·临床研究·

基于倾向性评分匹配法对比开腹与腹腔镜在老年胆囊结石并肝硬化中的应用

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【摘 要】 **目的** 基于倾向性评分匹配法分析比较开腹手术与腹腔镜手术在老年胆囊结石合并肝硬化中的应用效果。**方法** 回顾性收集2022年1月至2023年12月河北北方学院附属第一医院收治的159例老年胆囊结石合并肝硬化患者的临床资料,根据手术方式不同分为腹腔镜组(78例)与开腹组(81例),通过倾向性评分匹配法行1∶1匹配,比较两组患者手术相关指标、术前及术后3 d肝功能[丙氨酸氨基转移酶(ALT)、天冬氨酸氨基转移酶(AST)、胆碱酯酶活性(CHE)、前白蛋白(PA)、总胆红素(TBIL)、总胆汁酸(TBA)]、免疫功能[T淋巴细胞亚群($CD4^+$、$CD8^+$)、$CD4^+/CD8^+$]、应激反应[甲肾上腺素(NE)、肾上腺皮质激素(ACTH)、皮质醇(Cor)]差异,并评估两组并发症发生情况。采用SPSS 24.0软件进行数据分析。倾向性评分匹配采用R语言软件R3.6.1 Match It软件包。根据数据类型,组间比较分别采用t检验、χ^2检验及Fisher精确概率法。**结果** 未经倾向性评分匹配的两组老年患者在年龄、血清白蛋白、Child-Pugh分级的比较差异有统计学意义($P<0.05$),倾向性评分匹配消除不平衡变量后得到69对资料均衡的患者,匹配后的两组一般资料比较,差异无统计学意义($P>0.05$)。腹腔镜组手术时间、术中出血量、术后引流及住院时间均低于开腹组($P<0.05$)。术后3 d,两组ALT、AST、PA、TBIL、TBA及NE、ACTH、Cor均较术前显著升高($P<0.05$),但腹腔镜组术后ALT、AST、PA、TBIL、TBA、NE、ACTH、Cor低于开腹组($P<0.05$);两组CHE、$CD4^+$、$CD8^+$及$CD4^+/CD8^+$均较术前降低($P<0.05$),但腹腔镜组术后CHE、$CD4^+$、$CD4^+/CD8^+$高于开腹组($P<0.05$)。两组术中并发症比较,差异无统计学意义($P>0.05$);腹腔镜组术后并发症总发生率明显低于开腹组,差异有统计学意义[4.35%(3/69)和14.49%(10/69),$P<0.05$]。**结论** 相较于开腹胆囊切除术,腹腔镜胆囊切除术具有创伤小、恢复快的优势,能减少老年胆囊结石合并肝硬化患者术后肝功能损伤、免疫抑制及应激反应,安全性更高,更适合推广应用。

【关键词】 老年人;胆囊结石;肝硬化;腹腔镜;开腹;倾向性评分匹配法
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Comparison of open *versus* laparoscopic surgery for elderly patients with cholecystolithiasis and liver cirrhosis based on propensity score matching

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【**Abstract**】 **Objective** To compare the efficacy of open *versus* laparoscopic surgery for elderly patients with cholecystolithiasis complicated with liver cirrhosis based on propensity score matching. **Methods** The clinical data were retrospectively collected of 159 elderly patients with cholecystolithiasis and liver cirrhosis admitted to the First Affiliated Hospital of Hebei North University from January 2022 to December 2023. According to the surgical methods, they were divided into a laparoscopic group ($n=78$) and an open surgery group ($n=81$). The 1∶1 matching was performed by propensity score matching. Surgery-related indexes, liver function [alanine aminotransferase (ALT), aspartate aminotransferase (AST), cholinesterase activity (CHE), prealbumin (PA), total bilirubin (TBIL), total bile acid (TBA)], immune function [T lymphocyte subsets ($CD4^+$, $CD8^+$), $CD4^+/CD8^+$], stress response [norepinephrine (NE), adrenocorticotropic hormone (ACTH), cortisol (Cor)] before and 3 d after surgery were compared between the two groups, and complications were evaluated. SPSS 24.0 was used for data analysis. Propensity score matching used R language software R3.6.1 Match It package. Intergroup comparison was performed using t test, χ^2 test or Fisher's exact probability method depending on data type. **Results** Before propensity score matching, there were statistically significant differences between the two groups in age, serum albumin, and Child-Pugh grading ($P<0.05$). After propensity score matching eliminated the unbalanced variables, 69 pairs of patients with balanced data were obtained. There were no statistically significant differences in the general data between groups after matching

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(P>0.05). The laparoscopic group had shorter surgical time, less intraoperative blood loss, shorter postoperative drainage time, and shorter hospital stay than the open surgery group (P<0.05). At 3 d after surgery, ALT, AST, PA, TBIL, TBA, NE, ACTH, and Cor levels rose significantly compared with levels before surgery in both groups (P<0.05), but these values in the laparoscopic group were lower than those in the open surgery group after surgery (P<0.05). CHE, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ decreased in both groups as compared with before surgery (P<0.05), but CHE, $CD4^+$, and $CD4^+/CD8^+$ in the laparoscopic group were higher than those in the open surgery group after surgery (P<0.05). There were no statistically significant differences in intraoperative complications between the two groups (P>0.05). The total incidence of postoperative complications in the laparoscopic group was significantly lower than that in the open surgery group [4.35% (3/69) *vs* 14.49% (10/69); P<0.05], with a statistically significant difference. **Conclusion** Compared with open cholecystectomy, laparoscopic cholecystectomy has the advantages of less invasiveness and faster recovery. It can reduce postoperative liver function damage, immunosuppression, and stress response in elderly patients with cholecystolithiasis and liver cirrhosis, with higher safety, making it more suitable for promotion and application.

【Key words】 aged; cholecystolithiasis; liver cirrhosis; laparoscopes; open surgery; propensity score matching

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胆囊结石在我国的发病率为6%~9%,胆囊切除术是其有效治疗办法[1]。另外,肝硬化作为慢性肝损伤的修复反应,可造成胆囊结石风险升高。有报道指出,肝硬化患者胆囊结石发生率是非肝硬化患者的2~4倍[2]。老年人作为肝硬化及胆囊结石的好发人群,具有器官功能退化、预后差等特点,且肝硬化患者由于静脉曲张、门静脉压力较高,围术期出血风险高,故老年胆囊结石合并肝硬化患者的手术治疗一直受到临床广泛关注[3]。既往研究认为,腹腔镜建立的气腹可造成肝硬化患者肝缺血再灌注,加剧肝细胞损伤,故老年胆囊结石合并肝硬化更适合行开腹手术[4]。但近年研究发现,适当的气腹压力对肝组织压迫较小,且腹腔镜下还能观察腹壁曲张静脉,避免出血,用于肝硬化患者安全性良好[5]。基于此,本研究对比分析腹腔镜与开腹胆囊切除术对老年胆囊结石合并肝硬化患者的影响,为临床术式选择提供参考数据。

1 对象与方法

1.1 研究对象

回顾性收集2022年1月至2023年12月河北北方学院附属第一医院收治的159例老年胆囊结石合并肝硬化患者临床资料。纳入标准:经手术证实为胆囊结石;符合《肝硬化诊治指南》[6]中代偿期肝硬化诊断标准,即食管胃静脉曲张或消化道异位静脉曲张,或影像学检查提示肝硬化或门脉高压特征,且无腹水等门脉高压相关并发症;年龄≥60岁;行胆囊切除术;肝功能Child-Pugh分级为A~B级;实验室检查等资料完整。排除标准:合并急性胰腺炎;恶性肿瘤;活动性肝炎;自身免疫系统疾病;入院前1个月内行免疫抑制剂治疗;入院前1个月内饮酒史;既往腹部手术治疗史或腹部外伤史。

1.2 方法

1.2.1 倾向性评分匹配法 159例患者根据手术方式不同分为腹腔镜组(78例)与开腹组(81例),将两组患者组间不均衡一般资料作为协变量,纳入倾向性评分匹配模型的因素包括性别、年龄、体质量指数、胆囊壁厚度、结石直径、血红蛋白、白蛋白、Child-Pugh分级、肝硬化类型及基础疾病,经logistic回归计算对应的倾向性评分,使用最小毗邻法对两组倾向性评分相近的患者行1∶1匹配,匹配容差为0.02,最终每组各纳入患者69例。

1.2.2 手术方法 (1)腹腔镜组取头高脚低左侧倾斜位,气管插管全身麻醉,采用常规“四孔法”建立操作通道,腹壁穿刺时需注意避开腹壁的曲张静脉,气腹压力维持在10~12 mmHg(1 mmHg=0.133 kPa),充分显露、解剖胆囊三角,游离胆囊动脉及胆囊管并用钛夹夹闭,顺逆结合式从胆囊床切除胆囊,常规放置腹腔引流管,结束手术。(2)开腹组体位及麻醉方式同腹腔镜组,于右上肋缘下作一4~5 cm的切口,显露胆囊三角,使用电凝法分离并切除胆囊,放置1根腹腔引流管,结束手术。两组老年患者术后均给予预防感染、抑酸、护肝等对症支持治疗。

1.2.3 观察指标 (1)手术相关指标:记录手术时间、出血量、术后引流时间及术后住院时间。(2)肝功能:术前及术后3 d采集所有患者清晨空腹外周肘静脉血3~4 ml,使用全自动生化分析仪(日本OLYMPUS公司,型号:AU2700)检测丙氨酸氨基转移酶(alanine aminotransferase, ALT)、天冬氨酸氨基转移酶(aspartate aminotransferase, AST)、胆碱酯酶活性(cholinesterase, CHE)、前白蛋白(prealbumin, PA)、总胆红素(total bilirubin, TBIL)及总胆汁酸(total bile acid, TBA)水平。(3)免疫功能:使用流式细胞仪(美国BD公司,型号:FACSCanto Ⅱ)检测T淋巴细胞亚群($CD4^+$、$CD8^+$)占比,并计算$CD4^+/CD8^+$比值。(4)应激反应:使用酶联免疫分析法(德国SIgma-Aldrich公司)检测甲肾上腺素(norepinephrine, NE)、肾上腺皮质

激素(adrenocorticotropic hormone, ACTH)、皮质醇(cortisol, Cor)水平。(5)并发症发生情况:包括胆总管损伤等术中并发症,以及胆漏、出血等术后并发症。

1.3 统计学处理

采用SPSS 24.0统计软件进行数据分析。倾向性评分匹配采用R语言软件R3.6.1 Match It软件包。计量资料用均数±标准差($\bar{x}\pm s$)表示,采用t检验;计数资料用例数(百分率)表示,采用χ^2检验或Fisher精确概率法。$P<0.05$为差异有统计学意义。

2 结 果

2.1 两组患者一般资料匹配

未经倾向性评分匹配的两组老年患者在年龄、血清白蛋白、Child-Pugh分级比较差异有统计学意义($P<0.05$);倾向性评分匹配消除不平衡变量后得到69对资料均衡的患者,匹配后的两组一般资料比较,差异无统计学意义($P>0.05$;表1)。

2.2 两组患者手术相关指标

腹腔镜组术中未出现中转开腹病例,腹腔镜组手术时间、术中出血量、术后引流时间及住院时间均低于开腹组,差异均有统计学意义(均$P<0.05$;表2)。

2.3 两组患者手术前后肝功能指标

术后3 d,两组患者ALT、AST、PA、TBIL、TBA均较术前显著升高($P<0.05$),但腹腔镜组术后低于开腹组,差异均有统计学意义(均$P<0.05$);两组患者CHE均较术前显著降低,但腹腔镜组术后高于开腹组,差异均有统计学意义(均$P<0.05$;表3)。

2.4 两组患者免疫功能指标

术后3 d,两组患者$CD4^+$、$CD8^+$及$CD4^+/CD8^+$均较术前降低,但腹腔镜组术后$CD4^+$、$CD4^+/CD8^+$高于开腹组,差异均有统计学意义(均$P<0.05$;表4)。

2.5 两组患者手术前后应激反应指标

术后3 d,两组NE、ACTH、Cor均较术前显著升高($P<0.05$),但腹腔镜组术后低于开腹组,差异均有统计学意义(均$P<0.05$;表5)。

2.6 两组患者术中及术后并发症发生情况

两组术中并发症发生情况比较,差异无统计学意义($P>0.05$);腹腔镜组术后并发症总发生率明显低于开腹组,差异有统计学意义($P<0.05$;表6)。

表1 两组患者匹配前与匹配后一般资料比较

Table 1 Comparison of general data before and after matching between two groups

Item	Before matching				After matching($n=69$)			
	Laparoscopic group ($n=78$)	Open surgery group($n=81$)	χ^2/t	P value	Laparoscopic group	Open surgery group	χ^2/t	P value
Male/female(n)	48/30	49/32	0.018	0.893	45/24	44/25	0.032	0.859
Age(years, $\bar{x}\pm s$)	67.39±5.08	69.67±6.52	2.453	0.015	67.93±4.55	68.72±5.37	0.932	0.353
Body mass index(kg/m^2, $\bar{x}\pm s$)	24.13±2.18	24.32±2.33	0.530	0.597	24.19±2.05	24.30±2.27	0.299	0.766
Gallbladder wall thickness(mm, $\bar{x}\pm s$)	3.21±0.43	3.17±0.46	0.566	0.572	3.20±0.41	3.15±0.43	0.699	0.486
Stone diameter(mm, $\bar{x}\pm s$)	8.11±1.63	8.03±1.72	0.301	0.764	8.09±1.60	8.01±1.65	0.289	0.773
Hemoglobin(g/L, $\bar{x}\pm s$)	122.39±8.65	120.72±9.11	1.184	0.238	122.15±8.16	121.43±8.33	0.513	0.609
Albumin(g/L, $\bar{x}\pm s$)	41.39±4.52	38.25±4.27	4.504	<0.001	41.28±4.09	40.69±4.13	0.843	0.401
Child-Pugh grading[n(%)]			4.912	0.027			1.272	0.259
Grade A	70(89.74)	62(76.54)			64(92.75)	60(86.96)		
Grade B	8(10.26)	19(23.46)			5(7.25)	9(13.04)		
Liver cirrhosis type[n(%)]			0.258	0.879			0.552	0.759
Posthepatitic cirrhosis	59(75.64)	64(79.01)			58(84.06)	61(88.40)		
Alcoholic cirrhosis	10(12.82)	9(11.11)			7(10.14)	5(7.25)		
Other cirrhosis	9(11.54)	8(9.88)			4(5.80)	3(4.35)		
Hypertension [n(%)]	29(37.18)	33(40.74)	0.212	0.645	27(39.13)	30(43.48)	0.269	0.604
Diabetes mellitus[n(%)]	7(8.97)	8(9.88)	0.038	0.846	6(8.70)	4(5.80)	0.431	0.511
Coronary heart disease[n(%)]	6(7.69)	6(7.41)	0.005	0.946	5(7.25)	3(4.35)	0.133	0.716$^{\#}$

表2 两组患者手术相关指标比较

Table 2 Comparison of surgery-related indexes between two groups ($n=69$, $\bar{x}\pm s$)

Group	Surgical time(min)	Intraoperative blood loss(ml)	Postoperative drainage time(d)	Postoperative hospital stay(d)
Laparoscopic	55.28±10.13	35.42±7.06	2.07±0.41	5.21±1.03
Open surgery	76.49±13.57	68.79±9.22	3.12±0.68	7.19±1.26
t	10.404	23.870	10.984	10.106
P value	<0.001	<0.001	<0.001	<0.001

表 3 两组患者手术前后肝功能指标比较

Table 3 Comparison of liver function before and after surgery between two groups ($n=69$, $\bar{x}\pm s$)

Group	ALT(U/L)		AST(U/L)		CHE(U/L)	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
Laparoscopic	35.28±4.89	56.21±7.63 *	36.92±5.27	57.19±6.86 *	2 984.58±279.86	2 436.49±255.38 *
Open surgery	36.07±5.03	68.44±8.25 *	37.45±5.46	68.39±7.59 *	3 029.53±289.44	2 198.93±246.40 *
t	0.935	9.040	0.580	9.094	0.927	5.561
P value	0.351	<0.001	0.563	<0.001	0.355	<0.001

Group	PA(mg/L)		TBIL(μmol/L)		TBA(μmol/L)	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
Laparoscopic	133.89±22.06	165.46±21.33 *	16.48±0.80	18.89±1.24 *	14.19±2.35	16.89±2.56 *
Open surgery	135.94±23.18	178.44±19.52 *	16.39±0.72	20.06±1.36 *	13.68±2.19	18.06±2.87 *
t	0.532	3.729	0.695	5.281	1.319	3.823
P value	0.596	<0.001	0.489	<0.001	0.189	<0.001

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CHE: cholinesterase; PA: prealbumin; TBIL: total bilirubin; TBA: total bile acid. Compared with preoperative in the same group, * $P<0.05$.

表 4 两组患者手术前后 $CD4^+$、$CD8^+$及 $CD4^+/CD8^+$比较

Table 4 Comparison of $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ before and after surgery between two groups ($n=69$, $\bar{x}\pm s$)

Group	$CD4^+$(%)		$CD8^+$(%)		$CD4^+/CD8^+$	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
Laparoscopic	45.22±5.33	33.19±4.76 *	30.46±4.08	22.37±3.48 *	1.62±0.32	1.43±0.23 *
Open surgery	44.78±4.89	29.21±4.35 *	31.22±4.26	21.82±4.11 *	1.58±0.31	1.35±0.20 *
t	0.505	5.127	1.070	0.848	0.746	2.180
P value	0.614	<0.001	0.286	0.398	0.457	0.031

Compared with preoperative in the same group, * $P<0.05$.

表 5 两组患者手术前后 NE、ACTH 及 Cor 指标比较

Table 5 Comparison of NE, ACTH and Cor before and after surgery between two groups ($n=69$, $\bar{x}\pm s$)

Group	NE(ng/ml)		ACTH(pg/ml)		Cor(nmol/ml)	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
Laparoscopic	310.19±48.93	452.27±42.11 *	66.25±7.48	78.79±8.25 *	508.19±78.93	613.44±83.76 *
Open surgery	312.48±53.19	483.13±38.33 *	67.13±8.05	89.44±9.32 *	510.42±82.16	679.44±85.27 *
t	0.263	4.502	0.665	7.107	0.163	4.587
P value	0.793	<0.001	0.507	<0.001	0.871	<0.001

NE: norepinephrine; ACTH: adrenocorticotropic hormone; Cor: cortisol. Compared with preoperative in the same group, * $P<0.05$.

表 6 两组患者术中及术后并发症发生情况比较

Table 6 Comparison of intraoperative and postoperative complications between two groups [$n=69$, $n(\%)$]

Group	Intraoperative complications			Postoperative complication				
	Common bile duct injury	Gallbladder artery injury	Total	Bile leakage	Bleeding	Infection	Liver failure	Total
Laparoscopic	1(1.45)	0(0.00)	1(1.45)	1(1.45)	1(1.45)	1(1.45)	0(0.00)	3(4.35)
Open surgery	1(1.45)	1(1.45)	2(2.90)	1(1.45)	3(4.35)	4(5.80)	2(2.90)	10(14.49)
χ^2	0.507	–	0.341	–	0.258	0.830	–	4.161
P value	0.476	1.000	0.559	1.000	0.612	0.362	0.496	0.041

–: no datum.

3 讨 论

随机对照研究要求严格限定研究环境及人群,虽然具有明确因果关系,但偏离复杂临床环境,故研究结论在临床实际的应用仍待进一步观察[7]。真实世界研究是在真实诊疗环境下评估干预措施的应用效果及安全,但由于缺乏严格纳入及排除标准,组间基线资料常分布不均衡,缺乏可比性[8]。倾向性评分匹配法可优化混杂因素,对入组对象进行匹配,使基于真实世界研究的组间具有可比性[9]。本研究中,两组老年患者匹配前年龄、血清白蛋白、Child-Pugh 分级存在显著差异,考虑与临床实际对高龄、肝功能差的

患者更倾向于选择开腹手术有关[10],但倾向性评分匹配后两组患者一般资料分布均衡,可尽可能减少混杂因素造成的结果偏倚,提高研究结果可靠性。

肝硬化背景下,手术需尽可能避免对肝功能的损伤,既往研究认为,腹腔镜术中气腹造成周围器官对肝脏压迫增加,易造成肝组织缺血缺氧及再灌注损伤[11]。随着腹腔镜技术的飞速发展,气腹压力已无需维持较高水平,在12 mmHg(1 mmHg=0.133 kPa)左右的压力下能完成胆囊切除术[12]。本研究腹腔镜组气腹压力在10~12 mmHg下均完成手术操作,并无中转开腹病例,提示该气腹压力合适可靠。另外,腹腔镜组术后3 d ALT、AST、PA、TBIL、TBA低于开腹组,CHE高于开腹组,提示腹腔镜手术对老年胆囊结石合并肝硬化患者的肝损伤更轻微,考虑是因其气腹压力合适,不压迫肝组织,且创伤小,能避免局部组织炎症水肿对肝组织的压迫性损伤,故术后肝功能更佳[13]。不仅如此,腹腔镜组手术时间、术中出血量及术后引流、住院时间均低于开腹组,术后3 d血清NE、ACTH、Cor也低于开腹组,上述结果也符合腹腔镜手术的微创特征,且腹腔镜下能观察肝硬化背景下的腹壁曲张静脉,减少手术操作对曲张静脉的破坏,降低出血量,减轻应激反应,术后恢复也更快[14]。

另据文献报道,老年肝硬化患者常伴免疫功能紊乱,外科手术则进一步破坏其免疫功能,术后感染等风险较非肝硬化的老年患者更高[15]。本研究中,两组患者术后3 d $CD4^+$、$CD8^+$及$CD4^+/CD8^+$均较术前降低,开腹组术后$CD4^+$、$CD4^+/CD8^+$低于腹腔镜组,提示两种术式均造成患者免疫抑制进一步增加,但开腹手术的免疫抑制作用更大,考虑与开腹术式创伤大,炎症、应激反应更强,而免疫功能抑制更严重有关[16]。且腹腔镜组术后并发症总发生率明显低于开腹组,分析其原因为腹腔镜视野下能清晰观察、明确解剖组织与血管,减轻组织损伤,且切口小,术区暴露少,感染风险低,故并发症发生率更低[17]。本研究虽然使用倾向性评分分配法减轻了混杂因素对结果的影响,但作为单中心小样本量研究,代表性及可靠性有所欠缺,未来还需联合其他医疗机构开展多中心大样本量研究,对本研究结果加以验证。

综上,倾向性评分匹配一般资料后,腹腔镜胆囊切除术较开腹术式能缩短手术时间、降低手术创伤,减轻免疫抑制及应激反应,对老年胆囊结石合并肝硬化患者肝功能损伤更小,术后并发症更少,安全性更佳。

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