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《SHOCK》2024 年第 12 期新观点

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本期《SHOCK》杂志刊出了 6 篇文章,其中临床研究 3 篇,基础研究 3 篇。研究内容涵盖脓毒症预后、尿毒症患者血管内皮功能改变、重症热射病预后、创伤后肺炎血液微生物失调、烧伤合并吸入性损伤后的急性全身及肺部免疫反应、烧伤后骨髓造血微环境重塑。

Liu 等一方面采用多组学分析技术,鉴定脓毒症的新型生物标志物[1],另一方面通过单细胞 RNA 测序(scRNA-Seq)比较脓毒症存活组与死亡组以及创伤后对照患者的基因表达差异,结合 Viper 算法推断蛋白质活性,并通过数据非依赖性采集(DIA)蛋白质组学分析蛋白质表达水平,最终发现,SPI1、MEF2A 和 UBTF 的表达与脓毒症患者生存率呈正相关,而 CBX3 的高表达与不良预后相关。基因集变异富集分析表明,脓毒症不良结局与细胞凋亡和炎症通路异常密切相关。

慢性肾病中尿毒症毒素的蓄积可诱发炎症、氧化应激及内皮功能障碍。Li 等探讨了 NOD 样受体家族含 pyrin 结构域蛋白 3(NOD-like receptor family pyrin domain containing 3,NLRP3)炎性小体在尿毒症患者血清诱导的人主动脉内皮细胞功能障碍中的作用[2]。研究发现,尿毒症血清可激活 NLRP3 炎性小体并促进高迁移率族蛋白 B1(high mobility group box 1 protein,HMGB1)释放,抑制内皮功能受损和细胞增殖,破坏内皮细胞功能,而己酮可可碱的体外干预可显著逆转上述改变,进一步证实该磷酸二酯酶抑制剂在血管疾病中的治疗潜力。

热射病可引发多器官功能障碍。Xu 等通过回顾性临床研究分析 194 例热射病患者的系统性免疫炎症指数(SII,血小板计数×中性粒细胞计数/淋巴细胞计数)动态变化,发现热射病后第 3 天的 SII 值可有效预测患者预后,且联合序贯器官衰竭评估(sequential organ failure assessment,SOFA)评分可显著提升预测效能[3]。研究构建的列线图为临床评估重症热射病提供了新的量化工具。

临床研究表明,创伤患者肠道通透性增加与感染风险升高、全身炎症反应及多器官功能障碍综合征相关。Munley 等通过多部位创伤联合慢性束缚应激及细菌性肺炎的大鼠模型,发现创伤后肺炎可显著增加肠道通透性,且血液微生物组多样性呈现性别依赖性差异[4]。这一发现提示,创伤后脓毒症可能通过破坏肠道屏障功能和菌群失调影响严重创伤患者的结局。

吸入性损伤显著增加烧伤患者呼吸衰竭及全身并发症的发生率。Alves 等在烧伤伴烟尘吸入及铜绿假单胞菌感染的临床前模型中,评估了激活核因子 E2 相关因子 2(Nuclear factor erythroid 2-related factor 2,NRF2)抗氧化通路与抑制哺乳动物雷帕霉素靶蛋白(mammalian target of rapamycin,mTOR)通路的联合治疗效果[5]。研究采用负载 NRF2 激动剂与雷帕霉素的微颗粒进行多模式治疗,通过肺组织细胞因子及免疫基因转录组学分析证实,该策略可有效缓解烧伤诱导的免疫重编程,增强抗细菌感染能力,从而改善肺损伤。

烧伤可促使骨髓造血从红系向髓系偏移。Johnson 等利用小鼠烧伤模型,系统评估了应急造血过程中红系、髓系及淋巴系祖细胞的动态变化[6]。流式细胞术分析显示,烧伤早期可显著增加骨髓长期造血干细胞(LT-HSC)及短期造血干细胞/多能祖细胞(ST-HSC/MPP)比例,同时关键造血转录因子的 mRNA 表达水平验证了这一现象,揭示了烧伤后骨髓造血微环境重塑的分子机制。

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(收稿日期: 2024-11-12)
(本文编辑: 顾潇宵)

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(收稿日期: 2024-10-15)
(本文编辑: 顾潇宵)