·综述·

转移性脊柱肿瘤的手术并发症和预防策略

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【摘要】 随着肿瘤综合治疗水平的提高，癌症患者的平均预期寿命得到延长，转移性脊柱肿瘤的发病率也越来越高。转移性脊柱肿瘤作为一种全身性疾病，需要多学科的治疗方法。其中，手术治疗是重要组成部分，可以显著缓解疼痛，恢复脊柱稳定性，降低脊髓压迫的可能性，显著改善患者的生活质量。然而，由于这些患者的健康状况较差，手术治疗会增加围手术期并发症的风险。充分认识和了解可能发生的并发症原因和预防策略有助于降低不必要并发症的发生。本文重点综述转移性脊柱肿瘤手术相关的并发症、潜在的危险因素及预防策略，为脊柱转移瘤患者的治疗提供一定的参考价值。

【关键词】 脊柱肿瘤； 转移性肿瘤； 外科治疗； 并发症； 危险因素

Surgical complications and prevention strategies for metastatic spinal tumors

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【Abstract】 With the improvement of comprehensive treatment for cancer, the average length of life expectancy is increased, and the incidence of metastatic spinal tumors is increasing. As a systemic disease, metastatic spinal tumor requires multidisciplinary treatment. Among which, surgical treatment is an important part, which can significantly relieve pain, restore spinal stability, reduce the possibility of spinal cord compression, and significantly improve the quality of life of patients. However, surgery increases the risk of perioperative complications due to the poor health of these patients. Fully understanding the causes of the possible complications and prevention strategies might help reduce the incidence of unnecessary complications. This review article focuses on the complications, potential risk factors and prevention strategies related to the surgery of metastatic spinal tumor, providing a certain reference value for the treatment of patients with spinal metastatic tumor.

【Key words】 Spinal tumor; Metastatic tumor; Surgical treatment; Complication; Risk factor; Prevention strategy

脊柱是仅次于肺和肝脏之外第三最常见的转移部位，也是最常见的骨转移部位[1-2]。随着肿瘤综合治疗水平的提高，癌症患者的平均预期寿命得到延长，转移性脊柱肿瘤的发病率也越来越高[3]。据估计，在5～30%的原发性癌症中存在脊柱转移，最常见的原发癌为乳腺癌、前列腺癌和肾癌[4]。转移性肿瘤可累及椎体及其附件，导致病理性骨折、脊髓压迫或脊柱不稳定，从而引起严重疼痛和脊髓压迫，最终降低癌症患者的生活质量和预期寿命[5]。

转移性脊柱肿瘤的治疗是多学科的，包括放射治疗，如：常规/立体定向体放射治疗（Stereotactic Body Radiation Therapy，SBRT）、化疗、免疫治疗（靶向治疗）、手术治疗(微创治疗和开放手术治疗）等[6]。其中，手术治疗是转移性脊柱肿瘤患者治疗的重要组成部分[3]。手术治疗可以显著缓解疼痛，恢复脊柱稳定性，降低脊髓压迫的可能性，显著改善患者的生活质量[7-8]。然而，由于这些患者的健康状况较差，手术治疗会增加围手术期并发症的风险[9-10]。据报道，在接受脊柱转移手术的患者中，并发症的发生率从10%到66.7%不等[10-22]。术后并发症不仅给患者及家属带来了沉重的经济和心理负担，也给社会医疗系统带来了沉重的负担。充分认识和了解可能发生的并发症原因和预防策略有助于降低不必要并发症的发生。本文重点综述转移性脊柱肿瘤手术相关的并发症、潜在的危险因素及预防策略，为脊柱转移瘤患者的治疗提供一定的参考价值。

一、资料与方法

分别使用中文检索词：“癌症”、“转移瘤”、“脊柱”、“手术

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胡宏志和杨文博对本文有同等贡献

治疗”、“并发症”在中国知网（China National Knowledge Internet，CNKI）及万方数据库检索相关文献；并以英文检索词“Cancer”，“ Metastasis”，“Spine”，“Surgery”及“Complications”在PubMed、Web of Science 和 Embase 数据库进行检索，查找从2010年至2020年所有的相关文献，并同时纳入参考文献中的相关文献。文献纳入标准：（1）中文或英文文献；（2）文献类型为临床或成人标本试验研究；（3）研究内容为与脊柱转移瘤治疗相关并发症的文献。排除标准：（1）重复研究的文献；（2）无法获取全文的文献；（3）质量较低、证据等级不高的文献。共获得英文文献1 260篇、中文253篇，根据纳入及排除标准最终选取英文文献124篇，中文文献2篇（图1）。

二、治疗原则

目前，转移性脊柱肿瘤的治疗通常采取多学科的治疗方法来维持或改善患者的生存质量，但总体治疗效果仍不理想[23]。大部分患者的生存期较短，通常不到一年[24-27]。其治疗目标是减轻疼痛，预防或缓解脊髓压迫，保持或恢复神经功能和脊柱稳定性[24, 28]。对于预后极差的患者，非手术治疗（放疗、化疗、生物治疗等）或微创姑息治疗、椎体成形术或椎体后凸成形术在缓解疼痛方面取得了令人满意的效果[29]。对于脊柱不稳定、畸形、进行性神经功能障碍、脊髓受压严重、对非手术治疗无效的顽固性疼痛以及预期寿命超过3～6个月的患者，必须考虑手术治疗[30-32]。了解手术治疗潜在的并发症及其危险因素对权衡手术干预的风险至关重要[33]。以下将探讨转移性脊柱肿瘤围术期常见的相关并发症及其危险因素，并强调并发症的预防策略（表1）。

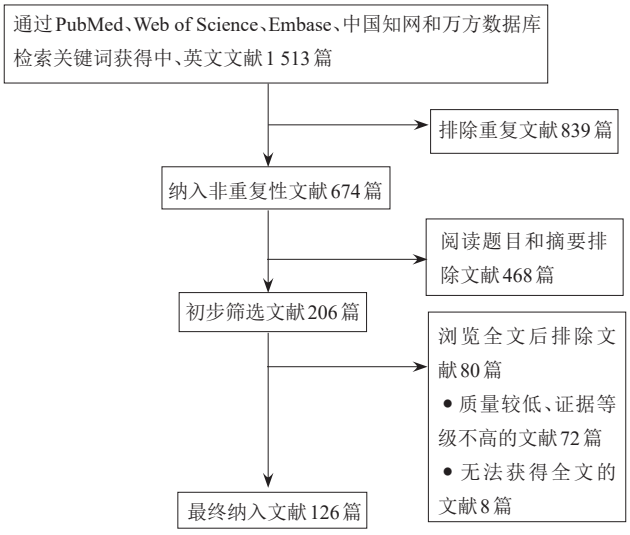

图1 纳入文献流程图

三、常见手术并发症与预防策略

（一）术中并发症

1.脊髓和神经根损伤：在转移性脊柱手术中，神经系统并发症的发生率从0.6%到14.5%不等[10, 18, 34-35]。常见的神经并发症包括脊髓、马尾和神经根损伤，导致永久性或暂时性的神经功能障碍，如截瘫、偏瘫和感觉功能障碍等[14, 17, 21-22, 34, 36]。除了手术过程中对神经的直接损伤外，供应脊髓的神经根动脉损伤会影响脊髓的灌注，从而使脊髓面临缺血性损伤的危险[29]。如Adamkiewicz动脉的损伤可能导致神经功能障碍，因为它为脊髓提供了重要的灌注来源，当进行下胸椎肿瘤切除时，应特别注意此动脉，无意中结扎可能导致脊髓缺血和截瘫[37]。此外，术后的硬膜外血肿形成可造成脊髓和神经根压迫，也会引起严重的神经功能障碍[29]。

术前常使用高剂量类固醇以减少创伤性脊髓水肿和潜在的肿瘤压迫[38]。术中神经电生理监测可对神经结构的功能完整性进行识别和实时监测[39]。在神经损伤的可逆阶段及早发现可以迅速纠正原因并避免造成永久性的损害。一旦电生理监测电位发生变化，手术医生和麻醉师应迅速作出反应。手术医生应注意是否存在可逆性压迫，并及时解除压迫。麻醉医生应确定是否是麻醉剂的影响，血压是否足以维持脊髓灌注。术后可人为提高患者血压水平，以维持脊髓灌注，并可给予类固醇激素[40]。在转移性脊柱肿瘤手术中，常常需要牺牲神经根来切除肿瘤[37]。如果遇到颈神经根或腰

表1 转移性脊柱肿瘤的常见手术并发症和预防策略

手术并发症类型	预防策略
术中并发症	
脊髓和神经根损伤	术前：高剂量类固醇；术中：神经电生理监测；术后：维持脊髓灌注、类固醇激素；
大量出血	术前：纠正凝血功能障碍、血管栓塞术、抗纤溶药物、低体温预防；术中：供瘤血管结扎、双极电凝止血、止血药品；术后：密切监测血压和引流量的变化；
硬脊膜损伤和脑脊液漏	术中：仔细分离肿瘤与硬膜的粘连、避免使用尖锐的器械、分离前彻底止血、直视下谨慎操作等；
术后并发症	
手术部位感染	术前：戒烟、纠正营养不良、控制血糖、预防使用抗生素；术中：遵守严格无菌操作原则、控制手术时间和术中出血量、严密缝合不留死腔；
静脉血栓栓塞	术后：术后行放疗的间隔时间至少一周；术后：抬高双侧下肢、物理预防（足底静脉泵、间歇充气加压装置、弹力袜等）、鼓励患者主动在床上做足踝部和关节的主动屈伸运动，争取早日下床活动、早期预防性应用抗凝剂；
内固定失败	术中：合理设计和选择内固定装置和固定方式；术后：早期下床活动，密切随访；
肿瘤复发	术后：对于富血供的原发肿瘤患者术后应密切随访。

神经根受压，则不建议牺牲神经根，因为这种手术本质上是姑息性的。然而在胸椎，除T_1外，胸椎神经根结扎通常能被患者很好地耐受，而且不会造成明显的术后神经功能障碍[37]。

2.大量出血：术中过多的失血会严重影响术区视野，延长手术时间，导致围手术期并发症增加，如严重的心脏不良事件、术后凝血障碍和急性肺损伤等[41-42]。据文献报道，转移性脊柱肿瘤术中出血量平均2 180 ml[43-47]，严重时可达5 000 ml以上[48]。影响术中出血量的因素有：肿瘤的病理类型、肿瘤的大小、浸润范围、手术时间及手术方式等[49]。其中，原发肿瘤的类型是判断术中出血量的关键因素。对于血管丰富的肿瘤如转移性肾细胞癌、肝细胞癌和甲状腺癌等，破坏肿瘤包膜常常导致持续出血[37,50]。此外，血液系统恶性肿瘤、肝癌及使用抑制骨髓药物的患者易发生凝血功能障碍，术中发生出血并发症的风险尤其高[40]。

对于转移性脊柱肿瘤患者，值得注意的是这些患者出血的主要原因包括凝血功能障碍以及术中操作不当导致血管损伤[40]。目前，减少术中失血的常规措施包括：凝血功能的评估和纠正、术前栓塞术、抗纤溶药物使用、低体温预防、术中供瘤血管结扎、使用双极电凝止血以及止血药品的使用等[51]。对于富血供的原发肿瘤为肾细胞癌、滤泡性甲状腺癌、神经内分泌肿瘤，以及术前影像学检查怀疑富血供肿瘤的患者可考虑术前栓塞[40]。对于术后出现严重或持续的低血压和/或贫血，应怀疑有隐匿性血管损伤，建议使用CT血管造影进行检查[42]。总之，制定充分的术前准备与周密的手术计划是避免大量出血发生的关键。

3.硬脊膜损伤和脑脊液漏：在脊柱退行性手术中，发生意外的硬脊膜撕裂的发生率为0.3%～35%[52-55]。转移性脊柱肿瘤的转移灶可能与硬脊膜紧密粘连，术中更易发生硬脊膜损伤[56]。此外，放疗会使硬膜外纤维化、粘连和硬脊膜变薄显著增加硬脊膜撕裂的风险[29]。大多数意外的硬脊膜撕裂可在术中被识别和处理，不需要再次手术或进一步的干预，但值得注意的是其导致的术后脑脊液漏及与脑脊液漏相关的并发症，如伤口感染[57-59]、低颅压症[60]、颅内蛛网膜下腔出血[61-63]、蛛网膜炎[64-65]、神经根卡压[66-67]、脑膜炎[68]及硬膜内肿瘤的播散[40]等。

许多硬脊膜损伤可以通过基本的外科原则来预防，如仔细分离肿瘤与硬膜粘连、避免使用尖锐的器械分离硬膜、分离前彻底止血、直视下谨慎操作等[69]。近年来，超声骨刀已经逐渐被引入脊柱外科，由于其拥有较大的骨切割精度和避免损伤周围软组织的潜力。但是，超声骨刀在脊柱手术中的安全性和有效性尚未得到很好的证实，有研究认为超声截骨术不太可能穿透硬脊膜[70]，但另一些研究者发现超声骨刀也能引起医源性硬脊膜撕裂[71]。需要注意的是，转移性脊柱患者更容易出现术后脑脊液漏，原因包括：营养不良、长期使用高剂量类固醇或需要辅助放化疗等[69]。持续的脑脊液漏导致住院时间延长，而且需要额外的干预，增加了医疗费用[72]。因此，早期有效的预防、识别和治疗术后脑脊液漏是避免一系列相关不良后果发生的关键[69]。

(二)术后并发症

1.手术部位感染（Surgical site infection，SSI）：SSI是转移性脊柱肿瘤最常见的术后并发症之一[6,73]。转移性脊柱肿瘤患者术后SSI的发病率是一般脊柱手术平均发生率的8～10倍[12,73-75]。发生SSI的患者治疗的经济成本明显高于未发生SSI的患者，住院时间延长是主要原因[1]。平均住院时间增加了100%，约为4周[1,75]。此外，SSI还会影响转移性脊柱肿瘤患者术后的生存率[75]。Awad等[76]研究发现发生SSI的患者比未发生SSI患者的生存率下降了4个月。有研究认为在发生SSI的患者中，38～75%的死亡可归因于SSI本身[76]。

2.转移性脊柱肿瘤SSI的危险因素：高龄、糖尿病、吸烟史、低白蛋白水平、术前使用类固醇、用不可吸收缝线缝合、手术时间≥4 h、术中出血≥2000 ml、多发脊柱转移灶、高ASA评分、术前神经功能损害、多节段固定手术、术前放疗等[1,6,73,75,77-78]。最近的研究结果表明ASA≥3、手术时间≥4 h、糖尿病和术前放疗是转移性脊柱肿瘤患者发生SSI的独立危险因素[73,75]。

为降低SSI的发生率，外科医生应警惕任何感染的迹象和症状，如肿胀、触痛、红斑、持续疼痛、恶心、食欲不振和疲劳等[29]。围手术期血糖控制和预防性抗生素的使用已被证明可以减少脊柱手术中伤口感染的发生率[79]。对于辅助放疗技术的使用，Itshayek等[80]认为术前或术后辅助放疗最佳间隔时间应至少为一周，以减少伤口并发症的发生。Demura等[73]发现PGE1可显著降低术前接受放射治疗的脊柱转移患者SSI的发生率。

3.静脉血栓栓塞（Venous thromboembolism，VTE）：VTE是癌症患者死亡的主要原因之一，包括深静脉血栓形成（Deep vein thrombosis，DVT）和肺栓塞（Pulmonary embolism，PE）[81-84]。与没有癌症的患者相比，癌症患者有47倍的风险发展为症状性VTE[85-86]。脊柱手术被认为是症状性VTE的独立危险因素[87-88]。此外，接受手术治疗的转移性脊柱肿瘤患者发生VTE的风险比其他需要手术的脊柱疾病（如椎间盘突出症或脊柱畸形）高[89]。文献中关于转移性脊柱肿瘤患者术后发生VTE的发生率不尽相同（从6.2%～16.9%不等），可能是由于研究方案、检测方法和研究人群的差异等造成的[81,84,90]。Groot等[84]报道的一项回顾性分析中637例转移性脊柱肿瘤患者接受手术治疗后90天内症状性VTE的发生率为11%（其中DVT为6.2%，PE为6.0%）。此外，该研究还表明VTE与术后1年的生存率下降相关。另一项回顾性分析研究中647例转移性脊柱肿瘤患者接受手术治疗后30 d内VTE的发生率为6.2%（其中DVT为4.5%，PE为3.6%）[90]。

多种因素可能与VTE的高发生率有关，包括高龄、肿瘤、严重的静脉淤滞、术后长时间的卧床等[87,91-92]。此外，Kim等[93]发现明较长的手术时间与较高的VTE的风险直接相关。目前，对于接受手术治疗的转移性脊柱肿瘤患者来说，仍然缺乏标准的指导方针和防治方案[81]。转移性脊柱肿瘤在手术干预后的第1天至第3天，除机械预防外，预防性应用抗凝剂可显著降低30 d内发生VTE的风险[81]。虽然需要在更大规模的前瞻性随机对照试验中进一步的研究，但这些发现表

明，早期预防性应用抗凝剂是一种相对安全的做法，可以潜在地降低血栓栓塞事件的风险。

4.内固定失败：许多脊柱转移瘤患者需要内固定来维持脊柱的稳定性和神经功能。伴随而来的是内固定失败的风险，这可能会导致再手术、再入院，在严重的情况下，还会导致神经系统的损害或死亡[94]。无内固定失败患者的平均生存时间几乎是有内固定失败患者的两倍[95]。据文献报道，转移性脊柱肿瘤患者的内固定失败率从1.8%到16%不等[22,95-101]。这种差异可能部分是由于患者情况、手术方法和重建方式的不同。

Amankulor等[97]确定了内固定失败的危险因素，包括肋骨切除后胸壁不稳定、跨越六个或多个相邻椎体长度的固定以及女性转移性硬膜外脊髓压迫的患者。Longo等[94]认为多发性骨髓瘤及美国东部肿瘤协作组评分（Eastern Cooperative Oncology Group score，ECOG）＞2是内固定失败的危险因素。Pedreira等[95]发现术前放疗与内固定失败有显著的相关性。既往研究已经证明放疗会导致骨坏死和纤维化[102-103]。也有证据表明术前放疗与术后椎旁肌肉愈合不良有关，这些肌肉群的力量下降使脊柱结构承受更大的压力，因此可能进一步导致内固定失败[104]。值得注意的是，术后放疗与手术治疗相结合可改善患者的生存质量[105-107]。因此，放疗的时机似乎会影响这一患者群体的预后，如果术前进行放疗，必须高度重视内固定失败的风险[95]。活动能力受损与内固定风险增加有关，因此，保证患者早期活动不仅可以缩短住院时间和减少术后并发症，还可以降低内固定失败的风险[94,108]。

5.肿瘤复发：随着治疗水平的提高，转移性脊柱患者的生存期延长，术后肿瘤复发率也不断增加[109]。肿瘤复发可压迫神经或脊髓导致脊柱不稳定和神经/脊髓压迫，严重影响患者的生活质量[110]。所有接受手术的转移性脊柱肿瘤患者应密切监测肿瘤的局部复发、活检通道的复发和远处转移。任何可疑的复发应密切关注，必要时进行活检，并及时治疗[40]。据文献报道，转移性脊柱肿瘤的术后复发率在5.5%~32.3%[12,14,111-114]。Lau等[111]随访99例患者转移性脊柱肿瘤患者，其中32例(32.3%)患者在初次手术后出现转移性疾病的局部复发，平均复发时间为9.8个月。Weigel等[112]对76例有症状性脊柱转移的患者进行了评估，17例（22%）患者术后出现肿瘤复发，平均复发时间为11.4个月。Lee等[12]回顾性分析了200例接受手术治疗的脊柱转移瘤患者，其中11例患者复发（8例原位复发，3例其他部位再发）。

目前的文献中已确定某些癌症类型，如肾癌明显与较高的复发率相关[112,115]。Chataigner等[115]认为肾癌脊柱转移有高复发的危险，必须进行全椎体切除术。Lau等[111]的研究表明复发率较的癌症包括肾细胞癌（63.6%）、平滑肌肉瘤（62.5%）、黑色素瘤（50.0%）、甲状腺（50.0%）。但是，通过多变量分析进行分层并对系统转移性疾病进行调整时，发现黑色素瘤是唯一与局部复发独立相关的癌症类型。转移性黑色素瘤和转移性肾细胞癌的共同之处在于，它们都是非常严重的血管病变[111]。目前尚不清楚这些转移病灶的血管分布是否增加了局部复发的风险。但是，有分子证据表明，在多种肿瘤类型中，血管生成的高水平与较高的复发率相关[116-117]。此外，与生存率增加相关的某些因素，包括年龄小于65岁、单一节段椎体转移、化疗、放疗等，与局部复发风险增加相关[111]，可能与这些因素与患者生存期延长有关[112,118]。

6.其他：除以上常见的并发症之外，文献中报道较少的并发症还包括围术期死亡[90]、血管事件（术中心脏骤停、心肌梗塞、心律失常和中风等）[25,119]、肺部及呼吸道并发症（胸腔积液、气胸、肺炎、肺脓肿和肺不张等）[17,18,22,36,42,44,120-121]、胃肠道并发症（胃溃疡、麻痹性肠梗阻、胃肠道出血等）[14,22,36,122]、肝功能衰竭[12]、邻近器官损伤（食管、气管、输尿管等）[40,123]、腹膜后出血[124]、脑膜炎[12]、高钙血症危象[125]、败血症[17]等。

降低手术相关的并发症发生率对转移性脊柱肿瘤患者治疗的成功至关重要。Patil等[10]对1993年至2002年在美国接受手术治疗的26 233例脊柱转移瘤患者死亡率、并发症及住院费用等进行分析，术后发生一例并发症，平均住院时间从10 d增加到17 d，死亡率从3%增加到14%，住院费用增加2万美元。Lau等[126]报道，发生并发症的患者的住院费用约为无并发症患者的两倍。随着过高的医疗成本成为一个日益紧迫的公共卫生问题，针对性减少手术相关并发症的必要性是显而易见的。

四、总结

转移性脊柱肿瘤的治疗需要多学科诊疗团队针对患者的个体情况共同制定个性化治疗方案，其中先进的外科技术大大改善了患者的生活质量。外科医生必须权衡手术治疗的高并发症发生率与手术治疗带来的益处，否则患者可能会经历不必要的手术，缩短患者的寿命，降低患者的生活质量。此外，术前充分的准备、术中精细的操作、术后密切的观察和及时的处理是降低手术并发症和改善患者预后的关键。

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