

肝衰竭诊治指南(2024年版)

中华医学会感染病学分会肝衰竭与人工肝学组 中华医学会肝病学会重型肝病与人工肝学组

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【摘要】 肝衰竭是临床常见的严重肝病症候群,病死率极高。多年来,各国学者对肝衰竭的定义、病因、分类、分型、诊断和治疗、预后等问题不断进行探索。根据国内外最新研究成果,中华医学会感染病学分会肝衰竭与人工肝学组和中华医学会肝病学会重型肝病与人工肝学组在我国《肝衰竭诊治指南(2018年版)》的基础上对指南进行了全面更新,以指导和规范肝衰竭的临床诊疗。

【关键词】 肝功能衰竭; 肝,人工; 诊断; 治疗; 指南

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Guideline for diagnosis and treatment of liver failure (2024 version)

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【Abstract】 Liver failure is a severe clinical syndrome of liver disease with an extremely high mortality rate. Over the years, scholars worldwide have continuously investigated various aspects of liver failure, including its definition, etiology, classification, types, diagnosis and treatment, and prognostic assessment. Based on the latest advances in research, Liver Failure and Artificial Liver Group, Chinese Society of Infectious Diseases, Chinese Medical Association along with Severe Liver Disease and Artificial Liver Group, Chinese Society of Hepatology, Chinese Medical Association have conducted a comprehensive update on the *Guidelines for Diagnosis and Treatment of Liver Failure (2018 version)*. This update aims to offer standardized protocols and evidence-based recommendations to guide the management of liver failure in clinical settings.

【Key words】 Liver failure; Artificial liver; Diagnosis; Treatment; Guideline

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肝衰竭是临床常见的严重肝病症候群,病死率极高^[1]。多年来,各国学者对肝衰竭的定义、病因、分类、分型、诊断和治疗、预后等问题不断进行探索。2005年,美国肝病学会(AASLD)发布了《急性肝衰竭处理》^[2]的建议书。2006年10月,中华医学会感染病学分会肝衰竭与人工肝学组和中华医学会肝病学会重型肝病与人工肝学组制订了我国

第一部《肝衰竭诊疗指南》^[3],从定义、诱因、分类、诊断和治疗等方面对我国肝衰竭进行了系统而精要的阐述,既与国际接轨,又独具中国特色,诊断分型突出了实用性,指导和规范了我国肝衰竭的临床诊疗,并于2012年、2018年进行了2次修订^[4-5]。亚太肝脏研究协会(APASL)于2009年首次提出针对慢加急性肝衰竭定义和诊断标准的专家共识^[6],分

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别于2014年、2019年进行了更新^[7-8]。欧洲肝病学会(EASL)和北美终末期肝病研究联盟(NACSELD)分别于2013和2014年提出了慢加急性肝衰竭诊断标准^[9-10]。2017年,中国重型乙型肝炎研究小组(COSSH)基于乙型肝炎人群的多中心、前瞻性 & 大样本的研究,提出了慢加急性肝衰竭诊断的 COSSH 中国标准^[11]。上述四大标准均被收录至欧洲 2023 年发布的《慢加急性肝衰竭临床实践指南》^[12]和美国 2024 年发布的《慢加急性肝衰竭和危重肝硬化患者管理实践指南》^[13]。中华医学会感染病学分会肝衰竭与人工肝学组和中华医学会肝病学会分会重型肝病与人工肝学组根据国内外最新研究成果,再次对我国《肝衰竭诊治指南(2018 年版)》进行更新。

《肝衰竭诊治指南(2024 年版)》(简称《指南》)旨在使临床医师对肝衰竭的诊治有进一步了解,并做出较为合理的决策,并非强制性标准。鉴于肝衰竭是由多种病因引起的复杂病理生理过程,本指南不可能包括或解决肝衰竭诊治中的所有问题。因此,在针对具体病情,临床医师应参照本《指南》,充分了解肝衰竭的最佳临床证据和现有的医疗资源,在全面考虑患者具体病情及其意愿的基础上,制订合理的诊治方案。

随着对肝衰竭发病机制及诊断、治疗研究的逐渐深入,本《指南》将根据最新的临床医学证据不断更新和完善。本《指南》的制订遵守了国内外权威学术组织制订的基本流程和程序,采用英国牛津大学循证医学中心证据分级(2011 年版)进行证据评估,根据 GRADE 推荐标准对推荐强度进行评估^[14]

(表 1 和 2)。

表 1 英国牛津大学循证医学中心证据分级(2011 年版)

证据级别	描述
1	基于随机对照试验的系统评价、全或无研究、效应量大的观察性研究
2	单个随机对照试验、效应量大的观察性研究
3	非随机对照的队列研究、随访研究
4	病例系列、病例对照研究、回顾性对照研究
5	专家意见(基于机制的推理)

表 2 GRADE 推荐标准

推荐级别	描述
A	强烈推荐:明确显示干预措施利大于弊或弊大于利
B	较弱的推荐:利弊不确定或无论质量高低的证据均显示利弊相当

1 肝衰竭的定义和病因

1.1 定义 肝衰竭是由多种因素引起的严重肝脏损害,导致肝脏合成、解毒、代谢和生物转化功能严重障碍或失代偿,出现以黄疸、凝血功能障碍、肝肾综合征、肝性脑病及腹水等为主要表现的一组临床症状候群。

1.2 病因 在我国引起成人肝衰竭的主要病因是肝炎病毒(尤其是乙型肝炎病毒),其次是药物及肝毒性物质(如酒精、化学制剂等)^[11, 15]。儿童肝衰竭多见于遗传代谢性疾病。肝衰竭的常见病因见表 3。

2 肝衰竭的分类和诊断

肝衰竭分类与诊断对于临床精准诊治管理极

表 3 肝衰竭的常见病因

病因	常见分类
肝炎病毒	甲型、乙型、丙型、丁型、戊型肝炎病毒(HAV、HBV、HCV、HDV、HEV)
其他病毒	巨细胞病毒(CMV)、EB病毒(EBV)、新型布尼亚病毒、黄热病毒、裂谷热病毒等
药物	对乙酰氨基酚、抗结核药物、抗肿瘤药物、部分中草药、抗风湿病药物、抗代谢药物、膳食补充剂等
肝毒性物质	酒精、毒蕈、植物、有毒的化学物质等
细菌及寄生虫等	严重或持续感染(如脓毒症、血吸虫病等)
遗传代谢	肝豆状核变性、遗传性糖代谢障碍等
免疫相关	自身免疫性肝病、肿瘤免疫治疗、乙肝不规范抗病毒治疗等
肝脏其他疾病	肝脏肿瘤、肝脏手术、妊娠急性脂肪肝、肝移植术后、肝脏血管疾病(如布加综合征)等
胆道疾病	先天性胆道闭锁、胆汁淤积性肝病等
循环衰竭	缺血缺氧、休克、充血性心力衰竭等
其他	创伤、热射病等
原因不明	-

注:“-”无相关数据

其重要,并与病因、诱因及发病机制等密切相关^[11, 16-17]。28 d、90 d 生存情况是患者长期预后的关键时间点,关注肝衰竭的动态转归分型有助于临床早诊早治与预后判断^[18-20]。

2.1 分类 基于基础肝病病史、起病特点及病情进展速度,肝衰竭分为4类:急性肝衰竭(acute liver failure, ALF)、亚急性肝衰竭(subacute liver failure, SALF)、慢加急性(亚急性)肝衰竭[acute(subacute)-on-chronic liver failure, ACLF 或 SACLf]和慢性肝衰竭(chronic liver failure, CLF),见表4。

2.2 组织病理学表现 组织病理学检查在肝衰竭诊断、分类及预后判定上具有重要价值,但由于肝衰竭患者的凝血功能严重障碍,实施经皮肝穿刺具有较高的风险,在临床工作中应特别注意,但也可根据临床实际情况,选择相对出血风险小的经颈内静脉肝穿刺。多项多中心的回顾性研究均表明,经颈静脉肝穿刺在凝血功能障碍、腹水等高危患者中具有较高的安全性^[21-23]。

肝衰竭发生时(慢性肝衰竭除外),肝脏组织学可观察到广泛的肝细胞坏死,坏死的部位和范围因病因和病程的不同而不同。按照坏死的范围,可分为大块坏死(坏死范围超过肝实质的2/3)、亚大块坏死(约占肝实质的1/2~2/3)、融合性坏死(相邻成片的肝细胞坏死)及桥接坏死(较广泛的融合性坏死,并破坏肝实质结构)。在不同病程肝衰竭肝组织中,可观察到一次性或多次性的、新旧不一的肝细胞坏死病灶。最新转录、蛋白和代谢等多组学研究揭示,慢加急性肝衰竭发病机制涉及系统性炎症反应和免疫代谢失衡等,发病早期固有免疫激活、炎症因子风暴,进而发生适应性免疫抑制或耗竭、代谢紊乱,导致肝脏和/或肝外多器官衰竭^[24-27]。

2.2.1 急性肝衰竭 肝细胞呈一次性坏死,可呈大块或亚大块坏死,或桥接坏死,伴存活肝细胞严重变性,肝窦网状支架塌陷或部分塌陷。

2.2.2 亚急性肝衰竭 肝组织呈新旧不等的亚大块坏死或桥接坏死;较陈旧的坏死区网状纤维塌

陷,或有胶原纤维沉积,残留肝细胞有程度不等的再生,并可见细、小胆管增生和胆汁淤积。

2.2.3 慢加急性(亚急性)肝衰竭 在慢性肝病病理损伤的基础上,发生新旧程度不等的肝细胞亚大块坏死性病变,伴有汇管周围的小胆管增生,有肝硬化基础的患者,部分硬化结节结构仍然存在。

2.2.4 慢性肝衰竭 弥漫性肝脏纤维化,以及异常增生结节形成,可伴有分布不均的肝细胞坏死。

2.3 临床诊断 肝衰竭的临床诊断需要依据病史、临床表现和辅助检查等综合分析而确定。

2.3.1 急性肝衰竭 无基础肝病病史,急性起病,4周内出现Ⅱ级及以上肝性脑病(按Ⅳ级分类法划分)并有以下表现者:(1)乏力厌食、腹胀、恶心及呕吐等严重消化道症状;(2)凝血功能障碍,国际标准化比值(international normalized ratio, INR)≥1.5或凝血酶原活动度(prothrombin time activity, PTA)≤40%,并排除其他原因者;(3)总胆红素(total bilirubin, TBil)进行性升高。

2.3.2 亚急性肝衰竭 无基础肝病病史,起病较急,4~24周出现以下表现者:(1)乏力、厌食、腹胀、恶心及呕吐等严重消化道症状;(2)严重黄疸, TBil≥10×ULN 或每日上升≥1 mg/dL;(3)凝血功能障碍, INR≥1.5 或 PTA≤40%,并排除其他原因者;(4)腹水,伴或不伴肝性脑病。

2.3.3 慢加急性(亚急性)肝衰竭 慢加急性肝衰竭是在慢性肝病(无论有无肝硬化)基础上,不同诱因导致的急性肝功能恶化,伴随肝脏和/或肝外器官衰竭,短期内高病死率的复杂临床综合征^[10]。多个国际肝衰竭联盟根据各自区域的人群特征建立了相应的慢加急性肝衰竭诊断标准(表5)。

基于中国人群特征的 COSSH 诊断标准,将慢加急性肝衰竭划分为1、2、3三个等级^[11]。

慢加急性肝衰竭1级(早期):肝衰竭(TBil≥12 mg/dL)合并2.5≥INR≥1.5,或合并肾功能障碍(肌酐1.5~1.9 mg/dL),或合并Ⅰ~Ⅱ级肝性脑病(A1)。

慢加急性肝衰竭2级(中期):出现2个器官衰

表4 肝衰竭的分类

分类	定义
急性肝衰竭	急性起病,无基础肝病史,4周以内出现以Ⅱ级以上肝性脑病为特征的肝衰竭
亚急性肝衰竭	起病较急,无基础肝病史,4~24周出现肝功能衰竭的临床表现
慢加急性(亚急性)肝衰竭	在慢性肝病基础上(有无肝硬化),各种诱因导致短期内出现急性肝功能恶化,以肝脏和/或肝外器官衰竭和短期高病死率(28 d病死率>15%)为主要特征的复杂临床综合征
慢性肝衰竭	在肝硬化基础上,缓慢出现肝功能进行性减退导致的以反复腹水和(或)肝性脑病等为主要表现的慢性肝功能失代偿

表 5 慢加急性肝衰竭(ACLF)诊断标准

项目	COSSH-ACLF ^[11]	EASL-ACLF ^[9]	NACSELD-ACLF ^[10]	APASL 专家共识 ^[8]	世界胃肠病学组织 ^[17]
临床研究类型	多中心、前瞻性、观察性队列研究	多中心、前瞻性、观察性队列研究	多中心、前瞻性数据库分析	专家共识	专家共识
主要病因	HBV	酒精、HCV	HCV、酒精	HBV、酒精	-
发病诱因	肝内(HBV再激活)、肝外(细菌感染)或两者兼有	肝内(酒精性肝炎),肝外(感染、静脉曲张出血),或两者兼有	肝内型、肝外型,或两者兼有	肝内型	-
研究人群	乙肝相关慢性肝病急性失代偿(不论有无肝硬化)	肝硬化急性失代偿	肝硬化急性失代偿	慢性肝病急性失代偿(有失代偿史除外)	-
慢加急性肝衰竭定义	在慢性肝病(无论肝硬化与否)基础上出现的急性肝功能恶化,伴随肝脏和/或肝外器官衰竭(肝、肾、脑、凝血、呼吸和循环)以及短期高病死率(28 d病死率≥15%)的一组复杂临床综合征	肝硬化急性失代偿患者出现多器官功能衰竭(肝、肾、脑、凝血、呼吸和循环),伴随短期高病死率(28d病死率≥15%)的一组复杂临床综合征	合并感染的肝硬化患者出现2个及以上肝外器官衰竭(肾、脑、呼吸和循环)合并短期(30 d)高病死率	在既往已知或未知的慢性肝病基础上出现急性肝损伤(TB≥5 mg/dL和INR≥1.5)伴有4周内出现腹水或HE,并有28天高病死率	慢性肝病患者无论先前是否诊断为肝硬化,在诱因引起急性肝功能失代偿导致肝功能衰竭(黄疸和国际标准化比例延长)和一个或多个肝外器官衰竭,28 d和3个月内病死率增加将慢加急性肝衰竭分为3型: A型:在慢性非肝硬化肝病基础上发生; B型:在代偿期肝硬化基础上发生; C型:在既往发生失代偿的肝硬化基础上发生
慢加急性肝衰竭分级	ACLF-1级:肝衰竭(总胆红素≥12 mg/dL)合并2.5>INR≥1.5,或合并肾功能障碍(肌酐1.5~1.9 mg/dL),或合并I~II级肝性脑病; ACLF-2级:2个器官衰竭; ACLF-3级:≥3个器官衰竭	ACLF-1级:1个器官衰竭,包括(1)肾衰竭;(2)肝脏、凝血、循环或呼吸衰竭之一合并或肾功能障碍(肌酐1.5~1.9 mg/dL)或1~2级肝性脑病;(3)脑衰竭合并肾功能障碍(肌酐1.5~1.9 mg/dL); ACLF-2级:2个器官衰竭; ACLF-3级:≥3个器官衰竭	-	1级:AARC评分5~7分; 2级:AARC评分8~10分; 3级:AARC评分11~15分	-
器官衰竭定义	肝脏:总胆红素≥12 mg/dL;肾脏:肌酐≥2 mg/dL或使用连续性肾脏替代治疗; 凝血功能:国际标准化比值>2.5; 脑:West Haven 分级3~4级HE或因HE使用机械通气; 循环系统:血管活性药物的使用; 呼吸系统:PaO ₂ /FiO ₂ ≤200或SpO ₂ /FiO ₂ ≤214或使用非HE的使用机械通气	同COSSH标准下器官衰竭定义	肾脏:使用透析或其他形式的连续性肾脏替代治疗; 脑:West Have 分级3~4级; 循环系统:尽管有液体复苏和足够的心输出量,但平均动脉压<60 mmHg或收缩压较基础值降低40 mmHg; 呼吸系统:使用机械通气	肝脏:总胆红素≥5 mg/dL; 脑:临床肝性脑病	-
等级分布	1级:61%; 2级:33%; 3级:6%	1级:49%; 2级:35%; 3级:16%	2个器官衰竭:43%; 3个器官衰竭:41%; 4个器官衰竭:16%	-	-
短期病死率	28 d 1级:23%; 2级:61%; 3级:93%	28 d 1级:22%; 2级:32%; 3级:77%	30 d 2个器官衰竭:49%; 3个器官衰竭:64%; 4个器官衰竭:77%	28 d 1级:13%; 2级:45%; 3级:86%	-

注:“-”无相关数据

竭(肝、肾、脑、凝血、呼吸和循环)(A1)。

慢加急性肝衰竭3级(晚期):出现3个或3个以上器官衰竭(肝、肾、脑、凝血、呼吸和循环)(A1)。

本指南的慢加急性肝衰竭COSSH分级标准中的1、2、3三个等级相当于《肝衰竭诊治指南

(2018年版)》中慢加急性肝衰竭的早、中、晚期。

2.3.4 慢性肝衰竭 在肝硬化基础上,缓慢出现肝功能进行性减退和失代偿:(1)血清TBil升高,常<10×ULN;(2)白蛋白明显降低;(3)血小板计数明显下降,INR≥1.5(或PTA≤40%),并排除其他原因者;(4)有顽固性腹水或门静脉高压等表现;

(5) 肝性脑病。

在未到达亚急性肝衰竭和慢加急性肝衰竭诊断标准但患者极度乏力,有严重的消化道症状、丙氨酸转氨酶(alanine aminotransferase, ALT)和/或天冬氨酸转氨酶(aspartate aminotransferase, AST)大幅升高,黄疸进行性加深($5 \leq \text{Tbil} < 12 \text{ mg/dL}$)或每日上升 $\geq 1 \text{ mg/dL}$,有出血倾向, $40\% < \text{PTA} \leq 50\%$ ($\text{INR} < 1.5$),考虑存在肝衰竭前期,要提高警惕,须密切关注病情发展。

2.4 肝衰竭诊断格式 肝衰竭不是一个独立的临床诊断,而是一种功能判断。在临床实际应用中,完整的诊断应包括病因、临床类型及分级,建议按照以下格式书写:

肝衰竭(分类、分级)

疾病病因诊断(病毒、药物、酒精、免疫、寄生虫等)

例如:(1)慢加急性肝衰竭 1 级

乙型病毒性肝炎

(2)急性肝衰竭

病因待查

2.5 疗效判断

2.5.1 疗效指标 肝衰竭主要疗效指标是短期生存率(4 及 12 周无移植生存率)。次要疗效指标包括:(1)症状:患者乏力、纳差、腹胀、恶心及呕吐等临床症状的改善;(2)并发症:肝性脑病、腹水、上消化道出血、感染等并发症的缓解;(3)器官衰竭如呼吸、循环、肾脏等器官功能的恢复;(4)实验室指标:血液生化学检查示 TBil、PTA、INR 等好转。

2.5.2 疗效判断标准

2.5.2.1 临床治愈率 急性肝衰竭、亚急性肝衰竭以临床治愈率作为判断标准:(1)乏力、纳差、腹胀、尿少、出血倾向和肝性脑病等临床症状消失;(2)肝功能指标基本恢复;(3)INR 或 PTA 恢复正常。

2.5.2.2 临床好转率 慢加急性(亚急性)肝衰竭以临床好转率作为判断标准:(1)乏力、纳差、腹胀、出血等临床症状明显好转,肝性脑病消失;(2)黄疸、腹水等体征明显好转;(3)肝功能指标明显好转($\text{Tbil} \leq 5 \times \text{ULN}$, $\text{INR} \leq 1.5$ 或 $\text{PTA} \geq 40\%$)。

2.5.2.3 临床恶化 急性肝衰竭、亚急性肝衰竭、慢加急性(亚急性)肝衰竭临床恶化标准:(1)乏力、纳差、腹胀、出血等临床症状及体征加重;(2)肝功能指标加重;(3)新发并发症和/或肝外脏器官衰竭,或原有并发症加重。

2.6 预警预后评估 肝衰竭预警预后评估应贯穿诊疗全程,尤其强调早期、动态预后评估的重要性。传统临床预后工具包括终末期肝病模型(model for end-stage liver disease, MELD)^[28]、MELD 联合血清 Na (MELD-Na)^[29]、iMELD^[30]、皇家医学院医院(King's College Hospital, KCH)标准^[31]、序贯器官衰竭评估(sequential organ failure assessment, SOFA)^[32]等。KCH 标准适用于急性肝衰竭。MELD、MELD-Na 等可用于判断慢加急性肝衰竭预后结局,但敏感度和特异度较差。国内外学者基于上述不同诊断标准,建立并更新了各自标准下慢加急性肝衰竭预后评分模型,包括 CLIF-C ACLF 评分^[33]、COSSH-ACLF 评分^[11]、COSSH-ACLF II 评分^[34]、APASL-AARC 评分^[35]和 NACSELD-ACLF 评分^[36](表 6)。动态评估 COSSH 研究基于乙型肝炎人群的前瞻性开放性大队列,建立了预警慢加急性肝衰竭发生的 COSSH-onset-ACLF 评分模型^[37]。除基于传统临床指标的模型之外,近年来国内外学者利用多组学技术等发现了一系列有助于提高肝衰竭临床预警预后模型准确度的标志物,但仍有待进一步的验证和临床转化^[24-26, 38-43]。

3 肝衰竭的治疗

目前肝衰竭的治疗包括 3 个方面:一是内科综合治疗,二是人工肝治疗,三是肝移植治疗。原则上强调早诊断、早治疗,采取相应的病因治疗和综合治疗措施,并积极防治并发症,维持或支持器官功能稳定。整个治疗过程中应动态评估病情、加强监护,及时联合人工肝、桥接肝移植,减低病死率。

3.1 内科综合治疗

3.1.1 一般支持治疗

(1)卧床休息,减少体力消耗,减轻肝脏负担,病情稳定后加强适当运动(A5)。

(2)加强病情监护:评估精神状态,监测生命体征,记录体质量、腹围及二便变化等;建议完善病因及病情评估相关实验室检查,如 INR/凝血酶原时间(Prothrombin time, PT)、纤维蛋白原、乳酸脱氢酶、血常规、肝功能、血糖、血脂、电解质、血肌酐、尿素氮、血氨、动脉血气和乳酸、内毒素、肝衰相关病原微生物、铜蓝蛋白、自身免疫性肝病相关抗体检测,以及肝脏影像学等检查,定期检测评估,门静脉高压者应酌情完善胃镜^[44](A5)。有条件单位可完成血栓弹力图或旋转式血栓弹力计、凝血因子 V、凝血因子 VII、人类白细胞抗原(human leukocyte



表 6 慢加急性肝衰竭预警预后评分

评分模型	应用人群	评价指标	评分公式	应用
预后评分模型				
COSSH-ACLF IIs ^[34]	慢性肝病急性失代偿(不论有无肝硬化)	INR、HE 等级、中性粒细胞、TB、血尿素、年龄	$=1.649 \times \ln(\text{INR}) + 0.457 \times \text{HE 评分} + 0.425 \times \ln(\text{中性粒细胞}) + 0.396 \times \ln(\text{TB}) + 0.576 \times \ln(\text{血尿素}) + 0.033 \times \text{年龄}$	患者病死率的个体评估; 危险分层, 28 d 病死率: <7 分(低风险), 8.2%/18.7%; 7~<8.4 分(中风险), 49.7%/65.8%; ≥8.4 分(高风险), 76.3%/87.7%
COSSH-ACLFs ^[11]	慢性肝病急性失代偿(不论有无肝硬化)	HBV-SOFA 评分(包括肾、脑、循环和呼吸功能的判断)、INR、TB、年龄	$=0.741 \times \text{INR} + 0.523 \times \text{HBV-SOFA} + 0.026 \times \text{年龄} + 0.003 \times \text{TB}(\mu\text{mol/L})$	-
CLIF-C ACLFs ^[33]	肝硬化急性失代偿性	CLIF-OF 评分(包括肝、凝血、肾、脑、循环和呼吸功能的判断)、年龄、白细胞	$=10 \times [0.33 \times \text{CLIF OFs} + 0.04 \times \text{年龄} + 0.63 \times \ln(\text{白细胞}) - 2]$	患者病死率的个体评估
APASL-AARCs ^[35]	慢性肝病急性恶化	TB、Cre、INR、HE 等级、血乳酸	-	危险分层, 28 d 病死率: 5~7 分/ACLF-1 级: 13%; 8~10 分/ACLF-2 级: 45%; 11~15 分/ACLF-3 级: 86%
NAC-SELD-ACLFs ^[36]	肝硬化急性失代偿	HE 等级、肾脏替代治疗、机械通气、平均动脉压	-	≥2 个器官衰竭的 30 d 病死率: 41%
预警评分模型				
COSSH-on-set-ACLFs ^[37]	慢性肝病急性失代偿(不论有无肝硬化)	ALT、TB、INR、铁蛋白	$=0.101 \times \ln(\text{ALT}) + 0.819 \times \ln(\text{TB}) + 2.820 \times \ln(\text{INR}) + 0.016 \times \ln(\text{铁蛋白})$	预测肝衰竭发生率; 危险分层, 7/14/28 d 发生率: <6.3 分(低风险), 2.5%/3.2%/3.7%; ≥6.3 分(高风险), 42.6%/49.2%/50.0%

注:“-”. 无相关数据

antigen, HLA) 分型、间接测热法测定静息能量消耗(resting energy expenditure, REE) 等。

(3) 推荐对肝衰竭患者直接进行详细营养评定, 以确定营养不良的类型和程度^[45-46], 制订个体化营养支持方案。根据疾病情况、营养状态、消化吸收功能等综合因素逐步达到每日 1.3 倍 REE 或 30~35 kcal·kg⁻¹·d⁻¹ 的能量摄入目标^[45-48]。营养支持途径首选经口进食, 推荐分餐及夜间加餐、补充维生素和微量元素等, 必要时予肠内营养或肠外营养^[44, 49-50](A4), 其中肝衰竭合并肝性脑病患者的营养支持详见 3.1.4。

(4) 积极纠正低蛋白血症, 补充白蛋白或新鲜血浆, 并酌情补充凝血因子^[51](A5)。

(5) 监测血气分析和乳酸水平, 注意纠正水电解质及酸碱平衡紊乱, 特别要注意纠正低钠、低氯、低钾、低镁血症(A5)。

(6) 注意消毒隔离, 加强口腔护理、肺部及肠道管理, 预防医院感染发生(A5)。

3.1.2 对症治疗

3.1.2.1 抗炎护肝药物的应用 推荐使用具有抗炎、抗氧化、解毒、利胆和肝细胞膜修复保护作用的药物, 如异甘草酸镁、水飞蓟素、还原型谷胱甘肽、腺苷蛋氨酸、多烯磷脂酰胆碱等^[48, 49]。不同护肝药物分别通过抑制炎症反应、清除活性氧、解毒、免疫

调节、调节能量代谢、改善肝细胞膜稳定性、完整性及流动性等途径, 达到减轻肝脏组织损害, 促进肝细胞修复和再生, 减轻肝内胆汁淤积, 改善肝功能的目 的(A5)。

3.1.2.2 微生态调节治疗 越来越多的证据表明, 肠道微生物群参与肝脏疾病的发病机制^[52-53]。肝衰竭患者存在肠道微生态失衡, 表现为肠道乳酸杆菌、双歧杆菌等有益菌减少, 韦荣球菌、链球菌等条件致病菌增多^[54], 导致继发感染、肝性脑病。而应用肠道微生态调节剂, 如双歧杆菌、乳酸杆菌、戊糖片球菌等益生菌, 乳果糖等益生元, 以及益生菌和益生元组成的合生元, 可改善肝衰竭肠道微生态^[55-56](A5), 维持微生态平衡, 减少继发感染, 降低肝性脑病患者的血氨水平和改善心理测量测试, 改善肝衰竭患者预后^[57]。粪便菌群移植(faecal microbiota transplantation, FMT)可快速重建健康、平衡的肠道微生态系统, 恢复肠道功能, 减少感染风险, 改善肝功能, 可作为一种治疗肝衰竭尤其是肝性脑病的新技术^[58]。因此, 建议肝衰竭患者尽早开展肠道优势菌群十联检检测, 及时发现肠道微生态失衡, 为及时干预提供依据^[59]。

3.1.2.3 免疫调节剂的应用 肾上腺皮质激素在肝衰竭治疗中的应用尚存在不同意见, 肾上腺皮质激素使用时机、类型和剂量尚无共识。非病毒感染

性肝衰竭,如自身免疫性肝炎、药物诱导的自身免疫性肝炎及急性酒精中毒(重症酒精性肝炎)等,可考虑肾上腺皮质激素治疗(甲泼尼龙,1.0~1.5 mg·kg⁻¹·d⁻¹)(A1),治疗中需密切监测,及时评估疗效与并发症。其他原因所致的急性肝衰竭前期或早期,若病情发展迅速且无严重感染、出血等并发症者,可酌情短期使用^[60](B3)。

有报道胸腺肽 α 1治疗慢加急性肝衰竭,尤其是合并感染患者,有助于降低90 d病死率^[61](B2)。对肝衰竭合并感染患者建议早期应用。粒细胞集落刺激因子(granulocyte colony-stimulating factor, G-CSF)治疗能促进慢加急性肝衰竭患者CD34(+)细胞的动员,有望提高疗效^[62](B2)。

其余免疫调节剂多应用于自身免疫性肝炎相关肝衰竭的治疗,例如吗替麦考酚酯、他克莫司、环孢素,可作为使用标准疗法(泼尼松龙单用或联合硫唑嘌呤)无效的自身免疫性肝炎患者二线用药,西罗莫司、英夫利昔单抗和利妥昔单抗等可作为三线用药^[63](A2)。

3.1.3 病因治疗

明确肝衰竭病因对指导治疗及判断预后具有重要价值,包括查明发病原因及诱因两类。对其尚不明确者应积极寻找病因以期达到正确处理的目的^[64]。

3.1.3.1 去除诱因 去除如重叠感染、应激、饮酒、劳累、药物、出血等诱因。

3.1.3.2 针对不同病因治疗 (1)肝炎病毒感染: HBsAg阳性乙型肝炎患者,不论其HBV DNA是否阳性,及HBV DNA载量高低,建议立即使用核苷(酸)类药物抗病毒治疗。在肝衰竭前、早、中期开始抗病毒治疗疗效相对较好。对慢加急性肝衰竭的有关研究指出,早期快速降低HBV DNA载量是治疗的关键,若HBV DNA载量在2周内能下降2 lg IU/mL,患者存活率可提高^[65]。抗病毒药物应优先选择快速强效的核苷(酸)类药物,如恩替卡韦、替诺福韦、丙酚替诺福韦、艾米替诺福韦等^[65-68](A2)。

丙型肝炎病毒(hepatitis C virus, HCV)RNA阳性的肝衰竭患者,可根据肝衰竭发展情况选择抗病毒时机及药物治疗。若MELD评分<18~20,可在移植术前尽快开始抗病毒治疗,部分患者经治疗后可从移植列表中退出;若MELD评分 \geq 18~20,可先行移植术,术后再行抗病毒治疗。如果等待移植时间超过6个月,可在移植前行抗病毒治疗。移植后患者一旦出现HCV RNA阳性,应及时抗病毒治疗。

抗病毒治疗首选无干扰素的直接抗病毒药物(direct acting antiviral agents, DAAs)治疗方案,必要时根据HCV基因型、患者耐受情况等进行个体化治疗。NS3/4A蛋白酶抑制剂、干扰素禁用于失代偿期肝硬化患者。在治疗过程中应定期监测血液学指标、HCV RNA及不良反应等^[69-70](A1)。

有研究报道,戊型肝炎病毒(HEV)导致的肝衰竭患者接受利巴韦林治疗,可快速清除HEV^[71],但目前尚未证实在甲型、戊型病毒性肝炎引起的急性肝衰竭中,抗病毒治疗有效(B5)。

其他病毒感染:确诊或疑似疱疹病毒或水痘-带状疱疹病毒感染导致急性肝衰竭的患者,应使用阿昔洛韦(5~10 mg/kg, 1次/8 h, 静脉滴注)或更昔洛韦(5 mg/kg, 1次/12 h, 静脉滴注)等治疗,且危重者可考虑进行人工肝、肝移植。

(2)药物性肝损伤:因药物肝毒性所致急性肝衰竭,应停用所有可疑的药物,并避免再次使用可疑或同类药物。追溯过去6个月服用的处方药、某些中草药、非处方药和膳食补充剂的详细信息(包括服用数量和最后一次服用的时间),尽可能确定非处方药的成分。N-乙酰半胱氨酸(NAC)对药物性肝损伤所致急性肝衰竭有效^[72-73]。怀疑对乙酰氨基酚(acetaminophen, APAP)中毒的急性肝衰竭患者也可应用NAC,必要时进行人工肝治疗。在非APAP引起的急性肝衰竭患者中,静脉注射NAC能改善I~II级早期肝性脑病患者的无肝移植生存率,但III~IV级重度肝性脑病的患者通常需要肝移植^[74]。确诊或疑似毒蕈中毒的急性肝衰竭患者,考虑应用青霉素G和水飞蓟素^[75-77](A5)。

肝毒性是免疫检查点抑制剂(ICIs)治疗相关不良事件之一,肿瘤患者在接受ICIs治疗前应进行评估,并在治疗过程中进行肝脏功能的监测^[78]。在ICIs所致的3级以上肝损伤患者(ALT \geq 5~20 \times ULN, TB \geq 3~10 \times ULN)中,应立即停用ICIs,开始使用大剂量肾上腺皮质激素治疗(每日1~2 mg/kg 甲基强的松龙或相当剂量激素),如治疗3~5 d后无明显改善,可考虑加用麦考酚酯或他克莫司^[79-80](A3)。药物治疗效果不佳时,尽早联合人工肝治疗。

(3)妊娠期急性脂肪肝(acute fatty liver of pregnancy, AFLP)/HELLP综合征导致的肝衰竭:当发生HELLP综合征、AFLP使孕妇病情迅速恶化的情况时,应在诊断明确和疾病稳定后立即终止妊娠^[81-82](A1)。如果终止妊娠后病情仍继续进展,需考虑人工肝和肝移植治疗。

(4)肝豆状核变性:肝移植可以挽救肝豆状核变性所致慢加急性肝衰竭患者的生命,提高患者的长期生存率^[83](A3)。人工肝联合铜螯合剂可用于肝豆状核变性导致的急性肝衰竭患者,在较短时间内改善病情,有利于过渡到肝移植手术^[84-85](A4)。对于术前存在明显神经系统症状的肝豆状核变性患者,在肝移植术后应继续低铜饮食,并加小剂量锌剂治疗^[86]。

3.1.4 并发症的内科综合治疗

3.1.4.1 脑水肿

(1)有颅内压增高者,给予甘露醇0.5~1.0 g/kg或者高渗盐水治疗^[87](A3),对于存在肾功能损伤时不宜使用甘露醇,宜使用高渗盐水^[88](A3);

(2)襻利尿剂,一般选用呋塞米,可与渗透性脱水剂交替使用;

(3)应用人血白蛋白,特别是肝硬化白蛋白偏低的患者,提高胶体渗透压,可能有助于降低颅内压,减轻脑水肿症状;

(4)人工肝支持治疗;

(5)肾上腺皮质激素不推荐用于控制颅内高压^[88](A1)。

3.1.4.2 肝性脑病

(1)识别并去除诱因,如严重感染、出血及电解质紊乱等;

(2)调整蛋白质摄入及营养支持,为减轻肝脏负担及预防肝性脑病的发生和加重,建议减少蛋白摄入,一般情况下蛋白质摄入量维持在1.2~1.5 g·kg⁻¹·d⁻¹,Ⅲ级以上肝性脑病者蛋白质摄入量为0.5~1.2 g·kg⁻¹·d⁻¹^[46](A4),在总蛋白摄入量不超过限制的前提下,可考虑用植物蛋白和乳蛋白替代动物蛋白^[89-90](B4)。对不能耐受口服蛋白质摄入的患者可考虑补充支链氨基酸(branched-chain amino acids,BCAA)^[47,91](B5)。营养支持能量摄入在危重期推荐25~35 kcal·kg⁻¹·d⁻¹,病情稳定后推荐35~40 kcal·kg⁻¹·d⁻¹^[46](A4)。一旦病情改善,可给予标准饮食。建议在白天少食多餐,夜间睡前可食用适量碳水^[92](B5);

(3)应用乳果糖或低聚果糖,口服或高位灌肠,可酸化肠道,促进氨的排出,调节微生态,减少肠源性毒素吸收^[93-95](A1)。利福昔明可作为乳果糖的辅助用药,推荐作为二级预防用药^[96-99](A2);

(4)视患者电解质和酸碱平衡情况酌情选择精氨酸、门冬氨酸-鸟氨酸等降氨药物^[100](A2)。益生菌和微生物粪便移植可能会改善显性肝性脑病的

发展,降低血氨^[58,101-103](A2);

(5)Ⅲ~Ⅳ级肝性脑病患者可酌情使用BCAA或BCAA与精氨酸混合制剂以纠正氨基酸失衡^[91,104](B5);

(6)Ⅲ级以上的肝性脑病患者存在误吸风险,GCS评分≤7分的患者可转移至重症监护病房(ICU)接受治疗^[13,105](A4);

(7)抽搐患者可酌情使用半衰期短的药物,例如丙泊酚、右美托咪定来镇静和镇痛,不推荐预防用药^[13](B5);

(8)人工肝支持治疗可改善肝性脑病症状^[106-108](A2)。

3.1.4.3 感染

(1)推荐常规进行血液和体液的病原学及感染相关检查;

(2)除肝移植前围手术期患者外,不推荐常规预防性使用抗感染药物;

(3)一旦出现感染征象,应首先明确感染部位,根据经验选择抗感染药物,并及时根据病原学检测及药敏试验结果调整用药^[109-110](A4);

(4)应用广谱抗感染药物,联合应用多个抗感染药物,以及应用肾上腺皮质激素类药物等治疗时,应注意防治继发真菌感染^[111](A4)。

3.1.4.4 低钠血症及顽固性腹水 低钠血症是常见并发症。而低钠血症、顽固性腹水与急性肾损伤(acute kidney injury, AKI)等并发症相互关联。水钠潴留所致稀释性低钠血症是其常见原因,托伐普坦作为精氨酸加压素V2受体阻滞剂,可通过选择性阻断集合管主细胞V2受体,促进自由水的排泄,用于治疗低钠血症及顽固性腹水^[112](A4)。对顽固性腹水患者:(1)限制钠盐的摄入,每日钠盐摄入量不超过4~6 g^[113]; (2)推荐螺内酯联合呋塞米起始联用,应答差者,可应用托伐普坦^[114](B2); (3)特利加压素1~2 mg/次,1次/12 h; (4)腹腔穿刺放腹水; (5)输注白蛋白^[115](A3); (6)经颈静脉肝内门腔静脉分流术(transjugular intrahepatic portosystemic shunt, TIPS)治疗。

3.1.4.5 AKI及肝肾综合征(hepatorenalsyndrome, HRS) 对于肝衰竭患者,应积极预防AKI的发生:系统性抗炎治疗,积极控制感染,降低胆红素水平,纠正低血容量和维持高平均动脉压,避免肾毒性药物和非甾体类药物等,需用静脉造影剂的检查者需权衡利弊后选择^[8,116-119](B3)。

AKI患者的治疗应综合评估病因、严重程度、



血流动力学及全身情况等:(1)当诊断为AKI时,应尽快调查其病因并积极控制,对于疑似细菌感染的患者,建议采集培养标本后,尽早给予经验性抗生素^[120](A4);(2)应立即停用利尿治疗和/或 β 受体阻滞剂,并停用可能肾损伤药物、血管扩张剂和非甾体消炎药^[121-122](A3);(3)根据液体丢失的原因和程度进行扩容量和补液,肾前性的患者可以使用晶体液治疗,而急性消化道出血患者应给予浓缩红细胞,以维持血红蛋白水平在70~90 g/L^[123-124](A3);(4)在停用利尿剂并控制诱因后,按照 $1\text{ g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ 剂量(最大剂量100 g/d)连续2 d静脉输注20%白蛋白扩充血容量,无效者需考虑是否存在肝肾综合征^[125](A3)。

肝肾综合征患者应立即接受白蛋白输注联合血管收缩药物治疗,改善肾脏灌注:(1)对于HRS-AKI优先推荐特利加压素(2 mg/24 h)联合白蛋白(20~40 g/d),治疗2 d且血肌酐下降 $\leq 25\%$,特利加压素可逐步增加至6 mg/24 h^[126-131](A1)。若有效,疗程7~14 d;若无效,停用特利加压素。(2)去甲肾上腺素(0.5~3.0 mg/h)联合白蛋白(10~20 g/L)在HRS-AKI患者的治疗上与特利加压素有相似的效果^[131-135](A1)。在休克患者的治疗上,优先推荐使用去甲肾上腺素^[13](A5)。(3)米多君联合奥曲肽,仅在无法获取特利加压素及去甲肾上腺素时推荐使用^[124, 131, 136](B2)。(4)肾脏替代治疗(RRT)的时机应根据个体情况综合评估,对于药物治疗效果欠佳且有机会接受肝移植的患者,RRT作为肾功能恶化、电解质紊乱或容量过载的桥接治疗^[137-140](A2)。(5)TIPS可用于改善HRS-NAKI患者的肾功能、控制难治性腹水,但尚不倡导在HRS-AKI患者中使用TIPS^[141-142](B3)。

3.1.4.6 消化道出血

(1)常规推荐使用质子泵抑制剂^[143](A1);

(2)对确诊门静脉高压性出血的患者,应立即使用血管活性药物降低门静脉压力,首选特利加压素、生长抑素类似物或奥曲肽,持续治疗3~5 d^[121, 144-146](A1)。急性出血期应避免使用 β 受体阻滞剂和血管扩张剂^[124];

(3)建议在发生出血后即开始抗生素预防性治疗,降低感染发生率并改善出血(A1),推荐使用头孢曲松或喹诺酮类药物^[147-149];

(4)尽早开始扩容补液,恢复和维持血流动力学稳定,保证组织灌注(A5),红细胞输注阈值为血红蛋白低于70 g/L,并维持70~90 g/L^[150-152](A2);

(5)在血流动力学恢复后,应尽早完善内镜治疗,行内镜下套扎、硬化剂注射或组织黏合剂治疗止血^[150, 153-154](A1);

(6)食管胃底静脉曲张所致出血者可用三腔管压迫止血作为内镜难以治疗的过渡治疗^[121](B5);

(7)对于Child-Pugh评级C级(<14分),或Child-Pugh评级B(评分>7分)合并活动性出血的患者,可考虑早期行TIPS^[155-156](B2)。对于药物联合内镜治疗后仍持续出血的患者,应首选TIPS治疗^[121](A5)。

3.1.4.7 肝肺综合征和门脉性肺动脉高压
 $\text{PaO}_2 < 80\text{ mmHg}$ ($1\text{ mmHg} = 0.133\text{ kPa}$)时给予氧疗,通过鼻导管或面罩给予低流量氧(2~4 L/min),对于氧流量需要增加的患者,可以加压面罩给氧或者气管插管。重度门脉性肺动脉高压(POPH)患者进行肝移植风险极高,前列环素等扩血管药物可能改善POPH患者的血液动力学^[157]。

3.2 非生物型人工肝支持治疗

3.2.1 概述 人工肝是治疗肝衰竭的有效方法之一,通过一个体外的机械、理化和生物装置,清除各种有害物质,补充必需物质,改善内环境,暂时替代衰竭肝脏的部分功能,为肝细胞再生及肝功能恢复创造条件或等待机会进行肝移植。

人工肝支持系统分为非生物型、生物型和混合型3种。非生物型人工肝已在临床广泛应用并被证实有一定疗效^[106, 158-171](A3),生物型和混合型人工肝尚在研发阶段,临床应用仍需积极探索。本指南中主要介绍非生物型人工肝治疗。

目前在临床上常用的人工肝系统是李氏非生物型人工肝(Li's Non-Bioartificial Liver, Li-NBAL)。Li-NBAL系统自1986年开始研究,经历了3个发展阶段, Li-NBAL 1.0系统主要是以置换、吸附和滤过等单一治疗模式为特征。在此基础上持续发展,又创建了一系列根据不同病情进行不同组合的Li-NBAL 2.0系统,包括血浆透析滤过(plasmadialfiltration, PDF)、血浆置换联合血液滤过(plasma exchange with hemofiltration, PERT)、配对血浆置换吸附滤过(coupled plasma exchange filtration adsorption, CPEFA)、双重血浆分子吸附系统(double plasma molecules adsorption system, DPMAS)。

为了实现临床治疗方案系统化、技术操作标准化、治疗功能集成化, Li-NBAL系统进一步得到发展,形成了功能更全面的Li-NBAL 3.0系统。Li-NBAL 3.0系统以小剂量血浆置换为基础,通过

对置换过程中分离的血浆进行血浆吸附(阴离子树脂、活性炭等)、血浆滤过多次循环,补充少量新鲜血浆及白蛋白,同时全面清除血浆中各种毒素物质,能实现解毒代谢、合成和平衡功能,提高了临床治疗效果,节省了血浆用量,而且使人工肝治疗流程更规范、更标准、更简便。

Li-NBAL 3.0 系统功能介绍简述如下:(1)解毒代谢功能:通过血浆吸附、血液/血浆滤过分别清除炎性介质、胆红素、血氨、芳香族氨基酸及内毒素等多种有害物质;(2)合成功能:通过血浆分离法选择性地从循环血液中除去病理血浆或血浆中的某些大分子致病物质,同时补充白蛋白和凝血因子等有益物质,提高机体胶体渗透压、物质转运载体水平,改善凝血因子;(3)平衡功能:通过血液/血浆滤过保持水、电解质和酸碱平衡。各医疗单位可根据实际情况,结合患者病情,选择上述功能单独使用,也可以对各功能进行组合使用。

其他还有分子吸附再循环系统(molecular absorbent recycling system, MARS)、连续白蛋白净化治疗(continuous albumin purification system, CAPS)、成分血浆分离吸附(fractional plasma separation and adsorption, FPSA)等。推荐人工肝治疗肝衰竭方案采用联合治疗方法为宜,注意操作的规范化。

3.2.2 适应证

(1)各种病因引起的急性肝衰竭、亚急性肝衰竭和慢加急性肝衰竭 COSSH 分级 1~2 级(早、中期)的患者;COSSH 分级 3 级(晚期)的慢加急性肝衰竭患者病情重、并发症多,应权衡利弊,慎重进行治疗,同时积极寻求肝移植机会^[106, 158-166](A3);

(2)肝衰竭患者肝移植前等待肝源、肝移植术后排斥反应及移植肝无功能、ABO 血型不合肝移植围手术期脱敏治疗的患者^[166-169](A4)。

3.2.3 相对禁忌证

- (1)活动性出血或弥漫性血管内凝血者;
- (2)对治疗过程中所用耗材、血制品或药物等严重过敏者;
- (3)血流动力学不稳定者;
- (4)心脑血管意外所致梗死非稳定者;
- (5)血管外溶血者。

虽有相对禁忌证,但病情治疗需要,经与患者或其家属充分知情同意,仍可通过选择相对安全的治疗模式进行治疗^[172-173](A5)。

3.2.4 并发症 人工肝治疗的并发症有出血、凝

血、深静脉血栓、低血压、继发感染、过敏反应、失衡综合征、高枸橼酸盐血症和肝素诱导的血小板减少症等。需要在人工肝治疗前充分评估并预防并发症的发生,在人工肝治疗中和治疗后严密观察并发症。随着人工肝技术的发展,并发症发生率逐渐下降,一旦出现,可根据具体情况给予相应处理^[172-173](A5)。

3.3 肝移植 肝移植是治疗各种原因所致的终末期肝功能衰竭的最有效方法^[174],适用于经积极内科综合治疗和/或人工肝治疗疗效欠佳,不能通过上述方法好转或恢复者。

3.3.1 适应证

(1)对于急性/亚急性肝衰竭、慢性肝衰竭患者,MELD 评分是评估肝移植的主要参考指标,MELD 评分为 15~40 分是肝移植的最佳适应证^[175-179]。此外,超紧急状态(IA)患者拥有供肝分配最高优先级^[174, 180-181](A1);

(2)对于慢加急性肝衰竭,经过积极的内科综合治疗及人工肝治疗后 CLIF-C 分级为 2~3 级的患者,建议尽早行肝移植;AARC 评分中,ACLF I~II 级治疗 1 周内评分无下降患者和 AARC ACLF III 级患者应优先行肝移植治疗^[182](B2);

(3)对于合并肝癌的肝衰竭患者,优先选择符合肿瘤无大血管侵犯及肝外转移,肿瘤累计直径≤8 cm 或肿瘤累计直径>8 cm、术前 AFP≤400 ng/mL 且组织学分级为高/中分化^[183](B2);

(4)对于合并严重肾损伤或终末期肾病的肝衰竭患者可考虑肝肾联合移植^[184](B3)。

3.3.2 禁忌证^[179](B2)

- (1)严重脑水肿并发脑疝;
- (2)严重循环功能衰竭,对血管活性药物剂量增加无反应;
- (3)持续严重的感染,细菌或真菌引起的败血症,感染性休克,活动性肺结核^[185-186];
- (4)合并存在肝外弥漫多发未控制的恶性肿瘤;
- (5)合并存在未控制的严重精神疾病。

4 展望

肝衰竭的预警和诊疗仍是国际难题,需进一步研究揭示肝衰竭的发病机制,融合应用生物技术、细胞技术和人工智能技术发现和筛选肝衰竭的精准宿主标志物,结合关键临床参数,早期识别和监测肝衰竭的高危人群,建立高循证医学证据等级的

预警预测体系、早期诊断和分级分期标准;进一步研发智能型非生物型和生物型人工肝脏技术、肝脏3D打印技术、细胞治疗技术,肝移植技术,实现肝衰竭高效的个性化治疗,促进肝细胞再生,恢复肝脏功能;研究大数据、人工智能、物联网等技术实现肝衰竭恢复期患者的远程监控和智能化管理,攻克肝衰竭高病死率的国际难题。

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