风险、血栓范围和位置、操作人员专业知识以及患者个人偏好等方面的影响。因此目前迫切需要强有力的前瞻性随机对照试验来证明这些血管腔内治疗对急性PE的长期以及潜在益处。

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