上海交通大學
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关注患者心理，再谈癌痛治疗

癌痛治疗及案例分享

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20180821

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Shanghai Sixth People's Hospital

NCCN NATIONAL COMPREHENSIVE CANCER NETWORK FOUNDATION®
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肿瘤患者的心理变化

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- 否定 对癌症的恐惧心理，希望判断是错误的
- 愤怒 其他人都好好的，为什么我倒霉？
- 讨价还价 较能配合，希望减轻痛苦，延长生命
- 忧伤 虚弱和痛苦，主导情绪是失望、沮丧
- 自暴自弃 放弃了自身防御机理对疾病产生积极的影响

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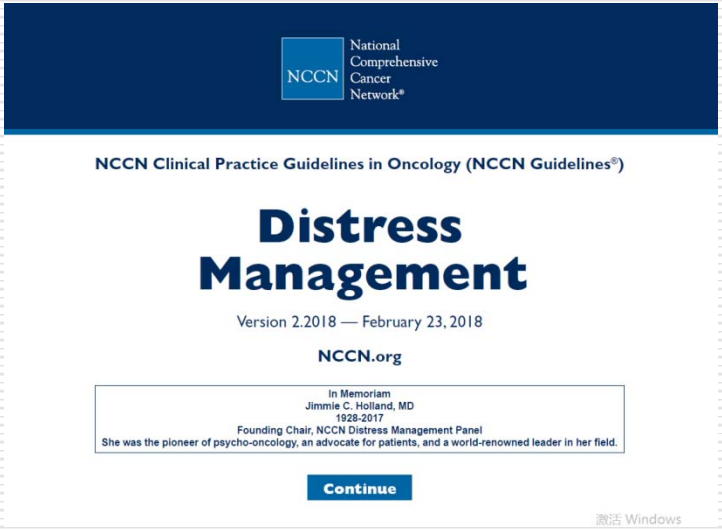
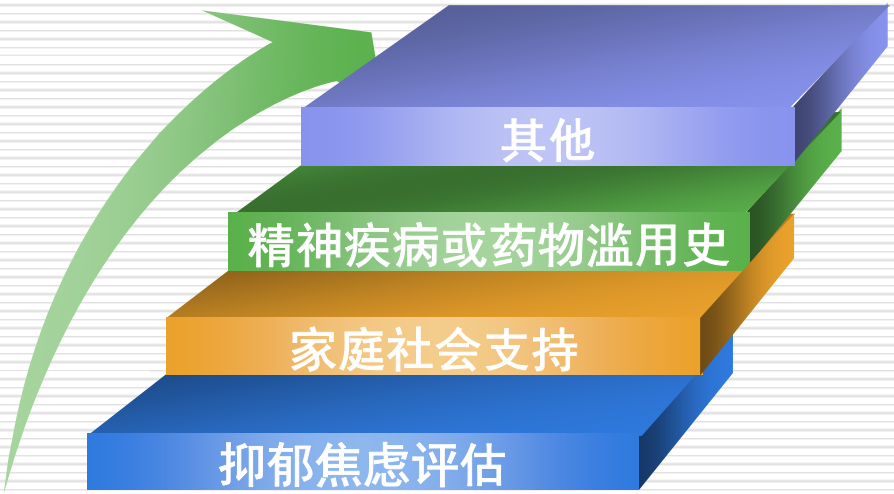
心理痛苦管理


National Comprehensive Cancer Network
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Distress Management
Version 2.2018 — February 23, 2018
NCCN.org
In Memoriam
Jimmie C. Holland, MD
1928-2017
Founding Chair, NCCN Distress Management Panel
She was the pioneer of psycho-oncology, an advocate for patients, and a world-renowned leader in her field.
Continue


其他
精神疾病或药物滥用史
家庭社会支持
抑郁焦虑评估

NCCN：心理痛苦的定义

上海交通大學

*D*istress is an unpleasant experience of a mental,physical,social,or spiritual nature.*I*t can affect the way you think,feel,or act.*D*istress may make it harder to cope with having cancer,its symptoms,or its treatment.

- By definition,being distressed isn't pleasant.
- Distress may affect how well you function.
- Distress may interfere with your health decisions or actions.
- Distress may worsen your health.

Guide 1. Symptoms of distress

Some symptoms of distress are:
• Sadness, fear, and helplessness
• Anger, feeling out of control
• Questioning your faith, your purpose, the meaning of life
• Pulling away from too many people
• Concerns about illness
• Concerns about your social role (ie, as mother, father, caregiver)
• Poor sleep, appetite, or concentration
• Depression, anxiety, panic
• Frequent thoughts of illness and death

心理痛苦的评估

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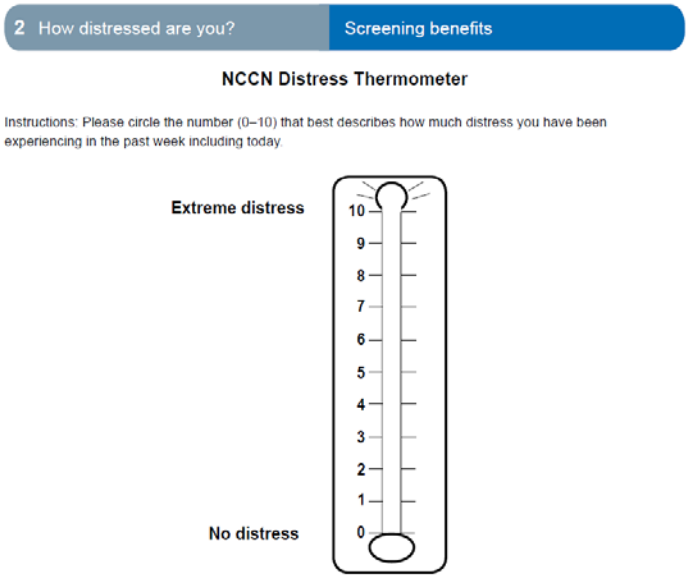
- 核心症状
  - 情绪低落
  - 兴趣丧失
  - 快感缺乏
- 躯体表现：
  - 睡眠障碍
  - 疲劳
  - 食欲紊乱
  - 体重改变



2 How distressed are you? | Screening benefits

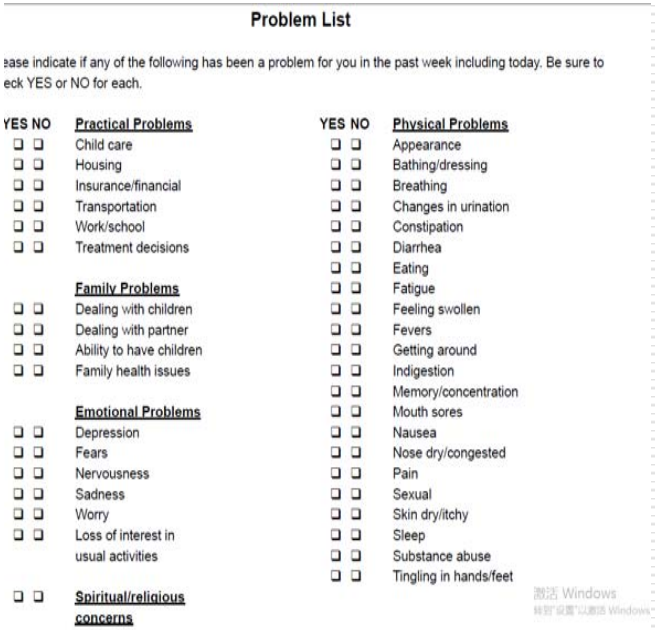
NCCN Distress Thermometer

Instructions: Please circle the number (0–10) that best describes how much distress you have been experiencing in the past week including today.

Extreme distress

10 9 8 7 6 5 4 3 2 1 0

No distress



Problem List

ease indicate if any of the following has been a problem for you in the past week including today. Be sure to eck YES or NO for each.

YES	NO	Practical Problems
❑	❑	Child care
❑	❑	Housing
❑	❑	Insurance/financial
❑	❑	Transportation
❑	❑	Work/school
❑	❑	Treatment decisions
		Family Problems
❑	❑	Dealing with children
❑	❑	Dealing with partner
❑	❑	Ability to have children
❑	❑	Family health issues
		Emotional Problems
❑	❑	Depression
❑	❑	Fears
❑	❑	Nervousness
❑	❑	Sadness
❑	❑	Worry
❑	❑	Loss of interest in usual activities
❑	❑	**Spiritual/religious concerns**

YES	NO	Physical Problems
❑	❑	Appearance
❑	❑	Bathing/dressing
❑	❑	Breathing
❑	❑	Changes in urination
❑	❑	Constipation
❑	❑	Diarrhea
❑	❑	Eating
❑	❑	Fatigue
❑	❑	Feeling swollen
❑	❑	Fevers
❑	❑	Getting around
❑	❑	Indigestion
❑	❑	Memory/concentration
❑	❑	Mouth sores
❑	❑	Nausea
❑	❑	Nose dry/congested
❑	❑	Pain
❑	❑	Sexual
❑	❑	Skin dry/itchy
❑	❑	Sleep
❑	❑	Substance abuse
❑	❑	Tingling in hands/feet

IAHPC肿瘤姑息治疗基本药品目录2007

- WHO遴选基本药品的条件：
  常见疾病；有证据表明入选药品有效、安全、费效比合理。
- 癌症姑息治疗33种基本药品缓解癌症患者症状

严重干扰癌症患者生活质量及生命的18种症状：

疼痛	乏力	食欲减退		
多汗	恶病质	口腔问题	呼吸困难	终末期呼吸问题
恶心	呕吐	呃逆	便秘	腹泻
抑郁	焦虑	失眠	谵妄	终末期烦乱不安


癌症疼痛


呼吸系统症状


消化系统症状


精神系统症状

IAHPC止痛治疗基本药品

- 癌症疼痛：IAHPC止痛治疗疾病药品符合WHO癌症三阶梯止痛治疗原则，反映推行WHO三阶梯原则临床实践进展。

IAHPC止痛治疗基本药品	
轻度、中度疼痛	对乙酰氨基酚、布洛芬、双氯芬酸、曲马多、可待因
中度、重度疼痛	吗啡（即释剂或缓释剂）、芬太尼（透皮贴剂）、羟考酮（即释剂或缓释剂），美沙酮（即释剂）
神经病理性疼痛	阿米替林、卡马西平、地塞米松、加巴喷丁
内脏疼痛	丁溴东莨菪碱

IAHPC呼吸系统症状基本药品

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- 在终末期癌症患者中，约有50%-70%出现呼吸困难。
- NCCN：对预期生存时间较短的晚期癌症患者出现呼吸困难，处理重点是提高患者舒适度。
- 吗啡是唯一被推荐使用的有效药物。

IAHPC呼吸系统症状基本药品	
呼吸困难	吗啡
临终呼吸道堵塞	丁溴东莨菪碱


降低对呼吸困难的反应敏感程度


减少机体氧耗量，提高机体耐受性


减慢浅快呼吸，改善通气状况


改善焦虑、紧张情绪，提高舒适度

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IAHPC精神系统症状基本药品

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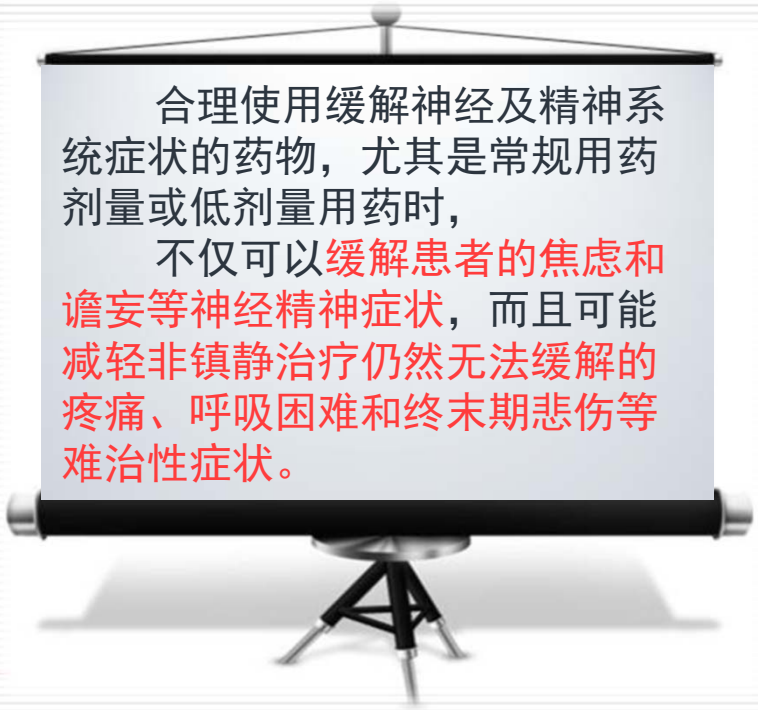
IAHPC精神系统症状基本药品	
失眠	劳拉西泮、曲唑酮、唑吡坦
抑郁	阿米替林、西酞普兰、米氮平
焦虑	安定、劳拉西泮、咪达唑仑
谵妄	氟哌啶醇、左美丙嗪
临终躁动	氟哌啶醇、左美丙嗪、咪达唑仑



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IAHPC消化系统症状基本药品

- 晚期癌症及终末期癌症患者常存在不同程度的消化系统症状，包括食欲减退、厌食、恶心、呕吐、便秘、腹泻。

IAHPC消化系统症状基本药品	
厌食	醋酸甲地孕酮、地塞米松、氢化可的松
恶心、呕吐	灭吐灵、氟哌啶醇、丁溴东莨菪碱、地塞米松、苯海拉明、奥曲肽
便秘	番泻叶、比沙可啶、矿物油灌肠剂
腹泻	口服 补液盐、洛哌丁胺、奥曲肽

疼痛与抑郁

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- 68%的疼痛患者伴有焦虑、抑郁。
- 13%的疼痛患者可以诊断为重度抑郁。
- 疼痛的定义：

An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. *

一种与实际的或潜在的组织损伤有关的不愉快的感觉和情绪体验，或对这种损伤所做的描述。

- 研究发现，疼痛和抑郁有一条潜在的神经化学通路。

* The International Association for the study of pain，1994

抑郁产生的生化基础

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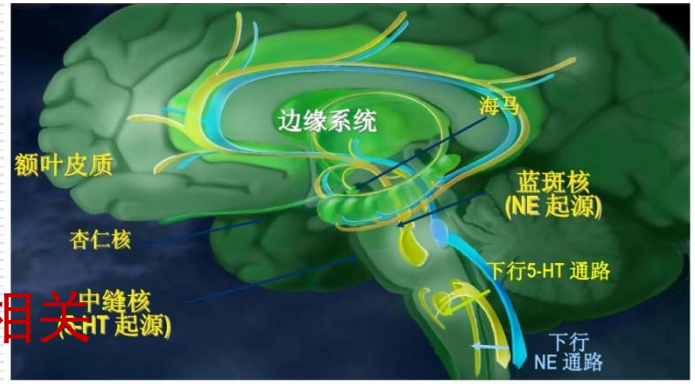
- 5-HT能神经元主要集中在中脑的中缝核
- NE能神经元主要集中在蓝斑核
- 5-HT和NE能神经元的上行神经纤维多相伴投射脑部的共同区域
  - 5-HT能神经纤维投射到基底节(调节运动)和睡眠中枢(调节睡眠-觉醒节律)
  - NE能神经元纤维投射到额叶皮层(调节认知功能和注意力)和小脑(调节精细运动)
- 大脑内5-HT和NE的失调与抑郁高度相关



Cooper JR, et al. *The Biochemical Basis of Neuropharmacology*. 8th ed. New York: Oxford University Press; 2003.

疼痛的病理生理机制

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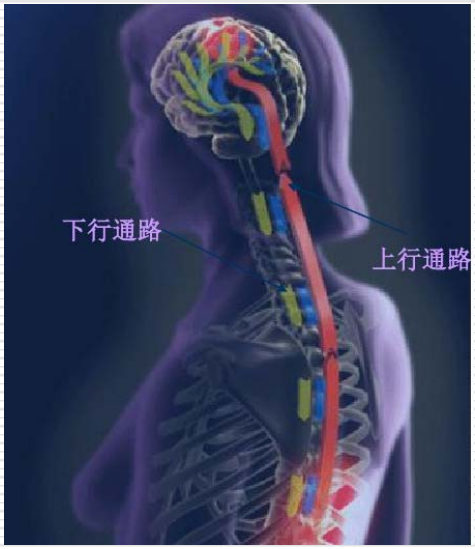
- NE和5-HT是痛觉下行抑制通路的主要神经递质。
- 在疼痛信号的加工处理和疼痛的调节中起重要作用。
- 下行通路调节上传信号，决定对疼痛的感知
- 疼痛的发生与痛觉上行通路的兴奋增强和抑制降低有关。



疼痛性躯体症状在抑郁患者中非常普遍。

疼痛与抑郁

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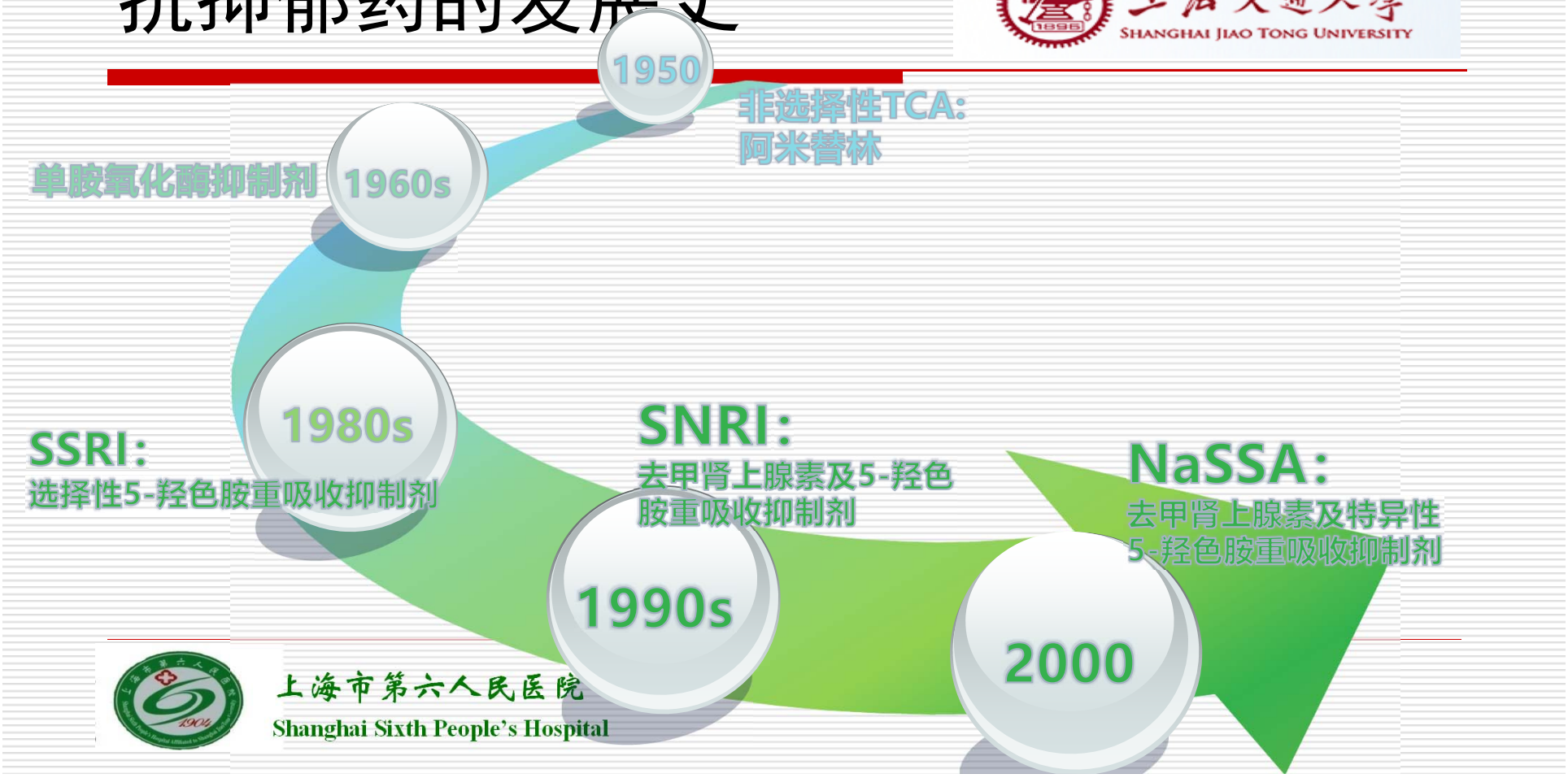
- NE和5-HT缺乏是抑郁焦虑障碍的生化基础，也是疼痛产生的主要原因。
- 增强NE和5-HT功能可以加强中枢的疼痛抑制。

抗抑郁药的发展史



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癌症患者的抗抑郁药

抗抑郁药分类	药品(英文，商品名)	起始剂量	维持剂量
TCA	阿米替林(amitriptyline)	25-50mg qn	50-200mg/d
SSRI	氟西汀(fluoxetine，百忧解)	10-20mg/d	20-60mg/d
	帕罗西汀(paroxetine，赛乐特)	10mg/d	20-60mg/d
	艾司西酞普兰(escitalopram，百适可)	5-10mg/d	10-20mg/d
	舍曲林(sertraline，左洛复)	25mg/d	50-150mg/d
	西酞普兰(citalopram，喜普妙)	10mg/d	20-40mg/d
SNRIs	文拉法辛(venlafaxine，怡诺思)	37.5-75mg/d	75-225mg/d
	度洛西汀(duloxetine，欣百达/博乐欣)	20mg/d	60mg/d
	米氮平(mirtazapine，瑞美隆)	15mg qn	15-45mg qn
	曲唑酮(trazodone，每素玉)	25mg/d	50-100mg/d

肾功能损坏患者使用阿片药物

Review

MEDICINE

A systematic review of the use of opioid medication for those with moderate to severe cancer pain and renal impairment: A European Palliative Care Research Collaborative opioid guidelines project

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K Forbes *Department of Palliative Medicine, University of Bristol, Bristol Oncology and Haematology Centre, UK*
GW Hanks *Department of Palliative Medicine, University of Bristol, Bristol Oncology and Haematology Centre, UK*
CJ Ferro *University Hospitals Birmingham NHS Trust, UK*
EJ Chambers *North Bristol NHS Foundation Trust, UK*

Abstract

Background: Opioid use in patients with renal impairment can lead to increased adverse effects. Opioids differ in their effect in renal impairment in both efficacy and tolerability. This systematic literature review forms the basis of guidelines for opioid use in renal impairment and cancer pain as part of the European Palliative Care Research Collaborative's opioid guidelines project.

Objective: The objective of this study was to identify and assess the quality of evidence for the safe and effective use of opioids for the relief of cancer pain in patients with renal impairment and to produce guidelines.

Search strategy: The Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, MedLine, EMBASE and CINAHL were systematically searched in addition to hand searching of relevant journals.

Selection criteria: Studies were included if they reported a clinical outcome relevant to the use of selected opioids in cancer-related pain and renal impairment. The selected opioids were morphine, diamorphine, codeine, dextropropoxyphene, dihydrocodeine, oxycodone, hydromorphone, buprenorphine, tramadol, alfentanil, fentanyl, sufentanil, remifentanil, pethidine and methadone. No direct comparator was required for inclusion. Studies assessing the long-term efficacy of opioids during dialysis were excluded.

Data collection and analysis: This is a narrative systematic review and no meta-analysis was performed. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess the quality of the studies and to formulate guidelines.

Main results: Fifteen original articles were identified. Eight prospective and seven retrospective clinical studies were identified but no randomized controlled trials. No results were found for diamorphine, codeine, dihydrocodeine, buprenorphine, tramadol, dextropropoxyphene, methadone or remifentanil.

Conclusions: All of the studies identified have a significant risk of bias inherent in the study methodology and there is additional significant risk of publication bias. Overall evidence is of very low quality. The direct clinical evidence in cancer-related pain and renal impairment is insufficient to allow formulation of guidelines but is suggestive of significant differences in risk between opioids.

Recommendations: Recommendations regarding opioid use in renal impairment and cancer pain are made on the basis of pharmacokinetic data, extrapolation from non-cancer pain studies and from clinical experience. The risk of opioid use in renal impairment is stratified according to the activity of opioid metabolites, potential for accumulation and reports of successful or harmful use. Fentanyl, alfentanil and methadone are identified, with caveats, as the least likely to cause harm when used appropriately. Morphine may be associated with toxicity in patients with renal impairment.

Oxycodone

Oxycodone can be excreted in conjugated and unconjugated (8%–14%) form with the main metabolites noroxycodone and oxymorphone also found in urine.[172] The production of noroxycodone, the most abundant metabolite, is catalysed by CYP3A4, whilst oxymorphone results from the action of CYP2D6. Oxycodone itself exhibits a prolongation of its elimination half life when used in renal failure[173] and the metabolites may also have delayed elimination and increased blood levels.[173,174]

Oxymorphone is active as an opioid receptor agonist and as an analgesic in humans.[175–177] Noroxycodone has some analgesic properties in animal models but is thought to have minimal clinical effect in humans under normal conditions.[178] The role of active metabolites in mediating either the therapeutic or toxic effects of oxycodone is unclear.

There are case reports of toxicity in association with oxycodone use in renal impairment, and increased sedation and accumulation of oxycodone and its metabolites in renal failure has been reported.[174,179,180]

- 肾功能损坏患者使用阿片药物会导致不良反应增加。
- 肾功能损坏对不同阿片药物的影响各异。
- 肾功能损坏导致羟考酮及代谢产物蓄积。

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肾功能损坏患者使用阿片药物

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Table 4. Metabolite activity and risk stratification

Group 1 (No clinically significant active metabolites)
Fentanyl, alfentanil and methadone
Group 2 (Active or probably active metabolites-stratified according to degree of toxicity or risk of accumulation)

a) Tramadol and hydromorphone (possible reduced risk of toxicity)

b) Morphine, diamorphine, codeine, dihydrocodeine and oxycodone

c) Pethidine and dextropropoxyphene (high risk of toxicity recommend against use)

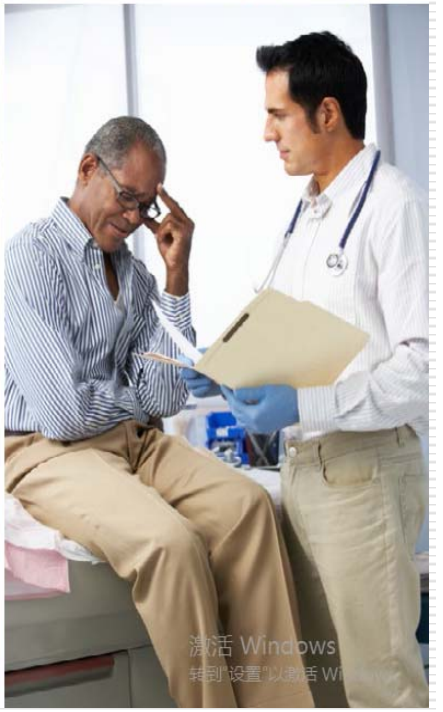
Group 3 (Insufficient evidence or experience to make a recommendation for chronic use)
Buprenorphine and sufentanil (active metabolites). Remifentanil (inactive metabolites)

Table 5. Mild to moderate renal impairment

Recommendations for the use of opioids in cancer related pain:
Estimated glomerular filtration rate (GFR)
30–89 ml/min (mild to moderate renal impairment)
The presence of renal failure should not be a reason to delay the use of an opioid for those with cancer pain when needed

- All opioids that are appropriate for cancer pain can be used with consideration of reduced dose or frequency at a lower eGFR
- Monitor for changes in renal function and consider a pre-emptive change of opioid in rapidly deteriorating renal function
- Assess for any reversible factors
- Be aware that estimations of GFR may be less accurate in the presence of cachexia, low protein states, oedema and with acute renal failure. An estimated GFR at the lower end of the moderate renal impairment range should therefore prompt consideration of a change of opioid to one considered safer in renal impairment.


BODY
MIND
SPIRIT
BALANCE

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