

论著·循证医学

口腔癌患者张口受限患病率的meta分析

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[摘要] **目的**·通过meta分析研究口腔癌患者张口受限患病率。**方法**·检索中国知网(CNKI)、中文科技期刊数据库(VIP)、万方数据知识服务平台(Wanfang)、中国生物医学文献数据库(CBM)、PubMed、Ovid、EMbase、Cochrane Library、Web of Science/SciSearch、ClinicalTrials.gov数据库关于口腔癌患者张口受限患病率的观察性研究(包括前瞻性研究、回顾性研究以及横断面研究),检索时限为建库到2022年4月30日。由2位研究人员按照纳入与排除标准对所获文献独立进行筛选、提取,采用非随机对照试验方法学评价指标(methodological index for non-randomized studies, MINORS)进行文献质量评价。以张口受限患病率为结局指标合并数据,采用Stata 15.0软件进行meta分析,并根据检测时间、肿瘤部位和肿瘤分期进行亚组分析。使用GRADE profiler 3.6软件,依据GRADE(Grading of Recommendations Assessment, Development, and Evaluation)证据质量分级系统对结局指标的证据质量进行评价。**结果**·初检共获得3 719篇文献,最终纳入18篇文献,包括2 701例调查对象。Meta分析结果显示,口腔癌患者张口受限总患病率为42.7%(95%CI 27.0%~59.1%)。亚组分析结果显示,手术前、术后3个月、术后6个月和术后1年及以上的口腔癌患者张口受限患病率分别为29.6%(95%CI 9.0%~55.8%)、75.2%(95%CI 68.3%~81.5%)、59.1%(95%CI 38.8%~77.9%)、22.3%(95%CI 2.0%~54.3%)。T1~T2期和T3~T4期口腔癌患者张口受限患病率分别为38.6%(95%CI 26.0%~52.0%)、99.6%(95%CI 93.9%~100.0%)。磨牙后三角区、牙龈、舌部、唾液腺、口底和唇部口腔癌患者张口受限患病率分别为93.1%(95%CI 68.5%~100.0%)、68.1%(95%CI 52.9%~81.7%)、46.1%(95%CI 11.6%~82.7%)、26.1%(95%CI 15.9%~37.5%)、21.9%(95%CI 0.7%~54.0%)、3.1%(95%CI 0~9.3%)。GRADE证据质量分级系统表明结局指标的证据质量为极低。**结论**·口腔癌患者张口受限总患病率较高,近50%;其中术后3个月、术后6个月、T3~T4期或肿瘤位于磨牙后三角区的患者患病率更高。

[关键词] 口腔肿瘤; 张口受限; 患病率; meta分析

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A meta-analysis of prevalence of mouth opening restriction in patients with oral cancer

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[Abstract] **Objective**·To study the prevalence of mouth opening restriction in oral cancer patients by meta-analysis. **Methods**·China National Knowledge Infrastructure (CNKI), Chinese Science and Technology Journal Database (VIP), Wanfang Data (Wanfang), Chinese BioMedical Literature Database (CBM), PubMed, Ovid, EMbase, Cochrane Library, Web of Science/SciSearch, and ClinicalTrials.gov were searched for observational studies about the prevalence rate of restricted mouth opening in oral cancer patients (including prospective, retrospective, and cross-sectional studies). The time limit for retrieval was from the database establishment to April 30th, 2022. The obtained documents were independently screened and extracted according to the inclusion and exclusion criteria, and the literature quality evaluation was performed by using methodological index for non-randomized studies (MINORS). The data were combined with the mouth-opening-restricted prevalence rate as the outcome indicator, the meta-

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analysis was performed by using Stata 15.0 software, and the subgroup analysis was performed based on the detection time, tumor site, and tumor stage. The evidence quality of outcome indicators was evaluated by using GRADE profiler 3.6 software according to GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system. **Results** A total of 3 719 documents were obtained during the initial examination, and 18 documents were finally included, including 2 701 objects. The meta-analysis results showed that the total prevalence rate of mouth opening restriction in oral cancer patients was 42.7% (95%CI 27.0%–59.1%). The results of subgroup analysis showed that the prevalence rates of mouth opening restriction in patients with oral cancer before surgery, and 3 months, 6 months and 1 year or more after surgery were 29.6% (95%CI 9.0%–55.8%), 75.2% (95%CI 68.3%–81.5%), 59.1% (95%CI 38.8%–77.9%) and 22.3% (95%CI 2.0%–54.3%), respectively. The prevalence rates of mouth opening restriction in patients with oral cancer at T1–T2 stage and T3–T4 stage were 38.6% (95%CI 26.0%–52.0%) and 99.6% (95%CI 93.9%–100.0%) respectively. The prevalence rates of mouth opening restriction in patients with oral cancer in the retromolar triangle, the gingiva, the tongue, the salivary gland, the floor of mouth and the lip were 93.1% (95%CI 68.5%–100.0%), 68.1% (95%CI 52.9%–81.7%), 46.1% (95%CI 11.6%–82.7%), 26.1% (95%CI 15.9%–37.5%), 21.9% (95%CI 0.7%–54.0%), and 3.1% (95%CI 0–9.3%), respectively. The GRADE system for evidence quality grading indicated that the quality of evidence for outcome indicator was extremely low. **Conclusion** The total prevalence rate of mouth opening restriction in patients with oral cancer is high, nearly 50%; the patients at 3 months after surgery, at 6 months after surgery, at T3–T4 stage or whose tumor located in the retromolar triangle have higher prevalence rates.

[Key words] oral neoplasm; mouth opening restriction; prevalence; meta-analysis

口腔癌 (oral cavity cancer, OCC) 在全球最常见恶性肿瘤中居第 11 位, 发病率较高, 正日益成为全球公共卫生领域关注的问题^[1]。2020 年全球癌症统计数据^[2]显示: 口腔癌全球新发病例为 377 713 例, 占 1 930 万癌症新发病例的 2.0%; 新死亡病例为 177 757 例, 占全球 1 000 万癌症新死亡病例的 1.8%。

张口受限是口腔癌术后或放射治疗 (放疗) 后的常见并发症之一, 但也可能发生在治疗前^[3]。张口受限又称张口困难, 定义为成人最大切牙间距离 (maximal interincisal opening, MIO) ≤ 35 mm^[4]。张口受限可能是自限性的, 但在部分患者中, 张口受限也可能表现为进行性发展, 甚至造成患者永久性伤害; 中度至重度张口受限会降低言语清晰度, 并损害进食或咀嚼功能 (甚至出现吞咽困难), 严重影响患者的健康和生活质量^[5-6]。因此, 预防张口受限对于口腔癌患者至关重要。目前, 口腔癌患者张口受限的流行病学特征尚缺乏系统的研究和分析。基于此, 本研究收集关于国内外口腔癌患者张口受限患病率的观察性研究, 主要分析不同检测时间、肿瘤部位、肿瘤分期的口腔癌患者张口受限的患病率, 旨在为口腔癌张口受限的防治提供循证依据。

1 资料与方法

1.1 纳入标准与排除标准

纳入标准: ① 研究类型为口腔癌患者张口受限的观察性研究 (包括前瞻性研究、回顾性研究以及横

断面研究)。② 研究对象是明确诊断为口腔癌的患者。③ 结局指标包括口腔癌患者张口受限的患病率 (张口受限定义为成人 MIO ≤ 35 mm^[4])。

排除标准: ① 排除关节、炎症、创伤等其他因素引起的张口受限。② 非中英文文献。③ 重复发表文献。④ 无法提取数据的文献。⑤ 综述。

1.2 文献检索策略

计算机检索中国知网 (CNKI)、中文科技期刊数据库 (VIP)、万方数据知识服务平台 (Wanfang)、中国生物医学文献数据库 (CBM)、PubMed、Ovid (仅搜索 Medline 数据库)、EMbase、Cochrane Library、Web of Science/SciSearch、ClinicalTrials.gov 数据库, 检索时限为建库到 2022 年 4 月 30 日。同时, 追溯纳入文献的参考文献, 以补充获取相关文献。此外, 在科技会议录索引 (ISTP)、OCLC Firstsearch 检索系统和中国学术会议论文数据库 (CACP) 中检索会议学术报告; 在 ProQuest 学位论文全文库 (PQDT)、数字化博硕士论文文摘数据库 (PQDD)、CALIS 高校学位论文库、中国学位论文全文数据库 (CDDb)、中国优秀硕士学位论文全文数据库 (CMFD) 中检索学位论文。检索词采用主题词和自由词相结合的方式, 中文检索词包括: “口腔肿瘤” “口腔癌” “口癌” “口腔鳞癌”, 以及 “张口困难” “张口受限” 等; 英文检索词包括: "Mouth Neoplasms" "Neoplasm, Mouth" "Oral Neoplasm" "Oral Neoplasms" "Mouth Cancers" "Oral Cancer" "Cancer of Mouth", 以及 "Trismus" "Lockjaw" "Lock Jaw" "Restricted Mouth

Opening" "Restricted Jaw Movement" "Limited Mouth" "Restricted Jaw Movement"等。

1.3 文献筛选与资料提取

由2名评价员独立筛选文献、提取资料并交叉核对,如遇分歧,则咨询第三方协助判断,缺乏的资料尽量与作者联系补充。文献筛选时首先阅读文题和摘要,在确定为相关的文献后,进一步阅读全文,以确定最终是否纳入。资料提取的内容包括第一作者、发表年份、研究类型、研究对象等。

1.4 文献质量评价

对纳入研究进行单个率的meta分析,由于纳入研究缺乏对照组,故采用非随机对照试验方法学评价指标(methodological index for non-randomized studies, MINORS)进行文献质量评价^[7]。该评价体系由SLIM等制定,共12条评价指标,如果针对无对照组的研究,评价指标仅8条;每1条分值为0~2分,总分为16分。计分方法:0分代表未报道,1分代表有报道但数据不充分,2分代表信息完整。由2位研究者根据评分标准,独立进行评价^[8]。

1.5 统计学分析

采用Stata 15.0软件对纳入文献进行meta分析,效应分析统计量采用合并率和95%CI表示。对研究

文献进行异质性检验,采用 χ^2 检验($\alpha=0.05$,结合 I^2 值)确定。若 $P \geq 0.1$ 且 $I^2 \leq 50\%$,表明研究间具有同质性,选择固定效应模型进行分析。若 $P < 0.1$ 且 $I^2 < 50\%$,说明研究间具有异质性但在可接受的范围内,采用固定效应模型进行合并。若 $P < 0.1$ 且 $I^2 > 50\%$,说明研究间存在异质性,需采用随机效应模型进行分析;当异质性较大时,采用亚组分析探究异质性来源,分别以不同检测时间、肿瘤部位和肿瘤分期作为分组因素。通过敏感性分析评价meta分析结果的稳定性。根据漏斗图,结合Egger's检验和Begg's检验判断是否存在发表偏倚。 $P < 0.05$ 表示差异有统计学意义。

1.6 证据等级

使用GRADE profiler 3.6软件,依据GRADE(Grading of Recommendations Assessment, Development, and Evaluation)证据质量分级系统对结局指标的证据质量进行评价^[9]。主要从5个方面进行评价:偏倚性、不一致性、间接性、精确性和发表偏倚。证据质量分级包括高、中、低和极低4个等级。

2 结果

2.1 文献筛选流程

初检共获得3 719篇文献,经逐层筛选后,最终纳入18篇研究^[3,10-26],文献筛选流程见图1。

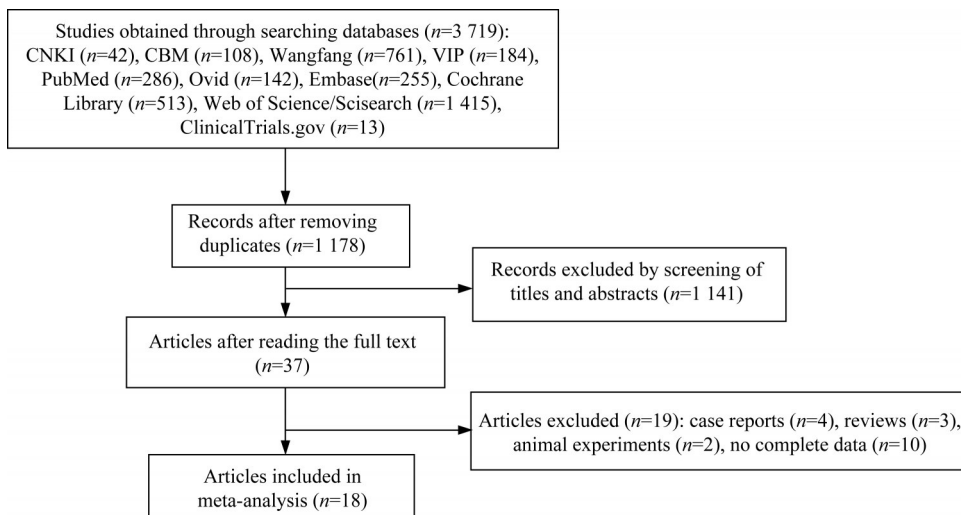


图1 文献筛选流程图

Fig 1 Flow diagram of literature screening

2.2 纳入研究的基本特征与偏倚风险评价结果

18篇研究^[3,10-26]共纳入2 701例研究对象,其中

样本量最少为22例,最多为730例,纳入研究的基本特征见表1,文献质量评价结果见表2。

表1 纳入研究的基本特征

Tab 1 Basic characteristics of the included studies

Study	Research type	Population	n	Outcome index
FU, et al (2014) ^[10]	Prospective study	Oral cancer patients	104	①②
GONDIVKAR, et al (2021) ^[11]	Prospective study	Oral cancer patients	100	①②③④
MARTINS, et al (2020) ^[12]	Prosepective study	Oral cancer patients	35	①③
PANTVAIDYA, et al (2019) ^[13]	Prosepective study	Oral cancer patients	401	①②
AGARWAL, et al (2016) ^[14]	Prosepective study	Oral cancer patients	30	②③④
MINHAS, et al (2017) ^[15]	Cross-sectional study	Patients with oral squamous cell carcinoma	81	①
OWOSHO, et al (2016) ^[16]	Retrospectivel study	Oral cancer patients	54	①③
SCOTT, et al (2011) ^[17]	Prosepective study	Oral cancer patients	98	②
WETZELS, et al (2014) ^[18]	Prospective study	Oral cancer patients	143	②
HSIEH, et al (2014) ^[19]	Prospective study	Patients with oral squamous cell carcinoma	22	①
VAN DER GEER, et al (2019) ^[20]	Cross-sectional study	Oral cancer patients	730	③
STEINER, et al (2015) ^[21]	Prospective study	Oral cancer patients	45	①
ASTRADSSON, et al (2018) ^[22]	Prospective study	Oral cancer patients	27	①②
JOHNSON, et al (2010) ^[3]	Prospective study	Oral cancer patients	246	③
PEI-LING, et al (2019) ^[23]	Cross-sectional study	Oral cancer patients	69	②
BATISTA, et al (2017) ^[24]	Prospective study	Oral cancer patients	100	①
NIKHAR, et al (2017) ^[25]	Prospective study	Oral cancer patients	156	①
MISHRA, et al (2005) ^[26]	Prospective study	Oral cancer patients	260	①

Note: ① The overall rate of mouth opening restriction. ② The rates of mouth opening restriction at different time points. ③ The rates of mouth opening restriction of the patients with lesions in different locations. ④ The rates of mouth opening restriction of the patients with different TNM tumor stages.

2.3 Meta分析结果

2.3.1 张口受限总患病率 共纳入 12 篇文献^[10-13, 15-16, 19, 21-22, 24-26], 异质性检验 $I^2=97.1\%$ ($P=$

0.000), 采用随机效应模型进行meta分析。分析结果显示, 口腔癌患者张口受限总患病率为 42.7% (95%CI 27.0%~59.1%), 详见图2。

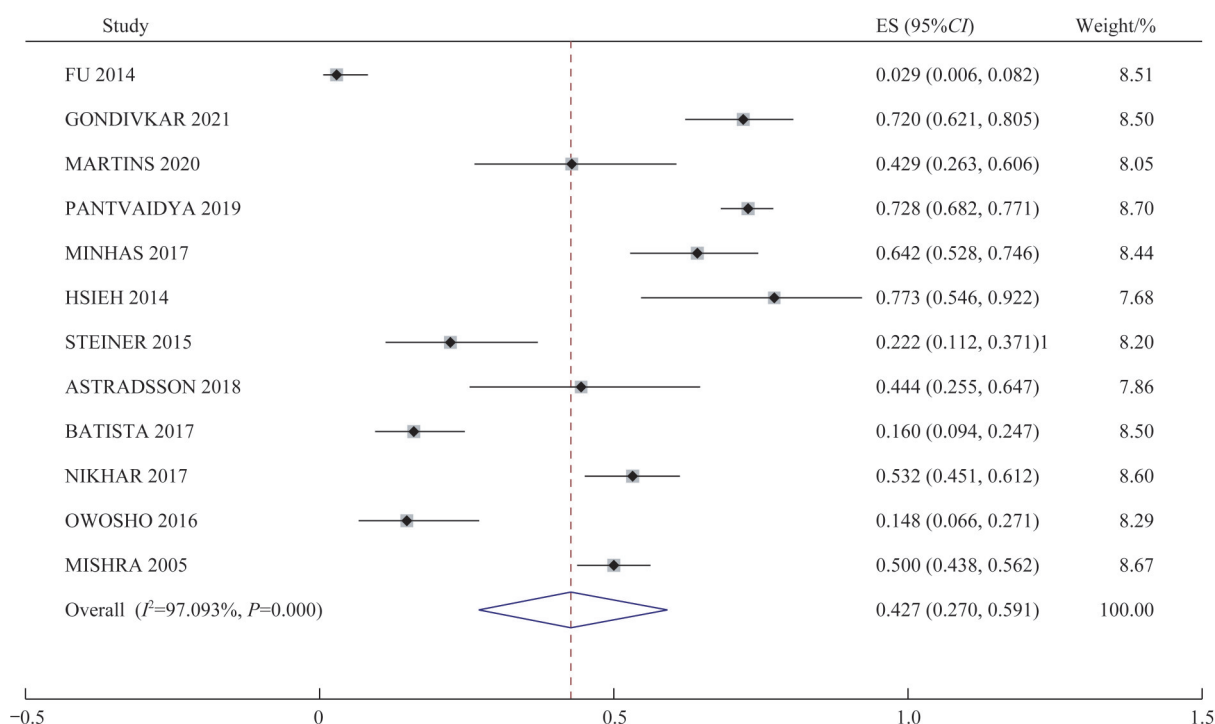


图2 口腔癌患者张口受限总患病率的森林图

Fig 2 Forest plot of the total prevalence rate of mouth opening restriction in the patients with oral cancer

表2 纳入研究的质量评价结果

Tab 2 Quality evaluation results of the included studies

Study	Score of item/point								Total score of MINORS/point
	①	②	③	④	⑤	⑥	⑦	⑧	
FU, et al (2014) ^[10]	2	2	2	2	0	2	2	0	12
GONDIVKAR, et al (2021) ^[11]	2	2	2	2	0	0	2	2	12
MARTINS, et al (2020) ^[12]	2	2	2	2	0	2	2	0	12
PANTVAIDYA, et al (2019) ^[13]	2	2	2	2	0	2	2	0	12
AGARWAL, et al (2016) ^[14]	2	2	2	2	0	2	2	0	12
MINHAS, et al (2017) ^[15]	2	2	2	2	0	2	2	0	12
OWOSHO, et al (2016) ^[16]	2	2	2	2	0	0	2	2	12
SCOTT, et al (2011) ^[17]	2	2	2	2	0	2	2	0	12
WETZELS, et al (2014) ^[18]	2	2	2	2	0	2	2	0	12
HSIEH, et al (2014) ^[19]	2	2	2	2	0	2	2	0	12
VAN DER GEER, et al (2019) ^[20]	2	2	2	2	0	2	2	0	12
STEINER, et al (2015) ^[21]	2	2	2	2	0	2	2	0	12
ASTRADSSON, et al (2018) ^[22]	2	0	2	2	0	0	2	2	10
JOHNSON, et al (2010) ^[3]	2	2	2	2	0	2	2	0	12
PEI-LING, et al (2019) ^[23]	2	2	2	2	0	2	2	0	12
BATISTA, et al (2017) ^[24]	2	2	2	2	0	0	0	0	8
NIKHAR, et al (2017) ^[25]	2	2	2	2	0	2	2	0	12
MISHRA, et al (2005) ^[26]	2	2	2	2	0	2	2	0	12

Note: ① A clearly stated aim: the question addressed should be precise and relevant in the light of available literature. ② Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion). ③ Prospective collection of data: data were collected according to a protocol established before the beginning of the study. ④ Endpoints appropriate to the aim of the study: unambiguous explanation of the criteria was used to evaluate the main outcome which should be in accordance with the question addressed by the study. Also the endpoints should be assessed on an intention-to-treat basis. ⑤ Unbiased assessment of the study endpoint: blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints. Otherwise the reasons for not blinding should be stated. ⑥ Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events. ⑦ Loss to follow up less than 5%: all patients should be included in the follow up. Otherwise the proportion lost to follow up should not exceed the proportion experiencing the major endpoint. ⑧ Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% confidence interval according to the expected incidence of the outcome event, and information about the level for statistical significance and estimates of power when comparing the outcomes.

2.3.2 亚组分析 分别以检测时间、肿瘤部位、肿瘤分期作为分组因素,进行亚组分析(表3)。

检测时间亚组分析:手术前,口腔癌患者张口受限患病率为29.6%;术后3个月,患病率为75.2%;术后6个月,患病率为59.1%;术后1年及以上,患病率为22.3%。

肿瘤分期亚组分析:T1~T2期,张口受限患病率

为38.6%;T3~T4期,患病率为99.6%。

肿瘤部位亚组分析:肿瘤位于磨牙后三角区,张口受限患病率为93.1%;位于牙龈处,患病率为68.1%;位于舌部,患病率为46.1%;位于唾液腺,患病率为26.1%;位于口底,患病率为21.9%;位于唇部,患病率为3.1%。

表3 口腔癌患者张口受限患病率的亚组分析结果

Tab 3 Results of subgroup analyses of the prevalence rates of mouth opening restriction in oral cancer patients

Subgroup	Study/n	I ² /%	P value	Effects model	Mouth opening restriction rate (95%CI)/%
Time					
Before surgery	5	96.2	0.000	Random	29.6 (9.0–55.8)
3 months after surgery	2	0	0.000	Fixed	75.2 (68.3–81.5)
6 months after surgery	5	94.7	0.000	Random	59.1 (38.8–77.9)
1 year or above after surgery	3	95.7	0.000	Random	22.3 (2.0–54.3)

Subgroup	Study/n	$I^2/\%$	P value	Effects model	Mouth opening restriction rate (95%CI)/%
Tumor stage					
T1-T2 phase	2	0	0.000	Fixed	38.6 (26.0-52.0)
T3-T4 phase	2	0	0.000	Fixed	99.6 (93.9-100.0)
Tumor site					
Retromolar triangle	2	0	0.000	Fixed	93.1 (68.5-100.0)
Gingiva	2	0	0.000	Fixed	68.1 (52.9-81.7)
Tongue	5	92.8	0.000	Random	46.1 (11.6-82.7)
Salivary glands	2	0	0.000	Fixed	26.1 (15.9-37.5)
Mouth floor	4	53.2	0.093	Random	21.9 (0.7-54.0)
Lip	4	0	0.465	Fixed	3.1 (0-9.3)

2.4 敏感性分析

采用逐一剔除单个研究的方法进行敏感性分析,结果显示:口腔癌患者张口受限患病率最低为39.7% (95%CI 23.4%~56.2%),异质性检验 $I^2=96.1\%$ ($P=0.000$);最高为47.7% (95%CI 27.0%~59.1%),异质性检验 $I^2=95.3\%$ ($P=0.000$)。此结果与最初合并结果42.7% (95%CI 34.2%~61.3%)相近,表明meta分析结果较为稳定。

2.5 发表偏倚

对12篇文献^[10-13, 15-16, 19, 21-22, 24-26]进行漏斗图分析,结果显示:研究分布大致对称(图3)。Begg's检验 $Z=0.00$ ($P=1.000$), Egger's检验 $t=-1.47$ ($P=0.172$),提示本研究存在较小的发表偏倚。

2.6 GRADE 评价结果

采用GRADE法对纳入文献合并后的结果进行质

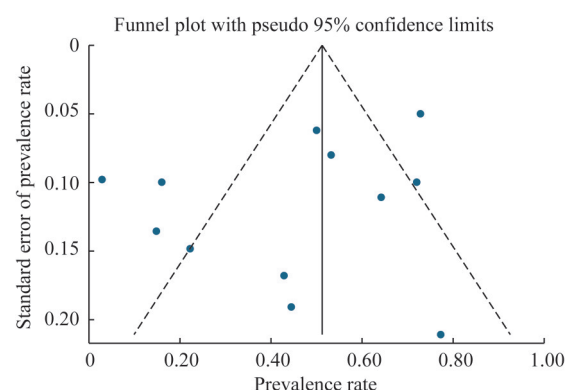


图3 口腔癌患者张口受限总患病率漏斗图

Fig 3 Funnel plot of the total prevalence rates of mouth opening restriction in the patients with oral cancer

量评价。观察性研究的初始等级为低,经过偏倚风险、不一致性、间接性、精确性和发表偏倚5个方面的评估,结果显示结局指标的证据质量等级均为极低(表4)。

表4 GRADE 证据质量等级评价表

Tab 4 Quality of evidence graded by the GRADE system

Outcome	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality
Total rate	Serious	Serious	No	No	No	Very low
Time						
Before surgery	Serious	Serious	No	Serious	—	Very low
3 months after surgery	Serious	No	No	Serious	—	Very low
6 months after surgery	Serious	Serious	No	Serious	—	Very low
1 year or above after surgery	Serious	Serious	No	Serious	—	Very low
Tumor stage						
T1-T2 phase	Serious	No	No	Serious	—	Very low
T3-T4 phase	Serious	No	No	Serious	—	Very low
Tumor site						
Retromolar triangle	Serious	No	No	Serious	—	Very low
Gingiva	Serious	No	No	Serious	—	Very low

Continued Tab

Outcome	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality
Tongue	Serious	Serious	No	Serious	—	Very low
Salivary glands	Serious	No	No	Serious	—	Very low
Mouth floor	Serious	Serious	No	Serious	—	Very low
Lip	Serious	No	No	Serious	—	Very low

Note: "—" represents not applicable.

3 讨论

本研究对18篇观察性研究^[3,10-26]进行汇总分析。MINORS质量评价结果显示纳入评分为8~12分,表明纳入文献质量有限。敏感性分析和发表偏倚检验均显示本研究meta分析结果较稳定。有文献^[3,18,27-31]报道,头颈肿瘤张口受限患病率的变化范围为28%~79%。本研究meta分析结果显示,口腔癌患者张口受限总患病率为42.7%,处于较高水平。因此医务工作者应该制定更加科学的策略来预防张口受限的发生。目前,物理治疗是张口受限的主要治疗方法,如颞下颌关节区及颈部肌肉的按摩、热敷和骨牵引等。但头颈肿瘤引起的张口受限仅靠物理治疗很难取得较好效果。有研究^[32-33]表明,物理治疗与下颌康复运动拉伸器联合治疗对头颈肿瘤患者张口受限具有较好的效果,可使用TheraBite和Dynasplint等运动康复系统装置进行张口训练。但关于张口训练开始的时间,文献中的建议未达成一致。RAPIDIS等^[29]认为在放疗完成后立即开始,LOH等^[30]认为在放疗期间即可开始。目前,普遍接受的观点是临床上患者一旦确诊为张口受限,应尽快开始张口锻炼;由于张口受限可能不断加重并出现不可逆的结果,尽早开展治疗尤为关键^[31]。

在对口腔癌患者张口受限总患病率进行合并时,发现纳入文献存在较大的异质性。因此,本研究根据不同检测时间、肿瘤部位、肿瘤分期,对纳入研究进行亚组分析。亚组分析的异质性检验结果显示,除了术前、术后3个月、术后1年及以上和舌部的口腔癌患者张口受限患病率异质性仍较高,其余各组异质性均明显下降,据此进行亚组分析能够在一定程度上降低组内异质性。本研究发现,不同检测时间、肿瘤分期和肿瘤部位的口腔癌患者张口受限患病率有明显差异。就检测时间而言,口腔癌患者张口受限患病率,在最初就诊时最低,在术后3~6个月上升,在术后1年以后有所下降。WATTERS等^[34]的研究也得到

了类似的结果:头颈肿瘤张口受限的患病率从基线时的17.3%,上升至6个月时的44.1%,1年后下降至36.1%,3年后下降至32.6%。这可能与术后放疗有关:由于放疗可引起咀嚼肌纤维化,并持续数月,进而导致肌肉组织挛缩,造成张口受限;同时放疗引起的局部血流灌注损失也可加重张口受限^[29-30,35]。放疗剂量越高,张口受限越严重,超过60 Gy的水平更容易引起张口受限。与首次接受治疗的患者相比,接受过放疗且目前正在放疗的患者出现张口受限的风险更高^[29,36]。就肿瘤分期而言,处于早期阶段的口腔癌张口受限患病率较低,处于晚期阶段的口腔癌张口受限患病率高。VAN DER GEER等^[20]发现,肿瘤的体积是发生张口受限的影响因素。较大的口腔肿瘤通常涉及部分颌骨切除。下颌骨是颌面部骨中唯一可活动的骨骼,参与构成颌面部下1/3的轮廓外形,在对舌体、下颌牙列以及口底肌肉的支撑中起主要作用,确保咀嚼、吞咽和呼吸等运动的正常进行^[37]。因此部分颌骨的切除可能会导致口腔癌患者张口受限。就肿瘤部位而言,各个部位张口受限的患病率各不相同,但高发部位都位于颞下颌关节。这可能由于颞下颌关节的原发性或转移性肿瘤可导致关节结构破坏,使关节无法正常旋转和平移^[38-40]。

虽然亚组分析在一定程度上能降低组内异质性,但研究间仍存在较大的异质性。可能是因为既往研究纳入人群特征不同,口腔癌的种类和病理类型有多种,但是既往观察性研究仅关注某种类型口腔癌患者或者某种病理特征的患者,没有对所有患者进行全面的考虑。既往研究类型包括前瞻性研究、回顾性研究以及横断面研究,这导致了张口受限检测的时间不同,有的研究是在口腔癌患者随访3个月、6个月和1年之后检测的,有些则在就诊时进行检测,因此张口受限患病率差异较大。除此之外,张口受限的检测方法和标准在不同研究中也稍有不同。这些因素也是导致本研究异质性较大的主

要原因。

本研究存在一些局限性:①受限于单个率meta分析的特点,纳入研究的异质性较高,虽然本研究根据纳入研究的特征,按检测时间、肿瘤分期、肿瘤部位分别进行亚组分析,但部分组别的研究异质性仍然较高,这可能影响meta分析的准确性。②研究范围仅覆盖了国内外部分国家,覆盖面有限,结果不足以反映口腔癌张口受限的总体患病率。③多篇文献未提供足够详细的资料,使得分组后部分组包含文献数量过少,缺乏代表性,影响了结果的可靠性。④所有结局指标的证据质量等级均为极低。

今后关于口腔癌患者张口受限的研究方向包括:

- ①当前国内缺少对口腔癌张口受限患病率的研究。可使用统一的标准,尝试在国内开展大样本的调查。
- ②目前为止,头颈肿瘤患者张口受限的最佳干预措施并未达成明确共识^[41];因此需要针对口腔癌患者张口受限的预防、治疗和管理开展更多高质量的研究,尤其是随机对照试验。

利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。

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作者贡献/Authors' Contributions

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