·综述·

# ICU 获得性衰弱的早期防控：基于时间窗的干预策略

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【摘要】 ICU 获得性衰弱（ICU-AW）作为重症监护病房（ICU）常见的并发症，因其可以造成存活者严重的功能障碍，越来越受到临床医生的关注。早期的研究重点多集中于 ICU-AW 的定义、诊断、病理生理机制以及危险因素，鲜见按照病情进展进行阶梯式干预的系统性研究。现有指南也仅提倡 ICU 患者进行早期活动，但具体时间及干预内容并未细化。本文筛选国内外相关研究，对 ICU-AW 基于时间窗的发病机制及干预措施进行综述，旨在找出 ICU-AW 基于时间窗的防控策略，并结合我国 ICU 资源配置特点优化实施路径。

【关键词】 ICU 获得性衰弱；　早期诊断；　康复；　时间窗
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**Early prevention and control of ICU-acquired weakness: intervention strategies based on the time window**

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【Abstract】 ICU-acquired weakness (ICU-AW), as a common complication in the intensive care unit (ICU), has received increasing attention from clinicians due to its potential to cause severe functional impairments in survivors. Early research primarily focused on the definition, diagnosis, pathophysiology, and risk factors of ICU-AW, while systematic studies on stepwise interventions aligned with disease progression remain scarce. Current guidelines merely advocate for early mobilization, without specifying the timing or content of interventions. This paper reviews relevant domestic and international studies to summarize the time-window-based pathogenesis and intervention measures of ICU-AW, aiming to identify time-window-based prevention and control strategies for ICU-AW and optimize the implementation pathway based on the characteristics of ICU resource allocation in China.

【Key words】 ICU-acquired weakness;　Early diagnosis;　Rehabilitation;　Time window
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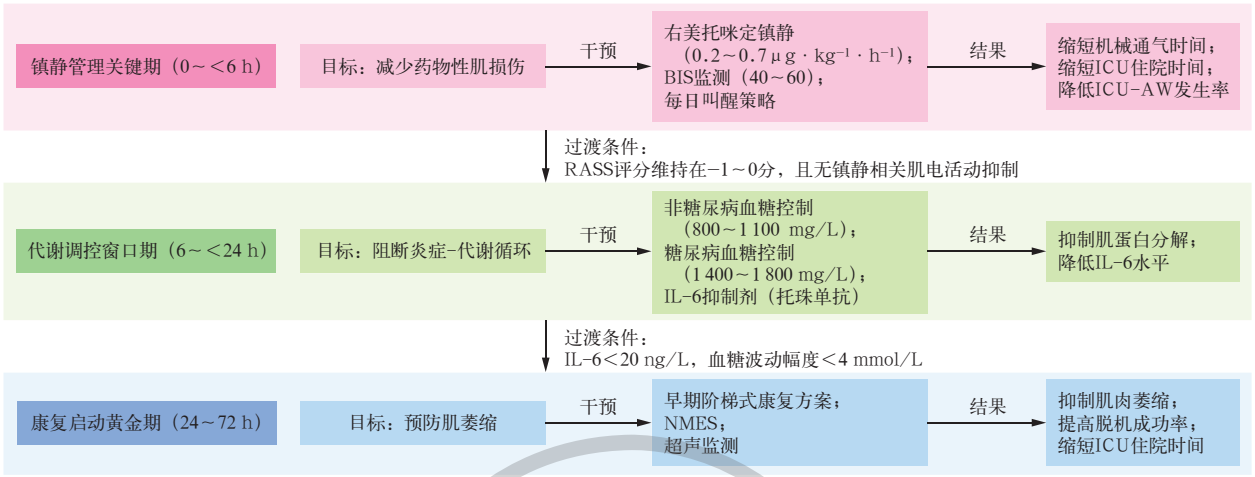
过去几十年，危重病患者的病死率降低了 35%，但存活者的功能障碍问题却愈发受到关注。约 1/3 的患者在转出重症监护病房（intensive care unit，ICU）后存在功能障碍，即重症监护后综合征（post-intensive care syndrome，PICS），主要表现为身体、心理和认知功能的受损。即使在转出 ICU 5 年后，患者的身体功能仍无法达到正常水平，且 1/3 的幸存者再也无法重返工作岗位。而 ICU 获得性衰弱（ICU-acquired weakness，ICU-AW）是导致 PICS 的重要因素[1]。

ICU-AW 是指危重患者因炎症反应、长期制动及药物毒性等因素导致的广泛性肌无力综合征，其诊断标准为清醒患者英国医学研究理事会（Medical Research Council，MRC）肌力评分＜48 分且持续＞24 h[2]；机械通气患者通过单向阀门测压计测得最大吸气压（maximum inspiratory pressure，MIP）＜36 $cmH_2O$（1 $cmH_2O$=0.098 kPa），此法也适用于昏迷患者[3]。研究显示，ICU-AW 总体发生率呈上升趋势，国外报道 ICU-AW 的发生率为 40%～50%[4-5]，个别研究中甚至超过 80%，机械通气患者发生率更高[6]。ICU 患者早期肌肉显著萎缩，平均每日丢失约 2% 的肌肉质量，与不良结局密切相关[7]。然而目前对 ICU-AW “早期干预”的定义普遍模糊，更鲜见基于时间窗下的明确管理。本文聚焦 ICU-AW 的早期防控，基于近年来相关研究，提出围绕 ICU-AW 病理生理发展过程的时间轴进行干预防控，将其划分为 3 个时期，即镇静管理关键期（0～＜6 h）、代谢调控窗口期（6～＜24 h）、康复启动黄金期（24～72 h），并对相应具体干预措施进行综述，以期优化 ICU-AW 防控路径，最终提高 ICU-AW 患者预后，具体干预路径见图 1。

## 1　基于时间窗划分及干预路径

**1.1**　镇静管理关键期（0～＜6 h）：ICU 重症患者早期（0～＜6 h）因机械通气、疼痛及躁动往往需要深度镇静，但镇静药物（如丙泊酚、苯二氮䓬类）通过抑制线粒体呼吸链复合物活性而降低线粒体质量和功能[8]，可直接导致肌纤维三磷酸腺苷（triphosadenine，ATP）合成减少，肌肉兴奋性降低，影响肌电活动，长期使用可导致肌肉无力或萎缩，影响自主呼吸和康复活动[9-13]，诱发药物性肌损伤。为此，有研究建议在患者病情允许的情况下尽可能给予轻度镇静，使用短效镇静剂，并避免使用苯二氮䓬类药物[14]。所以此阶段干预的核心在于选择神经肌肉毒性较低的镇静策略，并缩短深镇静时长。

早期治疗确实需要深镇静的患者，建议使用脑电双频指数（bispectral index，BIS）来监测镇静深度。BIS 是一种通




注：ICU-AW 为 ICU 获得性衰弱，BIS 为脑电双频指数，ICU 为重症监护病房，RASS 为 Richmond 躁动-镇静评分，IL-6 为白细胞介素-6，NMES 为神经肌肉电刺激

**图 1　基于时间窗划分的 ICU-AW 干预路径**

过分析脑电信号来评估麻醉深度和意识状态的量化指标，数值范围为 0（无脑电活动）～100（清醒状态）。可以指导临床精准调控镇静药物剂量，降低药物暴露风险。研究显示，BIS 引导的深度镇静〔Richmond 躁动-镇静评分（Richmond agitation-sedation scale，RASS）为 −4 或 −5 分〕可以减少镇静药物的使用，增加无昏迷天数[15]。

以前的理念是深度镇静可让患者在危重病缓解期间“休息”，避免痛苦记忆；但现有研究指出，深度镇静往往更有害，会延长或延迟患者的康复[14]，所以建议使用轻度镇静的短效药物。典型代表药物右美托咪定通过选择性激动 $\alpha_2$ 受体，抑制交感神经兴奋性而减少儿茶酚胺释放，避免过度肌颤搐抑制[16-19]。已有不少研究证实，与传统镇静剂（苯二氮䓬类药物和异丙酚）比较，右美托咪定可以缩短机械通气时间和 ICU 住院时间[20-23]，而机械通气时间和 ICU 住院时间又是 ICU-AW 的独立危险因素[24]，但右美托咪定是否可以降低 ICU-AW 的发生率仍需进一步研究验证。研究显示，轻度镇静联合每日唤醒策略，可以减少镇静药物的蓄积，从而降低对运动神经元的持续抑制[14,25]，促进早期活动，维持肌电活动和肌肉功能，缩短机械通气时间[25-27]。

综上所述，此阶段镇静管理需遵循镇痛优先的策略，并通过短效药物（如右美托咪定）实现轻度镇静（RASS 评分维持在 −2～−1 分或 BIS 目标值维持在 60～80，且无镇静相关肌电活动抑制[28]），避免使用苯二氮䓬类药物。具体方法：阿片类药物（如瑞芬太尼）联合右美托咪定的多模式镇痛镇静[29]。同时使用 RASS 评分或 BIS 进行镇静深度的监测，尤其是 BIS，可以引导精准镇静，减少镇静药物用量，研究证实 RASS 评分和 BIS 具有非常好的相关性[30]。

**1.2**　代谢调控窗口期（6～<24 h）：此阶段患者炎症达到峰值、代谢出现紊乱、线粒体功能障碍。研究显示，脓毒症和创伤早期（6～<24 h）处于低代谢期，肿瘤坏死因子-α（tumor necrosis factor-α，TNF-α）、白细胞介素-6（interleukin-6，IL-6）等促炎症因子水平急剧升高并达到峰值[31]，并通过激活泛素-蛋白酶体系统（ubiquitin-proteasome system，UPS）使肌球蛋白重链降解速率增加 3 倍[32-33]，从而加速肌肉蛋白降解[33-34]。代谢紊乱体现在出现高血糖、胰岛素抵抗，也可以通过激活 UPS 系统促进肌蛋白分解[35-37]。干预重点在于控制血糖、抗炎、抗氧化治疗，具体措施及依据如下。

**1.2.1**　精准血糖控制：高血糖和延长机械通气时间作为 ICU-AW 的独立危险因素[24]，对 ICU-AW 的病情进展起着至关重要的作用。与耐受高达肾脏阈值的高血糖相比，旨在使血糖正常化的胰岛素治疗显著降低了危重症神经病/危重症肌病电生理体征的发生率，以及长期在内科 ICU[38] 和外科 ICU[39-40] 住院的重症患者对延长机械通气的需求。研究显示，强化胰岛素治疗，即血糖水平控制在 4.4～6.1 mmol/L（800～1 100 mg/L）可大大降低 ICU-AW 的发生率[38]。因为胰岛素除了能降低血糖外，还可以促进肌肉合成代谢[41]。但对 ICU 重症患者实施严格的血糖控制却增加了低血糖的发生率[42]，尤其对于糖尿病患者，发生低血糖的概率更高[43]。重症专业协会提出的住院糖尿病患者的血糖目标〔7.8～10.0 mmol/L（1 400～1 800 mg/L）〕似乎是目前优化临床结局的同时避免低血糖的最佳折衷方案[44]。

研究显示，血糖波动幅度对 ICU-AW 也有一定影响，当血糖波动>4 mmol/L 时，通过下调 E3 泛素连接酶 WWP1，抑制 Kruppel 样因子 15（Kruppel like factor 15，KLF15）蛋白的泛素化降解，导致 KLF15 在骨骼肌中积累，从而激活肌肉萎缩相关基因（如 Atrogin-1、MuRF1），促进蛋白质分解并抑制合成，最终导致肌纤维萎缩，糖尿病模型小鼠的肌纤维横截面积以每日 5.2% 的速度减少[45]。

**1.2.2**　抗炎与抗氧化治疗：IL-6 在宿主对感染和组织损伤的防御中起着至关重要的作用，并且是多种不同类型“细胞因子风暴”的生物标志物。有证据表明，重组人源化抗免疫球蛋白 G1（immunoglobulin G1，IgG1）单克隆抗体托珠单抗可以有效阻断 IL-6 信号传导，在嵌合抗原受体 T 细胞疗法诱导的“细胞因子风暴”及新型冠状病毒感染中发挥了有益

作用[46]。研究显示，IL-6 抑制剂托珠单抗治疗降低了患有严重脓毒症 / 脓毒性休克的发热性中性粒细胞减少症患儿的病死率，但仍需大样本的随机对照试验进一步验证其是否能降低 ICU-AW 的发生率[44,47]。作为抗炎治疗的辅助手段，抗氧化治疗在此阶段也发挥了重要作用。N- 乙酰半胱氨酸（N-acetylcysteine，NAC）是临床常用的抗炎和抗氧化辅助药物。有研究显示，NAC 可以改善微循环，降低乳酸水平，缩短 ICU 住院时间[48]。2021 年一项针对老年患者补充甘氨酸和 NAC 的临床研究显示，连续补充甘氨酸和 NAC 可以改善氧化应激、线粒体功能、炎症反应、胰岛素抵抗，并改善了力量、步态速度、认知和身体成分[49]。

此阶段成功标准：IL-6＜20 ng/L[50]，血糖波动幅度＜4 mmol/L[51]。

**1.3**　康复启动黄金期（24～72 h）：此阶段由于病情因素及有创机械通气等设备的使用，患者常处于制动状态[52]，会导致肌肉快速萎缩[53]。研究显示，即使是健康志愿者，卧床也会使下肢肌肉每日萎缩 0.2%～0.6%[54-55]，而机械通气时间超过 48 h 的 ICU 重症患者骨骼肌萎缩更为迅速[32,56]，每日萎缩率可达 1.2%～3.0%[53]。所有肌肉萎缩中，膈肌萎缩出现最早，动物实验显示完全控制通气 12～18 h 即可导致大鼠横膈膜的肌纤维明显萎缩损伤[57-58]，而长时间机械通气是显著萎缩的独立危险因素[59]。研究显示，早期康复通过机械负荷激活哺乳动物雷帕霉素靶蛋白（mammalian target of rapamycin，mTOR）通路，促进肌原纤维合成。尽管早期物理康复可能改善预后[60-63]，但随机试验结果不一致，需进一步研究优化干预策略[64-65]。为此，针对机械通气的患者，有学者提出了阶梯式康复活动方案（图 2）[66]。

尽管针对重症患者的早期康复活动存在争议，但是此阶段物理康复干预仍是重要的手段。研究显示，功能性活动与多成分疗法逐步康复（从床上活动到站立行走[67]）治疗可降低 ICU-AW 风险〔风险比（risk ratio，*RR*）＝0.49〕[68]，多成分干预（如电刺激、阻力训练）可能改善功能结局[63]。对于无法主动活动的患者，每日进行神经肌肉电刺激（neuromuscular electrical stimulation，NMES）和早期体育锻炼可以保留肌肉力量，也能够降低 ICU-AW 发生的风险，并缩短机械通气时间和 ICU 住院时间[69-70]。被动或主动床上康复踏车训练可改善肌肉力量[71-72]，但单独使用效果有限，需结合其他干预措施。倾斜床、动态倾斜台等可促进早期站立，但对 MRC 评分改善无显著差异[73]。

## 2　我国针对 ICU-AW 的早期干预措施的挑战与对策

我国针对 ICU-AW 的早期干预措施的挑战主要是人力资源的限制和技术设备短缺。

**2.1**　人力资源的限制：① 护士人力配置不足，国家卫健委在《重症医学专业医疗质量控制指标（2024 年版）》[74]中明确指出，综合 ICU 推荐床护比为 1∶2.5～1∶3.0。2022 年 12 月，国家卫健委医政司司长焦雅辉公布，全国三级医疗机构 ICU 床位为 13.81 万张，重症专业护士 22 万人，由此推算三级医疗机构 ICU 床护比约为 1∶1.59，距离推荐的目标值差距较大[75]。护士人力不足导致早期康复措施（如体位管理、被动活动）执行率不足。② 康复人员短缺，由于我国康复医学起步较晚，目前康复服务存在需求大、服务能力差、人才缺口大、培养能力不足的问题，尤其是康复治疗人才缺乏是国内康复医学事业发展的瓶颈[76-77]。国家卫健委等部门提出，到 2025 年全国 ICU 专职康复治疗师需达到 0.5 人 /10 张床位[76]。③ 多学科协作机制不完善，康复治疗师参与率不足。④ 沟通效率低下，医生、护士、康复师间的信息传递依赖纸质记录，导致干预延迟。

改善人力资源限制的策略：① 政策层面优化配置，增加编制与待遇：参照《中国重症医学科建设和发展指南（2025 版）》，要求三级医院 ICU 床护比逐步达到 1∶2.5～1∶3.0，并纳入医院评级考核[78]。② 创新工作模式，护士主导的阶梯式康复：培训 ICU 护士掌握基础康复技能（如 NMES 操作、关节活动），提升每日被动活动执行率。③ 强化多学科协作，制定 ICU-AW 多学科协作专家共识，明确医生、护士、康复师、营养师的职责分工与交接节点。④ 信息化支持，开发 ICU 专用移动终端（如 ICU-AW 防控 APP），实时共享患者肌力评分、镇静深度等数据，缩短决策延迟。

**2.2**　技术设备短缺：① 康复设备资源配置不均衡，东部地区 ICU 是西部地区的 2～3 倍，县级医院设备缺口显著。尤其是 NMES 等进口设备普及率更低，集中在发达城市的三级教学医院，基层普及率低[79]。② 肌肉功能评估工具不足，超声设备缺口明显，尤其是基层，无法动态监测肌肉厚度与

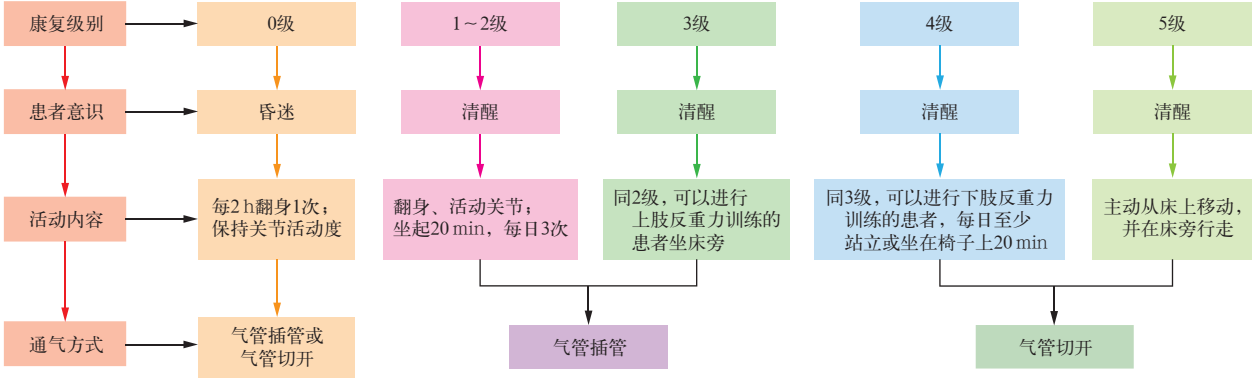



**图 2　有创机械通气患者阶梯式康复方案**

回声强度。③ 生物标志物检测滞后：大部分基层医院因价格或技术等原因，不能常规检测 IL-6、可溶性 CD14 亚型等炎症标志物，能检测的医疗机构出结果的时间也较长。

改善技术设备短缺的策略：① 加速国产设备研发与推广，降低成本；② 推进便携式超声普及，培训护士掌握肌肉厚度测量技术；③ 即时检验（point-of-care testing，POCT），引入全自动微流控芯片分析仪，实现 IL-6、肌酸激酶（creatine kinase，CK）等标志物 15 min 出结果。

## 3　未来方向

开发人工智能预警系统，从电子病例系统提取生物标志物、影像及结构数据（机械通气时间、序贯器官衰竭评分等），采用 XGBoost 算法构建预测模型。主要挑战是存在数据孤岛问题，需要医院信息科开发标准化数据接口，建立 ICU 专属数据平台，实现多源数据实时融合。研究表明，传统中医可以提高 ICU-AW 的临床疗效，提高肌肉力量和日常生活能力，缩短机械通气时间、ICU 住院时间和总住院时间，降低 TNF-α 和 IL-6 水平[80]。因此，可以考虑采取中西医协同方案对 ICU-AW 进行早期干预。目前该方向面临的主要挑战是中医师与康复师协调不足，可以考虑跨学科培训。

综上所述，人工智能预警系统可提前识别高风险患者，降低 ICU-AW 发生率；中西医协同方案通过抗炎与肌纤维激活双重机制，使肌力恢复时间缩短。两者结合有望成为 ICU-AW 防控的新模式，需进一步推进多中心随机对照试验验证长期疗效。

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