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甲状腺全切术治疗分化型甲状腺癌的疗效观察及临床研究探讨*

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摘要 目的: 研究甲状腺全切术治疗分化型甲状腺癌的疗效观察及临床研究探讨。方法: 收集 2014 年 3 月至 2015 年 3 月我院收治的 90 例分化型甲状腺癌患者, 按抽签法分为实验组和对照组, 每组 45 例。对照组采用次全切除术治疗, 实验组采用甲状腺全切术治疗。观察两组患者的治疗疗效、手术时间、术中出血量、住院时间、复发率、治疗前后血清 TNF- α 、IL-6、Gal-3、VEGF 水平及并发症的发生情况。结果: 治疗后, 实验组总有效率显著高于对照组 [93.33%(42/45) vs 68.89%(31/45)] ($P < 0.05$)。两组住院时间比较差异无统计学意义 ($P > 0.05$), 实验组手术时间、术中出血量、复发率均显著低于对照组 [(70.36 \pm 12.72)min vs (109.75 \pm 15.37)min, (50.28 \pm 10.64)mL vs (91.62 \pm 13.50)mL, 2.22%(1/45) vs 15.56%(7/45)] ($P < 0.05$); 治疗后血清 TNF- α 、IL-6、Gal-3、VEGF 水平均显著低于对照组 [(506.30 \pm 78.23)pg/mL vs (621.25 \pm 83.54)pg/mL, (73.29 \pm 10.32)pg/mL vs (102.58 \pm 12.49)pg/mL, (3.40 \pm 0.80)ng/mL vs (4.82 \pm 0.81)ng/mL, (16.21 \pm 4.02)pg/mL vs (20.75 \pm 5.23)pg/mL] ($P < 0.05$)。实验组和对照组并发症总发生率分别为 15.56%、6.66%, 两组比较差异无统计学意义 ($P > 0.05$)。结论: 甲状腺全切术治疗分化型甲状腺癌的疗效优于次全切除术治疗, 可彻底清除病灶, 降低复发率, 可能与有效降低患者血清 TNF- α 、IL-6、Gal-3、VEGF 水平有关, 但其并发症较多, 对于低危或术后无需放射治疗的患者可采用次全切除术治疗, 应慎重选择手术方式。

关键词: 甲状腺全切术; 分化型甲状腺癌; 肿瘤坏死因子- α ; 白细胞介素-6; 半乳糖血凝素-3; 血管内皮生长因子

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The Effect of Total Thyroidectomy in the Treatment of Differentiated Thyroid Carcinoma and Its Clinical Study*

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ABSTRACT Objective: To study the effect of total thyroidectomy in the treatment of differentiated thyroid carcinoma and its clinical study. **Methods:** 90 patients of differentiated thyroid carcinoma who were treated from March 2014 to March 2015 in our hospital were selected as the research objects, and divided into the experimental group and the control group according to the draw method, 45 cases in each group. The control group was treated with subtotal resection, while the experimental group was treated with total thyroidectomy. Then the treatment effect, operation index (operation time, intraoperative blood loss, hospital stay) and recurrence rate, the levels of serum TNF- α , IL-6, Gal-3, VEGF levels before and after treatment and the incidence of complications of two groups were compared. **Results:** After treatment, the total effective rate of experimental group was significantly higher than that of the control group [93.33%(42/45) vs. 68.89%(31/45)] ($P < 0.05$). There was no difference in the hospital stay between the two groups ($P > 0.05$), the operation time, intraoperative blood loss and recurrence rate of experimental group were significantly lower than those of the control group [(70.36 \pm 12.72)min vs. (109.75 \pm 15.37)min, (50.28 \pm 10.64)mL vs. (91.62 \pm 13.50)mL, 2.22%(1/45) vs 15.56%(7/45)] ($P < 0.05$). After treatment, the serum TNF- α , IL-6, Gal-3, VEGF levels were significantly lower than those of the control group [(506.30 \pm 78.23)pg/mL vs. (621.25 \pm 83.54)pg/mL, (73.29 \pm 10.32)pg/mL vs. (102.58 \pm 12.49)pg/mL, (3.40 \pm 0.80)ng/mL vs. (4.82 \pm 0.81)ng/mL, (16.21 \pm 4.02)pg/mL vs. (20.75 \pm 5.23)pg/mL] ($P < 0.05$). The incidence of complications in the experimental group and the control group was 15.56%, 6.66%, there was no significant difference between the two groups ($P > 0.05$). **Conclusion:** Total thyroidectomy was more effective for differentiated thyroid cancer than subtotal resection, it could completely clear the lesions and reduce the recurrence rate, which might be related to the decrease of serum TNF- α , IL-6, Gal-3 and VEGF levels, but there were many complications, and patients with low risk or no postoperative radiation therapy should be treated by subtotal resection.

Key words: Total thyroidectomy; Differentiated thyroid carcinoma; Tumor necrosis factor- α ; Interleukin-6; Galectin-3; Vascular en-

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前言

甲状腺癌是临床上常见的恶性肿瘤疾病,包括分化型和未分化型,以分化型居多,由于早期无明显特异性,常出现误诊^[1]。甲状腺癌的发病机制复杂多样,临床研究显示缺碘及高碘的饮食、体内过高的雌激素、接触过量的放射线等均为其致病因素,临床表现为颈部淋巴结肿大,出现单一体积较大且坚硬的甲状腺结节^[2]。由于分化型组织较好,生长缓慢,恶性程度不高,因此,积极采取治疗后能够达到良好的预后,但仍不可忽视复发及死亡^[3]。手术是治疗分化型甲状腺癌的主要方法,甲状腺全切除术能够彻底的清除病灶,降低术后复发率,但会对甲状腺功能造成一定的影响,因此,目前临床对于手术切除范围仍存在较大的争论^[4]。本研究旨在探讨甲状腺全切除术治疗分化型甲状腺癌的疗效观察及临床研究探讨。

1 资料与方法

1.1 一般资料

收集 2014 年 3 月至 2015 年 3 月我院收治的 90 例分化型甲状腺癌患者,均经病理学诊断^[5]。纳入未合并其他恶性肿瘤疾病;无过手术治疗史;配合研究患者;初次治疗;20~80 岁患者;无手术禁忌证;排除术前出现声音嘶哑或声带固定;颈部淋巴结转移者;患有精神疾病;无法进行后期随访者;本研究家属及患者均签署知情同意书,且经医院伦理委员会许可,按抽签法分组。实验组 25 例女,20 例男,病程 4 个月~9 年,平均病程(5.18± 1.04)年,年龄 24~70 岁,平均年龄(40.23± 7.15)岁,其中 29 例单侧癌,16 例双侧癌;乳头状腺癌 30 例,滤泡状癌 15 例;肿瘤直径:28 例> 1.0 cm,17 例≤ 1.0c m。对照组 24 例女,21 例男,病程 5 个月~9 年,平均病程(5.76± 1.05)年,年龄 25~70 岁,平均年龄(41.08± 7.10)岁,其中 27 例单侧癌,18 例双侧癌;乳头状腺癌 29 例,滤泡状癌 16 例;肿瘤直径:29 例> 1.0 cm,16 例≤ 1.0 cm。两组一般临床资料比较差异均无统计学意义

(P>0.05),具有可比性。

1.2 治疗方法

两组术前均进行相关常规检查,采用全身麻醉,术后给予内分泌治疗。实验组进行甲状腺全切除术治疗,指导患者取仰卧位,将切口定于胸骨切迹上方两横指处,作一弧形切口,将皮瓣和颈前肌群分离,充分暴露甲状腺体,首先对其上下极进行处理,将进入到甲状腺处的上、中、下静脉实施结扎,从而充分暴露甲状腺后背侧,切除腺叶、峡部以及对侧全部腺叶,清扫其区域的淋巴结后进行创面冲洗,于气管旁放置引流管,逐层缝合创口。对照组进行次全切除术治疗。

1.3 观察指标

1.3.1 临床疗效观察 根据《甲状腺疾病防止指导》进行疗效评定^[6]。临床症状完全消失,无并发症为显效;临床症状明显减轻,无并发症为有效;临床症状无改善或加重为无效。

1.3.2 指标检测 于入院及治疗后空腹抽取 5 mL 静脉血,以 3000 r/min 分离,血清 TNF-α、IL-6、Gal-3、VEGF 水平均采用 ELISA 进行检测,采用 MR-96 全自动酶标仪分析,试剂盒购至美国 ADL 公司。

1.3.3 复发率及并发症的发生情况 两组患者均进行术后 1 年随访,采用超声、CT 等检查观察其复发情况,以及低血钙症、甲状旁腺损伤、声音嘶哑、喉上神经损伤并发症的发生情况。

1.4 统计学分析

选择 SPSS18.0 进行统计学分析,计量资料用($\bar{x} \pm s$)表示,组间比较采用 t 检验,计数资料用[(例)%]表示,组间比较采用 χ^2 检验比较,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组治疗疗效的比较

实验组总有效率为 93.33%,显著高于对照组 68.89%(P< 0.05),见表 1。

表 1 两组治疗疗效的比较[(n)%]

Table 1 Comparison of the therapeutic effect between two groups[(n)%]

Groups	Cure	effective	invalid	total effective rate
Experimental group(n=45)	35(77.78)	7(15.56)	3(6.67)	42(93.33) [#]
Control group(n=45)	26(57.78)	5(11.11)	14(31.11)	31(68.89)

Note: Compared with the control group after treatment, [#]P<0.05.

2.2 两组手术指标及复发率的比较

两组住院时间比较差异无统计学意义(P>0.05),实验组手

术时间、术中出血量、复发率均显著低于对照组(P<0.05),见表 2。

表 2 两组手术指标及复发率的比较($\bar{x} \pm s$)

Table 2 Comparison of the operation index and recurrence rate between two groups($\bar{x} \pm s$)

Groups	Operation time(min)	Intraoperative blood loss (mL)	Hospitalization time(d)	Recurrence rate(%)
Experimental group(n=45)	70.36± 12.72 [#]	50.28± 10.64 [#]	6.40± 1.02	1(2.22) [#]
Control group(n=45)	109.75± 15.37	91.62± 13.50	6.42± 1.03	7(15.56)

Note: Compared with the control group after treatment, [#]P<0.05.

2.3 两组治疗前后血清 TNF-α、IL-6、Gal-3、VEGF 水平的比较
 两组治疗前血清 TNF-α、IL-6、Gal-3、VEGF 水平比较差异无统计学意义(P>0.05); 治疗后, 两组血清 TNF-α、IL-6、VEGF

水平均较治疗前显著降低, 血清 Gal-3 水平明显上升, 且实验组以上指标改善较对照组更明显(P<0.05), 见表 3。

表 3 两组治疗前后血清 TNF-α、IL-6、Gal-3、VEGF 水平的比较

Table 3 Comparison of the serum TNF-α, IL-6, Gal-3, VEGF levels between two groups before and after treatment ($\bar{x} \pm s$)

Groups		TNF-α(pg/ml)	IL-6(pg/ml)	Gal-3(ng/ml)	VEGF(pg/ml)
Experimental group (n=45)	Before treatment	973.62± 201.40	180.36± 30.46	5.30± 1.03	27.09± 7.35
	After treatment	506.30± 78.23*#	73.29± 10.32*#	3.40± 0.80*#	16.21± 4.02*#
Control group(n=45)	Before treatment	972.36± 202.36	179.76± 30.61	5.19± 0.90	26.97± 7.30
	After treatment	621.25± 83.54*	102.58± 12.49*	4.82± 0.81*	20.75± 5.23*

Note: Compared with before treatment, *P<0.05; compared with the control group after treatment, #P<0.05.

2.4 两组并发症的发生情况比较

组比较差异无统计学意义(P>0.05), 见表 4。

实验组并发症的总发生率为 15.56%, 对照组为 6.66%, 两

表 4 两组并发症发生情况的比较[例(%)]

Table 4 Comparison of the incidence of complications between two groups[n(%)]

Groups	Hypocalcemia	Parathyroid injury	Hoarseness	Jets nerve injury	Complication rate
Experimental group(n=45)	2(4.44)	1(2.22)	3(6.66)	1(2.22)	7(15.56)
Control group(n=45)	1(2.22)	0(0.00)	2(4.44)	0(0.00)	3(6.66)

3 讨论

分化型甲状腺癌多为良性肿瘤, 大多数患者可存活 10 年及以上, 由于其容易出现颈淋巴结转移, 在手术过程中清扫淋巴结可能会对甲状旁腺造成损伤^[7]。因此, 对于切除范围以及颈淋巴结清扫范围还有所争议。以往学者认为^[8]可在甲状腺全切除时不进行颈淋巴结清扫, 但近年来大量研究结果显示可采用甲状腺全切除术联合中央区颈淋巴结清扫进行治疗。

甲状腺全切除术能够将其病灶及潜在的腺体内转移灶完整的切除, 可减少病灶残留, 从而能够显著的降低复发率, 无需进行二次手术, 减轻患者的痛苦^[9]。国内外研究显示^[10]约 60% 左右的患者病灶位于双侧, 次全切除术无法彻底的清除病灶, 使肿瘤组织残留, 术后容易复发, 且二次手术因术区粘连致密, 术后易出现不良反应。本研究显示采用全切除术治疗的患者复发率显著低于采用次全切除术治疗的患者, 说明全切除术能够更加彻底的清除病灶, 减少肿瘤残留, 避免术后复发。此外, 采用全切除术治疗还有利于后期对甲状腺球蛋白的检测, 可观察是否出现复发或转移; 有利于促进放射性碘对病灶的作用, 能够降低肺部转移率和病死率^[11,12]。在本研究中, 采用全切除术的患者治疗疗效以及手术时间、术中出血量显著优于采用次全切除术的患者, 说明全切除术较次全切除术存在一定的优势。

但部分学者认为^[13]全切除术本身是一种致残性手术, 术后可能导致甲状腺功能的完全丧失, 还会出现甲状旁腺损伤以及喉返神经损伤。国外资料也显示^[14]全切除术的此类并发症高于次全切除术。本研究显示采用全切除术的患者并发症总发生率较高, 但两组比较差异无统计学意义。其中, 低血钙症可能是由于术后大量的补液使血钙得到稀释, 增加了尿钙的排出, 或因手术产生的应激反应使钙磷代谢出现紊乱^[15]。因此, 临床认为低危患者的切除范围可相对保守, 高危患者可扩大切除范围。

但本研究并未得出手术方式对患者预后的总生存率存在较大的影响。

国外研究发现^[16]甲状腺癌患者的血清 TNF-α、IL-6、Gal-3、VEGF 水平显著高于正常人。TNF-α 生物学活性广泛, 可促进血管形成, 调控炎症期间的细胞迁移, 参与促进肿瘤细胞的发生过程, 与 VEGF 的表达密切相关^[17]。VEGF 能够促进生成淋巴管, 可发生淋巴转移, 且与 TNF-α 随着病情的加重而升高^[18]。IL-6 能够调节免疫, 促进上皮细胞或成纤维细胞增殖, 与肿瘤的发展有关, 由于分化型甲状腺癌患者本身免疫功能出现紊乱, 其 T、B 淋巴细胞的失调也可促使 IL-6 升高^[19]。Gal-3 是一种 R- 半乳糖特异凝集素, 能够促进细胞生长及增殖, 可促使血管生成, 在肿瘤发生及转移起促进作用, 且转移者的 Gal-3 水平更高, 但其无法辨别良恶性^[20]。在本研究中, 采用全切除术的患者血清 TNF-α、IL-6、Gal-3、VEGF 水平显著较采用次全切除术的患者低, 说明全切除术能够更加显著的降低炎症血清的水平, 抑制肿瘤分化, 将其作为术后检查标志能够有利于对预后进行预测。

综上所述, 甲状腺全切除术治疗分化型甲状腺癌的疗效优于次全切除术治疗, 可彻底清除病灶, 降低复发率, 可能与有效降低患者血清 TNF-α、IL-6、Gal-3、VEGF 水平有关, 但其并发症较多, 对于低危或术后无需放射治疗的患者可采用次全切除术治疗, 应慎重选择手术方式。

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