

# 经超声射频消融术在颈部疾病治疗中的有效性和安全性

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## 摘要

射频消融(Radiofrequency ablation, RFA)是目前应用最广泛的微创技术之一,已应用于越来越多的临床科室。可弥补传统首选开放手术的不足,为更多患者提供多元化治疗。微创手术已被公认为手术风险高的患者的替代选择,或作为积极希望接受微创治疗的患者的首选。本文将对射频消融治疗甲状腺结节、原发性小而低风险甲状腺癌(即乳头状癌)和甲状旁腺功能亢进症的安全性和有效性评估的文献进行综述。

## 关键词

射频消融, 甲状腺结节, 甲状腺微小乳头状癌, 甲状旁腺功能亢进症

# The Efficacy and Safety of the Ultrasonic Radiofrequency Ablation in the Treatment of Neck Disease

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## Abstract

Radiofrequency ablation (RFA) is one of the most widely used minimally invasive techniques and has been used in more and more clinical departments. It can make up for the shortcomings of the

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traditional first choice of open surgery in China and provide diversified treatment for more patients. Minimally invasive surgery has been recognized as an alternative option for patients at high surgical risk, or as the first choice for patients who actively wish to undergo minimally invasive treatment. This article will review the literature on the safety and evaluation of the effectiveness of radiofrequency ablation in the treatment of thyroid nodules, primary small and low-risk thyroid cancer (*i.e.*, papillary carcinoma), recurrent thyroid cancer and hyperparathyroidism.

## Keywords

Radiofrequency Ablation, Thyroid Nodules, Micropapillary Carcinoma of the Thyroid Gland, Hyperparathyroidism

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## 1. 引言

常见的颈部疾病包括甲状腺和甲状旁腺相关疾病, 如甲状腺良性结节、甲状腺恶性肿瘤、甲状旁腺功能亢进症等。随着各个医院对高分辨率超声的应用, 导致在过去的 30 年中甲状腺结节的检出率大幅上升, 高达 65%, 其中 90% 以上为良性结节[1], 5%~15% 为恶性结节[2]。因甲状腺疾病无任何不适感, 大多都是由常规体检检出, 女性和老人的检出率更高[3]; 其中大多数甲状腺良性结节体积较小, 患者无任何异常感; 但仍然还有一部分患者的良性结节会随时间渐进性增大, 从而导致组织被压迫, 出现呼吸不畅、吞咽不适, 声音改变等[4] [5]。这类良性结节患者则需要择期进行手术治疗。

近年来, 越来越多学者开始尝试使用微创手术治疗甲状腺和甲状旁腺疾病, 弥补了传统手术的短板, 可作为传统开放手术治疗的补充方法, 能满足更广大颈部无瘢痕、有美容需求的人群[4]。包括 95% 乙醇消融(Ethanol ablation, EA)、经皮激光消融甲状腺术(Percutaneous laser ablation, PLA)和通过超声协助的射频消融术(radio-frequency ablation, RFA) [6] [7] [8] [9]; 其中, 95% 乙醇消融术只适合用于治疗甲状腺全囊性结节[10], 由于治疗受众群体的局限, 已经逐渐被射频消融术所取代; 激光消融和射频消融在最新指南中都被推荐为一线治疗方法[11] [12] [13], 两者的受众群体和安全性相似, 但目前有研究表明在良性结节的体积减小率方面, 射频消融术更占优。

射频消融术是通过 200~1200 kHz 范围内振荡得到的高频交流电产生的摩擦和传导热的配合从来破坏目标组织[14] [15]。射频消融术为局麻手术[14], 术前须在皮肤穿刺部位和甲状腺肿物的周围注射足量的局麻药(常用 2% 利多卡因); 用射频穿刺针穿入甲状腺瘤体内, 在超声的提示引导下不断调整进针方向, 在多个方向对肿物进行消融[16]。目前对于可以行甲状腺射频消融术治疗的患者, 还没有严格的结节大小或体积的定义标准[16] [17], 对于该手术的指征较为宽泛。射频消融术是通过减小结节的体积, 来减轻大的甲状腺结节引起颈部美容问题或压力症状, 从而改善临床问题[18]。

本文章我们回顾了通过经超声协助的射频消融术治疗甲状腺良性结节、原发小的低风险甲状腺癌(即乳头状癌)和甲状旁腺功能亢进症的安全性和有效性的文献。

## 2. 研究现状

### 2.1. 射频消融在甲状腺良性结节治疗中的应用

对于有症状的甲状腺良性结节患者, 已经满足了传统开放性手术的手术指征, 但是传统手术并不是

对所有患者都是最优选。传统手术包括开放性甲状腺肿物切除和腔镜下甲状腺肿物切除术, 虽然传统手术是一种被广泛使用且有效的治疗方案, 但其创伤性大, 恢复慢, 影响患者颈部皮肤美观, 术后并发症多见[18], 如术后甲状腺功能的永久减退, 需终身服用甲状腺素替代治疗[19], 术中是可能会损伤到一侧或两侧的喉返神经, 引起患者术后声音改变; 术中也可能损伤喉上神经, 术后患者出现吞咽困难、饮水呛咳、音调低钝等; 多发性甲状腺良性结节几乎占据整个甲状腺组织, 术中极有可能做甲状腺全切或者近全切, 那么术后发生永久性甲状旁腺减退的几率极高, 术后出现低钙血症[20]、严重者窒息需气管切开等, 患者需要长期口服大量的钙剂、促进钙吸收的药物, 还要补充其他缺失的电解质。对于腔镜手术术后可能出现高碳酸血症而导致死亡, 还可能出现皮下气肿等。且对于因年龄大、肺功能差、严重心血管疾病, 无法耐受全麻的患者, 无法选择传统手术治疗[15]。近年来, 越来越多医院开始尝试局麻下甲状腺肿物射频消融术, 作为甲状腺良性结节传统治疗的安全有效的替代方法, 能满足更广大人群的不同需求[17][20]。

许多报告已经阐述了通过超声协助的射频消融术(radio-frequency ablation, RFA)在减少甲状腺良性结节体积方面的长期、短期的有效性(6~48个月)和安全性。Wei-Che Lin 等人的回顾性研究中共纳入了 136 例因考虑到传统手术后的并发症和美观性而拒绝行传统手术治疗的甲状腺良性结节患者; 随着术后 6 个月的随访, 通过超声协助的射频消融术(radio-frequency ablation, RFA)术后的整体结节体积显著减少, 中结节(10 ml~30 ml)结节体积减少率(volume reduction rate, VRR)显著高于小结节(<10 ml)结节体积减少率(volume reduction rate, VRR)。在一篇前瞻性单中心队列研究中, 3 个月和 12 个月时的平均总结节体积减少率(VRR)分别为  $68\% \pm 16\%$  和  $82\% \pm 13\%$ 。在射频消融术后 12 个月, 较小的囊性和主要为囊性结节的平均 VRR 比其他组高 8.8% 和 14.5% [21]。

在另一项多中心回顾性研究中比较了通过超声协助的射频消融术(radio-frequency ablation, RFA)和激光消融(Laser Ablation, LA)在治疗甲状腺良性结节的有效性和安全性, 纳入了通过超声协助的射频消融术和激光消融(Laser Ablation, LA)治疗后跟踪随访 5 年的患者, 两者均可降低患者甲状腺良性结节的体积; 然而通过超声协助的射频消融术术后较激光消融术后有更低的再生和再处理率, 20% 接受通过超声协助的射频消融术(radio-frequency ablation, RFA)治疗的患者(43/216)和 38% 接受激光消融(Laser Ablation, LA)治疗的患者(72/190)中检查发现甲状腺结节有再生的情况; 通过超声协助的射频消融术(radio-frequency ablation, RFA)再处理率为 14%, 然而, 激光消融(Laser Ablation, LA)再处理率为 32% [22][23]。

## 2.2. 射频消融在甲状腺微小乳头状癌治疗中的应用

全球甲状腺癌确诊率一直处于上升趋势, 大多数是甲状腺乳头状癌[22], 其中包含甲状腺乳头状微小癌(papillary thyroid microcarcinoma, PTMC), 世界卫生组织首次将直径小于等于 10 mm 的甲状腺乳头状癌定义为甲状腺微小乳头状癌[21]-[26]。越来越多地区开始尝试使用经通过超声协助的射频消融术治疗甲状腺乳头状微小癌, 尤其是对于无法耐受传统手术或拒绝接受传统手术治疗的人群, 可作为传统开放手术的替代治疗法[18][23][24][27]。在一项荟萃分析中, 此次研究中共纳入分析了 1770 例经通过超声协助的射频消融术(通过超声协助的射频消融术(radio-frequency ablation, RFA)治疗的甲状腺微小乳头状癌(papillary thyroid microcarcinoma, PTMC)患者, 从而探究经通过超声协助的射频消融术对于甲状腺乳头状微小癌(papillary thyroid microcarcinoma, PTMC)的有效性和安全性。其中, 接受通过超声协助的射频消融术(radio-frequency ablation, RFA)治疗的 PTMC 患者在通过超声协助的射频消融术(radio-frequency ablation, RFA)后的 12 个月时的随访检查中, 完全消失率的合并比例为 66% [21], 即为随访超声检查结果提示肿瘤组织完全消失的患者占比; 12 个月后平均甲状腺肿瘤体积缩小率的汇总比例为 92.1%, 其中主要并发症的发生率汇总比例为 0%。

另一项为期 5 年的回顾性随访研究中, 共纳入了 174 例甲状腺乳头状微小癌(papillary thyroid microcarcinoma, PTMC)患者作为研究对象, 研究分为传统开放手术组与通过超声协助的射频消融术组; 与通过超声协助的射频消融术(radio-frequency ablation, RFA)组相比, 传统手术组手术时间更长, 失血量更多, 住院时间更长, 治疗费用也更高, 而传统手术组的整体生活质量低于射频消融组; 传统手术组共有 3 名患者是有出现了终身性的喉返神经破坏和终身性的甲状旁腺功能减退, 而射频消融组并没有患者出现并发症; 在随访期间传统手术组中有 1 例患者未经治疗的中央颈部淋巴结转移, 通过超声协助的射频消融术(radio-frequency ablation, RFA)组随访期间无颈部淋巴结转移的患者; 两组患者均未发现远处转移 [24]。

### 2.3. 射频消融在甲状旁腺功能亢进症治疗中的应用

甲状旁腺功能亢进症是因为四个甲状旁腺中的一个或多个过度分泌甲状旁腺激素所致[25], 以甲状旁腺激素(Parathyroid hormone, PTH)升高和高钙血症为特征, 药物治疗无效时则需手术进行干预, 甲状旁腺切除术和甲状旁腺微创手术的治愈率相似, 然而微创手术术后恢复快, 并发症少[19] [28] [29] [30]; 所以虽然甲状旁腺切除术是无症原发性甲状旁腺功能亢进症患者(primary hyperparathyroidism, PHPT)的首选治疗方法[30] [31], 但对于无法耐受甲状旁腺切除手术或拒绝进行全麻手术治疗的患者可以有其他的选择手术方式, 可以进行超声引导射频消融术(radio-frequency ablation, RFA), 目前甲状旁腺微创手术已经得到了广泛的普及[28] [29], 尤其对于单个甲状旁腺腺瘤疾病的患者[13]和无症状 PHPT 患者[30]更为推荐, 无症原发性甲状旁腺功能亢进(PHPT)患者是某些(PHPT)者缺乏传统上与 PTH 分泌过量或高钙血症相关的特定症状或体征, 中国 PHPT 无症状患者目前也处于不断增加状态[32]。

在一项前瞻性研究中招募了 2018 年 9 月 1 日至 2021 年 1 月 31 日内浙江省人民医院的 39 名甲状旁腺功能亢进症患者, 其中经治疗后有 38 名患者实现了完全消融, 手术成功率为 97.4% (38/39), 术后症状都有明显的减轻。FAR 术后 12 个月内血清 PTH、钙和磷水平显著改善, 甲状旁腺腺瘤体积显著减少。通过超声协助的射频消融术(radio-frequency ablation, RFA)术后 6 个月和 12 个月, 生化治愈率分别为 82.1% (32/39)和 84.4% (27/32), 临床治愈率分别为 100% (39/39)和 96.9% (31/32), 复发率仅为 2.6% (1/39)。在通过超声协助的射频消融术(radio-frequency ablation, RFA)后 1、3、6 和 12 个月的随访中, 分别有 44.7% (17/38)、34.3% (12/35)、15.8% (6/38)和 12.5% (4/32)的患者出现了甲状旁腺激素水平的升高和喉返神经麻痹发生率为 5.1% (2/39) [19]。

在 Eun Ju Ha 等人的这项回顾队列性研究中, 共纳入了符合标准的 19 例甲状旁腺功能亢进症患者, 其中包括 11 例原发性甲状旁腺功能亢进症患者(PHPT)和 8 例继发性甲状旁腺功能亢进症患者(Secondary hyperparathyroidism, SHPT); 两组患者均行通过超声协助的射频消融术, 在术后 12 个月内的随访中甲状旁腺腺瘤的平均大小和体积都有显著减小(前者  $p=0.003$ , 后者  $p=0.001$ ); 在 PHPT 组, 术后 12 个月中的甲状旁腺激素(PTH)和 Ca 水平均逐渐降低并恢复到正常水平, 然而在 SHPT 组内无显著变化[29]。

在该回顾性研究中, 收集了 10 例无法耐受甲状旁腺腺瘤切除术风险评估的患者, 这些患者都是有单个甲状旁腺腺瘤所引起的甲状旁腺功能亢进症, 这些患者都是因自身基础疾病无法耐受全麻手术; 该研究是对其进行了超声引导下甲状旁腺射频消融术的有效性和安全性的评估, 经手术治疗后患者均实现了甲状旁腺腺瘤完全消融, 其 PTH 水平在术后一周内恢复正常, 血钙水平在术后 72 h 内即恢复正常水平。并且术后只有一例患者发生了声音改变, 但是在三周后即已恢复, 其余均无不良反应[33] [34]。Ying Wei [35]团队首次收集了大量样本, 进而研究报告了超声引导下甲状旁腺腺瘤射频消融术治疗继发性甲状旁腺功能亢进症的安全性、可行性和有效性; 共纳入 67 例 PHPT 患者。随访 12 个月后, 大多数患者的消融区域已经基本吸收。该研究报告的治愈率为 86.4% (19/22), PTH 水平在消融术后的 12 个月内恢复正常水



平; 术后出现了轻微并发症, 如声音嘶哑和低钙血症, 均在术后 2~3 月后得到自行缓解恢复, 在此期间并没有进行特殊治疗。

### 3. 研究结论

在目前的研究中, 术后短期的随访内, 射频消融术与传统手术的肿物体积减小率并无明显差异, 我们预估射频消融术可能会在临床上有更广泛更常规的使用。但是目前的研究样本量可收集的数量较少, 还需要更大样本量的进一步验证; 另外随访时长较短, 需更长期的术后追踪, 证实该治疗手段的更长期有效性; 我们仍然需要在不同人群中进行大型的前瞻性试验。

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