

甲状腺乳头状癌颈侧区清扫术治疗现状

黑 虎,秦建武

(郑州大学附属肿瘤医院,河南省肿瘤医院,河南 郑州,450003)

摘 要:甲状腺乳头状癌容易发生颈部淋巴结转移,侧颈部是常见受累部位之一。颈部清扫术是治疗甲状腺癌颈转移的标准手段,但其清扫范围存在争议,应视颈部淋巴结转移的不同区域而定。广泛的侧颈部转移,建议治疗性的改良根治性颈清扫;颈部淋巴结转移不广泛者,特别是术前影像学检查或查体未发现ⅡB区和ⅤA区转移者,建议行ⅡA、Ⅲ、Ⅳ、ⅤB区的择区性颈清扫;cN₀患者不主张行预防性颈清扫术。建议同时采用cN分期和pN分期来区别对待颈部淋巴结。

关键词:甲状腺乳头状癌;侧颈部;淋巴结清扫

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Current Treatment Status of Lateral Neck Dissection in Papillary Thyroid Cancer

HEI Hu, QIN Jian-wu

(The Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, 450003 China)

Abstract: Papillary thyroid cancer is prone to cervical lymph node metastasis. One of the regions that are commonly involved is lateral neck compartment. The standard procedure for oncologic treatment of cervical metastases is neck dissection. However, the extent of neck dissection is controversial with the different levels of cervical lymph node involvement. Therapeutic modified radical neck dissection is recommended for cases of gross node metastasis, while selective neck dissection including level ⅡA, Ⅲ, Ⅳ, and ⅤB is recommended for those without evidence of involvement in level ⅡB and level ⅤA by preoperative imaging or clinical evaluation. Prophylactic neck dissection is not recommended for lymph node-negative patients. To distinguish different status of neck lymph nodes, combined utilization of clinical and pathologic nodal staging is proposed.

Key words: papillary thyroid cancer; lateral neck compartment; neck dissection

乳头状癌(papillary thyroid cancer, PTC)是分化型甲状腺癌中最常见病理类型,约占85%以上^[1]。颈部淋巴结转移率高,中央区为20%~90%^[2],侧颈区可达40%左右^[3]。

侧颈区清扫术(lateral neck dissection)是治疗甲状腺乳头状癌颈转移首选的、最有效的治疗手段,国内外学者对这一原则已达成共识^[4,5]。按治疗目的不同,将颈清扫术分为治疗性颈清扫和预防性颈清扫。按清扫范围不同,分为根治性颈清扫(radical neck dissection, RND)、改良根治性颈清扫(modified radical neck dissection, MRND),又称功能性颈清扫

(FND)和择区性颈清扫(selective neck dissection, SND)]。

改良根治性颈清扫是治疗甲状腺癌颈转移的常用术式,但在具体操作细节方面仍存在较大分歧。主要表现在以下两方面:cN+(clinically node positive)患者,清扫范围仍无统一标准;cN₀(clinically node negative)患者,是否需行预防性颈清扫。

1 cN+的清扫范围

“cN+”是指通过术前查体、影像学检查或术中探查发现明显转移淋巴结^[6]。是否所有cN+病例均需行Ⅱ~Ⅴ区(颈部淋巴结分区见Figure 1)清扫仍

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通讯作者:秦建武, E-mail: qinjianwu62@163.com

不明确,部分学者认为甲状腺乳头状癌颈侧区淋巴结转移常发生于ⅡA~Ⅳ区,ⅡB和Ⅴ区(特别是ⅤA区)较少转移,而ⅡB、ⅤA区清扫会增加副神经和耳大神经损伤几率。

1.1 Ⅴ区是否需常规清扫

支持Ⅴ区清扫的学者多考虑肿瘤治疗的彻底性,认为颈清扫手术为常规手术,如果由经验丰富医生操作,手术并发症较低或可以接受。Kupferman等^[8]对70例甲状腺癌颈清扫患者进行研究,发现Ⅴ区转移率53%,并且与甲状腺癌多灶性和侧颈部受累程度相关。2009年,Spriano等^[9]对1503例PTC患者进行回顾性研究,Ⅴ区转移率仅为8%,但该作者也建议行Ⅱ~Ⅴ区广泛清扫。

建议行Ⅴ区选择性清扫的学者认为:仅当多个区域存在转移时,Ⅴ区才发生转移^[10]。另外,虽然有16%患者存在Ⅴ区隐匿性转移风险,但是多伴随Ⅳ区有明显转移或超声提示^[11]。同时,如果仅对术前发现Ⅴ区转移患者行清扫手术,术后Ⅴ区复发率未见升高^[12]。

对Ⅴ区亚区(ⅤA区、ⅤB区)淋巴结转移规律的研究,较多文献支持仅行ⅤB区清扫。Eskander等^[13]的荟萃分析发现ⅤA区转移率(8%)明显低于ⅤB区(22%)。Roh等^[10]将副神经以上定为ⅤA区,副神经以下定为ⅤB区,发现所有转移都发生在ⅤB区。但值得说明的是,Roh对ⅤA区、ⅤB区的划分与传统的颈部淋巴结分区(以环状软骨下缘作为ⅤA、ⅤB区分界标志)^[7]存在偏差。2009年,Farrag等^[14]对53例患者研究发现,虽然16例发生Ⅴ区转移,但没有一例转移到ⅤA区。当Ⅳ区有阳性转移,或Ⅱ、Ⅲ区有多个阳性淋巴结,或术前彩超、术中探查提示ⅤB区转移时,才行ⅤB区清扫术^[15]。由于副神经位于ⅤA区,从而避免副神经损伤。多数情况下,术中只需将胸锁乳突肌向外方牵拉,在胸锁乳突肌深方将ⅤB区与Ⅱ~Ⅳ区整块切除^[15]。仅当ⅤA和ⅤB区都有转移时,才常规清扫Ⅴ区,此时Ⅴ区清扫为治疗性清扫。

1.2 ⅡB区是否需常规清扫

支持ⅡB区常规清扫的学者认为:甲状腺癌颈转移常累及多个区域,尽管ⅡB区转移率低,但存在跳跃转移可能,应常规清扫^[16]。2013年,Eskander等^[13]对2002~2012年18项研究进行荟萃分析,显示Ⅱ区转移率为53.4%,其中ⅡA区53.1%,ⅡB区

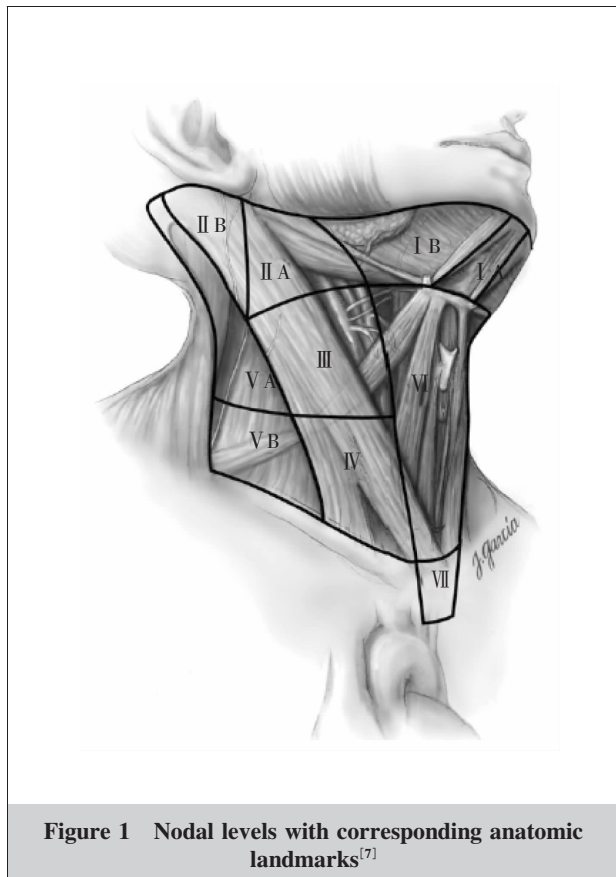


Figure 1 Nodal levels with corresponding anatomic landmarks^[7]

15.5%,该作者亦建议常规清扫ⅡB区。

反对ⅡB区常规清扫的学者则认为:如果没有ⅡA区或颈部多个区域广泛转移,ⅡB区转移可能性很低,ⅡB区清扫必要性不大^[17]。Vayisoglu等^[17]的研究中,只有一例发生ⅡB区转移,同时伴有ⅡA区、Ⅲ区、Ⅳ区和Ⅴ区多发转移。另外5例患者发生ⅡA转移,但ⅡB区未受累。Koo等^[18]发现ⅡB区转移率为11.8%(9/76)。并且,仅当ⅡA区存在阳性淋巴结或侧颈部多个区域转移时,ⅡB区转移率才会升高。在Lee等^[19]研究中,所有ⅡB区转移亦伴有ⅡA区转移。因此,作者也建议如果ⅡA区没有转移,不需要清扫ⅡB区。

甲状腺癌侧颈淋巴结清扫,需要平衡手术并发症和肿瘤治疗彻底性。综合以上研究,2012年美国甲状腺协会专家共识^[7]建议对于明显的颈部转移癌,应行择区性淋巴结清扫,清扫范围包括ⅡA、Ⅲ、Ⅳ、ⅤB区。没有必要常规ⅡB区清扫,除非ⅡB区或ⅡA区有明显可疑淋巴结。如果术前超声检查ⅤA区无异常淋巴结,常规ⅤA区清扫也无必要。

2 cN₀ 是否需行预防性侧颈清扫

以治愈为目的的单侧/双侧治疗性颈清扫已被认可,但是预防性侧颈清扫仍存在争议。

反对者认为预防性侧颈清扫并不能改善患者生存预后。预防性侧颈清扫是无根据的^[7]。由于需要长期随访来获得有意义结论,而甲状腺乳头状癌预后较好,大样本前瞻性随机对照研究很难实施^[1],目前尚缺乏预防性颈清扫提高疾病特异生存率的确切证据^[20]。

支持者认为即便术前彩超阴性的患者,仍有15%几率存在隐匿性转移^[21]。预防性侧颈清扫虽然不能显著提高生存率,但是可能减少局部复发率^[2]。Dralle 等^[20]建议 cN₀ 的 PTC 患者,当原发灶位于上极和/或同侧中央区有明显的广泛转移时,应行预防性单侧侧颈清扫;当双侧中央区淋巴结广泛转移时,应行双侧预防性侧颈清扫。Ito 等^[3]认为:在术前或术中,如果存在以下两项或两项以上:男性、年龄≥55岁、明显的腺体外侵犯、肿瘤直径大于3cm,侧颈淋巴结转移可能性高,建议行预防性颈清扫。

3 cN₁bpN₁b 与 cN₀pN₁b

cN₁bpN₁b 是指颈部淋巴结巨大或广泛转移患者,cN₀pN₁b 是针对临床不明显的镜下淋巴结转移患者,两者术后颈部淋巴结复发率不同。cN₀pN₁b 颈部复发率与 cN₀pN₀ 类似,只有4%^[22];而 cN₁bpN₁b 颈部淋巴结复发率可高达32%^[23,24]。另外,多因素分析发现:cN₁bpN₁b 对患者疾病特异生存率存在影响,是重要的预后判断指标,而 cN₀pN₁b 则不是^[3]。

cN₁bpN₁b 患者由于淋巴结广泛转移,导致临床 TNM 分期提高是可以理解的;但对于 cN₀pN₁b,由于淋巴结微转移导致 TNM 分期升高,从而需行与 cN₁bpN₁b 类似的治疗性颈清扫,可能是过度治疗,这些低危患者也并不能从中受益^[6]。对于这类患者,能否行超择区性淋巴结清扫(如仅清扫Ⅲ区、Ⅳ区),需要进一步研究。

目前 AJCC 分期并未将转移淋巴结的特点(如大小、数目、结外侵犯)作为进一步评价复发和死亡的指标。临床工作中,医生可以同时使用 cN 和 pN 分期来区分不同的淋巴结转移情况,制定个体化治

疗方案和随访建议,判定复发风险及对患者生存率的影响^[6]。Randolph 等^[6]亦建议,可以依据复发风险高低对颈部淋巴结分层(见 Table 1)。

Table 1 Risk factors that modify standard N₁ risk of recurrence estimates^[6]

Lower-risk N ₁ disease (<5% risk of recurrence)	Higher-risk N ₁ disease (>20% risk of recurrence)
Clinically N ₀	Clinically detectable LN metastases (cN ₁)
Micrometastases, small lymph node metastases	Metastatic LN>3 cm
≤5 small lymph node metastases	> 5 metastatic LNs

总之,甲状腺乳头状癌容易发生颈部淋巴结转移,常见转移部位为颈部中央区 and 侧颈部。明显的侧颈部转移,需行规范的清扫术,目前主张行择区性淋巴结清扫,但对清扫范围存在异议,倾向于ⅡA、Ⅲ、Ⅳ、VB 区淋巴结清扫。ⅡB 及 VA 区是否清扫,需视术前影像学检查及其它区域淋巴结转移情况而定。手术应由经验丰富的外科医生实施,以减少手术并发症,特别是副神经损伤。不提倡预防性侧颈淋巴结清扫。为降低术后颈部淋巴结复发率,对于 cN₀pN₁b 是否可以实施超择区性淋巴结清扫(如仅清扫Ⅲ、Ⅳ区)需要进一步研究。

近年来,甲状腺乳头状癌分子生物学研究取得显著进展^[25]:*BRAF* 基因突变或融合、*RAS* 基因突变、*TERT* 启动子突变、*RET/PTC* 基因重排等。这些遗传学改变在甲状腺乳头状癌的发生、淋巴结转移、预后转归方面均发挥重要作用。藉此研究,可以对乳头状癌进行分子分型^[25],也可以预测不同遗传学改变与淋巴结转移或复发的关系^[26,27],从而指导临床,对颈部淋巴结区别处理,个体化治疗。

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