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· 述评 ·

## 经口入路腔镜甲状腺手术的现状与展望

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### 摘要

经口入路腔镜甲状腺手术 (TOET) 是一种经自然腔道的腔镜手术 (NOTES)。2008年 Witzel 等首次在新鲜尸体和活体猪上完成经口底入路的腔镜甲状腺手术尝试, 国内王存川教授则首次在国际上提出了三孔经口腔前庭的腔镜甲状腺手术 (TOETVA) 技术。这也是目前应用最广泛的 TOET 入路方式, 其主要优势是对口底的结构损伤少, 器械操作也较灵活; 体表完全无疤痕, 根治疾病的同时, 能满足美容和隐私保护的双重需求。TOETVA 拥有从上而下视角, 由于其天然的视角优势, 解决了中央区低位淋巴结清扫的问题。因此, TOETVA 是分化型甲状腺癌合并中央区淋巴结转移病例的优选术式。自 2013 年该技术诞生, 中国国内首先开始发展, 2015 年多个中心开始尝试, 到目前为止, 国内已经有数百家单位可以开展此术式。TOETVA 的技术要点和难点主要包括: 空间的建立与维持、喉返神经的显露与保护、甲状旁腺辨认及功能保留、淋巴结清扫。相比经胸前入路, TOET 有更长的学习曲线, 一般需要 40~50 例操作才能克服, 同开放手术和其他入路的无疤痕腔镜甲状腺手术比较, 除了常规出血、神经损伤、旁腺损伤、皮瓣损伤等并发症外, 尚有以下特殊的并发症, 包括: 颈神经损伤, 感染, CO<sub>2</sub> 气体栓塞, 胸膜损伤, 下颌区域功能异常反应等。TOETVA 具有较好的肿瘤根治和整形美容效果, 在过去的十年中经历了飞速的发展。它作为 NOTES 手术体系的一部分, 代表了内镜外科、微创外科发展的趋势, 科学应用和推广 TOETVA 技术是未来工作的重点。毫无疑问, 严格遵循手术适应证是重中之重, 只有坚持“治病第一, 功能保护第二, 美容第三”的基本原则, 才能科学、规范地推广 TOETVA。此外, 教学医院应发挥带头作用, 积极推动指南共识的普及, 并在临床工作中不断示教手术操作。适应证拓展、操作方法改进和新技术研发是 TOETVA 未来研究的热点。TOETVA 的手术适应证并非绝对, 随着操作者技术的不断提升, 手术难度可以逐渐增大。但需要指出, 任何超出当前指南专家共识的术式, 都属于非常规手术, 目前 TOETVA 适应证的拓展, 主要以颈侧区清扫为代表, 但清扫 II 区相当困难。因此, 对于 TOETVA 颈侧区清扫能否达到根治性效果, 目前存在争议。本文结合国内外文献及本中心相关经验, 对于该入路的现状及展望作一综述。

### 关键词

甲状腺切除术; 自然腔道内镜手术; 口腔

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## Current status and prospects of transoral endoscopic thyroid surgery

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### Abstract

Transoral endoscopic thyroidectomy (TOET) is a type of natural orifice transluminal endoscopic surgery (NOTES). In 2008, Witzel et al. first attempted transoral endoscopic thyroidectomy through the oral floor in fresh cadavers and live pigs. Professor Wang Cunchuan in China was the first to propose the three-port transoral endoscopic thyroidectomy vestibular approach (TOETVA) internationally. Currently, this is the most widely used transoral endoscopic approach for thyroid surgery, with the main advantages of minimal damage to the oral floor structures and greater instrument maneuverability. It leaves no visible scars on the skin surface, meets the dual requirements of disease cure and aesthetic appearance, and ensures privacy protection. TOETVA provides a top-down view, which, due to its natural visual advantage, resolves the problem of low-level lymph node dissection in the central region. Therefore, TOETVA is the preferred surgical procedure for cases of differentiated thyroid cancer with central lymph node metastasis. Since its introduction in 2013, TOETVA has been initially developed in China, and multiple centers started attempting it in 2015. To date, there are already hundreds of institutions in China capable of performing this procedure. The technical key points and challenges of TOETVA mainly include the establishment and maintenance of space, exposure and protection of the recurrent laryngeal nerve, identification and preservation of the parathyroid glands, and lymph node dissection. Compared to the transthoracic approach, transoral endoscopic thyroid surgery has a steeper learning curve, typically requiring 40-50 cases to overcome. In comparison to open surgery and other scarless endoscopic thyroidectomy approaches, in addition to common complications such as bleeding, nerve injury, parathyroid injury, and flap injury, transoral endoscopic thyroid surgery has the following special complications: mental nerve injury, infection, CO<sub>2</sub> gas embolism, pleural injury, and abnormal functional reactions in the mandibular region, among others. TOETVA has shown good tumor control and aesthetic outcomes, experiencing rapid development over the past decade. As part of the NOTES surgical system, it represents the trend of endoscopic and minimally invasive surgery. The future focus is on scientific application and promotion of TOETVA technology, with strict adherence to surgical indications being of utmost importance. Only by adhering to the basic principles of "treating the disease first, preserving function second, and considering aesthetics third" can TOETVA be scientifically and standardizedly promoted. Additionally, teaching hospitals should take the lead in actively promoting the dissemination of guidelines and consensus, while continually demonstrating surgical procedures in clinical practice. Expanding indications, improving surgical techniques, and developing new technologies are the hotspots of future research in TOETVA. The surgical indications for TOETVA are not absolute, and as the operator's skills improve, the surgical difficulty can gradually increase. However, it should be noted that any procedure beyond the current guidelines and expert consensus is considered unconventional surgery. Currently, the expansion of indications for TOETVA is mainly represented by lateral neck dissection, but dissection of level II lymph nodes remains challenging. Therefore, there is controversy regarding whether TOETVA can achieve a radical effect with lateral neck dissection. This article provides an overview of the current status and prospects of this approach based on domestic and international literature and our center's relevant experience.

**Key words** Thyroidectomy; Natural Orifice Endoscopic Surgery; Mouth

**CLC number** R653.2

近三十年来分化型甲状腺癌表现出有别于其它恶性肿瘤的三大特点：发病率持续增长，病死率呈持平或下降，患者群体年轻化且生存期长<sup>[1]</sup>。患者对于生活质量的需求，特别是颈部美容的需求日趋显现。微创美容治疗的理念应运而生，以胸前、腋窝、经口等多种入路为代表的颈部无瘢痕腔镜甲状腺手术（scarless in the neck endoscopic thyroidectomy, SET）不断涌现并发展迅速<sup>[2-7]</sup>。其中经口入路腔镜甲状腺手术（transoral endoscopic thyroidectomy, TOET）与其他入路相比，有其独特的优势和操作技巧，本文结合本中心的经验和相关文献报道，就此入路的发展历史与现状，操作技巧及未来发展趋势作一总结和探讨。

## 1 TOET的设计理念与优势

无论是胸前还是腋窝等入路，体表疤痕仍难以完全避免；而对低位中央区淋巴结清扫的限制也是这些入路备受争议的原因之一。TOET是经自然腔道的腔镜手术（natural orifice transluminal endoscopic surgery, NOTES）<sup>[8-9]</sup>，将切口隐藏在口腔内，达到体表完全无疤的效果。TOET从2008年Witzel等<sup>[10]</sup>动物实验开始至今已有14年，经过了人体尸体实验到人体手术的探索，经历了从口底，颌下到经口腔前庭入路的探索<sup>[11-12]</sup>。最终目前甲状腺外科界都普遍认为，经口腔前庭的腔镜甲状腺手术（transoral endoscopic thyroidectomy vestibular approach, TOETVA）既创伤及并发症可控，安全，操作相对简便，同时可以在直视下做中央区淋巴结清扫，没有视觉盲区，不存在对肿瘤根治效果的质疑；作为一种距离入路，也可以更好地应用于肥胖人群及肌肉发达男性<sup>[13]</sup>。

目前的TOETVA体系最早由Nakajo等<sup>[7]</sup>奠定，他们对8例患者进行前瞻性研究，采用口腔前庭下唇后方正中2.5 cm横切口，长隧道进入颈部皮下作为观察孔，双侧唇角进入操作孔。使用克氏针抬起颈部前皮肤，通过免充气方式创建和维持皮下操作空间。此后大部分中心开展的TOETVA均以此

为蓝本，略有改进。如笔者中心通过低CO<sub>2</sub>灌注压联合特制悬吊拉钩进行混合空间维持<sup>[14]</sup>，其优点是手术空间较稳定，对于体型条件较好患者，也可以通过单纯低压灌注维持，操作相对简单。方静团队<sup>[15]</sup>改进了免充气悬吊体系，加大拉力空间更稳定，烟雾气体干扰相对较少。彭小伟团队<sup>[16]</sup>通过解剖颈神经的方法（在颈神经内侧或分支间置入5 mm小Trocar）来减少颈神经损伤。也有团队增加腋窝作辅助操作口降低操作难度，利用颈部mini-lap提供牵拉辅助以利于神经和旁腺保护。这些尝试都旨在完善经口手术的操作和流程，提高效率 and 安全性。经过10年改进和临床证实<sup>[17]</sup>，许多中心都发表了TOET的初步经验和早期结果，泰国的Anuwong等<sup>[18]</sup>回顾性分析了425例大样本TOETVA，与216例开放手术对比，TOETVA的手术时间明显延长，而长期和短期并发症发生率总体相当，包括切口感染率。

综上所述，目前国际国内，经口腔前庭入路三孔法是经口的主流方式，优势是不涉及口底，手术入径短，损伤少，器械操作灵活；体表完全无疤，淋巴结清扫到位，满足治病美容隐私保护的多重需求，因此具有良好的临床应用前景<sup>[19]</sup>。

## 2 TOET的适应证发展与变迁

作为从上而下视角的TOETVA，由于其天然的视角优势，解决了中央区低位淋巴结清扫的问题，因此，是分化型甲状腺癌合并中央区淋巴结清扫时优先选择。从2013年该术式诞生，中国国内首先开始发展，2015年多个中心开始尝试，到目前为止，国内已经有数百家单位可以或尝试开展此术式。

根据“经口腔前庭入路腔镜甲状腺手术专家共识（2018版）”<sup>[20]</sup>，对于有较强美容需求的患者且符合以下条件可行TOETVA。(1) 如为良性结节，最大径≤4 cm。对于囊性为主的良性结节，在有条件的中心可以适当放宽指征。(2) 分化型甲状腺癌，肿瘤直径≤2 cm，且无颈侧区淋巴结转移或

者全身远处器官转移,无影像学中央区淋巴结转移提示或转移淋巴结直径 $\leq 2$  cm且未融合固定。(3) II度以下肿大的原发性甲状腺功能亢进。(4)最大径 $\leq 4$  cm的胸骨后甲状腺肿。禁忌证为:(1)因口腔条件(口腔畸形、口腔局部感染等)导致手术操作受限或感染风险增加者。(2)髓样癌、甲状腺未分化癌。(3)合并严重的甲状腺炎性疾病。(4) III度肿大的甲状腺功能亢进。(5)肿瘤靠近喉返神经(recurrent laryngeal nerve, RLN)入喉处或较大肿瘤位于上极。(6)既往有颈部手术史、消融治疗史或颈部放射史。(7)伴有其他器官或系统合并症不能耐受手术创伤或全身麻醉者。

### 3 TOET的技术要点与难点

#### 3.1 空间建立与维持

TOETVA切口选择,观察孔位于口腔前庭,下唇系带前方,远离牙龈根部1 cm以上,为横行或者弧形切口;操作孔位于两侧第一前磨牙根部水平,远离牙龈根部1 cm处。为纵行切口。或者下唇正中单孔2~3 cm的大切口。空间建立的层次在颈阔肌后方,通过钝性分离导引,电刀或者超声刀分离,建立从上至甲状软骨上缘,下至胸骨颈静脉切迹,两侧至胸锁乳突肌胸骨头外侧缘的操作空间<sup>[14]</sup>。

对于手术空间的维持,目前最主流的方法是通过低CO<sub>2</sub>灌注压联合特制悬吊拉钩进行混合空间维持,其优点是手术空间较稳定,同时对于体型条件较好患者,也可以通过单纯低压灌注维持,操作相对简单。

#### 3.2 RLN暴露与保护

左右侧的RLN暴露方法略有不同。

右侧RLN暴露有两种方法,一是入喉处暴露<sup>[21]</sup>,自上而下神经隧道法保护切除甲状腺:将甲状腺上级离断,暴露至环状软骨和第一气管环连接处食道壁前侧,靠近上位旁腺内侧暴露,至暴露上位旁腺后,将甲状腺整体往中间牵拉,以上位旁腺、甲状腺外侧缘和食道前壁形成区域为标志,入喉处暴露神经;如果能使用RLN监测就更容易定位。此处血管丛丰富,分离时容易出血,要注意动作轻柔,辨认神经予以保护后再行凝闭血管。二是在RLN下方贴近右侧颈总动脉处暴露。以胸骨颈静脉切迹上方2~2.5 cm投影处为标记,从

下而上,逐步分离RLN并离断神经前方的组织,直到入喉处。此法的优势是即使没有神经监测,也容易定位和暴露神经,缺点是从下而上需要多次逐步分离组织,速度相对较慢<sup>[22-24]</sup>。

左侧RLN的暴露一般选择入喉处暴露法。多数术者都是右利手,而右侧操作钳容易被气管阻挡,暴露难度大;要学会采用左手持钳分离与超声刀。这对术者的技术要求较高,应具有双手操作的能力与技巧。左利手的操作者,同样可以从下极开始显露RLN;右利手的操作者,也可以从甲状腺下极的内侧显露RLN,尤其在行甲状腺次全切除治疗良性疾病之时。

#### 3.3 甲状旁腺辨认和保护

根据笔者的经验,TOETVA对于上位旁腺的保护其实相比其他术式更有优势。因为将上级血管离断后,可以紧贴上级背侧将甲状腺上级翻起,有利于保护上动脉后支。而下位旁腺保护由于甲状腺阻挡的问题,难以辨认,同时缺少有效提拉,有时即使辨认也难以保护。可以通过引入mini-lap提拉等方式,提高保护效率。必要时采用主动移植策略。

#### 3.4 淋巴结清扫

TOETVA,一般采用和甲状腺同时en-bloc淋巴结清扫的方法。在清扫过程中要注意三点<sup>[25-26]</sup>:(1)善用拉钩和口腔内支撑器械,用于暴露术区,包括牵拉带状肌,推气管等。(2)神经要全层显露,由于常规只有左手一把牵拉器械,建议先离断神经周围纤维血管组织,在处理气管和动脉周围组织时,有利于利用拉钩等进行牵拉,提供一定张力。(3)低位淋巴结清扫时要注意保护无名血管,避免误伤胸膜等。

### 4 TOET特有的并发症

TOET除了常规甲状腺手术出血、神经损伤、旁腺损伤、皮瓣损伤等并发症外,尚有以下特殊的并发症,应予以关注<sup>[27]</sup>。(1)颈神经损伤:TOETVA的特有并发症,发生率为1%~5%<sup>[28-29]</sup>,临床表现有下唇/下巴感觉下降(麻木和/或感觉异常和/或无法感知热液体)。笔者中心的经验是操作时尽量避免暴露颈神经,两侧5 mm的操作孔切口要远离第一前磨牙根部,避免损伤颈神经主干。(2)感染:为各种入路均有可能发生的并发症,多发生



于术后3~7 d, 据报道<sup>[30]</sup>, 经过术前完善准备, 经口的感染发生几率并不高于其他入路方式。处理仍以局部引流, 联合抗生素使用为主, 需排除气管与食道的损伤。(3) CO<sub>2</sub>气体栓塞: TOET罕见的并发症, 虽发生概率较低, 后果严重, 多发生于管径较粗的静脉所致。主要表现为心率先增快后减慢, 甚至心律失常, 同时伴有呼气末CO<sub>2</sub>压力升高以及血压下降, 严重者会出现心跳骤停。紧急治疗包括立即吸入100% O<sub>2</sub>, 大量补液以减少血管阻力并增加侧支循环血流。采取头低脚高左侧卧位, 可降低脑血管栓塞风险<sup>[31]</sup>。(4) 胸膜损伤: 中央区淋巴结清扫过低, 层次掌握不合理所致。术中发现, 应尽量缝合破口; 对于缝合困难者, 常规放置高负压引流, 延迟拔管, 避免发生气胸; 理论上, 所有切口缝合良好, 胸膜损伤是没有影响的。如有气胸者, 按照原则处理。(5) 下颌区域功能异常反应: 与开放手术颈前区功能障碍类似, TOET术后部分患者有下颌区域不适主诉, 甚至有些患者难以缓解。包括下颌麻木, 活动受限, 张口异常, 咀嚼不适等, 但外观和颈神经功能均没有异常。可能与局部疤痕粘连, 下颌肌群损伤有关。建议建腔过程尽量避免损伤下颌肌群, 隧道宜长宜窄<sup>[32-33]</sup>。

## 5 TOET的发展和展望

TOETVA具有较好的肿瘤根治和整形美容效果, 在过去的十年中经历了飞速的发展。TOETVA作为NOTES手术体系的一部分, 代表了内镜外科、微创外科发展的趋势和将来。对TOETVA未来的发展, 可以从手术规范化推广、适应证拓展, 操作方法改进和新技术研发等4个方面进行展望。

### 5.1 手术规范化推广

目前, 国内对TOETVA已经形成专家共识, 这对于规范化国内TOETVA手术操作具有划时代的意义。

如何面向基层医院推广和普及手术, 是未来十年的工作重点。毫无疑问, 严格遵循手术适应证是重中之重, 只有坚持“治病第一, 功能保护第二, 美容第三”的基本原则, 才能科学、规范地推广TOETVA。此外, 教学医院应发挥带头作用, 积极推动指南共识的普及, 并在临床工作中不断示教手术操作。

对于基层医院的初学者而言, 为了能更好地渡过学习曲线, 应选择合适的病例。女性, 右侧中下极肿瘤, 不伴桥本甲状腺炎或甲亢, 无临床淋巴结转移的患者, 是最佳的病例。有条件的单位可以配备神经监测, 对于初学者保护RLN和缩短学习曲线有一定帮助<sup>[34]</sup>。

### 5.2 适应证拓展

TOETVA的手术适应证并非绝对, 随着操作者技术的不断提升, 手术难度可以逐渐增大。但需要指出, 任何超出当前指南专家共识的术式, 都属于非常规手术, 主要面向对于有坚实硬件基础的医院(特别是大型三甲和教学医院), 以及具备相当手术经验的术者(特别是学科带头人)。超适应证手术需要符合3个条件, 第一是对患者病情的可控性有科学和严谨的评估, 第二是术者能够娴熟和规范地完成腺叶切除和中央区清扫, 第三是充分知情同意后患者有强烈手术需求。

目前TOETVA适应证的拓展, 主要以颈侧区清扫为代表, 已经有经口入路的择区性侧区清扫的报道<sup>[35]</sup>, 个别中心开展胸口联合颈侧区清扫, 将经口作为经胸入路侧区清扫的补充<sup>[36]</sup>。也有部分学者<sup>[37]</sup>对T3期肿瘤进行了尝试。总的来说, TOETVA自上而下的视角, 对清扫IV区具有明显优势, 有经验的术者亦能胜任III区清扫, 但清扫II区相当困难。因此, 对于TOETVA颈侧区清扫能否达到根治性效果, 目前存在争议。国内最新的研究指出, 对于合适的病例, 可以选择超择区清扫(III、IV区清扫)作为颈侧区清扫的基本术式, 但这有待未来大宗临床数据加以佐证<sup>[38-41]</sup>。

### 5.3 操作方法改进

对于空间的维持, 目前混合空间维持法是最主流、最易操作的方法。近几年, 部分学者开始尝试免充气TOET。Fang等<sup>[42]</sup>采用免充气悬吊法来维持手术空间, 通过吸引器持续吸引保持腔内气体流通, 减少烟雾并提供支撑, 具有视野更清晰、规避高碳酸血症或者空气栓塞等严重并发症的优点。但免充气方法在建腔操作初期, 手术0-p空间狭小, 对操作者的技术要求高, 对于初学者难度较大<sup>[43-44]</sup>。

对于颈神经的保护, 目前最主流的方法是通过合理化设计切口和Trocar穿刺方向, 规避颈神经走行区域。彭小伟团队<sup>[16]</sup>通过主动解剖显露颈神经的方法(在颈神经内侧或分支间置入5 mm小

Trocar)来减少神经损伤,特别是减少神经主干的损伤。但对于初学者来说,显露神经本身也有一定的难度与损伤,所以目前仍以规避法为主。

对于甲状旁腺的保护,经典TOETVA术式的En-bloc淋巴结清扫方法可能导致下位旁腺无法原位保留。研究提出的“胸腺层面-血管-下位甲状旁腺”概念,为原位保留下位旁腺及其血供提供了理论依据<sup>[45-47]</sup>。也有研究<sup>[48]</sup>认为,通过近红外自体荧光显像技术可以更好地识别和保护甲状旁腺。总之,如何改善TOETVA淋巴结清扫方法,以更好地精化解剖下位甲状旁腺,实现其血供的原位保留,将是后续研究的重点之一。

#### 5.4 新技术研发

神经监测对于TOETVA来说是一项非常重要的新技术,能够帮助初学者发现并保护RLN,减少RLN相关手术并发症。近期的研究<sup>[49-50]</sup>发现持续性RLN监测较间断性RLN监测对于减少神经的损伤更有优势。TOETVA开展初期由于担心气管插管对操作的影响,因此设计使用经鼻插管。由于鼻插管尺寸限制,不能使用神经监测。本中心在国际上率先采用经口插管,将气管导管固定于左侧口角,并不妨碍手术操作,从而使TOETVA可以常规使用神经监测技术<sup>[21]</sup>。这对于TOETVA的发展和适应证的拓展,起到了推动作用。目前在本中心,TOETVA的适应证拓展到巨大肿瘤,胸骨后甲状腺肿,甚至Ⅲ度甲亢也有开展和尝试。未来,随着国产神经监测的研发和推广,以及医疗成本的降低,更多的基层医院将有条件引入神经监测技术。这对于推广TOETVA将会有非常大的帮助。

## 6 总结

TOET在过去近二十年的发展过程中,已经形成了以TOETVA为首选入路的规范化手术体系。科学应用和推广TOETVA技术是未来工作的重点。适应证拓展、操作方法改进和新技术研发是TOETVA未来研究的热点。

利益冲突:所有作者均声明不存在利益冲突。

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