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·论　著·

原发性肝癌肝切除术后预防性抗凝对术后并发症的影响

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［**摘要**］ **目的**　探究原发性肝癌（PLC）患者术后预防性抗凝治疗能否降低术后并发症的发生风险，并探讨术后并发症的影响因素。**方法**　收集 2019 年 2 月至 2021 年 5 月在海军军医大学（第二军医大学）第三附属医院接受 PLC 肝切除手术治疗的 495 例患者的临床资料，根据术后是否进行预防性抗凝将患者分为抗凝组（287 例，术后接受预防性低分子肝素抗凝治疗）和常规治疗组（208 例）。对比两组患者术后并发症发生情况，并采用 logistic 回归模型分析并发症发生的影响因素。**结果**　495 例患者肝切除术后总体并发症发生率为 30.7%（152/495），按照发生率由高到低依次为感染（9.1%，45/495）、急性呼吸窘迫综合征（ARDS；6.5%，32/495）、出血（6.3%，31/495）、肝切除术后肝功能衰竭（PHLF；6.1%，30/495）、静脉血栓栓塞症（VTE；2.8%，14/495）。抗凝组术后 VTE、ARDS、PHLF 发生率均低于常规治疗组［1.4%（4/287）vs 4.8%（10/208）、3.8%（11/287）vs 10.1%（21/208）、3.8%（11/287）vs 9.1%（19/208），均 $P<0.05$］，但两组间术后出血的发生率差异无统计学意义（$P>0.05$）。多因素 logistic 回归分析显示，年龄、门静脉高压、肿瘤数量是 VTE 的独立危险因素，门静脉高压、术中出血、术中输血、术前降钙素原是 PHLF 的独立危险因素，腹水、术前胆红素是 ARDS 的独立危险因素，而术后预防性抗凝是 VTE、ARDS 的独立保护因素（均 $P<0.05$）。**结论**　PLC 患者肝切除术后预防性抗凝可以降低 VTE、PHLF、ARDS 的发生风险，且不会增加术后出血风险。年龄、门静脉高压、肿瘤数量、术中出血、术中输血、腹水、术前降钙素原、术前胆红素是 PLC 患者肝切除术后并发症发生的危险因素。

［**关键词**］ 肝肿瘤；肝切除术；原发性肝癌；预防性抗凝；静脉血栓栓塞症；急性呼吸窘迫综合征；肝功能衰竭；出血
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Effects of prophylactic anticoagulation on postoperative complications after hepatectomy for primary liver cancer

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［**Abstract**］ **Objective**　To investigate whether prophylactic anticoagulation therapy can reduce the risk of postoperative complications in patients with primary liver cancer (PLC) after hepatectomy, and to explore the influencing factors of postoperative complications. **Methods**　The clinical data of 495 patients undergoing hepatectomy for PLC in The Third Affiliated Hospital of Naval Medical University (Second Military Medical University) from Feb. 2019 to May 2021 were collected. The patients were divided into anticoagulation group ($n=287$, receiving prophylactic low-molecular-weight heparin after surgery) and conventional treatment group ($n=208$). The postoperative complications were compared between the 2 groups, and the influencing factors were analyzed using logistic regression model. **Results**　The postoperative overall complication incidence of the 495 patients after hepatectomy was 30.7% (152/495), ranking as infection (9.1%, 45/495), acute respiratory distress syndrome (ARDS; 6.5%, 32/495), bleeding (6.3%, 31/495), post-hepatectomy liver failure (PHLF; 6.1%, 30/495), and venous thromboembolism (VTE; 2.8%, 14/495). The incidence rates of postoperative VTE, ARDS, and PHLF were significantly lower in the anticoagulation group than those in the conventional treatment group (1.4%［4/287］vs 4.8%［10/208］, 3.8%［11/287］vs 10.1%［21/208］, and 3.8%［11/287］vs 9.1%［19/208］; all $P<0.05$), but there was no significant difference in the incidence of postoperative bleeding between the 2 groups ($P>0.05$). Multivariate logistic

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regression analysis showed that age, portal hypertension, and tumor number were independent risk factors for postoperative VTE; portal hypertension, intraoperative blood loss, intraoperative blood transfusion, and preoperative procalcitonin (PCT) were independent risk factors for PHLF; ascites and preoperative bilirubin were independent risk factors for ARDS; and postoperative prophylactic anticoagulation was an independent protective factor for VTE and ARDS (all $P<0.05$). **Conclusion** Prophylactic anticoagulation can reduce the risks of VTE, PHLF, and ARDS in PLC patients after hepatectomy, without increasing the risk of postoperative bleeding. Age, portal hypertension, number of tumors, intraoperative blood loss, intraoperative blood transfusion, ascites, preoperative PCT, and preoperative bilirubin are risk factors for postoperative complications of PLC patients after hepatectomy.

［**Key words**］ liver neoplasms; hepatectomy; primary liver cancer; prophylactic anticoagulation; venous thromboembolism; acute respiratory distress syndrome; liver failure; hemorrhage

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全世界范围内超过 54% 的原发性肝癌（primary liver cancer，PLC）发生在我国，严重威胁我国人民的健康和生命[1]。在我国 PLC 患者中大多数有慢性肝病史，HBV 感染是其主要原因，合并肝硬化者占比更是高达 85% 以上[2]，由此可见未来我国原发性肝细胞癌（hepatocellular carcinoma，HCC）仍是主要的卫生问题。肝切除和肝移植是目前 HCC 主要的、最有效的治疗手段，但是由于器官短缺，肝移植受到限制，因此肝切除手术仍然是 HCC 患者的首选治疗方案。尽管现代手术的安全性得以提升，但是肝切除手术依然是所有腹部外科手术中风险较高且并发症最多的手术之一，文献报道其并发症发生率为 40.2%～55.5%[3-4]。即便肝切除手术死亡率已经从历史最高点的 32% 下降至目前的 1%～10%[4-6]，肝切除术后的高并发症及高死亡率还困扰着许多临床医师，不仅导致住院时间长、住院费用居高不下，也严重影响着患者的生命安全[7]。

既往已经有研究探讨，肝脏外科医师由于意识到术后出血风险而拒绝开具抗凝剂的化学预防处方[8]。然而有研究表明，术后抗凝血剂能有效降低门静脉血栓形成的发生率，且术后静脉血栓栓塞症（venous thromboembolism，VTE）的发生率远高于出血的发生率，因而支持肝切除术后常规进行 VTE 化学预防[9-10]。同时抗凝剂也具有抗炎、抗病毒、促进伤口愈合、预防贫血等重要的药理作用[11]。目前我国临床上肝切除术后预防性使用抗凝药物的病例相对较少，其原因之一就是顾虑术后出血的风险，而且目前肝切除术后预防性应用抗凝药物的结论大多基于国外临床研究。研究肝切除术后预防性抗凝对于临床医师提高 VTE 防治意识、规范诊疗行为、减少术后并发症、降低病死率、提高患者生活质量具有重要意义。本研究回顾性分析了肝切除术后预防性抗凝和非抗凝治疗对术后并发症的影响，并分析术后发生并发症的危险因素，旨在为临床降低术后并发症的发生率提供依据。

1　对象和方法

1.1　*研究对象与分组*　选择 2019 年 2 月至 2021 年 5 月在海军军医大学（第二军医大学）第三附属医院接受 PLC 肝切除手术的 495 例患者为研究对象。纳入标准：（1）不存在抗凝治疗的禁忌证；（2）知情同意病例数据用于研究；（3）能严格遵医嘱接受治疗；（4）入组前 1 个月内未进行过溶栓、抗凝、抗血小板等治疗；（5）术前检查无静脉血栓；（6）Child 分级 A 级，且一般状况良好，美国麻醉师协会分级为Ⅰ级或Ⅱ级。排除标准：（1）治疗依从性低者；（2）合并血液、颅脑、肾脏、心脏等其他系统疾病者；（3）由于无法切除或其他原因未行肝切除术，仅行剖腹探查＋活检术者。本研究通过海军军医大学（第二军医大学）第三附属医院医学伦理委员会审批（EHBHKY2021-K-011）。

以术后预防性抗凝与否将患者分为两组：（1）抗凝组 287 例，术后 24 h 内接受低分子肝素抗凝治疗（低分子肝素钙注射液，商品名为速碧林，0.4 mL、1 次 /12 h 皮下注射），并予广谱抗生素预防感染、抑酸、化痰、肠外营养（包括氨基酸、中长链脂肪乳、葡萄糖溶液、多种维生素）、白蛋白、利尿、控制血压、维持内环境稳定及水、电解

质平衡等常规术后处理；（2）常规治疗组 208 例，仅给予广谱抗生素预防感染、抑酸、化痰、肠外营养（包括氨基酸、中长链脂肪乳、葡萄糖溶液、多种维生素）、白蛋白、利尿、控制血压、维持内环境稳定及水、电解质平衡等常规术后处理。

1.2　观察指标　（1）凝血功能指标：分别在治疗前、后抽取患者 3 mL 静脉血，以 3 500 r/min（离心半径为 5 cm）离心 15 min 获得血浆，检测国际标准化比值、凝血酶原时间等凝血功能指标。（2）急性呼吸窘迫综合征（acute respiratory distress syndrome，ARDS）发生情况：ARDS 的诊断需满足以下条件。①在已知临床损害发生的 1 周内出现新的呼吸系统症状；②X 线片或 CT 检查示双肺致密影，并且用胸腔积液、肺叶 / 肺塌陷或结节不能完全解释；③无法用心力衰竭或体液超负荷完全解释，对于不存在危险因素的患者需要排除静水压相关性肺水肿；④存在中到重度氧合指数下降，其中氧合指数定义为 PaO_2/FiO_2（PaO_2 为动脉氧分压，FiO_2 为吸入氧浓度）。（3）肝切除术后肝功能衰竭（post-hepatectomy liver failure，PHLF）发生情况：PHLF 是指各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，从而出现以黄疸、凝血功能障碍、肝肾综合征、肝性脑病、腹水等为主要表现的一组临床症候群。（4）VTE 发生情况：VTE 包括深静脉血栓形成、肺动脉栓塞、门静脉血栓，其中深静脉血栓形成的诊断采用二维超声检查，肺动脉栓塞的诊断采用 CT 血管成像，门静脉血栓的诊断采用超声、CT 和 MRI 检查。（5）收集患者治疗过程中的白细胞计数、中性粒细胞比例、CRP、降钙素原、血红蛋白、血细胞比容及术中出血、术中输血、术后出血等情况。

1.3　统计学处理　采用 SPSS 25.0 软件进行统计学分析。对计量资料行正态性检验，符合正态分布的计量资料以 $\bar{x}\pm s$ 表示，组间比较采用 Z 检验；不符合正态分布的计量资料以中位数（下四分位数，上四分位数）表示，组间比较采用秩和检验。计数资料以例数和百分数表示，组间比较采用 χ^2 检验。将单因素 logistic 回归分析中 $P<0.05$ 的变量纳入多因素 logistic 回归模型，分析并发症发生的独立影响因素。采用 ROC 曲线和 AUC 描述和比较不同指标对术后并发症预测的准确性。检验水准（α）为 0.05。

2　结　果

2.1　两组患者一般资料的比较　抗凝组 287 例，男 236 例、女 51 例，年龄为 18～90（56.00±12.43）岁。常规治疗组 208 例，男 166 例、女 42 例，年龄为 20～79（57.00±11.02）岁。两组患者性别、年龄、高血压病史、糖尿病史、吸烟史、既往肝脏手术史、肝硬化病史、门静脉高压病史等差异均无统计学意义（均 $P>0.05$）。抗凝组有腹水、术中输血的患者比例均低于常规治疗组（均 $P<0.05$），术中肝门阻断时间长于常规治疗组（$P<0.001$）。见表 1。

将预防性抗凝组患者以抗凝开始时间是否在术后 12 h 内分为 2 个亚组，其中术后 12 h 内抗凝的患者有 112 例、手术 12 h 后抗凝的患者有 175 例。2 个亚组患者的年龄、性别、吸烟史、糖尿病史、高血压病史、既往肝脏手术史、肝硬化病史等临床特征差异均无统计学意义（均 $P>0.05$），术后 12 h 内抗凝的患者肿瘤大小和术前 CRP 水平均低于手术 12 h 后抗凝的患者（均 $P<0.05$）。见表 2。

2.2　两组患者术后并发症的比较　495 例患者肝切除术后总体并发症发生率为 30.7%（152/495），按照发生率由高到低依次为感染、ARDS、术后出血、PHLF、VTE。抗凝组术后 VTE、ARDS、PHLF 发生率均低于常规治疗组（均 $P<0.05$），但与常规治疗比较预防性抗凝并未增加术后出血的发生率（$P>0.05$）。见表 3。

2.3　术后 VTE 影响因素的 logistic 回归分析　单因素 logistic 回归分析结果提示，年龄、肝硬化、门静脉高压、肿瘤数量、预防性抗凝、术前 PLT 与术后 VTE 有关（均 $P<0.05$，表 4）；多因素 logistic 回归分析结果提示，年龄、门静脉高压、肿瘤数量是术后 VTE 的独立危险因素，而预防性抗凝是术后 VTE 的独立保护因素（均 $P<0.05$，表 5）。

2.4　PHLF 影响因素的 logistic 回归分析　单因素 logistic 回归分析结果提示，门静脉高压、腹水、肿瘤数量、肿瘤大小、术中出血、术中输血、预防性抗凝、术前降钙素原、术前 PLT、术前国际标准化比值均与 PLC 患者术后发生 PHLF 与否有关（均 $P<0.05$，表 6）；多因素 logistic 回归分析结果提示，门静脉高压、术中出血、术中输血、术前降钙素原均是 PLC 患者术后发生 PHLF 的独立危险因素（均 $P<0.05$，表 7）。

表 1　两组 PLC 患者一般临床资料的比较

Tab 1　Comparison of general clinical data of PLC patients between 2 groups

Index	Total N=495	Anticoagulation group N=287	Conventional treatment group N=208	P value
Gender, n (%)				0.496
Female	93 (18.8)	51 (17.8)	42 (20.2)	
Male	402 (81.2)	236 (82.2)	166 (79.8)	
Age/year, $\bar{x}\pm s$	56.00±11.86	56.00±12.43	57.00±11.02	0.296
History of hypertension, n (%)	113 (22.8)	66 (23.0)	47 (22.6)	0.917
History of diabetes mellitus, n (%)	54 (10.9)	31 (10.8)	23 (11.1)	0.928
Smoking history, n (%)	198 (40.0)	115 (40.1)	83 (39.9)	0.970
Drinking history, n (%)	150 (30.3)	85 (29.6)	65 (31.2)	0.696
History of hepatitis B, n (%)	229 (46.3)	130 (45.3)	99 (47.6)	0.612
Previous history of liver surgery, n (%)	52 (10.5)	34 (11.8)	18 (8.7)	0.253
Cirrhosis, n (%)	224 (45.3)	133 (46.3)	91 (43.8)	0.567
Ascites, n (%)	56 (11.3)	25 (8.7)	31 (14.9)	0.032
Intraoperative blood loss, n (%)	31 (6.3)	14 (4.9)	17 (8.2)	0.136
Intraoperative blood transfusion, n (%)	115 (23.2)	47 (16.4)	68 (32.7)	＜0.001
Surgical method, n (%)				0.405
Open surgery	482 (97.4)	278 (96.9)	204 (98.1)	
Laparoscopic surgery	13 (2.6)	9 (3.1)	4 (1.9)	
Liver resection range, n (%)				0.570
≤3 liver segments	333 (67.3)	196 (68.3)	137 (65.9)	
＞3 liver segments	162 (32.7)	91 (31.7)	71 (34.1)	
Antiviral therapy, n (%)	155 (31.3)	98 (34.1)	57 (27.4)	0.110
Abnormal prothrombin time, n (%)	188 (38.0)	105 (36.6)	83 (39.9)	0.453
Portal hypertension, n (%)	82 (16.6)	51 (17.8)	31 (14.9)	0.397
Preoperative PLT/(L^{-1}, $\times10^9$), $\bar{x}\pm s$	163.66±69.10	162.33±67.86	165.50±70.91	0.615
Preoperative INR, $\bar{x}\pm s$	0.99±0.09	0.99±0.09	1.00±0.09	0.562
Preoperative neutrophil ratio, $\bar{x}\pm s$	0.59±0.11	0.58±0.12	0.58±0.11	0.984
Tumor maximum diameter/cm, M (Q_L, Q_U)	5.00 (3.00, 7.00)	5.00 (3.00, 7.00)	5.00 (3.00, 8.25)	0.079
Porta hepatis occlusion time/min, M (Q_L, Q_U)	17.0 (0.0, 31.0)	21.0 (8.0, 38.0)	4.5 (0.0, 21.5)	＜0.001
Preoperative bilirubin/(U•L^{-1}), M (Q_L, Q_U)	12.60 (9.00, 17.20)	12.80 (9.00, 17.20)	12.20 (8.65, 19.10)	0.415
Preoperative ALT/(U•L^{-1}), M (Q_L, Q_U)	26.0 (18.0, 40.0)	26.0 (17.0, 41.0)	24.5 (19.0, 30.7)	0.236
Preoperative AST/(U•L^{-1}), M (Q_L, Q_U)	26.0 (19.0, 38.0)	26.0 (19.0, 39.0)	23.0 (19.5, 37.2)	0.377
Preoperative LDH/(U•L^{-1}), M (Q_L, Q_U)	173.0 (147.0, 200.0)	175.0 (151.0, 200.0)	167.0 (138.2, 208.5)	0.931
Preoperative CRP/(mg•L^{-1}), M (Q_L, Q_U)	5 (5, 5)	5 (5, 5)	5 (5, 5)	0.639
Preoperative WBC/(L^{-1}, $\times10^9$), M (Q_L, Q_U)	5.12 (3.94, 6.38)	5.16 (3.97, 6.28)	5.04 (3.86, 6.43)	0.244

PLC: Primary liver cancer; PLT: Platelet count; INR: International normalized ratio; ALT: Alanine transaminase; AST: Aspartate transaminase; LDH: Lactate dehydrogenase; CRP: C reactive protein; WBC: White blood cell count; M (Q_L, Q_U): Median (lower quartile, upper quartile).

表 2　不同抗凝时机 PLC 患者的一般临床资料比较

Tab 2　Comparison of general clinical data among PLC patients with different anticoagulation timings

Index	Anticoagulation within 12 h after surgery N=112	Anticoagulation after 12 h of surgery N=175	P value
Gender, n (%)			0.327
Female	23 (20.5)	28 (16.0)	
Male	89 (79.5)	147 (84.0)	
Age/year, $\bar{x}\pm s$	56.78±11.21	54.75±13.12	0.179
History of hypertension, n (%)	32 (28.6)	34 (19.4)	0.073
History of diabetes mellitus, n (%)	17 (15.2)	14 (8.0)	0.056
Smoking history, n (%)	47 (42.0)	68 (38.9)	0.600
Drinking history, n (%)	37 (33.0)	48 (27.4)	0.310
History of hepatitis B, n (%)	49 (43.8)	81 (46.3)	0.635

续表 2

Index	Anticoagulation within 12 h after surgery N=112	Anticoagulation after 12 h of surgery N=175	P value
Previous history of liver surgery, n (%)	12 (10.7)	22 (12.6)	0.217
Cirrhosis, n (%)	58 (51.8)	75 (42.9)	0.139
Ascites, n (%)	10 (8.9)	15 (8.6)	0.917
Intraoperative blood transfusion, n (%)	13 (11.6)	34 (19.4)	0.411
Surgical method, n (%)			0.722
Open surgery	109 (97.3)	169 (96.6)	
Laparoscopic surgery	3 (2.7)	6 (3.4)	
Liver resection range, n (%)			0.514
≤3 liver segments	79 (70.5)	117 (66.9)	
>3 liver segments	33 (29.5)	58 (33.1)	
Antiviral therapy, n (%)	44 (39.3)	54 (30.9)	0.142
Abnormal prothrombin time, n (%)	43 (38.4)	62 (35.4)	0.611
Portal hypertension, n (%)	16 (14.3)	35 (20.0)	0.217
Preoperative PLT/(L^{-1}, $\times10^9$), $\bar{x}\pm s$	163.96±66.29	161.30±69.01	0.549
Preoperative INR, $\bar{x}\pm s$	0.99±0.11	0.99±0.08	0.143
Preoperative neutrophil ratio, $\bar{x}\pm s$	0.57±0.11	0.58±0.12	0.833
Tumor maximum diameter/cm, M (Q_L, Q_U)	4.00 (3.00, 6.00)	5.00 (3.00, 7.50)	0.009
Porta hepatis occlusion time/min, M (Q_L, Q_U)	24.0 (15.0, 37.5)	20.0 (7.0, 38.0)	0.538
Preoperative bilirubin/($U\cdot L^{-1}$), M (Q_L, Q_U)	13.2 (9.00, 17.30)	12.60 (8.90, 17.10)	0.845
Preoperative ALT/($U\cdot L^{-1}$), M (Q_L, Q_U)	24.0 (15.0, 38.0)	29.0 (18.0, 42.0)	0.146
Preoperative AST/($U\cdot L^{-1}$), M (Q_L, Q_U)	24.0 (18.0, 36.0)	27.0 (19.0, 41.0)	0.319
Preoperative LDH/($U\cdot L^{-1}$), M (Q_L, Q_U)	172.0 (145.3, 199.8)	177.0 (152.0, 201.0)	0.208
Preoperative CRP/($mg\cdot L^{-1}$), M (Q_L, Q_U)	5 (5, 5)	5 (5, 5)	0.047
Preoperative WBC/(L^{-1}, $\times10^9$), M (Q_L, Q_U)	5.00 (3.70, 6.10)	5.20 (4.10, 6.40)	0.121

The mean ranks of preoperative CRP were 138.67 and 147.41 in the subgroups of anticoagulation within 12 h and after 12 h of surgery, respectively. PLC: Primary liver cancer; PLT: Platelet count; INR: International normalized ratio; ALT: Alanine transaminase; AST: Aspartate transaminase; LDH: Lactate dehydrogenase; CRP: C reactive protein; WBC: White blood cell count; M (Q_L, Q_U): Median (lower quartile, upper quartile).

表 3　PLC 患者术后并发症发生情况的比较

Tab 3　Comparison of postoperative complications in PLC patients

n (%)

Complication	Total N=495	Anticoagulant group N=287	Conventional treatment group N=208	P value
VTE	14 (2.8)	4 (1.4)	10 (4.8)	0.024
Infection	45 (9.1)	28 (9.8)	17 (8.2)	0.545
ARDS	32 (6.5)	11 (3.8)	21 (10.1)	0.005
PHLF	30 (6.1)	11 (3.8)	19 (9.1)	0.015
Bleeding	31 (6.3)	14 (4.9)	17 (8.2)	0.135

PLC: Primary liver cancer; VTE: Venous thromboembolism; ARDS: Acute respiratory distress syndrome; PHLF: Post-hepatectomy liver failure.

表 4　PLC 患者术后 VTE 影响因素的单因素 logistic 回归分析

Tab 4　Univariate logistic regression analysis of influencing factors of postoperative VTE in PLC patients

Variable	Regression coefficient	Standard error	Wald	OR (95% CI)	P value
Gender	−17.881	4 167.817	0.000	0.000	0.997
Age	0.063	0.026	5.738	1.065 (1.012, 1.122)	0.017
History of hypertension	−0.588	0.771	0.581	0.556 (0.122, 2.520)	0.446
History of diabetes mellitus	−0.476	1.048	0.206	0.621 (0.080, 4.844)	0.650
Smoking history	1.023	0.566	3.271	2.781 (0.918, 8.425)	0.071
Drinking history	0.860	0.544	2.503	2.364 (0.814, 6.862)	0.114
Previous history of liver surgery	0.877	0.669	1.722	2.404 (0.649, 8.914)	0.189
Cirrhosis	1.529	0.658	5.403	4.613 (1.271, 16.747)	0.020
Portal hypertension	2.309	0.572	16.286	10.060 (3.278, 30.871)	<0.001
Ascites	−0.518	1.048	0.244	0.596 (0.076, 4.643)	0.621
Number of tumors	0.480	0.200	5.757	1.616 (1.092, 2.392)	0.016

续表 4

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
Tumor maximum diameter	0.046	0.062	0.553	1.047 (0.928, 1.181)	0.457
Hepatic hilum obstruction	−0.276	0.323	0.726	0.759 (0.403, 1.431)	0.394
Porta hepatis occlusion time	0.005	0.008	0.460	1.005 (0.990, 1.021)	0.498
Intraoperative blood loss	0.000	0.000	2.322	1.000 (1.000, 1.001)	0.128
Intraoperative blood transfusion	0.288	0.601	0.229	1.333 (0.410, 4.334)	0.632
Laparoscopic surgery	−17.693	11 147.524	0.000	0.000	0.999
Liver resection range	0.137	0.566	0.058	1.146 (0.378, 3.478)	0.809
Prophylactic anticoagulation	−1.273	0.599	4.523	0.280 (0.087, 0.905)	0.033
Antiviral therapy	−0.527	0.659	0.640	0.590 (0.162, 2.147)	0.424
HBV DNA	0.154	0.542	0.081	1.167 (0.403, 3.377)	0.776
Preoperative ALP	−0.209	0.548	0.145	0.812 (0.277, 2.377)	0.703
Preoperative bilirubin	−0.033	0.042	0.623	0.968 (0.892, 1.050)	0.430
Preoperative ALT	0.005	0.005	1.150	1.005 (0.996, 1.015)	0.284
Preoperative AST	0.005	0.005	0.950	1.005 (0.995, 1.015)	0.330
Preoperative LDH	−0.008	0.007	1.322	0.992 (0.978, 1.006)	0.250
Preoperative CRP	−0.004	0.027	0.021	0.996 (0.945, 1.050)	0.885
Preoperative WBC	−0.281	0.176	2.539	0.755 (0.535, 1.067)	0.111
Preoperative neutrophil ratio	−0.001	0.023	0.002	0.999 (0.954, 1.046)	0.965
Preoperative PCT	0.044	0.032	1.901	1.045 (0.982, 1.112)	0.168
Preoperative PLT	−0.016	0.006	7.981	0.984 (0.974, 0.995)	0.005
Preoperative INR	1.224	2.619	0.218	3.400 (0.020, 576.555)	0.640

PLC: Primary liver cancer; VTE: Venous thromboembolism; HBV: Hepatitis B virus; ALP: Alkaline phosphatase; ALT: Alanine transaminase; AST: Aspartate transaminase; LDH: Lactate dehydrogenase; CRP: C reactive protein; WBC: White blood cell count; PCT: Procalcitonin; PLT: Platelet count; INR: International normalized ratio; *OR*: Odds ratio; *CI*: Confidence interval.

表 5　PLC 患者术后 VTE 影响因素的多因素 logistic 回归分析

Tab 5　Multivariate logistic regression analysis of influencing factors of postoperative VTE in PLC patients

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
Age	0.072	0.030	5.707	1.075 (1.013, 1.141)	0.017
Portal hypertension	1.981	0.793	6.237	7.248 (1.532, 34.298)	0.013
Number of tumors	0.678	0.266	6.478	1.970 (1.169, 3.319)	0.011
Prophylactic anticoagulation	−1.360	0.635	4.585	0.257 (0.074, 0.891)	0.032

PLC: Primary liver cancer; VTE: Venous thromboembolism; *OR*: Odds ratio; *CI*: Confidence interval.

表 6　PLC 患者 PHLF 影响因素的单因素 logistic 回归分析

Tab 6　Univariate logistic regression analysis of influencing factors of PHLF in PLC patients

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
Gender	−0.431	0.550	0.614	0.650 (0.221, 1.910)	0.433
Age	0.008	0.016	0.266	1.008 (0.977, 1.041)	0.606
History of hypertension	0.564	0.403	1.956	1.757 (0.798, 3.872)	0.162
History of diabetes mellitus	−0.103	0.626	0.027	0.902 (0.264, 3.079)	0.869
Smoking history	0.290	0.378	0.588	1.336 (0.637, 2.803)	0.443
Drinking history	0.605	0.382	2.503	1.831 (0.866, 3.873)	0.114
Previous history of liver surgery	−0.523	0.747	0.490	0.593 (0.137, 2.564)	0.484
Cirrhosis	0.203	0.377	0.290	1.225 (0.585, 2.564)	0.590
Portal hypertension	1.167	0.400	8.505	3.213 (1.466, 7.039)	0.004
Ascites	1.516	0.417	13.200	4.554 (2.010, 10.319)	＜0.001
Number of tumors	0.411	0.156	6.914	1.508 (1.110, 2.049)	0.009
Tumor maximum diameter	0.096	0.039	5.976	1.101 (1.019, 1.189)	0.014
Hepatic hilum obstruction	−0.001	0.170	0.000	0.999 (0.716, 1.395)	0.996
Porta hepatis occlusion time	0.006	0.005	1.376	1.006 (0.996, 1.017)	0.241
Intraoperative blood loss	0.002	0.000	24.294	1.002 (1.001, 1.002)	＜0.001
Intraoperative blood transfusion	1.893	0.396	22.873	6.639 (3.056, 14.422)	＜0.001
Laparoscopic surgery	−18.490	11 147.524	0.000	0.000	0.999
Liver resection range	0.186	0.392	0.225	1.204 (0.559, 2.594)	0.636

续表 6

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
Prophylactic anticoagulation	−0.925	0.390	5.615	0.396 (0.184, 0.852)	0.018
Antiviral therapy	−0.634	0.467	1.845	0.530 (0.212, 1.325)	0.174
HBV DNA	0.017	0.378	0.002	1.017 (0.485, 2.133)	0.963
APTT	0.379	0.410	0.855	1.460 (0.650, 3.260)	0.355
Preoperative bilirubin	0.008	0.004	3.287	1.008 (0.999, 1.017)	0.070
Preoperative ALT	0.003	0.004	0.545	1.003 (0.995, 1.012)	0.460
Preoperative AST	0.003	0.004	0.562	1.003 (0.995, 1.012)	0.454
Preoperative LDH	0.003	0.002	2.879	1.003 (1.000, 1.006)	0.090
Preoperative CRP	−0.011	0.022	0.239	0.989 (0.947, 1.033)	0.625
Preoperative WBC	−0.018	0.058	0.095	0.982 (0.877, 1.100)	0.758
Preoperative neutrophil ratio	0.031	0.018	3.076	1.032 (0.996, 1.069)	0.079
Preoperative PCT	0.064	0.024	6.921	1.066 (1.016, 1.118)	0.009
Preoperative PLT	−0.009	0.003	7.759	0.991 (0.984, 0.997)	0.005
Preoperative INR	5.100	1.624	9.865	164.031 (6.804, 3 954.512)	0.002

PLC: Primary liver cancer; PHLF: Post-hepatectomy liver failure; HBV: Hepatitis B virus; APTT: Activated partial thromboplastin time; ALT: Alanine transaminase; AST: Aspartate transaminase; LDH: Lactate dehydrogenase; CRP: C reactive protein; WBC: White blood cell count; PCT: Procalcitonin; PLT: Platelet count; INR: International normalized ratio; *OR*: Odds ratio; *CI*: Confidence interval.

表 7　PLC 患者 PHLF 影响因素的多因素 logistic 回归分析

Tab 7　Multivariate logistic regression analysis of influencing factors of PHLF in PLC patients

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
Portal hypertension	1.046	0.427	6.003	2.848 (1.233, 6.577)	0.014
Intraoperative blood loss	0.001	0.000	5.368	1.001 (1.000, 1.002)	0.021
Intraoperative blood transfusion	1.032	0.522	3.907	2.807 (1.009, 7.811)	0.048
Preoperative PCT	0.054	0.025	4.633	1.055 (1.005, 1.108)	0.031

PLC: Primary liver cancer; PHLF: Post-hepatectomy liver failure; PCT: Procalcitonin; *OR*: Odds ratio; *CI*: Confidence interval.

2.5　术后 ARDS 影响因素的 logistic 回归分析　单因素和多因素 logistic 回归结果均提示，腹水、术前胆红素是 PLC 患者术后发生 ARDS 的独立危险因素，而预防性抗凝是术后发生 ARDS 的独立保护因素（均 $P<0.05$，表 8、9）。

表 8　PLC 患者术后 ARDS 影响因素的单因素 logistic 回归分析

Tab 8　Univariate logistic regression analysis of influencing factors of postoperative ARDS in PLC patients

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
Gender	−0.237	0.501	0.223	0.789 (0.296, 2.107)	0.636
Age	0.032	0.017	3.781	1.033 (1.000, 1.067)	0.052
History of hypertension	0.463	0.397	1.357	1.589 (0.729, 3.462)	0.244
History of diabetes mellitus	0.691	0.478	2.089	1.995 (0.782, 5.090)	0.148
Smoking history	0.434	0.366	1.407	1.544 (0.753, 3.164)	0.235
Drinking history	0.487	0.374	1.698	1.628 (0.782, 3.389)	0.193
Previous history of liver surgery	−0.135	0.625	0.046	0.874 (0.257, 2.975)	0.829
Cirrhosis	0.204	0.366	0.310	1.226 (0.599, 2.510)	0.577
Portal hypertension	0.371	0.446	0.691	1.449 (0.605, 3.471)	0.406
Ascites	1.058	0.436	5.899	2.882 (1.227, 6.771)	0.015
Number of tumors	−0.288	0.302	0.908	0.750 (0.415, 1.356)	0.341
Tumor maximum diameter	0.037	0.043	0.752	1.038 (0.954, 1.129)	0.386
Hepatic hilum obstruction	−0.292	0.219	1.778	0.747 (0.487, 1.147)	0.182
Porta hepatis occlusion time	−0.008	0.009	0.843	0.992 (0.975, 1.009)	0.359
Intraoperative blood loss	0.000	0.000	1.428	1.000 (1.000, 1.001)	0.232
Intraoperative blood transfusion	0.000	0.000	3.352	1.000 (1.000, 1.001)	0.067
Laparoscopic surgery	0.193	1.057	0.033	1.212 (0.153, 9.629)	0.855
Liver resection range	−0.586	0.439	1.785	0.556 (0.235, 1.315)	0.182
Prophylactic anticoagulation	−1.036	0.384	7.276	0.355 (0.167, 0.753)	0.007
Antiviral therapy	−0.163	0.406	0.161	0.850 (0.384, 1.882)	0.688

续表 8

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
HBV DNA	−0.385	0.377	1.046	0.680 (0.325, 1.424)	0.306
Preoperative ALP	0.318	0.393	0.653	1.374 (0.636, 2.969)	0.419
Preoperative bilirubin	0.011	0.004	8.140	1.012 (1.004, 1.020)	0.004
Preoperative ALT	0.006	0.004	2.403	1.006 (0.999, 1.013)	0.121
Preoperative AST	0.003	0.004	0.568	1.003 (0.995, 1.012)	0.451
Preoperative LDH	0.001	0.002	0.101	1.001 (0.996, 1.005)	0.750
Preoperative CRP	0.014	0.012	1.372	1.014 (0.991, 1.037)	0.241
Preoperative WBC	−0.016	0.054	0.088	0.984 (0.885, 1.094)	0.766
Preoperative neutrophil ratio	−0.003	0.016	0.041	0.997 (0.967, 1.028)	0.840
Preoperative PCT	0.038	0.026	2.128	1.039 (0.987, 1.094)	0.145
Preoperative PLT	−0.001	0.003	0.184	0.999 (0.994, 1.004)	0.668
Preoperative INR	−0.645	2.085	0.096	0.525 (0.009, 31.267)	0.757

PLC: Primary liver cancer; ARDS: Acute respiratory distress syndrome; HBV: Hepatitis B virus; ALP: Alkaline phosphatase; ALT: Alanine transaminase; AST: Aspartate transaminase; LDH: Lactate dehydrogenase; CRP: C reactive protein; WBC: White blood cell count; PCT: Procalcitonin; PLT: Platelet count; INR: International normalized ratio; *OR*: Odds ratio; *CI*: Confidence interval.

表 9　PLC 患者术后 ARDS 影响因素的多因素 logistic 回归分析

Tab 9　Multivariate logistic regression analysis of influencing factors of postoperative ARDS in PLC patients

Variable	Regression coefficient	Standard error	Wald	*OR* (95% *CI*)	*P* value
Prophylactic anticoagulation	−0.934	0.391	5.697	0.393 (0.183, 0.846)	0.017
Ascites	0.886	0.454	3.800	2.425 (0.995, 5.909)	0.041
Preoperative bilirubin	0.011	0.004	5.899	1.011 (1.002, 1.019)	0.015

PLC: Primary liver cancer; ARDS: Acute respiratory distress syndrome; *OR*: Odds ratio; *CI*: Confidence interval.

3　讨　论

我国是世界上肝病发生率最高的国家之一，也是世界上肝切除病例最多的国家之一，目前肝切除术仍然是 PLC 患者的首选治疗方法。美国胸科医师学会抗栓治疗指南推荐腹部手术患者术后使用抗凝药物治疗[10]，这一治疗方案同样对肝切除患者适用。在我国的实际临床工作中，因考虑到术后抗凝存在出血风险，即使在没有术后活动性出血的患者中，术后预防性抗凝仍未被普遍应用。本研究探究了 PLC 患者肝切除术后使用预防性抗凝治疗是否可降低术后并发症的发生率。

数据表明，普通外科未使用预防措施的患者术后深静脉血栓形成的发生率为 6.1%[12-13]。由于手术时间长、术中出血多、肿瘤患者血液高凝等原因，接受 PLC 肝切除手术的患者被视为术后 VTE 发生的中－高风险人群，肝切除术后 VTE 发生率高达 2.1%～4.7%[14-18]。本研究结果显示，VTE 的总发生率为 2.8%（14/495），其中抗凝组 VTE 的发生率为 1.4%（4/287），低于常规治疗组的 4.8%（10/208），进一步 logistic 回归分析结果显示术后发生 VTE 的独立危险因素包括年龄、门静脉高压和肿瘤数量，而术后预防性抗凝是 VTE 的独立保护因素。该结果与既往报道结果[16]一致，再次印证了 PLC 患者行肝切除术后 VTE 的发生率较高，术后早期预防性抗凝可降低 VTE 的发生率且不会增加出血风险。

HiSCO-05 研究是一项中心随机对照试验，旨在分析肝切除术后使用抗凝血酶Ⅲ对 PHLF 发生率的影响[16]。HiSCO-05 研究结果表明，使用抗凝血酶Ⅲ作为次要终点的方案是安全的，然而未观察到主要终点的疗效，即 PHLF 发生率降低。该研究同时指出，BMI≥25 kg/mm^2 和总胆红素≥15 mg/L 为 PHLF 的独立危险因素。本研究结果显示，常规治疗组与抗凝组在 PHLF 发生率方面存在差异，进一步行单因素及多因素 logistic 回归分析发现，PLC 患者发生 PHLF 的独立危险因素包括门静脉高压、术中出血、术中输血、术前降钙素原。本研究结果与 HiSCO-05 研究结果[16]存在差异，考虑本研究样本量较小，所得结果可能存在误差，且尚无大型临床研究明确肝切除术后抗凝与 PHLF 的发生相关或为 PHLF 发生的独立危险因素，故该结果仍需进一步验证。

有研究报道 PLC 术后肺部感染的发生率高达 10% 左右，原因可能为术后呼吸肌张力下降等导致肺活力降低及痰液淤积导致感染或术前原有疾病加

重引起感染等[19]。但尚无临床研究证实肝切除术后肺部感染与 ARDS 有关，也未见有关肝切除术后 ARDS 危险因素的报道。本研究结果显示，常规治疗组与抗凝组在 ARDS 发生率方面存在差异，进一步分析发现 PLC 患者发生术后 ARDS 的独立危险因素包括腹水、术前胆红素，而预防性抗凝则是独立保护因素。但本研究样本量较小，后期仍需扩大样本量进一步验证该结果。

综上所述，PLC 患者术后早期预防性抗凝可降低 VTE、PHLF、ARDS 的发生率，且不会增加术后出血的风险。但本研究为单中心研究，受到样本量、研究经费等因素限制，研究结果可能存在偏倚，后续将进一步扩大样本量进行多中心研究以验证该结果。

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