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· 临床研究 ·

55例口腔颌面头颈部恶性肿瘤患者围手术期死亡病例回顾性分析

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【摘要】 目的 探讨口腔颌面头颈部恶性肿瘤患者围手术期死亡病例的临床特点。方法 回顾1999年1月~2019年12月于上海交通大学医学院附属第九人民医院口腔颌面头颈肿瘤科治疗并发生围手术期死亡的口腔颌面头颈部恶性肿瘤患者的一般资料、病理诊断以及临床治疗信息;围手术期死亡因素分为外科因素、内科因素、复合因素(内科因素联同外科因素)以及个人因素,使用SPSS17.0软件统计分析不同前提下死亡因素组成差异。结果 最终纳入55例患者:男性39例,女性16例。12例具有吸烟史,28例患有基础性疾病。20例接受过术前放疗,9例接受过术前化疗。37例病理学诊断为鳞状细胞癌,9例肿瘤位于上颌骨及颅底区域。围手术期死亡4例发生于术前,1例发生于术中,50例发生于术后。死亡主要因素中:外科因素以颈总动脉破裂为主(8例),内科因素以肺部感染为主(6例),复合因素以血肿合并肺部感染为主(4例),个人因素死亡2例。美国麻醉医师协会(American Society of Anesthesiologist, ASA)评分越高的患者,死亡因素中内科因素占比更高($P=0.039$)。结论 口腔颌面头颈部恶性肿瘤患者围手术期死亡因素组成较为复杂:颈总动脉破裂是最常见、最致命的外科因素,尤其针对术前接受过放疗的患者;肺部感染是最常见内科并发症;ASA评分越高,围手术期死亡内科因素占比越高。

【关键词】 口腔颌面头颈部恶性肿瘤; 围手术期死亡; 颈总动脉破裂; 放疗; 化疗; 肺部感染; ASA评分

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55 cases of perioperative mortality in oral maxillofacial head and neck cancer patients: a retrospective analysis

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【Abstract】 **Objective** To analyze the characteristics of perioperative mortality (POM) in oral maxillofacial head and neck cancer patients. **Methods** A retrospective study was adapted for head and neck cancer patients who were treated and had POM in the department of oral maxillofacial & head and neck oncology in Shanghai Ninth People's Hos-

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pital from Jan 1999 to Dec 2019. Demographic information, disease characteristic and clinical records were collected. The factors of POM were classified into surgical complication, medical complication, mixed complication (surgical and medical) and personal complication. SPSS 17.0 software was used to analyze the cause composition for POM under different condition. **Results** 55 patients were included: 39 were male, and 16 were female. A total of 12 patients had a smoking history. Furthermore, 28 patients had general comorbidities. 20 underwent preoperative radiotherapy and 9 received preoperative chemotherapy. Squamous cell carcinoma was the most frequent pathological diagnosis in 37 patients. A total of 9 patients had tumors in the maxilla and skull base. In addition, 4 patients had POM preoperatively, 1 patient had POM within the operation, and 50 patients had POM postoperatively. The leading causes of death were as follows: rupture of the carotid artery was the most frequent (8), and the surgical complication of pulmonary infection was the main medical complication (6). Pulmonary infection and hemorrhage were regarded as the main mixed complication (4). Two patients had POM due to personal complications. The higher the American Society of Anesthesiologists (ASA) score, the higher the proportion of medical factors in POM ($P = 0.039$). **Conclusion** The composition of POM in oral maxillofacial- head and neck cancer (OMHNC) patients was complicated. Carotid artery rupture was the most common and fatal surgical complication, especially for those who underwent preoperative radiotherapy. Pulmonary infection was the most frequent medical complication, and those who had a higher ASA grade tended to have more complication.

【Key words】 oral maxillofacial- head and neck cancer; perioperative mortality; rupture of carotid artery; radiotherapy; chemotherapy; pulmonary infection; ASA grade

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口腔颌面头颈部恶性肿瘤(oral maxillofacial-head and neck cancer, OMHNC)连同上消化道恶性肿瘤居全身恶性肿瘤第七位,其发病趋势逐年递增^[1]。发展中国家OMHNC患者多数在就诊时已经处于疾病晚期^[2]。手术、辅助化疗、辅助放疗在内的多项治疗措施被用于治疗上述疾病,对于自身情况可以耐受全麻手术的患者,肿瘤切除或切取活检被视为优先治疗方案。随着近年来手术以及麻醉技术的进步,OMHNC患者围手术期并发症比例显著下降,但是围手术期死亡(perioperative mortality, POM)仍时有发生^[3]。文献回顾可知:发达国家此类疾病患者围手术期死亡率(perioperative mortality rate, POMR)约为0.2%~9.8%,我国OMHNC患者的围手术期死亡率尚不明确,相关报道也罕见于文^[4]。OMHNC患者围手术期死亡是多种因素单独或共同作用的结果:心肌梗死、血肿、肺栓塞、肺部感染等因素均见诸于文献^[5]。既往临床研究侧重于OMHNC患者预后,围手术期死亡病例的关注力度相对有限。研究OMHNC患者围手术期死亡的临床表现及相关因素,有利于临床医生了解POM风险并采取针对性措施降低此类事件的发生概率。本研究旨在分析OMHNC患者围手术期死亡的临床特点及相关因素,以为临床医师提供参考。

1 病例资料

1.1 一般资料、临床治疗信息

筛选1999年1月~2019年12月于上海上海交

通大学医学院附属第九人民医院口腔颌面头颈肿瘤科接受治疗的患者。纳入标准:①收治入院拟接受或已经全麻手术治疗(肿瘤切除或切取活检);②病理诊断为口腔颌面头颈部恶性肿瘤(未接受手术患者以术前病理诊断为准);③出现围手术期死亡。排除标准:①未接受或未曾计划进行全麻手术治疗(肿瘤切除或切取活检);②病理诊断非头颈部恶性肿瘤;③未出现围手术期死亡。

收集纳入患者的基本信息、病理、影像、临床治疗信息。基本信息包括年龄、性别、吸烟史以及酗酒史。所有病理学诊断均由两位高年资病理学医师分别审核后共同得出。肿瘤发病部位则参照临床症状、影像学资料以及术中肿瘤标本综合分析后得出。临床治疗信息包括既往治疗记录,术前评估、手术记录以及术后治疗信息:既往治疗记录侧重于术前放疗、化疗以及头颈部手术史,术前评估主要参照美国麻醉协会(American Society of Anesthesiologists, ASA)评分;手术记录主要采集肿瘤切除(切取)方式、术中出血、手术时间、修复方式、术中突发情况;术后治疗信息重点关注手术结束至围手术期死亡发生期间的临床症状、化验/检查指标,围手术期死亡发生时的抢救记录以及化验指标均由两位高年资医师共同审阅。

围手术期死亡因素被分为4类:外科因素、内科因素、复合因素(外科因素联合内科因素)以及个人因素(非治疗相关因素)。

1.2 统计学分析

使用SPSS 17.0对上述数据进行分析:Fisher检验被用于比较不同因素下口腔颌面头颈部恶性肿瘤患者围手术期死亡组成因素的差异, $P < 0.05$ 为差异具有统计学意义。

2 结果

1999年1月~2019年12月笔者所在科室OMHNC手术患者总计16 112例,55例符合纳入标准:男39例,女16例,年龄24~88岁,平均年龄(63.24 ± 13.63)岁;12例有吸烟史,28例患有基础性疾病。24例既往接受过头颈部肿瘤相关手术,20例本次术前接受过放疗,9例既往接受过化疗。

ASA I级1例,ASA II级33例,ASA III/IV/V级21例。手术时长60~780 min,平均手术时长(373 ± 200.19)min;术中失血50~1 400 mL,平均($572.73 + 336.76$)mL。3例术中行喉切除术,37例行气管切开(表1)。

基础性疾病以高血压(15例)以及冠心病(13例)为主,部分患者患有多种基础性疾病(表2)。

肿瘤部位较为分散:14例发病部位为下颌骨,10例位于颊部,7例位于舌体;病理诊断以鳞状细胞癌为主(37例),其次为黏液表皮样癌(5例),详细病理学诊断及肿瘤部位见表3。

4例围手术期死亡病例发生于术前,均为内科因素所致:心肌梗死1例,肺栓塞1例,心衰以及电解质失衡2例。术中1例死于失血过多。50例围手术期死亡发生于术后:最常见也是最危险的外科因素为颈总动脉破裂(8例),主要内科因素为肺栓塞(6例),最常见复合因素为肺部感染合并血肿(4例),个人因素死亡2例(意外跌落1例,患者家属阻碍医生施救1例)(表4)。不同因素围手术期死亡时间组成见表5。

单因素分析可知:不同ASA评分患者,围手术期死亡的内外科因素组成差异具有统计学意义($P = 0.039$,表6)。

3 讨论

随着近年来外科以及麻醉技术的进步,头颈部恶性肿瘤患者POMR显著下降,但是POM仍时有发生^[6]。过去20年间:我科OMHNC患者围手术期死亡例数从1999年的6例降至2019年的1例。

OMHNC患者围手术期死亡,内科因素占主导地位:心肌梗死、肺栓塞以及肺部感染最为常

表1 基本信息以及临床治疗信息

Table 1 Clinical and demographic characteristics of the

| patients | | n = 55 |
|--|------------------|----------------|
| Variable | | n |
| Age [median number (min-max), y] | | 63 (24-88) |
| Sex | Male | 39 |
| | Female | 16 |
| Smoking history | Yes | 12 |
| | No | 43 |
| General morbidity | Yes | 28 |
| | No | 27 |
| Tumor recurrence | Yes | 20 |
| | No | 35 |
| Previous operation | Yes | 24 |
| | No | 31 |
| Previous radiotherapy | Yes | 20 |
| | No | 35 |
| Previous chemotherapy | Yes | 9 |
| | No | 46 |
| Receive operation (this time) | Yes | 51 |
| | No | 4 |
| ASA grade | I | 1 |
| | II | 33 |
| | III | 16 |
| | IV | 4 |
| | V | 1 |
| Operation time [median number (min-max), min] | | 420 (60-780) |
| Operative blood loss [median number (min-max), mL] | | 600 (50-1 400) |
| Airway management | Tracheotomy | 37 |
| | Throat colostomy | 2 |
| | No | 6 |
| POM time classification | Preoperative | 4 |
| | Intraoperative | 1 |
| | Postoperative | 50 |
| POM complication classification | Surgical | 12 |
| | Medical | 31 |
| | Mixed | 10 |
| | Personal | 2 |

POM: perioperative mortality

见^[7-10]。机体状况较差的患者有一定概率出现多脏器衰竭(multiple organ dysfunction, MODS);并且口腔颌面头颈部恶性肿瘤本身也被认为是围手术期内科并发症的主要危险因素之一^[11-14]。高血压、糖尿病在内的基础性疾病以进一步提高围手术期并发症乃至死亡风险^[14]。本研究纳入患者逾50%年龄大于60岁且患有基础性疾病,这在一定程度上解释了为何围手术期死亡以内科因素为主。

25%(1/4)的术前死亡以及10%(5/50)的术后死亡直接源于心肌梗死:心肌梗死在OMHNC患者

表2 基础性疾病组成

Table 2 Composition of systemic comorbidities

| Systemic comorbidity | Number |
|----------------------|--------|
| Hypertension | 15 |
| Diabetes | 6 |
| Cerebral infarction | 2 |
| Epilepsy | 1 |
| COPD | 3 |
| Premature beat | 2 |
| Hypoproteinemia | 1 |
| Cerebral hemorrhage | 1 |
| MI | 4 |
| CHD | 13 |
| SS | 1 |
| Raynaud's disease | 1 |
| CGN | 1 |
| Asthma | 1 |

COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; CHD: coronary heart disease; SS: Sjogren's syndrome; CGN: chronic glomerulonephritis; some patients had more than one kind of general morbidity

表3 病理诊断及肿瘤部位

Table 3 Pathological diagnosis and tumor region

| Diagnosis and region | n | |
|--|------------------------|----|
| Squamous cell carcinoma mucosa | Maxilla and skull base | 2 |
| | Mandible | 10 |
| | Buccal | 8 |
| | Tongue | 7 |
| | Cervical | 4 |
| | Parapharyngeal | 5 |
| | Parotid | 1 |
| Osteosarcoma | Maxilla and skull base | 1 |
| Chondrosarcoma | Maxilla and skull base | 1 |
| Malignant hemangioendothelioma | Buccal | 1 |
| Ameloblastoma | Mandible | 1 |
| ACC | Maxilla and skull base | 1 |
| MEC | Cervical | 3 |
| | Parotid | 1 |
| Lymphoma | Maxilla and skull base | 1 |
| Epidermoid carcinoma | Infraorbital | 1 |
| Inflammatory myofibroblastic tumor with local malignancy | Maxilla and skull base | 3 |
| | Mandible | 3 |
| Malignant hemangioendothelioma | Buccal | 1 |
| Total | 55 | |

ACC: adenoid cystic carcinoma; MEC: mucoepidermoid carcinoma

中占比不足5%,其可在极短时间内导致死亡^[12-14]。肺栓塞在OMHNC患者围手术期治疗中受

表4 围手术期死亡因素组成

Table 4 Etiology composition of perioperative mortality

| POM | Number | |
|--|---|---|
| Preoperative POM-Medical | MI | 1 |
| | Heart failure | 1 |
| | Electrolyte disturbance | 1 |
| Intraoperative POM- Surgical | Pulmonary infection | 1 |
| | Hemorrhage | 1 |
| Postoperative POM- Surgical | Rupture of carotid artery | 8 |
| | Asphyxia caused by hematoma | 3 |
| Postoperative POM-Medical | Pulmonary embolism | 5 |
| | MI | 5 |
| | Heart failure | 1 |
| | Electrolyte disturbance | 1 |
| | Pulmonary infection | 6 |
| | Cardiopulmonary arrest | 2 |
| | Pancreatitis | 1 |
| | MODS | 7 |
| | MODS+DIC | 1 |
| | Shock | 1 |
| | Mix | |
| | Pulmonary infection+Hemorrhage | 4 |
| | Aspiration+ Pulmonary infection+ MODS+ Hemorrhage | 2 |
| | Postoperative hemiplegia+ | 1 |
| | Pulmonary infection | |
| Pulmonary embolism+ Urinary tract infection | 1 | |
| MODS+DIC+ Hemorrhage | 1 | |
| Personal: fall from cycling | 1 | |
| Personal: patient's relatives refuses rescue | 1 | |
| Total | 55 | |

POM: perioperative mortality; MI: myocardial infarction; MODS: multiple organ dysfunction syndrome; DIC: disseminated intravascular coagulation

到的重视程度相比于心肌梗死略低,既往文献回顾可知肺栓塞在此类患者围手术期发生的概率不足1%^[14],10%(5/50)的患者因肺栓塞在术后死亡;血管化游离皮瓣是OMHNC手术常用的修复手段,接受此类手术的患者在术后被要求严格卧床3d,这会进一步增加下肢深静脉血栓(deep venous thrombosis, DVT)以及肺栓塞形成的风险,合理使用抗凝药物以下肢气压泵可以降低此类情况的风险(表4)。我科接受皮瓣修复的OMHNC患者术前

表5 不同因素下围手术期死亡发生时间

Table 5 The time characteristic of perioperative mortality under different variables

| Variable | | Median time (day) | Range (day) |
|---------------------------|------------------|----------------------|----------------|
| Age (years) | ≤ 65 | 11 | 3-65 |
| | > 65 | 10 | 2-120 |
| Sex | Male | 10 | 2-120 |
| | Female | 16 | 3-42 |
| Smoking history | Yes | 13 | 5-35 |
| | No | 10 | 2-120 |
| General morbidity | Yes | 8 | 2-65 |
| | No | 11 | 2-120 |
| Tumor recurrence | Yes | 14.5 | 3-30 |
| | No | 10 | 2-120 |
| Previous operation | Yes | 11 | 3-65 |
| | No | 10 | 2-120 |
| Previous radiotherapy | Yes | 10 | 2-65 |
| | No | 11 | 2-120 |
| Previous chemotherapy | Yes | 8 | 2-65 |
| | No | 11 | 2-120 |
| ASA grade | I | 10 | - |
| | II | 11 | 3-120 |
| | III | 10 | 2-65 |
| | IV | 5 | 2-8 |
| | V | 8 | - |
| Operation time (min) | ≤ 420 | 10 | 3-65 |
| | > 420 | 10 | 2-120 |
| Operative blood loss (ml) | ≤ 600 | | |
| | > 600 | 12 | 3-120 |
| Airway management | Tracheotomy | 10 | 2-65 |
| | Throat colostomy | 7.5 | 5-10 |
| | No | 14 | 3-120 |
| Mortality composition | Surgical | 10 | 3-15 |
| | Medical | 14 | 2-120 |
| | Mix | 12.5 | 3-30 |
| | Personal | 12 | 2-22 |

POM: perioperative mortality

均接受 Autar DVT 风险评估,高风险者术后 12~72 h 常规使用速碧林(低分子肝素钙,0.4 mL/支)半支 Q12H 皮下注射预防下肢深静脉血栓,术后 1~5 d 常规使用气动加压装置改善下肢血液循环并日常检测 DD(D-dimer, DD)二聚体,根据检测结果调整速碧林使用剂量;针对出现下肢肿胀、血氧饱和度异常等症状的患者,在下肢制动的前提下予以 B 超以及胸部 CT 以排查 DVT、肺栓塞,必要时由血管外科进行取栓治疗。

喉造瘘以及气管切开可以降低气道阻塞风险,同时也会便于细菌在呼吸道定植与感染;吸烟

表6 不同情况下围手术期死亡因素分析

Table 6 Analysis of the composition of perioperative mortality under different condition

| Condition | POM composition | | | | P |
|-----------------------|-----------------|---------|-----|----------|-------|
| | Surgical | Medical | Mix | Personal | |
| ASA | 1 | 1 | 0 | 0 | 0.039 |
| | 2 | 9 | 15 | 8 | |
| | 3 | 2 | 12 | 2 | |
| | 4 | 0 | 3 | 0 | |
| | 5 | 0 | 1 | 0 | |
| Age | ≤ 65 | 9 | 15 | 6 | 0.170 |
| | > 65 | 3 | 16 | 4 | |
| Airway management | Yes | 10 | 22 | 6 | 0.594 |
| | No | 2 | 9 | 4 | |
| General morbidity | Yes | 4 | 17 | 6 | 0.571 |
| | No | 8 | 14 | 4 | |
| Previous radiotherapy | Yes | 5 | 10 | 5 | 0.509 |
| | No | 7 | 21 | 5 | |
| Previous chemotherapy | Yes | 4 | 4 | 1 | 0.323 |
| | No | 8 | 27 | 9 | |
| Tumor recurrence | Yes | 6 | 11 | 3 | 0.514 |
| | No | 6 | 20 | 7 | |
| Blood loss (mL) | ≤ 600 | 7 | 19 | 7 | 0.674 |
| | > 600 | 5 | 12 | 3 | |
| Operation time (min) | ≤ 420 | 7 | 15 | 6 | 0.896 |
| | > 420 | 5 | 16 | 4 | |

ASA: American Society of Anesthesiologist; POM: perioperative mortality

史以及呼吸系统相关基础性疾病可使得上述情况更加糟糕^[15-16]。虽大大剂量抗生素的使用较为普遍,肺部感染在本研究中较为常见(表4):26%(13/50)术后死亡病例直接或间接由肺部感染引起;患者自身体质下降、耐药菌定植可能是肺部感染的附加风险因素。MODS 涉及免疫应答、神经功能、基础代谢等多方面,在大型手术术后具有较高的出现几率^[17]。本次研究纳入患者多数肿瘤恶性程度高、基础状况差:18%(9/50)患者术后因 MODS 死亡。除上述因素外:电解质失衡、胰腺炎等也导致部分死亡,但是占比较为有限;全身基础状况的全围手术期监测与及时适当纠正,可有效降低内科并发症及后续死亡风险^[18]。对于 OMHNC 患者尤其是高龄患者,我科经验如下:基础性疾病的治疗应当将术前阶段也作为重点,力争患者术前达到机体平衡状态;术后 1~5 d 日常(5 d 以后,改为每 3 天)检测电解质等指标并针对性修改补液组成,气管切开切口以及喉造瘘口分泌物接受药敏试验并调整抗生素使用。力争将体液指标以及感染在初始阶段予以控制,为后续治疗提供便利。

外科因素是OMHNC患者围手术期死亡的重要组成部分,术中及术后均可发生^[19]。100%术中死亡病例(1/1)以及22%(11/50)术后死亡由外科因素导致。颈总动脉破裂是最常见也是最为致命的外科因素:短时间内的大量失血可迅速引起患者死亡;既往放疗则可增加此类风险;血肿引起的窒息可导致患者脑部不可逆损伤进而引起死亡^[20]。OMHNC患者有较高概率接受颈淋巴结清扫,对于颈总动脉直接暴露于术野内尤其是术后颈部需要放疗的患者,术中应尽量使用邻近软组织或者游离皮瓣覆盖上述血管以起到保护作用。不同因素围手术期死亡时间组成见表5。

ASA评分系统是一种基于患者术前各项检查结果的外科风险评估系统,可在一定程度上评估围手术期死亡风险^[21]。本次研究纳入患者ASA评分较高者的死亡因素的组成中内科因素占比高于ASA评分较低者($P=0.039$,表6)。对于术前ASA评分较高的患者,围手术期应适当强化对应治疗措施。

口腔颌面头颈部恶性肿瘤患者围手术期死亡因素组成较为复杂:颈总动脉破裂是最常见、最致命的外科因素,尤其是对于术前接受过放疗的患者;肺部感染是最常见的内科因素;ASA评分越高,围手术期死亡因素会偏向内科方面。有效的术前排查、术中针对性保护以及术后定期检测、治疗可降低OMHNC患者围手术期死亡的发生率。

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