·专题综述·

新型血液炎症标志物与缺血性卒中出血性转化关系研究进展

黄云秀 王亚楠 刘东 吴波 刘峻峰

【摘要】 出血性转化是缺血性卒中的自然病程或静脉溶栓、机械取栓等治疗的严重并发症之一，增加患者不良预后风险，影响临床治疗决策。血脑屏障损伤是出血性转化的核心机制，炎症反应通过激活内皮细胞、招募中性粒细胞和巨噬细胞等免疫细胞，释放蛋白酶、活性氧等炎性介质，加剧血管损伤和血脑屏障损伤，促进出血性转化。血液炎症标志物可反映这一病理改变过程，为出血性转化的早期识别和风险分层提供重要信息。经典炎症标志物如基质金属蛋白酶-9、铁蛋白等已被证实可用于预测出血性转化，中性粒细胞明胶酶相关脂质运载蛋白、高迁移率族蛋白B1和核苷酸结合寡聚化结构域样受体蛋白3炎症小体等新型标志物在出血性转化中的作用机制及预测潜力逐渐成为研究热点。本文聚焦新型血液炎症标志物，阐述其与出血性转化的临床关联及研究进展，旨在为出血性转化的机制解析、精准预测及个性化治疗提供依据。

【关键词】 缺血性卒中； 脑出血； 炎症； 生物标记； 血液； 综述

Research progress on the relationship between novel blood inflammatory markers and hemorrhagic transformation after ischemic stroke

HUANG Yun-xiu[1], WANG Ya-nan[2], LIU Dong[3], WU Bo[1], LIU Jun-feng[1]

[1]Department of Neurology, [2]Center of Cerebrovascular Diseases, West China Hospital, Sichuan University, Chengdu 610041, Sichuan, China

[3]Department of Neurology, The Second People's Hospital of Deyang, Deyang 618000, Sichuan, China

HUANG Yun-xiu and WANG Ya-nan contributed equally to the article

Corresponding author: LIU Jun-feng (Email: junfengliu225@outlook.com)

【Abstract】 Hemorrhagic transformation (HT) is one of the severe complications of ischemic stroke, which may occur either during the natural course or as a consequence of treatments such as thrombolysis and thrombectomy. HT is associated with poor prognosis after ischemic stroke and influences clinical treatment decisions. Disruption of blood-brain barrier (BBB) has been demonstrated as the main mechanism underlying HT. Inflammatory responses contribute to this process by activating endothelial cells, recruiting immune cells such as neutrophils and macrophages, and releasing inflammatory mediators including proteases and reactive oxygen species, which further exacerbate vascular injury and BBB permeability, thereby promoting HT. Blood inflammatory markers may reflect these pathological processes and offer valuable biological information for early identification and risk stratification of HT. Classical inflammatory markers, such as matrix metalloproteinase-9 (MMP-9) and ferritin, have been demonstrated predictive value for HT. Recently increasing attention has been paid to investigate the mechanism and predictive potential of novel markers, such as neutrophil gelatinase-associated lipocalin (NGAL), high-mobility group box 1 (HMGB1) and nucleotide-binding oligomerization domain-like receptor protein 3 (NLRP3) inflammasome, for predicting HT. This review focuses on the novel blood inflammatory markers and systematically describes their correlation with HT, with the aim of providing a scientific basis for the mechanism investigation,

doi:10.3969/j.issn.1672-6731.2025.05.002

基金项目：国家自然科学基金资助项目（项目编号：82371323）；四川大学华西医院专职博士后研发基金资助项目（项目编号：2024HXBH139）；2023年四川省德阳市社会发展领域重点研发指导类项目（项目编号：2023SZZ037）

作者单位：610041 成都，四川大学华西医院神经内科（黄云秀、吴波、刘峻峰），脑血管病中心（王亚楠）；618000 四川省德阳市第二人民医院神经内科（刘东）

黄云秀与王亚楠对本文有同等贡献

通讯作者：刘峻峰，Email：junfengliu225@outlook.com

accurate prediction and individualized therapeutic strategies of HT.

【Key words】 Ischemic stroke; Cerebral hemorrhage; Inflammation; Biomarkers; Blood; Review

This study was supported by the National Natural Science Foundation of China (No. 82371323), Postdoctor Research Fund of West China Hospital, Sichuan University (No. 2024HXBH139), and 2023 Key Research and Development Guidance Project in the Field of Social Development of Deyang in Sichuan (No. 2023SZZ037).

Conflicts of interest: none declared

脑卒中是全球病残和病死的首位病因,在我国呈现高患病率、高发病率和高病死率的特点[1]。最新流行病学调查数据显示,2020年我国脑卒中患病例数达1780万例,新发340万例,死亡230万例,给患者家庭和社会带来沉重负担[2]。出血性转化(HT)是缺血性卒中的严重并发症,可能是缺血性卒中自然病程的一部分,也可能发生于治疗后(如机械取栓、静脉溶栓、抗血小板和抗凝治疗等)[3-4]。出血性转化不仅是缺血性卒中患者预后不良的危险因素[5],而且是导致上述治疗方法临床应用受限的重要原因[6]。既往认为血脑屏障损伤是出血性转化的关键发生机制,炎症反应在血脑屏障损伤过程中发挥重要作用,可引起内皮细胞激活及炎症反应,导致紧密连接蛋白破坏和血脑屏障通透性增加[7];此外,炎症反应还通过激活和招募多种炎性细胞,释放蛋白酶和氧自由基等炎性介质,引起血脑屏障和血管损伤,进而增加出血性转化风险[8-9]。某些血液标志物可以反映炎症反应机制,作为出血性转化早期诊断与风险评估的重要工具。本文综述缺血性卒中出血性转化相关血液炎症标志物最新研究进展,旨在提高对出血性转化发生机制的理解,为出血性转化标志物研究提供新的方向。

一、基质降解效应因子

1.基质金属蛋白酶 基质金属蛋白酶(MMPs)是一类锌离子依赖性内肽酶,其核心功能是降解细胞外基质(ECM)。脑缺血时基质金属蛋白酶-9(MMP-9)以酶原形式从神经元、神经胶质细胞及浸润的中性粒细胞中释放,特异性水解Ⅳ型胶原(基底膜主要结构蛋白)并破坏内皮细胞间紧密连接,其血清水平与血脑屏障通透性呈正相关[10]。动物实验显示,安宫牛黄丸通过抑制大脑中动脉闭塞(MCAO)模型大鼠血清MMP-9活性,减少细胞外基质降解,减轻延迟静脉溶栓后血脑屏障损伤程度并降低出血性转化发生率[11]。临床研究显示,发生出血性转化的急性缺血性卒中患者发病24 h内血清MMP-9水平显著高于非出血性转化患者[12]。对于未接受再灌注治疗的急性缺血性卒中患者,血清MMP-9水平升高已被证实是出血性转化的危险因素[13];接受静脉溶栓治疗的患者,血清MMP-9联合尿酸可显著提高对出血性转化的预测能力[14];接受机械取栓的颅内大动脉闭塞患者,出血性转化组入院时和发病6 h血清MMP-9水平显著高于非出血性转化组[15];前循环大血管闭塞患者,入院时血清MMP-9水平升高且与脑实质血肿(PH)相关[16]。基于液体活检技术的研究显示,机械取栓术前缺血区侧支循环MMP-9水平升高,且与出血性转化呈正相关,提示MMP-9可能通过介导侧支循环的血管内炎症反应,参与超早期出血性转化[17]。一项纳入11项临床研究的Meta分析显示,MMP-9联合纤维连接蛋白可以早期识别急性缺血性卒中出血性转化高危患者[18]。亦有研究显示,*MMP9*基因位点之间的协同作用可显著增加发病14 d内出血性转化风险[19];MMP-9相关微小RNA(miRNA)如miRNA-21-5p、miRNA-206和miRNA-3123在心源性卒中出血性转化患者中显著表达上调[20],miRNA-206可能通过上调*MMP9*基因表达加速血脑屏障损伤,增加自发性出血性转化风险,为研究出血性转化的遗传学机制提供新的视角[21]。降低MMP-9水平是否可以减轻血脑屏障损伤,进而减少出血性转化的发生?一项多中心Ⅱ期临床试验显示,Otaplimastat(MMP-9抑制剂)联合阿替普酶治疗急性缺血性卒中并未显著增加出血性转化风险,但其能否降低出血性转化风险尚待更大规模临床试验进一步验证[22]。尽管有研究显示低剂量阿替普酶联合自由基清除剂依达拉奉无法抑制静脉溶栓后血清MMP-9水平升高[23];但一项纳入3项临床研究共1118例急性缺血性卒中患者的Meta分析证实,依达拉奉可以显著降低缺血性卒中出血性转化风险[24]。此外,常压高氧联合

血管内治疗可以降低缺血性卒中发病后24 h和7 d血清MMP-9水平及术后24 h对比剂外渗率，提示常压高氧可通过调控MMP-9通路降低出血性转化风险[25]。未来尚待进一步探索MMP-9作为出血性转化治疗靶点的临床价值。

2.中性粒细胞明胶酶相关脂质运载蛋白　中性粒细胞明胶酶相关脂质运载蛋白（NGAL）是脂质运载蛋白超家族成员，其在介导天然免疫反应、炎症反应、铁代谢、细胞迁移与分化等方面发挥重要作用[26]。体外研究和动物实验显示，NGAL可直接降低内皮细胞跨内皮电阻并增加其通透性；而*NGAL*基因缺陷的大脑中动脉闭塞模型小鼠则表现出更轻微的神经炎症反应和血脑屏障损伤，提示NGAL可直接作用于内皮细胞或通过活化星形胶质细胞、激活炎症小体等途径参与血脑屏障损伤[27-28]。光血栓性卒中大鼠模型显示，NGAL通过高迁移率族蛋白B1（HMGB1）相关通路诱导内皮细胞铁死亡，进而导致血脑屏障损伤[29]。缺血性卒中患者入院时血清NGAL水平与静脉溶栓后24 h出血性转化呈正相关，且出血性转化患者血清NGAL水平亦与入院时血清铁蛋白水平呈正相关[29]。尽管已证实NGAL抑制剂（ZINC006440089）在血栓栓塞性脑卒中大鼠模型中可减轻血脑屏障损伤，但尚缺乏临床研究验证其疗效和安全性[29-30]。

3.肝配蛋白A1　肝配蛋白A1（ephrin A1）作为糖基磷脂酰肌醇（GPI）锚定蛋白，通过肝细胞受体介导的双向信号转导机制调控细胞迁移、黏附等生理过程[31]。病理状态（如病毒感染）下，ephrin A1通过下调细胞间紧密连接蛋白和黏连蛋白表达，破坏内皮细胞间的结构完整性，从而导致组织屏障功能受损[32]；还可通过激活促红细胞生成素产生肝细胞受体A2（EphA2），促进血管生成素-2（Ang-2）释放，破坏血管内皮完整性并加剧炎症反应[33]。大脑中动脉闭塞小鼠模型显示，血清ephrin A1水平与血脑屏障损伤和脑水肿程度呈正相关[34]。前瞻性队列研究显示，发病7 d内发生脑实质血肿的缺血性卒中患者入院时血清ephrin A1水平显著高于未发生脑实质血肿患者，提示ephrin A1具有识别出血性转化高危患者的潜力[35]。

二、损伤相关分子模式触发因子

1.高迁移率族蛋白B1　HMGB1是一种非组蛋白核蛋白，生理状态下参与DNA修复及基因转录调控；脑组织缺氧缺血等病理状态下从坏死细胞中释放，与Toll样受体（TLR）、晚期糖基化终末产物受体（RAGE）等结合，激活下游炎症反应通路并触发炎症级联反应、氧化应激反应，最终导致血脑屏障损伤[36]。HMGB1可直接诱导小胶质细胞向促炎表型转化，促进促炎因子释放，加重神经血管单元（NVU）损伤[37]；褪黑素则通过抑制HMGB1释放维持血脑屏障完整性，降低出血性转化风险[38]；动物实验亦显示，甘草酸（HMGB1抑制剂）通过抑制过氧亚硝酸盐介导的HMGB1/TLR2通路，降低大脑中动脉闭塞模型大鼠出血性转化风险[39]，上述研究均提示HMGB1有可能成为出血性转化的潜在治疗靶点。有研究发现，急性缺血性卒中患者发病24 h内血清HMGB1水平与过氧亚硝酸盐水平呈正相关，支持HMGB1可能参与氧自由基介导的出血性转化过程[39]。亦有研究显示，与静脉溶栓后24 h未发生出血性转化的患者相比，发生出血性转化患者入院时血清HMGB1水平显著升高，提示其可作为预测静脉溶栓后出血性转化风险的生物学标志物[40]。

2.S-100蛋白B　S-100蛋白B（S-100B）主要表达于中枢神经系统星形胶质细胞和少突胶质细胞，生理状态下参与细胞内钙稳态维持、细胞代谢及信号转导等[41]；脑缺血等病理状态下，S-100B在小胶质细胞中呈高表达，促进小胶质细胞向促炎M1型极化，促进促炎因子释放，触发核因子-κB（NF-κB）等炎症反应通路，诱发炎症反应[42]。脂多糖诱导的神经炎症大鼠模型显示，S-100B通过激活NF-κB等信号转导通路增强炎症级联反应，使血脑屏障通透性增加[43]。一项多中心前瞻性队列研究显示，急性缺血性卒中发病24 h内血清S-100B水平与症状性出血性转化风险呈正相关[44]。接受静脉溶栓的急性缺血性卒中患者发病24 h内发生出血性转化者其入院时血清S-100B水平显著高于非出血性转化者[45-46]。一项多中心前瞻性研究发现，血清S-100B水平＞0.20 ng/ml是静脉溶栓后出血性转化的危险因素[47]。但一项Meta分析显示，血清S-100B预测出血性转化的准确性较低，其预测价值尚待进一步探索[48]。

三、铁超载损伤标志物

血清铁蛋白是一种反映机体铁存储的蛋白质，主要表达于巨噬细胞和肝细胞。病理状态下，铁蛋白异常释放可以导致组织铁超载，加剧氧化应激反应和炎症反应[49]。大脑中动脉闭塞大鼠模型显示，铁超载通过升高MMP-9水平破坏血脑屏障完整性，

诱发出血性转化，铁螯合剂去铁胺可以有效降低MMP-9水平，减少出血性转化的发生[50]。铁死亡抑制剂Ferrostatin-1通过降低NGAL水平，减轻静脉溶栓后血脑屏障损伤，提示铁蛋白通过调控血管内皮细胞铁死亡途径参与出血性转化的病理过程[29]。研究发现，急性缺血性卒中后发生出血性转化者发病48 h内血清铁蛋白水平显著升高，且铁蛋白>171.80 ng/ml是症状性出血性转化的危险因素[51]。一项纳入30项临床研究的Meta分析显示，基线血清铁蛋白水平升高可以预测急性缺血性卒中出血性转化，其合并诊断比值比（DOR）为24.032（95%CI：2.557～225.871），但是由于95%CI宽泛，其独立诊断效能有限，需与MMP-9等高特异性标志物联合应用以提高预测效能[48]。因此，铁蛋白作为出血性转化的独立预测生物学标志物尚待进一步探索。

四、神经胶质损伤标志物

胶质纤维酸性蛋白（GFAP）是星形胶质细胞的主要中间丝蛋白，参与细胞骨架构成，在神经胶质细胞激活、血脑屏障通透性调控，以及神经炎症反应中发挥重要作用[52]。泛素羧基末端水解酶L1（UCH-L1）表达于神经细胞胞质，通过泛素化清除体内多余蛋白，其血清水平可以反映神经细胞损伤程度[53]。GFAP与UCH-L1已被美国食品与药品管理局（FDA）批准用于辅助评估颅脑创伤（TBI），并指导轻型颅脑创伤的影像学检查决策[54-55]。一项多中心前瞻性队列研究显示，静脉溶栓24 h内血清GFAP和UCH-L1水平均与出血性转化呈正相关[56]。亦有研究显示，机械取栓术后24 h血清GFAP水平与症状性出血性转化呈正相关[57]，血清GFAP和UCH-L1水平与脑实质血肿显著相关[58]。因此，认为GFAP和UCH-L1有望成为预测出血性转化的血液炎症标志物。

五、炎症小体相关标志物

核苷酸结合寡聚化结构域样受体蛋白3（NLRP3）是核苷酸结合寡聚化结构域（NOD）样受体蛋白家族成员，是先天性免疫系统的一种模式识别受体（PRR）。NLRP3通过与凋亡相关斑点样蛋白质（ASC）和半胱氨酸蛋白酶-1组装形成NLRP3炎症小体，介导白细胞介素-1β和18（IL-1β和IL-18）等促炎因子成熟和释放，增强炎症级联反应[59]。高血糖-脑缺血再灌注小鼠模型显示，NLRP3炎症小体异常活化通过促进血管内皮细胞焦亡，增加静脉溶栓后血脑屏障通透性[60]。而抑制NLRP3炎症小体活化可抑制小胶质细胞向促炎M1型极化，阻断细胞焦亡通路，降低大脑中动脉闭塞模型大鼠延迟静脉溶栓后出血性转化发生率[61]。组织蛋白酶B（CTSB）是一种溶酶体内半胱氨酸蛋白水解酶，生理状态下参与蛋白降解与细胞稳态调控；脑缺血或脑出血等病理状态下，铁超载、氧自由基增加，干扰溶酶体膜稳定性，导致CTSB释放至胞质[62]。脑出血大鼠模型显示，血肿周围CTSB动态表达上调与NLRP3炎症小体活化同步，提示CTSB通过活化NLRP3炎症小体、诱导MMPs释放，引起炎症级联反应，进而损伤血脑屏障[63]。此外，高血糖相关出血性转化小鼠模型显示，CTSB可能是高血糖引发神经血管损伤的关键分子机制[60]。临床研究发现，急性缺血性卒中发病后6～24 h血清NLRP3水平呈动态升高趋势，提示NLRP3可能参与脑卒中后早期炎症反应进程[64]。亦有研究显示，CTSB与急性缺血性卒中患者神经功能缺损程度呈正相关[65]。但一项针对前循环梗死的小样本队列研究显示，脑实质血肿组与非脑实质血肿组血清CTSB和NLRP3水平无明显差异[66]。因此，CTSB和NLRP3作为出血性转化的血液炎症标志物尚待进一步探究。

六、其他

紧密连接蛋白如闭合蛋白（occludin）和紧密连接蛋白5（claudin-5）是血脑屏障内皮细胞间连接的核心成分，其功能异常导致血脑屏障通透性改变，与出血性转化密切相关[67]。尽管紧密连接蛋白自身并不介导炎症反应，但作为MMPs、ephrin A1等炎性因子的作用靶点，可反映血脑屏障损伤程度及潜在的神经炎症状态[68]。大脑中动脉闭塞小鼠模型显示，组织型纤溶酶原激活物（t-PA）通过激活血小板衍生生长因子-CC（PDGF-CC）信号转导通路，诱导occludin S490位点磷酸化，导致血脑屏障通透性增加，诱发出血性转化[69]。临床研究显示，发生出血性转化的缺血性卒中患者入院时血清闭合蛋白水平高于未发生出血性转化的患者[70-71]。接受血管再通治疗（静脉溶栓、机械取栓、静脉溶栓桥接机械取栓）的患者中，治疗36 h内发生出血性转化者血清闭合蛋白水平仍较高，且联合入院时血清闭合蛋白、Alberta脑卒中计划早期CT评分（ASPECTS）、血管再通治疗方式构建风险预测模型，对出血性转化风险预测具有较高的准确性[67]。此外，还有研究发现，接受机械取栓术的前循环大血管闭塞患者入院时血清claudin-5水平与发病7 d内出血性转化相

关[16],且发病12 h内血清claudin-5水平可以有效预测48 h内出血性转化风险[72],表明血清紧密连接蛋白在预测出血性转化方面具有良好应用前景。其他标志物方面,出血性转化患者入院后24和48 h和肽素(copeptin)水平高于非出血性转化患者[73];基线蛋白羰基化(PC)水平可以预测缺血性卒中发病后48 h的出血性转化风险[74]。但是由于样本量均较小,这些标志物能否作为出血性转化的血液炎症标志物尚待进一步探索。

综上所述,缺血性卒中出血性转化的病理生理学机制涉及多维度炎症反应,血脑屏障损伤是核心环节。血液炎症标志物通过不同炎症反应通路参与出血性转化的发生,联合应用可显著提高出血性转化的预测效能。部分标志物如MMP-9目前已进入临床试验阶段,提示其潜在应用价值。然而,现有研究存在诸多局限性,如部分血液炎症标志物的独立预测效能有限、作用机制尚未阐明,且靶向干预策略缺乏大规模临床试验验证等。随着新技术如液体活检等的应用,针对侧支循环损伤的研究可能为出血性转化的机制研究提供新的思路。未来将深入探索血液炎症标志物动态变化及相互作用,进一步理解出血性转化的炎症机制,并构建动态综合风险预测模型;同时聚焦关键炎症反应通路的靶向干预研究,推动出血性转化风险分层与个性化治疗的发展。

利益冲突 无

参 考 文 献

[1] Wu S, Liu M. Global burden of stroke: dynamic estimates to inform action[J]. Lancet Neurol, 2024, 23:952-953.

[2] Tu WJ, Zhao Z, Yin P, Cao L, Zeng J, Chen H, Fan D, Fang Q, Gao P, Gu Y, Tan G, Han J, He L, Hu B, Hua Y, Kang D, Li H, Liu J, Liu Y, Lou M, Luo B, Pan S, Peng B, Ren L, Wang L, Wu J, Xu Y, Xu Y, Yang Y, Zhang M, Zhang S, Zhu L, Zhu Y, Li Z, Chu L, An X, Wang L, Yin M, Li M, Yin L, Yan W, Li C, Tang J, Zhou M, Wang L. Estimated burden of stroke in China in 2020[J]. JAMA Netw Open, 2023, 6:e231455.

[3] Álvarez-Sabín J, Maisterra O, Santamarina E, Kase CS. Factors influencing haemorrhagic transformation in ischaemic stroke[J]. Lancet Neurol, 2013, 12:689-705.

[4] Chinese Society of Neurology; Chinese Stroke Society. Consensus on diagnosis and treatment of hemorrhagic transformation after acute ischemic stroke in China 2019[J]. Zhonghua Shen Jing Ke Za Zhi, 2019, 52:252-265.[中华医学会神经病学分会, 中华医学会神经病学分会脑血管病学组. 中国急性脑梗死后出血转化诊治共识2019[J]. 中华神经科杂志, 2019, 52:252-265.]

[5] Wang Y, Maeda T, You S, Chen C, Liu L, Zhou Z, Robinson TG, Lindley RI, Delcourt C, Mair G, Wardlaw JM, Chalmers JP, Arima H, Huang Y, Kim JS, Lavados PM, Lee TH, Levi C, Parsons MW, Martins SC, Pandian JD, Pontes-Neto OM, Sharma VK, Nguyen TH, Wang J, Wu S, Liu M, Anderson CS, Chen X; ENCHANTED Investigators. Patterns and clinical implications of hemorrhagic transformation after thrombolysis in acute ischemic stroke: results from the ENCHANTED study[J]. Neurology, 2024, 103:e210020.

[6] Wu S, Wu B, Liu M, Chen Z, Wang W, Anderson CS, Sandercock P, Wang Y, Huang Y, Cui L, Pu C, Jia J, Zhang T, Liu X, Zhang S, Xie P, Fan D, Ji X, Wong KL, Wang L; China Stroke Study Collaboration. Stroke in China: advances and challenges in epidemiology, prevention, and management[J]. Lancet Neurol, 2019, 18:394-405.

[7] Liu C, Xie J, Sun S, Li H, Li T, Jiang C, Chen X, Wang J, Le A, Wang J, Li Z, Wang J, Wang W. Hemorrhagic transformation after tissue plasminogen activator treatment in acute ischemic stroke[J]. Cell Mol Neurobiol, 2022, 42:621-646.

[8] Li Q, Ye J, Li Z, Xiao Q, Tan S, Hu B, Jin H. The role of neutrophils in tPA thrombolysis after stroke: a malicious troublemaker[J]. Front Immunol, 2024, 15:1477669.

[9] Liu Q, Shi K, Wang Y, Shi FD. Neurovascular inflammation and complications of thrombolysis therapy in stroke[J]. Stroke, 2023, 54:2688-2697.

[10] Bani-Sadr A, Mechtouff L, De Bourguignon C, Mauffrey A, Boutelier T, Cho TH, Cappucci M, Ameli R, Hermier M, Derex L, Nighoghossian N, Berthezene Y. Blood-brain barrier permeability and kinetics of inflammatory markers in acute stroke patients treated with thrombectomy[J]. Neurology, 2023, 101:e502-e511.

[11] Chen H, Luo Y, Tsoi B, Gu B, Qi S, Shen J. Angong Niuhuang Wan reduces hemorrhagic transformation and mortality in ischemic stroke rats with delayed thrombolysis: involvement of peroxynitrite-mediated MMP-9 activation[J]. Chin Med, 2022, 17:51.

[12] Yuan R, Tan S, Wang D, Wu S, Cao X, Zhang S, Wu B, Liu M. Predictive value of plasma matrix metalloproteinase-9 concentrations for spontaneous haemorrhagic transformation in patients with acute ischaemic stroke: a cohort study in Chinese patients[J]. J Clin Neurosci, 2018, 58:108-112.

[13] Ling C, Cao S, Kong X. Changes of FSTL1 and MMP-9 levels in patients with acute cerebral infarction and its relationship with hemorrhagic transformation[J]. J Clin Neurosci, 2022, 99:164-168.

[14] Fu Y, Zheng S, Kong H, Ying M, Chen H, Wang J, Yuan X. Clinical value of combined detection of UA and MMP-9 in evaluating bleeding transformation and prognosis after thrombolysis in acute cerebral infarction[J]. Appl Biochem Biotechnol, 2022, 194:5236-5254.

[15] Wang D, Wang GJ, Zhao XY, Zhang J. Clinical study of serum MMP-9 in predicting bleeding transformation in large vessel occlusive stroke patients after mechanical thrombectomy[J]. Zhonghua Lao Nian Xin Nao Xue Guan Bing Za Zhi, 2023, 25:720-724.[王丹, 王功锦, 赵学渊, 张晶. 血清基质金属蛋白酶9预测大血管闭塞性脑卒中患者机械取栓术后出血转化的临床研究[J]. 中华老年心脑血管病杂志, 2023, 25:720-724.]

[16] Iwamoto T, Kitano T, Oyama N, Yagita Y. Predicting hemorrhagic transformation after large vessel occlusion stroke in the era of mechanical thrombectomy[J]. PLoS One, 2021, 16:e0256170.

[17] Kollikowski AM, Pham M, März AG, Feick J, Vogt ML, Xiong Y, Strinitz M, Vollmuth C, Essig F, Neugebauer H, Haeusler KG, Hametner C, Zimmermann L, Stoll G, Schuhmann MK. MMP-9 release into collateral blood vessels before endovascular thrombectomy to assess the risk of major intracerebral

haemorrhages and poor outcome for acute ischaemic stroke: a proof-of-concept study[J]. EBioMedicine, 2024, 103:105095.
[18] Wang L, Deng L, Yuan R, Liu J, Li Y, Liu M. Association of matrix metalloproteinase 9 and cellular fibronectin and outcome in acute ischemic stroke: a systematic review and Meta-analysis [J]. Front Neurol, 2020, 11:523506.
[19] Yi X, Sui G, Zhou Q, Wang C, Lin J, Chai Z, Zhou J. Variants in matrix metalloproteinase - 9 gene are associated with hemorrhagic transformation in acute ischemic stroke patients with atherothrombosis, small artery disease, and cardioembolic stroke[J]. Brain Behav, 2019, 9:e01294.
[20] Zheng L, Xiong Y, Liu J, Yang X, Wang L, Zhang S, Liu M, Wang D. MMP-9-related microRNAs as prognostic markers for hemorrhagic transformation in cardioembolic stroke patients[J]. Front Neurol, 2019, 10:945.
[21] Song X, Liu J, Wang Y, Zheng L, Liu M. Serum microRNA miR-491-5p/miR-206 is correlated with poor outcomes/spontaneous hemorrhagic transformation after ischemic stroke: a case control study[J]. Brain Sci, 2022, 12:999.
[22] Kim JS, Lee KB, Park JH, Sung SM, Oh K, Kim EG, Chang DI, Hwang YH, Lee EJ, Kim WK, Ju C, Kim BS, Ryu JM; SAFE-TPA Investigators. Safety and efficacy of otaplimastat in patients with acute ischemic stroke requiring tPA (SAFE-TPA): a multicenter, randomized, double - blind, placebo - controlled phase 2 study[J]. Ann Neurol, 2020, 87:233-245.
[23] Tsuruoka A, Atsumi C, Mizukami H, Imai T, Hagiwara Y, Hasegawa Y. Effects of edaravone, a free radical scavenger, on circulating levels of MMP-9 and hemorrhagic transformation in patients with intravenous thrombolysis using low-dose alteplase [J]. J Stroke Cerebrovasc Dis, 2014, 23:2894-2899.
[24] Kashbour M, Shata A, Wagdy M, Alnajjar AZ, Aldemerdash MA, Tarakhan H, Abouelmagd ME. Efficacy and safety of edaravone dexborneol in acute ischemic stroke: systematic review and meta - analysis of randomized controlled trials [J]. Naunyn Schmiedebergs Arch Pharmacol, 2025.[Epub ahead of print]
[25] Li W, Hu W, Yuan S, Chen J, Wang Q, Ding J, Chen Z, Qi Z, Han J. Enhancing blood-brain barrier integrity in patients with acute ischemic stroke via normobaric hyperoxia[J]. J Am Heart Assoc, 2024, 13:e036474.
[26] Zhao RY, Wei PJ, Sun X, Zhang DH, He QY, Liu J, Chang JL, Yang Y, Guo ZN. Role of lipocalin 2 in stroke[J]. Neurobiol Dis, 2023, 179:106044.
[27] Jin M, Kim JH, Jang E, Lee YM, Soo Han H, Woo DK, Park DH, Kook H, Suk K. Lipocalin - 2 deficiency attenuates neuroinflammation and brain injury after transient middle cerebral artery occlusion in mice [J]. J Cereb Blood Flow Metab, 2014, 34:1306-1314.
[28] Li J, Xu P, Hong Y, Xie Y, Peng M, Sun R, Guo H, Zhang X, Zhu W, Wang J, Liu X. Lipocalin - 2 - mediated astrocyte pyroptosis promotes neuroinflammatory injury via NLRP3 inflammasome activation in cerebral ischemia/reperfusion injury [J]. J Neuroinflammation, 2023, 20:148.
[29] Liu J, Pang SY, Zhou SY, He QY, Zhao RY, Qu Y, Yang Y, Guo ZN. Lipocalin-2 aggravates blood-brain barrier dysfunction after intravenous thrombolysis by promoting endothelial cell ferroptosis via regulating the HMGB1/Nrf2/HO-1 pathway[J]. Redox Biol, 2024, 76:103342.
[30] Laohavisudhi K, Sriwichaiin S, Attachaipanich T, Wittayachamnankul B, Chattipakorn N, Chattipakorn S. Mechanistic insights into Lipocalin-2 in ischemic stroke and hemorrhagic brain injury: integrating animal and clinical studies [J]. Exp Neurol, 2024, 379:114885.
[31] Wu Y, Du Z, Mou J, Qiu X, Chen J, Cai S, Ren D, Xiao F, Zhou G, Yuan C. The functions of EphA1 receptor tyrosine kinase in several tumors[J]. Curr Med Chem, 2023, 30:2340-2353.
[32] Shin JM, Han MS, Park JH, Lee SH, Kim TH, Lee SH. The EphA1 and EphA2 signaling modulates the epithelial permeability in human sinonasal epithelial cells and the rhinovirus infection induces epithelial barrier dysfunction via EphA2 receptor signaling[J]. Int J Mol Sci, 2023, 24:3629.
[33] Khan N, Kumar V, Li P; RAPIDS Study Group; Schlapbach LJ, Boyd AW, Coulthard MG, Woodruff TM. Inhibiting Eph/ephrin signaling reduces vascular leak and endothelial cell dysfunction in mice with sepsis[J]. Sci Transl Med, 2024, 16:eadg5768.
[34] Chen F, Liu Z, Peng W, Gao Z, Ouyang H, Yan T, Ding S, Cai Z, Zhao B, Mao L, Cao Z. Activation of EphA4 induced by EphrinA1 exacerbates disruption of the blood - brain barrier following cerebral ischemia - reperfusion via the Rho/ROCK signaling pathway[J]. Exp Ther Med, 2018, 16:2651-2658.
[35] Wu X, Tao W, Wang Y, Wu Q, Ye C, Song X, Guo X, Liu J. Increased serum EphrinA1 is associated with parenchymal hematoma after ischemic stroke[J]. Cerebrovasc Dis, 2023, 52:651-657.
[36] Nishibori M, Wang D, Ousaka D, Wake H. High mobility group box-1 and blood-brain barrier disruption[J]. Cells, 2020, 9:2650.
[37] Li J, Wang Z, Li J, Zhao H, Ma Q. HMGB1: a new target for ischemic stroke and hemorrhagic transformation [J]. Transl Stroke Res, 2025, 16:990-1015.
[38] Chen S, Sun Y, Li F, Zhang X, Hu X, Zhao X, Li Y, Li H, Zhang J, Liu W, Zheng GQ, Jin X. Modulation of α7nAchR by melatonin alleviates ischemia and reperfusion - compromised integrity of blood - brain barrier through inhibiting HMGB1 - mediated microglia activation and CRTC1 - mediated neuronal loss[J]. Cell Mol Neurobiol, 2022, 42:2407-2422.
[39] Chen H, Guan B, Wang B, Pu H, Bai X, Chen X, Liu J, Li C, Qiu J, Yang D, Liu K, Wang Q, Qi S, Shen J. Glycyrrhizin prevents hemorrhagic transformation and improves neurological outcome in ischemic stroke with delayed thrombolysis through targeting peroxynitrite - mediated HMGB1 signaling[J]. Transl Stroke Res, 2020, 11:967-982.
[40] Zhu YY, Liu J, Wang J, Liu DL, Yun Y, Wen L, Wang ZQ, Kang BQ. High - mobility group box - 1 protein predicts hemorrhagic transformation after intravenous thrombolysis in patients with acute ischemic stroke[J]. Guo Ji Nao Xue Guan Bing Za Zhi, 2019, 27:881-885.[朱远远, 刘杰, 王进, 刘大磊, 云宇, 闻亮, 王志强, 康保全. 高迁移率族蛋白B1预测急性缺血性卒中静脉溶栓后出血性转化[J]. 国际脑血管病杂志, 2019, 27:881-885.]
[41] Arrais AC, Melo LHMF, Norrara B, Almeida MAB, Freire KF, Melo AMMF, Oliveira LC, Lima FOV, Engelberth RCGJ, Cavalcante JS, Araújo DP, Guzen FP, Freire MAM, Cavalcanti JRLP. S100B protein: general characteristics and pathophysiological implications in the central nervous system [J]. Int J Neurosci, 2022, 132:313-321.
[42] Zhou S, Zhu W, Zhang Y, Pan S, Bao J. S100B promotes microglia M1 polarization and migration to aggravate cerebral ischemia[J]. Inflamm Res, 2018, 67(11/12):937-949.
[43] Seady M, Schirmbeck G, Taday J, Fróes FT, Baú JV, Jantsch J, Guedes RP, Gonçalves CA, Leite MC. Curcumin attenuates neuroinflammatory damage induced by LPS: implications for the role of S100B[J]. J Nutr Biochem, 2025, 135:109768.
[44] Honegger T, Schweizer J, Bicvic A, Westphal LP, Schütz V, Inauen C, Pokorny T, Bracher K, Arnold M, Fischer U, Bonati

LH, De Marchis GM, Nedeltchev K, Kahles T, Cereda C, Kägi G, Montaner J, Bustamante A, Palù E, Ntaios G, Foerch C, Luft A, Spanaus K, Saleh L, von Eckardstein A, Arnold M, Katan M. Serum S-100B adds incremental value for the prediction of symptomatic intracranial hemorrhage and brain edema after acute ischemic stroke[J]. Eur Stroke J, 2023, 8:309-319.

[45] Foerch C, Wunderlich MT, Dvorak F, Humpich M, Kahles T, Goertler M, Alvarez-Sabín J, Wallesch CW, Molina CA, Steinmetz H, Sitzer M, Montaner J. Elevated serum S100B levels indicate a higher risk of hemorrhagic transformation after thrombolytic therapy in acute stroke[J]. Stroke, 2007, 38:2491-2495.

[46] Chen R, Jiang G, Liu Y, Pan H, Yan L, Zhao L, Zhao Y, Ji Q. Predictive effects of S100β and CRP levels on hemorrhagic transformation in patients with AIS after intravenous thrombolysis: a concise review based on our center experience [J]. Medicine (Baltimore), 2023, 102:e35149.

[47] Qu Y, Jin H, Abuduxukuer R, Qi S, Si XK, Zhang P, Zhang KJ, Wang SJ, Zheng XY, Zhang Y, Gao JH, Zhang XK, Liu XD, Li CY, Li GC, Wang J, Jin H, He Y, Jiang L, Liu L, Jiang Y, Teng RH, Jia Y, Zhang BJ, Chen Z, Qi Y, Liu X, Li S, Sun X, Nguyen TN, Yang Y, Guo ZN; Biomarkers of Brain Injury Investigator Study Group. The association between serum S100β levels and prognosis in acute stroke patients after intravenous thrombolysis: a multicenter prospective cohort study[J]. BMC Med, 2024, 22:304.

[48] Krishnamoorthy S, Singh G, Jose KJ, Soman B, Foerch C, Kimberly WT, Millán M, Świtońska M, Maestrini I, Bordet R, Malhotra K, Mechtouff L, Sylaja PN. Biomarkers in the prediction of hemorrhagic transformation in acute stroke: a systematic review and Meta-analysis[J]. Cerebrovasc Dis, 2022, 51:235-247.

[49] Jia J, Wang M, Meng J, Ma Y, Wang Y, Miao N, Teng J, Zhu D, Shi H, Sun Y, Liu H, Cheng X, Su Y, Ye J, Chi H, Liu T, Zhou Z, Wan L, Chen X, Wang F, Zhang H, Ben J, Wang J, Yang C, Hu Q. Ferritin triggers neutrophil extracellular trap-mediated cytokine storm through Msr1 contributing to adult-onset Still's disease pathogenesis[J]. Nat Commun, 2022, 13:6804.

[50] Wu Q, Wei C, Guo S, Liu J, Xiao H, Wu S, Wu B, Liu M. Acute iron overload aggravates blood-brain barrier disruption and hemorrhagic transformation after transient focal ischemia in rats with hyperglycemia[J]. IBRO Neurosci Rep, 2022, 13:87-95.

[51] Choi KH, Park MS, Kim JT, Nam TS, Choi SM, Kim BC, Kim MK, Cho KH. The serum ferritin level is an important predictor of hemorrhagic transformation in acute ischaemic stroke[J]. Eur J Neurol, 2012, 19:570-577.

[52] Abdelhak A, Foschi M, Abu-Rumeileh S, Yue JK, D'Anna L, Huss A, Oeckl P, Ludolph AC, Kuhle J, Petzold A, Manley GT, Green AJ, Otto M, Tumani H. Blood GFAP as an emerging biomarker in brain and spinal cord disorders[J]. Nat Rev Neurol, 2022, 18:158-172.

[53] Giovannini G, Meletti S. Fluid biomarkers of neuro-glial injury in human status epilepticus: a systematic review[J]. Int J Mol Sci, 2023, 24:12519.

[54] Korley FK, Jain S, Sun X, Puccio AM, Yue JK, Gardner RC, Wang KKW, Okonkwo DO, Yuh EL, Mukherjee P, Nelson LD, Taylor SR, Markowitz AJ, Diaz-Arrastia R, Manley GT; TRACK-TBI Study Investigators. Prognostic value of day-of-injury plasma GFAP and UCH-L1 concentrations for predicting functional recovery after traumatic brain injury in patients from the US TRACK-TBI cohort: an observational cohort study[J]. Lancet Neurol, 2022, 21:803-813.

[55] Bazarian JJ, Biberthaler P, Welch RD, Lewis LM, Barzo P, Bogner-Flatz V, Gunnar Brolinson P, Büki A, Chen JY, Christenson RH, Hack D, Huff JS, Johar S, Jordan JD, Leidel BA, Lindner T, Ludington E, Okonkwo DO, Ornato J, Peacock WF, Schmidt K, Tyndall JA, Vossough A, Jagoda AS. Serum GFAP and UCH-L1 for prediction of absence of intracranial injuries on head CT (ALERT-TBI): a multicentre observational study[J]. Lancet Neurol, 2018, 17:782-789.

[56] Guo ZN, Qu Y, Abuduxukuer R, Jin H, Zhang P, Wang J, Zhang KJ, Qi S, Zheng XY, Zhang Y, Gao JH, Pan DW, Liu XD, Li CY, Chen LP, Chen JH, Gu JL, Wang AY, Jiang L, Liu L, Jiang Y, Wang CF, Jia Y, Xin H, Jiang CL, Qi YB, Hu XF, Li S, Sun X, Nguyen TN, Yang Y; Biomarkers of Brain Injury Investigator Study Group. Serum GFAP and UCH-L1 levels for the assessment of the absence of hemorrhagic transformation: a multicenter prospective cohort study[J]. Stroke, 2025, 56:22-29.

[57] Li M, Liu H, Xu M, Yu B, Guo M, Wang X, Shi G, Zhou R. Glial fibrillary acidic protein as a potential indicator for symptomatic intracranial hemorrhage in acute ischemic patients undergoing endovascular thrombectomy[J]. Clin Interv Aging, 2024, 19:123-132.

[58] Chen CH, Chu HJ, Hwang YT, Lin YH, Lee CW, Tang SC, Jeng JS. Plasma neurofilament light chain level predicts outcomes in stroke patients receiving endovascular thrombectomy[J]. J Neuroinflammation, 2021, 18:195.

[59] Zhang X, Zeng W, Zhang Y, Yu Q, Zeng M, Gan J, Zhang W, Jiang X, Li H. Focus on the role of mitochondria in NLRP3 inflammasome activation: a prospective target for the treatment of ischemic stroke (review)[J]. Int J Mol Med, 2022, 49:74.

[60] Salman M, Ismael S, Li L, Ahmed HA, Puchowicz MA, Ishrat T. Acute hyperglycemia exacerbates hemorrhagic transformation after embolic stroke and reperfusion with tPA: a possible role of TXNIP-NLRP3 inflammasome[J]. J Stroke Cerebrovasc Dis, 2022, 31:106226.

[61] Pan Y, Nie L, Chen W, Guan D, Li Y, Yang C, Duan L, Wan T, Zhuang L, Lai J, Li W, Zhang Y, Wang Q. Buyang Huanwu Decoction prevents hemorrhagic transformation after delayed t-PA infusion via inhibiting NLRP3 inflammasome/pyroptosis associated with microglial PGC-1α[J]. J Ethnopharmacol, 2025, 340:119275.

[62] Xie Z, Zhao M, Yan C, Kong W, Lan F, Narengaowa, Zhao S, Yang Q, Bai Z, Qing H, Ni J. Cathepsin B in programmed cell death machinery: mechanisms of execution and regulatory pathways[J]. Cell Death Dis, 2023, 14:255.

[63] Zhou Y, Dong W, Wang L, Ren S, Wei W, Wu G. Cystatin C attenuates perihematomal secondary brain injury by inhibiting the cathepsin B/NLRP3 signaling pathway in a rat model of intracerebral hemorrhage[J]. Mol Neurobiol, 2024, 61:9646-9662.

[64] Wang X, Kou W, Kong W, Ma S, Xue Q, Zou Y, Song A. Magnetic resonance images, pathological features of thrombus, and expression of NLRP inflammasome in patients with acute ischemic stroke [J]. Contrast Media Mol Imaging, 2022: ID3464042.

[65] Bu LX. Study on the relationship between serum cathepsin B and acute cerebral infarction[J]. Zhongguo Yao Wu Yu Lin Chuang, 2017, 17:1352-1354.[卜丽霞. 血清组织蛋白酶B与急性脑梗死的关系研究[J]. 中国药物与临床, 2017, 17:1352-1354.]

[66] Wang Y, Huang H, He W, Zhang S, Liu M, Wu S. Association between serum NLRP3 and malignant brain edema in patients with acute ischemic stroke[J]. BMC Neurol, 2021, 21:341.

[67] Yuan S, Ma Q, Hou C, Li W, Liu KJ, Ji X, Qi Z. The

combination model of serum occludin and clinical risk factors improved the efficacy for predicting hemorrhagic transformation in stroke patients with recanalization[J]. Heliyon, 2024, 10: e25052.

[68] Li Y, Quan X, Hu J, Han Y, Chen J, Zhou M, Zhang F, Yang Y, Liao M, Wang B, Zhao Y. BMSCs-derived small extracellular vesicles antagonize cerebral endothelial Caveolin-1 driven autophagic degradation of tight-junction proteins to protect blood-brain barrier post-stroke[J]. Int J Biol Sci, 2025, 21:842-859.

[69] Goncalves A, Su EJ, Muthusamy A, Zeitelhofer M, Torrente D, Nilsson I, Protzmann J, Fredriksson L, Eriksson U, Antonetti DA, Lawrence DA. Thrombolytic tPA-induced hemorrhagic transformation of ischemic stroke is mediated by PKCβ phosphorylation of occluding[J]. Blood, 2022, 140:388-400.

[70] Shi CX, Zhang F, Han XY. Relationships between serum occludin level and severity, hemorrhagic transformation and prognosis of acute ischemic stroke[J]. Guo Ji Jian Yan Yi Xue Za Zhi, 2022, 43:2060-2064.[石晨旭, 张芾, 韩鲜艳. 血清Occludin水平与急性缺血性脑卒中严重程度、出血性转化和预后的关系[J]. 国际检验医学杂志, 2022, 43:2060-2064.]

[71] Li W, Qi Z, Kang H, Qin X, Song H, Sui X, Ren Y, Ji X, Ma Q, Jian Liu K. Serum occludin as a biomarker to predict the severity of acute ischemic stroke, hemorrhagic transformation, and patient prognosis[J]. Aging Dis, 2020, 11:1395-1406.

[72] Krishnamoorthy S, Sylaja PN, Sreedharan SE, Singh G, Damayanthi D, Gopala S, Madhusoodanan UK, Ramachandran H. Biomarkers predict hemorrhagic transformation and stroke severity after acute ischemic stroke[J]. J Stroke Cerebrovasc Dis, 2023, 32:106875.

[73] Spagnolello O, De Michele M, Lorenzano S, Cerulli Irelli E, Naitana F, Falcou A, Letteri F, Bachetoni A, Collepardo D, Bertazzoni G, Toni D. Copeptin kinetics in acute ischemic stroke may differ according to revascularization strategies: pilot data[J]. Stroke, 2019, 50:3632-3635.

[74] Błaż M, Natorska J, Bembenek JP, Członkowska A, Ząbczyk M, Polak M, Undas A. Protein carbonylation contributes to prothrombotic fibrin clot phenotype in acute ischemic stroke: clinical associations[J]. Stroke, 2023, 54:2804-2813.

（收稿日期：2025-03-30）
（本文编辑：许畅）

·小词典·

中英文对照名词词汇（一）

阿尔茨海默病 Alzheimer's disease（AD）

氨基末端B型利尿钠肽前体 N-terminal pro-B-type natriuretic peptide（NT-proBNP）

白细胞介素-1β interleukin-1β（IL-1β）

表达数量性状基因座 expression quantitative trait locus（eQTL）

丙氨酸转氨酶 alanine aminotranferase（ALT）

超氧化物歧化酶 superoxide dismutase（SOD）

出血性转化 hemorrhagic transformation（HT）

穿支动脉粥样硬化病 branch atheromatous disease（BAD）

磁敏感加权成像 susceptibility-weighted imaging（SWI）

磁敏感血管征 susceptibility vessel sign（SVS）

促肾上腺皮质激素 adrenocorticotropic hormone（ACTH）

大动脉粥样硬化 large artery atherosclerosis（LAA）

大脑后动脉 posterior cerebral artery（PCA）

大脑前动脉 anterior cerebral artery（ACA）

大脑中动脉 middle cerebral artery（MCA）

大脑中动脉闭塞 middle cerebral artery occlusion（MCAO）

单纯球囊扩张血管成形术 percutaneous transluminal angioplasty（PTA）

低密度脂蛋白胆固醇 low-density lipoprotein cholesterol（LDL-C）

β-淀粉样蛋白 amyloid β-protein（Aβ）

凋亡相关斑点样蛋白质 apoptosis-associated speckle-like protein containing a CARD（ASC）

动脉血氧饱和度 artery oxygen saturation（SaO_2）

动脉血氧分压 arterial partial pressure of oxygen（PaO_2）

动脉自旋标记 arterial spin labeling（ASL）

动态步态指数 Dynamic Gait Index（DGI）

动态视敏度 dynamic visual acuity（DVA）

豆纹动脉 lenticulostriate artery（LA）

短暂性脑缺血发作 transient ischemic attack（TIA）

对比增强经颅多普勒超声 contrast-enhanced transcranial Doppler ultrasound（cTCD）

反常性栓塞 paradoxical embolism（PDE）

反常性栓塞风险评分 Risk of Paradoxical Embolism Score（RoPE）

泛素羧基末端水解酶L1 ubiquitin carboxy-terminal hydrolase L1（UCH-L1）

非高密度脂蛋白胆固醇 non-high-density lipoprotein cholesterol（non-HDL-C）

肺动静脉瘘 pulmonary arteriovenous fistula（PAVF）

肺动脉压 pulmonary arterial pressure（PAP）

CT肺动脉造影 computed tomographic pulmonary angiography（CTPA）

肺泡-动脉血氧分压差 alveolar-artery oxygen partial pressure gradient（$PA\text{-}aO_2$）

肺泡氧分压 partial pressure of oxygen in alveolar gas（PAO_2）

改良Rankin量表 modified Rankin Scale（mRS）

甘油三酯 triglyceride（TG）

甘油三酯-葡萄糖 triglyceride glucose（TyG）

感兴趣区 region of interest（ROI）

高分辨率血管壁磁共振成像 high resolution-vascular wall magnetic resonance imaging（HR-VWI）