DOI:10.16016/j.2097-0927.202507027

# 慢性肝病患者术后转入ICU首日液体入量对术后7天死亡风险的MIMIC-IV回顾性队列研究

占 卓,杨纯勇,舒 欣,朱易紫婷,鲁开智,邵建良 陆军军医大学(第三军医大学)第一附属医院麻醉科,重庆

[摘要] **目的** 慢性肝病患者常表现出独特的血流动力学异常与代谢紊乱,术后液体管理面临诸多挑战,尤其是术后入住重症监护室(intensive care unit,ICU)的重症患者,亟待深入探究术后液体治疗方案与预后之间的关系。**方法** 本研究基于MIMIC-IV数据库中2 414名慢性肝病、接受手术治疗,并术后转入ICU的患者,对纳排后最终得到的2 143名患者数据进行回顾性队列研究。采用多变量调整Logistic回归模型,分析术后转入ICU首日液体治疗方案与术后7天死亡风险的关联,并通过限制性立方样条(restricted cubic spline,RCS)分析剂量-反应关系。**结果** 多因素分析指出限制性补液为独立保护因素,相较于非限制性补液组,限制性补液显著降低了术后7天死亡率(6.4% *vs* 12.4%,*OR*=0.44,95%*CI*:0.22~0.88,*P*=0.021)。减少了机械通气的使用(42.9% *vs* 72.3%,*OR*=0.29,95%*CI*:0.24~0.35,*P*<0.001)和ICU停留时长(1.86 d *vs* 3.47 d,*OR*=0.81,95%*CI*:0.78~0.84,*P*<0.001)。RCS曲线显示,术后首日液体入量与术后7天死亡风险呈现J型曲线关系,拐点为1 850 mL,超过该阈值后,术后7天死亡风险随之增加。亚组分析结果表明,限制性补液的保护作用在不同年龄、合并症群体中均呈现出一致性。**结论** 慢性肝病患者术后首日采取限制性补液方案可有效降低短期死亡风险,且液体入量与7天死亡风险呈非线性剂量效应关联,液体入量超过1 850 mL时,死亡风险显著升高。

[关键词] 慢性肝病;MIMIC-IV数据库;液体治疗;术后短期死亡率;限制性补液

[中图法分类号] R181.32;R472.9;R575 [文献标志码] A

# Effect of first-day fluid intake after transferring to ICU on 7-day risk for death in patients with chronic liver disease after surgery: a retrospective cohort study based on MIMIC-IV database

ZHAN Zhuo, YANG Chunyong, SHU Xin, ZHU Yiziting, LU Kaizhi, SHAO Jianliang Department of Anesthesiology, First Affiliated Hospital, Army Medical University (Third Military Medical University), Chongqing, China

[**Abstract**] Objective Patients with chronic liver diseases often exhibit unique hemodynamic abnormalities and metabolic disorders. Postoperative fluid management presents numerous challenges, especially for critically ill patients admitted to the intensive care unit (ICU) after surgery. This study aimed at exploring the relationship between postoperative fluid therapy and prognosis. Methods Based on 2 414 patients with chronic liver diseases who underwent surgical treatment and were subsequently transferred to the ICU in the MIMIC-IV database, a retrospective cohort study was conducted on the final 2 143 patients after

[基金项目] 国家重点研发计划(2018YFC0116700)

[通信作者] 鲁开智,E-mail:lukaizhi2010@163.com

邵建良,E-mail:654708721@qq.com

2097-0927/Copyright © 2025,陆军军医大学(第三军医大学)。这篇开放获取文章遵循CC BY许可协议(https://creativecommons.org/licenses/by/4.0/)

**引用格式**:占卓,杨纯勇,舒欣,等.慢性肝病患者术后转入ICU首日液体入量对术后7天死亡风险的MIMIC-IV回顾性队列研究[J].陆军军医大学学报,2025,47(16):1931-1939.DOI:10.16016/j.2097-0927.202507027.

**Citation**:ZHAN Z,YANG C Y,SHU X,*et al*. Effect of first-day fluid intake after transferring to ICU on 7-day risk for death in patients with chronic liver disease after surgery: a retrospective cohort study based on MIMIC-IV database[J]. J Army Med Univ,2025,47(16):1931-1939. DOI:10.16016/j.2097-0927.202507027.

our inclusion and exclusion criteria. Multivariate adjusted logistic regression model was used to analyze the association between fluid therapeutic regimens on the first day after ICU admission and the risk of 7-day death after surgery. Restricted cubic spline (RCS) was applied to analyze the dose-response relationship. **Results** Multivariate analysis indicated that restrictive fluid resuscitation was an independent protective factor. Compared with the non-restrictive fluid resuscitation group, restrictive fluid resuscitation significantly reduced the 7-day postoperative mortality rate (6.4% *vs* 12.4%, *OR*=0.44, 95%*CI*: 0.22~0.88, *P*=0.021), decreased the use of mechanical ventilation (42.9% *vs* 72.3%, *OR*=0.29, 95%*CI*: 0.24~0.35, *P*<0.001), and shortened the ICU stay (1.86 *vs* 3.47 d, *OR*=0.81, 95%*CI*: 0.78~0.84, *P*<0.001). RCS curve showed that the fluid intake on the first postoperative day and the 7-day postoperative mortality risk presented a J-shaped curve relationship, with an inflection point at 1 850 mL. Beyond this threshold, the 7-day postoperative mortality risk was increased. Subgroup analysis results indicated that the protective effect of restrictive fluid resuscitation was consistent across different age and comorbidity groups. **Conclusion** For patients with chronic liver diseases, adopting a restrictive fluid therapy on the first day after surgery can effectively reduce the risk of short-term death. Moreover, there is a non-linear dose-effect relationship between the fluid intake and the 7-day mortality risk. When the fluid intake exceeds 1 850 mL, the risk of death significantly increases.

[**Key words**] chronic liver disease; MIMIC-IV Database; fluid therapy; chronic liver diseases; fluid restriction

Supported by the National Key Research and Development Program (2018YFC0116700). Corresponding authors: LU Kaizhi, E-mail: lukaizhi2010@163.com; SHAO Jianliang, E-mail: 654708721@qq.com

我国年手术量已突破8 000万例,作为肝病大国,我国慢性肝病患者接受手术治疗的需求持续上升[1]。这类患者往往存在凝血功能障碍、代谢解毒功能受损及门静脉高压等病理生理改变,术后并发症发生率高,严重影响患者预后[1-2]。尤其是术后入ICU的患者,病情更为危急,有较高的死亡风险[3-4]。液体管理作为术后管理以及重症监护治疗的核心环节,直接影响组织灌注、器官功能及电解质平衡,优化术后早期液体治疗方案对于改善患者预后至关重要[5-8]。然而,对于手术及创伤患者,目前仍缺乏具有针对性和器官特异性的液体治疗方案,现有方案在临床上应用效果不佳[9]。

当慢性肝病进展至肝硬化时,患者普遍存在有效循环血容量不足、高动力循环及毛细血管渗漏等病理生理改变[10-11],过度限制性液体治疗可能导致组织低灌注及器官功能障碍,而过度补液策略则可能诱发局部炎症反应、肺部并发症等不良事件[12-15]。尽管现行指南提出了目标导向液体治疗(goal-directed fluid therapy,GDFT)、限制性输液等管理方案,但针对不同手术类型及风险分层患者的策略选择仍存在争议,目前尚缺乏专门针对慢性肝病患者术后早期液体管理的明确推荐方案[16-19]。亟需开展系统性研究以明确术后早期液体管理对慢性肝病患者预后的影响,并建立剂量-效应关系模型。

本研究旨在系统评估术后早期液体入量是否构成慢性肝病手术患者术后死亡的独立危险因素,探究是否存在安全剂量阈值,并分析不同临床亚组间的异质性。拟通过构建多阶段调整模型和限制性立方样条(restricted cubic spline,RCS)分析,为慢性肝病患者术后液体管理策略的制定提供参考。

## 1 资料与方法

### 1.1 研究人群与数据提取

本研究数据来源于MIMIC-IV v2.2数据库[20]。该公开获取的临床数据库收录了2008年至2019年间贝斯以色列女执事医疗中心(Beth Israel deaconess medical center,BIDMC)收治患者的脱敏临床数据,经去标识化处理以保障患者隐私。研究团队已通过协作机构培训倡议(collaborative institutional training initiative,CITI)程序认证,获得数据库访问权限(认证编号:46086293)。

慢性肝病患者定义参照Charlson合并症指数(Charlson comorbidity index, CCI)中"轻度至中重度肝脏疾病"评分标准[21],研究人群筛选的纳入标准:①确诊慢性肝病且接受手术治疗患者;②年龄为18~89岁;③术后24 h内转入ICU。排除标准:①数据记录异常(包括极端值、异常值等);②术后24 h内无液体输注记录。

纳入分析的变量包括:①术前相关变量:人口统计学资料(年龄、性别、体质量);术前合并疾病(充血

性心力衰竭、慢性肺部疾病、糖尿病、肾脏疾病、恶性肿瘤、CCI);②手术相关变量:手术类型(非肝脏手术和肝脏手术);③术后相关变量:术后首次实验室检查,包括白蛋白、血红蛋白、肝功能[丙氨酸氨基转移酶(alanine aminotransferase, ALT)、天门冬氨酸氨基转移酶(aspartate aminotransferase, AST)、总胆红素(total bilirubin, TBIL)]、凝血功能[国际标准化比值(international normalized ratio, INR)、凝血酶原时间(prothrombin time, PT)、活化部分凝血活酶时间(activated partial thromboplastin time, APTT)]、肾功能(血肌酐、术后首日尿量);术后首次序贯性器官功能衰竭评分(sequential organ failure assessment, SOFA);术后首日血管活性药物(是否使用及使用的总量),其中血管加压药包含去甲肾上腺素、多巴胺、肾上腺素、去氧肾上腺素和血管加压素,根据剂量对应关系转换为去甲肾上腺素当量;术后首日是否使用机械通气及术后首日静脉液体输注量,液体治疗为所有静脉液体入量,包含晶体、胶体、血制品等,并将其转换为等张液体当量。术后首日液体治疗方案根据静脉液体输注总量是否小于2 000 mL,划分为限制性补液与非限制性补液[22]。本研究的主要结局为术后7天死亡,次要结局包括院内死亡、术后90天死亡、住院时长、ICU停留时长及术后持续机械通气时长。

### 1.2 统计分析

采用SPSS 26.0软件(IBM Corp., Armonk, NY, USA)和R软件(version 4.2.2, R Core Development Team, Vienna, Austria)进行数据分析。限制性立方样条函数(restricted cubic spline,RCS)曲线的绘制采用R语言的rms包,方差膨胀系数(variance inflation factor,VIF)的计算通过car包,而亚组分析森林图则是基于forestploter包实现。正态分布的计量资料用$\bar{x}\pm s$表示,组间比较采用$t$检验;偏态分布的计量资料用$M$($P_{25}$, $P_{75}$)表示,组间比较采用Mann-Whitney $U$检验。计数资料采用例(%)表示,组间比较采用$\chi^2$检验或Fisher确切概率法。

采用多变量调整的Logistic回归模型分析术后首日液体管理策略对术后7天死亡风险的影响。构建四个递进式模型进行协变量逐步调整:模型1为单变量模型,仅纳入液体治疗方案,模型2调整人口统计学特征纳入液体治疗方案+人口统计学资料,模型3纳入液体治疗方案+人口统计学资料+术前相关变量,模型4纳入液体治疗方案+人口统计学资料+术前相关变量+手术及术后相关变量。所有模型均采用赤池信息准则(Akaike information criterion, AIC)进行拟合优度检验。

为探索效应修饰作用,按年龄(<65岁 *vs* ≥65岁)、性别(男 *vs* 女)、手术类型(肝脏手术 *vs* 非肝脏手术)、术前合并疾病(是 *vs* 否)及术后首日血管活性药物使用(是 *vs* 否)进行分层分析,通过似然比检验(likehood ratio test,LRT)评估交互作用显著性。剂量-反应关系分析采用RCS,节点数量由最小AIC确定,针对非线性关系进行Wald $\chi^2$检验,并绘制调整后优势比(odds ratio,*OR*)及95%*CI*的平滑曲线图,并对不同节点方案进行敏感性分析,以验证结果的稳健性。所有统计检验均为双侧,$P<0.05$为差异有统计学意义。

## 2 结果

### 2.1 慢性肝病手术患者基线信息

本研究最终纳入符合标准的慢性肝病手术患者2 143例(图1)。根据术后7日的生存状态将研究对象分为存活组($n$=1 946)与死亡组($n$=197),总体术后7日死亡率为9.19%,基线信息如表1所示。相较于存活组,死亡组年龄更大,术前合并心力衰竭、恶性肿瘤的占比更多,非肝脏手术患者占比更高(均$P<0.05$)。在术后首日,死亡组补液总量显著更高,凝血功能、AST及肾功能恶化程度更严重,白蛋白更低,术后首日首次SOFA评分更高,机械通气的比例及时间均更长,血管活性药物使用率更高(均$P<0.05$);而两组患者在性别、体质量、慢性肺部疾病、糖尿病、肾脏疾病及术后首次血红蛋白水平上差异无统计学差异。

相较于非限制性补液组,限制性补液组机械通气使用比例更低、使用时长更短,ICU停留时长、住院时

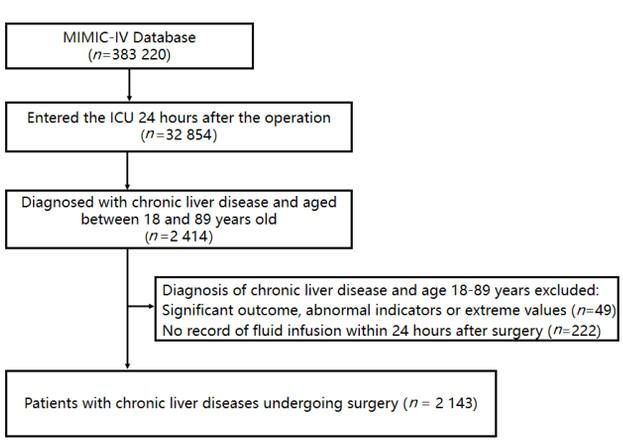



**图1 研究病例纳入排除流程图**

**Figure 1 Flowchart for inclusion and exclusion of the participants**

**表1 慢性肝病患者术后7天死亡的基线信息**[$\bar{x}\pm s$,$M(P_{25}, P_{75})$,例(%)]

**Table 1 Baseline data of the patients with chronic liver diseases on 7 d after surgery**[$\bar{x}\pm s$,$M(P_{25}, P_{75})$, cases (%)]

| Variable | The survival group $n$=1 946(90.81%) | The death group $n$=197(9.19%) | $P$ |
|---|---|---|---|
| Preoperative information | | | |
| Male, n (%) | 1276 (65.6) | 125 (63.5) | 0.605 |
| Age (years) | 59.77 (51.58, 68.10) | 64.14 (54.05, 76.97) | <0.001 |
| Weight (kg) | 80.95 (70.0, 96.0) | 80.0 (68.10, 95.0) | 0.154 |
| Congestive heart failure, n (%) | 383 (19.7%) | 54 (27.4%) | 0.013 |
| Chronic lung diseases, n (%) | 439 (22.6%) | 46 (23.4%) | 0.870 |
| Diabetes, n (%) | 632 (32.5%) | 53 (26.9%) | 0.129 |
| Kidney diseases, n (%) | 414 (21.3%) | 46 (23.4%) | 0.558 |
| Cancer, n (%) | 328 (16.9%) | 50 (25.4%) | 0.004 |
| CCI(score) | 5.0(4.0,7.0) | 6.0 (5.0,9.0) | <0.001 |
| Type of surgery, n (%) | | | 0.001 |
| Non-liver surgery | 1 697 (87.2%) | 188 (95.4%) | |
| Liver surgery | 249 (12.8%) | 9 (4.57%) | |
| Postoperative information | | | |
| Hemoglobin (g/dL) | 98.0 (83.0, 113.0) | 100.0 (83.0, 118.0) | 0.185 |
| Albumin (g/dL) | 31.0 (26.0, 36.0) | 27.0 (21.0, 34.0) | 0.002 |
| Creatinine (mg/dL) | 1.0 (0.70, 1.60) | 1.50 (0.90, 2.55) | 0.001 |
| ALT(U/L) | 37.0 (23.0, 100.0) | 63.0 (25.5, 191.75) | 0.149 |
| AST(U/L) | 66.0 (36.0,158.0) | 133.0 (60.0,685.50) | 0.019 |
| TBIL(mg/dL) | 1.90 (0.80,4.40) | 2.0 (1.00,6.40) | 0.046 |
| INR | 1.40 (1.20,1.80) | 1.80 (1.40,2.35) | <0.001 |
| PT(s) | 15.90 (13.60,19.50) | 19.10 (15.35,25.25) | <0.001 |
| APTT(s) | 34.40 (29.85,42.90) | 41.7 (33.80,63.10) | <0.001 |
| First SOFA (score) | 2.0 (0,5.0) | 4.0 (1.0,6.0) | <0.001 |
| First-day urine volume (mL) | 1 985.35(1 175.79,3201.62) | 721.32 (305.22,1 698.11) | <0.001 |
| First-day limited fluids, n (%) | 1066 (54.8%) | 73 (37.1%) | <0.001 |
| First-day total fluid (mL) | 1 731.21(766.54,3374.34) | 2 798.11(1 115.25,4 721.10) | <0.001 |
| First-day vasoactive agent, n (%) | 868 (44.6) | 165 (83.8) | <0.001 |
| First-day vasoactive agent dosages (mg) | 0. 0(0.0,0.28) | 1.48 (0.86,4.71) | <0.001 |
| Mechanical ventilation, n (%) | 1 066 (54.8%) | 149 (75.6%) | <0.001 |
| Duration of mechanical ventilation (h) | 19.79 (0.0,67.0) | 23.0 (1.0,61.25) | 0.540 |
| Length of ICU(day) | 2.33 (1.48,4.24) | 2.47 (1.31,4.53) | <0.001 |
| Hospital stay(day) | 9.15(5.58,16.39) | 3.30 (1.51,6.28) | <0.001 |
| Hospital deaths, n (%) | 127 (6.53%) | 191 (97.0%) | <0.001 |
| 90-day death after surgery, n (%) | 328 (16.9%) | 197 (100%) | <0.001 |

长更短,院内死亡风险、术后7天与术后90天死亡风险更低($P$<0.001),且术后首日尿量更多($P$=0.005,表2)。

### 2.2 多因素Logistic回归分析情况

拟纳入的多变量中,INR与PT存在严重多重共线性(均VIF>10,容差值<0.1),且条件指数达17.17;为确保模型稳健性,剔除INR与PT,剩余变量的条件指数降至4.21,不存在多重共线性(表3),纳入构建递进式回归模型。

如表4所示,在对慢性肝病手术患者术后7天死亡风险的Logistic回归分析中,术后首日实施限制性补液策略与术后7天死亡风险显著降低相关(模型1:$OR$=0.49,95%$CI$:0.36~0.66,$P$<0.001),该关联在逐步调整人口统计学资料(模型2:$OR$=0.46,0.33~0.62,$P$<0.001)、术前相关变量(模型3:$OR$=0.47,0.34~0.64,$P$<0.001)后保持高度稳定,调整手术及术后相关变量后(模型4:$OR$=0.44,0.22~0.88,$P$=0.021)效应值略有减弱且置信区间增宽,但仍具有统计学显著性。综上,术后首日的限制性补液与慢性肝病手术患者术后7天死亡风险显著降低相关,且这一关联在综合考虑多种潜在混杂因素后依然稳健。

分层分析表明,术后首日实施限制性补液与术后死亡风险降低相关,不受患者年龄($OR$:0.51~0.56,

表2 慢性肝病患者术后首日补液的结局信息[$M(P_{25}, P_{75})$,例(%)]

**Table 2 Outcomes of patients with chronic liver diseases with different fluid replacement on the first day after surgery** [$M(P_{25}, P_{75})$, cases (%)]

| Variable | Non-restrictive fluid therapy ($n$=1 004) | restrictive fluid therapy ($n$=1 139) | Odds Ratio (95%*CI*) | *P* |
|---|---|---|---|---|
| First-day urine volume (mL) | 1 672.25 (938.33, 2 795.68) | 2 116.29 (1 244.83,3 328.27) | 1.00 (1.00~1.00) | 0.005 |
| Mechanical ventilation(n) | 726 (72.3) | 489 (42.9) | 0.29 (0.24~0.35) | <0.001 |
| Duration of mechanical ventilation(h) | 19.79 (0.0,67.0) | 0.0 (0.0,10.43) | 0.99 (0.98~0.99) | <0.001 |
| Length of ICU(d) | 3.47 (2.05,6.54) | 1.86 (1.19,2.95) | 0.81 (0.78~0.84) | <0.001 |
| Hospital stay(d) | 10.65 (6.66,20.81) | 6.77 (4.16,12.01) | 0.96 (0.95~0.96) | <0.001 |
| Hospital deaths | 207 (20.60) | 111 (9.75) | 0.42 (0.32~0.53) | <0.001 |
| 7-day death after surgery | 124 (12.40) | 73 (6.41) | 0.49 (0.36~0.66) | <0.001 |
| 90-day death after surgery | 284 (28.3) | 241 (21.2) | 0.68 (0.56~0.83) | <0.001 |

表3 Logistic回归的共线性诊断

**Table 3 Collinearity diagnostics of logistic regression**

| Variable | VIF | Tolerance value |
|---|---|---|
| Preoperative information | | |
| Gender | 1.19 | 0.84 |
| Age | 1.77 | 0.56 |
| Weight | 1.25 | 0.80 |
| Congestive heart failure | 1.40 | 0.72 |
| Chronic lung diseases | 1.18 | 0.85 |
| Diabetes | 1.24 | 0.81 |
| Kidney diseases | 1.65 | 0.60 |
| Cancer | 1.48 | 0.67 |
| CCI | 2.81 | 0.36 |
| Type of surgery | 1.24 | 0.81 |
| Postoperative information | | |
| Hemoglobin | 1.25 | 0.80 |
| Albumin | 1.29 | 0.77 |
| Creatinine | 1.64 | 0.61 |
| ALT | 2.62 | 0.38 |
| AST | 2.80 | 0.36 |
| TBIL | 1.65 | 0.61 |
| INR | 71.64 | 0.01 |
| PT | 74.17 | 0.01 |
| APTT | 1.30 | 0.77 |
| First SOFA score | 1.57 | 0.64 |
| First-day limited fluids | 1.21 | 0.83 |
| First-day vasoactive agent dosages | 1.30 | 0.77 |
| Duration of mechanical ventilation | 1.30 | 0.77 |

$P$<0.05,交互$P$=0.465)和性别影响(男性$OR$=0.44,$P$<0.001;女性$OR$=0.76,$P$=0.316,交互$P$=0.186)。在非肝脏手术患者中,限制性补液显著降低死亡风险($OR$=0.52,$P$<0.001),而肝脏手术患者无显著关联($OR$=2.11,$P$=0.396),交互$P$=0.147。充血性心力衰竭、慢性肺部疾病、糖尿病和肾脏疾病亚组中,限制性补液多与死亡风险降低相关($P$<0.05),但交互作用无统计学差异。恶性肿瘤亚组间交互显著($P$=0.002),无恶性肿瘤患者中保护作用显著($OR$=0.41,$P$<0.001)。无论是否使用血管活性药物,限制性补液均显著降低风险($OR$:0.50~0.83,$P$<0.05,交互$P$=0.409),详见图2。

### 2.3 限制性立方样条分析

在慢性肝病手术患者中,术后首日液体输入量与术后7天全因死亡率呈非线性关联,具体表现为J型曲线特征,当节点为3时,AIC最小,其拐点位于1 850 mL处:当液体输入量高于该阈值时,死亡风险随输入量增加呈增加趋势(图3A)。敏感性分析表明,该关系在不同节点方案下保持一致,结果稳健。

亚组分析显示,不同性别、年龄、手术类型患者的液体输注量与死亡风险关系存在差异。具体而言,男性患者液体输注量与死亡风险正相关更显著(图3B),年龄大于65岁的高龄患者,液体输注量增加时死亡风险上升更明显(图3C),而非肝脏手术患者液体输注量与死亡风险的关系更密切(图3D)。

## 3 讨论

慢性肝病患者术后并发症发生率和死亡率显著高于普通患者[23],在术后早期液体管理方面,由于该群体独特的病理生理状态,如有效循环血容量相对不足、门静脉高压、低蛋白血症、高动力循环、潜在的肾损伤风险等,目前临床指南对于这类患者尚未达成共识[16-19],因此,深入探索并优化慢性肝病患者术后早期液体管理方案具有重要临床意义。本研究基于MIMIC-IV数据库,通过多变量调整的Logistic回归模型和限制性立方样条分析,系统评估了慢性肝病手术患者术后入住ICU首日液体入量与术后短期死亡风险的关系,不仅明确了限制性液体治疗策略在降低该人群死亡风险中的关键作用,还通过RCS分析确立了具有潜在临床指导价值的液体入量阈值(1 850 mL/24 h),

表4 慢性肝病手术患者术后7天死亡与术后首日限制性补液的Logistic回归分析模型

**Table 4 Logistic regression analysis model for postoperative 7-day mortality in patients with chronic liver disease after surgery and restrictive fluid administration on the first postoperative day**

| The risk of death 7 days after the operation | Odds Ratio(*OR*) | *AIC* |
|---|---|---|
| Model 1 (Liquid Therapy Plan) | 0.49 (0.36~0.66, *P*<0.001) | 1 297.04 |
| Model 2 (Liquid Therapy Plan+Demographic data) | 0.46 (0.33~0.62, *P*<0.001) | 1 270.08 |
| Model 3 (Liquid Therapy Plan+Demographic data + Preoperative related variables) | 0.47 (0.34~0.64, *P*<0.001) | 1 254.86 |
| Model 4 (Liquid Therapy Plan+Demographic data+Preoperative related variables+ Surgical and postoperative related variables) | 0.44 (0.22~0.88, *P*=0.021) | 313.60 |

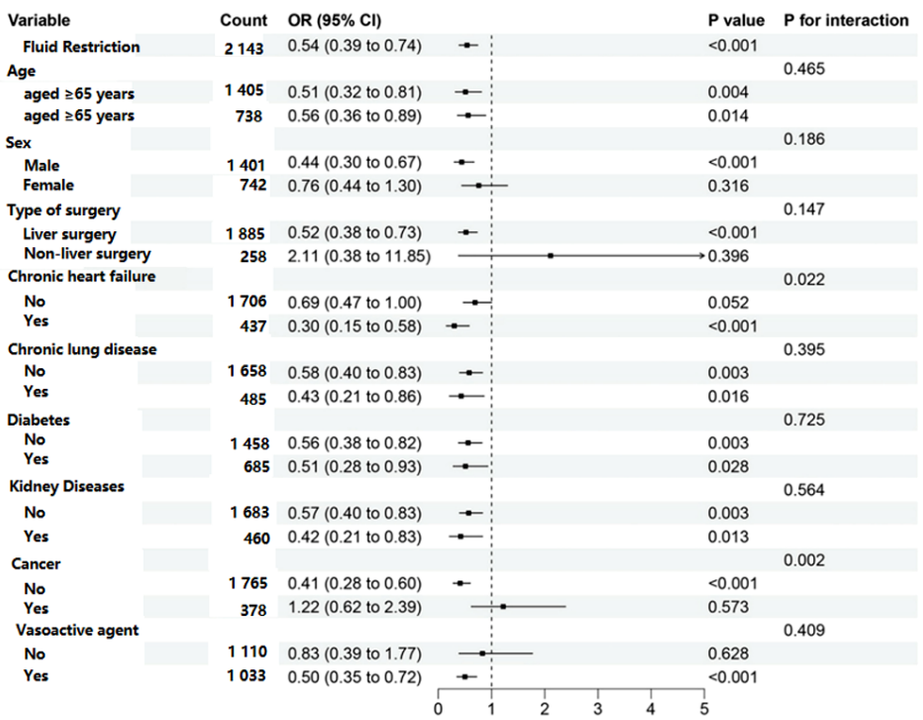



图2 多因素Logistic回归亚组分析森林图

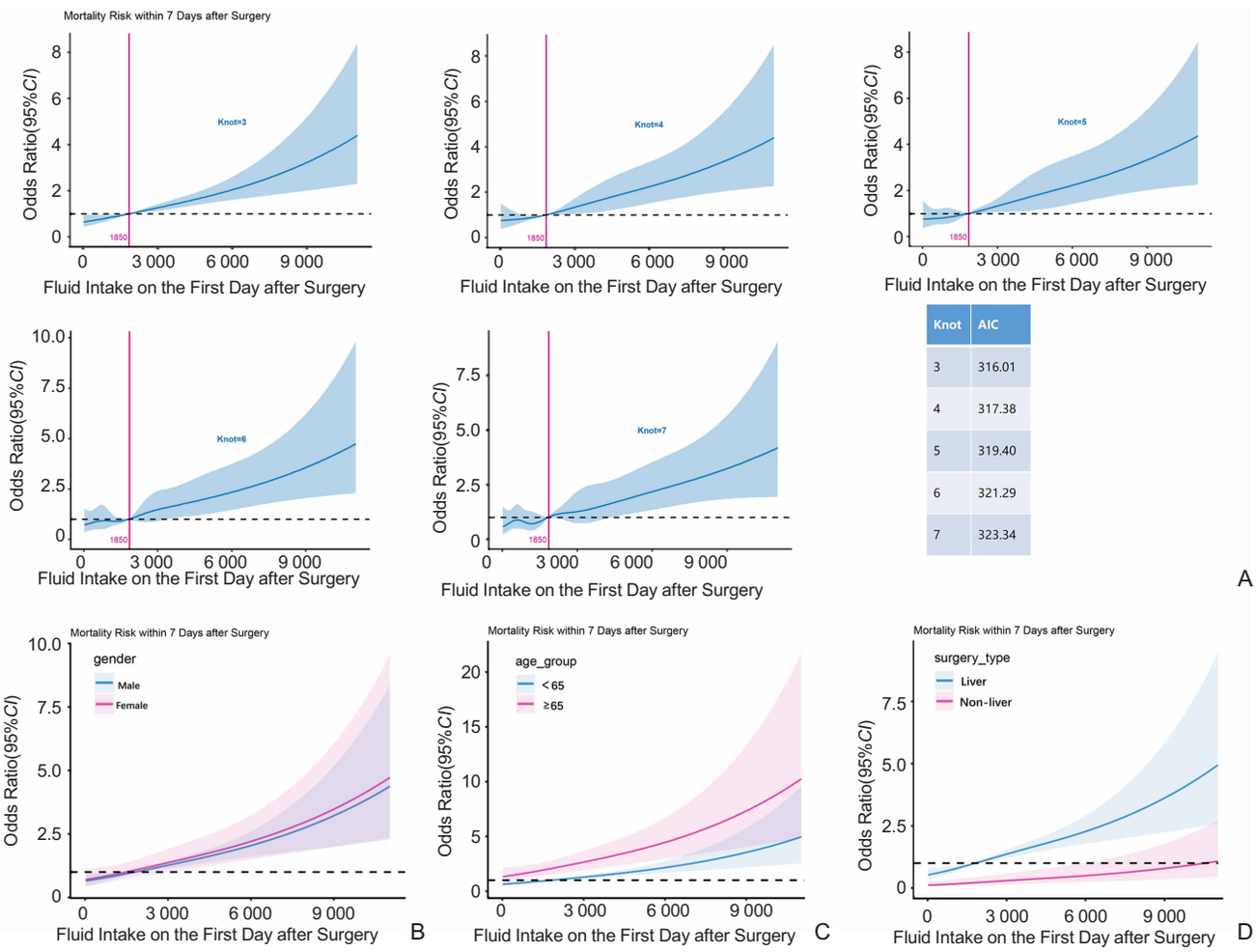
**Figure 2 Forest plot of multivariate logistic regression in subgroup analysis**

可为临床医生在该复杂人群中实施液体管理提供重要参考。

3.1 限制性补液可改善慢性肝病患者术后短期结局

与既往在普通外科术后人群中支持限制性液体管理的研究结论一致[24],本研究证实并量化了限制性补液对慢性肝病手术患者术后7 d死亡风险的保护效应,多变量调整模型显示,限制性液体治疗可使术后7 d死亡率降低6%(*OR*=0.44,95%*CI*:0.22~0.88,*P*=0.021),且这一保护效应在不同年龄组和合并症患者中均保持稳定。另外,亚组分析与敏感性分析均证实了1 850 mL这一阈值的稳健性。相较于既往普通术后人群研究,本研究聚焦慢性肝病患者,明确了限制性补液在该特殊群体中的保护作用。

慢性肝病患者固有的有效循环血容量不足及高动力循环状态使其对容量负荷的耐受性更差。过多的液体入量极易加剧门静脉高压,加速组织器官水肿,并可能稀释凝血因子,从而诱发或加重腹水、肺水肿、心功能不全及凝血功能障碍等一系列严重并发症。因此,慢性肝病患者对液体管理的精准性要求远高于普通人群。本研究发现限制性补液不仅降低死亡风险,还显著缩短了机械通气时间和住院时长,提示限制性策略可能通过多重途径改善预后:一方面,在维持足够有效灌注的前提下,避免了液体过载对器官功能的直接损害(如组织水肿、氧弥散障碍、腹内压增高等);另一方面,可能减少了因液体正平衡导致的炎症介质稀释和转运障碍,间接减轻了全身炎症反应,最终促进了患者整体预后的改善。




A: RCS curve of fluid intake-mortality risk; B: RCS curve by gender; C: RCS curve by age; D: RCS curve by surgical type; Solid line: the odds ratio of mortality risk 7 d after surgery; Shaded area: the corresponding 95% confidence interval. RCS: restricted cubic spline

**图3 慢性肝病手术患者术后首日液体入量-术后7天死亡风险RCS曲线**

**Figure 3 RCS curve of fluid intake on the first day after surgery for patients with chronic liver disease-risk of 7-day death after surgery**

### 3.2 不同亚组存在异质性,提示个体化管理的必要性

尽管限制性补液的总体获益明确,但亚组分析进一步揭示了限制性液体治疗效果的异质性,提示个体化精准管理的必要性。限制性策略在不同年龄、性别及常见合并症(如高血压、糖尿病、慢性肾病)患者中均显示出相对一致的保护效应,提示其基础获益具有较广泛的适用性。然而,在肝脏手术患者和恶性肿瘤患者亚组中,限制性补液的保护作用呈现减弱趋势。

肝脏手术本身具有术中出血风险高、肝功能储备进一步受损、手术创伤大的特点。更重要的是,为减少手术出血与保障操作顺利,术中常常规采用低中心静脉压技术和限制性补液策略[25]。这使得患者术后早期往往处于相对或绝对的容量负平衡状态。术后继续严格限制液体入量可能无法充分满足组织灌注需求,甚至可能加剧潜在的肾脏灌注不足风险。因此,对于肝脏手术患者,术后液体管理需要在避免容量过载与预防容量不足之间寻求更精细的平衡,结合血流动力学监测、乳酸、尿量、组织灌注等指标来指导个体化的容量复苏目标,而非单纯依赖一个固定的总量阈值。恶性肿瘤作为一种系统性疾病,其病理生理机制高度复杂[26]。肿瘤本身可能通过释放炎症因子、影响代谢、导致恶病质或引起特定器官功能障碍等方式影响机体的内环境稳态和容量反应性。此外,抗肿瘤治疗常伴随多种并发症(如心功能损害、肺毒性、肾功能损伤、毛细血管渗漏综合征等),这些都可能显著

改变患者的液体分布、血管通透性以及对液体治疗的反应性。例如,血管内皮生长因子抑制剂的使用可能增加高血压和蛋白尿风险,影响液体管理目标[27]。因此,肿瘤患者的液体管理需要综合考虑肿瘤负荷、治疗方案及其副作用,策略可能更为复杂和个体化。

### 3.3 研究局限与未来方向

本研究作为回顾性研究,不可避免存在残余混杂,虽然通过多变量模型进行了调整,但仍无法完全排除混杂因素的影响,可能存在未测量混杂因素的偏倚。其次,液体治疗方案的划分基于术后首日的总入量,未详细考虑补液的类型(晶体/胶体比例、白蛋白及血液制品情况等)及速度等因素,这些因素可能对患者预后产生重要影响。另外,数据库缺乏详细的术中液体管理数据,这使得无法全面评估整个围术期的液体状态对结果的潜在影响。本研究肝脏手术亚组样本量相对较小($n$=258),可能降低了该亚组分析的统计效力,并限制了对该群体进行更深入分层分析(如不同肝切除范围、不同基础肝功能)的能力。后续研究拟纳入多中心数据,扩大样本量以增强统计效能,针对液体管理进行细化指标分析,实现更精准的个体化液体管理。此外,还需开展前瞻性队列研究及随机对照试验(RCT)进一步验证限制性液体治疗(<1 850 mL)的临床效用。

综上所述,本研究为慢性肝病患者术后首日液体管理提供了重要参考。术后首日限制性液体治疗(<1 850 mL)可显著降低术后7天死亡风险($OR$ 0.44,$P$=0.020),并有助于缩短机械通气时间和住院时长。这一保护效应在不同年龄、并发症亚组中均保持稳定,尤其对高龄、危重患者更具临床价值。此外,亚组分析提示肝脏手术和恶性肿瘤患者中个体化管理的重要性。未来还需要更深入的前瞻性研究和个体化管理方案的探索,以进一步优化这一脆弱群体的围术期预后。

**利益冲突** 本文所有作者声明不存在利益冲突

## 参考文献:

[1] XIAO J, WANG F, WONG N K, *et al*. Global liver disease burdens and research trends: Analysis from a Chinese perspective[J]. J Hepatol, 2019, 71(1): 212-221. DOI: 10.1016/j.jhep.2019.03.004.

[2] JADAUN S S, SAIGAL S. Surgical risk assessment in patients with chronic liver diseases[J]. J Clin Exp Hepatol, 2022, 12(4): 1175-1183. DOI: 10.1016/j.jceh.2022.03.004.

[3] SCHOCKAERT B R, VAN BRUCHEM R M, ENGEL M F, *et al*. Outcomes following extended postoperative recovery unit admission in noncardiac surgery: a systematic review and meta-analysis[J]. Eur J Anaesthesiol, 2025, 42(5): 407-418. DOI: 10.1097/EJA.0000000000002145.

[4] CURRAN T F, SUNKARA B, LEIS A, *et al*. Outcomes after prolonged ICU stays in postoperative cardiac surgery patients[J]. Fed Pract, 2022, 39(Suppl 5): S6-S11c. DOI: 10.12788/fp.0300.

[5] GIGLIO M, BIANCOFIORE G, CORRIERO A, *et al*. Perioperative goal-directed therapy and postoperative complications in different kind of surgical procedures: an updated meta-analysis[J]. J Anesth Analg Crit Care, 2021, 1(1): 26. DOI: 10.1186/s44158-021-00026-3.

[6] PHOTHIKUN N, PANTATONG O, KULPANUN M, *et al*. The impact of perioperative positive fluid balance on postoperative acute kidney injury in patients undergoing open hepatectomy: a retrospective single center cohort study[J]. PLoS One, 2025, 20(4): e0319856. DOI: 10.1371/journal.pone.0319856.

[7] PISARSKA-ADAMCZYK M, TORBICZ G, GAJEWSKA N, *et al*. The impact of perioperative fluid therapy on the short-term outcomes after laparoscopic colorectal cancer surgery with ERAS protocol: a prospective observational study[J]. Sci Rep, 2023, 13(1): 22282. DOI: 10.1038/s41598-023-49704-y.

[8] MILLER T E, MYLES P S. Perioperative fluid therapy for major surgery[J]. Anesthesiology, 2019, 130(5): 825-832. DOI: 10.1097/ALN.0000000000002603.

[9] 刘良明.战创伤休克早期救治研究进展与思考[J].陆军军医大学学报,2022,44(20):2025-2029. DOI: 10.16016/j.2097-0927.202205151.
LIU L M. Advances and thinking for early treatment of war wound and traumatic shock[J]. J Army Med Univ, 2022, 44(20): 2025-2029. DOI: 10.16016/j.2097-0927.202205151.

[10] ARROYO V, ANGELI P, MOREAU R, *et al*. The systemic inflammation hypothesis: Towards a new paradigm of acute decompensation and multiorgan failure in cirrhosis[J]. J Hepatol, 2021, 74(3): 670-685. DOI: 10.1016/j.jhep.2020.11.048.

[11] ENGELMANN C, CLÀRIA J, SZABO G, *et al*. Pathophysiology of decompensated cirrhosis: Portal hypertension, circulatory dysfunction, inflammation, metabolism and mitochondrial dysfunction[J]. J Hepatol, 2021, 75(Suppl 1): S49-S66. DOI: 10.1016/j.jhep.2021.01.002.

[12] KASHABI K, OMER T, SHAW A D. The intensivist's perspective of shock, volume management, and hemodynamic monitoring. Clin J Am Soc Nephrol, 2022, 17

(5):706-716. DOI: 10.2215/CJN.14191021.

[13] KIM J A, AHN H J, OH A R, *et al*. Restrictive intraoperative fluid management was associated with higher incidence of composite complications compared to less restrictive strategies in open thoracotomy: a retrospective cohort study [J]. Sci Rep, 2020, 10(1): 8449. DOI: 10.1038/s41598-020-65532-w.

[14] OH E J, KIM J, KIM B G, *et al*. Intraoperative factors modifying the risk of postoperative pulmonary complications after living donor liver transplantation [J]. Transplantation, 2023, 107(8): 1748-1755. DOI: 10.1097/TP.0000000000004544.

[15] KENDRICK J B, KAYE A D, TONG Y R, *et al*. Goal-directed fluid therapy in the perioperative setting [J]. J Anaesthesiol Clin Pharmacol, 2019, 35(Suppl 1): 29. DOI: 10.4103/joacp.JOACP_26_18.

[16] AGARWAL V, DIVATIA J V. Enhanced recovery after surgery in liver resection: current concepts and controversies [J]. Korean J Anesthesiol, 2019, 72(2): 119-129. DOI: 10.4097/kja.d.19.00010.

[17] MUNGROOP T H, GEERTS B F, VEELO D P, *et al*. Fluid and pain management in liver surgery (MILESTONE): a worldwide study among surgeons and anesthesiologists [J]. Surgery, 2019, 165(2): 337-344. DOI: 10.1016/j.surg.2018.08.013.

[18] MESSINA A, ROBBA C, CALABRÒ L, *et al*. Perioperative liberal versus restrictive fluid strategies and postoperative outcomes: a systematic review and metanalysis on randomised-controlled trials in major abdominal elective surgery [J]. Crit Care, 2021, 25(1): 205. DOI: 10.1186/s13054-021-03629-y.

[19] FROGHI F, GOPALAN V, ANASTASIOU Z, *et al*. Effect of post-operative goal-directed fluid therapy (GDFT) on organ function after orthotopic liver transplantation: Secondary outcome analysis of the COLT randomised control trial [J]. Int J Surg, 2022, 99: 106265. DOI: 10.1016/j.ijsu.2022.106265.

[20] JOHNSON A E W, BULGARELLI L, SHEN L, *et al*. MIMIC-IV, a freely accessible electronic health record dataset [J]. Sci Data, 2023, 10(1): 1. DOI: 10.1038/s41597-022-01899-x.

[21] CHARLSON ME, CARROZZINO D, GUIDI J, *et al*. Charlson comorbidity index: a critical review of clinimetric properties [J]. Psychother Psychosom, 2022, 91(1): 8-35. DOI: 10.1159/000521288.

[22] 中华医学会麻醉学分会老年人麻醉与围术期管理学组, 国家老年麻醉联盟, 国家老年疾病临床医学研究中心, 等. 中国成人患者围手术期液体治疗临床实践指南(2025版)[J]. 中华医学杂志, 2025, 105(2): 128-154. DOI: 10.3760/cma.j.cn112137-20241003-02245.
Geriatric Anesthesiology and Perioperative Management Group Chinese Medical Association, National Geriatric Anesthesia Alliance, National Clinical Research Center for Geriatric Disorders, *et al*. Clinical practice guidelines for perioperative fluid therapy in Chinese adult patients (2025 edition) [J]. Natl Med J China, 2025, 105(2): 128-154. DOI: 10.3760/cma.j.cn112137-20241003-02245.

[23] ABBAS N, FALLOWFIELD J, PATCH D, *et al*. Guidance document: risk assessment of patients with cirrhosis prior to elective non-hepatic surgery [J]. Frontline Gastroenterol, 2023, 14(5): 359-370. DOI: 10.1136/flgastro-2023-102381.

[24] PANG Q Y, LIU H L, CHEN B, *et al*. Restrictive and liberal fluid administration in major abdominal surgery [J]. Saudi Med J, 2017, 38(2): 123-131. DOI: 10.15537/smj.2017.2.15077.

[25] 邬雪涵, 梁兰美, 尉昆, 等. 肝切除术中应用控制性低中心静脉压的有效性及安全性: meta分析[J]. 中华麻醉学杂志, 2022, 42(11): 1353-1359. DOI: 10.3760/cma.j.cn131073.20220927.01117. WU X H,
LIANG L M, YU K, *et al*. Efficacy and safety of controlled low central venous pressure applied during hepatectomy: a meta-analysis [J]. Chin J Anesthesiol, 2022, 42(11): 1353-1359. DOI: 10.3760/cma.j.cn131073.20220927.01117.

[26] SWANTON C, BERNARD E, ABBOSH C, *et al*. Embracing cancer complexity: Hallmarks of systemic disease [J]. Cell, 2024, 187(7): 1589-1616. DOI: 10.1016/j.cell.2024.02.009.

[27] 杨晓蕾, 管博, 吕海辰, 等. 抗癌药物血管内皮生长因子抑制剂相关高血压的管理策略[J]. 中华心血管病杂志, 2021, 49(10): 957-962. DOI: 10.3760/cma.j.cn112148-20210824-00727.
YANG X L, GUAN B, LV H C, *et al*. Management strategy on hypertension induced by anti-cancer therapy with vascular endothelial growth factor inhibitor [J]. Chin J Cardiol, 2021; 49(10): 957-962. DOI: 10.3760/cma.j.cn112148-20210824-00727.

(收稿:2025-07-07;修回:2025-07-28)

(编辑 李 玥)