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· 临床研究 ·

肝门部胆管癌根治术联合血管切除重建术治疗肝门部胆管癌的荟萃分析

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摘要: **目的** 用荟萃分析的方法评价肝门部胆管癌根治术联合血管切除重建术治疗肝门部胆管癌的围术期安全性和远期疗效。**方法** 计算机检索 PubMed、Web of Science、Embase、Cochrane library、中国生物医学文献数据库、中国知网和万方数据库关于联合血管切除重建与不切除血管根治性切除治疗肝门部胆管癌的临床对照研究, 检索时间限定为 2010 年 1 月 1 日至 2021 年 3 月 1 日。对纳入的文献数据采用 RevMan 5.3 进行分析, 比较两种治疗方法的安全性和有效性。**结果** 共纳入 21 篇文献 (均为回顾性研究), 共 4 124 例患者, 血管切除重建组 1283 例, 包括门静脉切除重建组 718 例、肝动脉切除重建组 302 例和联合切除重建组 263 例, 未切除组 2841 例。血管切除重建组与未切除组在术后总体并发症 ($OR=1.16$, $95\%CI: 0.98\sim1.37$, $P=0.08$)、术中失血量 ($MD=150.92$, $95\%CI: -9.19\sim311.04$, $P=0.06$)、术后死亡率 ($OR=1.37$, $95\%CI: 0.97\sim1.93$, $P=0.07$) 和术后复发率 ($OR=0.78$, $95\%CI: 0.37\sim1.64$, $P=0.52$) 等方面比较, 差异均无统计学意义; 在术后 1、3 和 5 年生存率 ($OR=0.68$, $95\%CI: 0.51\sim0.90$, $P<0.01$; $OR=0.62$, $95\%CI: 0.50\sim0.75$, $P<0.01$; $OR=0.54$, $95\%CI: 0.43\sim0.68$, $P<0.01$) 和 R0 切除率 ($OR=0.63$, $95\%CI: 0.52\sim0.76$, $P<0.01$) 方面, 血管切除重建组均小于未切除组。门静脉和肝动脉切除重建组亚组的 5 年生存率 ($OR=0.51$, $95\%CI: 0.36\sim0.73$, $P<0.01$; $OR=0.55$, $95\%CI: 0.39\sim0.76$, $P<0.01$) 均小于未切除组; 肝动脉切除重建亚组术后死亡率 ($OR=1.89$, $95\%CI: 1.04\sim3.42$, $P=0.04$) 大于未切除组。血管切除重建组肝功能衰竭发生率 ($OR=1.91$, $95\%CI: 1.09\sim3.36$, $P=0.02$) 大于未切除组。**结论** 肝门部胆管癌根治术联合血管切除重建术治疗肝门部胆管癌总体上是安全的, 联合血管切除重建的术式可以改善局部进展期患者预后, 延长患者生存期, 有肝门血管侵犯的肝门部胆管癌不应是手术的禁忌证。

关键词: 肝门部胆管癌; 肝门部胆管癌根治术; 血管切除重建术; 荟萃分析

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Radical resection combined with vascular resection plus reconstruction in treatment of hilar cholangiocarcinoma: A meta-analysis

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Abstract: Objective To evaluate the perioperative safety and long-term efficacy of radical resection combined with vascular resection plus reconstruction in the treatment of hilar cholangiocarcinoma by meta-analysis. **Methods** The clinical controlled study of radical resection of hilar cholangiocarcinoma combined with vascular resection plus reconstruction and without vascular resection was searched from PubMed、Web of Science、Embase、Cochrane library、China Biology Medicine disc (SinoMed CBM), China National Knowledge Infrastructure (CNKI) and Wangfang databases. The retrieval time was limited to January 1st, 2010–March 1st, 2021. The included literature data were analyzed by RevMan 5.3 to compare the safety and effectiveness of the two treatment methods. **Results** A total of 21 literatures (all retrospective studies) were included, involving 4 124 patients, including 1 283 patients in the vascular resection plus reconstruction group (718 patients in the portal vein resection and reconstruction group, 302 patients in the hepatic artery resection and reconstruction group, and 263 patients in the combined resection and reconstruction group), and 2 841 patients in the unresected group. Compared the vascular resection and reconstruction group with the unresected group, the overall postoperative complications ($OR=1.16$, $95\%CI$: $0.98-1.37$, $P=0.08$), intraoperative blood loss ($MD=150.92$, $95\%CI$: $-9.19-311.04$, $P=0.06$), postoperative mortality ($OR=1.37$, $95\%CI$: $0.97-1.93$, $P=0.07$) and postoperative recurrence rate ($OR=0.78$, $95\%CI$: $0.37-1.64$, $P=0.52$) had no significant difference. The postoperative 1-, 3- and 5-year survival rates ($OR=0.68$, $95\%CI$: $0.51-0.90$, $P<0.01$; $OR=0.62$, $95\%CI$: $0.50-0.75$, $P<0.01$; $OR=0.54$, $95\%CI$: $0.43-0.68$, $P<0.01$) and R0 resection rates ($OR=0.63$, $95\%CI$: $0.52-0.76$, $P<0.01$) were lower in the vascular resection and reconstruction group than in the unresected group. The 5-year survival rate of the portal vein and hepatic artery resection and reconstruction subgroups ($OR=0.51$, $95\%CI$: $0.36-0.73$, $P<0.01$; $OR=0.55$, $95\%CI$: $0.39-0.76$, $P<0.01$) were both lower than that of the unresected group, and the postoperative mortality rate of the hepatic artery resection subgroup ($OR=1.89$, $95\%CI$: $1.04-3.42$, $P=0.04$) was higher than that of the unresected group. The incidence of liver failure in the vascular resection and reconstruction group ($OR=1.91$, $95\%CI$: $1.09-3.36$, $P=0.02$) was higher than that in the unresected group. **Conclusions** Radical resection of hilar cholangiocarcinoma combined with vascular resection and reconstruction is generally safe. The combined vascular resection and reconstruction can improve the prognosis of patients with locally advanced cholangiocarcinoma and prolong the survival of patients. Hilar cholangiocarcinoma with hilar vascular invasion should not be regarded as a contraindication.

Key words: hilar cholangiocarcinoma; radical resection of hilar cholangiocarcinoma; vascular resection plus reconstruction; meta-analysis

肝门部胆管癌约占胆管癌的60%，是胆管癌最常见的类型^[1]，由于早期缺乏明显的症状，就诊时常常已是晚期，手术仍是根治肝门部胆管癌的唯一手段^[2]。根治性切除的目标是R0切除，目前的标准包括完整的肝外胆管切除联合肝大部切除、根治性淋巴结清扫和胆道重建术^[3-4]。在根治术的基础上联合血管切除重建被视为一种比较激进的手术方式，但患者更有可能获得无瘤生存^[5]。肝门部胆管癌因其特殊的解剖位置，常有门脉血管的侵犯。术中行血管的切除重建的研究已在临床广泛开展，但血管切除重建的术式对于患者术后并发症以及远期预后的影响仍然存在争议。因此，本文通过荟萃分析比较术中联合血管切除重建与

不行血管切除治疗肝门部胆管癌的有效性及安全性，以期对临床手术方式决策提供参考。

1 资料与方法

1.1 文献检索

计算机检索PubMed、Web of Science、Embase、Cochrane library、中国生物医学文献数据库、中国知网和万方数据库，检索有关肝门部胆管癌手术治疗的临床研究。英文检索词为“perihilar cholangiocarcinoma”、“hilar cholangiocarcinoma”、“Klatskin tumor”、“vascular resection and reconstruction”、“portal vein resection”和“hepatic artery resection”，中文检索词为“胆管肿瘤”、“肝门部

胆管癌”、“血管切除重建”、“门静脉切除”和“肝动脉切除”，检索方式为主题词结合自由词，并对部分文献的参考文献进行手工搜索，检索时间限定为 2010 年 1 月 1 日至 2021 年 3 月 1 日。

1.2 文献纳入与排除标准

1.2.1 纳入标准 (1) 研究类型为经手术联合肝动脉或门静脉切除重建治疗的肝门部胆管癌的临床对照研究，语种限定为中英文文献。(2) 研究对象为术后病理证实的肝门部胆管癌患者。(3) 干预措施为术中行门静脉或肝动脉切除或联合切除重建。(4) 结局指标至少包含以下一项：1、3 和 5 年生存率，术后并发症（胆漏、肝功能衰竭和血管相关并发症）发生率，术后死亡率，R0 切除率，复发率以及术中失血量。

1.2.2 排除标准 (1) 非肝门部原发的胆管癌患者。(2) 无对照组或对照不符合要求。(3) 未行根治性切除。(4) 数据报告不完整或关键数据无法获取。(5) 个案报道或动物实验。

1.3 数据提取及文献质量评价

由 2 名评价者独立进行资料提取并交叉核对，如有分歧则通过双方讨论或征求第 3 名评论者的意见。数据不全时，尽可能通过与通信作者联系获取。提取如下内容：作者、发表年份、国家、研究类型、实验组与对照组样本量，结局指标以及研究偏倚风险评估特征等。纳入文献质量采用纽卡斯堡-渥太华量表 (Newcastle-Ottawa Scale, NOS)^[6] 进行评定，评分 ≥ 5 分者为高质量文献。

1.4 统计学分析

采用 Review Manager 5.3 软件对结局指标进行分析。二分类变量采用比值比 (odds ratio, OR) 为分析统计量，计量资料采用均数差 (mean difference, MD) 为效应分析统计量，各统计量均采用 95%CI 表示，以 $P < 0.05$ 为差异具有统计学意义。检验各组研究的异质性时，当 $I^2 \leq 50\%$ 、 $P > 0.1$ 时采用固定效应模型分析；当 $I^2 > 50\%$ 、 $P < 0.1$ 时表明研究异质性较大，采用随机效应模型分析，并进行亚组或敏感性分析。以森林图形式呈现分析结果。以漏斗图检验发表偏倚。

2 结果

2.1 文献检索结果

通过检索数据库最终获得 1 130 篇文献，排除重复文献 234 篇，进一步阅读标题及摘要，剔除不符合纳入标准的文献后剩余 28 篇，9 篇无法获

得全文无法提取数据，检索参考文献有 2 篇符合要求，最终纳入 21 篇文献^[7-27]，均为回顾性研究。总样本量为 4 124 例，其中血管切除重建组 1 283 例，对照组 2 841 例。筛选文献过程如图 1。

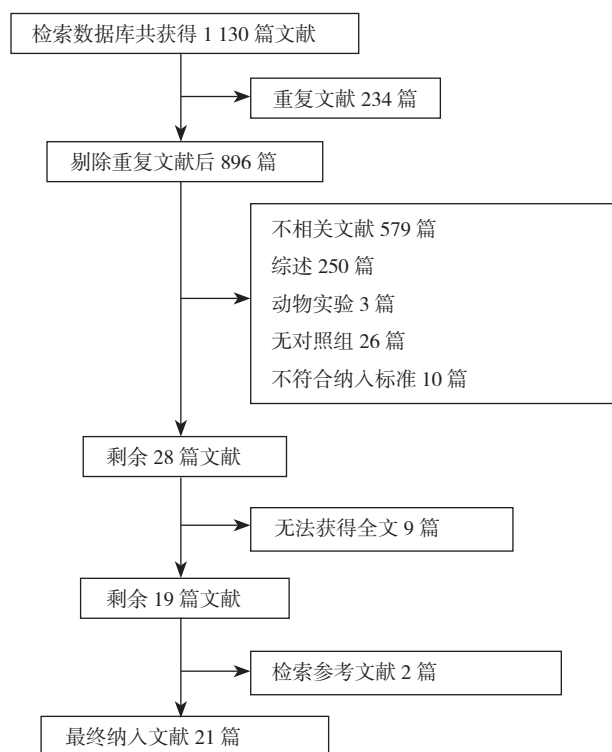


图 1 文献筛选流程图

Fig. 1 Flow chart of literature screening

2.2 纳入文献基本特征及质量评价

纳入的 21 篇文献中，有 1 篇中文文献，其余均为英文文献。纳入文献评分均 > 5 分 (表 1)。

2.3 Meta 分析结果

2.3.1 术后死亡率

有 16 项研究^[7-8, 10-11, 13-20, 22-23, 26-27]报道了术后总体死亡率，共有 2 943 例患者，结果显示， $I^2=19\%$ ， $P=0.24$ ，采用固定效应模型；血管切除重建组与未切除重建组术后总体死亡率比较，差异无统计学意义 ($OR=1.37$ ，95%CI: 0.97~1.93， $P=0.07$ ；图 2)。亚组分析显示，门静脉切除重建组与未切除组比较，差异无统计学意义 ($OR=1.44$ ，95%CI: 0.90~2.31， $P=0.13$)，而肝动脉切除重建组与未切除组比较，差异具有统计学意义 ($OR=1.89$ ，95%CI: 1.04~3.42， $P=0.04$ ；图 3)。

2.3.2 术中失血量

有 5 项研究^[12, 15, 17-18, 27]报道了术中失血量，共 695 例患者。结果显示， $I^2=87\%$ ， $P < 0.01$ ，采用随机效应模型；血管切除重建组与未切除组术中失血量比较，差异无统计学意义 ($MD=150.92$ ，95%CI: -9.19~311.04， $P=0.06$ ；图 4)。

表 1 纳入文献特征及 NOS 评分

Table 1 Features of the included literatures and NOS score

作者	年份	国家	研究类型	样本量 (例)				NOS 评分
				PVR 组	HAR 组	PVR+HAR 组	未切除组	
She 等 ^[7]	2020	中国	回顾性	17	5	—	68	6
Mizuno 等 ^[8]	2020	日本	回顾性	157	46	100	484	8
Sugiura 等 ^[9]	2019	日本	回顾性	—	12	—	24	7
Higuchi 等 ^[10]	2019	日本	回顾性	56	6	13	174	8
Schimizzi 等 ^[11]	2018	美国	回顾性	19	10	2	169	6
戴海栗等 ^[12]	2018	中国	回顾性	47	24	—	174	7
Yu 等 ^[13]	2017	中国	回顾性	10	6	3	67	7
Nuzzo 等 ^[26]	2012	意大利	回顾性	35	5	2	334	8
Nagino 等 ^[24]	2010	日本	回顾性	92	12	50	211	7
Tamoto 等 ^[22]	2012	日本	回顾性	36	—	—	13	6
Dumitrașcu 等 ^[14]	2017	罗马尼亚	回顾性	21	—	—	102	6
Yu 等 ^[21]	2014	中国	回顾性	17	47	—	174	5
Peng 等 ^[15]	2016	中国	回顾性	—	26	—	35	8
Noji 等 ^[16]	2016	日本	回顾性	—	—	28	181	7
Matsuyama 等 ^[17]	2016	日本	回顾性	54	44	—	74	7
Wang 等 ^[18]	2015	中国	回顾性	16	6	18	114	7
Noji 等 ^[19]	2015	日本	回顾性	—	—	21	18	7
Hoffmann 等 ^[20]	2015	德国	回顾性	21	—	—	39	5
de Jong 等 ^[23]	2012	美国	回顾性	51	—	—	173	7
Igami 等 ^[25]	2010	日本	回顾性	69	53	—	176	6
张潇等 ^[27]	2021	中国	回顾性	—	—	26	37	7

注 NOS : 纽卡斯堡 - 渥太华量表 (Newcastle-Ottawa Scale) ; PVR : 门静脉切除重建 (portal vein resection) ; HAR : 肝动脉切除重建 (hepatic artery resection)

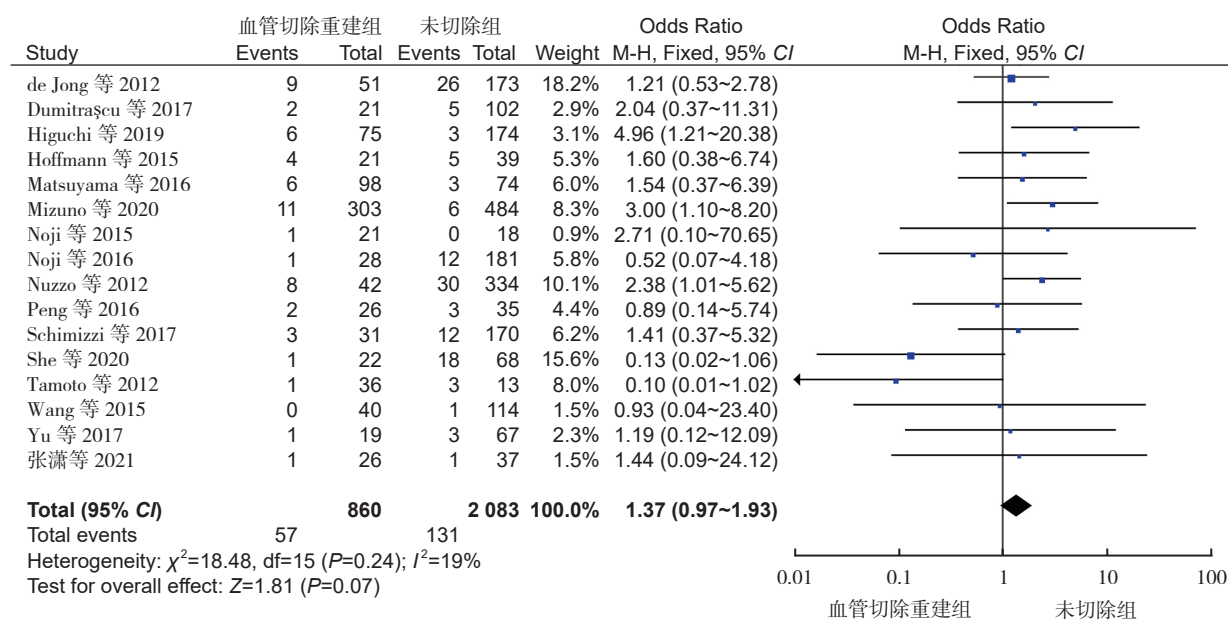


图 2 血管切除重建组和未切除组术后总体死亡率比较

Fig. 2 Comparison of overall postoperative mortality between the vascular resection and reconstruction group and the unresected group

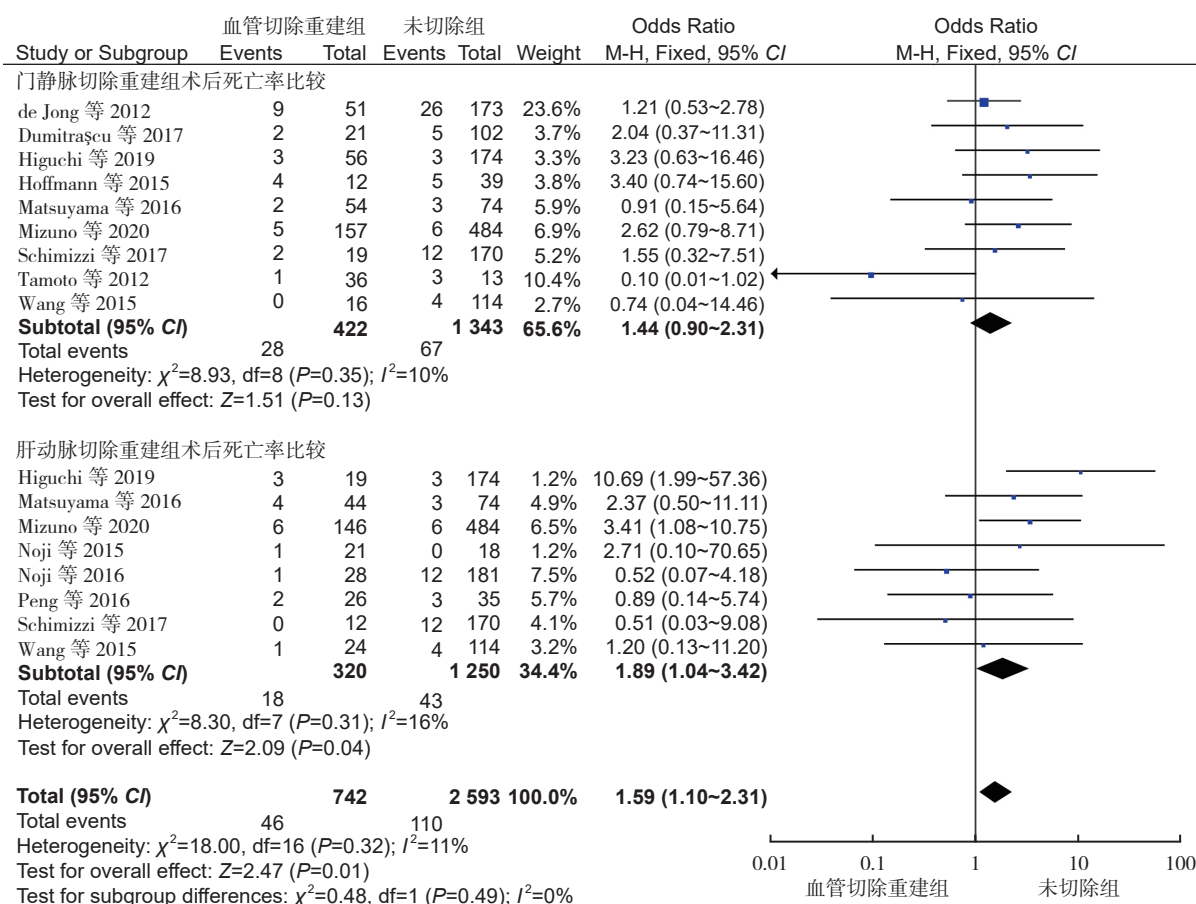


图 3 门静脉切除重建组和肝动脉切除重建组与未切除组术后死亡率亚组比较

Fig. 3 Subgroup comparison of postoperative mortality between the portal vein resection and hepatic artery resection and reconstruction groups and the unresected group

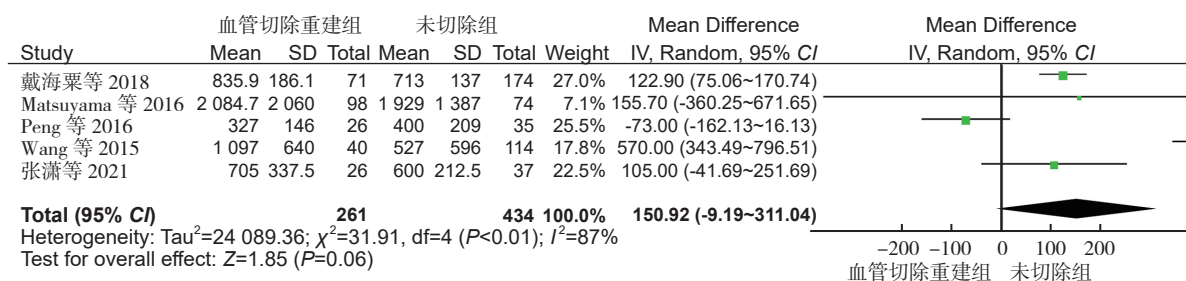


图 4 血管切除重建组与未切除组术中失血量比较

Fig. 4 Comparison of intraoperative blood loss between the vascular resection and reconstruction group and the unresected group

2.3.3 术后并发症 有 17 项研究^[7-22, 27]报道了术后并发症, 共有 2 862 例患者。结果显示, $I^2=33\%$, $P=0.09$, 采用固定效应模型; 血管切除重建组与未切除组术后总体并发症发生率比较, 差异无统计学意义 ($OR=1.16$, $95\%CI: 0.98\sim1.37$, $P=0.08$; 图 5)。在亚组分析方面, 门静脉切除重建组与肝动脉切除重建组和未切除组比较, 差异均无统计学意义 ($OR=0.80$, $95\%CI: 0.49\sim1.32$, $P=0.39$; $OR=1.15$, $95\%CI: 0.91\sim1.45$, $P=0.25$; 图 6)。

胆漏和血管相关并发症亚组与未切除组比较, 差异均无统计学意义 ($OR=1.89$, $95\%CI: 0.93\sim3.58$, $P=0.08$; $OR=0.91$, $95\%CI: 0.68\sim1.22$, $P=0.53$), 而在肝功能衰竭方面, 差异具有统计学意义 ($OR=1.91$, $95\%CI: 1.09\sim3.36$, $P=0.02$; 表 2)。

2.3.4 R0 切除率 有 13 项研究^[7-11, 14-17, 20-21, 23, 27]报道了 R0 切除率, 共有 2 513 例患者, 结果显示, $I^2=45\%$, $P=0.04$, 采用固定效应模型, 血管切除重建组与未切除组 R0 切除率比较, 差异具有统计学

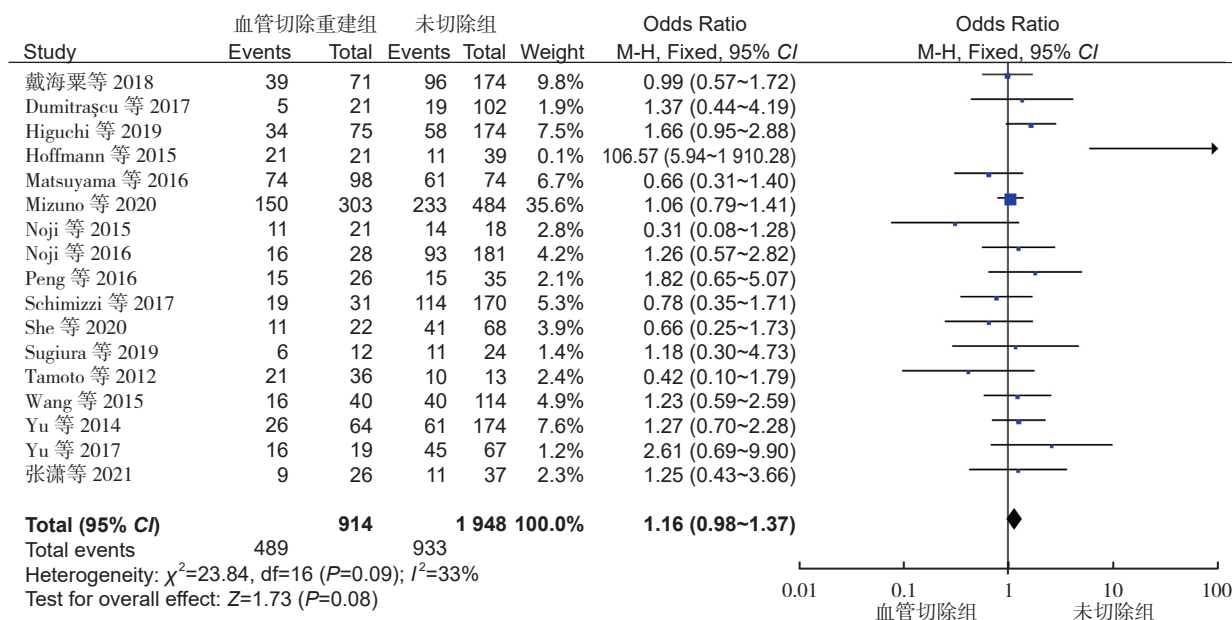


图5 血管切除重建组与未切除组术后总体并发症比较

Fig. 5 Comparison of overall postoperative complications between the vascular resection and reconstruction group and the unresected group

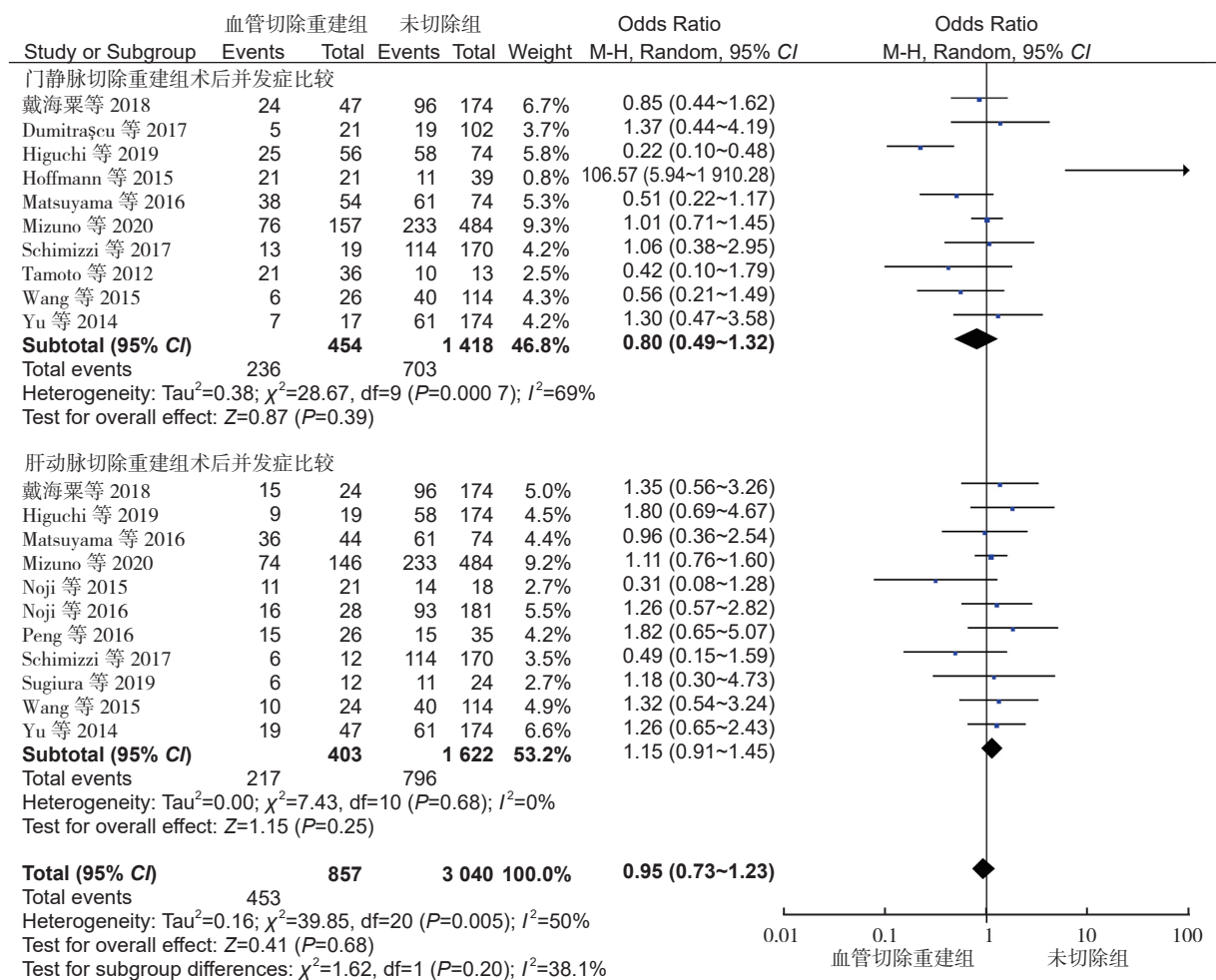


图6 门静脉切除重建组和肝动脉切除重建组与未切除组术后并发症亚组比较

Fig. 6 Subgroup comparison of postoperative complications between the portal vein resection and hepatic artery resection and reconstruction groups and the unresected group

差异 ($OR=0.63$, $95\%CI:0.52\sim0.76$, $P<0.01$;图 7)。

2.3.5 术后复发率 有 6 项研究^[7, 9, 11, 17, 20, 22]报道了术后复发率,共 608 例患者;结果显示, $I^2=70\%$, $P=0.005$,采用随机效应模型,血管切除组与未切除组在复发率方面比较,差异无统计学意义 ($OR=0.78$, $95\%CI:0.37\sim1.64$, $P=0.52$;图 8)。

2.3.6 术后 1、3 和 5 年生存率 有 11 项研究^[8-9, 12, 16-19, 22, 24-25, 27]报道了 5 年生存率,共 2 323 例患者;结果显示, $I^2=0\%$, $P=0.54$,采用固定效应模型,血管切除重建组与未切除组 5 年生存率

比较,差异具有统计学意义 ($OR=0.54$, $95\%CI:0.43\sim0.68$, $P<0.01$;图 9)。5 年生存率亚组分析显示,门静脉切除重建组及肝动脉切除重建组与未切除组比较,差异均具有统计学意义 ($OR=0.51$, $95\%CI:0.36\sim0.73$, $P=0.000\ 2$; $OR=0.55$, $95\%CI:0.39\sim0.76$, $P=0.000\ 4$;图 10)。有 10 项研究^[8-9, 11-12, 16, 19, 22, 24-25, 27]报道了 3 年生存率,共 2 188 例患者;结果显示, $I^2=22\%$, $P=0.24$,采用固定效应模型,血管切除重建组与未切除组 3 年生存率比较,差异具有统计学意义 ($OR=0.62$,

表 2 血管切除重建组与未切除组不同并发症亚组比较

Table 2 Subgroup comparison of complications between the vascular resection and reconstruction groups and the unresected group

并发症	血管切除重建组		未切除组		OR	95%CI	P 值
	并发症例数	总例数	并发症例数	总例数			
肝衰	194	734	236	1 465	1.91	1.09~3.36	0.02
胆漏	137	696	283	1 327	0.91	0.68~1.22	0.53
血管相关并发症*	55	536	56	1 102	1.89	0.93~3.58	0.08

注 * 包括血栓、出血、狭窄和血管瘤等

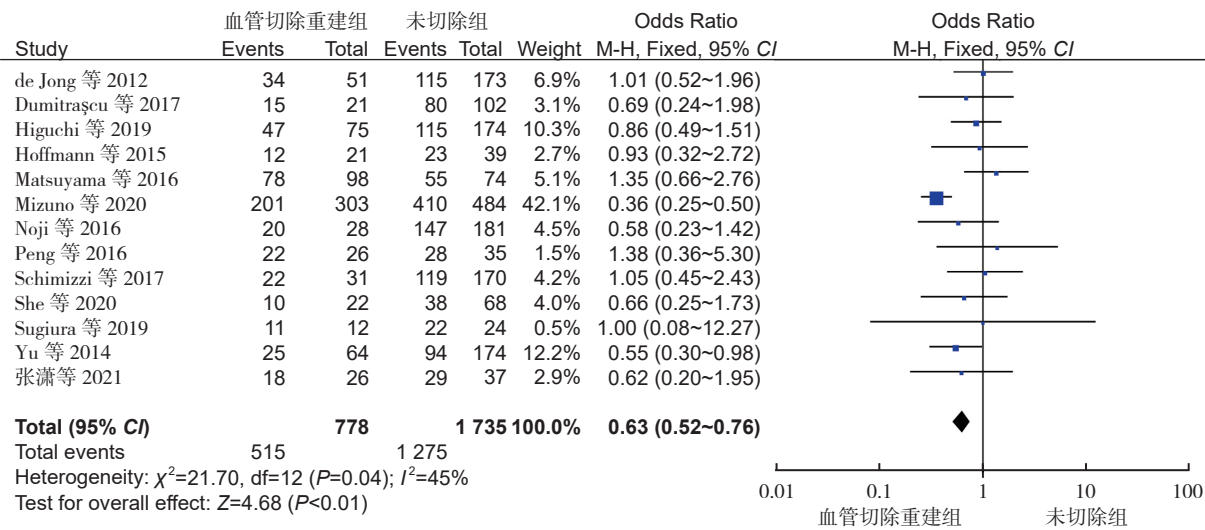


图 7 血管切除重建组与未切除组 R0 切除率比较

Fig. 7 Comparison of R0 excision rates between the vascular resection and reconstruction group and the unresected group

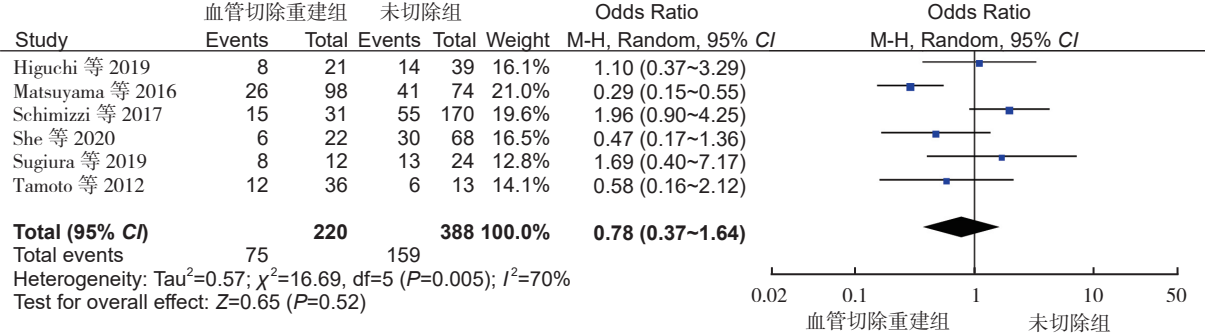


图 8 血管切除重建组与未切除组术后复发率比较

Fig. 8 Comparison of postoperative recurrence rates between the vascular resection and reconstruction group and the unresected group

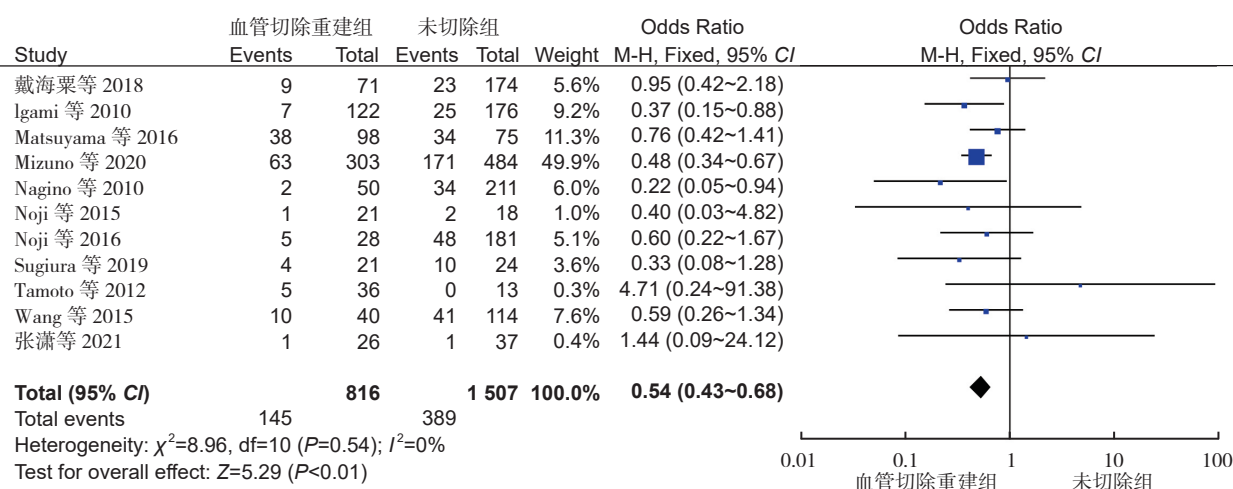


图9 血管切除重建组与未切除组 5 年生存率比较

Fig. 9 Comparison of 5-year survival rates between the vascular resection and reconstruction group and the unresected group

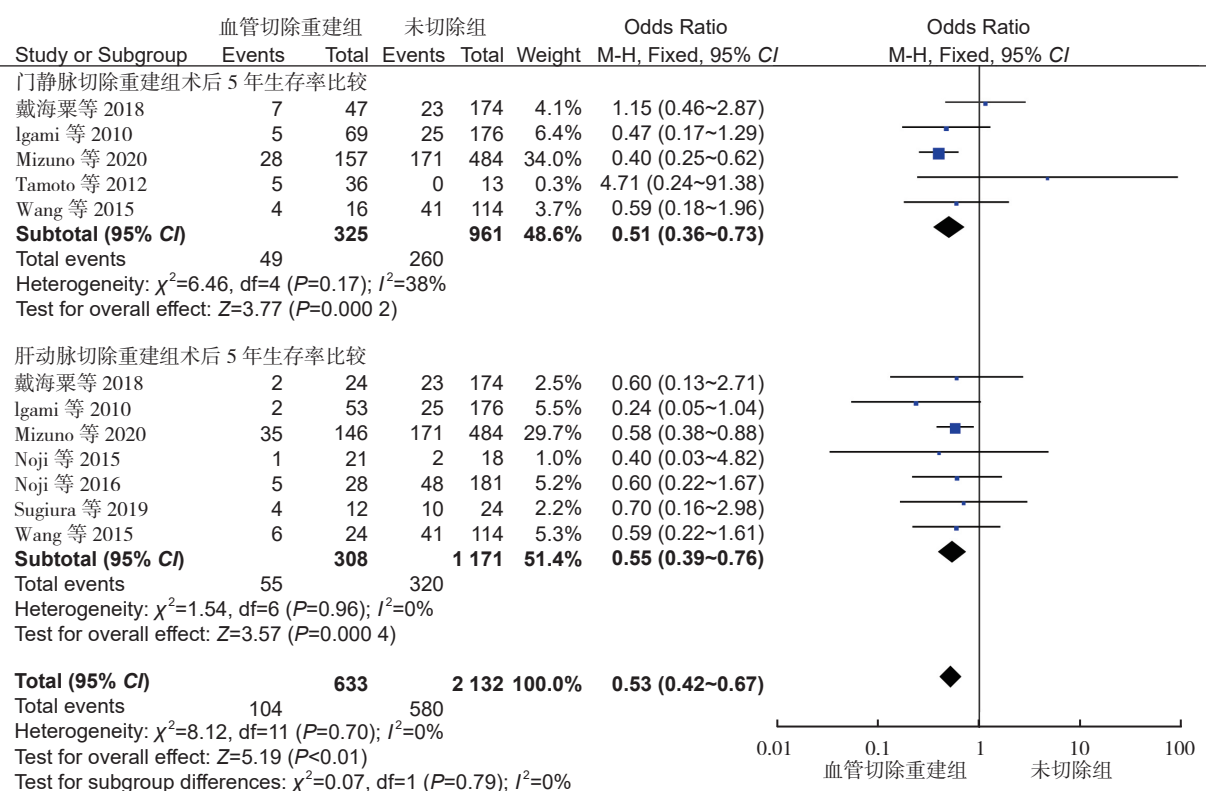


图10 门静脉切除重建组和肝动脉切除重建组与未切除组 5 年生存率亚组比较

Fig. 10 Subgroup comparison of 5-year survival rates in the portal vein resection and hepatic artery resection and reconstruction groups and the unresected group

95%CI: 0.50~0.75, $P<0.01$; 图 11)。有 9 项研究^[9, 11-12, 16, 19, 22, 24-25, 27]报道了 1 年生存率, 共 1 401 例患者; 结果显示, $I^2=47\%$, $P=0.07$, 采用固定效应模型, 血管切除重建组与未切除组 1 年生存率比较, 差异具有统计学意义 ($OR=0.68$, 95%CI: 0.51~0.90, $P=0.006$; 图 12)。

2.4 发表偏倚

采用 Revman 5.3 软件绘制漏斗图来评价研究

间的发表偏倚。可见漏斗图对称性较好, 存在发表偏倚可能性很小 (图 13)。

3 讨论

肝门部胆管癌因解剖位置的特殊性, 侵犯肝门血管非常常见, III~IV 型肝门部胆管癌门静脉侵犯率可高达 65.5%^[28], 而门脉血管的侵犯与糟糕的预后有密切关系^[29]。由于胆管癌对于放化疗的

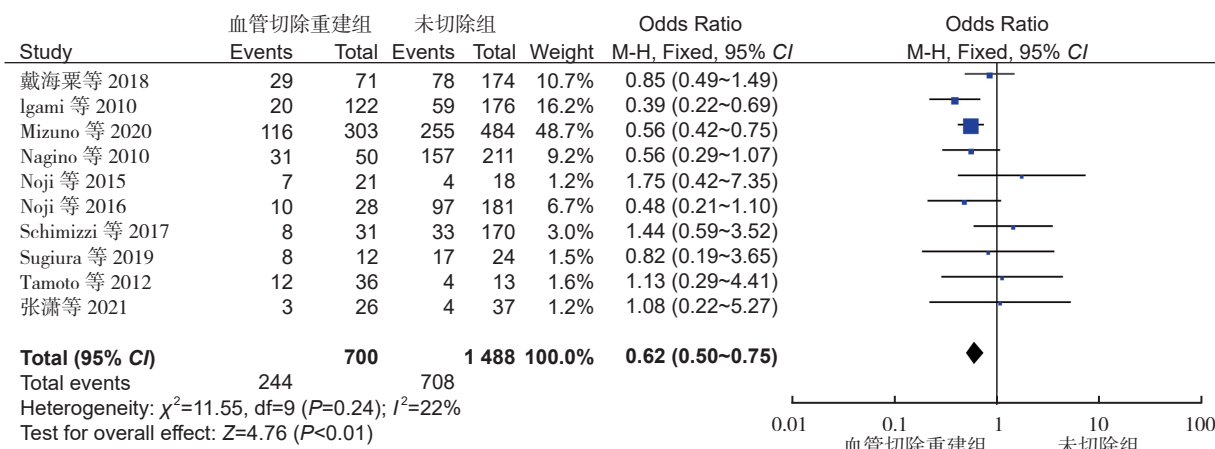


图 11 血管切除重建组与未切除组 3 年生存率比较

Fig. 11 Comparison of 3-year survival rates between the vascular resection and reconstruction group and the unresected group

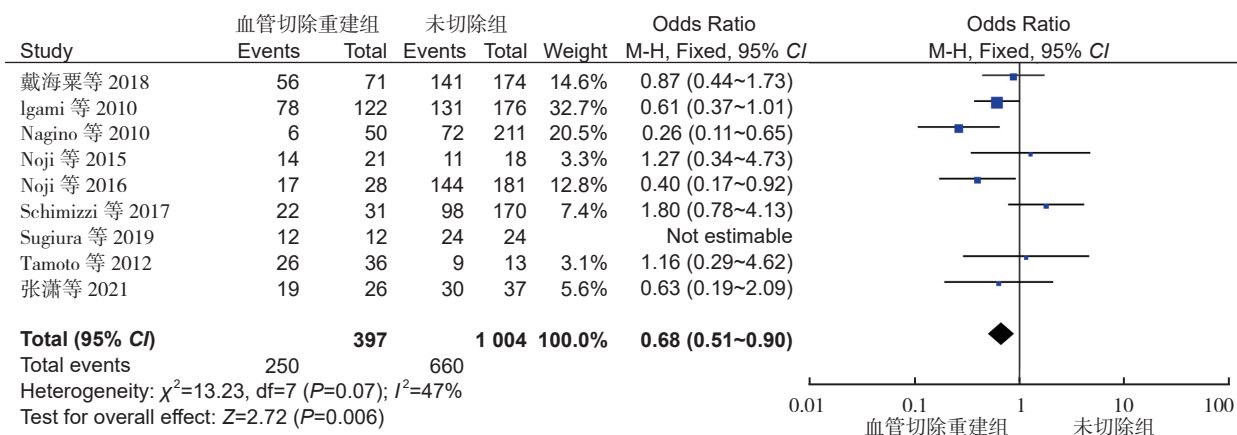


图 12 血管切除重建组与未切除组 1 年生存率比较

Fig. 12 Comparison of 1-year survival rates between the vascular resection and reconstruction group and the unresected group

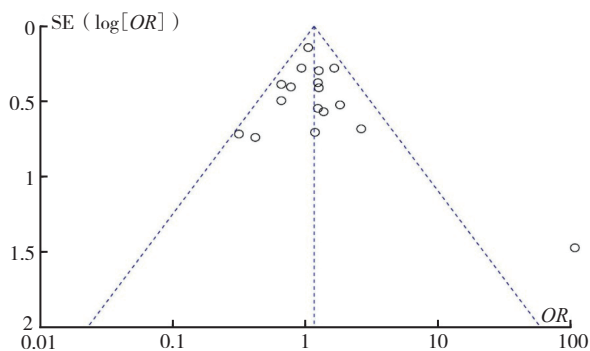


图 13 发表偏倚漏斗图

Fig. 13 Funnel plot of publication bias

不敏感性, 免疫和靶向治疗也还在探索过程中, 根治性切除仍是治疗胆管癌相对最有效的方法。过去认为肝门部胆管癌有血管的侵犯是手术的相对禁忌证^[30], 因为手术风险大于患者获益; 但是随着显微外科技术的进步和肝移植经验的积累以及围手术期管理经验的丰富, 门静脉和肝动脉的切除重建有可能使患者获得根治性切除, 此术式逐

渐变得可接受^[31]。

随着近年来血管吻合技术的成熟、人造血管和自体血管移植技术的进步以及围手术期管理经验的积累, 本研究选择纳入 2010 年以后发表的文献进行分析。既往研究认为行血管切除重建的肝门部胆管癌患者死亡率高^[32], Abbas 等^[33]的荟萃分析也得到相同的结果 ($P=0.008$)。然而本研究的结论相反: 血管切除重建组死亡率 (6.6%) 略高于未切除组 (6.2%), 但差异无统计学意义 ($P=0.07$); 亚组分析表明, 门静脉切除重建组与未切除组术后死亡率比较, 差异无统计学意义 ($P=0.13$), 而肝动脉切除重建组与未切除组比较, 差异有统计学意义 ($P=0.04$)。从纳入的多篇文献^[11-12, 15, 18]分析来看, 无论是门静脉切除重建组还是肝动脉切除重建组, 死亡率高与肿瘤的侵袭性更强、恶性程度更高以及为分期更晚的 III 或 IV 型肿瘤有关。门静脉切除的过程中会阻断肝血流, 肝动脉的切除会减少保留

侧肝脏的血供,并且肝动脉浸润严重的患者,切除重建困难,肝脏缺血时间延长,血栓发生率较高,重建成功后再通率较低,大范围切除后对残肝造成严重的缺血性损伤,这些因素都易诱发致死性肝功能衰竭,增加了术后死亡率^[21, 32, 34]。其次,本研究也得出血管切除重建组术中失血量确实大于未切除组,虽然差异无统计学意义($P=0.06$)。Nuzzo等^[26]也指出术中输血是术后死亡的独立预测因子。

在术后总体并发症方面,血管重建组的并发症发生率(53.5%)高于未切除组(47.9%),但差异无统计学意义($P=0.08$);而Abbas等^[33]和Yu等^[21]的荟萃分析显示,血管切除重建组并发症高于未切除组,且差异均具有统计学意义(均 $P<0.05$)。亚组分析结果表明,门静脉切除与肝动脉切除组并发症都稍高于未切除组,但差异无统计学意义($P=0.39$, $P=0.25$)。血管切除重建组和未切除组在常见并发症如胆漏和血管相关并发症发生率方面比较,差异均无统计学意义(均 $P>0.05$)。而血管切除重建组肝衰发生率大于未切除组,差异具有统计学意义($P=0.02$)。笔者认为可能是肝动脉切除增加肝功能衰竭的发生率,而Chen等^[35]的荟萃分析仅对门静脉切除的患者进行分析发现,肝功能衰竭的发生率并没有增加($P=0.5$)。同时肝动脉切除或肝动脉与门静脉联合切除重建增加了血管重建技术难度,术中失血过多,血管阻断时间过长,加之肝门部胆管癌患者大多有梗阻性黄疸,肝功能受损降低了肝脏缺血灌注耐受程度,肝脏发生不可逆的缺血性损伤,相继诱发了肝功能衰竭和其他并发症。本研究显示,肝门部胆管癌患者行血管切除重建术是安全可行的,其并发症在可接受范围内,但是对肝动脉的切除重建应更加谨慎。

因为肝门部胆管癌易侵犯血管,理论上联合血管切除可能会提高R0切除率,但是本研究的结果显示,血管切除重建组R0切除率低于未切除组($P<0.01$),这与Chen等^[35]的荟萃分析结果一致。Abbas等^[33]的研究则显示,血管切除重建与未切除的R0切除率比较,差异无统计学意义($P=0.1$)。Nagino等^[36]的研究早已指出,R0切除可以改善肝门部胆管癌患者长期生存率,但是R0切除率的提高仅仅切除受侵犯的血管可能是不够的,尾状叶在肝门部胆管癌患者中更容易受到侵犯,连同尾状叶一同切除甚至扩大的左或右半肝切除才有可能达到R0切除。Tamoto等^[37]使用“no-touch”技术对肝门部胆管癌患者行门静脉切除改善了患

者的预后生存时间,这可能归功于减少了肿瘤细胞的脱落和微栓塞。肝门部胆管癌患者有侵犯血管就提示了肿瘤的侵袭性强,术中肉眼难以察觉的周围组织侵犯,所以要提高R0切除率仅仅切除受侵犯的血管是不够的,可能还需要扩大切除范围、提高手术切除技术减少术中肿瘤细胞的扩散。

在复发率方面,本研究结果显示,血管切除重建组复发率低于未切除组,但差异无统计学意义($P=0.52$)。复发可能与肝门周围的微小残留灶,肿瘤细胞的微扩散以及周围神经浸润有关^[9, 38]。有研究表明,积极的R0切除可以降低复发率^[39],但Hoffmann等^[20]观点则认为切缘状况与复发率无相关性。本研究纳入的病例中一部分患者接受了术后放化疗,所以无法评价R0切除与复发的关系;但考虑到血管切除重建组的肿瘤恶性程度更高,侵袭性更强,与未切除组复发率比较并无差异,说明血管切除重建对于肝门部胆管癌患者预后来说是有积极意义的。

如何提高长期生存率改善预后一直是肝门部胆管癌治疗的最终目的。本研究结果表明,血管切除重建组1、3和5年生存率以及门静脉和肝动脉切除亚组分析的5年生存率都低于未切除组,且差异均具有统计学意义(均 $P<0.05$)。有研究指出,淋巴结转移是影响肝门部胆管癌术后生存率的独立因素^[40-41],并且纳入的研究也表明,与血管未切除组比较,血管切除重建组患者淋巴结转移比例更高,尤其是肝动脉切除组^[12, 18, 26, 42],这意味着血管切除重建组的肿瘤恶性程度更高,侵袭性更强,尽管术中行淋巴结清扫,但是在术前可能已经有血液系统的转移^[21]。这也就不难解释为何血管切除重建组生存率低于对照组。虽然血管切除重建组的总体生存率低于对照组,但高于姑息治疗组^[8, 25, 27];所以和姑息性治疗比较,血管切除的获益是大于风险的。

综上所述,根治性手术切除目前是可以改善肝门部胆管癌患者预后相对最有效的治疗方法,血管切除重建对肝门部胆管癌患者总体上来讲是安全的,虽然术后死亡率以及并发症等风险有所增加,但在可接受范围内。有血管侵犯的肝门部胆管癌患者在充分评估可切除能为患者带来生存获益的情况下,应积极考虑行血管切除重建术。本研究纳入的均为回顾性研究,偏倚风险无法避免,所以要准确评估血管切除重建的安全性和有效性还需要大量的、多中心前瞻性的随机对照试验。

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