

甲状腺切除术对性功能的影响

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摘要

有临床证据显示甲状腺切除术可引起性功能改变, 特别是勃起功能障碍。既往有许多研究探索了甲状腺切除术后患者出现一系列的身体变化, 如甲状腺激素水平异常、慢性虚弱、体重增加、焦虑、抑郁等, 这些身体和心理变化都是性功能改变的原因。目前针对甲状腺切除术对性功能的影响缺乏大样本的研究, 其中的具体机制也尚不明确, 因此未来需进一步研究这两者的关系。本文对甲状腺切除术对性功能的影响进行综述, 本综述提示临床医师应该关注甲状腺切除术对患者性功能产生的不利影响, 也为制定适合的治疗方案提供依据。

关键词

甲状腺切除术, 性功能障碍

The Impact of Thyroidectomy on Sexual Function

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Abstract

There is clinical evidence that thyroidectomy can cause sexual changes, especially erectile dysfunction. Many previous studies have explored a series of physical changes in patients after thy-

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roidectomy, such as abnormal thyroid hormone levels, chronic weakness, weight gain, anxiety, depression, etc. These physical and psychological changes are the causes of sexual function changes. At present, there is a lack of large sample research on the impact of thyroidectomy on sexual function, and the specific mechanism is not clear, so the relationship between the two needs to be further studied in the future. This article reviews the impact of thyroidectomy on sexual function. This review suggests that clinicians should pay attention to the adverse effects of thyroidectomy on the sexual function and provides a basis for formulating a suitable treatment plan.

Keywords

Thyroidectomy, Sexual Dysfunction

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1. 引言

甲状腺是重要的内分泌器官, 其分泌功能受下丘脑 - 垂体 - 甲状腺轴的调节。甲状腺疾病与性功能关系密切, 甲状腺切除术所致甲状腺缺失也可引起性功能变化, 导致患者术后生活质量下降, 据报道约30%的甲状腺癌患者在甲状腺切除术后出现性功能障碍[1]。本综述从多方面分析男性患者行甲状腺切除术后性功能改变的现状, 提示医生应关注甲状腺切除术后的性功能改变, 同时为甲状腺切除术后性功能改变的应对方案提供参考依据。

2. 甲状腺切除术与男性性功能障碍

正常的性功能需要正常的性欲、完整的下丘脑 - 垂体 - 性腺轴、生殖器的神经血管完整性以及性激素的生理水平, 同时甲状腺轴在性功能中也起着重要的作用[2]。男性性功能障碍主要指性欲低下、勃起功能障碍和射精功能障碍(早泄、延迟射精)。既往有许多研究证实甲状腺功能亢进(甲亢)和甲状腺激素减退(甲减)可导致男性勃起功能障碍(ED)、射精功能障碍以及性欲低下[3]-[8]。甲状腺切除术导致神经 - 内分泌调节系统受到极大的影响, 其引起的身体及心理状态变化也可导致性功能障碍。既往关于甲状腺术后性功能改变的研究较为局限, 本文通过回顾甲状腺切除术及性功能障碍相关的文献, 分析男性患者甲状腺切除术对性功能改变的影响。

3. 甲状腺切除术后性功能障碍的可能原因

甲状腺主要由滤泡细胞和滤泡旁细胞组成, 滤泡细胞主要合成和分泌甲状腺激素, 滤泡旁细胞可分泌降钙素及多种调节肽, 甲状腺切除术可从分泌功能、下丘脑 - 垂体 - 性腺轴、生理和心理状态等多方面影响性功能。

3.1. 术后分泌功能变化

3.1.1. 滤泡上皮细胞

甲状腺中滤泡上皮细胞主要合成和分泌甲状腺激素, 氨基酸在滤泡上皮细胞中形成甲状腺球蛋白, 甲状腺球蛋白在滤泡腔中经过碘化后进一步水解为大量的四碘甲腺原氨酸和少量三碘甲腺原氨酸两种甲

甲状腺激素。甲状腺激素可通过复杂的网络信号传导路径对性功能产生重要影响。

术后患者甲状腺激素水平异常时可直接或间接影响性功能。Eleonora 等人在人类阴茎海绵体中发现了甲状腺激素受体 TR α 1, TR α 2 和 TR β 的存在, 这些受体存在于海绵体的内皮细胞和阴茎平滑肌细胞中 [9], 影响阴茎平滑肌的收缩与松弛, 这说明甲状腺激素对阴茎勃起发挥直接控制作用。另外, 甲状腺激素可通过上调 β -肾上腺素受体密度来增强对肾上腺素激动剂的敏感性, 进一步增加交感神经兴奋性 [10], 最终可能导致 ED 或射精障碍, 且肾上腺素能张力的改变可导致阴茎海绵体松弛和静脉闭塞功能发生障碍 [3], 这也是甲状腺激素水平异常导致勃起功能障碍原因之一。甲状腺激素的产生由下丘脑 - 垂体 - 甲状腺轴调节, 而下丘脑 - 垂体 - 甲状腺轴与下丘脑 - 垂体 - 性腺轴是两条平行的调节系统, 它们之间的关系密切, 也可相互影响, 如甲状腺功能减退可导致性腺激素释放激素的减少 [11]。甲状腺激素缺乏通过负反馈作用引起促甲状腺激素和促甲状腺激素释放激素增多, 增多的促甲状腺激素释放激素刺激垂体前叶释放更多的催乳素 (PRL)。高催乳素血症可通过抑制促性腺激素释放激素 (GnRH) 的释放将甲状腺功能减退和性腺功能障碍联系起来, 睾酮、性激素结合球蛋白 (SHBG)、去氢表雄酮 (DHEA) 和 DHEA 代谢物的减少可最终导致性功能障碍, 主要包括 ED 和性欲下降 [4]。甲状腺激素增多则会导致 SHBG 增加, 而 SHBG 与雄激素结合的亲和力比雌激素高, 从而导致相对高雌激素 [10], 同时, 升高的雌二醇可与睾丸间质细胞内相应的受体结合, 抑制睾酮合成酶, 从而降低睾酮生成量 [12], 这也是甲状腺激素异常引起性功能障碍的可能原因之一。一些学者对甲亢动物的研究发现海绵体组织的一氧化氮 (NO) 依赖性松弛受损 [13], 甲亢兔海绵体中乙酰胆碱含量和电刺激诱导的松弛都受到影响, 这表明甲状腺激素对阴茎 NO 形成的影响是动物和人类勃起机制的关键媒介 [14]。

甲状腺切除术导致甲状腺滤泡上皮细胞减少或缺失, 若术后未规范补充甲状腺激素, 长期处于甲状腺激素水平异常状态则可通过以上多条途径影响勃起或射精过程。同时术后 TSH 抑制治疗导致的亚临床甲亢状态对性功能的改变也是不可忽视的, Corona 等人观察到 TSH 小于 0.2 mU/L 的患者射精功能障碍的患病率更高 (57.1% 比 26.5%) [7]。另外, 有研究认为甲状腺激素和睾酮的联合治疗可能是治疗男性甲状腺功能减退诱发的 ED 的治疗方法 [15], 与原发性甲状腺功能异常不同之处在于, 甲状腺的缺失对交感神经通路和下丘脑 - 垂体 - 甲状腺轴的影响可能无法通过补充甲状腺激素来弥补。

3.1.2. 滤泡旁细胞

甲状腺滤泡旁细胞位于滤泡之间和滤泡上皮之间, 能够分泌多种调节肽。学者们在哺乳动物的滤泡旁细胞中发现了多种调节肽, 包括降钙素 (CT)、降钙素基因相关肽 (CGRP)、生长抑素、促甲状腺激素释放激素等。其中降钙素和降钙素基因相关肽 (CT/CGRP) 由同一基因编码翻译出来的两种物质, CGRP 分为 α 和 β 两种亚型 [16], 这两种亚型相似度 > 90%, 具有相似的生物活性 [17]。CGRP 是一种高效、持久的微血管扩张剂, 可通过影响外周动脉血管中的 NO 扩张微血管 [18] [19] [20], C G Stief 等人在猴子中观察到 CGRP 免疫反应性的组织学染色显示海绵状动脉壁和海绵状平滑肌内的神经纤维样染色 [21], 还有研究发现 CGRP 是参与人类阴茎勃起的重要神经递质 [22], 海绵体内 CGRP 可增加海绵动脉血流量, 诱导海绵体平滑肌松弛和静脉流出道闭塞, Champion 等人发现向海绵体内注射 CGRP 可使麻醉猫产生勃起反应, 且加入 CGRP 受体拮抗剂后可减这种勃起反应 [23]。这些研究表明 CGRP 可能在勃起反应中发挥重要作用, 甲状腺被切除后, 由甲状腺滤泡旁细胞分泌的 CGRP 来源消失, 这也是甲状腺切除术引起 ED 的一种可能机制。

3.2. 术后慢性虚弱

甲状腺切除后一些患者出现慢性虚弱、体重增加、生活质量下降等, 这些改变都可能引起性功能改

变。据观察有 25%至 49%的患者在甲状腺全切术后出现慢性虚弱[24] [25] [26] [27], 且年龄、性别、BMI 与虚弱没有明显相关性[26]。即使在 TSH 维持正常水平的前提下, 甲状腺全切术后 12 个月后患者的虚弱程度仍有加重趋势, 而单侧腺叶切除的患者则逐渐好转[25]。在与其他手术相比时, 甲状腺全切组在手术后 6 个月时发生虚弱, 术后 1 年虚弱情况几乎保持不变, 甲状旁腺切除术组术前虚弱评分平均较高, 随访时明显下降, 而胆囊切除术组三个时期之间的虚弱评分没有显著变化[27]。这些研究结果表明甲状腺的分泌功能远比我们目前所研究的多, 一些未知激素的缺失导致了患者术后的身体负向变化, 这种长期处于虚弱的身体状态也是引起性功能变化的可能原因。

3.3. 术后体重增加

一些研究发现甲状腺全切术后患者出现体重增加, Jonklaas 等人对比甲状腺全切术后替代治疗维持甲状腺功能正常的患者、已有甲状腺功能减退行替代治疗的患者以及健康人群的体重变化, 发现甲状腺全切的患者术后 1 年比先前存在甲状腺功能减退症的匹配患者体重增加更多[28]。Rotondi 等人发现甲状腺切除术与体重显著增加有关, 并且术前甲状腺功能、术后 TSH 水平都不影响体重增加[29]。Zihni 等人发现尽管有有效的 LT4 替代, 在接受全甲状腺切除术的患者中, 平均体重指数和腰围在 24 个月和 59 个月的随访中显著增加[30]。甲状腺切除术后出现的体重增加可引起患者的身体和心理状态变化, 从多个角度进一步导致性欲下降或其他类型的性功能改变。

3.4. 术后心理状态改变

甲状腺术后生活质量下降还表现在精神方面[31] [32] [33] [34], 患者行甲状腺切除术后更容易出现沮丧、忧郁、焦虑和注意力下降, 一些患者术后还出现畏寒、怕热、关节疼痛等, 由此导致的整体生活质量下降也包含性功能障碍。甲状腺切除术后激素补充不当导致甲减或甲亢是心理状态改变的原因之一, 甲减引起新陈代谢减慢以及情绪障碍(难治性抑郁症、焦虑等), 甲亢则与心动过速、易怒、情绪不稳定等有关, 这些都可能造成性功能障碍。除此以外, 一些研究发现甲状腺术后患者可出现与激素水平无关的情绪变化, 如甲状腺术后患者更容易出现抑郁、焦虑[35], 以及慢性的心理衰弱[36], 术后发生甲状旁腺功能减退的患者更容易出现认知和情绪障碍[37], 还有一些患者术后无法正常工作导致情绪焦虑[38], 这些心理状态的变化都是正常性功能的不利因素。

4. 小结

男性患者在甲状腺切除术后可能出现勃起功能障碍、射精功能障碍、性欲低下等问题, 严重影响患者的生活质量。本综述分析了甲状腺缺失导致性功能改变的可能原因, 但明确甲状腺与性功能之间的关系仍需大量的研究。在行甲状腺手术治疗前应考虑到手术对性功能的可能影响, 手术后需规范调控甲状腺激素, 同时应关注患者术后的性功能变化, 必要时及时给予医疗干预。

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