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· 专家共识 ·

口咽癌外科治疗专家共识

中国抗癌协会头颈肿瘤专业委员会, 中国抗癌协会口腔癌整合防筛专业委员会

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【摘要】 随着人乳头瘤病毒(human papilloma virus, HPV)感染在口咽癌致病因素中的占比越来越高,口咽癌的外科治疗也随之发生了一系列变化,治疗模式改进的同时,仍存在着诸多问题,包括诊断与治疗模式的不统一、修复重建技术的不普及、治疗后康复体系的不完善以及有效预防措施未建立等,尤其是在治疗模式上,对于早期口咽癌,是单纯手术还是单纯放疗,机器人微创手术是否比放疗具有更好的功能保护,尚存争议;对于中晚期口咽癌,治疗模式的争议更大,是采用同期放化疗或诱导化疗加同期放化疗的非手术治疗模式,还是采用手术加术后放(化)疗的治疗模式仍不明确。为规范中国口咽癌的外科治疗,明确口咽癌外科治疗的适应证,本专家共识根据中国口咽癌的发病特点和诊疗现状,结合国内外最新理论和实践,在口咽癌的外科术前评估、手术指征确定、原发肿瘤切除、颈淋巴结清扫、术后缺损修复、术后并发症处理、预后及随访等多方面形成共识性意见,重点包括:①口咽癌治疗前应当检测p16蛋白表达以明确HPV状态;②手术前进行颌面部

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增强磁共振检查从而清晰评估口咽癌浸润深度、侵袭方向,指导口咽癌的精准外科切除;开口度与气道评估对于外科手术的路径决策和术后风险预测具有重要意义;③较大口咽癌手术,预估口腔内1~2月不能有效进食者,建议术前接受经皮内镜胃造瘘,有效提升治疗期间的营养摄入;④对于早期口咽癌患者,可以选择单纯手术治疗或是单纯放疗;对于中晚期患者,HPV相关性口咽癌一般首选放射治疗,并根据肿瘤的临床分期酌情选择是否增加同步化疗;非HPV相关性口咽鳞状细胞癌(包括原发和复发)、放化疗后复发性HPV相关性口咽鳞状细胞癌建议首选手术治疗;⑤原发外生性的T1-2口咽癌,首选经口入路直接手术或达芬奇机器人手术,T3-4的中晚期口咽癌患者建议酌情采用下颌骨暂时离断入路或是舌骨上入路进行手术;⑥肿瘤浸润深度>3 mm的cT1-2N0口咽癌患者以及cT3-4N0的非HPV相关性口咽癌患者建议行I B-IV区的预防性颈淋巴清扫,cN+的非HPV相关性口咽癌患者建议进行I-V区的治疗性颈淋巴清扫;⑦HPV相关性口咽癌放疗后12周或更长时间的PET-CT扫描显示颈淋巴结中有较强的氟代脱氧葡萄糖(fludeoxyglucose, FDG)摄取,或影像学提示淋巴结持续增大,建议进行颈淋巴清扫;⑧术前怀疑包膜外侵犯的患者,颈淋巴清扫时应当切除淋巴结周边的肌肉脂肪结缔组织;⑨口咽癌的缺损修复需要遵循修复重建阶梯原则,优先选择邻近瓣,次选远位带蒂瓣,最后游离瓣,组织量丰富的股前外侧皮瓣可以作为术后大范围缺损的首选皮瓣。

【关键词】 口咽癌; 人乳头瘤病毒; 外科治疗; 术前评估; 手术适应证; 颈淋巴清扫; 包膜外侵犯; 缺损修复; 并发症; 专家共识

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Expert consensus on surgical treatment of oropharyngeal cancer

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【Abstract】 With the increasing proportion of human papilloma virus (HPV) infection in the pathogenic factors of oropharyngeal cancer, a series of changes have occurred in the surgical treatment. While the treatment mode has been improved, there are still many problems, including the inconsistency between diagnosis and treatment modes, the lack of popularization of reconstruction technology, the imperfect post-treatment rehabilitation system, and the lack of effective preventive measures. Especially in terms of treatment mode for early oropharyngeal cancer, there is no unified conclusion whether it is surgery alone or radiotherapy alone, and whether robotic minimally invasive surgery has better functional protection than radiotherapy. For advanced oropharyngeal cancer, there is greater controversy over the treatment mode. It is still unclear whether to adopt a non-surgical treatment mode of synchronous chemoradiotherapy or induction chemotherapy combined with synchronous chemoradiotherapy, or a treatment mode of surgery combined with postoperative chemoradiotherapy. In order to standardize the surgical treatment of oropharyngeal cancer in China and clarify the indications for surgical treatment of oropharyngeal cancer, this expert consensus, based on the characteristics and treatment status of oropharyngeal cancer in China and combined with the international latest theories and practices, forms consensus opinions in multiple aspects of preoperative evaluation, surgical indication determination, primary tumor resection, neck lymph node dissection, postoperative defect repair, postoperative complication management prognosis and follow-up of oropharyngeal cancer patients. The key points include: ① Before the treatment of oropharyngeal cancer, the expression of P16 protein should be detected to clarify HPV status; ② Perform enhanced magnetic resonance imaging of the maxillofacial region before surgery to evaluate the invasion of oropharyngeal cancer and guide precise surgical resection of oropharyngeal cancer. Evaluating mouth opening and airway status is crucial for surgical approach decisions and postoperative risk prediction; ③ For oropharyngeal cancer patients who have to undergo major surgery and cannot eat for one to two months, it is recommended to undergo percutaneous endoscopic gastrostomy before surgery to effectively improve their nutritional intake during treatment; ④ Early-stage oropharyngeal cancer patients may opt for either surgery alone or radiation therapy alone. For intermediate and advanced stages, HPV-related oropharyngeal cancer generally prioritizes radiation therapy, with concurrent chemotherapy considered based on tumor staging. Surgical treatment is recommended as the first choice for HPV unrelated oropharyngeal squamous cell carcinoma (including primary and recurrent) and recurrent HPV related oropharyngeal squamous cell carcinoma after radiotherapy and chemotherapy; ⑤ For primary exogenous T1-2 oropharyngeal cancer, direct surgery through the oral approach or da Vinci robotic surgery is preferred. For T3-4 patients with advanced oropharyngeal cancer, it is recommended to use temporary mandibulectomy approach and lateral pharyngotomy approach for surgery as appropriate; ⑥ For cT1-2N0 oropharyngeal cancer patients with tumor invasion depth >3 mm and cT3-4N0 HPV unrelated oropharyngeal cancer patients, selective neck dissection of levels IB to IV is recommended. For cN+ HPV unrelated oropharyngeal cancer patients, therapeutic neck dissection in regions I-V is advised; ⑦ If PET-CT scan at 12 or more weeks after completion of radiation shows intense FDG uptake in any node, or imaging suggests continuous enlargement of lymph nodes, the patient should undergo neck

dissection; ⑧ For patients with suspected extracapsular invasion preoperatively, lymph node dissection should include removal of surrounding muscle and adipose connective tissue; ⑨ The reconstruction of oropharyngeal cancer defects should follow the principle of reconstruction steps, with priority given to adjacent flaps, followed by distal pedicled flaps, and finally free flaps. The anterolateral thigh flap with abundant tissue can be used as the preferred flap for large-scale postoperative defects.

【Key words】 oropharyngeal cancer; human papilloma virus; surgical treatment; preoperative evaluation; surgical indication; neck dissection; extranodal extension; defect reconstruction; complication; expert consensus

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口咽癌是原发于舌根、扁桃体、软腭、口咽侧壁与口咽后壁的恶性肿瘤,约占全身恶性肿瘤的0.5%^[1-2]。口咽癌90%以上为鳞状细胞癌,相对于口腔癌,口咽癌发病位置隐蔽,早期发现较难,淋巴结转移率较高,临床治疗效果欠佳,尤其是人乳头瘤病毒(human papilloma virus, HPV)非相关口咽癌患者,5年生存率明显较低,仅为50%左右^[3-4]。此外,口咽癌治疗也会对患者的言语、吞咽和咀嚼功能产生较大影响,患者生存质量明显较差。近年来,口咽癌在全球范围内的发病率明显上升,在美国,1988年到2004年的16年间,尽管吸烟人群在逐年减少,但口咽癌的整体发病率还是增长了近30%,其中,HPV相关口咽癌的增长幅度更是高达225%。从2004年到2017年的13年间,美国口咽癌的总发病率又增长了约30%^[5-6]。在我国,近10年口咽癌发病率和死亡率也明显增加,尤其是男性和农村地区,分别增加了30.7%和61.1%,严重影响人民群众的生命健康^[7]。

口咽癌治疗在过去的几十年中也发生了显著变化。由于口咽位置特殊,是呼吸、进食的共同通道,因此,治疗上越来越强调肿瘤根治和生活质量之间的平衡。现阶段的口咽癌治疗,主要以手术和放疗为主,随着HPV病毒感染在口咽癌致病因素中的占比越来越高,口咽癌的诊疗也随之发生了一系列变化,治疗模式改进的同时,也存在诸多问题,包括诊断与治疗模式的不统一、修复重建技术的不普及、治疗后康复体系的不完善以及有效预防措施未建立等,尤其是在治疗模式上,对于早期口咽癌存在的争议有:是单纯手术还是单纯放疗;机器人微创手术是否比放疗具有更好的功能保护。对于中晚期口咽癌,治疗模式的争议更大,

是采用同期放化疗或诱导化疗加同期放化疗的非手术治疗模式,还是采用手术加术后放(化)疗的治疗模式仍不明确。对于HPV阳性的口咽癌是否能够降低治疗强度也存在争议,尤其是在减少放疗剂量和缩小手术范围等方面,有待于临床研究进一步明确。为规范中国口咽癌外科治疗,明确口咽癌的手术适应证,提高口咽癌患者的生存率和生存质量,中国抗癌协会头颈肿瘤专业委员会和中国抗癌协会口腔癌整合防筛专业委员会组织国内相关领域专家,根据中国口咽癌的发病特点和诊疗现状,结合国内外最新理论和经验,在口咽癌的手术指征确定、外科术前评估、原发肿瘤切除、颈淋巴清扫、术后缺损修复、术后并发症处理、预后及随访等多方面形成共识性意见,以期的口咽癌的临床工作和相关研究提供参考和指导。

1 口咽的解剖与组织学特点

口咽(oropharynx)位于咽的中部,是食物和空气的共同通道,承担着呼吸、言语和吞咽等多项重要生理功能。口咽上界为软腭平面,连鼻咽,下界为会厌上缘平面,接喉咽,前方借咽峡通向口腔,后壁紧贴颈椎椎体和椎前肌,两侧有颈部的大血管,尤其是颈动脉及其分支。按照部位,口咽可以划分为5个区域,分别是舌根、扁桃体、软腭、咽侧壁与咽后壁。与口腔不同,口咽部淋巴组织丰富,包括扁桃体、淋巴结和淋巴滤泡,这些淋巴组织互相通连,构成咽淋巴环,即“瓦尔代尔(Waldeyer)淋巴环”^[8]。Waldeyer淋巴环又进一步分为内环和外环,内环位于呼吸道和消化道的入口处,由咽扁桃体、咽鼓管扁桃体、腭扁桃体、舌扁桃体、咽侧索、咽后壁淋巴滤泡等构成。外环则位于颈外侧,由

咽后淋巴结、下颌下淋巴结和颈下淋巴结组成。内外两环间淋巴组织互相通连,内环淋巴流向外环,外环淋巴流向颈深淋巴结。口咽部的Waldeyer淋巴环,对呼吸道和消化道上端起着重要的免疫防御作用,但同时也是口咽癌高发淋巴结转移特性的组织解剖学基础。

2 口咽癌治疗前评估与准备

2.1 全身评估

口咽癌患者术前全身评估的重点是明确全身麻醉风险及手术耐受性。常规评估项目包括体格检查,血常规,凝血功能,肝、肾功能,心电图和胸片等。高龄患者以及有特殊疾病的口咽癌患者,还需要增加相关评估,包括动态心电图、心脏彩超、冠脉造影、心肌酶谱等检查以评估心脏情况,血栓弹力图、颈动脉B超和下肢B超评估凝血状态、动脉斑块和下肢血栓情况。合并高血压或糖尿病患者,还需要动态监测血压、血糖,并调控在安全范围内。长期服用抗凝药物患者,尤其是氯吡格雷等药物,需要进行低分子肝素替代治疗。术前接受化疗和(或)免疫治疗的患者,还需要明确是否存在骨髓抑制及免疫性肺炎等情况。此外,由于吞咽功能受影响,口咽癌患者都会出现不同程度的营养不良甚至是恶病质状态,术前往往往需要纠正电解质紊乱、贫血和脱水等。最后,建议有条件的口咽癌患者在外科治疗前接受一次PET-CT检查,排除可能存在的远处脏器转移。

2.2 局部评估

口咽癌患者术前局部评估的重点是原发肿瘤情况和颈部淋巴结情况。术前内镜检查可以评估原发肿瘤的具体位置、大小、生长方式、是否带蒂以及表面是否破溃。颌面部增强MRI具有良好的软组织分辨力,无辐射,可以清晰显示口咽肿瘤的浸润深度、与周围软组织的关系,包括对毗邻血管、神经、肌肉及器官结构的精细显影与受累评估。颌面部增强CT检查可以评估中晚期口咽癌对邻近骨质的侵犯情况,包括舌根癌导致的舌骨破坏、扁桃体癌导致的下颌骨后份牙槽骨质以及舌侧骨皮质的受累情况,软腭咽侧壁癌导致的上颌骨硬腭及翼钩破坏情况,咽后壁癌导致的椎体骨质破坏情况等。B超可以评估颈部淋巴结大小与淋巴门结构情况,判断是否早期淋巴结转移。CBCT薄层小视野图像有助于精细评估下颌骨骨皮质的受累程度,辅助制定下颌骨的外科处理方

式^[9]。临床与影像学的局部及全身评估是确定口咽癌临床分期的重要参考,准确的口咽癌分期对患者预后和治疗决策至关重要,目前口咽癌分期主要参照美国癌症联合委员会(American Joint Committee on Cancer, AJCC)第八版的TNM分期标准^[10-11],基于大数据的人工智能分期具有潜在的临床应用前景^[12]。最后,建议完成全身及局部各项检查的口咽癌患者,都进行多学科诊疗(multi-disciplinary treatment, MDT)讨论,以确定最终治疗方案。

2.3 病理评估

病理学诊断是口咽癌确诊和制定临床治疗方案的最重要依据。在病理类型上,口咽部恶性肿瘤包括鳞状细胞癌、腺癌、恶性淋巴瘤及软组织肉瘤等,口咽癌主要是指口咽部的鳞状细胞癌和腺癌。治疗前的病理诊断需要明确口咽癌的具体病理类型:对于鳞状细胞癌,需要行p16蛋白免疫组织化学检测和(或)HPV DNA或RNA检测。当p16阳性细胞数 $\geq 70\%$ 、阳性表达定位于细胞核和细胞质、且为中等至强阳性,并且组织学形态为非角化型鳞状细胞癌时,应报告“HPV相关性(p16+)鳞状细胞癌”。HPV DNA或RNA检测阳性者,应报告“HPV相关性鳞状细胞癌”^[13-15]。口咽非HPV相关性鳞状细胞癌需要根据肿瘤细胞的分化程度分为高分化、中分化和低分化,口咽HPV相关性鳞状细胞癌则无需进行组织学分级。若为小涎腺癌,需要尽量明确小涎腺癌具体病理类型,包括腺样囊性癌、黏液表皮样癌、恶性混合瘤和透明细胞癌等,恶性淋巴瘤也需明确具体类型,便于选择合理的药物治疗方案。对于分化较差且伴有淋巴组织背景的癌,还应行EB病毒原位杂交检测,以明确肿瘤是否与EB病毒感染相关^[16-17]。

口咽癌,尤其是口咽鳞状细胞癌患者,术后病理还需提供切缘状况、有无神经侵犯、有无淋巴管血管侵犯、是否有淋巴结转移,如有淋巴结转移,还应明确转移淋巴结的个数、部位等相关信息。此外,条件许可时,还应提供距切缘的距离等影响患者预后的相关病理指标^[13]。

2.4 治疗前准备

口咽癌患者在接受外科治疗前,首先需要进行开口度评估和气道评估。开口度一般以上下切牙之间的距离进行分类,大于或等于三指并排的宽度,为正常开口,大约是4.5 cm;若为一到两指,为轻度开口受限;若小于一指,为重度开口受

限。气道评估多采用 Mallampati 法^[18-19],具体分为四级:开口可看到软腭、咽腭弓、腭垂、硬腭者为Ⅰ级;可看到软腭、腭垂、硬腭者为Ⅱ级;只能看到软腭和硬腭者为Ⅲ级;仅能看到硬腭者为Ⅳ级。开口度与气道评估对于外科手术的入路决策和术后风险预测具有重要意义。

口腔口咽部为污染创口,存在大量细菌和微生物,外科治疗前,需用抗菌含漱液漱口,全口牙周洁治,去除牙垢结石,治疗相关龋齿,创造良好的手术区域。对于术前营养不良或预估术后长期不能口腔进食的口咽癌患者,可以通过微创内镜手术在胃前壁与腹壁之间造一人工通道,即经皮内镜胃造瘘,直接将食物研磨成食糜并输入胃部,有效改善营养摄入^[20-21]。对于需要股前外侧皮瓣修复术后缺损的患者,可在术前进行超声血管定位,明确旋股外侧动静脉是否缺如及伴行状况,判断血管走行、穿支分布情况,测量穿支管径、血流速度等,便于皮瓣的微创制备与适形修复^[22]。

3 口咽癌手术指征与手术方式

口咽癌的治疗方式包括放疗、化疗,手术治疗以及靶向免疫治疗等。对于早期口咽癌患者,可以选择单纯手术治疗或是单纯放疗;对于中晚期患者,HPV 相关性口咽癌一般首选放射治疗,并根据肿瘤的临床分期酌情选择是否增加同步化疗;非 HPV 相关性口咽癌则首选手术,手术前可酌情选择是否接受新辅助药物治疗,手术后根据具体临床病理分期,酌情进行术后放疗或是放化疗。

3.1 手术指征

①对于原发性非 HPV 相关性口咽鳞状细胞癌,若无全身麻醉绝对禁忌和远处脏器转移,早中期患者可直接进行手术;局部晚期患者,常规采取手术及术后辅助治疗。随着免疫治疗的发展,以 PD-1 单抗为代表的免疫检查点抑制剂治疗成为复发或转移头颈癌的一线用药。对于条件合适的局部晚期患者,可进行临床研究,尝试完成新辅助免疫化疗后接受手术^[23-25]。②对于原发性 HPV 相关性口咽鳞状细胞癌,早期患者可以直接进行手术,也可以选择放疗;中晚期患者,应进行多学科评估^[26],以选择合适的放化疗方案。③对于复发性口咽癌患者(包括 HPV 相关性口咽鳞状细胞癌),未侵犯颅底、颈动脉、翼腭窝,无远处脏器转移,可以实施开放性根治性手术。④对于复发性口咽癌患者,侵犯颅底、颈动脉、翼腭窝,无远处脏器转

移,可以实施开放性救治性手术。⑤对于口咽区小唾液腺癌原发及复发患者(腺样囊性癌和黏液表皮样癌),无颅底、颈动脉、翼腭窝侵犯,无远处脏器转移,首选手术;⑥口咽癌治疗并发症较为严重的患者,如放射性颌骨坏死、化学性颌骨坏死、咽痿患者,保守治疗无效或无明显缓解者,也可选择手术治疗。

3.2 口咽部病灶的外科切除

口咽癌的外科切除入路包括经口入路、下颌骨暂时离断入路和舌骨上入路3种^[1, 27-29]。经口入路包括直接经口切除,经口激光显微外科切除以及经口机器人手术^[29-30]。

对于开口度良好,口咽结构显露充分,无心、脑、肺合并症,肿物为原发外生性的 T1-2 期口咽癌患者,首选经口入路手术,包括机器人手术。切除超过 50% 以上舌根组织或 75% 以上软腭组织的口咽癌,则不适用于经口手术入路。由于大部分经口手术的口咽癌术区创面采用裸露自愈方式,因此,长期使用抗凝药或罹患免疫缺陷相关性疾病的患者的出血及感染风险会大大增加,不建议使用口内入路创面裸露愈合的手术方式。

下颌骨暂时离断入路手术,主要用于经口暴露不充分的口咽癌患者,包括各类原发及复发性口咽癌,侵犯翼内肌、下颌骨、上颌结节、舌骨或咽旁结构(咽侧壁收缩肌)的患者,以及累及颅底、包绕大血管、口咽部肿瘤与颈部肿块相连通的患者^[31-32]。下唇一般为正中切开,也可在颊肌表面皮肤处设计弧形切口或“Z”形切口,以减轻术后瘢痕挛缩。下颌骨暂时离断的部位可以在正中,也可以在颏孔前方,从而避免下牙槽神经损伤。口腔内沿颌舌沟切开,到达口咽部肿瘤外围,充分显露病灶。

口咽癌的舌骨上入路切除手术,主要用于经口入路不畅,尤其是肿瘤位于低位口咽的患者,可以避免下颌骨连续性中断,减轻术后放疗导致的并发症。

舌骨上入路可分为侧方舌骨上入路和正中舌骨上入路,侧方舌骨上入路可充分显露低位舌根癌和咽侧壁癌,做到直视下切除肿瘤,并可同时进行咽旁淋巴结的探查与摘除;正中舌骨上入路可充分显露低位咽后壁肿瘤,进行直视下切除,并在有咽后淋巴结受累的情况下,进行充分暴露与摘除。

临床实际操作中,一般根据口咽癌的具体发

病部位,选择合适的手术方式。对于舌根癌,由于浸润深度往往明显大于舌体癌(特别是在肿瘤表面积相近的情况下),因此,对于靠近人字沟的T1期舌根癌,可采用口腔内暴露切除;位于靠近会厌隙的T1期舌根癌,建议采用舌骨上入路暴露切除肿瘤^[33-34]。对于T2-4期舌根癌,建议采用下唇正中切口或侧方切口下颌骨暂时离断的方式暴露肿瘤。出现开口受限的患者,提示翼内肌或翼外肌可能受到侵犯,需要追到肌肉起止点进行切除;必要时,可选择切除下颌支。对于下颌骨受侵犯的口咽癌患者,可同期进行下颌骨边缘切除或截段性切除。对于扁桃体癌,原发性T1-2期扁桃体癌可经口入路在口腔内直视下切除;原发性T3-4期扁桃体癌,或放化疗后复发性扁桃体癌,建议颈部切口暴露颈内动脉,用纱布遮挡保护后,再进行扁桃体的扩大根治手术。软腭癌可以口腔内暴露切除,累及硬腭时可切除部分硬腭,过中线的软腭癌需要进行全软腭切除,包括两侧的舌腭弓,直至咽侧壁。咽侧壁与咽后壁的口咽癌,原发肿瘤位置较高,口腔内显露良好的T1-2期患者,可经口入路切除^[35-36],T3-4期患者则需要下颌骨暂时离断,充分暴露后切除。对于位置较低,口腔内显露不佳,尤其是合并淋巴结转移的患者,均建议舌骨上入路切除。

4 口咽癌颈淋巴清扫

口咽部淋巴组织和淋巴引流丰富,相互沟通并形成咽淋巴环,向下汇入颈深淋巴结,口咽癌的最主要局部扩散途径是区域性淋巴结转移。口咽鳞状细胞癌的总体淋巴结转移率高达53%~80%,淋巴结转移与肿瘤位置、肿瘤大小、病理类型、浸润深度以及HPV状态等因素密切相关^[37-38]。口咽鳞状细胞癌的颈部淋巴结转移以II区最常见,其次为III-IV区,I区及V区少见。口咽唾液腺癌的总颈部淋巴结转移率较低,约为10%;但高度恶性黏液表皮样癌及舌根腺样囊性癌的淋巴结转移率则较高,分别达到66%和20%^[39-41]。

4.1 颈淋巴清扫适应证和禁忌证

口咽癌患者接受颈淋巴清扫的适应证包括:①原发性无远处转移的非HPV相关口咽鳞状细胞癌,cT1-2N0且MRI检查提示肿瘤浸润深度>3mm;②原发性无远处转移的非HPV相关口咽鳞状细胞癌,cT3-4N0期;③原发性无远处转移的非HPV相关口咽鳞状细胞癌,cN+;④原发性无远处转移的

HPV相关口咽鳞状细胞癌,cT0-3N0-2期;⑤复发性无远处转移的非HPV相关口咽鳞状细胞癌;⑥复发性无远处转移的HPV相关性口咽鳞状细胞癌;⑦放化疗后的口咽鳞状细胞癌,12周或更长时间的PET-CT扫描显示淋巴结中有较强的氟代脱氧葡萄糖(fludeoxyglucose,FDG)摄取;⑧放化疗后的口咽鳞状细胞癌,12周或更长时间的影像学检查怀疑淋巴结持续增大,直径超过1cm;⑨原发性无远处转移的舌根中高度恶性黏液表皮样癌;⑩原发性舌根腺样囊性癌,无远处转移或远处转移仅限于肺部且无肺功能障碍患者。

口咽癌患者接受颈淋巴清扫的相对禁忌证包括:①经活检或穿刺证实有远处转移的患者(ACC肺转移除外);②cN+口咽癌患者,明确有肿瘤淋巴结包膜外侵犯累及颈动脉或颅神经。此外,出现下述情况的口咽癌患者,一般也不推荐颈淋巴清扫:①T0-2,N1(同侧单个淋巴结转移,最大径>3cm或同侧多个淋巴结转移,最大径≤6cm)或T0-2,N2-3或T3-4,N0-3 HPV相关口咽癌患者,且出现转移淋巴结融合或是明显淋巴结包膜外侵犯等不良特征者;②放疗/放化疗完成后12周或更长时间的PET-CT未显示淋巴结FDG摄取,且患者无异常增大淋巴结的口咽癌患者;③完成放疗/放化疗并在治疗后12周或更长时间接受解剖学横断面成像(CT或MRI),显示之前异常的淋巴结已消退的患者^[42]。

4.2 颈淋巴清扫时机

口咽癌的颈淋巴清扫手术,一般与原发肿瘤切除手术同期进行,同期手术可为口咽癌的术后病理分期提供重要信息,及时确定是否给予后续辅助治疗及方案(辅助治疗通常在初次手术干预后的4~6周内开始)。同期手术过程中,先行颈淋巴清扫,可以有效识别、结扎有风险的口咽部供血血管,有效控制切除原发肿瘤过程中的出血,减少术后出血的严重性和发生率。此外,在口咽部肿瘤(如扁桃体或咽侧壁癌)范围与颈动脉之间的关系尚不清楚时,可以通过颈部的清扫切口,找到颈动脉,在颈动脉和口咽之间放置纱布或棉垫,以保护颈动脉,尤其是颈内动脉,使其在口咽肿瘤切除过程中免受意外损伤。对于经口口咽癌手术,颈淋巴清扫可在经口肿瘤切除时进行,也可在经口肿瘤切除后2~3周进行,后者可以避免口咽和颈部之间产生瘘道,避免颈部回流障碍引起的口咽部水肿,降低预防性气管切开的需要,还可为外科

医师提供第二次机会,解决延迟的阳性手术切缘。

4.3 颈淋巴清扫范围

口咽癌颈淋巴清扫的范围一般遵循以下8点:①单侧原发口咽癌患者的颈淋巴清扫,一般为患侧的ⅠB~Ⅳ区且包括至少18个淋巴结,当肿瘤向前侵犯时,可能需要清扫ⅠA区;②N0择区性颈淋巴清扫患者,至少清扫Ⅱ~Ⅳ区淋巴结;N1-N2a-c患者接受择区性或根治性颈淋巴清扫;N3期患者接受根治性颈淋巴清扫;③接近中线的T1-2、N0-1原发肿瘤,术中切缘阴性,可实施单侧颈淋巴清扫;若术中首次切缘出现阳性,则需同时实施对侧淋巴清扫;④接近中线的T1-2、N0-1原发肿瘤,术后病理出现阳性切缘,或出现不良病理特征(淋巴结包膜外侵犯、阳性切缘、接近阳性切缘、pT3或pT4原发肿瘤分期、pN2或pN3淋巴结分期、Ⅳ或Ⅴ区淋巴结转移、神经侵犯、血管侵犯和淋巴管侵犯),可以二期清扫对侧淋巴结;⑤接近中线的T3-4期口咽癌患者,需实施双侧颈淋巴清扫;⑥累及中线的口咽癌,尤其是舌根癌和软腭癌患者,或涉及口咽后壁的患者,除非计划进行双侧辅助放疗,否则应进行双侧颈淋巴清扫;⑦Ⅲ区及Ⅳ区无淋巴结转移的患者,可以不清扫Ⅴ区;⑧术前怀疑包膜外侵犯的患者,颈淋巴清扫时应切除淋巴结周边的肌肉脂肪结缔组织。

5 口咽癌术后缺损的外科修复

由于口咽解剖与生理的复杂性,所以口咽癌术后缺损修复成为头颈外科领域最具挑战性的工作之一。成功的口咽缺损重建需要对吞咽和腭咽闭合发音功能的正常解剖和生理机制有详细的了解,在此基础上,依据口咽缺损的位置和大小,遵循重建阶梯原则^[43-44],结合外科专业知识和洞察力,选择能产生最高功能水平的最简单的重建修复方式,包括人工黏膜(生物补片)修复、邻近组织瓣修复、远位带蒂组织瓣修复以及血管化游离组织瓣修复。口咽癌术后缺损修复中,长期服用类固醇的患者、有头颈部放射史、骨面炎症暴露史或有口咽颈部瘻道史、糖尿病史或营养状况不良史的患者,可能会更加受益于血管化游离组织瓣修复^[45-47]。

舌根T1-2口咽癌术后的组织缺损修复,可采用邻近组织瓣修复,包括邻近的舌体组织、舌下腺腺体组织、下颌下腺腺体组织等。T3-4口咽癌术后的组织缺损修复,可以首选股前外侧皮瓣或前

臂皮瓣^[48],腹直肌瓣和背阔肌瓣等则适用于较大软组织缺损修复。如果颈部血管条件困难,也可采用远位带蒂胸大肌皮瓣或背阔肌皮瓣等进行修复。舌根肿瘤累及上、下颌骨时,切除病灶后可选用自体骨移植修复,目前临床上应用最广泛的是腓动脉供血的腓骨移植和旋髂深动脉供血的髂骨移植^[49-50]。合适的数字化技术辅助有利于更为精准的骨缺损修复^[51-52]。肿瘤累及造成的神经缺损则可采用人工神经材料或移植自体神经修复,条件合适时应术中修复,因为早期修复,特别是即刻修复,功能恢复的效果更佳。

软腭缺损修复以重建腭咽闭合为目的,具有一定的挑战性。软腭作为一个肌性阀门,可以产生正常语音共鸣所需要的口腔压力,因此,手术治疗导致的软腭缺损应根据切除范围进行修复,修补方式包括膈肌瓣修复和自体组织修补。利用自体组织修补时,当缺损组织少于软腭的50%时,可采用局部皮瓣修复,包括岛状腭瓣、颏下岛状瓣和颞肌瓣等,重建腭咽闭合,提升发音功能;当缺损组织大于软腭的50%,或同时伴有邻近组织的大范围缺损时,可采用游离组织瓣进行修复重建,以更好地恢复外形,可供选择的组织瓣包括前臂皮瓣、股前外侧皮瓣等^[53]。

对于扁桃体癌及咽侧壁癌的术后缺损,较小者可直接进行原位缝合,或邻近组织瓣转移修复,较大者则应进行适当的游离或远位皮瓣/肌皮瓣修复重建,从而最大程度地恢复言语和吞咽功能。咽后壁癌术后缺损一般可以旷置,上皮细胞爬行于肉芽创面从而自行愈合。补片或植皮并打包,或用其他组织瓣修补,可能增加气道狭窄,甚至窒息的风险。

6 口咽癌术后常见并发症与处理

口咽癌术后常见并发症包括气道阻塞、出血、感染、咽痿等^[54-55]。气道阻塞是口咽癌术后最危险的并发症。口咽属于上呼吸道的起始部分,口咽部术后肿胀,尤其是颈部同期清扫患者,气道阻塞风险明显增加。经口口咽癌切除的患者,术后出血也会导致呼吸道阻塞。术后高风险气道患者,建议预防性气管切开,以保持呼吸道通畅,或是带鼻插管,观察2~3d,度过肿胀期。口咽癌术后出血发生率为4.6%~15.6%^[56-58],术后早期出血多为黏膜慢性渗血,或手术期间收缩或痉挛的血管扩张而导致的快速出血。黏膜慢性渗血可通过冰

敷、局部加压、避免使用抗凝药物以及床旁电凝止血进行处理,血管开放引起的快速出血需要在保持呼吸道通畅的情况下(包括麻醉插管或紧急气管切开)快速找到出血位置及相关血管,采用床旁局麻或手术室内全麻下结扎止血。术后后期出血多为感染所致,在充分清理创面并止血的同时,还需加强抗炎治疗与营养支持。

口咽癌术后3~4 d切口疼痛加重,或减轻后又加重,并有体温升高,白细胞计数增高,检查口腔或颈部有红、肿、热和压痛的典型体征,提示可能存在感染。早期感染,可根据药敏选择有效的抗菌药物,如果已形成脓肿应敞开切口,通畅引流。咽瘘是指唾液贮积于皮下或切口下组织,形成脓腔破溃至皮肤或切口缘,使咽腔与皮肤相通成瘘管,患者进食时,唾液、水和食物可以通过瘘口流出皮肤外。作为口咽癌术后常见的并发症,咽瘘发生率为4.3%~12%^[29,59]。保守的治疗方法包括瘘口清创、胶原蛋白填充、膈肌修复等。保守治疗无效时,可通过手术进行咽瘘修补,包括局部创面清理后严密缝合、邻近组织瓣以及远位带蒂或游离皮瓣进行修补^[60]。口咽癌术后长期卧床加上吞咽功能不良可能导致食物或唾液误吸,随后发展为肺炎^[61]。肺炎患者通常出现低热、白细胞计数升高和粘稠恶臭的气管分泌物,此时需要加强针对肺部炎症的抗感染治疗,如左氧氟沙星,必要时进行纤维支气管镜肺部灌洗,有效清理肺部吸入物。

腭咽闭合不全和吞咽障碍是口咽癌术后较常见的功能相关并发症。口咽癌术后软腭缺损,会导致患者出现鼻咽反流和鼻音加重。软腭切除量小于50%,可以保守治疗,愈合瘢痕与对侧软腭的收缩和后移最终起到狭窄鼻咽入口的作用。软腭缺失50%以上时,需行假体修复或游离组织瓣修复,最大限度地恢复腭咽闭合。吞咽是一种原始而复杂的反射性动作,主要有25对肌肉和6对脑神经参与,口咽部肿瘤切除手术会对这些肌肉和神经造成损伤,从而引起不同程度的吞咽障碍^[62-64]。吞咽障碍会进一步造成患者营养不良、抵抗力下降,发生吸入性肺炎的风险大大增加。吞咽障碍的治疗方法包括:①营养支持治疗,改善吞咽障碍患者的营养状况,促进康复;②物理疗法,包括颈部肌肉按摩、吞咽反射刺激等,增强吞咽相关肌肉力量和协调性,改善吞咽功能;③吞咽功能训练,在医师指导下进行口腔运动协调性训练、吞

咽反射诱发训练等系列活动,有助于恢复或改善吞咽功能,减少误吸风险^[65-66]。此外,对于存在心理压力过大等问题的患者,还应给予适当的心理疏导。

7 口咽癌术后辅助治疗与随访

早期口咽癌病变较小,侵及范围较浅,单纯手术可获得理想的治疗效果,一般不需要术后放疗等辅助治疗。中晚期口咽癌术后一般需要做辅助放疗,特别是肿瘤浸润深度大于5 mm、合并神经、血管侵犯以及淋巴结转移的患者,如切缘阳性或淋巴结有包膜外侵犯,需要进行术后同期放化疗^[15,67-69]。对于术前进行过放化疗的原发性或复发性口咽癌患者,术后一般不进行再程放疗或化疗,建议通过MDT获得综合治疗方案。

口咽癌手术完成后2~3周进行第一次随访,关注伤口愈合情况,包括伤口是否感染,是否开裂,是否存在咽瘘等。术后第一年,每1~3个月在门诊接受1次复查;术后第二年,每2~6个月在门诊接受1次复查;术后3至5年,每4~8个月复查1次;术后5年以上,每12个月复查1次。复查方式包括触摸检查、鼻咽纤维镜检查 and 颈部B超检查,每半年1次颌面部增强MRI检查,每年1次胸部平扫CT。根据患者需求,也可每年进行1次PET-CT检查,可疑复发或转移时,加强随访频率,动态观察可疑病灶变化,早期发现及时处理。

8 专家共识

①口咽位置隐蔽,解剖复杂,淋巴及腺体组织丰富,多种微生物聚居,肿瘤病理类型多样,以鳞状细胞癌最为常见;②口咽鳞状细胞癌原发部位以舌根和扁桃体多见,软腭及咽侧壁咽后壁相对少见;③根据HPV状态,口咽鳞状细胞癌可以分为HPV相关和非相关口咽癌,近年来,非HPV相关口咽癌的发病有所降低,但是,HPV相关口咽癌的发病率明显上升;④HPV状态是口咽鳞状细胞癌治疗选择的重要参考因素,p16蛋白的检测,可以提示口咽鳞状细胞癌的HPV状态,建议作为外科治疗前的常规检测;⑤术前颌面部增强磁共振检查可以清晰评估口咽癌浸润深度、侵袭方向,指导口咽癌的精准外科切除;⑥较大口咽癌手术,预估口腔内1~2月不能有效进食者,尤其是术后还需要接受放疗的患者,建议术前接受经皮内镜胃造瘘,有效提升治疗期间的营养摄入;⑦对于原发性

HPV相关口咽鳞状细胞癌,早期患者可以直接进行手术或放疗,中晚期患者应进行多学科评估;⑧原发性非HPV相关性口咽鳞状细胞癌、复发性口咽鳞状细胞癌、口咽部位唾液腺癌均首选手术治疗,淋巴瘤则首选放化疗;⑨原发外生性的T1-2口咽癌,首选经口入路直接手术或达芬奇机器人手术;⑩侵犯翼内肌、下颌骨、上颌结节、舌骨或咽旁结构(咽侧壁收缩肌)的患者,以及侵犯颅底、包绕大血管、原发性肿瘤和颈部疾病相连通的原发性或复发性口咽癌,建议采用下颌骨暂时离断入路进行切除;⑪低位T3-4的口咽癌,尤其是舌根癌以及咽侧壁咽后壁癌,可以采用舌骨上入路进行切除,在直视下切除肿瘤的同时,可以进行颈动脉的暴露保护以及咽旁淋巴结的探查;⑫cT1-2N0且磁共振检查提示肿瘤浸润深度>3mm和cT3-4N0的非HPV相关性口咽癌患者,cN0的高度恶性黏液表皮样癌以及位于舌根的腺样囊性癌患者,建议进行预防性颈淋巴清扫,清扫范围为I B-IV区;⑬cN+的非HPV相关性口咽癌患者以及口咽唾液腺癌患者,建议进行治疗性颈淋巴清扫,清扫范围为I-V区;原发或复发肿瘤接近或跨过中线时,建议进行双侧颈部淋巴清扫;⑭放化疗后的口咽鳞状细胞癌,尤其是HPV相关性口咽癌,12周或更长时间的PET-CT扫描显示淋巴结中有较强的FDG摄取,或影像学提示淋巴结持续增大,建议进行颈淋巴清扫;⑮Ⅲ区及Ⅳ区无淋巴结转移的患者,可以不清扫V区;术前怀疑包膜外侵犯的患者,颈淋巴清扫时应当切除淋巴结周边的肌肉脂肪结缔组织;⑯口咽癌的缺损修复需要遵循修复重建阶梯原则,优先选择邻近瓣,次选远位带蒂瓣,最后游离瓣,面积广泛的浅表缺损可以使用前臂皮瓣或是削薄的股前外侧皮瓣,间室切除后的深大缺损或贯穿性缺损,建议使用组织量丰富的股前外侧皮瓣、背阔肌皮瓣或是胸大肌皮瓣进行修复。

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