

doi: 10.13241/j.cnki.pmb.2021.01.013

胸腹腔镜联合 Ivor Lewis 食管癌根治术对食管癌患者肺功能、红细胞免疫及应激反应的影响*

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摘要 目的:探讨胸腹腔镜联合 Ivor Lewis 食管癌根治术对食管癌患者红细胞免疫、肺功能及应激反应的影响。**方法:**选取 2016 年 5 月~2018 年 6 月期间我院收治的食管癌患者 150 例。根据随机数字表法将患者分为 A 组(n=75)和 B 组(n=75),A 组予以开胸 Ivor Lewis 食管癌根治术,B 组予以胸腹腔镜联合 Ivor Lewis 食管癌根治术,比较两组围术期指标、肺功能、红细胞免疫、应激反应及并发症。**结果:**B 组手术时间、住院时间短于 A 组,术中出血量少于 A 组($P<0.05$);两组清扫淋巴结数目比较无差异($P>0.05$)。两组术后 1 个月第 1 秒末用力呼气容积(FEV₁)、用力呼吸肺活量(FVC)、FEV₁/FVC 均降低,但 B 组高于 A 组($P<0.05$)。两组术后 3d 白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、C 反应蛋白(CRP)均升高,但 B 组低于 A 组($P<0.05$)。两组术后 3d 红细胞免疫复合物花环率(RBC-ICR)升高,但 B 组低于 A 组($P<0.05$);红细胞 C3b 受体花环率(RBC-C3bRR)、肿瘤红细胞花环率(TRR)降低,但 B 组高于 A 组($P<0.05$)。两组患者术后并发症发生率比较差异无统计学意义($P>0.05$)。**结论:**胸腹腔镜联合 Ivor Lewis 食管癌根治术治疗食管癌患者,可有效改善围术期各项指标,减轻对机体肺功能、红细胞免疫及应激反应的影响,且不增加并发症发生率。

关键词:胸腹腔镜;Ivor Lewis 食管癌根治术;食管癌;肺功能;红细胞免疫;应激反应

中图分类号:R735.1 **文献标识码:**A **文章编号:**1673-6273(2021)01-66-04

The Effect of Thoracoscope Combined with Ivor Lewis Esophagectomy on Pulmonary Function, RBC Immunity and Stress Response in Patients with Esophageal Cancer*

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ABSTRACT Objective: To investigate the effect of thoracoscopic combined with Ivor Lewis esophagectomy on red cell immunity, lung function and stress response in patients with esophageal cancer. **Methods:** 150 patients with esophageal cancer were selected from May 2016 to June 2018. The patients were divided into group A (n=75) and group B (n=75) according to the method of random number table. Group A was treated with radical resection of Ivor Lewis esophageal cancer and group B with laparoscopic resection of Ivor Lewis esophageal cancer. The perioperative indexes, lung function, red cell immunity, stress response and complications were compared between the two groups. **Results:** The operation time and hospitalization time of group B were shorter than that of group A, and the amount of bleeding during operation was less than that of group A ($P<0.05$). There was no difference in the number of lymph nodes cleaned between the two groups ($P>0.05$). The forced expiratory volume (FEV₁), forced respiratory vital capacity (FVC) and FEV₁/FVC decreased at 1 month after operation, but group B was higher than group A ($P<0.05$). The levels of interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), C-reactive protein (CRP) were all increased in the two groups at 3d after operation, but the group B was lower than that in group A ($P<0.05$). The rosette rate of RBC immune complex (RBC-ICR) in group B was lower than that in group A at 3d after operation ($P<0.05$), while the erythrocyte C3b receptor rosette rate (RBC-C3bRR), tumor rosette rate (TRR) decreased, and the group B were lower than those in group A ($P<0.05$). There was no significant difference in the incidence of postoperative complications between the two groups ($P>0.05$). **Conclusion:** Thoracoscopy combined with Ivor Lewis esophagectomy for esophageal cancer can effectively improve the perioperative indicators, reduce the impact on lung function, red cell immunity and stress response, and do not increase the incidence of complications.

Key words: Thoracoscope; Ivor Lewis esophagectomy; Esophageal cancer; Lung function; RBC immunity; Stress response

Chinese Library Classification(CLC): R735.1 **Document code:** A

Article ID: 1673-6273(2021)01-66-04

* 基金项目:北京市科技计划项目(Z111107076113068)

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(收稿日期:2020-03-31 接受日期:2020-04-27)

前言

食管癌是临床常见的消化道恶性肿瘤,多发于40岁以上的男性,早期临床症状不典型,疾病中晚期症状会表现为吞咽困难、背痛、腹腔积液以及胸痛等^[1,2]。近年来,随着人们生活方式的改变,饮食结构的不断变化,加之人口老龄化进程的加快,我国食管癌的发病率呈不断升高趋势,且逐渐趋于年轻化^[3,4]。目前该病的治疗方法以根治手术为主,传统的开胸 Ivor Lewis 食管癌根治术是治疗该病的常用术式,但此类术式术后创伤大,并发症多,影响患者预后^[5,6]。近年来,随着手术技术的进步及腔镜器械的发展,胸腹腔镜联合 Ivor Lewis 食管癌根治术以其创伤小、失血量少、肿瘤切除便捷等优点逐渐受到临床医师的重视^[7,8]。但有关其具体疗效尚存在一定的争议。鉴于此,本研究通过设置对照试验,探讨胸腹腔镜联合 Ivor Lewis 食管癌根治术对食管癌患者红细胞免疫、肺功能及应激反应的影响,以期治疗该病手术方式的选择提供数据支持。

1 资料与方法

1.1 一般资料

选取2016年5月~2018年6月期间我院收治的食管癌患者150例。纳入标准:(1)均经病理活检、术前CT以及术后病理学检查确诊;(2)患者及其家属知情本研究并签署同意书;(3)均符合手术指征者,择期行食管癌根治术者;(4)未进行过胸部手术者。排除标准:(1)代谢紊乱、药物过敏者;(2)合并严重心肺等脏器功能障碍者;(3)合并精神疾患,无法正常沟通交流者;(4)合并其他恶性肿瘤者;(5)妊娠或哺乳期妇女;(6)合并免疫系统疾病者;(7)影像学显示肿瘤浸润或者远处转移者。根据随机数字表法将患者分为A组($n=75$,开胸 Ivor Lewis 食管癌根治术)和B组($n=75$,胸腹腔镜联合 Ivor Lewis 食管癌根治术),其中A组男41例,女34例,年龄38~65岁,平均(50.26 ± 4.82)岁;肿瘤部位:上段29例,中段31例,下段15例;临床分期:I期23例,II期26例,III期26例;病理类型:腺癌29例,鳞癌32例,其他14例。B组男39例,女36例,年龄40~68岁,平均(49.91 ± 5.36)岁;肿瘤部位:上段32例,中段30例,下段13例;临床分期:I期24例,II期25例,III期26例;病理类型:腺癌30例,鳞癌29例,其他16例。两组一般资料比较无差异($P>0.05$),具有可比性。本研究经医院伦理委员会批准。

1.2 方法

B组给予胸腹腔镜联合 Ivor Lewis 食管癌根治术,腹腔镜具体操作如下:患者取仰卧位,双肺通气。主操作孔:腹部脐下缘1.0 cm,2个副操作孔:左右锁骨中线肋下缘2.0 cm以及脐平处。气腹压力维持12~14 mmHg,置入Trocarr后,依次游离大弯侧胃网膜血管弓、胃短动静脉、幽门、贲门,保留胃网膜右血管弓。清扫淋巴结。采用线型吻合器沿胃大弯作管状胃,在右胸顶做食管与胃管机械吻合器吻合,关闭切口。胸腔镜具体操作如下:患者取左侧卧位,单肺通气。2个切口:第8肋间腋后线后2 cm处以及腋中线第8肋间。2辅助孔:肩胛骨尖端后方、第4肋间腋前线。依次置入胸腔镜及超声刀,离断并夹闭奇静脉,游离胸段食管,打开膈肌食管裂孔,接通胸腹腔,切除食管

标本并取出,将管状胃提至胸腔并用吻合器吻合。A组给予开胸 Ivor Lewis 食管癌根治术,患者取平卧位,取上腹部剑突至脐上作一切口,游离全胃后清扫淋巴结。随后患者呈左侧卧位,取右胸第5肋间后外侧作一切口,行淋巴结清扫。除开腹方式外,手术方法及手术范围同B组。

1.3 观察指标

(1)围术期指标:记录两组患者清扫淋巴结数目、手术时间、住院时间、术中出血量。(2)肺功能指标:于术前、术后1个月采用意大利COSMED公司生产QuarkPFT4自动肺功能检测仪对两组肺功能指标进行测定,包括第1秒末用力呼气容积(Forced expiratory volume at the end of the first second, FEV₁)和用力呼吸肺活量(Forced breathing vital capacity, FVC),并计算FEV₁/FVC。(3)红细胞免疫及应激反应指标:于术前、术后3d采集患者清晨空腹静脉血4ml,每次采集均分为两管,一管经肝素抗凝后冷藏,待测。镜检并测定红细胞C3b受体花环率(Rosette rate of C3b receptor in erythrocytes, RBC-C3bRR)、红细胞免疫复合物花环率(Rosette rate of RBC immune complex, RBC-ICR)、肿瘤红细胞花环率(Rosette rate of tumor erythrocytes, TRR)。另一管经离心半径8 cm,3500 r/min离心8 min,取上清液,置于-30℃冰箱中待测。选用上海基免生物科技有限公司生产的试剂盒,遵照试剂盒说明书,采用酶联免疫吸附试验检测患者白介素-6(Interleukin -6, IL-6)、肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)、C反应蛋白(C-reactive protein, CRP)。(4)并发症:记录两组术后并发症情况。

1.4 统计学方法

本研究所有数据均采用SPSS18.0统计学软件进行分析,计量资料以均值 $\pm$ 标准差($\bar{x} \pm s$)表示,行t检验;计数资料以比或率(%)表示,行 χ^2 检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组围术期指标比较

B组手术时间、住院时间短于A组,术中出血量少于A组($P<0.05$);两组清扫淋巴结数目比较无差异($P>0.05$);详见表1。

2.2 两组肺功能指标比较

两组患者术前FEV₁、FVC、FEV₁/FVC比较无差异($P>0.05$);两组术后1个月FEV₁、FVC、FEV₁/FVC均降低,但B组高于A组($P<0.05$);详见表2。

2.3 两组应激反应指标比较

两组患者术前IL-6、TNF- α 、CRP比较无差异($P>0.05$);两组术后3d的IL-6、TNF- α 、CRP均升高,但B组低于A组($P<0.05$);详见表3。

2.4 两组红细胞免疫指标比较

两组患者术前RBC-C3bRR、RBC-ICR、TRR比较无差异($P>0.05$);两组术后3dRBC-ICR升高,但B组低于A组($P<0.05$);RBC-C3bRR、TRR降低,但B组高于A组($P<0.05$);详见表4。

2.5 并发症发生率比较

B组出现肺部感染1例,急性呼吸窘迫症3例,肺栓塞1例,术后并发症发生率为6.67%(5/75);A组中出现肺部感染3

例,喉返神经损伤 1 例,胸腔积液 2 例,心功能不全 3 例,术后 较无差异($\chi^2=1.261, P=0.262$)。并发症发生率为 12.00%(9/75);两组患者术后并发症发生率比

表 1 两组围术期指标比较($\bar{x} \pm s$)

Table 1 Comparison of perioperative indexes between the two groups($\bar{x} \pm s$)

Groups	Operative time(min)	Number of lymph nodes cleaned(n)	Intraoperative hemorrhage (mL)	Length of stay(d)
Group A(n=75)	335.67±17.18	34.38±2.06	319.74±18.82	17.81±1.76
Group B(n=75)	296.89±18.23	33.96±2.72	234.68±16.79	12.45±1.52
t	13.407	1.066	29.208	19.961
P	0.000	0.288	0.000	0.000

表 2 两组肺功能指标比较($\bar{x} \pm s$)

Table 2 Comparison of lung function indexes between the two groups($\bar{x} \pm s$)

Groups	FEV ₁ (L)		FVC(L)		FEV ₁ /FVC	
	Before operation	1 month after operation	Before operation	1 month after operation	Before operation	1 month after operation
Group A(n=75)	2.67±0.73	1.78±0.56*	3.37±0.56	2.53±0.34*	0.79±0.11	0.70±0.08*
Group B(n=75)	2.73±0.64	2.19±0.58*	3.31±0.49	2.91±0.38*	0.82±0.08	0.75±0.07*
t	0.535	4.404	0.698	6.454	1.910	4.073
P	0.593	0.000	0.486	0.000	0.058	0.000

Note: compared with before operation, * $P<0.05$.

表 3 两组应激反应指标比较($\bar{x} \pm s$)

Table 3 Comparison of stress response indexes between the two groups($\bar{x} \pm s$)

Groups	IL-6(ng/mL)		TNF- α (ng/mL)		CRP(mg/L)	
	Before operation	3d after operation	Before operation	3d after operation	Before operation	3d after operation
Group A(n=75)	1.79±0.23	6.24±0.22*	1.08±0.13	5.74±0.19*	3.18±0.95	11.54±1.32*
Group B(n=75)	1.83±0.18	3.53±0.23*	1.12±0.15	3.68±0.23*	3.23±0.73	6.56±2.01*
t	1.186	53.698	1.745	59.861	0.361	17.935
P	0.237	0.000	0.083	0.000	0.718	0.000

Note: compared with before operation, * $P<0.05$.

表 4 两组红细胞免疫指标比较($\bar{x} \pm s, \%$)

Table 4 Comparison of RBC immune indexes between the two groups($\bar{x} \pm s, \%$)

Groups	RBC-C3bRR		RBC-ICR		TRR	
	Before operation	3d after operation	Before operation	3d after operation	Before operation	3d after operation
Group A(n=75)	23.36±2.18	13.52±2.42*	26.16±2.15	34.53±2.54*	27.02±3.18	16.46±2.26*
Group B(n=75)	23.19±3.87	17.83±2.31*	25.93±2.36	29.13±2.27*	26.94±3.73	21.83±2.71*
t	0.331	11.157	0.624	13.728	0.141	13.179
P	0.741	0.000	0.534	0.000	0.888	0.000

Note: compared with before operation, * $P<0.05$.

3 讨论

食管癌是发生于食管上皮组织的一种多发恶性肿瘤,在世界癌症相关病死率中排名第 6 位,严重威胁着人类的生命健康^[9,10]。目前临床中治疗食管癌的基本策略是手术、化疗和放疗相结合的综合治疗方案,以外科手术切除为主^[11,12]。Ivor Lewis 是经右胸、经腹二切口食管癌根治术,可充分暴露右胸,是介于

经三野根治术与左胸切口手术之间的一个较好选择^[13,14]。以往通常使用开胸 Ivor Lewis 食管癌根治术治疗,但此类术式创伤大、术后并发症相对较多、病死率相对较高^[15,16]。以往研究结果显示^[17],食管癌术后吻合口瘘发生率国内报道为 3%~5%,胸内吻合口瘘病死率高达 50%。近年来,胸腹腔镜联合 Ivor Lewis 食管癌根治术这一微创术式已逐渐在临床普及^[18,19]。但有关该术式能否降低红细胞免疫损害、改善患者术后肺功能和应激反

应的研究报道尚较少。

本次研究结果显示,相比于开胸 Ivor Lewis 食管癌根治术,胸腹腔镜联合 Ivor Lewis 食管癌根治术治疗者的大部分围术期指标情况均更有优势。这可能是因为胸腹腔镜下手术可将病灶局部视野放大,清晰暴露食管及周围组织结构,利于术者在术中精准完成各项操作,避免损伤喉返神经和胸导管等正常结构,可最大限度减轻损伤,促进患者术后恢复^[20-22]。而两组清扫淋巴结数目比较差异无统计学意义,可见这两种术式肿瘤学治疗效果相当,均能够达到足够的肿瘤切除及淋巴结清扫需求。本次研究结果还显示,两组患者均存在不同程度的肺功能下降,红细胞免疫反应降低及炎症应激状态,但胸腹腔镜联合 Ivor Lewis 食管癌根治术可有效减轻对机体肺功能、红细胞免疫及应激反应的影响。分析其原因,红细胞中含有多种免疫物质如 RBC-C3bRR、RBC-ICR、TRR 等,在机体的免疫调控中发挥重要作用,可通过直接黏附于肿瘤细胞而增强吞噬细胞的吞噬功能^[23,24]。由于手术创伤可对红细胞免疫产生抑制作用,而胸腹腔镜下操作可明显减少手术创伤,使其对机体红细胞免疫的抑制作用减弱,利于患者术后早期恢复。手术产生的应激反应是影响患者术后恢复及疾病转归的关键,IL-6、TNF- α 、CRP 是机体重要的炎症因子,其水平上升可间接反映机体损伤及应激程度^[25,26]。胸腹腔镜微创手术创伤小,诱发体内的炎症反应较轻,这可能是因为胸腹腔镜下视野清晰,可减少对各脏器的机械牵拉,进而减轻应激反应^[27,28]。此外胸腹腔镜联合 Ivor Lewis 食管癌根治术可减轻对机体肺功能损害的原因可能在于开胸手术术后疼痛会导致咳嗽反射抑制,加重术后肺泡塌陷等肺功能损伤,而胸腹腔镜下操作可保持胸腹腔的完整性,减小对呼吸肌群的损害,有效减轻肺功能损害^[29,30]。另两组术后并发症发生率比较差异无统计学意义,可见胸腹腔镜联合 Ivor Lewis 食管癌根治术安全性较好。

综上所述,胸腹腔镜联合 Ivor Lewis 食管癌根治术治疗食管癌患者,可有效改善围术期各项指标,减轻对机体肺功能、红细胞免疫及应激反应的影响,且不增加并发症发生率。

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