Advances in Clinical Medicine 临床医学进展, 2023, 13(3), 3709-3715
Published Online March 2023 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2023.133532

Hans汉斯

继发性甲状旁腺功能亢进症治疗进展

刘　毅，钟　玲*

重庆医科大学附属第二医院肾内科，重庆

收稿日期：2023年2月13日；录用日期：2023年3月9日；发布日期：2023年3月16日

摘　要

继发性甲状旁腺功能亢进(secondary hyperparathyroidism, SHPT)是慢性肾脏病(CKD)病人常见的严重并发症之一。甲状旁腺通过分泌甲状旁腺激素调节血钙水平来维持内分泌稳态。然而，SHPT会导致全身多个器官和系统的结构发生改变，这不仅会降低患者的生活质量，还会影响死亡率。因此对SHPT患者有效治疗及规范管理显得尤为重要，我们对SHPT的治疗做一综述，并且将重点叙述微创治疗进展。

关键词

慢性肾脏病，继发性甲状旁腺功能亢进，甲状旁腺激素，微创治疗

Progress in the Treatment of Secondary Hyperparathyroidism

Yi Liu, Ling Zhong*

Department of Nephrology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing

Received: Feb. 13th, 2023; accepted: Mar. 9th, 2023; published: Mar. 16th, 2023

Abstract

Secondary hyperparathyroidism (SHPT) is one of the common and serious complications in patients with chronic kidney disease (CKD). Parathyroid gland maintains endocrine homeostasis by secreting parathyroid hormone to regulate the level of blood calcium. However, SHPT can lead to structural changes in multiple organs and systems throughout the body, which will not only reduce the quality of life of patients, but also affect mortality. Therefore, the effective treatment and standardized management of patients with SHPT are particularly important. We review the treatment of SHPT, and will focus on the progress of minimally invasive treatment.

*通讯作者。

文章引用: 刘毅, 钟玲. 继发性甲状旁腺功能亢进症治疗进展[J]. 临床医学进展, 2023, 13(3): 3709-3715.
DOI: 10.12677/acm.2023.133532

Keywords

Chronic Kidney Disease, Secondary Hyperparathyroidism, Parathyroid Hormone, Minimally Invasive Treatment

Copyright © 2023 by author(s) and Hans Publishers Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/
Open Access

1. 引言

慢性肾脏病(chronic kidney disease, CKD)的患病率日益增长，已成为影响公共卫生健康的全球性问题。据统计我国 CKD 的患病率高达 10.8% (11.7%~15.1%) [1]。继发性甲状旁腺功能亢进(secondary hyperparathyroidism, SHPT)是 CKD 病人常见的严重并发症之一。其特征是体内钙磷代谢紊乱引起甲状旁腺代偿性增生及全段甲状旁腺素(intact parathyroid hormone, iPTH)的分泌增加。持续的甲状旁腺激素分泌异常增多和血钙、血磷的异常，可引起骨骼系统、神经精神系统、血液系统及心脑血管等多系统的损害[2] [3] [4]，是全因和心血管死亡率的独立危险因素[5]，成为透析患者的长期生活困扰，严重影响患者日常生活及工作，是目前亟需解决的临床问题。因此，对 SHPT 患者有效治疗及规范管理显得尤为重要。本文将结合国内外最新报道，对 SHPT 的综合治疗做一综述，我们将重点叙述微创治疗进展，为临床医生制定个体化治疗决策提供参考。

2. 发病机制

SHPT 的发病机制复杂，随着肾功能逐渐恶化，肾小管合成 1,25-(OH)2-D3 的 1-α 羟化酶减少，使 1,25-(OH)2-D3 水平不断降低，导致肠道对钙的吸收降低，血钙下降，造成低钙血症。CKD 患者肾小球滤过率下降，肾脏对血清磷的清除能力减弱，随着肾衰竭尿磷排泄不断减少造成体内磷潴留，形成高磷血症。最新的机制研究提示，成骨细胞产生成纤维生长因子-23 (fibroblast growth factor-23, FGF-23)在 SHPT 的发展中起着重要作用，随着 FGF-23 的增加进一步降低活性维生素 D 的水平，共同对抗维生素 D 介导的抑制 PTH 生成和促进肠道重吸收磷的生理活动[6]。并且 FGF23 已被证明能促进慢性肾病小鼠甲状旁腺细胞增殖和甲状旁腺激素分泌[7]。

细胞外钙和活性维生素 D 浓度是调节甲状旁腺激素分泌的主要因素，CaSR 是细胞外钙浓度的传感器，CaSR 检测到低钙血症，使 PTH 基因表达和 PTH 释放增加，以恢复正常的血钙[8]。VDR 检测到 1,25-(OH)2-D3 水平降低，导致 PTH 基因抑制系统的抑制，使得 PTH 生成增多[9]。而在尿毒症动物模型和 SHPT 患者的甲状旁腺组织中 CaSR 和 VDR 表达降低[10] [11] [12] [13]，这种异常与 SHPT 的进展密切相关。高磷血症、低钙血症、PTH 抵抗及活性维生素 D 受体和改敏感受体减少等因素的共同刺激导致 CKD 患者形成 SHPT。

3. 内科治疗

在早期阶段，SHPT 可以通过内科治疗进行有效管理。比如磷结合剂、维生素 D 及其类似物、钙敏感受体激动剂、钙盐等在疾病的早期阶段可以在一定程度上控制患者甲状旁腺激素水平。目前临床上常用的磷结合剂是司维拉姆，它通过迅速降低血磷的浓度来抑制甲状旁腺细胞增殖，进而使甲状旁腺激素水平降低[14] [15]。维生素 D 及其类似物常用药物包括骨化三醇、骨化醇和阿法骨化醇，通过抑制破骨

细胞、促进成骨细胞和肠道钙吸收来调节钙磷代谢，抑制甲状旁腺激素的产生[16]。甲状旁腺中的钙敏感受体是重要治疗靶点，西那卡塞是最常使用的拟钙剂，同时也是钙敏感受体的变构激活剂，它通过增加钙敏感受体对细胞外钙的敏感性，并与受体变构结合以抑制甲状旁腺激素的分泌[17] [18]。这些药物可能出现严重的胃肠道反应、药物之间的相互作用以及高钙、高磷血症等副作用极大地降低了患者的依从性，同时随着患者病情的进展，耐药性增加会使疗效进一步降低[14] [19] [20] [21] [22]。这使得单纯药物治理方案无法成功实现对 SHPT 的充分控制。

4. PTX

对于药物治疗失败或晚期 SHPT 患者仍需要外科手术干预[23]。目前，主要的手术方法是甲状旁腺切除术(PTX)。外科 PTX 手术主要有全甲状旁腺切除术(tPTX)、次全甲状旁腺切除术(sPTX)、全甲状旁腺切除加自体移植术(tPTX-AT)。以上手术方式可以有效控制 HPT、iPTH、钙、磷等生化指标，皮肤瘙痒、骨骼畸形、皮肤异位钙化等临床症状也有所改善，减少并发症和死亡率[24] [25]。但是由于甲状旁腺周围解剖结构较为复杂，有许多神经和其他重要结构，使得甲状旁腺体手术技术要求高，并且 PTX 具有侵入性、创伤大，手术的可重复性较差。许多一般情况欠佳的患者，尤其是心肺功能较差的患者，不能耐受 PTX。术后复发性 SHPT、甲状旁腺功能减退的发生率也很高。这些因素都导致外科手术仍然有一定的局限性。

5. 微创治疗

随着微创技术的发展，微创治疗已应用到了 SHPT 治疗领域。SHPT 的微创治疗自上世纪九十年代即有报道，初期主要采用超声引导下无水乙醇注射等[26]。近十年来，以微波、射频为主的热消融技术在 SHPT 的治疗中逐步进入临床医生的视野，具有侵袭性小、可重复性高的优势，在安全性和有效性方面并不逊色于 PTX [27] [28] [29]。并且，在最新的研究中经皮局部注射维生素 D 类似物也为治疗 SHPT 提供了新的临床治疗方案。

5.1. 超声引导下经皮无水乙醇注射

超声引导下经皮无水乙醇注射术也称化学性 PTX。研究显示经皮在甲状旁腺腺体内注射无水乙醇，使组织硬化，可减少病变甲状旁腺的体积、数目，并且可有效降低血清 iPTH 值[30] [31]。虽然经皮注射乙醇最早使用，但因为长期疗效不确定和无水乙醇弥散的不可控性等因素使其的应用有所限制[32]。虽然无水乙醇注射术相较于其他手术方式治疗效果有局限性，但同时具有一定的安全性，或可作为切除术后的辅助治疗方案。

5.2. 热消融治疗

热消融术是逐渐发展的超声介入技术，原理是利用微波或射频技术使组织中的极性分子(主要是水)发生高频振荡产生热量，通过升高温度破坏局部组织，使组织发生凝固性坏死，但对周围组织的损伤很小[33]。与 PTX 相比，热消融降低了低钙血症的风险，具有侵袭性小、易于操作、恢复快和可重复使用的优点而被青睐于手术风险较高的甲旁亢患者[33]。迄今为止，射频消融(RFA)，微波消融(MWA)和高强度聚焦超声(HIFU)被用于甲状旁腺功能亢进的治疗[34]。然而一项 meta 分析结果表明，热消融和 PTX 都是 SHPT 的有效治疗选择，但是热消融术增加了甲状旁腺功能亢进症持续存在或复发的风险[33]。

有临床研究显示 RFA 能适度有效地改善血清钙、血清磷、PTH 水平，降低低钙血症的发病率，并且与 PTX + AT 相比 RFA 的并发症，如神经损伤，出血，感染，创伤和发烧，更少，恢复时间更短[35] [36]。同时，严重的低钙血症一直是热消融术后的关键问题，这可能与治疗的时间和疗程有关。相关研究人员

通过评估单次与两次射频治疗 SHPT 患者对低钙血症的影响发现，进行两次 RFA 患者的低钙血症相对较轻，尤其是基线 ALP > 566 mmol/L 的患者应进行两次 RFA，以避免消融术后出现严重的低钙血症[37]。但是关于 RAF 是否有益于长期预后的研究尚不足。

MWA 已广泛用于介入治疗，特别是在肿瘤的治疗中。与 RFA 一样作为微创治疗的方式之一，它还有许多其他优点，包括更可预测的消融区、同时治疗多个病变的能力、大消融量和快速消融时间[38]。超声引导下 MWA 经验证为可行、安全、有效地破坏甲状旁腺组织，维持正常的血钙和磷浓度，也可用于治疗 SHPT 异位结节[39] [40] [41]。MWA 术后主要并发症包括喉返神经损伤和低钙血症[42]。在操作中应经常注意邻近的组织和器官，如食管和喉返神经，尤其是对于 MWA 前已经有不可逆单侧喉返神经损伤的患者。然而，一项研究表明大多数(16/26)维持性血液透析的重度 SHPT 患者对 MWA 没有明显反应[35]，因此不建议作为此类患者的一线治疗方案。

目前关于 HIFU 治疗 HPT 的报道相对较少。有研究者于 2010 年首次提出将 HIFU 用于 PHPT 治疗。研究涉及的所有四名患者接受了 2 次 HIFU 手术一年后，其中 3 名患者的 PTH 水平和血清钙水平恢复到正常水平[43]。在 2012 年报道了 5 例重度 SHPT 患者在接受 1 次或多次 HIFU 治疗后，血清 iPTH 显著降低，同时血清钙和磷的控制也得到了改善[44]。副作用主要包括局部水肿、声带活动性和声音的短暂性损害。HIFU 作为非侵入式的热消融方法具有不可替代的优势，但样本数较少，还需更多的研究明确其安全性及有效性。

5.3. 超声引导下活性维生素 D 类药物注射

帕立骨化醇作为一种合成维生素 D2 类似物，通过选择性结合维生素 D 受体抑制 PTH 的分泌[45]。几项研究报道，帕立骨化醇是一种有效且安全的药物，可成功且快速地将完整的甲状旁腺激素浓度降至继发性甲状旁旁腺功能亢进的目标水平[46] [47] [48] [49]。

有研究证明静脉注射帕立骨化醇相较于骨化三醇能更快更有效地降低血清 PTH [50]。特别是，最近有研究表明经皮局部注射活性维生素 D 类似物可以直接作用于腺体，有效抑制腺体合成、分泌 PTH，使腺体体积缩小[51]。在一项纳入 46 例终末期肾脏病 SHPT 患者的研究中，经皮局部注射帕立骨化醇可有效降低患者的 iPTH，在经过 2 次治疗后可使甲状旁腺体积显著减少[52]。血清钙代谢紊乱是射频消融术、甲状旁腺切除术和外周使用帕立骨化醇后最常见的并发症。值得注意的是在此项研究中观察到术后未出现低钙血症，并且在为期 6 月的随访中未发生不良事件[52]，其安全性得到一定证实。但是因为随访时间短，其长期疗效和远期并发症需要进一步研究。

6. 未来具有治疗潜力的方法

光动力疗法最初是为治疗癌症而开发的，现在也被应用于皮肤、性病和血管疾病等各种临床领域。研究发现，大鼠腹腔注射 5-氨基乙酰丙酸(5-ALA)后，光照甲状旁腺可破坏甲状旁腺组织来治疗 SHPT [53]。这为 SHPT 的临床治疗提供了新的思路。

光遗传学是一项很有前途的强大技术，它可以利用光对神经元活动和细胞过程进行可逆控制[54]。有研究证实通过光刺激 SHPT 患者来源的甲状旁腺细胞可以诱导抑制人类甲状旁腺激素，机制为甲状旁腺的光激活通过去极化膜电位、升高细胞内钙和调节细胞信号通路来抑制甲状旁腺激素的分泌[55]。这为调节甲状旁腺并恢复继发性甲状旁腺功能亢进患者甲状旁腺激素释放提供了新方向。

7. 总结

近年来对 SHPT 的治疗方法不断改进。除了传统药物及外科手术治疗外，还有不断发展的创新微创治疗，这提高了干预的成功率，减少了术后并发症，也为相关疾病的患者提供了新的治疗方案。然而，

由于药物价格昂贵、术后并发症和较高的死亡率，目前对于 SHPT 的治疗仍面临挑战。未来进一步有效的药物开发、手术或微创质量的提高和治疗方案的个体化，对延缓或预防疾病的进展，提高患者的生活质量和生存率尤其重要。

参考文献

[1] Lv, J.C. and Zhang, L.X. (2019) Prevalence and Disease Burden of Chronic Kidney Disease. *Advances in Experimental Medicine and Biology*, **1165**, 3-15. https://doi.org/10.1007/978-981-13-8871-2_1

[2] Ishida, H., Komaba, H., Hamano, N., *et al*. (2020) Skeletal and Mineral Metabolic Effects of Risedronate in a Rat Model of High-Turnover Renal Osteodystrophy. *Journal of Bone and Mineral Metabolism*, **38**, 501-510. https://doi.org/10.1007/s00774-020-01095-0

[3] Tanaka, M., Komaba, H. and Fukagawa, M. (2018) Emerging Association between Parathyroid Hormone and Anemia in Hemodialysis Patients. *Therapeutic Apheresis and Dialysis*, **22**, 242-245. https://doi.org/10.1111/1744-9987.12685

[4] Kono, K., Fujii, H., Watanabe, K., Goto, S. and Nishi, S. (2021) Relationship between Parathyroid Hormone and Renin-Angiotensin-Aldosterone System in Hemodialysis Patients with Secondary Hyperparathyroidism. *Journal of Bone and Mineral Metabolism*, **39**, 230-236. https://doi.org/10.1007/s00774-020-01139-5

[5] Yang, B., Lu, C., Wu, Q., *et al*. (2016) Parathyroid Hormone, Cardiovascular and All-Cause Mortality: A Meta-Analysis. *Clinica Chimica Acta*, **455**, 154-160. https://doi.org/10.1016/j.cca.2016.01.034

[6] Quarles, L.D. (2012) Role of FGF23 in Vitamin D and Phosphate Metabolism: Implications in Chronic Kidney Disease. *Experimental Cell Research*, **318**, 1040-1048. https://doi.org/10.1016/j.yexcr.2012.02.027

[7] Kawakami, K., Takeshita, A., Furushima, K., *et al*. (2017) Persistent Fibroblast Growth Factor 23 Signalling in the Parathyroid Glands for Secondary Hyperparathyroidism in Mice with Chronic Kidney Disease. *Scientific Reports*, **7**, Article No. 40534. https://doi.org/10.1038/srep40534

[8] Brown, E.M. (1983) Four-Parameter Model of the Sigmoidal Relationship between Parathyroid Hormone Release and Extracellular Calcium Concentration in Normal and Abnormal Parathyroid Tissue. *The Journal of Clinical Endocrinology & Metabolism*, **56**, 572-581. https://doi.org/10.1210/jcem-56-3-572

[9] Demay, M.B., Kiernan, M.S., DeLuca, H.F. and Kronenberg, H.M. (1992) Sequences in the Human Parathyroid Hormone Gene That Bind the 1,25-Dihydroxyvitamin D3 Receptor and Mediate Transcriptional Repression in Response to 1,25-Dihydroxyvitamin D3. *Proceedings of the National Academy of Sciences of the United States of America*, **89**, 8097-8101. https://doi.org/10.1073/pnas.89.17.8097

[10] Brown. A.J., Ritter, C.S., Finch, J.L. and Slatopolsky, E.A. (1999) Decreased Calcium-Sensing Receptor Expression in Hyperplastic Parathyroid Glands of Uremic Rats: Role of Dietary Phosphate. *Kidney International*, **55**, 1284-1292. https://doi.org/10.1046/j.1523-1755.1999.00386.x

[11] Yano, S., Sugimoto, T., Tsukamoto, T., *et al*. (2000) Association of Decreased Calcium-Sensing Receptor Expression with Proliferation of Parathyroid Cells in Secondary Hyperparathyroidism. *Kidney International*, **58**, 1980-1986. https://doi.org/10.1111/j.1523-1755.2000.00370.x

[12] Fukuda, N., Tanaka, H., Tominaga, Y., *et al*. (1993) Decreased 1,25-Dihydroxyvitamin D3 Receptor Density Is Associated with a More Severe Form of Parathyroid Hyperplasia in Chronic Uremic Patients. *Journal of Clinical Investigation*, **92**, 1436-1443. https://doi.org/10.1172/JCI116720

[13] Patel, S.R., Ke, H.Q., Vanholder, R., Koenig, R.J. and Hsu, C.H. (1995) Inhibition of Calcitriol Receptor Binding to Vitamin D Response Elements by Uremic Toxins. *Journal of Clinical Investigation*, **96**, 50-59. https://doi.org/10.1172/JCI118061

[14] Lai, T., Frugoli, A., Barrows, B. and Salehpour, M. (2020) Sevelamer Carbonate Crystal-Induced Colitis. *Case Reports in Gastrointestinal Medicine*, **2020**, Article ID: 4646732. https://doi.org/10.1155/2020/4646732

[15] Xiao, X., Liu, Y., Zhong, X., *et al*. (2019) Sevelamer Hydrochloride Suppresses Proliferation of Parathyroid Cells during the Early Phase of Chronic Renal Failure in Rats. *Nephrology* (*Carlton*, *Vic*.), **24**, 127-133. https://doi.org/10.1111/nep.13215

[16] Thadhani, R.I., Rosen, S., Ofsthun, N.J., *et al*. (2020) Conversion from Intravenous Vitamin D Analogs to Oral Calcitriol in Patients Receiving Maintenance Hemodialysis. *Clinical Journal of the American Society of Nephrology*, **15**, 384-391. https://doi.org/10.2215/CJN.07960719

[17] Danese, M.D., Lubeck, D., Belozeroff, V., *et al*. (2020) Real World Use and Effects of Calcimimetics in Treating Mineral and Bone Disorder in Hemodialysis Patients. *American Journal of Nephrology*, **51**, 815-822. https://doi.org/10.1159/000510360

[18] Bucharles, S.G.E., Barreto, F.C. and Riella, M.C. (2019) The Impact of Cinacalcet in the Mineral Metabolism Markers

of Patients on Dialysis with Severe Secondary Hyperparathyroidism. *Journal Brasileiro de Nefrologia*, **41**, 336-344. https://doi.org/10.1590/2175-8239-jbn-2018-0219

[19] Tsukamoto, Y., Moriya, R., Nagaba, Y., *et al*. (1995) Effect of Administering Calcium Carbonate to Treat Secondary Hyperparathyroidism in Nondialyzed Patients with Chronic Renal Failure. *American Journal of Kidney Diseases*, **25**, 879-886. https://doi.org/10.1016/0272-6386(95)90570-7

[20] Pandey, R., Zella, J.B., Zhu, J.G., *et al*. (2017) Pharmacokinetics of a New Oral Vitamin D Receptor Activator (2-Methylene-19-Nor-(20S)-1α,25-Dihydroxyvitamin D3) in Patients with Chronic Kidney Disease and Secondary Hyperparathyroidism on Hemodialysis. *Drugs in R & D*, **17**, 597-605. https://doi.org/10.1007/s40268-017-0210-z

[21] Fukagawa, M., Shimazaki, R. and Akizawa, T. (2018) Head-to-Head Comparison of the New Calcimimetic Agent Evocalcet with Cinacalcet in Japanese Hemodialysis Patients with Secondary Hyperparathyroidism. *Kidney International*, **94**, 818-825. https://doi.org/10.1016/j.kint.2018.05.013

[22] Harada, K., Fujioka, A., Konno, M., *et al*. (2019) Pharmacology of Parsabiv® (Etelcalcetide, ONO-5163/AMG 416), a Novel Allosteric Modulator of the Calcium-Sensing Receptor, for Secondary Hyperparathyroidism in Hemodialysis Patients. *European Journal of Pharmacology*, **842**, 139-145. https://doi.org/10.1016/j.ejphar.2018.10.021

[23] 田文, 贺青卿, 姜可伟, 庄大勇, 周鹏. 慢性肾功能衰竭继发甲状旁腺功能亢进外科临床实践专家共识[J]. 中国实用外科杂志, 2016, 36(5): 481-486.

[24] Neagoe, R.M., Sala, D.T., Voidazan, S., *et al*. (2021) A Comparative Analysis of Three Types of Parathyroidectomies in Renal Hyperparathyroidism Single Centre Prospective Cohort of 77 Patients. *Annali Italiani di Chirurgia*, **92**, 6-12.

[25] 田武国, 汪玲俐, 赵健洁. 继发性甲状旁腺功能亢进手术治疗的现状及进展[J]. 重庆医科大学学报, 2022, 47(11): 1373-1375.

[26] Stratigis, S., Stylianou, K., Mamalaki, E., *et al*. (2008) Percutaneous Ethanol Injection Therapy: A Surgery-Sparing Treatment for Primary Hyperparathyroidism. *Clinical Endocrinology* (*Oxford*), **69**, 542-548. https://doi.org/10.1111/j.1365-2265.2008.03238.x

[27] 魏莹, 卓莉, 于明安, 王淑荣, 车颖, 钱林学, 余建军, 郭建琴. 继发性甲状旁腺功能亢进热消融治疗专家共识(2021 版) [J]. 中日友好医院学报, 2021, 35(4): 195-202.

[28] Hu, Z., Han, E., Chen, W., *et al*. (2019) Feasibility and Safety of Ultrasound-Guided Percutaneous Microwave Ablation for Tertiary Hyperparathyroidism. *International Journal of Hyperthermia*, **36**, 1129-1136. https://doi.org/10.1080/02656736.2019.1684576

[29] Ren, M., Zheng, D., Wu, J., *et al*. (2022) Efficacy and Safety of Radiofrequency Ablation versus Parathyroidectomy for Secondary Hyperparathyroidism in Dialysis Patients: A Single-Center Retrospective Study. *Scientific Reports*, **12**, Article No. 10289. https://doi.org/10.1038/s41598-022-14623-x

[30] 张凌, 刘亚绵. 超声引导下甲状旁腺无水酒精注射治疗继发性甲状旁腺功能亢进症[J]. 中华内科杂志, 2001(11): 58-60+77.

[31] 杜文泽, 陈乐, 吴晓云, 贾军利, 张卫东, 翟江. 超声引导下无水乙醇注射治疗继发性甲状旁腺功能亢进症的临床观察及安全性分析[J]. 中国临床医生杂志, 2017, 45(7): 73-76.

[32] 黄庆龙, 周健美. 继发性甲状旁腺功能亢进症的治疗现状[J]. 安徽医学, 2016, 37(5): 636-638.

[33] Gong, L., Tang, W., Lu, J. and Xu, W. (2019) Thermal Ablation versus Parathyroidectomy for Secondary Hyperparathyroidism: A Meta-Analysis. *International Journal of Surgery*, **70**, 13-18. https://doi.org/10.1016/j.ijsu.2019.08.004

[34] Chen, Z., Cheng, L., Zhang, W. and He, W. (2022) Ultrasound-Guided Thermal Ablation for Hyperparathyroidism: Current Status and Prospects. *International Journal of Hyperthermia*ermia, **39**, 466-474. https://doi.org/10.1080/02656736.2022.2028907

[35] Diao, Z., Wang, L., Li, D. and Liu, W. (2017) Efficacy of Microwave Ablation for Severe Secondary Hyperparathyroidism in Subjects Undergoing Hemodialysis. *Renal Failure*, **39**, 140-145. https://doi.org/10.1080/0886022X.2016.1256307

[36] Peng, C., Zhang, Z., Liu, J., *et al*. (2017) Efficacy and Safety of Ultrasound-Guided Radiofrequency Ablation of Hyperplastic Parathyroid Gland for Secondary Hyperparathyroidism Associated with Chronic Kidney Disease. *Head & Neck*, **39**, 564-571. https://doi.org/10.1002/hed.24657

[37] Zeng, Z., Peng, C.Z., Liu, J.B., *et al*. (2020) Efficacy of Ultrasound-Guided Radiofrequency Ablation of Parathyroid Hyperplasia: Single Session vs. Two-Session for Effect on Hypocalcemia. *Scientific Reports*, **10**, Article No. 6206. https://doi.org/10.1038/s41598-020-63299-8

[38] Jahangeer, S., Forde, P., Soden, D. and Hinchion, J. (2013) Review of Current Thermal Ablation Treatment for Lung Cancer and the Potential of Electrochemotherapy as a Means for Treatment of Lung Tumours. *Cancer Treatment Reviews*, **39**, 862-871. https://doi.org/10.1016/j.ctrv.2013.03.007

[39] Zhuo, L., Peng, L., Zhang, Y.M., *et al*. (2017) US-Guided Microwave Ablation of Hyperplastic Parathyroid Glands: Safety and Efficacy in Patients with End-Stage Renal Disease—A Pilot Study. *Radiology*, **282**, 576-584. https://doi.org/10.1148/radiol.2016151875

[40] Li, X., Wei, Y., Shao, H., *et al*. (2019) Efficacy and Safety of Microwave Ablation for Ectopic Secondary Hyperparathyroidism: A Feasibility Study. *International Journal of Hyperthermia*ermia, **36**, 646-652. https://doi.org/10.1080/02656736.2019.1627429

[41] Li, X., An, C., Yu, M. and Peng, L. (2019) US-Guided Microwave Ablation for Secondary Hyperparathyroidism in Patients after Renal Transplantation: A Pilot Study. *International Journal of Hyperthermia*, **36**, 322-327. https://doi.org/10.1080/02656736.2019.1566580

[42] Ma, H., Ouyang, C., Huang, Y., *et al*. (2020) Comparison of Microwave Ablation Treatments in Patients with Renal Secondary and Primary Hyperparathyroidism. *Renal Failure*, **42**, 66-76. https://doi.org/10.1080/0886022X.2019.1707097

[43] Kovatcheva, R.D., Vlahov, J.D., Shinkov, A.D., *et al*. (2010) High-Intensity Focused Ultrasound to Treat Primary Hyperparathyroidism: A Feasibility Study in Four Patients. *American Journal of Roentgenology*, **195**, 830-835. https://doi.org/10.2214/AJR.09.3932

[44] Kovatcheva, R.D., Vlahov, J.D., Stoinov, J.I., *et al*. (2012) High-Intensity Focussed Ultrasound (HIFU) Treatment in Uraemic Secondary Hyperparathyroidism. *Nephrology Dialysis Transplantation*, **27**, 76-80. https://doi.org/10.1093/ndt/gfr590

[45] Robinson, D.M. and Scott, L.J. (2005) Paricalcitol: A Review of Its Use in the Management of Secondary Hyperparathyroidism. *Drugs*, **65**, 559-576. https://doi.org/10.2165/00003495-200565040-00008

[46] Abboud, H., Coyne, D., Smolenski, O., *et al*. (2006) A Comparison of Dosing Regimens of Paricalcitol Capsule for the Treatment of Secondary Hyperparathyroidism in CKD Stages 3 and 4. *American Journal of Nephrology*, **26**, 105-114. https://doi.org/10.1159/000092033

[47] Coyne, D., Acharya, M., Qiu, P., *et al*. (2006) Paricalcitol Capsule for the Treatment of Secondary Hyperparathyroidism in Stages 3 and 4 CKD. *American Journal of Kidney Diseases*, **47**, 263-276. https://doi.org/10.1053/j.ajkd.2005.10.007

[48] Trillini, M., Cortinovis, M., Ruggenenti, P., *et al*. (2015) Paricalcitol for Secondary Hyperparathyroidism in Renal Transplantation. *Journal of the American Society of Nephrology*, **26**, 1205-1214. https://doi.org/10.1681/ASN.2013111185

[49] Cruzado, J.M., Lauzurica, R., Pascual, J., *et al*. (2018) Paricalcitol versus Calcifediol for Treating Hyperparathyroidism in Kidney Transplant Recipients. *Kidney International Reports*, **3**, 122-132. https://doi.org/10.1016/j.ekir.2017.08.016

[50] Zhang, T., Ju, H., Chen, H. and Wen, W. (2019) Comparison of Paricalcitol and Calcitriol in Dialysis Patients with Secondary Hyperparathyroidism: A Meta-Analysis of Randomized Controlled Studies: Paricalcitol and Calcitriol for Secondary Hyperparathyroidism. *Therapeutic Apheresis and Dialysis*, **23**, 73-79. https://doi.org/10.1111/1744-9987.12760

[51] 李丽, 李灿霞. 超声引导下治疗继发性甲状旁腺亢进的价值[J]. 中国超声诊断杂志, 2005(4): 300-301.

[52] Xie, S., Yu, Y., Liu, Y., *et al*. (2022) Effectiveness and Safety of Ultrasound-Guided Local Paricalcitol Injection in Treating Secondary Hyperparathyroidism in ESRD: A Retrospective Study. *Journal of Clinical Medicine*, **11**, 6860. https://doi.org/10.3390/jcm11226860

[53] Miyakogawa, T., Kanai, G., Tatsumi, R., *et al*. (2017) Feasibility of Photodynamic Therapy for Secondary Hyperparathyroidism in Chronic Renal Failure Rats. *Clinical and Experimental Nephrology*, **21**, 563-572. https://doi.org/10.1007/s10157-016-1335-z

[54] Campos, P. and Herbison, A.E. (2014) Optogenetic Activation of GnRH Neurons Reveals Minimal Requirements for Pulsatile Luteinizing Hormone Secretion. *Proceedings of the National Academy of Sciences of the United States of America*, **111**, 18387-18392. https://doi.org/10.1073/pnas.1415226112

[55] Liu, Y., Zhang, L., Hu, N., *et al*. (2022) An Optogenetic Approach for Regulating Human Parathyroid Hormone Secretion. *Nature Communications*, **13**, 771. https://doi.org/10.1038/s41467-022-28472-9