

胸痛风险评分在急性胸痛患者危险分层中应用的研究进展

于菁怡, 邢家璇, 徐雅妮*

山东大学齐鲁医院(第一临床学院), 山东 济南

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摘要

急性胸痛患者在急诊门诊就诊的患者中占比较大, 早期明确诊断并进行危险分层有利于改善患者预后。胸痛病因复杂, 分为心源性胸痛和非心源性胸痛, 其中较常见的为急性冠脉综合征。目前指南推荐的胸痛风险评分包括HEART评分、EDACS评分、ADAPT评分、hs-cTn评分、TIMI评分和GRACE评分, 这些评分各有优劣, 但均缺少我国人群数据支持, 且大多数建立在动态监测肌钙蛋白基础上, 未来有待进一步验证评分效能或创建基于我国人群的危险分层模型。

关键词

急性冠脉综合征, 胸痛风险评分, 危险分层, 预后

Research Progress on the Application of Chest Pain Risk Score in Risk Stratification of Patients with Acute Chest Pain

Jingyi Yu, Jiaxuan Xing, Yani Xu*

Qilu Hospital (The First Clinical College) of Shandong University, Jinan Shandong

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Abstract

Acute chest pain accounts for a large proportion of emergency outpatient patients, and early diagnosis and risk stratification are beneficial to improve patient prognosis. The etiology of chest

*通讯作者。

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pain is complex, including cardiogenic chest pain and non-cardiogenic chest pain, of which acute coronary syndrome is the most common. The chest pain risk scores recommended in the current guidelines include HEART score, EDACS score, ADAPT score, hs-cTn score, TIMI score, and GRACE score. Each of these scores has its advantages and disadvantages, but all of them lack the support of Chinese population data, and most of them are based on dynamic monitoring of troponin. In the future, it is necessary to further validate the scoring efficacy or create a risk stratification model based on Chinese population.

Keywords

Acute Coronary Syndrome, Chest Pain Risk Score, Risk Stratification, Prognosis

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1. 引言

胸痛是指胸部的疼痛不适感, 是许多心血管疾病的共同表现, 如急性冠脉综合征、主动脉夹层、心包炎、肺栓塞等。胸痛分为心源性胸痛和非心源性[1] [2], 终生患病率为 20%至 40% [3], 胸痛症状在女性中更为常见[4], 虽然导致胸痛的原因通常是非心脏源性的, 但冠状动脉疾病(CAD)仍然是导致胸痛患者死亡的主要原因[5]。

国内外胸痛患者的数量仍在持续增加。2017 年至 2022 年间, 我国胸痛中心共收治急性胸痛患者 863 万例, 其中急性心肌梗死患者 194 万例, 平均死亡率为 3.85%, 患者人数较前有所下降, 但死亡率仍较高[6]。在美国, 每年有近 400 万人因胸痛到门诊就诊, 是急诊室就诊的第二大常见原因[7] [8], 每年死亡人数超过 36.5 万人[5]。

胸痛的主要诊断依据是胸痛的性质、部位和持续时间等, 结合病史、心肌损伤标志物、心电图、超声心动图及胸部 CT 等辅助检查确定胸痛的病因。根据发病原因, 选择药物或手术治疗进行干预。如果胸痛因急性冠脉综合征引起, 则需要尽快行冠脉再通治疗, 辅以抗血小板及扩冠药物[9]; 如果病因是主动脉夹层, 则需尽快外科手术[10]; 如果因胃食管反流引起胸痛, 则需使用质子泵抑制剂缓解症状, 症状较重的年轻患者可选择胃底折叠术改善病情[11]。但由于胸痛病因复杂、临床表现多样、缺乏典型特征, 如果不及时采取正确有效的治疗措施, 则会增加患者的死亡风险。因此, 对于胸痛患者而言, 治疗重点是明确病因, 早期将患者按照危险程度分层[12], 及时采取干预措施。为实现这一点, 便需要进行有效且彻底的临床评估。

2. 胸痛常见原因

胸痛病因复杂、临床表现多样、缺乏典型特征, 主要分为心源性胸痛及非心源性胸痛。心源性胸痛包括急性冠脉综合征、主动脉夹层、心包炎, 非心源性胸痛包括胃食管反流病、肺栓塞、肋间神经炎等[2]。其中最常见为急性冠脉综合征, 是冠状动脉急性、持续性缺血缺氧引起的心肌坏死, 在胸痛患者中占比较大, 其预后取决于干预措施的选择和开始干预的时间。治疗以再灌注治疗为主, 包括冠脉介入治疗和溶栓治疗, 并辅以扩冠药物维持[9]。近年来, 我国每年新增胸痛病例至少 50 万例, 死亡率呈明显上升趋势[6]。据统计, 2020 年中国城市居民冠心病死亡率为 126.91/10 万, 农村为 135.88/10 万, 2020 年冠心病死亡率继续 2012 年以来的上升趋势, 农村地区上升明显, 到 2016 年已超过城市水平[13]。急性心梗在

欧美最为常见,美国每年约有 150 万人发生心肌梗死[5]。急性心肌梗死分为 ST 段抬高型心肌梗死(STEMI)和非 ST 段抬高型急性冠脉综合征(NSTE-ACS)。ST 段抬高型心肌梗死在心电图上易于识别,因此目前临床诊断难点主要是区分非 ST 段抬高型急性冠状动脉综合征与非心源性胸痛。

3. 胸痛危险评分

目前指南推荐的胸痛风险评分包括 HEART 评分、EDACS 评分、ADAPT 评分、hs-cTn 评分、TIMI 评分和 GRACE 评分[2]。HEART 评分是急诊胸痛患者的首个风险评分,包括病史、心电图、年龄、危险因素、肌钙蛋白(0 h, 3 h), 7~10 分为高危, 4~6 分为中危, 3 分以下为低危[14]。该评分的最大优点是考虑了典型的 ACS 症状,更符合胸痛患者的早期风险分层过程。EDACS 评分主要包括年龄、性别、危险因素、肌钙蛋白(0 h, 2 h),它简化了 HEART 评分,不需要心电图便可将胸痛病人快速分级,缺点在于特异性低,仅能识别低危患者(评分小于 16 分)[15]。ADAPT 评分主要包括 TIMI 评分 0~1 分、无缺血性心电图改变及肌钙蛋白(0 h, 2 h)[16]。TIMI 评分小于 1 分为低危, 2~4 分为中危, 5~7 分为高危[17]。GRACE 评分包括年龄、心率、收缩压、血清肌酐、心脏骤停、心电图、心肌损伤标志物和 Killip 分级[18],常用于不稳定型心绞痛和非 ST 段抬高型心肌梗死患者,是住院期间或发病后半年内进行死亡风险评估的有效工具。缺点是心肌损伤标志物的值需要在发病时和发病后 1、3、6 小时获得,较为复杂。患者分数<108 分属于低危患者, 108~140 属于中危患者, 140 以上属于高危患者[19]。或直接用肌钙蛋白评价心肌损伤程度,进一步分流患者[20]。

目前国内应用最广的生物标志物是高敏肌钙蛋白(hs-cTn),具有较高敏感度和特异性,是诊断的首选标准,可以更准确地识别和排除心肌损伤。但肌钙蛋白水平可能在心肌梗死后两小时内升高,也可能在 6 小时内不会出现[2]。对于任何生物标志物,患者症状发作后的送检时间可能会影响其对心肌缺血的识别能力。鉴于这一限制,急诊方案通常需要连续的肌钙蛋白结果[21],而大多数评分也建立在连续肌钙蛋白结果的基础上,所以若有新的评分或者化验检查方式可以简化这一步骤,将极大提高急诊和门诊对胸痛患者的分流效率,尽快确定治疗方案,降低死亡率。

然而,尽管在过去几十年中有广泛针对胸痛患者的研究,但快速识别或排除急诊科胸痛患者的急性心肌梗死仍然是一个巨大的挑战[22]。Simms 等人的回顾性研究[23]提出,目前已有的数据库可能无法收集所有八个 GRACE 预测变量[24]。鉴于此提出了 GRACE 风险评分的修改版本,该版本排除了肌酐和 Killip 分级,命名为 Mini-GRACE 评分,简化评分流程,提高临床危险分层效率。国内 Qing 等人在中华内科杂志上发表一篇回顾性研究[25],发现 CHA2DS2-VASc 评分较高的患者有更高的住院死亡率和更多的住院并发症,说明 CHA2DS2-VASc 评分是急性心肌梗死患者住院预后的独立预测因子,其预测价值与 Mini-GRACE 评分相当,可作为急性心肌梗死患者早期快速预后评估的简单工具。以上两个评分不建立在连续肌钙蛋白结果基础上,可早期快速识别高危患者,及时采取有效治疗措施,改善预后。

4. 人工智能在医学领域应用

人工智能是计算机科学的一个分支,随着人工智能不断发展,在医学领域的应用也在不断拓展,能够分析复杂的医疗数据,可用于许多临床场景的诊断、治疗,并预测临床结果[26]。近年来,多个临床领域都有人工智能的参与。Hashimoto 等人所著综述指出可使用人工智能监测术中麻醉深度、控制麻醉、预测事件和风险[27]。Gupta 等人发现深度学习算法可应用于多种药物发现过程[28]。Ellahham 等人研究示人工智能可帮助糖尿病患者更好自我管理,精准控制血糖[29]。国内医疗人工智能面向临床需求,结合医师临床经验,依靠人工智能技术计算、分析和决策能力,为临床诊断与治疗提供精确的智能辅助[30],多所高校医工交叉,将算法广泛应用于医学影像学诊断[31]、神经系统功能障碍和运动障碍分析[32]及康复机器人系统[33]等领域。在心血管医学领域,人工智能在诊断及治疗方面也有极大进展。Yasmin 等人研

究示通过结合算法,人工智能可以用来分析心脏成像技术(如超声心动图、计算机断层扫描、心脏 MRI 等)和心电图记录的原始图像数据。利用逻辑回归(LR)方法构建决策模型来诊断充血性心力衰竭,以及人工智能在早期发现未来死亡率和在不稳定事件中发挥巨大作用,在优化心血管疾病结局方面发挥了至关重要的作用[34]。对于心律失常尤其是房颤病人,人工智能有望实现无创消融治疗[35]。人工智能在介入心脏病学中的应用也不断出现,可评估冠脉狭窄程度,确定治疗方案[36] [37]。Kobayashi 等人[38]进行了一项临床试验,通过将超声心动图不同类型及其与血管参数和蛋白质组学特征相关联进行聚类分析,获得三种表型,后使用马尔默预防项目队列进行外部验证,得到超声心动图表型与心衰事件和心血管死亡的长期风险之间的关联,从而可以通过人工智能预测无症状个体的心力衰竭发病率。

机器学习(Machine Learning, ML)是人工智能的一个子领域,通过计算机模拟人类的学习行为,以获取新的知识或技能[39],也能够对多个数据集进行分析,以发现数据中从未被发现的规律[40]。机器学习可分为三种类型,即监督学习、无监督学习和强化学习[41]。通过机器学习对大数据进行分析,为评估大量复杂的医疗数据提供了相当大的便利[42]。同时,人工智能的出现为患者的治疗带来了新的可能性,通过大数据分析和机器学习,我们能够更准确地预测疾病的进展,并及时调整治疗方案[43]。近期机器学习能够对无症状的左心室收缩功能障碍进行分类[44]、用心电图检测异常心肌舒张[45]且有效地对有心衰风险的患者进行风险分层[46]。在一项针对接受择期非心脏手术的患者单中心研究中,使用机器学习衍生的早期预警系统可在低血压发生之前进行预测,从而降低术中低血压[47]。Pavel 等人[48]通过机器学习算法构建了新生儿癫痫发作识别模型,机器学习组正确识别的癫痫发作比例高于对照组。在一项随机对照试验中,通过机器学习对临床医生进行行为干预,会使癌症患者接受的临终治疗减少,可以改善癌症患者的预后[49]。尽管有这些优势,机器学习在临床实践中的应用依然存在挑战,需要根据实际临床问题对数据进行预处理、模型训练和系统改进[50]。

5. 人工智能在心电领域应用

近年来,应用于心电领域的机器学习预测模型的研究不断增加。一项多中心研究利用病史、心电图和晕厥情况的十个变量来训练和测试模型,来对急诊科患者的晕厥风险进行分层的短期预测[51]。且目前人工智能心电分析技术在识别心律失常、电解质紊乱、心脏瓣膜病、冠心病及循环系统、消化系统等疾病方面有广泛应用,进一步挖掘心电图的深层价值,从而实现多系统疾病的筛查、诊断和治疗[52]。同样,也有研究聚焦于急诊患者心脏骤停的风险预测,利用机器学习构建出了早期骤停预测模型[53]。在美国,急诊科分诊标准严重依赖主观评估,并且对患者进行风险分层的能力有限,一项对照研究成功的利用机器学习构建电子分诊系统,模型通过对大量的急诊就诊次数的学习与训练,使得急诊分诊效率得到提升[54]。目前还有研究不限于院内诊疗,通过机器学习模型最大程度帮助个人保持健康,比如在家里,利用机器学习早期发现疾病、监测对治疗的反应以及对治疗方案的依从性;在诊所或医院,帮助医疗专业人员诊断和调整个体患者的治疗,从而使患者获得最好的预后[50]。

机器学习的应用越来越多的被应用于急性胸痛的患者中,有研究纳入了 5695 例胸痛患者,基于高敏肌钙蛋白 T 的浓度构建模型,将其诊断效能与欧洲指南推荐的 hs-cTnT 的 0/1 和 0/3 小时算法做比较,结果显示机器学习模型诊断效能并不劣于指南的分类算法,并能使分类到中危组的病人的数量减少[55]。有学者对机器学习技术应用于急诊胸痛的成年患者的文章进行了系统综述,发现在诊断急性心肌梗死和预测 MACE 事件方面优于急诊医生的判断和当前的风险分层工具,但很少被整合到实践中,因为许多评估机器学习模型在急诊胸痛患者中的应用的研究存在高偏倚风险[55]。胸痛模型的外部验证结果并不理想,因此在常规诊疗中很少应用。但近年来的机器学习模型,似乎在一定程度上解决了这些问题,他们提出了不同的解决方案。Rohan 等人的研究通过开发并验证了三种机器学习模型,并将不同的机器学习模型

结合,发现了近乎完美的校准,在对患者进行了更精确的分类[56]。Márton 等人通过对胸部 X 线片进行深度学习,对急性胸痛综合征患者进行分类,这种模型可以根据胸部 X 线片对不同病因如急性冠脉综合征、肺栓塞、主动脉夹层所导致的急性胸痛患者进行分类,并在内部和外部测试集中都有良好的表现,能对急性胸痛患者进行更有效的分诊[57]。Martin 等人的研究团队提出一种对高敏肌钙蛋白进行机器学习的算法(MI³ 心肌缺血损伤指数),结合年龄,性别和高敏肌钙蛋白 I 的浓度及变化率,可以给出一个患者诊断为心肌梗死的可能性的值。在测试集中,MI³ 对低危患者的阴性预测值达到了 99.7%,敏感性为 97.8%。这项研究证明了 MI³ 表现优于 ESC 0/3 小时途径,证明通过使用机器学习,可以早期使可疑急性心梗的胸痛患者受益[58]。

心电图目前仍是急性胸痛患者诊疗中不可替代的工具,QRS 波和 ST 段是目前评估的重点。目前的研究已经提出了几个心电图参数对患者的住院的随访结局具有预后价值[59] [60]。深度学习是人工智能的其中一个领域,它是由多个处理层组成的计算模型,能对多个抽象的数据进行深度学习[61]。如果能够采用人工智能技术来评估这些参数,特别是能在预测患者预后方面起作用,成为了重要的研究方向[62]。

6. 展望

尽管当前指南推荐的胸痛风险评分种类多样,效能较好,但大多数评分建立在连续肌钙蛋白基础上,且均不包含中国人群数据。我国急诊接诊量大,医患信息不对等导致部分患者依从性欠佳,从而限制了以上评分在中国医疗环境中的使用。因此,未来的研究应聚焦于使用中国人群数据验证评分效能,或基于我国医疗现状,创建新的风险预测模型以评估患者病情,指导治疗并改善患者预后。

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