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腔镜下腺体切除术对早期乳腺癌患者血清免疫球蛋白及 TNF- α 、IL-10 水平变化的影响*

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摘要 目的:分析腔镜下腺体切除术对早期乳腺癌患者血清免疫球蛋白及 TNF- α 、IL-10 水平的影响,从而对其优势评估。**方法:**选择 2017 年 2 月 -2020 年 2 月于本院实施乳腺癌手术患者 100 例,根据其选择手术方式的不同分为 2 组:A 组(腔镜下腺体切除术,59 例)和 B 组(开放乳房皮下腺体切除术,41 例),分别统计患者手术时间、术后拔管时间以及住院时间;术后 1 个月,取患者外周血,离心取血清,采用免疫比浊法检测患者血清免疫功能相关指标 IgM 和 IgG 含量、采用人酶联免疫吸附实验(ELISA)试剂盒检测患者血清中炎症反应指标 TNF- α 和 IL-10 含量、统计术后两组患者出现术野皮下出血、皮下积液、乳头乳晕坏死等并发症的例数;术后一年,统计两组患者出现复发和淋巴结转移等现象的例数。**结果:**A 组患者手术时间显著长于 B 组,而其拔管时间和住院时间均显著短于 B 组($P < 0.05$)。A 组并发症发生率(5.00%)显著高于 B 组(25.71%)($P < 0.05$)。术前 1 d,两组患者血清免疫指标 IgM 和 IgG 水平和炎症反应指标 TNF- α 和 IL-10 水平相比差异无统计学意义($P > 0.05$),而术后 3 d~术后 1 m,A 组患者血清免疫指标 IgM 和 IgG 水平以及抗炎因子 IL-10 水平均显著高于 B 组,促炎因子 TNF- α 水平显著低于 B 组($P < 0.05$)。A 组患者术后 1 年内乳腺癌复发率(3.3%)与 B 组(10.0%)相比差异不具有统计学意义($P > 0.05$)。**结论:**腔镜下腺体切除术治疗早期乳腺癌具有拔管时间以及术后住院时间短、并发症发生率低等优势,其原因可能与该手术对患者血清免疫球蛋白 IgM 和 IgG 及炎症因子 TNF- α 、IL-10 水平影响程度较小、术后恢复较快有关。

关键词:腔镜手术;腺体切除术;早期乳腺癌;免疫球蛋白;炎症因子

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Effect of Endoscopic Gland Resection on Serum Immunoglobulin, TNF- α , IL-10 Levels in Patients with Early Breast Cancer*

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ABSTRACT Objective: To analyze the effect of endoscopic gland resection on serum immunoglobulin, TNF- α and IL-10 levels in patients with early breast cancer, so as to evaluate its advantages. **Methods:** 75 patients undergoing breast cancer surgery were selected and divided into 2 groups according to their choice of surgical methods: group A (laparoscopic surgery, 59 cases) and group B (open breast subcutaneous gland resection, 41 cases). The operation time, postoperative extubation time, and hospital stay were counted. One month after the operation, the peripheral blood of the patient was collected, and the serum was collected by centrifugation. The immuno-turbidimetric method was used to detect the serum immune function-related indicators of IgM and IgG. The human enzyme-linked immunosorbent assay (ELISA) kit was used to detect the serum levels of TNF- α and IL-10, and the number of postoperative complications such as subcutaneous hemorrhage, subcutaneous effusion, and nipple and areola necrosis in the two groups of patients was counted; one year after the operation, the number of cases of recurrence and lymph node metastasis in the two groups were counted. **Results:** The oper-

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ation time of patients in group A was significantly longer than that in group B, while their extubation time and hospital stay were significantly shorter than those in group B ($P<0.05$). The incidence of complications in group A (5.00%) was significantly higher than that in group B (25.71%)($P<0.05$). 1 day before surgery, there was no significant difference in serum immune index IgM and IgG levels and inflammation response index TNF- α and IL-10 levels between the two groups of patients($P>0.05$); From 3 days after operation to 1 m after operation, the serum immune index IgM and IgG levels and the anti-inflammatory factor IL-10 levels of group A patients were significantly higher than those of group B, and the level of pro-inflammatory factor TNF- α was significantly lower than that of group B ($P<0.05$). The breast cancer recurrence rate (3.3%) of group A patients within 1 year after operation was not statistically different from that of group B (10.0%) ($P>0.05$). **Conclusion:** Endoscopic gland resection for the treatment of early breast cancer has the advantages of extubation time, short postoperative hospital stay, and low complication rate. The reason may be related to the lesser effect of the operation on the patient's serum immunoglobulin IgM and IgG, inflammatory factors TNF- α and IL-10 levels, and faster postoperative recovery.

Key words: Laparoscopic surgery; Gland resection; Early breast cancer; Immunoglobulin; Inflammatory factor

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前言

乳腺癌是临床常见的多血管肿瘤，其发病人群以女性为主，与大多数肿瘤一样，该肿瘤的发生和进展为多因素共同的结果，但目前其发病机制尚未完全明确^[1-3]。近年来，随着我国经济发展以及国民生活节奏的加快，女性在工作与生活的双重压力下，其乳腺癌发病率逐年增长且呈年轻化趋势，已引起了医疗界的广泛关注^[4-5]。目前临幊上该肿瘤的治疗以手术治疗为主，但传统手术创伤大，对患者术后生活质量具有不良影响，因此近年来，个体化、精准化手术综合治疗对乳腺癌患者生存率的提升以及预后的改善具有重要意义，如：腔镜手术、保乳术等^[6-8]。本研究通过分析腔镜下腺体切除术对早期乳腺癌患者血清免疫球蛋白 IgM 和 IgG 及炎症因子 TNF- α 、IL-10 水平的影响，从而对其优势进行分析，以期对乳腺癌手术个体化和精准化发展提供理论基础。

1 资料与方法

表 1 一般资料

Table 1 General information

	Item	Group A(n=59)	Group B(n=41)
Average age(years)		48.19± 7.32	47.52± 8.11
BMI(kg/m ²)		22.66± 5.82	22.82± 4.96
Clinical Stage	Stage I	26	22
	Stage II	14	13
Lesion Size(cm)		2.61± 0.21	2.54± 0.25
Pathological Type	Invasive ductal carcinoma	27	25
	Ductal carcinoma in situ	13	10
Marital Status	Married	38	34
	Unmarried	2	1

1.2 方法

1.2.1 A 组 该组患者实施腔镜下乳房皮下腺体切除术，采用三孔法，所有患者实施插管全麻，平卧，并进行术前标记。以腺体下缘 2 m 与锁骨中线交汇处作为观察孔，置入直径 12 mm 的 Trocar；观察孔内侧约 10 cm 为操作孔，置入直径 5 mm 的 Trocar；

观察孔外侧约 10 cm 为操作孔兼标本取出孔，置入直径 12 mm 的 Trocar。溶脂并吸脂后，从操作孔注入 CO₂(压力 1064~1330 kPa)。腔镜下游离乳房后间隙并在接近皮瓣切断 Cooper 韧带，术中用爪钳将肿瘤浅层组织和乳头深方组织置入 Trocar 内，后将两者一同从操作孔取出，并将组织送检。止血并冲洗术野，取出腔

镜及 Trocar 并逐层缝合戳孔。

1.2.2 B 组 该组患者实施开放乳房皮下腺体切除术,麻醉剂手术体位等与 A 组相同,于乳实施放射状切口,采用电刀游离乳房腺体,然后离断乳头乳晕深方腺体,术中取肿瘤浅层组织和乳头深方组织,将胸大肌筋膜和腺体周围韧带离断后,取出完整病灶组织送检。止血、冲洗、缝合。

1.3 观察及检验指标

(1) 分别统计患者手术时间、术后拔管时间以及住院时间; (2) 分别于术前 1 d、术后 3 d 以及术后 1 个月, 收集患者外周血, 离心取血清, 采用免疫比浊法检测患者血清免疫功能相关指标 IgM 和 IgG 含量, 采用人酶联免疫吸附实验(ELISA)试剂盒检测患者血清中炎症反应指标 TNF- α 和 IL-10 含量, 具体检测步骤按照相应试剂盒说明书进行操作。

1.4 随访

表 2 两组患者一般手术指标比较($\bar{x} \pm s$)

Table 2 Comparison of general surgical indicators between the two groups($\bar{x} \pm s$)

Groups	n	Operation time/min	Extubation time/d	Hospital stay/d
Group A	59	139.88± 23.30*	6.25± 0.58*	8.02± 1.02*
Group B	41	62.20± 14.71	7.03± 0.80	9.17± 1.13

Note: Compared with Group B, *P<0.05.

2.2 两组患者术后 1 月并发症发生率比较

术后 A 组各类并发症总发生率为 5.00%(2/40), B 组患者

(1) 术后 1 个月内, 统计术后两组患者出现术野皮下出血、皮下积液、乳头乳晕坏死等并发症的例数; (2) 术后一年, 统计两组患者出现复发和淋巴结转移等现象的例数。

1.5 统计学方法

本研究所得数据通过 SPSS20.0 进行处理和分析, 数据均符合正态分布, 计量资料和计数资料分别采用($\bar{x} \pm s$)和[n(%)]表示, 分别通过 t 检验和卡方(χ^2)检验进行两组间比较, 检验水准: $\alpha=0.05$ 。

2 结果

2.1 两组手术指标比较

A 组患者手术时间显著长于 B 组, 而其拔管时间和住院时间均显著短于 B 组, 差异均具有统计学意义($P<0.05$)。见表 2。

术后各类并发症发生率为 25.71%(9/35), A 组并发症发生率显著高于 B 组($P<0.05$), 见表 3。

表 3 两组患者术后并发症发生率比较(例, %)

Table 3 Comparison of the incidence of postoperative complications between the two groups (cases, %)

Groups	n	Surgical field subcutaneous hemorrhage	Subcutaneous fluid	Nipple and areola necrosis	Total incidence
Group A	59	1(2.50)	1(2.50)	0(0.00)	2(5.00)*
Group B	41	4(28.57)	3(8.57)	2(5.14)	9(25.71)

Note: Compared with Group B, *P<0.05.

2.3 两组患者术后患者血清免疫指标水平变化比较

术后 3 d 两组患者血清免疫指标 IgM 和 IgG 水平均显著低于术前 1 d, 而术后 1 m 两组患者血清免疫指标 IgM 和 IgG 水平均显著高于术后 3 d($P<0.05$)。术前 1 d, 两组患者血清免

疫指标 IgM 和 IgG 水平相比差异无统计学意义($P>0.05$), 而术后 3 d~ 术后 1 m, A 组患者血清免疫指标 IgM 和 IgG 水平均显著高于 B 组($P<0.05$)。见表 4。

表 4 2 组患者术后患者血清免疫指标水平变化比较($\bar{x} \pm s$)

Table 4 Comparison of changes in serum immune index levels of patients in the two groups after surgery($\bar{x} \pm s$)

Groups	n	IgM(mg/mL)			IgG(mg/mL)		
		1 d before operation	3 d after operation	1 month after operation	1 d before operation	3 d after operation	1 month after operation
Group A	59	1.29± 0.49	0.93± 0.20*	2.23± 0.51*	10.66± 2.09	9.14± 1.27*	15.03± 3.49*
Group B	41	1.32± 0.37	0.77± 0.11	1.75± 0.42	10.40± 2.43	8.20± 0.09	12.87± 2.62

Note: Compared with Group B, *P<0.05.

2.4 两组患者术后患者血清炎症反应指标水平变化比较

术后 3 d 两组患者血清促炎因子 TNF- α 水平显著高于术前 1 d, 抗炎因子 IL-10 水平显著低于术前 1 d, 而术后 1 m 两组患者血清促炎因子 TNF- α 水平显著低于术前 1 d, 抗炎因子 IL-10 水平显著高于术前 1 d($P<0.05$)。术前 1 d, 两组患者血

清炎症反应指标 TNF- α 和 IL-10 水平相比差异无统计学意义($P>0.05$), 而术后 3 d~ 术后 1 m, A 组患者促炎因子 TNF- α 水平显著低于 B 组, 抗炎因子 IL-10 水平显著高于 B 组($P<0.05$)。见表 4。

表 5 2 组患者术后患者血清炎症反应指标水平变化比较($\bar{x} \pm s$)Table 5 Comparison of changes in serum inflammatory response index levels between the two groups of patients after surgery($\bar{x} \pm s$)

Groups	n	TNF- α (pg/mL)			IL-10(pg/mL)		
		1 d before operation	3 d after operation	1 month after operation	1 d before operation	3 d after operation	1 month after operation
Group A	59	113.16± 17.19	162.73± 21.76*	72.16± 13.08*	59.20± 8.43	40.18± 6.55*	68.30± 10.27*
Group B	41	118.53± 18.23	199.43± 25.44	100.46± 14.12	60.16± 8.77	31.77± 6.12	43.22± 7.52

Note: Compared with Group B, *P<0.05.

2.5 两组患者术后 1 年内复发率比较

A 组患者术后 1 年内乳腺癌复发率为 3.34%(2/59),B 组复发率为 12.20%(5/41),2 组患者术后 1 年内复发率比较差异不具有统计学意义($\chi^2=2.881,P=0.119$)。

3 讨论

乳腺癌是女性多发恶性肿瘤之一,男性由于生理原因其发病率通常为 1% 左右,但近年来,我国该肿瘤发病率逐年递增,且呈年轻化趋势^[9-11]。虽然医疗技术的进步促进了该肿瘤的诊断和治疗的发展,但由于 6% 的患者确诊时已出现转移,可切除性乳腺癌的主要标准治疗方法是接受或进行术后放射的根治性手术,从而产生了稳定的治疗效果^[12-15]。而腋窝淋巴结转移乳腺癌患者在术后早期复发的风险较高,因此该肿瘤的生存率目前仍不容乐观^[16-18]。相关研究显示:低龄乳腺癌(35 岁以下)侵袭性更强因而预后更差^[19,20]。目前该肿瘤以手术为主、放化疗为辅的方式进行治疗^[21-23]。但研究显示:乳腺癌手术对患者免疫功能具有较大影响,通常术后患者该功能底下,从而导致感染和肿瘤复发的风险增加,因此微创、精准的手术及操作对患者术后恢复及预后改善具有重要意义^[24,25]。

近年来,腔镜技术在乳腺癌外科治疗中占有重要地位,从理论上讲,相较于传统手术,腔镜的应用具有可视化术野,从而可达到解剖学意义上的精准切除,一定程度上可降低肿瘤复发率并最大程度减少皮瓣损伤^[26,27]。腔镜下腺体切除术治疗早期乳腺癌的临床效果分析结果表明:腔镜乳房皮下腺体切除术治疗早期乳腺癌术后切口皮下积液发生率低,拔管时间和住院时间短,术后美容效果好^[28]。本研究通过分析腔镜手术和开放乳房皮下腺体切除术对早期乳腺癌的临床治疗效果,并进一步比较两者的安全性,结果显示:A 组患者手术时间显著长于 B 组,而其拔管时间和住院时间均显著短于 B 组,表明:腔镜手术术中用时较长,但术后患者拔管时间和住院时间均显著缩短,其原因之一在于腔镜手术器械及操作更为复杂,另一方面其具有可视化术野从而为肿瘤组织的精准化、彻底化切除提供了更多可能性,因此相较于传统开放性手术,腔镜手术患者术后拔管时间和住院时间缩短,表明其术后恢复较快。另外,本研究还对不同术式患者手术前后免疫功能及炎症指标变化趋势进行分析,结果显示:两组治疗前后,术后 3 d 两组患者血清免疫指标 IgM 和 IgG 水平和抗炎因子 IL-10 水平均显著低于术前 1 d,促炎因子 TNF- α 水平显著高于术前 1 d,结合相关研究可知:通常乳腺癌手术会对患者造成较大创伤,因而术后患者应激反应严重、免疫功能低下,因此术后患者易发生感染或出现各种并发症,从而导致机体免疫功能指标及炎症反应指标出现大幅波

动,而而术后 1 m 两组患者血清免疫指标 IgM 和 IgG 水平和抗炎因子 IL-10 水平均显著高于术后 3 d,促炎因子 TNF- α 水平显著高于术后 3 d,说明随着患者手术创伤恢复及病情好转,患者免疫功能指标及炎症反应指标逐渐恢复平衡,与相关研究结果类似^[29,30]。另外,两组并发症发生、免疫功能指标及炎症反应指标比较结果表明:A 组各类并发症总发生率为 5.00%(2/40),B 组患者术后各类并发症发生率为 25.71%(9/35),A 组并发症发生率显著高于 B 组($P<0.05$);A 组患者术后 1 月血清中免疫指标 IgM 和 IgG 含量以及抗炎因子 IL-10 含量均显著高于 B 组,促炎因子 TNF- α 含量显著低于 B 组($P<0.05$)。以上结果表明:腔镜术后乳腺癌患者免疫功能指标和炎症反应指标水平平均显著优于传统开放手术患者,且患者术后并发症发生率也较低,结合上述研究^[29,30]推测:腔镜手术对患者造成的创伤程度以及对患者免疫功能的影响可能相对较小,且术后患者相关功能指标水平的恢复较快,因此有助于降低患者并发症发生率。另外,本研究中,A 组患者术后 1 年内乳腺癌复发率为 2.5%(1/40),B 组复发率为 8.57%(3/35),2 组患者术后 1 年内复发率比较差异不具有统计学意义($\chi^2=1.363,P=0.243$),表明:两种手术对患者术后复发率影响无差异,这可能与本研究纳入患者例数较少有关,后续将扩大样本量进一步证实该结论。

综上所述,腔镜下腺体切除术治疗早期乳腺癌具有拔管时间以及术后住院时间短、并发症发生率低等优势,其原因可能与该手术对患者血清免疫球蛋白 IgM 和 IgG 及炎症因子 TNF- α 、IL-10 水平影响程度较小、术后恢复较快有关。

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