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· 临床研究 ·

甲状腺手术不同术式对甲状旁腺功能影响的临床观察

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摘要

背景与目的: 手术是治疗甲状腺疾病的一种极为重要的方式, 而甲状旁腺功能减退是甲状腺手术的常见并发症之一。由于各类甲状腺疾病采取的手术方式不同, 对甲状旁腺功能的影响也可能不同。本研究探讨甲状腺不同术式对甲状旁腺功能影响的差异并分析原因。

方法: 回顾性分析 2017 年 8 月—2019 年 3 月收治的 319 例甲状腺手术患者的临床资料, 其中, 行甲状腺单侧腺叶切除 111 例(单侧切除组)、行甲状腺双侧腺叶切除 107 例(双侧切除组)、行甲状腺双侧腺叶切除+中央区淋巴清扫术 71 例(双侧切除+VI 区清扫组)、行甲状腺双侧腺叶切除+中央区淋巴清扫术+侧颈区淋巴清扫术 30 例(双侧切除+II~VI 区清扫组)。术中在患侧近峡部周围被膜选择 1~2 点, 每点注射 0.1~0.2 mL 纳米炭混悬注射液, 所有患者均采用精细被膜解剖法原位保留甲状旁腺, 若术中发现甲状旁腺无法原位保留则立即将该甲状旁腺剪成薄片或匀浆移植包埋于胸锁乳突肌中。观察并比较各组手术前后甲状旁腺激素(PTH)与血钙水平的变化以及术后甲状旁腺功能减退与低钙血症发生率。

结果: 各组术前一般资料及 PTH 与血钙水平均无统计学差异(均 $P>0.05$)。各组术后 PTH 和血钙浓度均较术前明显降低(均 $P<0.01$), 但两者的下降幅度在术后相同时间点随着手术范围扩大而明显增大, 即单侧切除组 < 双侧切除组 < 双侧切除+VI 区清扫组 < 双侧切除+II~VI 区清扫组, 差异均有统计学意义(均 $P<0.05$)。甲状旁腺功能减退与低钙血症的发生率同样随着手术范围扩大而升高, 单侧切除组、双侧切除组、双侧切除+VI 区清扫组、双侧切除+II~VI 区清扫组甲状旁腺功能减退发生率分别为 9.9%、32.7%、56.3%、73.3%, 低钙血症发生率分别为 0%、1.9%、19.7%、50.0%, 组间差异均有统计学意义(均 $P<0.05$)。所有患者随访至 24 周, 无永久性甲状旁腺功能减退发生。

结论: 各种甲状腺手术均对甲状旁腺功能有一定的影响, 且手术范围越大, 甲状旁腺受损的几率越大, 发生甲状旁腺功能减退的风险越高。因此, 无论何种术式术中均应对甲状旁腺实施保护, 术中精细操作, 减少对甲状旁腺血运影响, 从而尽可能地降低甲状旁腺功能减退的发生率。

关键词

甲状腺切除术; 手术后并发症; 甲状旁腺功能减退症

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Clinical observation of impacts of different types of thyroid surgery on parathyroid function

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Abstract

Background and Aims: Surgery plays an important role in the treatment of thyroid disease, and hypoparathyroidism is one of the common complications of thyroid surgery. However, different kinds of thyroid pathologies have different indications for different types of thyroid surgery, which may exert different impacts on parathyroid function. This study was conducted to investigate the differential influences of different types of thyroid surgery on parathyroid function and analyze the reasons.

Methods: The clinical data of 319 eligible patients who underwent thyroid surgeries from April 2017 to March 2019 were retrospectively analyzed. Of the patients, 111 cases underwent unilateral thyroid lobectomy (unilateral resection group), 107 cases underwent bilateral thyroid lobectomy (bilateral resection group), 71 cases underwent bilateral thyroid lobectomy with central lymph node dissection (bilateral resection plus level VI dissection group), and 30 cases underwent bilateral thyroid lobectomy with central and lateral neck dissection (bilateral resection plus level II–VI dissection group). During the operation, 1-2 points on the capsule around the affected side close to the isthmus region were selected, and 0.1-0.2 mL of nanocarbon suspension was injected at each point. Meticulous capsular dissection technique was adopted in all patients for in-situ preservation of the parathyroid glands. If the parathyroid glands failed to be retained in situ, they were immediately cut into pieces or homogenates and reimplanted into the sternocleidomastoid muscle. The changes in parathyroid hormone (PTH) and blood calcium levels before and after surgery as well as the incidence rates of postoperative hypoparathyroidism and hypocalcemia among groups of patients were observed and compared.

Results: The preoperative general data and PTH and blood calcium levels showed no significant differences among groups (all $P>0.05$). After surgery, both PTH and blood calcium levels were significantly decreased in all groups compared with their preoperative levels (all $P<0.01$), but their decreasing amplitudes were significantly magnified with the expansion of surgical scope, namely unilateral resection group < bilateral resection group < bilateral resection plus level VI dissection group < bilateral resection plus level II–VI dissection group, and all differences had statistical significance (all $P<0.05$). The incidence rates of hypoparathyroidism and hypocalcemia were likewise increased with the expansion of surgical scope, and in unilateral resection group, bilateral resection group, bilateral resection plus level VI dissection group and bilateral resection plus level II–VI dissection group, the incidence of hypoparathyroidism was 9.9%, 32.7%, 56.3% and 73.3%, and the incidence of hypocalcemia was 0, 1.9%, 19.7% and 50.0%, respectively. Follow-up was conducted for 24 weeks in all patients, and no permanent hypoparathyroidism was noted.

Conclusion: All kinds of thyroid surgery have certain impacts on the parathyroid function, and the possibility of parathyroid injury and risk of the occurrence of hypoparathyroidism will increase with the expansion of the surgical scope. So, the protective measures for parathyroid glands should be adopted in all thyroid surgeries, with meticulous dissection and reduced interference in the blood supply of the parathyroid glands, and thereby to decrease the incidence of hypoparathyroidism as far as possible.

Key words

Thyroid surgery; Postoperative Complications; Hypoparathyroidism

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在现代医学中，手术治疗是治疗甲状腺疾病的重要的方式，但是由于甲状腺与甲状旁腺“密不可分”，导致甲状旁腺功能减退成为甲状腺手术的常见并发症之一^[1]。患者电解质指标可由于术后甲状旁腺激素（parathyroid hormone, PTH）降低而出现低钙血症或高磷血症，严重者可出现反复手足抽搐或癫痫，极大降低了患者术后生活质量。各研究^[2-3]关于甲状腺术后甲状旁腺功能减退说法不一，有学者^[4]报道甲状腺手术术式能影响甲状旁腺术后功能。基于上述，本研究回顾性分

析甲状腺手术不同术式对甲状旁腺功能变化的影响，现报告如下。

1 资料与方法

1.1 一般资料

收集2017年8月—2019年3月湖南省人民医院集团祁东县人民医院乳甲外科行甲状腺手术治疗的患者共341例，符合入选标准319例，其中男52例，女267例；年龄29~68岁，中位年龄45岁。

319例患者中,行甲状腺单侧腺叶切除(单侧切除组)111例,行甲状腺双侧腺叶切除(双侧切除组)107例,行甲状腺双侧腺叶切除+中央区淋巴清扫术71例(双侧切除+VI区清扫组),行甲状腺双侧腺叶切除+中央区淋巴清扫术+侧颈区淋巴清扫术30例(双侧切除+II~VI区清扫组)。各组年龄、性别构成比无统计学差异(均 $P>0.05$),具

有可比性(表1)。入选标准:(1)初次手术的患者;(2)术者为同一手术团队;(3)资料完整;(4)患者术前PTH均在正常范围内。排除标准:(1)不来源于同一手术团队(7例);(2)再次手术病例(10例);(3)仅行峡部切除者(5例);(4)合并心、肝、肾等重要器官损害者。符合入选标准患者319例。所有患者均签署手术知情同意书。

表 1 各组患者年龄、性别构成情况

Table 1 The age and sex constitution of the groups of patients

资料	单侧切除组 (n=111)	双侧切除组 (n=107)	双侧切除+VI区清扫组 (n=71)	双侧切除+II~VI区清扫组 (n=30)	χ^2/t	P
性别[n(%)]						
男	23(20.7)	12(11.2)	13(18.3)	4(13.3)	4.02	0.26
女	88(79.3)	95(88.8)	58(81.7)	26(86.7)		
年龄(岁, $\bar{x}\pm s$)	46.28 \pm 9.02	45.20 \pm 7.29	43.73 \pm 9.40	42.63 \pm 11.42	1.95	0.12

1.2 手术方式

所有患者均采用全身麻醉,按手术方式分为甲状腺单侧腺叶切除111例,甲状腺双侧腺叶切除107例、甲状腺双侧腺叶切除+中央区淋巴清扫术71例、全甲状腺切除+中央区淋巴清扫术+侧颈区淋巴清扫术30例。术中注射纳米炭时间及方法:在暴露甲状腺后,在患侧近峡部周围被膜选择1~2点,每点注射0.1~0.2 mL纳米炭混悬注射液(重庆莱美药业,国药准字H20041829),待淋巴结黑染显色后行相应术式(图1A)。所有患者在术中均采取精细被膜解剖法原位保留甲状旁腺:打开甲状腺外科被膜,翻出甲状腺的背面并仔细辨认甲

状旁腺及其血管蒂。上甲状旁腺常位于甲状腺上1/3,而下甲状旁腺位置多变,可在纵膈内、胸腺内、甲状腺前或甲状腺内,但常见于甲状腺下极^[5](图1B)。在发现甲状旁腺后,可轻轻钳夹住甲状旁腺旁筋膜组织(不要长时间钳夹同一位置以减少对甲状旁腺的损伤),沿筋膜间隙轻柔分离甲状旁腺及血管蒂,这样能原位保护甲状旁腺及营养血管。若发现甲状旁腺供血不足或误切,立即将该甲状旁腺剪成薄片或匀浆移植包埋于胸锁乳突肌中^[6]。所有手术中止血均使用电刀、双极电凝刀或超声刀。

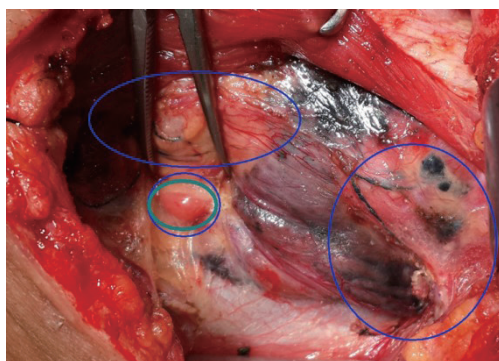


图 1 术中照片 A: 注射纳米炭后负显影的甲状旁腺(蓝圈内为显影淋巴结,绿圈内为负显影甲状旁腺); B: 左下甲状旁腺及血管(钳夹处为左下甲状旁腺)

Figure 1 Intraoperative pictures A: Negative contrast of the parathyroid gland after nanocarbon injection (positive contrast of the lymph nodes in the blue circle, and negative contrast of the parathyroid gland in the green circle); B: Left inferior parathyroid gland and its feeding vessels (left inferior parathyroid gland in the clamping point)

1.3 观察指标

血清PTH正常值15~68.3 pg/mL,术后任何1 d

PTH<15 pg/mL可认为甲状旁腺功能减退。血钙正常值2.1~2.8 mmol/L, <2.1 mmol/L为低钙血症。

统计分析各组术前及术后各时间点测定PTH水平及血钙浓度水平,以及甲状旁腺功能减退、低钙血症的发生率,对比分析4种术式对甲状旁腺术后功能的影响差异。

1.4 统计学处理

使用SPSS25.0处理数据,定量资料使用均值±标准差表示($\bar{x} \pm s$),计数资料使用构成比(%) [n (%)]表示,统计方法使用重复测量方差分析,配对 t 检验, χ^2 检验和Fisher精确检验。以 $\alpha=0.05$ 作为检验水准,双尾概率 $P<0.05$ 认为有统计学意义。

2 结果

2.1 PTH水平的变化

各组术前PTH水平差异无统计学意义($P>0.05$)。各组术后1、3、7 d的PTH水平均较术前明显降低(均 $P<0.01$),且均于术后1 d降至最低,术后3、7 d逐渐缓慢升高,但术后PTH降低幅度随着手术范围的增加而增大,即单侧切除组<双侧切除组<双侧切除+VI区清扫组<双侧

切除+II~VI区清扫组,差异均有统计学意义(均 $P<0.05$) (表2)。单侧切除组、双侧切除组、双侧切除+VI区清扫组、双侧切除+II~VI区清扫组的术前与术后7 d PTH差值依次增大,分别为:(5.21 ± 0.07) pg/mL、(8.47 ± 4.04) pg/mL、(18.23 ± 0.84) pg/mL、(22.58 ± 1.13) pg/mL,各组间PTH差值均有统计学差异(均 $P<0.05$)。

2.2 血钙水平的变化

各组术前血钙水平经比较无统计学意义($P>0.05$)。各组术后3 d血钙水平均较术前明显降低(均 $P<0.01$),但术后血钙水平降低幅度随着手术范围的增加而增大,即单侧切除组<双侧切除组<双侧切除+VI区清扫组<双侧切除+II~VI区清扫组,差异均有统计学意义(均 $P<0.05$) (表3)。单侧切除组、双侧切除组、双侧切除+VI区清扫组、双侧切除+II~VI区清扫组的术前与术后3 d血钙水平差值依次增大,分别为(0.04 ± 0.00) mmol/L、(0.10 ± 0.02) mmol/L、(0.18 ± 0.07) mmol/L、(0.26 ± 0.14) mmol/L,各组间血钙水平差值均有统计学差异(均 $P<0.05$)。

表2 各组术前与术后PTH水平比较(pg/mL, $\bar{x} \pm s$)

Table 2 Comparison of the PTH levels before and after surgery among groups (pg/mL, $\bar{x} \pm s$)

组别	术前	术后1 d	术后3 d	术后7 d	F	P
单侧切除组($n=111$)	41.68 ± 11.39	31.34 ± 12.19	33.21 ± 11.96	36.47 ± 11.32	97.09	<0.01
双侧切除组($n=107$)	41.60 ± 11.48	$25.32 \pm 14.92^{1)}$	$28.50 \pm 17.55^{1)}$	$33.13 \pm 15.52^{1)}$	105.91	<0.01
双侧切除+VI区清扫组($n=71$)	39.19 ± 11.98	$15.15 \pm 10.29^{1,2)}$	$17.07 \pm 11.13^{1,2)}$	$20.96 \pm 12.82^{1,2)}$	196.77	<0.01
双侧切除+II~VI区清扫组($n=30$)	39.43 ± 10.15	$12.79 \pm 10.79^{1,2,3)}$	$13.52 \pm 11.46^{1,2,3)}$	$16.85 \pm 11.28^{1,2,3)}$	90.96	<0.01
F	1.00	32.08	28.92	31.94	—	—
P	0.39	<0.01	<0.01	<0.01	—	—

注:1)与单侧切除组相同时间点比较, $P<0.05$;2)与双侧切除组相同时间点比较, $P<0.05$;3)与双侧切除+VI区清扫组相同时间点比较, $P<0.05$

Note: 1) $P<0.05$ vs. unilateral resection group at the same time point; 2) $P<0.05$ vs. bilateral resection group at the same time point; 3) $P<0.05$ vs. unilateral resection plus level VI dissection group at the same time point

表3 各组术前与术后血钙水平比较(mmol/L, $\bar{x} \pm s$)

Table 3 Comparison of the blood calcium levels before and after surgery among groups (mmol/L, $\bar{x} \pm s$)

组别	术前	术后3 d	F	P
单侧切除组($n=111$)	2.32 ± 0.07	2.28 ± 0.07	9.18	<0.01
双侧切除组($n=107$)	2.32 ± 0.06	$2.22 \pm 0.08^{1)}$	17.77	<0.01
双侧切除+VI区清扫组($n=71$)	2.33 ± 0.06	$2.15 \pm 0.13^{1,2)}$	12.03	<0.01
双侧切除+II~VI区清扫组($n=30$)	2.31 ± 0.01	$2.05 \pm 0.15^{1,2,3)}$	11.32	<0.01
F	0.39	50.44	—	—
P	0.76	<0.01	—	—

注:1)与单侧切除组相同时间点比较, $P<0.05$;2)与双侧切除组相同时间点比较, $P<0.05$;3)与双侧切除+VI区清扫组相同时间点比较, $P<0.05$

Note: 1) $P<0.05$ vs. unilateral resection group at the same time point; 2) $P<0.05$ vs. bilateral resection group at the same time point; 3) $P<0.05$ vs. unilateral resection plus level VI dissection group at the same time point

2.3 各组术后甲状旁腺功能减退与低钙血症发生率

各组间甲状旁腺功能减退的发生率有统计

学差异($P<0.01$);单侧切除组、双侧切除组、双侧切除+VI区清扫组、双侧切除+II~VI区清扫

组甲状旁腺功能减退的发生率依次升高,分别为9.9%、32.7%、56.3%、73.3%,组间比较,差异均有统计学意义(均 $P<0.05$)。各组间低钙血症的发生率有统计学差异($P<0.01$);单侧切除术后无低血钙患者出现,双侧切除组、双侧切除

+VI区清扫组、双侧切除+II~VI区清扫组低钙血症发生率逐渐增高,分别为1.9%、19.7%、50.0%,组间比较,差异均有统计学意义(均 $P<0.05$)(表4)。

表 4 各组术后甲状旁腺功能减退与低钙血症发生情况 [n (%)]

Table 4 The incidence rates of postoperative hypoparathyroidism and hypocalcemia in each group [n (%)]

组别	甲状旁腺功能减退	低钙血症
单侧切除组 (n=111)	11 (9.9)	0 (0.0)
双侧切除组 (n=107)	35 (32.7) ¹⁾	2 (1.9) ¹⁾
双侧切除+VI区清扫组 (n=71)	40 (56.3) ^{1),2)}	14 (19.7) ^{1),2)}
双侧切除+II~VI区清扫组 (n=30)	22 (73.3) ^{1),2),3)}	15 (50.0) ^{1),2),3)}
χ^2	65.39	34.22
P	<0.01	<0.01

注:1)与单侧切除组比较, $P<0.05$;2)与双侧切除组比较, $P<0.05$;3)与双侧切除+VI区清扫组比较, $P<0.05$

Note: 1) $P<0.05$ vs. unilateral resection group; 2) $P<0.05$ vs. bilateral resection group; 3) $P<0.05$ vs. unilateral resection plus level VI dissection group

2.4 随访情况

所有患者4周后门诊予以复查追踪,4周复查PTH正常后,改为每3个月复查;4周复查PTH仍低者,则第2次复查仍为4周后。依次进行,直至术后24周。随访至24周患者仍 $PTH<15$ pg/mL者认为是永久性甲状旁腺功能减退。所有患者术后12周内PTH均恢复正常,无永久性甲状旁腺功能减退发生。

3 讨论

甲状旁腺是位于甲状腺后方的小腺体,直径约3~6 mm,主要功能就是分泌甲状旁腺激素,该激素可以调节体内钙的代谢,维持体内钙磷平衡^[7]。甲状旁腺功能减退是甲状腺手术后最常见的并发症之一,暂时性甲状旁腺功能减退会出现暂时性低钙症状,通常能逐渐恢复;但永久性甲状旁腺功能低下会出现永久性低钙症状,如手足麻木和四肢抽搐,严重时可出现喉肌和膈肌痉挛导致窒息死亡^[8]。据报道^[9],在患者行甲状腺手术后,暂时性甲状旁腺功能减退的发生率达18%~54%,永久性甲状旁腺功能减退的发生率达0~5%,本组术后暂时性甲状旁腺功能减退发生率为33.86%(单侧切除组9.9%、双侧切除组32.7%、双侧切除+VI区清扫组56.3%、双侧切除+II~VI区清扫组73.3%),永久性甲状旁腺功能减退发生率为0,与文献报道相符。随着甲状腺手术范围的扩大,术后甲状旁腺功能减退的发生率增高,说明手术范围越大,甲状旁腺损伤的概率越大。

本研究中,各组PTH及血钙浓度水平在行甲状腺术后均有不同程度下降,且随着手术范围的

增大,PTH及血钙浓度下降幅度逐渐增加。说明只要实施甲状腺手术,就会对甲状旁腺产生损伤,从而可能导致甲状旁腺功能减退。这与靳凯等^[10]研究结果一致。本研究发现各组术后PTH第1天达到最低点。本研究还比较了各组手术前后PTH与血钙水平的差值,结果同样显示,两者的差值随着甲状腺手术范围的增大而增大。

笔者认为出现甲状腺手术后甲状旁腺功能减退的原因主要包括:(1)甲状旁腺的误切。甲状旁腺体积较小,颜色与脂肪或甲状腺组织相似,术中如未明确辨别则极易误切甲状旁腺组织。此外,术中出血以及甲状旁腺自身存在的广泛粘连都极易对手术视野形成干扰^[11]。(2)手术范围。甲状旁腺在甲状腺癌中较甲状腺良性疾病被误切的风险大^[12],可能是由于甲状腺癌手术范围较大所致。(3)甲状旁腺挫伤及血供障碍。术中对甲状旁腺不当的提拉、钳夹及缝扎均会挫伤甲状旁腺而造成甲状旁腺功能减退;血供障碍可能是甲状旁腺功能减退的主要原因,约80%的术后甲状旁腺功能减退是因结扎甲状腺下动脉主干而产生^[13]。有研究^[14]表明,上甲状旁腺的血供有55%来自甲状腺上动脉后支,其余来自甲状腺上、下动脉吻合支,这些血管非常纤细,极易被拉扯分离等刺激影响。有些甲状旁腺没有专门的营养血管,而是由穿过甲状腺实质的终末血管分支提供。甲状旁腺功能减退目前缺乏有效的治疗方法,只能靠口服钙剂及维生素D保持血钙浓度,但是最近甲状旁腺激素替代治疗受到广泛关注,该治疗方法相比应用钙剂和维生素D具有更多优势^[15]。PTH替代药物特立帕肽随着研究进展有望成为治疗永久性甲状旁

腺功能减退的标准药物^[16]。

对于甲状旁腺功能减退并发症最主要是靠术中的积极预防^[17-18]，术者应熟悉解剖结构，进行精确的操作，同时也应具有严谨的手术态度。无论何种术式术中均应对甲状旁腺实施保护，在甲状腺非全切术中，应注意避开甲状旁腺常见解剖位置，对残留的甲状腺不宜缝扎过深，以免使甲状旁腺缺血坏死^[12]。笔者认为，如此高的一过性甲状旁腺功能减退发生率与术后甲状旁腺滋养血管痉挛有关，甲状旁腺滋养血管细如发丝，被 Halsted 等^[20]称为“被茎悬吊的樱桃”。术后使用止血药易导致滋养血管血流瘀滞从而形成血栓影响甲状旁腺功能，故不主张术后常规使用。纳米炭是一种新型的淋巴结示踪剂，可使注射区域甲状腺及引流淋巴结黑色显影，甲状旁腺负显影^[21-23]，减少甲状旁腺损伤概率，如果纳米炭使用得当，可帮助术者在甲状腺手术中更好地分辨及保护甲状旁腺，避免误切^[24]。反之则会污染手术视野，反而影响甲状旁腺和周围组织的鉴别^[25-26]。现在，越来越多甲状旁腺示踪方法出现，如甲状旁腺自发荧光显像技术^[27]、基于光学相干断层成像术的分类识别系统^[28]等。

综上所述，只要实行甲状腺手术，就会对甲状旁腺产生影响；手术范围越大，对术后甲状旁腺功能影响越大，发生甲状旁腺功能减退的概率越高。虽然甲状旁腺识别及保护技术正飞速发展，但预防甲状旁腺功能减退还在于术者对甲状旁腺良好的保护意识以及手术技巧。本研究观察了原位保留甲状旁腺及注射纳米炭情况下甲状旁腺术后功能，未比较不同保护方法下甲状旁腺功能状况，这还有待于进一步探索。

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