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· 综述 ·

慢性硬膜下血肿术后复发危险因素的研究进展

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[摘要] 慢性硬膜下血肿(CSDH)是神经外科最常见疾病之一,随着人口老龄化和抗血栓药物的广泛使用,其发病率逐年上升。大部分CSDH患者通过手术治疗可获得较好的治疗效果,但仍有5%~30%的患者术后出现血肿复发需要再次入院治疗。CSDH术后复发的常见危险因素包括患者性别、年龄、基础疾病等自身因素,以及入院时血肿影像学形态、抗血栓药物的使用、麻醉方式、手术方式、辅助药物等。

[关键词] 慢性硬膜下血肿; 复发; 危险因素; 手术方式; 药物

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Risk factors of postoperative recurrence of chronic subdural hematoma: research progress

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[Abstract] Chronic subdural hematoma (CSDH) is one of the most common diseases in neurosurgery, and its incidence is increasing every year with the aging of the population and the widespread use of antithrombotic drugs. The majority of patients with CSDH have a good outcome with surgical treatment, but 5%-30% of patients still experience recurrence of hematoma and require readmission to the hospital. Common risk factors of hematoma recurrence include the patient factors such as gender, age and underlying disease, the imaging pattern of the hematoma at admission, the use of antithrombotic drugs, the mode of anesthesia, different surgical procedures, and adjuvant medications.

[Key words] chronic subdural hematoma; recurrence; risk factors; surgical procedures; drugs

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慢性硬膜下血肿(chronic subdural hematoma, CSDH)是神经外科最常见的疾病之一, CSDH的发病率为1/10万~5.3/10万,其发病率将随着人口老龄化的加剧而上升^[1]。CSDH的发生机制目前尚未明确,可能的原因包括脑损伤导致桥静脉破裂、炎症反应、急性硬膜下血肿转化和硬膜下新生血管渗漏等^[2]。随着疾病的进展, CSDH患者可出现多种临床表现,包括头痛、恶心、呕吐、精神异常、癫痫发作、感觉运动障碍、昏迷等^[3]。年轻患者常出现头痛和呕吐等颅内压增高症状,而50岁以上的患者经常出现肢体无力、语言障碍等大脑半

球损伤症状^[4]。对于症状明显或伴有严重神经功能缺损的患者,常采用钻孔引流等外科手术进行治疗,但仍有5%~30%的患者会出现术后血肿复发需要再次入院治疗^[5]。CSDH术后高复发率是目前临床面临的一个重要问题,额外的治疗增加了患者的经济负担,延长了住院时间,并导致潜在的不良预后^[6]。目前对于CSDH术后血肿复发的危险因素,如患者因素、手术相关因素、药物相关因素等未达成共识。本文就CSDH患者术后复发的危险因素进行综述。

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1 患者因素

患者性别、糖尿病、脑萎缩等与CSDH术后高复发显著相关^[7]。男性CSDH患者术后复发率为23.5%，女性患者复发率为12.7%，男性患者术后复发率约是女性患者的2倍^[8]。近年来有研究表明，患者血型、高密度脂蛋白水平、脱水状态等也可能与CSDH术后复发有关。Hirai等^[9]分析发现与其他血型相比，A型血与CSDH术后复发显著相关，A型血预测CSDH术后复发的灵敏度与特异度分别为64.9%和58.8%。血清中较高水平(>374.5 mg/L)的高密度脂蛋白与CSDH术后低复发率相关^[10]。入院时患者的脱水状态也是CSDH术后复发的一个独立预测因素，脱水介导的全身炎症反应可引起免疫细胞募集并分泌炎症介质，从而导致血肿复发^[11]。

患者入院时的影像学表现如血肿的单双侧、厚度、密度、体积、内部结构及中线移位情况等与CSDH术后复发密切相关。Chen等^[12]研究发现双侧CSDH患者术后血肿复发率是单侧血肿患者的2.5倍。meta分析显示高密度血肿、层状或分隔状结构的血肿均表现出较高的复发率^[13]。同时当术前血肿厚度 ≥ 10 mm和/或中线移位 ≥ 20 mm时术后血肿复发率显著增加^[14]。

CSDH患者常合并1种或多种需进行抗血栓药物治疗的基础疾病，目前关于需要行手术治疗的CSDH患者抗血栓药物的管理尚未达成共识，抗血栓药物是否为血肿术后复发的危险因素备受争议。早期研究表明接受抗血栓药物治疗的CSDH患者术后复发率是未接受抗血栓药物治疗患者的1.5~2.5倍^[15]。而Nathan等^[16]认为CSDH患者的复发率增高仅与抗凝药物的使用有关，与抗血小板药物的使用无关。最新研究则表明如果手术治疗充分，抗血栓药物的使用与CSDH术后复发无关，患者再出血可能是由于自身合并有出血倾向的其他慢性疾病(如高血压、肾功能障碍等)所致^[17]。对于CSDH手术治疗的患者，临床医师应充分考虑抗血栓药物治疗的适应证和患者相关合并症，筛选可能发生血栓栓塞事件的高危人群并早期恢复抗血栓治疗。

2 手术相关因素

2.1 麻醉方式 麻醉方式可能会对CSDH术后复

发造成影响。研究显示全身麻醉的CSDH患者术后血肿复发率明显低于局部麻醉的患者^[17]。而Wong等^[18]的研究则得出了相反的结论，全身麻醉组的手术后血肿复发率大约是局部麻醉组的5倍。全身麻醉可以避免患者术中活动，保障手术安全，同时减少局部麻醉操作时由于术中病情变化或患者不配合而需要转为全身麻醉带来的不便。局部麻醉可以减少患者术中的血流动力学波动及围手术期麻醉相关并发症。不同麻醉方式对术后血肿复发的影响仍存在争议，未来需要开展更多大样本、前瞻性的临床研究进行验证。

2.2 传统手术方式 钻孔引流术是治疗症状性CSDH的主流方法^[19]。在CSDH的手术管理中，缺乏有关最佳手术技术选择和规范化操作的指南与共识。术中钻孔的数量、冲洗、引流等对术后血肿复发的影响都存在争议。

研究认为单孔引流可能会导致引流不充分而造成血肿复发，因此更倾向采用双孔引流的方法^[20]。而2019年的一项meta分析显示，单孔和双孔引流在血肿复发率和手术并发症率方面差异均无统计学意义，单孔引流方式具有创伤小、手术时间短等特点，可以优先考虑^[21]。此外，术中冲洗与引流同样影响CSDH术后复发率。meta分析显示，冲洗组和非冲洗组之间的CSDH患者术后血肿复发率差异无统计学意义($P>0.05$)，但引流组的复发率低于非引流组($P<0.01$)，因此研究者认为CSDH术后引流有利于降低血肿复发率，而是否冲洗与血肿复发率无关^[22-23]。但Saito等^[24]认为血肿腔内的高浓度成分可能导致再出血风险增加。从这个角度来看，术中冲洗是有利的，冲洗可以稀释血肿并促进引流，进一步促进残余血肿的排出，有利于降低CSDH术后复发率。

与此同时，研究表明术中冲洗液的类型和温度也可能与术后血肿复发相关。相较于生理盐水，使用人工脑脊液冲洗可明显降低血肿复发率，这可能是因为人工脑脊液减轻了伤口周围组织水肿和细胞损伤，实现了更快的止血效果^[25-26]。此外，Bartley等^[27]分别使用室温(22℃)和生理温度(37℃)下的林格氏液对血肿进行冲洗，发现生理温度下的林格氏液更有利于血肿的稀释与引流，患者术后血肿复发率明显低于室温组($P<0.05$)。常用的引流方式有硬膜下引流和骨膜下引流，meta分析显

示术后骨膜下引流患者的血肿复发率低于硬膜下引流患者^[28]。骨膜下引流技术简单,与脑实质无直接接触,可减少脑组织损伤、脑内血肿形成和癫痫发作的发生,更加安全^[29]。此外,术后残余血肿的体积($>50\text{ cm}^3$)、颅内积气($>10\text{ mL}$)也与CSDH高复发率相关^[30-31]。术后残留的硬膜下积气、积血可能引起血肿内外包膜之间不完全粘连,进而导致CSDH复发。因此建议术中彻底冲洗、充分排气,以降低术后血肿复发率。

2.3 神经内镜血肿清除术 有少数研究讨论了CSDH神经内镜下手术治疗与术后血肿复发的关系。神经内镜因具有可视化特点,可以充分打开血肿分隔并完全清除血肿,且能有效清除较厚的血肿包膜及血凝块,较传统手术治疗更具优势^[32]。神经内镜术后血肿复发率明显低于传统手术(5.33% vs 15.07%),同时在术后24~48 h内的血肿清除率、住院时间、Markwalder评分等方面均优于传统钻孔引流手术^[33-34]。

2.4 脑膜中动脉栓塞术(middle meningeal artery embolization, MMAE) MMAE是治疗CSDH的一项新技术。Ishihara等^[35]最早报道了7例采用MMAE治疗的CSDH患者,均取得了良好的治疗效果。血肿包膜内新生微血管出血是CSDH复发的可能机制之一,组织学与影像学检查证实这些新生血管由脑膜中动脉供血^[36]。对血肿腔的供血动脉进行栓塞可有效降低CSDH的复发率,meta分析显示MMAE治疗后CSDH的复发率仅为4.1%,治疗效果优于传统外科钻孔引流术^[37]。海军军医大学(第二军医大学)第一附属医院脑血管病中心率先报道了国内使用液态栓塞材料行MMAE治疗的19例CSDH患者资料,术后3个月的随访期内所有患者均未见血肿复发^[38]。由此可见,MMAE可能是一种安全、有效且应用前景广阔的CSDH治疗方法。目前国际上已有多项MMAE的随机对照试验正在进行,期待这些研究能带来MMAE治疗CSDH更高级别的证据。

3 药物相关因素

阿托伐他汀、糖皮质激素等药物常作为CSDH患者手术的辅助治疗或替代治疗。阿托伐他汀可以将巨噬细胞极化为M2型并调节炎症反应来缓解CSDH的症状,促进血肿消融^[39]。阿托伐他汀已

被证明是CSDH患者的一种安全、有效的治疗药物,能够显著减小CSDH患者血肿体积,然而其是否影响CSDH术后复发还不清楚^[40]。最新的研究发现,术后使用阿托伐他汀的CSDH患者血肿复发率为7.0%,没有使用阿托伐他汀的患者复发率为5.6%,两组复发率差异无统计学意义($P>0.05$)^[41]。这提示他汀类药物可能不会降低CSDH患者的术后血肿复发率。单纯糖皮质激素治疗或作为CSDH患者术后的辅助治疗手段均可以降低CSDH患者的血肿复发率($P<0.001$)^[42]。但在辅助性使用糖皮质激素时,患者精神症状明显增多,需要临床医师平衡相关风险并根据患者具体情况个体化用药。

4 小结

CSDH传统外科手术后血肿复发率高是临床面临的重要问题。研究血肿复发危险因素对于降低CSDH术后复发率具有重要意义。以MMAE为代表的新型血管内治疗方法显示出较传统外科手术更好的效果,能够显著降低血肿复发率,但今后还需要高级别循证医学证据进一步评价MMAE的安全性和有效性。

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