·专　论　Special comment·

从评分到人工智能——经颈静脉肝内门体分流术后肝性脑病预测的演变与挑战

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【摘要】 该文探讨了经颈静脉肝内门体分流术（TIPS）后肝性脑病（hepatic encephalopathy，HE）的影响因素及预测方法，重点分析了人工智能（AI）技术在预测 TIPS 术后 HE 的应用潜力和挑战。具体系统梳理了包括患者基线特征、TIPS 相关参数及其他相关因素，并评估传统评分系统如 Child-Pugh 评分、终末期肝病模型（model for end-stage liver disease，MELD）评分和白蛋白-胆红素（ALBI）评分预测 HE 的准确性。同时探讨了 AI 技术如何通过处理多维数据集提高预测准确性，并讨论 AI 模型在临床应用中的优势与挑战。该文强调构建全面动态预测模型的重要性，以改善 TIPS 术后患者生活质量和生存率。

【关键词】 经颈静脉肝内门体分流术；肝性脑病；人工智能；预测模型

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From scoring to artificial intelligence: the evolution and challenges in predicting hepatic encephalopathy after TIPS

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【Abstract】 This paper discusses the factors influencing the occurrence of hepatic encephalopathy (HE) after transjugular intrahepatic portosystemic shunt (TIPS) and the prediction methods for HE, focusing on the potential and challenges of artificial intelligence (AI) technology in predicting HE after TIPS. The related factors including patient's baseline characteristics, TIPS-related parameters, and other related factors are systematically summarized, and the accuracy of the traditional scoring systems such as Child-Pugh score, Model for End-Stage Liver Disease (MELD) score, and albumin-bilirubin (ALBI) score in predicting HE is evaluated. Besides, the mechanism by which AI techniques improve prediction accuracy through processing multidimensional datasets is discussed, and the advantages of AI model and its challenges in clinical application are also introduced. This paper emphasizes the importance of constructing comprehensive dynamic prediction models so as to improve the quality of life and survival rate of patients after TIPS.

【Key words】 transjugular intrahepatic portosystemic shunt; hepatic encephalopathy; artificial intelligence; prediction model

经颈静脉肝内门体分流术（TIPS）是一种常用于治疗门静脉高压症及其并发症（如食管胃底静脉曲张出血和复发性腹水）的微创介入技术，通过建立门静脉与肝静脉间分流通道降低门静脉压力[1-2]。然而，分流通道的建立可能导致部分并发症，其中肝性脑病（hepatic encephalopathy，HE）最为突出，也是限制 TIPS 广泛应用的主要因素[3]。研究表明，TIPS 术后 HE 发生率为 11%～50%，多数出现于术后 1～3 个月[4-6]。这种神经精神综合征不仅会延长住院时间、增加医疗费用，还严重影响患者生活质

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量，甚至增加死亡风险[7-8]。

当前，尽管 Child-Pugh 评分、终末期肝病模型（model for end-stage liver disease，MELD）评分、白蛋白-胆红素（albumin-bilirubin，ALBI）评分等传统评价工具在预测 TIPS 术后 HE 中有所应用，但其准确性和普适性受到一定限制[9-10]。近年人工智能（artificial intelligence，AI）技术在医学领域广泛应用，为提升 HE 预测能力提供了全新视角[11-15]。本文系统梳理 TIPS 术后 HE 影响因素及预测方法，并重点探讨 AI 技术在这一领域的应用潜力和未来发展方向。

1　TIPS 术后 HE 影响因素

HE 本质是一种代谢性脑病，表现形式从轻度认知障碍到昏迷不等。TIPS 术后分流通道使门静脉血液绕过肝脏直接进入体循环，使毒素（尤其是氨）清除减少；其他机制如炎症反应、肠道菌群失调和脑组织代谢异常等，也在 HE 发生中起重要作用[14-15]。HE 病理基础复杂，涉及多种因素，如肝功能不全、内脏血液分流至全身循环、高氨血症、炎症反应以及肠道微生物学改变等。这些因素相互作用增加了 HE 复杂性[16-17]。

TIPS 术前基线特征如年龄和肝功能，是报道最多的影响因素。许多研究提及 60 岁及以上患者术后发生 HE 风险显著更高，在这一人群中进行详细风险评估非常有必要[14,18]。血清白蛋白和胆红素水平等肝功能相关指标，除了与 HE 发生风险有关外，也可能反映肝硬化患者其他疾病状态，如营养不良和全身炎症[19]。

手术相关参数也是重要影响因素。多个研究证实，门静脉压力梯度（portal pressure gradient，PPG）过度降低会增加 TIPS 术后 HE 风险[4,20-23]，因此在降低 PPG 时需要同步考量过度分流带来的 HE 风险。此外，支架直径、类型和穿刺部位等也已证明是影响 HE 发生的关键因素[24-25]。

其他影响因素，如认知功能、肌肉含量、营养状况、药物影响、显性 HE 病史、糖尿病、肌酐水平升高以及肝硬化病因等，均与 TIPS 后 HE 发病率增加有关[26-29]。因此，综合分析这些因素能更好地预测和降低 HE 风险，改善患者治疗结果和生活质量。

2　现有评分系统与预测模型

TIPS 术后 HE 评估应包括详尽的病史收集、体格检查、神经心理测试以及各种生化指标分析等多维度指标。生化指标提供了患者代谢状态和肝功能直接信息，如胆红素、白蛋白、血氨、胆碱酯酶、白细胞介素（interleukin，IL）-6 等，目前这些是临床常用 HE 预测评分系统的基本组成部分。

2.1　血氨

血氨浓度是 HE 评估的关键指标，广泛用于 HE 诊断和监测[30-31]。研究表明，高血氨水平与 HE 发生密切相关，提示肝脏解毒能力降低和系统性氨积累。利福昔明可显著降低血氨水平，持续改善肝功能，并提高患者生活质量[32]。然而一些研究表明，仅依赖血氨水平评估 HE 缺乏特异性；高血氨患者不一定会发生 HE，而即使血氨水平正常，也可能出现 HE。各种外在因素也可能影响血氨水平，导致误诊[33-34]。此外，氨离体后不稳定性对样本收集和处理提出了特殊要求，采样后样本应置于 4 ℃，且最好在 30 min 内完成检测。临床中若未严格操作，可能影响其作为诊断指标的准确性[35]。因此，仅依赖血氨水平不足以充分评估和预测 HE。

2.2　IL-6

除了血氨以外，全身炎症反应被认为是参与 HE 发病的关键因素之一。其中，IL-6 与 HE 关联较为紧密，可作为预测 HE 风险的标志物[36-38]。有研究表明，IL-6 水平超过 9 pg/mL 肝硬化患者发生 HE 风险显著增加，其预测效能胜于 Child-Pugh 评分和 C 反应蛋白[38]。然而，IL-6 对 HE 预测能力存在一定的局限性，其作为一种多功能细胞因子，参与免疫调节、代谢控制、炎症反应及神经调节，意味着其缺乏疾病特异性。肝硬化患者中高 IL-6 水平与 HE 关联的具体病理机制尚不清楚，这种不确定性使得 IL-6 水平作为 HE 标志物还有待明确。

2.3　胆碱酯酶

胆碱酯酶是近年来报道较多的 HE 预测因子。胆碱酯酶水平在 HE 患者中显著降低，且与 HE 诊断后 1 年内死亡率增加存在显著关联，其可作为 HE 和死亡的独立预测因子[39-40]。胆碱酯酶与血氨、血小板计数、谷氨酰转肽酶等多项指标联合检测，对 HE 诊断具有更高的预测价值[41-43]。但许多中心都没有常规测量胆碱酯酶，这可能导致其预测价值被低估。

2.4　Child-Pugh 评分

Child-Pugh 评分系统被广泛用于衡量肝硬化严重程度。既往研究已证实 Child-Pugh 评分在预测 HE 发展方面的有效性，拓宽了其在临床实践中

的应用价值[44]。尤其是在 TIPS 术后,Child-Pugh 评分与少肌症评估、术后 PPG 相结合建立的模型,可进一步提升其预测效能(C 指数:0.77 比0.68)[45]。有研究表明,较高 Child-Pugh 评分(>6.5 分)和较小脾脏体积(<773 cm^3)与 TIPS 术后高 HE 风险相关,符合这两个条件患者术后发生 HE 风险可达 40.7%[46]。虽然 Child-Pugh 评分结合了生化标志物和临床判断,但在评估腹水和 HE 时存在主观因素,可能影响评分结果的一致性[47]。此外,该系统并未包含所有与肝脏病理改变相关的因素,尤其是反映肾功能的肌酐和尿素氮。

2.5 MELD 评分

MELD 评分最初用于评估肝硬化患者生存预后,为肝移植等待名单建立优先级标准。组成部分是可量化的实验室结果,使其成为一客观评价指标。如今临床上,MELD 评分的应用已从肝移植评估扩展到对接受 TIPS 患者进行生存预后评估[48]。其在预测 TIPS 术后 HE 发生率方面也很重要。Kim 等[49]发现 MELD 模型 3.0 也可用于 TIPS 术后 HE 预测,其准确性更高。MELD 评分联合肌少症评估建立的 MELD-肌少症评分,对于 HE 患者 30 d 内再入院率有更好的预测效能,再入院患者评分明显更高(25.0 比 19.5)[50]。尽管 MELD 评分很有价值,但其用于肾功能受损或有肝肾综合征患者时,对血清肌酐水平重度依赖可能导致高估 HE 风险[51-53]。

2.6 ALBI 评分

ALBI 评分仅需血清白蛋白和胆红素水平两指标,通过公式“ALBI = log10(胆红素) − 0.085 × 白蛋白”即可计算得出。这两个指标在常规临床检查中容易获取,无需复杂的检测设备和技术,大大提高了临床可操作性。ALBI 评分能有效预测肝硬化患者预后,也能反映患者肝脏储备功能,用于肝癌术前评估患者预后[54-56]。有研究比较了 ALBI 评分、Child-Pugh 评分、MELD 评分和 FIB-4 评分,结果显示 ALBI 评分在预测包括 HE 在内的失代偿事件发生率方面优于其他评分(AUC = 0.86)[57]。另一研究显示,ALBI 评分联合年龄因素相较于单独 ALBI 评分有更高的预测效能(AUC:0.80 比 0.72)[25]。需要注意的是,ALBI 评分在特殊情况下可能会因胆红素或白蛋白异常而影响判断。

2.7 Freiburg TIPS 术后生存指数

Freiburg TIPS 术后生存指数(Freiburg index of post-TIPS survival,FIPS)通过结合生化参数及患者年龄估算 TIPS 术后生存率,关键组成部分包括肌酐、胆红素、白蛋白和年龄[47,58]。FIPS 能够准确识别出 TIPS 术后预后不良高危患者。在训练集、验证集中,高风险组患者中位生存期分别为 5.0 个月、3.1 个月[47]。最初 FIPS 主要应用于预测患者 TIPS 术后生存时间,近期研究扩展了 FIPS 应用范围,提出其可作为一种客观的评分系统评估 TIPS 术后 HE 风险(AUC = 0.744),FIPS 较高患者(FIPS> − 0.97)术后发生 HE 比率显著更高[59]。最新一多中心、大样本、队列研究表明,高 FIPS 患者 TIPS 术后更易发生肝衰竭(18%比 8%),发生包括 HE 在内的急性失代偿事件风险也增加(*HR* = 1.974)[60]。尽管许多研究者看好 FIPS 前景,但 FIPS 缺少 TIPS 手术相关因素和营养状态评估,在广泛应用前还需要进一步验证。

2.8 PPG

除了基于术前资料建立的评分外,手术相关因素也与 HE 密切相关。关于 8 mm 和 10 mm 支架的探讨已持续多年[61],但随着可控直径支架的应用,支架直径可在植入后进一步调整。目前更关注的是术后 PPG 对结局的影响,关键在于如何确定最适合的术后 PPG 目标范围[62-63]。近期一大样本、队列研究表明,将 TIPS 术后 PPG 目标设定在 11~14 mmHg(1 mmHg = 0.133 kPa),或相对于基线降低 20%~50%,可在保证降压效果的同时避免过度分流增加 HE 风险,因此可用于指导可控直径支架的调整[64]。有研究提出,亚扩张小直径 TIPS(6~7 mm)相较“标准”直径 TIPS(8~10 mm)可降低 HE 风险[65]。用 6 mm 球囊对支架亚扩张相较于常规扩展,患者术后 HE 发生率明显降低(11.0%比 29.5%),与预防静脉曲张再出血的效果并无差别[66]。国内有研究比较 7 mm 和 8 mm 支架,发现两者 TIPS 术后 HE 发生率无显著差别[67]。因此,新研发和上市的可控直径支架直径范围也已调整至 6~10 mm,有望在将来实现更加个性化的合理分流。

3 AI 在预测 TIPS 术后 HE 中应用

3.1 AI 潜力

传统的评分系统和临床生化标志物至关重要,但由于数据复杂性,其有效性通常受到限制。大数据出现和计算能力提高为 AI 在医学领域应用铺平了道路。包括机器学习和深度学习算法在内的 AI 技术彻底改变了 HE 风险评估方法。AI 在预测

HE 方面拥有巨大潜力，其模型能够从大规模临床数据集中提取复杂模式，以实现准确的 HE 风险预测。这些模型的准确性得益于其能够同时处理多维数据，包括生物标志物、影像数据和病史资料[68-69]。一项针对 TIPS 患者进行非靶向代谢组学的研究采集术前和术后肝静脉血，通过肝静脉血代谢组学分析的代谢物差异可判断肝脏中发生的肝内分流和生化转化，发现 TIPS 前后肝静脉代谢组差异较大者发生术后 HE 风险更高[70]。集成学习方法如结合多个模型结果，可以减少单个模型偏差，并进一步改善预测性能。Zhang 等[13]采用人工神经网络这一机器学习方法，展示了 AI 模型在预测 HE 患者 28 d 病死率方面有更好的区分度（AUC = 0.837）。

3.2　基于影像数据的 AI 模型

基于 CT 成像数据的 AI 模型已被多项研究证实可用于预测 TIPS 术后 HE 风险[11,26,71]。特别是机器学习算法，其在分析和解释大型影像数据集方面更有优势，不仅能够自动检测和量化重要的影像特征，而且还能通过将这些特征与临床证据相结合提供风险评估。Ronald 等[72]采用 AI 分析了 TIPS 患者腹部 CT 图像，发现与超重或肥胖相关的相对肌肉损失是 TIPS 后死亡的重要风险因素，但与 HE 发作频率间无显著相关性，突显了 AI 简化复杂影像数据集的能力。Cai 等[73]通过 CT 影像评估髂腰肌密度、面积等数据，建立的逆向逐步逻辑回归模型（AUC = 0.743）预测准确性优于 MELD、ALBI 和 Child-Pugh 评分等经典评分系统，髂腰肌密度＜51.24 HU 患者发生 TIPS 术后 HE 风险更高。

整合生化标志物与影像信息的预测模型在 AI 辅助评估 TIPS 后 HE 风险方面取得了显著进展。Zhong 等[12]采用多变量逻辑回归分析识别与 TIPS 后 3 个月内发生 HE 相关独立风险因素，并开发出一人工神经网络模型和预后列线图，能够准确预测接受优先 TIPS 患者术后早期 HE 发作、肝损伤和死亡风险。Ince 等[74]结合临床资料、实验室和影像数据，开发了 3 个基于支持向量机、逻辑回归和 CatBoost 算法的机器学习模型，在识别 TIPS 术后 HE 高危个体方面表现出显著优势。这两项研究均基于单中心、小样本、队列患者数据，样本量仅为 200 余人，建立的预测模型也无外部验证，因此其临床适用性还有待加强。尽管不够完善，但这些预测模型的成功开发，进一步强调了 AI 技术在改善 TIPS 后 HE 风险评估方面的重要作用。

3.3　优化与挑战

在当今医疗领域，AI 预测模型构建、打磨、临床应用以及广泛普及面临一系列复杂且关键环节，这一进程绝非一蹴而就，而是需要经历漫长且严谨的阶段。在模型开发与验证起始阶段，要投入大量资源开展大规模、多中心临床试验研究。通过在不同地域、不同医疗环境下收集海量且多样化临床数据，以此全方位、多维度地检验 AI 模型的可靠性和有效性，确保其在真实世界场景中稳定表现[75]。随着技术在不断实践中持续成熟，以及在试点应用中积累丰富经验，AI 工具有望突破现有局限，在更广泛的医疗场景中大放异彩，从辅助诊断、疾病预测到个性化治疗方案制定等关键环节，都将成为其发挥关键作用的舞台，为医疗行业变革与发展注入强劲动力。

在医疗领域，许多 AI 预测模型，尤其是深度学习模型，因其复杂的结构和高维数据处理能力，常常被视为“黑箱”。这些模型通常无法提供预测过程的直观解释，这在医疗应用中构成了显著挑战。医疗决策过程要求清晰且可解释的依据，以确保医生能够理解和信任所使用的工具。例如 Das 等[76]在阿尔茨海默病诊断中使用了随机森林和支持向量机模型进行预测，尽管这些模型在诊断中表现出 84％灵敏度和 67％特异度，但其纳入的变量及复杂的决策过程使得医生难以理解其模型组建背后的逻辑，从而影响了其在实际临床中应用和推广。

4　结论

综上所述，TIPS 术后 HE 是一种不可忽视的术后并发症，对于患者预后而言，精准的风险预测与有效的预防策略至关重要。传统评分系统虽已奠定基础，但存在局限性，亟需通过组合、优化与补充来提升其预测效能。AI 技术作为一种强有力的工具，在预测 HE 风险方面展现了显著优势和巨大潜力。未来研究应聚焦于构建更加全面且动态的预测模型，通过多中心研究验证其在临床的适用性和可靠性，并将其深度融入患者管理流程，以切实改善患者 TIPS 术后生活质量和生存率，为临床决策提供更为精准、有力的支持。

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