

·指南·共识·解读·

中国慢性癌症相关性疼痛诊疗指南(2024版)

中国慢性癌症相关性疼痛诊疗指南制订专家组,中国老年保健协会疼痛病学会

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【摘要】 慢性癌症相关性疼痛是严重危害癌症患者身心健康的一类疾病。消除癌痛是癌症患者的基本权益,控制和消除癌痛是医护人员的职责。本指南专家组依据国内外近10年来发表的慢性癌症相关性疼痛诊疗高质量循证医学研究证据,经严格论证和专家投票,对常见的慢性癌症相关性疼痛治疗方法形成推荐意见,旨在为慢性癌症相关性疼痛规范诊疗提供参考。

【关键词】 慢性癌症相关性疼痛; 癌痛; 指南

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A Chinese guideline for the diagnosis and treatment of chronic cancer-related pain (2024 edition)

Expert Group for the Development of Chinese Chronic Cancer-related Pain Diagnosis and Treatment Guidelines,
Society of Painology, Chinese Aging Well Association

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【Abstract】 Chronic cancer-related pain can seriously damage physical and mental health of cancer patients. Eliminating cancer pain is basic right of cancer patients, controlling and eliminating cancer pain is the responsibility of medical staff. Based on high quality evidence of medical researches on the diagnosis and treatment of chronic cancer-related pain published domestically and internationally in the past 10 years, the expert group has formed recommendations for common treatment methods through rigorous argumentation and expert voting, to provide references for standardized diagnosis and treatment of chronic cancer-related pain.

【Key words】 Chronic cancer-related pain; Cancer pain; Guideline

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慢性癌症相关性疼痛 (chronic cancer-related pain, CCRP) 严重危害患者身心健康, 加速疾病进展, 恶化生理功能, 甚至被迫中断抗肿瘤治疗, 导致生存期缩短^[1]。相比死亡, 癌症患者更恐惧癌痛。消除癌痛是癌症患者的合理诉求和基本权益, 控制和消除癌痛是医护人员的职责。虽然国内外学术组织、机构或专家团队已经发布了很多针对 CCRP 管理的原则、规范、专家共识及临床指南, 但完全基于国际疾病分类-11 (International Classification of Diseases-11, ICD-11) 的 CCRP 临床诊疗指南未见公布。为进一步提升 CCRP 诊疗服务能力, 满足临床诊疗需求, 我们组织国内疼痛学科领域的相关专家制订了《中国慢性癌症相关性疼痛诊疗指南》。需要注意的是, 由于篇幅所限, 本指南无法涵盖 CCRP 诊疗每一个方面的所有细节。

指南的制订方法

文献检索时限为 2014 年 1 月至 2024 年 5 月。中文检索词包括癌痛、癌症相关性疼痛、内脏癌性疼痛、骨性癌性疼痛、神经病理性癌性疼痛、癌症药物治疗

后疼痛、放射治疗后疼痛、癌症术后疼痛、癌性爆发痛等, 英文检索词包括 cancer pain, chronic cancer-related pain, chronic post-cancer treatment pain, visceral cancer pain, bone cancer pain, neuropathic cancer pain, post-cancer medicine pain, post-radiotherapy pain, post-cancer surgery pain, breakthrough cancer pain 等, 系统检索了万方、知网、PubMed、Cochrane Library 等国内外知名数据库, 主要选择系统评价 (systematic review)、Meta 分析 (Meta analysis)、随机对照试验 (randomized controlled trial, RCT)、专家共识 (consensus)、临床指南 (guideline) 等高质量循证医学证据文献, 采用推荐分级的评估、制订与评价 (Grading of Recommendations Assessment, Development and Evaluation, GRADE) 分级系统证据质量分级及推荐强度 (表 1) 和共识会议法, 经过多次反复讨论, 并进行在线投票, 最终制订本指南^[2-4]。

慢性癌症相关性疼痛概述

一、CCRP 的定义

CCRP 是由癌症本身或转移所致的疼痛以及癌

症治疗引起的慢性疼痛^[5-6]。

二、CCRP的流行病学

CCRP在癌症的各个阶段均可出现,约25.0%新诊断恶性肿瘤患者,75.0%转移性癌症患者和59.0%目前正在接受抗癌治疗的患者报告疼痛,且1/3的患者即使在完成根治治疗后仍感到疼痛^[7]。在患有晚期癌症、濒临死亡的患者中,有66.0%的患者经历过疼痛,55.0%的患者为中至重度疼痛^[5-6]。

三、分类^[5-6]

根据疼痛的原因,CCRP分为慢性癌性疼痛(chronic cancer pain, CCP)和慢性癌症治疗后疼痛(chronic post-cancer treatment pain, CPCTP)(图1)。

1. CCP 主要包括慢性内脏癌痛(chronic visceral cancer pain, CVCP)、慢性骨性癌痛(chronic bone cancer pain, CBCP)、慢性神经病理性癌痛(chronic neuropathic cancer pain, CNCP)等。

(1) CVCP 指原发肿瘤和肿瘤转移损伤了头颈部或胸腹腔内的内脏器官所引起的慢性疼痛。例如肝转移灶、胰腺肿瘤侵犯腹腔神经丛所致的疼痛,

食管或肺肿瘤局部进展所致的胸骨后疼痛。

(2) CBCP 指由原发肿瘤和肿瘤转移破坏或损伤骨骼引起的慢性疼痛,是最常见的CCP类型。由于原发性骨肿瘤比较罕见,所以其他部位肿瘤转移到骨骼所致的疼痛是最常见的CBCP类型。

(3) CNCP 指由原发肿瘤或肿瘤转移破坏或损伤外周或中枢神经系统引起的慢性疼痛。慢性外周性神经病理性癌性疼痛包括胸部原发或转移性肿瘤破坏臂丛神经,或腹盆腔肿瘤损伤腰骶神经丛等。脊髓压迫(癌症骨转移导致的椎体塌陷)可导致慢性中枢性神经病理性癌性疼痛。

2. CPCTP 主要包括癌症药物治疗后的慢性疼痛(chronic post-cancer medicine pain, CPCMP)、慢性放射治疗后疼痛(chronic post-radiotherapy pain, CPRP)、慢性癌症术后疼痛(chronic post-cancer surgery pain, CPCSP)等。

(1) CPCMP 指由任何抗癌药物引起的慢性疼痛,包括全身化疗、激素治疗和生物治疗等使用的药物。慢性痛性化疗后多发神经病变(chronic painful

表1 GRADE系统证据质量分级及推荐强度说明

级别	说明
证据质量	
高质量(A)	非常有把握估计值接近真实值
中等质量(B)	对估计值有中等把握:估计值有可能接近真实值,但也有可能差别很大
低质量(C)	对估计值的把握有限:估计值可能与真实值有很大差别
极低质量(D)	对估计值几乎没有把握:估计值与真实值极大可能有很大差别
推荐强度	
强推荐(1)	大部分患者在此情况下会选择使用推荐方案,只有少数患者不会;大多数医生应该接受干预措施;70%以上专家组成员赞成
弱推荐(2)	大部分患者在此情况下会选择使用推荐方案,还有很多患者不会;医生亲自仔细查找证据或证据摘要,准备与患者就证据以及他们的价值观和意愿进行讨论;50%~70%专家组成员赞成
没有明确推荐意见(3)	利弊相当;未确定目标人群;制订推荐意见的证据不足;50%以下专家组成员同意

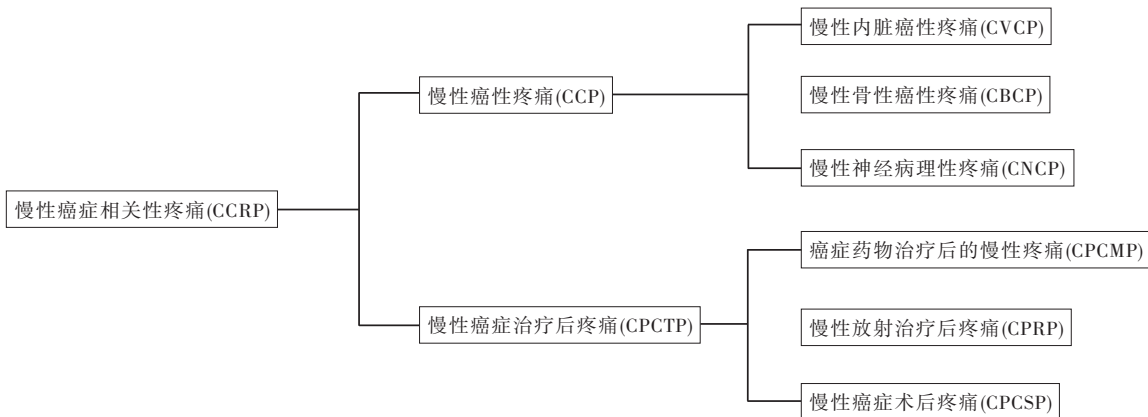


图1 慢性癌症相关性疼痛的分类

chemotherapy-induced polyneuropathy, CIPN)是ICD-11的一个诊断类别。在接受激素治疗的女性乳腺癌患者中,45%伴有慢性关节痛,表现为对称性的关节疼痛,最常见的部位是手腕、双手和膝盖。慢性痛性化疗后神经病变(chronic painful chemotherapy-induced neuropathy, CPCIN)是指由于治疗原发肿瘤或肿瘤转移采用了口服或静脉化疗而引起的慢性周围性神经病理性疼痛。

(2) CPRP 指对原发肿瘤或转移性肿瘤进行放射治疗时,照射野内神经、骨骼或软组织的延迟性损害所致的慢性疼痛。这类疼痛的发生可始于放疗结束后几个月内或数年后,发生的危险因素包括总治疗剂量过大、每次放疗剂量过大以及联合使用手术或化疗治疗。

(3) CPCSP 指癌症手术或有创操作(组织活检或胸引流管插入)引起的疼痛。乳腺癌术后(乳房切除术后疼痛)或肺癌术后(开胸后疼痛)尤为常见。

慢性癌症相关性疼痛的发生机制

CCRP发生机制复杂且独特,涉及肿瘤组织、正常组织、肿瘤微环境、神经系统及免疫系统之间的相互作用^[8-9]。

一、癌症相关伤害性疼痛机制

癌症发生、发展过程中的肿瘤组织浸润、压迫和转移会产生前列腺素E₂、缓激肽、P物质、肿瘤坏死因子等炎症因子,通过直接与受体或离子通道相互作用,支配癌症组织的外周感觉神经引起疼痛^[9]。癌症骨转移相关的疼痛可由溶骨性病变或溶骨性侵袭诱发,骨破坏过程中分泌大量的炎症因子,从而刺激敏感的神纤维,导致严重疼痛^[10]。

二、癌症相关神经病理性疼痛机制

癌症影响到躯体感觉神经系统改变是主要机制,肿瘤细胞直接侵袭神经周围或通过免疫细胞侵袭,瘤体直接压迫神经,甚至放疗和化疗的影响以及癌症的手术治疗等因素均可引起神经损伤,可能导致轴突运输中断,离子通道和受体活性变化,神经元损伤和炎症,氧化应激和线粒体损伤等改变,进一步导致外周和中枢神经系统敏化,诱发神经病理性疼痛^[9,11]。

三、其它机制

如癌症相关内脏疼痛,患者心理状态改变,压力增加等也是导致CCRP的重要机制^[12]。

慢性癌症相关性疼痛的临床特点

一、持续慢性疼痛,伴随整个病程,夜间痛和静息痛为其特点。

二、常伴有严重的难以忍受的爆发痛。

三、常呈现全方位疼痛(total pain),包括躯体的、心理的、精神的、社会的等多种表现。

慢性癌症相关性疼痛的辅助检查

一、实验室检查

血常规、肝肾功能、电解质、凝血功能、肿瘤标志物等。

二、影像学检查

1. X线检查 空间分辨率很高,但密度分辨率不足,适用于骨和含气组织的显像,主要用于识别骨折等。

2. 计算机化X线体层照相(CT) 可清晰显示人体多数组织和器官,包括骨骼等。注射造影剂进行强化,可进一步提高组织密度和分辨率。

3. 磁共振成像(MRI) 更适合软组织(组织对比度更佳)和神经组织检查,常用于椎管受侵的识别。

4. 正电子发射计算机断层扫描(PET) 高效、安全、无创,保证诊断准确性,在疑似多发性转移病例中具有优势。

5. 单光子发射计算机断层显像(ECT) 不仅显示脏器或病变组织的形态结构,还提供脏器或病变的功能和代谢信息,对转移性骨肿瘤有很高的灵敏度。

6. 超声 不仅可观察内脏的细微结构和功能状态,而且可实时观察肌肉、肌腱的运动情况,在腹部、盆腔及四肢软组织疾病的诊断中发挥重要作用。

7. 医用红外热成像 借助于敏感的体表温度变化,进行双侧对比观察,可早期发现能够引起体表温度变化的病变,如血管运动不良、炎症、肿瘤等。

慢性癌症相关性疼痛的诊断标准与疼痛评估

一、诊断标准

1. 有明确癌症病史。

2. 如无明确的病理学诊断,需有癌症临床表现,并有影像学、实验室检查等证据。

3. 患者的疼痛是源于肿瘤的发生发展或治疗所

引发。

二、疼痛评估

癌痛评估是CCRP获得合理、有效治疗的前提。

1. 评估原则^[13]

(1) 首诊评估 首次接诊癌症患者时医护人员须筛查和评估疼痛。

(2) 常规评估 每日进行1次评估。

(3) 量化评估 采用疼痛强度评估量表,量化并记录患者描述的疼痛强度。

(4) 全面评估 评估疼痛类型、发作情况、诱发因素、治疗效果等。

(5) 动态评估 接诊后对癌痛患者持续疼痛评估,包括门诊就诊、住院期间、出院后,以及癌痛治疗实施前后疼痛变化。

2. 评估工具

根据患者个人情况不同,采用合适的疼痛强度评估量表,记录患者疼痛强度,必要时可进行心理状态评估。常用疼痛评估工具包括^[13]:

(1) 数字分级评分法(numerical rating scale, NRS)。

(2) 视觉模拟评分法(visual analogue scale, VAS)。

(3) 面部表情评分量表(faces pain scale, FPS)。

(4) 简明疼痛评估量表(brief pain inventory, BPI)。

(5) 心理痛苦温度计(distress thermometer, DT)。

(6) 健康问卷抑郁量表(patient health questionnaire-9, PHQ-9)。

(7) 广泛性焦虑自评量表(generalized anxiety disorder-7, GAD-7)。

慢性癌症相关性疼痛的治疗

一、治疗原则与目标

1. 治疗原则

CCRP发病机制复杂,需要根据疼痛的病因、特点和患者身体情况进行个体化治疗^[14-15]。世界卫生组织(World Health Organization, WHO)提出的癌痛三阶梯药物治疗原则仍是目前控制癌痛的主要方式^[16]。实施标准化的疼痛评估、规范化治疗^[17]、安宁疗护(姑息治疗)^[18-19]可有效缓解疼痛,提高生活质量。

2. 治疗目标

癌痛控制的“5A”目标^[14-15]:

(1) 镇痛(analgesia) 优化镇痛(缓解疼痛)。

(2) 活动(activities) 优化日常生活活动(心理社会功能)。

(3) 不良反应(adverse effects) 尽量减少不良事件。

(4) 异常用药(aberrant behavior) 监控异常的药物治疗行为。

(5) 情绪(affect) 疼痛与情绪之间的关系。

二、治疗方法

CCRP治疗首先是病因治疗,尤其是抗肿瘤治疗,再采取针对性的个体化镇痛治疗,如一般治疗、药物治疗、物理治疗、中医治疗、心理治疗、数字医疗、微创介入治疗等^[20]。

1. 一般治疗

一般治疗主要包括健康教育、自我管理(表2)。

(1) 健康教育 对患者及其家属进行健康教育的内容主要包括治疗目标、治疗方法、可能出现的不良反应等。健康教育可培养患者良好的自我控制能力,提高患者的治疗依从性,显著减少疼痛发作的强度和频率,提高患者的生活质量^[21]。

(2) 自我管理 癌痛自我管理是指患者管理自己的疼痛,将疼痛缓解策略融入日常生活的过程^[21]。有效的癌痛管理不仅需要医护人员的专业指导,还需要患者自身的积极参与和自我管理。

表2 一般治疗的循证医学证据质量分级及推荐强度

治疗方式	证据级别	推荐强度
健康教育 ^[22-24]	A	1
自我管理 ^[25-27]	A	1

2. 药物治疗

(1) 概述

药物治疗是CCRP治疗最为重要和常用的方法,规范、有效的药物治疗能够缓解80%~90% CCRP。强效阿片类药物是CCRP治疗的基石,吗啡是强效阿片类药物的金标准^[28]。

(2) 癌痛治疗的药物种类

用于CCRP治疗的药物主要有镇痛药物和辅助镇痛药物。

① 镇痛药物(表3^[28-29, 41-71])

A. 非甾体类抗炎药(non-steroidal anti-inflammatory drugs, NSAIDs) 如塞来昔布、布洛芬、吲哚美辛、双氯芬酸、右酮洛芬氨丁三醇^[29]等。

B. 阿片类药物 吗啡、羟考酮、芬太尼等。吗啡或羟考酮是中重度CCRP治疗的一线口服阿片类



药物^[28,30]。与口服阿片类药物相比,使用透皮芬太尼治疗中重度CCRP具有更多优势^[31-32],因而经皮给药是阿片稳定需求患者的最佳治疗选择^[33]。芬太尼透皮贴剂优选人群主要有:不能或不愿经口服给药、中重度肝肾功不全、恶性肠梗阻、慢性便秘及顽固性便秘、口服阿片类药物出现不可耐受的严重恶心及呕吐、对口服药依从性差的人群等^[34]。

C. 生物毒素 眼镜蛇神经毒素、河豚毒素^[35-36]、肉毒杆菌毒素^[37-38]等。中华眼镜蛇神经毒素被制备成镇痛药物,用于CCRP的治疗^[39-40]。

② 辅助镇痛药物(表4^[43,63,74-85])

A. 钙离子通道药物 加巴喷丁、普瑞巴林等。

B. 三环类抗抑郁药物 阿米替林、多塞平等。

C. 5-羟色胺和去甲肾上腺素再摄取抑制剂 (serotonin-norepinephrine reuptake inhibitors, SNRIs)

度洛西汀、文拉法辛等。

D. 其他药物 利多卡因、辣椒素、氯胺酮、糖皮质激素、汉防己甲素、脾多肽注射液等^[72-73,82-84]。

(3) 阿片类药物剂量转换、滴定、常见不良反应及处理方法、使用原则

① 阿片类药物剂量转换(表5)

阿片类药物轮换是指用一种阿片类药物替代另一种阿片类药物,或者是同一阿片类药物不同剂型之间的转换,以寻求疼痛控制和不良反应之间的平衡。阿片类药物轮换能够提高患者镇痛效果及患者满意度^[86]。

② 阿片类药物剂量滴定原则

A. 目的是尽快有效镇痛,按需给药治疗爆发痛。

B. 滴定应简单、灵活,提倡采用短效药物滴定与控缓释剂型相结合的原则,实现对基础性疼痛和

表3 镇痛药物循证医学证据质量分级及推荐强度

药物种类	药物名称	CVCP	CNCP	CPCMP	CPRP
NSAIDs	吲哚美辛 ^[29,41]			B2	B2
	双氯芬酸 ^[29,42-43]	B2			B2
类阿片类	曲马多 ^[44-45]	A2			
弱阿片类	可待因 ^[46]	A2			
强阿片类	吗啡 ^[30,47-49]	A1			
	羟考酮 ^[28,47,49-52]	A1			
	芬太尼 ^[32,47-48,53]	A1			
	氢吗啡酮 ^[54-57]	A1			
	丁丙诺啡 ^[47,58]	A2			
	美沙酮 ^[59-64]	B2	B2		B2
	地佐辛 ^[45,65-66]	B2			
	羟考酮纳洛酮缓释片 ^[67-70]	A1			
复合止痛	氨酚羟考酮片 ^[71]	B2			

注:CVCP为慢性内脏癌性疼痛,CNCP为慢性神经病理性癌痛,CPCMP为癌症药物治疗后的慢性疼痛,CPRP为慢性放射治疗后疼痛,NSAIDs为非甾体抗炎药物

表4 辅助镇痛药物循证医学证据质量分级及推荐强度

药物种类	药物名称	CVCP	CNCP	CPCMP	CPRP	CPCSP
钙离子通道药物	加巴喷丁 ^[63,74]	A2			B2	
	普瑞巴林 ^[63,74-78]	A1	A1	A1	A1	
三环类抗抑郁药物	阿米替林 ^[43,74]	B2			B2	
	多塞平 ^[43,77]			B2	B2	
SNRIs	度洛西汀 ^[75-76,79-81]		A1	A1		
	文拉法辛 ^[74,79]	A2		B2		
其他	利多卡因 ^[82]	B2				
	辣椒素 ^[83-84]	B2				B2
	氯胺酮 ^[63,85]	B2			B2	

注:CVCP为慢性内脏癌性疼痛,CNCP为慢性神经病理性癌痛,CPCMP为癌症药物治疗后的慢性疼痛,CPRP为慢性放射治疗后疼痛,CPCSP为慢性癌症术后疼痛,SNRIs为去甲肾上腺素再摄取抑制剂

爆发痛的控制。

C. 当需要快速剂量滴定时,推荐使用快速起效的短效药物,优先推荐使用经皮下或静脉途径给药。

D. 阿片类药物滴定是实现中度至重度癌症疼痛缓解和可耐受不良反应平衡的最佳方法,快速剂量滴定有助于实现早期镇痛^[87]。

③ 阿片类药物常见不良反应及处理方法(表6^[88])。

④ 阿片类药物使用原则

A. 癌痛药物治疗的5项基本原则:无创给药(口服、皮肤或粘膜)、按时给药、按阶梯给药、个体化用药及细节化用药。

B. 其他原则:尽早应用、改变给药途径、阿片类药物转换、联合用药等。

(4) 癌痛三阶梯药物治疗原则

① 第一阶梯 针对轻度疼痛,使用非阿片类药物,如NSAIDs等。这些药物存在最大有效剂量的问题,即所谓的“天花板效应”。

② 第二阶梯 对于中度疼痛,使用弱阿片类药物,如可待因、曲马多等,并可与NSAIDs联合使用。弱阿片类药物也存在“天花板效应”。

③ 第三阶梯 重度疼痛的治疗则使用强阿片类药物,如吗啡等,且没有“天花板效应”。这类药物

可以持续增加剂量。

3. 物理治疗

物理治疗主要包括光生物调节疗法(photobiomodulation therapy, PBMT)、低能量激光治疗(low-level laser therapy, LLLT)、经皮神经电刺激(transcutaneous electrical nerve stimulation, TENS)、加扰器疗法(scrambler therapy, ST)、经颅直流电刺激(transcranial direct current stimulation, tDCS)、手法治疗(manual therapy, MT)、运动疗法、立体定向放疗(stereotactic body radiotherapy, SBRT)、MRI引导聚焦超声(magnetic resonance-guided focused ultrasound, MRgFUS)、放射性核素等,在CCRP治疗中应用广泛(表7^[89-109])。

4. 中医治疗

基于辩证论治的理论,CCRP中医治疗主要有中医内治和外治法。

(1) 中医内治法 主要包括中药汤剂和中成药两种形式,可以止痛并改善阿片类药物不良反应,作为癌痛辅助治疗方法。见表8^[110-114]。

(2) 中医外治法 主要包括针刺、针灸、电针、按摩、耳穴疗法、穴位注射、芳香疗法等。见表9^[115-133]。

5. 心理治疗

心理治疗(psychotherapy)是指应用心理学原理

表5 常用阿片类药物不同给药途径的剂量转换

吗啡(mg/d) 静脉/皮下/硬膜外/鞘内	芬太尼(μg/h)			羟考酮(mg/d)		可待因(mg/d)	
	口服	肠外	贴剂	静脉/皮下	口服	静脉/皮下	口服
20	60	25	25	15	30	130	200
40	120	50	50	30	60	260	400
60	180	75	75	45	90	390	600
80	240	100	100	60	120	520	800

表6 阿片类药物常见不良反应及处理方法

副作用	特点	处理方法
恶心呕吐	呈剂量依赖和自限性,一般在用药后3~7 d可耐受	甲氧氯普胺、异丙嗪、氟哌啶醇及氯丙嗪。静脉注射格拉司琼及昂丹司琼
便秘		治疗药物有甲基纳曲酮 ^[88] 等,通便药物有润滑性药物多库酯钠、番泻叶、比沙可啶、容积性药物植物纤维素、渗透性药物乳果糖、大便软化剂等。非药物方法也有效,如增加液体摄入和活动、规律排便等
呼吸抑制	剂量依赖性,静脉注射易发生。开始应用药物后5~7 d可耐受呼吸抑制	唤醒患者,给予疼痛刺激,可诱发呼吸。应用纳洛酮拮抗
尿滞留		应用非药物,例如听流水声、会阴部热敷、膀胱部位轻度按摩、针灸等如果没有效果,可插管导尿
瘙痒		抗组胺药物仍是治疗瘙痒的一线药物,常用药物包括苯海拉明、异丙嗪、赛庚啶等。基础治疗包括加强皮肤护理,穿着纯棉柔软内衣等
镇静、嗜睡	多在1周内消失。	需减量或更换其他阿片类药物,也可使用小剂量中枢兴奋药物治疗

表7 CCRP物理治疗循证医学证据质量分级及推荐强度

治疗方法	CVCP	CNCP	CPCMP	CPRP	CPCSP
PBMT ^[89-90]				A2	
LLLT ^[91-93]			B2		A2
TENS ^[94-96]	A2		B2		
ST ^[97]			B2		
tDCS ^[98]	B2				
MT ^[99-100]	B2		B2	A2	A2
运动疗法 ^[101-102]			B2		
SBRT ^[103-106]	B2	A1			
放射性核素 ^[107-108]		A2			
MRgFUS ^[109]		B2			

注:PBMT为光生物调节疗法,LLLT为低能量激光治疗,TENS为经皮神经电刺激,ST为加扰器疗法,tDCS为经颅直流电刺激,MT为手法治疗,SBRT为立体定向放疗,MRgFUS为引导聚焦超声治疗,CVCP为慢性内脏癌性疼痛,CNCP为慢性神经病理性癌痛,CPCMP为癌症药物治疗后的慢性疼痛,CPRP为慢性放射治疗后疼痛,CPCSP慢性癌症术后疼痛

表8 中成药治疗 CCRP 循证医学证据质量分级及推荐强度

中成药	CVCP	CBCP
复方苦参注射液 ^[111-112]	B2	B2
华蟾素 ^[113]	B2	
双柏散 ^[114]	B2	

注:CVCP为慢性内脏癌性疼痛,CBCP为慢性骨性癌性疼痛

表9 常见中医外治法循证医学证据质量分级及推荐强度

中医外治法	CVCP	CBCP	CPCMP	CPRP	CPCSP
针刺 ^[116-117]	B3		B3		
针灸 ^[118-125]	A2	A2	A2		A2
电针 ^[126]	B2				
体针 ^[127]	B2	B2		B2	
穴位注射 ^[128]	B3				
耳穴疗法 ^[129]	B3				
耳穴贴压 ^[130]	B3				
按摩 ^[131-132]	B3		B3		
芳香疗法 ^[133]	B2				

注:CVCP为慢性内脏癌性疼痛,CBCP为慢性骨性癌性疼痛,CPCMP为癌症药物治疗后的慢性疼痛,CPRP为慢性放射治疗后疼痛,CPCSP为慢性癌症术后疼痛

和方法,与患者建立良好治疗关系与互动,应用专业的理论和技术,对患者进行治疗的过程。癌痛患者常表现出焦虑、恐惧、抑郁等情绪障碍,甚至产生自杀倾向,对癌痛患者开展心理治疗非常必要。癌痛治疗常用的心理治疗方法主要有认知行为疗法(cognitive-behavioural therapy, CBT)、基于正念的认知疗法(mindfulness-based cognitive therapy, MBCT)、

基于正念的减压疗法(mindfulness-based stress reduction, MBSR)、催眠、音乐疗法、引导想象疗法、肌肉放松训练、身心疗法、神经反馈疗法(neurofeedback, NFB)等。见表10^[134-153]。

表10 常见心理治疗方法循证医学证据质量分级及推荐强度

治疗方法	证据分级	推荐强度
CBT ^[134]	A	2
身心疗法 ^[135]	A	2
MBCT ^[136-140]	A	1
MBSR ^[139-141]	A	2
催眠 ^[142-144]	B	2
肌肉放松训练 ^[137, 145]	B	2
引导想象疗法 ^[137, 145]	B	3
音乐疗法 ^[146-150]	B	2
NFB ^[151-153]	B	2

注:CBT为认知行为疗法,MBCT为基于正念的认知疗法,MBSR为基于正念的减压疗法,NFB为神经反馈疗法

6. 数字医疗

数字医疗是把现代数字信息技术应用于整个医疗过程的一种新型医疗方式,已经由电子医疗、远程医疗和移动医疗发展到数字疗法(digital therapeutics, DTx)。见表11^[26, 154-164]。

表11 常见数字医疗循证医学证据质量分级及推荐强度

治疗方法	证据级别	推荐强度
电子医疗 ^[154]	B	2
远程医疗 ^[155-156]	B	2
移动医疗 ^[26, 157-161]	B	2
数字疗法 ^[157, 162-164]	B	2

7. 微创介入治疗

微创介入治疗方法主要有自控镇痛(patient controlled analgesia, PCA)、神经毁损术、经皮椎体成形术、放射性粒子植入术、鞘内药物输注系统(intrathecal drug delivery system, IDDS)等。

(1) PCA 技术

① 定义

PCA是一种由医护人员根据患者疼痛程度和身体情况,预先设置镇痛药物的剂量,再交由患者“自我管理”的一种疼痛管理技术^[165]。PCA具有起效迅速、血药浓度波动小、镇痛效果好、按需给药、个体化程度高等优点。

② 分类

PCA主要包括患者静脉自控镇痛(patient

controlled intravenous analgesia, PCIA)、患者皮下自控镇痛(patient-controlled subcutaneous analgesia, PCSA)、硬膜外腔PCA(patient controlled epidural analgesia, PCEA)、鞘内PCA和区域阻滞PCA。

③ 适应证

A. 口服用药困难、胃肠道功能障碍或消化道肿瘤导致的肠梗阻患者。

B. 口服大量镇痛药但效果不佳或长期使用镇痛药出现耐受的患者。

C. 口服药物出现严重不良反应的患者。

D. 阿片类药物的滴定。

E. 癌性爆发痛频繁发作(每日 ≥ 5 次)的患者。

④ PCA数智化管理

癌痛的管理过程是长期的、动态的,同时涉及麻醉药品的应用和管理,因此需要信息化、智能化的平台管理。癌痛管理平台利用物联网,联结三级-二级-社区-居家等各级医疗机构、各级医护人员于同一癌痛管控医联体,在癌痛管理平台对各级医疗机构包括居家的癌痛患者进行同质化远程实时管理,实现医护人员之间、医患之间零距离交流,协助医疗单位高效管理癌痛及慢性疼痛患者,提升医疗服务质量与效率。数智化PCA(artificial intelligence PCA, Ai-PCA)利用物联网和人工智能技术,由终端、无线传输、中心控制3部分组成,赋予镇痛泵系统智能分析评估、智能报警、远程监控等功能,实现PCA的全程化、智能化及个体化管理^[166-169]。

(2) 神经毁损术

神经毁损技术是以介入手术方式将化学药物或物理因素作用于疼痛区域的责任神经,使神经组织变性、结构损伤,破坏部分或全部感觉传导功能,从而获得较长镇痛时间的方法。根据毁损的方法不同,神经毁损分为化学性毁损和物理性毁损。

① 化学性毁损

将化学药物通过介入方式精准作用于硬膜外腔、蛛网膜下腔、神经根、神经干、神经丛,甚至瘤体内神经末梢,以控制严重的癌性疼痛,而不会产生明显的不良反应。神经毁损药物包括无水乙醇、苯酚、阿霉素、亚甲蓝等,其中无水乙醇是最常用的药物。化学性毁损的镇痛作用一般维持2~4个月。

② 物理性毁损

利用物理方法对感觉神经产生物理性毁损,使神经组织的传导功能受到不同程度的中断或阻滞,从而

获得镇痛效果,主要包括内脏神经毁损术(splanchnic nerve neurolysis, SNN)、超声内镜下腹腔神经丛松解术(EUS-guided celiac plexus neurolysis, EUS-CPN)、射频消融术(Radiofrequency ablation, RFA)、EUS引导射频消融术(EUS-guided radiofrequency ablation, EUS-RFA)、经皮热消融术(percutaneous thermal ablation, PTA)、微波消融术(microwave ablation)、冷冻消融术(cryoablation)、高强度聚焦超声(high intensity focused ultrasound)等。

(3) 经皮椎体成形术

经皮椎体成形术,全称为经皮穿刺椎体成形术(percutaneous vertebro plasty, PVP),是向病变椎体内注入骨水泥(聚丙烯酸甲酯)或人工骨,以强化椎体的技术。球囊扩张椎体后凸成形术(percutaneous kyphoplasty, PKP)在PVP基础上改进而来,经过球囊扩张后再分次注入骨水泥,可减少骨水泥的渗漏。PKP更有助于椎体的稳定和椎间高度的维持。PVP可减轻椎体原发性肿瘤或转移瘤疼痛、强化椎体稳定性,同时对椎体肿瘤有一定杀伤作用,抑制肿瘤的进展。

(4) 放射性粒子植入术

放射性粒子植入术是在CT、DSA等引导下将微型粒子源(¹²⁵I)利用植入针准确植入肿瘤内,持续性释放 γ 射线及X射线,通过直接电离破坏DNA及间接电离产生氧自由基来杀灭肿瘤细胞,治疗中发现¹²⁵I粒子植入对癌性疼痛有一定作用。具有瘤内剂量高、瘤外剂量低,高度适形,并发症少,患者耐受性好等优点。

(5) IDDS

IDDS可将药物以精确控制的速度输送到蛛网膜下腔。由于鞘内给药可以绕过血脑屏障,直接作用于中枢神经系统,因此较小剂量即可产生显著的镇痛效果,从而减少全身不良反应。对于无法忍受药物不良反应和/或全身性阿片类药物无法有效控制疼痛的患者,应考虑鞘内途径给药^[170]。鞘内镇痛可作为癌症患者在疾病过程中任何时间的可选治疗方案,尤其是对于预期寿命有限的患者,优先考虑,及时减轻患者痛苦。根据《鞘内药物输注技术用于癌痛管理的中国专家共识(2022版)》,鞘内用药应以阿片类药物为主导,依据镇痛方案进行阶梯用药^[171]。阿片类药物或者阿片类药物与局麻药联合使用为癌痛鞘内治疗的一线用药。IDDS最常见的

并发症为低颅压性疼痛,常见不良反应包括尿潴留、恶心、呕吐等。

常用微创介入治疗循证医学证据质量级别及推荐强度。见表12^[55, 57, 165, 169-170, 172-204]。

表12 常用微创介入治疗循证医学证据质量级别及推荐强度

类型	方法	证据级别	推荐强度	
PCA	PCIA ^[57, 165, 172-174]	A	1	
	PCSA ^[55, 165, 174-176]	A	1	
	PCEA ^[177-178]	A	1	
化学性毁损术	[179-180]	B	1	
物理性毁损术	SNN ^[181]	A	1	
	EUS-CPN ^[182-185]	A	1	
	EUS-RFA ^[186]	A	2	
	PTA ^[187]	A	1	
	RFA ^[188-195]	A	1	
	微波消融 ^[191-192]	A	1	
	冷冻消融 ^[191-192, 196-197]	A	1	
	高强度聚焦超声 ^[191-192]	A	2	
	经皮椎体成形术	PVP ^[198-200]	A	1
		PKP ^[198-200]	A	1
放射性粒子置入术 ^[201-202]		A	1	
鞘内药物输注系统 ^[169-170, 203-204]		A	1	

注:PCA为患者自控镇痛,PCIA为患者静脉自控镇痛,PCSA为患者皮下自控镇痛,PCEA为患者硬膜外自控镇痛,SNN为内脏神经毁损术,EUS-CPN为超声内镜下腹腔神经丛松解术,EUS-RFA为超声内镜引导下射频消融术,PTA为经皮热消融术,RFA为射频消融术,PVP为经皮穿刺椎体成形术,PKP为球囊扩张椎体后凸成形术

8. 康复治疗

癌痛患者的康复治疗是一个综合性的、个体化的过程,应该根据患者的具体情况和需求进行定制。高级别证据支持长期随访护理、疲劳和心理社会/心理健康筛查的康复建议^[205],旨在帮助患者减轻疼痛、恢复身心健康,提高生活质量。

9. 安宁疗护

在诊断为癌症晚期后,患者的主要关注点包括躯体症状和不良反应、功能丧失,疾病进展的可能性以及生存期等。找到合适的安宁疗护方法,控制疼痛、营养支持、心理支持,尽可能提高生活质量^[18-19]。

癌性爆发痛

一、概念

癌性爆发痛(breakthrough cancer pain, BTcP)是

指在背景痛控制相对稳定、镇痛药物充分应用的前提下自发或在某些因素的诱发下,突然出现的短暂疼痛加重,其发生率可达33%~95%。BTcP可分为事件性(诱发性)BTcP和自发性(特发性)BTcP,前者一般由可预测的因素引起易于防治,而后者是由无法预测的活动或诱因引发疼痛,难以防治。BTcP为一种难治性癌痛,起病迅速、中度至重度强度、持续时间短、疼痛多不可预测,病理机制复杂,任何解救性药物均有滞后性。

二、诊断标准^[206]

1. 在过去的1周患者是否存在持续性疼痛(背景痛)。
2. 在过去的1周患者的背景痛是否充分控制(NRS≤3分)。
3. 患者是否存在短暂疼痛加重的现象(NRS≥4分)。

若上述问题的答案均为“是”,则可确诊患者存在BTcP。

三、治疗方法

病因治疗至关重要。BTcP治疗主要是基于阿片类药物为主导的解救治疗(多推荐芬太尼制剂)和微创介入治疗。

1. 药物治疗

国内目前多采用的方法:(1)快速起效的解救药物;(2)PCA,一般采用静脉或皮下途径给药。

常用的阿片类药物包括吗啡、氢吗啡酮注射剂等^[56],有趋势使用特色的芬太尼剂型,包括芬太尼透粘膜口服锭剂、芬太尼舌下含片、芬太尼鼻腔喷雾剂等^[207-211]。

2. 微创介入治疗

合理选择微创介入治疗可以提高癌痛的治疗效果,并降低BTcP的发作频率和程度。可根据病情选择的方法有:(1)针对瘤体进行治疗(粒子植入术、瘤体物理或化学毁损等);(2)阻断癌痛相关的神经传导通路(内脏神经节、神经干毁损,脊神经根、神经干毁损等);(3)改善和提升组织结构的稳定性(经皮椎体/骨成形术);(4)改变给药途径或方式,提高药物疗效、加快起效时间(IDDS、PCA等)。

慢性癌症相关性疼痛诊疗路径

CCRP的诊疗路径见图2。



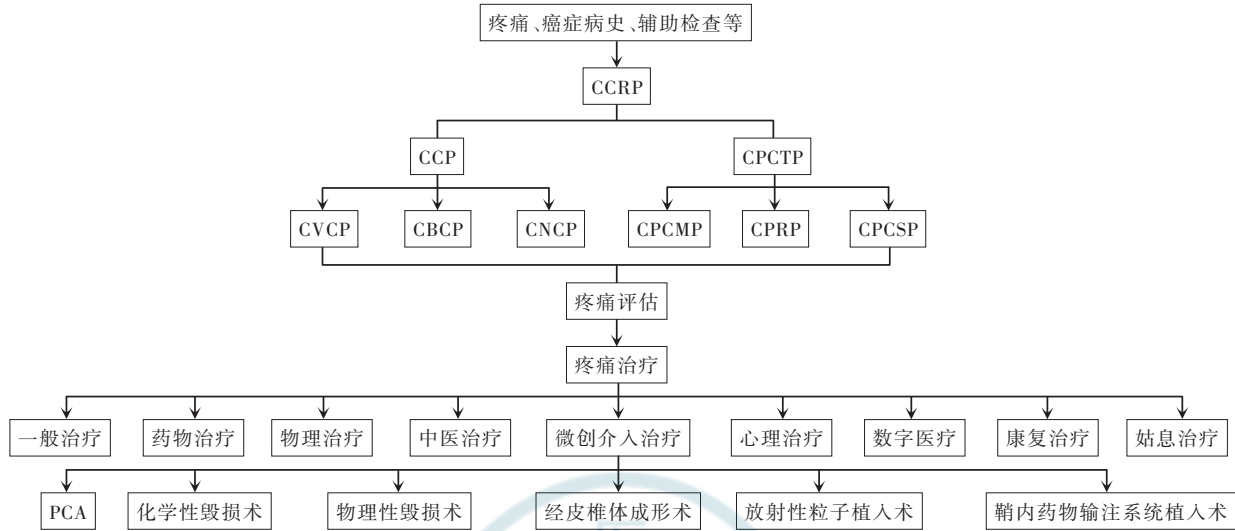


图2 CCRP诊疗路径

注:CCRP为慢性癌症相关性痛,CCP为慢性癌性疼痛,CVCP为慢性内脏癌性疼痛,CBCP为慢性骨性癌性疼痛,CNCP为慢性神经病理性癌痛,CPCTP为慢性癌症治疗后疼痛,CPCMP为癌症药物治疗后的慢性疼痛,CPRP为慢性放射治疗后疼痛,CPCSP为慢性癌症术后疼痛,PCA为患者自控镇痛

利益冲突 所有作者均声明无利益冲突

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