

论著·循证医学

冷冻疗法预防头颈癌患者放射性口腔黏膜炎的 meta 分析

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[摘要] **目的**·系统评价冷冻疗法在头颈癌患者放射治疗(放疗)所致口腔黏膜炎中的应用效果。**方法**·计算机检索中英文数据库(PubMed、EMbase、Cochrane Library、Web of Science、中国知网、万方、维普、中国生物医学文献数据库)中关于冷冻疗法对头颈癌患者放射性口腔黏膜炎影响的随机对照试验(randomized controlled trial, RCT), 检索时间从建库至2022年1月31日。2名研究者独立对所得文献进行筛选、数据提取及质量评价, 并运用RevMan 5.4及Stata 16.0软件进行meta分析。**结果**·共纳入36个RCT。Meta分析结果显示, 冷冻疗法组患者放射性口腔黏膜炎总发生率[比值比(odds ratio, OR)=0.30, 95%置信区间(confidence interval, CI) 0.23~0.39, P=0.000]及严重放射性口腔黏膜炎发生率(OR=0.17, 95%CI 0.14~0.21, P=0.000)明显低于对照组患者, 差异有统计学意义。**结论**·冷冻疗法有助于降低头颈癌放疗患者放射性口腔黏膜炎及严重放射性口腔黏膜炎发生率。

[关键词] 冷冻疗法; 头颈部肿瘤; 放射性口腔黏膜炎; meta分析; 随机对照试验

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Efficacy of preventive intervention of cryotherapy on radiation-induced oral mucositis in head and neck cancer: a meta-analysis

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[Abstract] **Objective**·To systematically review the efficacy of cryotherapy in head and neck cancer patients with radiation-induced oral stomatitis. **Methods**·PubMed, EMbase, Cochrane Library, Web of Science, CNKI, WanFang, VIP and CBM databases were searched to collect randomized controlled trials (RCTs) of cryotherapy in head and neck cancer patients with radiation-induced stomatitis from inception to January 31st, 2022. Literature screening, data extraction, and quality evaluation were performed independently by two researchers. Meta-analysis was then performed by using RevMan 5.4 and Stata 16.0 software. **Results**·A total of 36 RCTs were included. The results of meta-analysis showed that compared to control group, cryotherapy group had a lower total incidence of radiation-induced stomatitis [odds ratio (OR)=0.30, 95% confidence interval (CI) 0.23–0.39, P=0.000] and a lower incidence of severe radiation-induced stomatitis (OR=0.17, 95% CI 0.14–0.21, P=0.000). **Conclusion**·Cryotherapy may contribute to reducing the incidence of radiation-induced stomatitis and the incidence of severe radiation-induced stomatitis.

[Key words] cryotherapy; head and neck neoplasms; radiation-induced oral stomatitis; meta-analysis; randomized controlled trial

放射性口腔黏膜炎是头颈部肿瘤患者经放射治疗(放疗)后常见的不良反应, 常引起口腔疼痛、进食

困难、张口受限及继发感染等, 进而影响患者的营养状况、生活质量及预后, 严重时还会导致放疗中

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断^[1-4]。据报道,头颈部放疗所致口腔黏膜炎的发生率为85%~100%^[5-7]。因此,针对放疗所致口腔黏膜炎采取积极有效的预防措施是十分重要的。

口腔冷冻疗法(cryotherapy)是临床上一种简便、安全、低成本的干预方法,其利用低于人体温度的物质作用于口腔内或外,降低局部组织温度,促使局部血管收缩,减少口腔黏膜的血流量,减轻疼痛以及控制炎症扩散,进而减少口腔黏膜炎的发生。目前,已有多项关于冷冻疗法用于预防头颈癌放射性口腔黏膜炎的研究报道;然而,大多数研究样本量较小,或使用不同的评分方法,导致结论不一致。本研究旨在根据现有研究进行meta分析,以探讨冷冻疗法对预防头颈癌患者放射性口腔黏膜炎的有效性,为临床合理预防放射性口腔黏膜炎提供一定的参考依据。

1 资料与方法

1.1 纳入与排除标准

1.1.1 纳入标准 ①研究对象≥18岁,确诊为头颈癌并接受放疗的患者。②试验组在放疗开始时,同期接受冷冻疗法;对照组在放疗期间接受常规护理。③结局指标为严重口腔黏膜炎发生率。考虑到放射性口腔黏膜炎评估工具主要有世界卫生组织(World Health Organization, WHO)口腔黏膜炎分级标准、北美放射肿瘤治疗协作组(Radiation Therapy Oncology Group, RTOG)急性放射性黏膜反应分级标准、美国国家癌症研究所的常见毒性标准(National Cancer Institute Common Toxicity Criteria, NCI-CTC)等,各分级标准不一,本研究将以上口腔黏膜炎诊断评分表中Ⅲ~Ⅳ级判定为严重口腔黏膜炎^[1]。④研究类型为随机对照试验(randomized controlled trial, RCT)。

1.1.2 排除标准 排除非中、英文文献,以及重复发表、无法获取全文或数据不完整的文献。

1.2 文献检索策略

计算机检索PubMed、EMbase、Cochrane Library、Web of Science、中国知网、万方、维普、中国生物医学文献数据库(China Biology Medicine, CBM)数据库,检索时限均从建库至2022年1月31日。中文检索词:放射性口腔黏膜炎;放射性口腔炎;头颈部肿瘤;头颈癌;头颈部恶性肿瘤;鼻咽癌;冷冻疗法;冷疗

法;冰疗法;冰块;低温等。英文检索词: radiation-induced oral mucositis; radiotherapy-induced oral mucositis; head and neck cancer; nasopharyngeal neoplasms; cryotherapy; cold therapy; ice therapy; ice。检索以主题词与自由词相结合的方式进行,并根据各数据库特点进行调整;同时追溯纳入研究的参考文献。

1.3 文献筛选、资料提取与质量评估

由2名研究者根据研究的纳入和排除标准独立筛选文献、进行资料提取与质量评估,如有分歧,则通过讨论或与第三方协商解决。如有需要,联系原始研究作者获取相关信息。资料提取信息包括第一作者、发表时间、研究对象、样本量、干预措施、结局指标和结果测量数据等。

采用Cochrane系统评价手册5.1.0版本中的偏倚风险评估工具进行方法学质量评价^[8]。评价内容包括随机序列的产生、分配隐藏、选择性报告、盲法采用情况、结果数据不完整及其他偏倚(低风险、高风险、不清楚)。

1.4 统计学分析

采用RevMan 5.4及Stata 16.0软件进行统计分析。分类变量采用比值比(odds ratio, OR)为效应分析统计量,各效应量均采用其95%置信区间(confidence interval, CI)。结合 I^2 定量判断异质性大小。若纳入的各研究间无异质性或异质性较小($P>0.1$, $I^2<50%$),选用固定效应模型分析;若存在明显的异质性($P\leq 0.1$, $I^2\geq 50%$),选用敏感性分析、亚组分析等方法分析异质性来源,充分排除方法学异质性和临床异质性后,采用随机效应模型分析。 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 文献筛选流程及结果

初检共获得相关文献428篇。经逐层筛选,最终纳入36个RCT^[9-46]。文献筛选流程及结果见图1,纳入研究的基本特征见表1。

2.2 文献质量评价

所有研究均为RCT,均使用了随机分配。其中8项研究^[10-11,16,21,30,32,35,41]使用了随机数表法,1项研

究^[14]使用了计算机随机数字法,其余研究均仅提及随机分组而未描述具体的随机方法。所有研究均未提

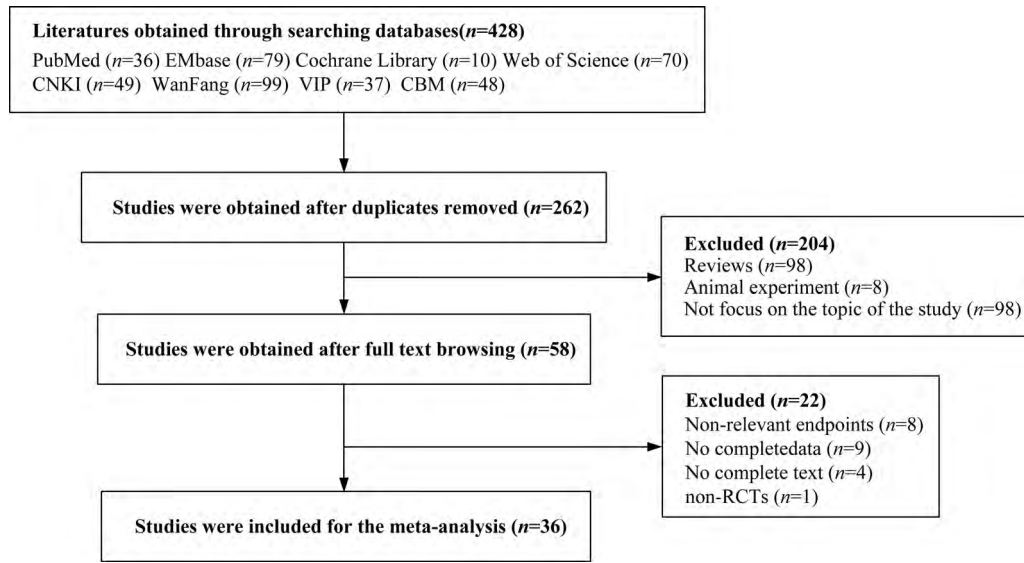


图1 文献筛选流程图

Fig 1 Flowchart of the study screening

表1 纳入研究的基本特征

Tab 1 Basic characteristics of the included studies

Study	Number of cases		Disease	Intervention		Assessment scale
	Exp	Con		Exp	Con	
GONG ^[9] , 2010	33	35	Head and neck cancer	RN+holding NS ice in the mouth	RN	RTOG
LI ^[10] , 2017	50	50	Nasopharyngeal cancer	RN+holding NS ice in the mouth	RN	WHO
XU ^[11] , 2021	80	80	Nasopharyngeal cancer	RN+holding NS ice in the mouth	RN	RTOG
CHEN ^[12] , 2012	48	42	Nasopharyngeal and oral cancer	RN+holding NS ice in the mouth+spraying rhEGF	RN+spraying rhEGF	WHO
ZHANG ^[13] , 2013	60	60	Nasopharyngeal cancer	RN+holding NS ice in the mouth+spraying rhEGF	RN+spraying rhEGF	WHO
GONG ^[14] , 2011	40	40	Nasopharyngeal cancer	RN+ice compress	RN	RTOG
Ji ^[15] , 2008	31	31	Head and neck cancer	RN+ice compress	RN	RTOG
QU ^[16] , 2019	44	44	Nasopharyngeal cancer	RN+ice compress+strengthening nursing	RN	WHO
YAN ^[17] , 2011	66	66	Nasopharyngeal cancer	RN+ice compress+spraying JUS	RN	WHO
CAI ^[18] , 2021	55	55	Nasopharyngeal cancer	RN+holding Kangfuxin ice in the mouth	RN	RTOG
LI ^[19] , 2010	22	18	Nasopharyngeal cancer	RN+holding Kangfuxin ice in the mouth	RN	WHO
MIN ^[20] , 2014	10	10	Nasopharyngeal cancer	RN+holding Kangfuxin ice in the mouth	RN	NCI-CTC

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Study	Number of cases		Disease	Intervention		Assessment scale
	Exp	Con		Exp	Con	
GU ^[21] , 2020	45	44	Nasopharyngeal cancer	RN+holding green tea ice in the mouth	RN	RTOG
XU ^[22] , 2019	39	41	Nasopharyngeal cancer	RN+holding green tea ice in the mouth	RN	RTOG
HUANG ^[23] , 2011	40	40	Nasopharyngeal cancer	RN+holding Kuding tea ice in the mouth	RN	WHO
ZHANG ^[24] , 2017	25	25	Head and neck cancer	RN+holding Kuding tea ice in the mouth	RN	WHO
ZHANG ^[25] , 2015	30	30	Nasopharyngeal cancer	RN+holding SB ice in the mouth	RN	WHO
YU ^[26] , 2011	30	30	Head and neck cancer	RN+holding SB ice in the mouth+aerosol inhalation with deproteinised calf blood extract	RN	WHO
ZHAO ^[27] , 2015	25	25	Oral cancer	RN+holding milk ice in the mouth	RN	RTOG
WAN ^[28] , 2011	99	99	Nasopharyngeal cancer	RN+holding milk ice in the mouth+drinking the herbal tea	RN	WHO
HUANG ^[29] , 2018	50	50	Nasopharyngeal cancer	RN+holding Glycyrrhiza and Wumei ice in the mouth	RN	WHO
JIN ^[30] , 2019	50	50	Nasopharyngeal cancer	RN+holding Chuanbeipagao and Yunnanbaiyao ice in the mouth	RN	WHO
LIU ^[31] , 2010	30	30	Nasopharyngeal cancer	RN+holding Glycyrrhiza ice in the mouth	RN	WHO
LU ^[32] , 2015	52	48	Nasopharyngeal cancer	RN+holding Biyafen ice in the mouth	RN+mouth-washing with Titai solution	RTOG
TANG ^[33] , 2018	20	20	Nasopharyngeal cancer	RN+holding carrot ice in the mouth	RN+drinking vitamin solution	RTOG
WANG ^[34] , 2016	40	40	Nasopharyngeal cancer	RN+holding Smecta ice in the mouth	RN+mouth-washing with warm Smecta solution	RTOG
LIU ^[35] , 2014	30	30	Oral and maxillofacial cancer	RN+holding ice cream in the mouth	RN	WHO
LU ^[36] , 2017	20	20	Head and neck cancer	RN+holding the frozen device in the mouth+mouth-washing with vitamin-B12 solution	RN	RTOG
GU ^[37] , 2016	47	47	Nasopharyngeal cancer	RN+holding sterile distilled water ice in the mouth+mouth-washing with icy saline solution	RN	WHO
HE ^[38] , 2018	50	50	Nasopharyngeal cancer	RN+mouth-washing with icy aloe solution	RN	WHO
QIN ^[39] , 2020	40	40	Nasopharyngeal cancer	RN+mouth-washing with icy mixed solution (which contains tea polyphenols, normal saline, lidocaine and dexamethasone)	RN+mouth-washing with NS solution	RTOG
QIN ^[40] , 2021	60	60	Nasopharyngeal cancer	RN+mouth-washing with icy mixed solution (which contains tea polyphenols, normal saline, lidocaine and dexamethasone)	RN+mouth-washing with sodium bicarbonate solution	RTOG
YANG ^[41] , 2019	36	36	Nasopharyngeal cancer	RN+mouth-washing with icy water+taking artificial cow-bezoar pills	RN	WHO
XIE ^[42] , 2019	30	30	Head and neck cancer	RN+mouth-washing with icy solution which contains G-CSF	RN	RTOG
PANG ^[43] , 2013	25	25	Head and neck cancer	RN+mouth-washing with icy mixed solution which contains thymus protein	RN+mouth-washing with Duobeier solution	WHO
BAI ^[44] , 2019	33	35	Head and neck cancer	RN+cryogenic aerosol inhalation(4-8 °C)	RN+normal aerosol inhalation(18-24 °C)	RTOG

Note: Exp—experimental group; Con—control group; RN—routine nursing; NS—normal saline; rhEGF—recombinant human epidermal growth factor; JUS—Jieyoushen, a long-acting antibacterial material; SB—sodium bicarbonate; G-CSF—granulocyte colony stimulating factor.

及分配隐藏, 试验过程中研究者和受试者的盲法设计以及结局评定人员设盲等方面, 无法进行评价。1项研究^[13]报道对照组1例因严重口腔黏膜炎终止放疗, 其余研究均未见病例脱落及失访等情况, 资料数据完整。

2.3 Meta分析结果

2.3.1 放射性口腔黏膜炎总发生率 有35项研究^[9-19, 21-44]报道了放射性口腔黏膜炎发生例数, 其中16项研究^[14-15, 17, 19, 23-26, 28, 30-31, 33-34, 37, 40-41]试验组和

对照组患者全部发生了放射性口腔黏膜炎, 其OR值, 即干预组中放射性口腔黏膜炎发生人数与未发生人数的比值除以对照组中发生人数与未发生人数的比值不可计算, 予以剔除后合并19项研究^[9-13, 16, 18, 21-22, 27, 29, 32, 35-36, 38-39, 42-44]显示各项研究之间无统计学异质性 ($P=0.10$, $I^2=31%$), 故应用固定效应模型合并效应量进行分析。结果显示: 2组患者放射性口腔黏膜炎发生率比较, 差异有统计学意义 ($OR=0.30$, $95\%CI 0.23\sim 0.39$, $P=0.000$)。Meta分析森林图见图2。

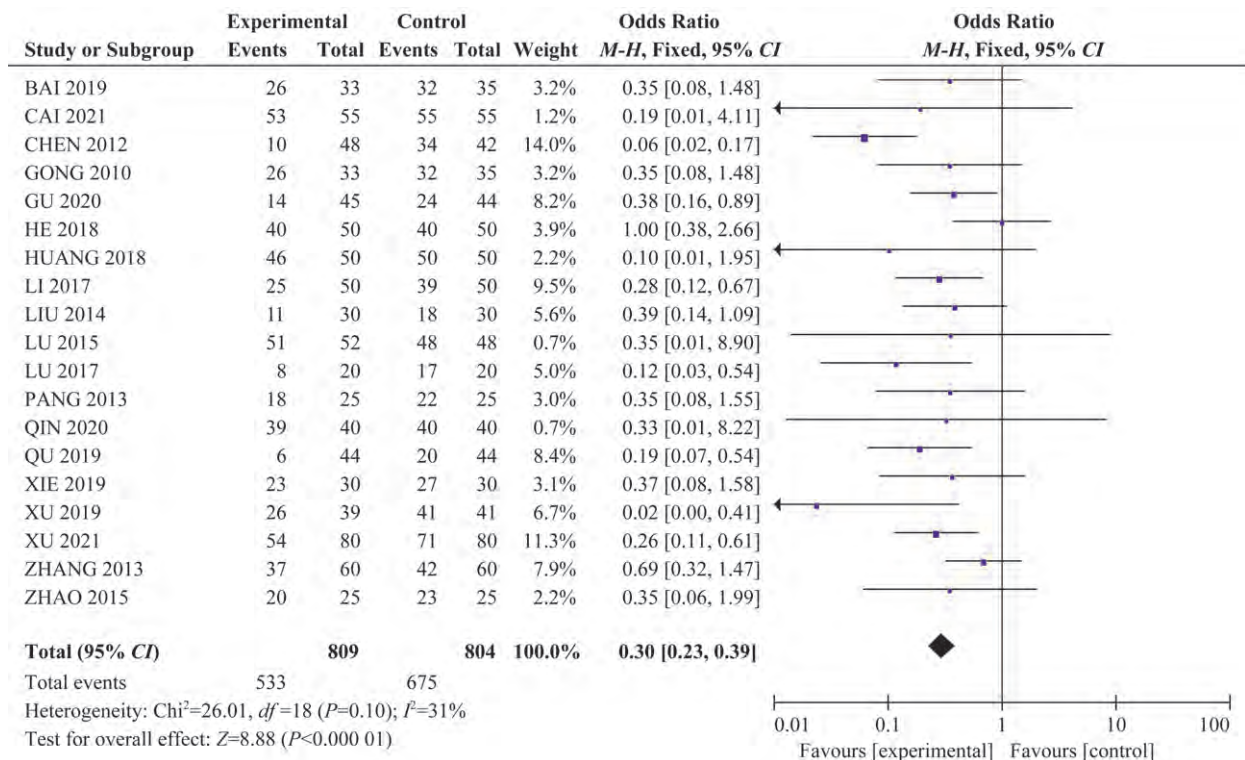


图2 冷冻疗法预防放射性口腔黏膜炎的meta分析结果及森林图

Fig 2 Meta-analysis and forest plots of cryotherapy for prevention of radiation-induced oral mucositis

2.3.2 严重放射性口腔黏膜炎发生率 共纳入36项研究^[9-44], 试验组1485例, 对照组1476例, 各项研究之间无统计学异质性 ($P=0.19$, $I^2=17%$), 故应用固定效应模型合并效应量进行分析。结果显示: 2组患者严重放射性口腔黏膜炎发生率比较, 差异有统计学意义 ($OR=0.17$, $95\%CI 0.14\sim 0.21$, $P=0.000$)。Meta分析森林图见图3。

对严重放射性口腔黏膜炎按照不同具体干预方式进行亚组分析, 结果显示: 口含生理盐水冰块组^[9-13] ($OR=0.25$, $95\%CI 0.14\sim 0.43$, $P=0.000$)、冰袋冰敷组^[14-17] ($OR=0.12$, $95\%CI 0.06\sim 0.22$, $P=0.000$)、口

含康复新冰块组^[18-20] ($OR=0.25$, $95\%CI 0.12\sim 0.49$, $P=0.000$)、口含绿茶冰块组^[21-22] ($OR=0.02$, $95\%CI 0.00\sim 0.19$, $P=0.000$)、口含苦丁茶冰块组^[23-24] ($OR=0.21$, $95\%CI 0.09\sim 0.51$, $P=0.000$)、口含碳酸氢钠冰块组^[25-26] ($OR=0.13$, $95\%CI 0.06\sim 0.31$, $P=0.000$) 严重放射性口腔黏膜炎发生率均低于对照组, 差异均有统计学意义。Meta分析森林图见图4。

2.4 发表偏倚评估

以放射性口腔黏膜炎总发生率及严重放射性口腔黏膜炎发生率为指标, 绘制漏斗图及采用Egger's检

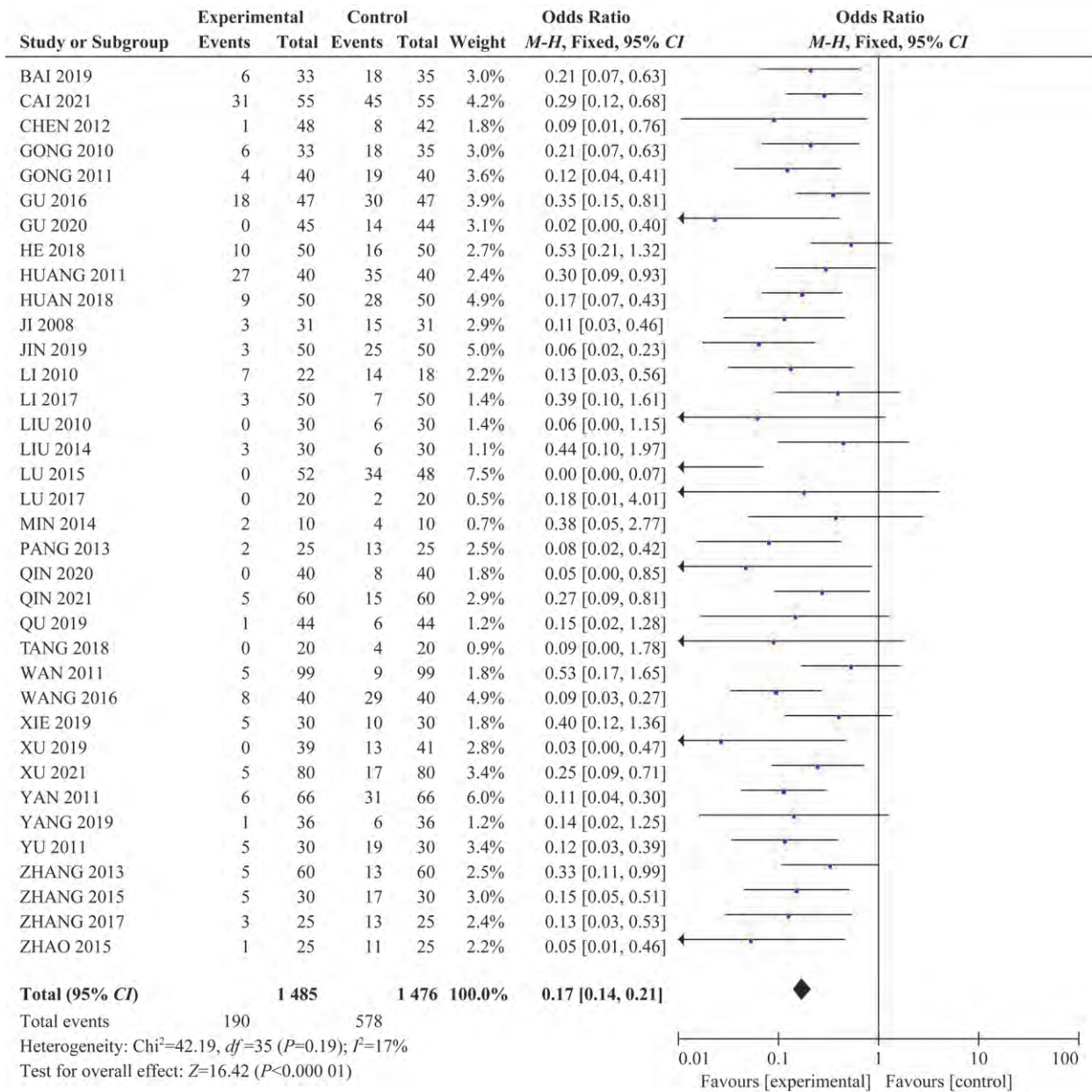


图3 冷冻疗法预防严重放射性口腔黏膜炎的meta分析结果及森林图

Fig 3 Meta-analysis and forest plots of cryotherapy for prevention of severe radiation-induced oral mucositis

验评估发表偏倚。放射性口腔黏膜炎总发生率的漏斗图呈现基本对称的形状 (图5); 进一步进行Egger's 检验 (P=0.191), 结果表明不存在明显的偏倚。严重放射性口腔黏膜炎发生率的漏斗图呈现不对称形状 (图6); Egger's 检验结果 (P=0.001) 表明存在一定的发表偏倚。

2.5 敏感性分析

对放射性口腔黏膜炎总发生率和严重放射性口腔黏膜炎发生率2项结局指标的meta分析结果, 分别逐一剔除纳入的单个研究后合并效应量重新进行分析,

结果未发生方向性改变, 且各研究的合并效应量未发生明显变化, 提示本研究结果稳定性较高。同时, 再应用失安全系数 (fail-safe number, N_{fs})^[45] 说明分析结果的稳定性。以P=0.05水平, 计算公式为: $N_{fs0.05} = (\sum Z/1.64)^2 - k$, 其中k为纳入研究个数, Z为各独立研究的Z值。放射性口腔黏膜炎总发生率的失安全系数 [$N_{fs0.05}=438.459 > (5k+10)$]、严重放射性口腔黏膜炎发生率的失安全系数 [$N_{fs0.05}=2 894.443 > (5k+10)$] 均较大, 说明本研究合并结果较为稳定, 结论不易被逆转, 可靠性高。

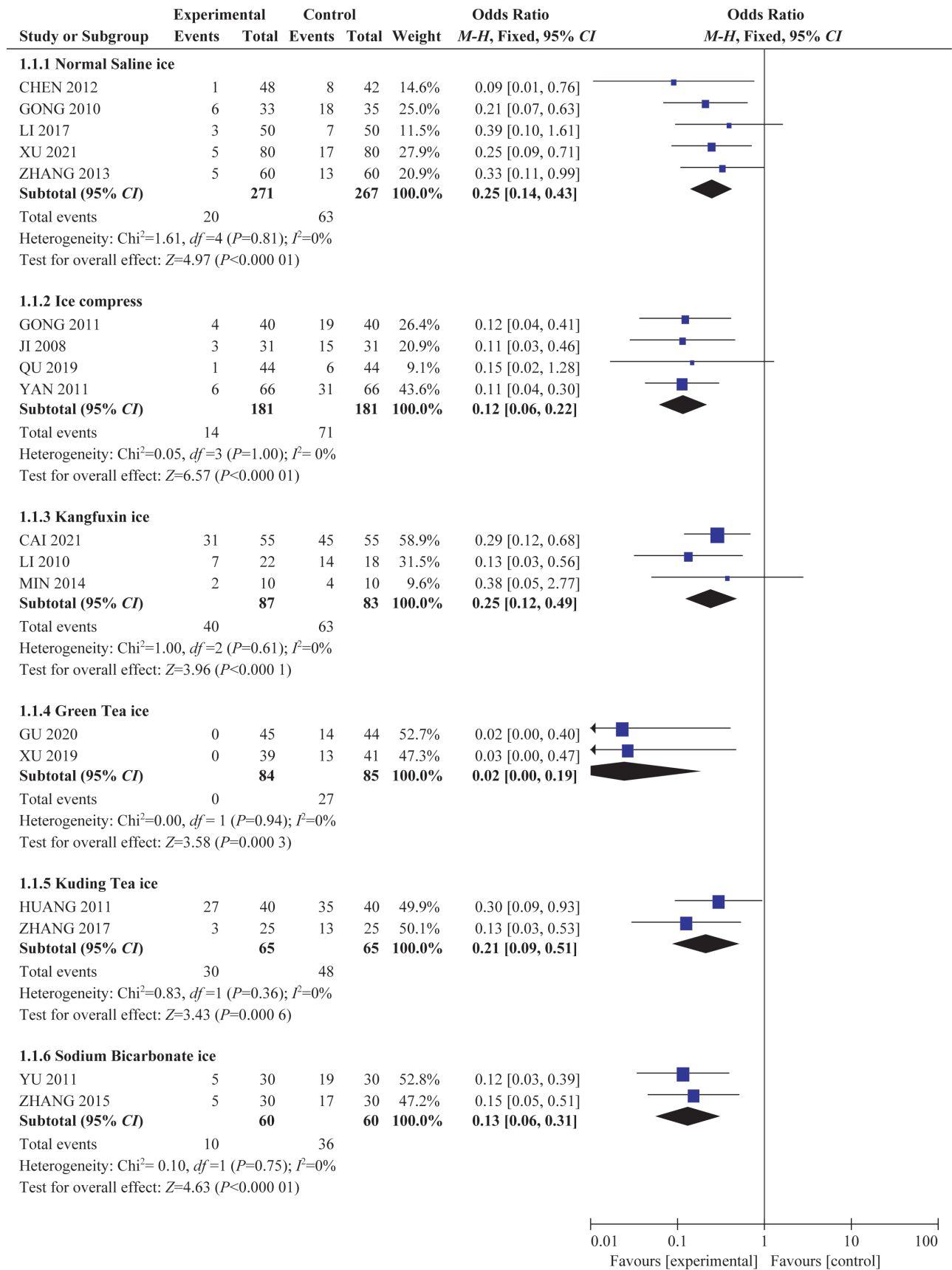


图4 试验组不同干预措施亚组分析的meta分析结果及森林图

Fig 4 Meta-analysis and forest plots of subgroup analysis of different intervention in experimental group

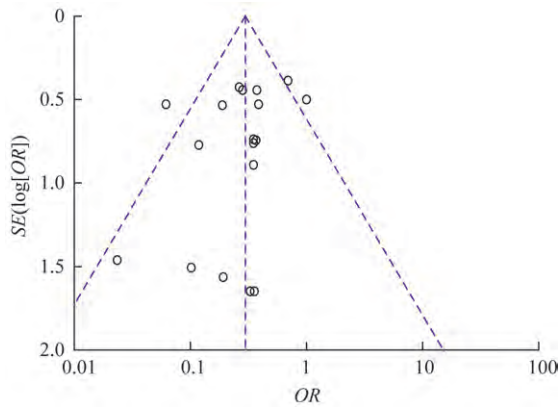


图5 冷冻疗法预防放射性口腔黏膜炎的漏斗图

Fig 5 Funnel plot of cryotherapy for prevention of radiation-induced oral mucositis

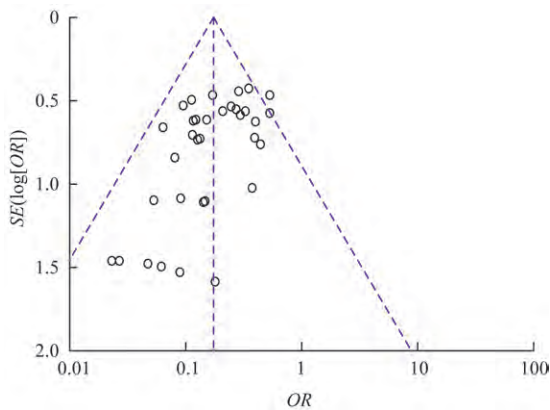


图6 冷冻疗法预防严重放射性口腔黏膜炎的漏斗图

Fig 6 Funnel plot of cryotherapy for prevention of severe radiation-induced oral mucositis

3 讨论

口腔黏膜炎是伴随头颈癌患者放疗发生的且令患者感到痛苦的并发症。有研究^[46]对头颈癌放疗患者进行调查, 93.1%的患者出现口腔黏膜炎, 其中66.3%的患者还发生了严重口腔黏膜炎。可见, 预防口腔黏膜炎发生至关重要。《放射性口腔黏膜炎防治策略专家共识》(2019)^[47]也提出: 放射性口腔黏膜炎重在预防。

冷冻疗法最初应用于外科手术中, 原理为冷冻对肿瘤细胞的杀伤作用可抑制肿瘤生长^[48-49]。近年来, 随着医学研究的深入和发展, 冷冻疗法在口腔护理中也得到应用和重视, 并取得了一定的疗效。RILEY等^[50]、裴露斯等^[51]、WANG等^[52]的多项meta分析研究结果均显示, 口腔冷冻疗法应用于接受化学治疗的非头颈部恶性肿瘤患者, 可降低口腔黏膜炎总发生率及严重口腔黏膜炎的发生率。

临床上针对放射性口腔黏膜炎的药物防治手段包括糖皮质激素、抗微生物漱口水、细胞保护剂、口腔黏膜保护剂、中医中药等^[53]。然而, 到目前为止, 尚没有令人满意的治疗措施, 且没有单一的干预措施可以完全预防头颈癌口腔黏膜炎, 可能需要联合预防性治疗策略来保证更确切的疗效^[54]。国外一项比较头颈癌患者放射性口腔黏膜炎的预防性治疗效果的网状meta分析^[55]也提出, 对患者仅进行标准口腔护理是远远不够的, 应联合其他预防措施, 以缓解患者的不适。

本研究纳入36项口腔冷冻疗法预防性干预头颈癌放疗所致口腔黏膜炎的RCT研究, 进行合并分析。结果显示: 对头颈癌患者, 在常规护理的基础上, 给予口腔冷冻疗法, 在降低放射性口腔黏膜炎的发生率及缓解严重程度方面具有积极有效的作用。在头颈部肿瘤放疗期间, 同步采取口腔冷冻疗法预防口腔黏膜炎发生的机制尚未明确, 可能有以下2个方面^[56-57]。①放疗过程中, 放射线导致细胞凋亡, 基底上皮细胞的更新减少, 对口腔黏膜有较强的直接损伤作用; 而口腔降温措施可引起组织血管收缩, 一定程度上增强了口腔黏膜上皮细胞的耐受性, 起到对黏膜的保护作用。②放疗过程中, 由于口腔含化冰块或冰水含漱, 增加了漱口的次数, 改善了口腔卫生条件, 减少口腔炎症反应, 从而减轻口腔黏膜的破坏。

此外, 本研究根据不同的干预内容再进行了亚组分析。合并5篇文献^[9-13]结果表明, 与常规护理组相比, 生理盐水冰块对于预防头颈癌严重放射性口腔黏膜炎有一定作用。康复新液是美洲大蠊虫干燥提取物, 是一种纯中药制剂, 已有研究^[58]表明其防治头颈癌放射性口腔黏膜炎效果显著。而研究^[18-20]显示, 将康复新制成冰块含化也有效缓解了放射治疗对口腔黏膜的毒性, 且对比常温康复新液效果更佳。碳酸氢钠性质温和, 用于漱口不仅能提高患者的口腔舒适度, 也有助于维持口腔黏膜湿度和酸碱度, 从而降低继发感染的风险^[59]。有2项研究^[25-26]将冷冻疗法与碳酸氢钠相结合, 也减少了严重口腔黏膜炎发生的概率; 合并2项绿茶冰块研究^[21-22]结果显示, 联合茶多酚成分在预防放射性口腔黏膜炎中取得良好的效果, 这也与EBERT等^[60]的研究结果一致。合并2篇文献^[23-24]结果显示苦丁茶制成冰块含化在降低放射性口腔黏膜炎严重程度, 效果也优于常规护理组。

中医认为,放射线为一种热毒外邪。《本草纲目》记述苦丁茶具有清热利湿、消肿止痛之功效,因而在预防头颈癌放射性口腔黏膜炎中也发挥着一定的临床作用^[61]。在本研究亚组分析中,在常规护理与冷冻疗法的基础上,联合使用康复新液、碳酸氢钠、绿茶、苦丁茶等可缓解口腔黏膜炎的症状,进一步验证了联合疗法的有效性。但亚组分析中纳入的文献较少,需辩证看待此结论。故今后可尝试将冷冻疗法联合各种有效物质,开展更多高质量、多中心 RCT 研究进行验证。

本研究存在一定局限性。① 本研究仅探讨口腔冷冻疗法对口腔黏膜炎及严重口腔黏膜炎发生情况的影响。36 项试验中,某些终点测量指标(口腔黏膜炎相关疼痛、口腔舒适度、黏膜炎持续和愈合时间等)不一致和表达形式不同,导致难以提取数据,因此本研究未探讨涉及的这些结局指标。② 纳入的所有研究的样本量都少于 100 例,且大多数未报道随机方法、分配隐藏及盲法,可能存在选择、实施、测量等多种偏倚。③ 研究使用了 3 个口腔黏膜炎评价标准(RTOG、WHO 和 NCI-CTC),缺乏评估黏膜炎严重程度的一致标准,也可能产生偏倚。④ 纳入的研究多为中国学者发表的研究,可能存在地域和人种差异,因而影响结果的代表性和推广性。

综上所述,当前证据显示,在头颈部肿瘤放疗期间采用口腔冷冻疗法能够有效预防放射性口腔黏膜炎及严重性放射性口腔黏膜炎的发生。冷冻疗法以其独特的优势成为预防口腔黏膜炎的有效措施,也是临床护理人员进行口腔护理过程中可以采用的有效护理方法。受纳入研究数量和质量限制,上述结论尚待更多高质量研究予以验证。

利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。

All authors disclose no relevant conflict of interests.

作者贡献/Authors' Contributions

陈卫宏负责论文的构思与设计,陈卫宏和杨玲参与了数据收集与整理、统计学处理、论文撰写;侯黎莉、毛艳和张金凤参与了文章的修订与审校。所有作者均阅读并同意了最终稿件的提交。

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