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Identifying pain-related concerns in routine follow-up clinics following oral and oropharyngeal cancer

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Abstract

AIM: To describe clinical characteristics of head and neck cancer (HNC) patients with pain and those wishing to discuss pain concerns during consultation.

METHODS: Cross-sectional, questionnaire study using University of Washington Quality of Life, version 4 (UW-QOL) and the Patients Concerns Inventory (PCI) in disease-free, post-treatment HNC cohort. Significant pain on UW-QOL and indicating "Pain in head and neck" and "Pain elsewhere" on PCI.

RESULTS: One hundred and seventy-seven patients

completed UW-QOL and PCI. The prevalence of self-reported pain issues was 38% (67/177) comprising 25% (44/177) with significant problems despite medications and 13% (23/177) with lesser or no problems but wishing to discuss pain. Patients aged under 65 years and patients having treatment involving radiotherapy were more likely to have pain issues. Just over half, 55% (24/44) of patients with significant pain did not express a need to discuss this. Those with significant pain or others wanting to discuss pain in clinic had greater problems in physical and social-emotional functioning, reported suboptimal QOL, and also had more additional PCI items to discuss in clinic compared to those without significant pain and not wishing to discuss pain.

CONCLUSION: Significant HNC-related pain is prevalent in the disease-free, posttreatment cohort. Onward referral to a specialist pain team may be beneficial. The UW-QOL and PCI package is a valuable tool that may routinely screen for significant pain in outpatient clinics.

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Key words: Pain; Health related quality of life; Patient Concerns Inventory; Head and neck cancer; Mouth neoplasm; Quality of life; Questionnaire

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INTRODUCTION

Pain can be experienced at various time points in the cancer journey of an individual with head and neck cancer (HNC)^[1]. Cancer-related pain is due to the direct effect of the tumor and/or the consequence of HNC treatment. Non-cancer related pain can co-exist and may contribute to the overall pain experience^[2,3]. Pain experienced by HNC patients may have a detrimental impact on their general well-being^[4], cause dysfunction^[5,6] and distress^[7,8], is associated with poor sleep quality^[9] and poor health-related quality of life^[10], can mark the onset of malignant transformation^[11] and recurrence^[12], and reduces survival rate^[13]. Although the impact of pain in HNC patients is significant, its management is difficult^[14] and often inadequate^[2]. There are several obstacles to optimal pain management in this group of patients. There is an incomplete understanding of the HNC-related pain experience, particularly in the post-diagnosis period^[3]. Current approach to cancer-related pain management emphasizes heavily on the pharmacological approach based on the World Health Organization (WHO) pain ladder^[1,15] with less consideration on the psycho-cognitive aspects underlying pain and how this influences coping^[16]. Involvement of the pain specialist in HNC cases may be limited in many HNC set-ups^[2,5]. There may be an inadequate appreciation by non-pain specialist practitioners of the neuropathic mechanisms involved in HNC-related pain^[17] with consequential bearing on symptom management^[2]. Health professionals' reluctance towards opioid use^[3] and patients' reservations due to fear of addiction^[16] may hinder adequate pain control, especially for breakthrough pain, which is common among HNC patients^[2,18]. Finally, HNC patients may have difficulty self-reporting pain to their medical care providers^[19] and routine screening may assist them in conveying this issue to the clinician.

Opportunistic evaluation of pain in HNC patients is achievable by using Health Related Quality Of Life tools. Pain is frequently assessed as part of HNC patient-reported outcomes using various health-related quality of life tools^[3], including the University of Washington Quality of Life version 4 questionnaire (UW-QOL)^[20]. When the UW-QOL is used in routine oncology clinical practice, this tool may offer a platform to identify those with significant problems in any of the 12 domains assessed (including pain) and also provides a trigger mechanism for supportive intervention^[21]. The UW-QOL trigger for supportive intervention is based on defined cut-off points in the response scores of each domain, beyond which patients would be expected to encounter significant dysfunction/problems. This method correlated well with validated head and neck specific questionnaires e.g., Derriford Appearance Scale (DAS-24) and the MD Anderson Dysphagia Inventory, in identifying those with significant issues with appearance and swallowing respectively^[21]. However, in regard to the pain domain, the cut-off point for supportive intervention was not correlated with any pain-specific questionnaire due to the lack of a

suitable HNC pain-specific questionnaire that considers the complexity of HNC-related pain. The complexity of HNC-related pain is due to in part, the influence of multiple sources of somatic tissue and neural damage resulting from cancer and/or its treatment, and also from the personal and subjective nature of the pain experienced, which may be influenced by cultural learning, the meaning of the situation, attention, and other psychologic variables^[22].

The Patients Concerns Inventory (PCI) is a 55-item checklist tool introduced to assist HNC patients in highlighting the items of concern that they may wish to discuss with clinicians during routine oncology consultations^[23]. In the PCI item checklist, pain is covered in 2 items: "Pain in the head and neck" and "Pain elsewhere". The original PCI study found that the "Pain in the head and neck" and "Pain elsewhere" were indicated as items of concern in 20% (4th most common item) and 10% (15th most common item) respectively^[23]. As there is no limit to the number of PCI items that patients could choose from, patients may also indicate other items they perceive to be of concern and wish to be addressed during consultation. This includes other items that may be associated with or influence pain, such as fear of recurrence, anxiety, swallowing, saliva and shoulder^[10,12,16,24]. We have found that the PCI is a valuable tool in understanding a wider scope of issues that HNC patients may experience in the post-treatment period based on previous work^[25-29] and facilitates patient-clinical discussion regarding these issues and the need for supportive care.

There is a paucity of work relating specifically to the pain experience of HNC patients who have undergone treatment^[3]. The rationale for this work is to understand how post-treatment HNC patients with pain self-report their experience using the PCI in a routine clinic outpatient setting, which forms part of the on going work of this unit with the PCI. The aims of this paper are: First, to report the clinical characteristics of HNC patients with pain attending routine outpatients and those wishing to discuss the issue of pain in their consultation and second, to identify if the issue of pain was mentioned in the clinic letter and if onward referral was made.

MATERIALS AND METHODS

Prospective data collection from HNC patients attending routine follow-up clinics occurred from October 2008 to January 2011. Patients on the Liverpool oncology database were included if they were disease-free and under routine follow-up at least 6 wk after completing treatment. Patients were excluded if they were pretreatment, palliative, attending the clinic for other post-operative wound management or were part of another outcomes study in clinic.

Touch-screen technology (TST) was used by patients before their consultation to complete PCI, a holistic, self-reported screening tool for unmet needs/concerns and UW-QOL, version 4^[30]. Following registration to clinic,

patients were invited by a hospital volunteer to complete the TST questionnaire package. TST data was collected using Microsoft Access and placed directly on to a secure hospital server and was accessible to the clinician immediately before the consultation. The PCI measure asked patients to indicate which of 55 issues they would like to discuss during their consultation, and two of these issues involved pain – pain in the head and neck and pain elsewhere. Patients were also asked to select members of staff, from a list of 14 types of health professional, who they would “like to see or be referred to”.

The UW-QOL questionnaire is well established^[31]. For this study the UW-QOL was analysed in terms of its two subscale composite scores, “physical function” and “social-emotional function”^[32] as well as its domains and a single six-point Likert scale “overall” QOL measure. Physical function is the simple average of the swallowing, chewing, speech, saliva, taste and appearance domain scores whilst social-emotional function is the simple average of the activity, recreation, pain, mood, anxiety and shoulder domain scores. The pain domain is scored on a five point Likert scale as: (100) I have no pain, (75) There is mild pain not needing medication, (50) I have moderate pain – requires medication (e.g., paracetamol), (25) I have severe pain controlled only by prescription medicine (e.g., morphine), (0) I have severe pain, not controlled by medication. In earlier work^[21] we defined a “significant problem” with pain as being a UW-QOL domain score of (0) or (25) or also as (50) if pain had been one of the three most important domains to the patient over the previous week. We also refer to earlier work^[33] to provide normative reference scores for pain. In regard to the single item overall QOL scale, patients were asked to consider not only physical and mental health, but also other factors, such as family, friends, spirituality or personal leisure activities important to their enjoyment of life.

Details of onward referrals regarding pain arising subsequently from consultations were obtained from clinic letters. Clinical-demographic data came from the Liverpool HNC database.

Results were analysed mainly within three patient subgroups defined by reference to whether there was any evidence of significant pain from the UW-QOL and to whether pain issues were raised for discussion on the PCI. The χ^2 test compared the patient subgroups with regard to categorical patient characteristics including the presence or absence of significant problems on each of the other domains of the UW-QOL. The Kruskal-Wallis test compared the subgroups in regard to age, months from primary treatment, UW-QOL overall QOL Likert scale, UW-QOL subscale scores for physical and social-emotional function, number of PCI concerns raised and number of staff members selected. As the UW-QOL and PCI TST package is integrated into routine clinical practice in this setting, this study was approved by the University Hospital Aintree Clinical Audit department in the context of service evaluation.

RESULTS

There were 396 TST sets of data that included both PCI and UW-QOL, from 177 patients during the course of 79 clinic sessions. Nearly two-thirds of patients (63%, 112/177) attended clinic more than once during the study, with 53 attending two, 29 attending three, 19 attending four and 11 attending five to seven times. Males comprised 63% (112) and the mean (SD) age at first clinic was 62 (12) years (range 24–86 years). Most patients (89%, 158) had a primary diagnosis of squamous cell carcinoma, with others including: low grade polymorphous adenocarcinoma (4), adenoid cystic carcinoma (2), mucoepidermoid carcinoma (2), and verrucous carcinoma (2). Most (71%, 126) had oral tumors, with 23% (41) pharyngeal and 6% (10) others. Overall, 19% (34) had advanced T3-T4 tumors and 20% (36) were clinically neck node positive. Just over half (58%, 103) had been treated by surgery alone, 32% (56) by surgery with adjuvant radiotherapy, and 10% (18) without surgery (by radiotherapy/chemotherapy). Overall 43% (76) had free-flap primary surgery with selective neck dissection. At first clinic 41% (73) were within 12 mo of diagnosis, 13% (23) within 12–23 mo, 21% (37) within 24–47 mo and 25% (44) after 48 mo.

Before the first study clinic consultation, 25% (44/177) of patients reported significant problems with pain (i.e., scores of 0 or 25 or 50 and important on the UW-QOL). This contrasts with significant problem levels of 13% (44/349) in data reanalysed for non-cancer patients routinely attending ten general dental practices and 100% (23/23) for non-cancer patients attending these practices in an emergency^[33].

“Pain in the head and neck” was raised by patients on the PCI in 18% (32/177) of cases, and “Pain elsewhere” by 10% (17/177), with one or the other raised by 24% (43/177). A total of 38% (67/177) reported significant pain problems on the UW-QOL or highlighted issues of pain on the PCI for discussion (Table 1), with 25% (44/177) meeting the UW-QOL criteria while an extra 13% (23/177) met only the PCI criteria (more minor concerns they wanted to discuss). One-half (55%, 24/44) of those with a significant pain problem did not wish to discuss it. Subsequent analyses focus on three groups for comparison: the 62% (110) of patients without significant pain and with no wish to discuss pain (Group A), the 25% (44) with significant pain (Group B), and the 13% (23) without significant pain who wanted to discuss pain (Group C, 18 to discuss head and neck pain, 5 to discuss pain elsewhere).

Patients aged 65 years and older reported less significant pain and fewer wished to discuss pain than younger patients (Table 2). Patients having primary treatment without surgery reported higher levels of significant pain. Significant problems in physical functioning were reported more often by patients with significant pain (Table 3). Both Group B and C reported more problems relating to social and emotional function and to overall QOL than

Table 1 Touch-screen responses from 177 patients to questions about pain on the University of Washington Quality of Life questionnaire and on the Liverpool Patients Concerns Inventory before first study attendance at clinic from October 2008 to January 2011

UW-QOL Pain	Stated on PCI that patient wished to discuss the issue of "Pain in head and neck"			
	No (Stated on PCI that patient wished to discuss the issue of "Pain elsewhere")		Yes (Stated on PCI that patient wished to discuss the issue of "Pain elsewhere")	
	No	Yes	No	Yes
(0) I have severe pain, not controlled by medication	3 ²	2	2	2 ²
(25) I have severe pain controlled only by prescription medicine (e.g., morphine)	11 ²	3 ²	2 ²	1 ²
(50) I have moderate pain - requires medication (e.g., paracetamol)/and pain IMPORTANT ¹	10 ²	3 ²	6 ²	3 ²
(50) I have moderate pain - requires medication (e.g., paracetamol)/and pain NOT IMPORTANT ¹	13	2 ²	3 ²	2
(75) There is mild pain not needing medication	22	3 ²	8 ²	2
(100) I have no pain	75	2	7 ²	2

¹Pain was one of three issues most important to patient within the past week; ²Represents those who had reported "significant problems" on the University of Washington Quality of Life questionnaire, version 4 (UW-QOL) or those who had raised pain concerns on the Patients Concerns Inventory (PCI).

Table 2 Patient factors, by whether there was any evidence of significant pain from the University of Washington Quality of Life questionnaire and by whether pain issues were raised for discussion on the Patients Concerns Inventory at the first study clinic *n* (%)

	Patients	No significant pain and no wish to discuss pain (<i>n</i> = 110)	Significant pain (<i>n</i> = 44)	No significant pain but wish to discuss pain (<i>n</i> = 23)	<i>P</i> value ¹
Male	112	71 (63)	29 (26)	12 (11)	0.49
Female	65	39 (60)	15 (23)	11 (17)	
Age (< 55 yr)	45	23 (51)	15 (33)	7 (16)	0.03
Age (55-64 yr)	64	35 (55)	19 (30)	10 (16)	
Age (65+ yr)	68	52 (76)	10 (15)	6 (9)	
Squamous cell carcinoma	158	101 (64)	39 (25)	18 (11)	0.16
Other diagnosis	19	9 (47)	5 (25)	5 (26)	
Oral cavity tumor	126	83 (66)	28 (22)	15 (12)	0.71 (oral vs pharyngeal)
Pharyngeal	41	20 (49)	15 (37)	6 (15)	
Other site	10	7 (70)	1 (10)	2 (20)	
Clinical T1/T2	140	93 (66)	31 (22)	16 (11)	0.11
Clinical T3/T4	34	16 (47)	12 (35)	6 (12)	
Clinical N0	139	89 (64)	34 (24)	16 (12)	0.43
Clinical N+	36	20 (56)	9 (25)	7 (19)	
Primary surgery only	103	68 (66)	26 (25)	9 (9)	0.006
Primary surgery and RT	56	32 (57)	10 (18)	14 (25)	
No surgery, primary RT	18	10 (56)	8 (44)	- (-)	
Within 12 months of diagnosis	73	45 (62)	20 (27)	8 (11)	0.18
Within 12-23 mo of diagnosis	23	15 (65)	6 (26)	2 (9)	
Within 24-47 mo since diagnosis	37	23 (62)	10 (27)	4 (11)	
48 or more months from diagnosis	44	27 (61)	8 (18)	9 (20)	

¹ χ^2 test, apart from Kruskal-Wallis test for age and time from diagnosis and using the numerical values.

Group A. In particular, half of Group B and C patients had significant problems with mood and/or anxiety in contrast to 14% of Group A. Similarly, overall QOL was less than good for half of Group B and C patients compared to 18% for Group A.

In regard to PCI concerns, Figure 1 indicates that Group B and C raised considerably more issues to discuss than Group A. The median [interquartile range (IQR)] total number of concerns per patient were 7 (4-12), 7 (5-10) and 2 (1-5) respectively, $P < 0.001$. In total there were 940 issues raised by the 177 patients (Table 4): the 23% of all patients that form Group B raised 39% (369) of all issues, whilst the 13% in Group C raised 21% (195) of is-

ues and the 62% in Group A raised 40% (376) of issues.

There were no notable differences between groups in terms of selected members of staff (Figure 2) apart from Group B who more often wanted to see or be referred on to dental services. The median (IQR) total number selected per patient were 0 (0-1), 1 (0-1) and 0 (0-1) respectively, $P = 0.07$. For patients attending clinic more than once in the study, the median (IQR) time between first and second clinics was 4 (2-9) mo, 11 (5-15) mo between first and third and 13 (8-20) mo between first and fourth. The longitudinal perspective in following through the three clinical groups from first study clinic is shown in Table 5. Of those with significant pain at first

Table 3 Quality of life as measured by the University of Washington Quality of Life questionnaire, by whether there was any evidence of significant pain from the University of Washington Quality of Life questionnaire and by whether pain issues were raised for discussion on the Patients Concerns Inventory at the first study clinic *n* (%)

	No significant pain and no wish to discuss pain (<i>n</i> = 110)	Significant pain (<i>n</i> = 44)	No significant pain but wish to discuss pain (<i>n</i> = 23)	<i>P</i> value ²
Significant problems ³				
Appearance	5 (5)	14 (32)	2 (9)	< 0.001
Swallowing	17 (15)	14 (32)	3 (13)	0.05
Chewing	15 (14)	9 (20)	1 (4)	0.19
Speech	5 (5)	7 (16)	- (-)	0.02
Taste	15 (14)	7 (16)	- (-)	0.14
Saliva	17 (15)	12 (27)	7 (30)	0.04
Physical function subscale, median (IQR)	80 (62-95)	58 (45-72)	68 (54-72)	< 0.001
Significant problems ³				
Activity	7 (6)	8 (18)	4 (17)	0.06
Recreation	7 (6)	4 (9)	3 (13)	0.53
Shoulder	6 (5)	7 (16)	7 (30)	0.001
Mood	10 (9)	21 (48)	6 (26)	< 0.001
Anxiety	11 (10)	18 (41)	7 (30)	< 0.001
Mood and/or anxiety	15 (14)	23 (52)	11 (48)	< 0.001
Social-emotional subscale ¹ , median (IQR)	85 (73-94)	60 (45-73)	63 (54-79)	< 0.001
Overall QOL				
Very poor	- (-)	- (-)	- (-)	< 0.001
Poor	4 (4)	6 (14)	2 (9)	
Fair	16 (15)	17 (40)	9 (41)	
Good	32 (29)	13 (30)	6 (27)	
Very good	44 (40)	6 (14)	5 (23)	
Outstanding	14 (13)	1 (2)	- (-)	
% less than good	20 (18)	23 (53)	11 (50)	< 0.001

¹The social-emotional subscale score was computed using five domains only, i.e., after excluding pain; ² χ^2 test, apart from using the Kruskal-Wallis test with actual subscale scores and with the ordinal scale for overall Quality of Life (QOL); ³The criteria used for determining if there was a significant problem can be found in previous work^[21]. IQR: Interquartile range.

Table 4 The most common concerns raised by patients on the Patients Concerns Inventory for each clinical group

No significant pain and no wish to discuss pain (<i>n</i> = 110)		Significant pain (<i>n</i> = 44)		No significant pain but wish to discuss pain (<i>n</i> = 23)	
Issue	%	Issue	%	Issue	%
Fear of the cancer coming back	26	Fear of the cancer coming back	57	Pain in head and neck	78
Dental health/teeth	21	Dental health / teeth	46	Fear of the cancer coming back	61
Chewing / Eating	21	Chewing / Eating	39	Shoulder	44
Salivation	16	Fatigue / tiredness	39	Fatigue / tiredness	39
Swallowing	15	Swallowing	39	Dental health / teeth	35
Mucous production	13	Pain in head and neck	32	Swallowing	35
Fatigue/tiredness	13	Mood	30	Chewing / Eating	30
Mouth opening	12	Energy levels	30	Mood	30
Breathing	11	Pain elsewhere	27	Mucous production	26
Sleeping	11	Appearance	27	Sleeping	26
Weight	11	Depression	25	Salivation	26
Taste	11	Sleeping	25	Energy levels	26
		Anxiety	25		

clinic (Group B), 76% (16/21) reported significant pain at second clinic, 65% (9/14) at third clinic and 50% (2/4) at fourth clinic. Those no longer having significant pain did not wish to discuss it at subsequent clinics. Also, of the 12 patients reporting significant pain in their third study clinic 67% (8) had also reported significant pain at their first and second clinics. Of those with no significant pain and not wishing to discuss it at the first study clinic (Group A) about three-quarters (78%, 79% and 83% respectively in successive clinics) remained in the same

group. There was greater variability noted in later clinics for those without significant pain but wanting to discuss pain at the first clinic (Group C).

Those in Group B and C had pain mentioned in about half of the clinic letters subsequent to the clinic (Table 6), in contrast to just 12% of clinic letters from patients in Group A. The rates of onward referral for pain were 11%, 8% and 0.8% of clinics respectively for groups B, C and A. Details from the clinic letters as to whom the patient was referred, the medications that were

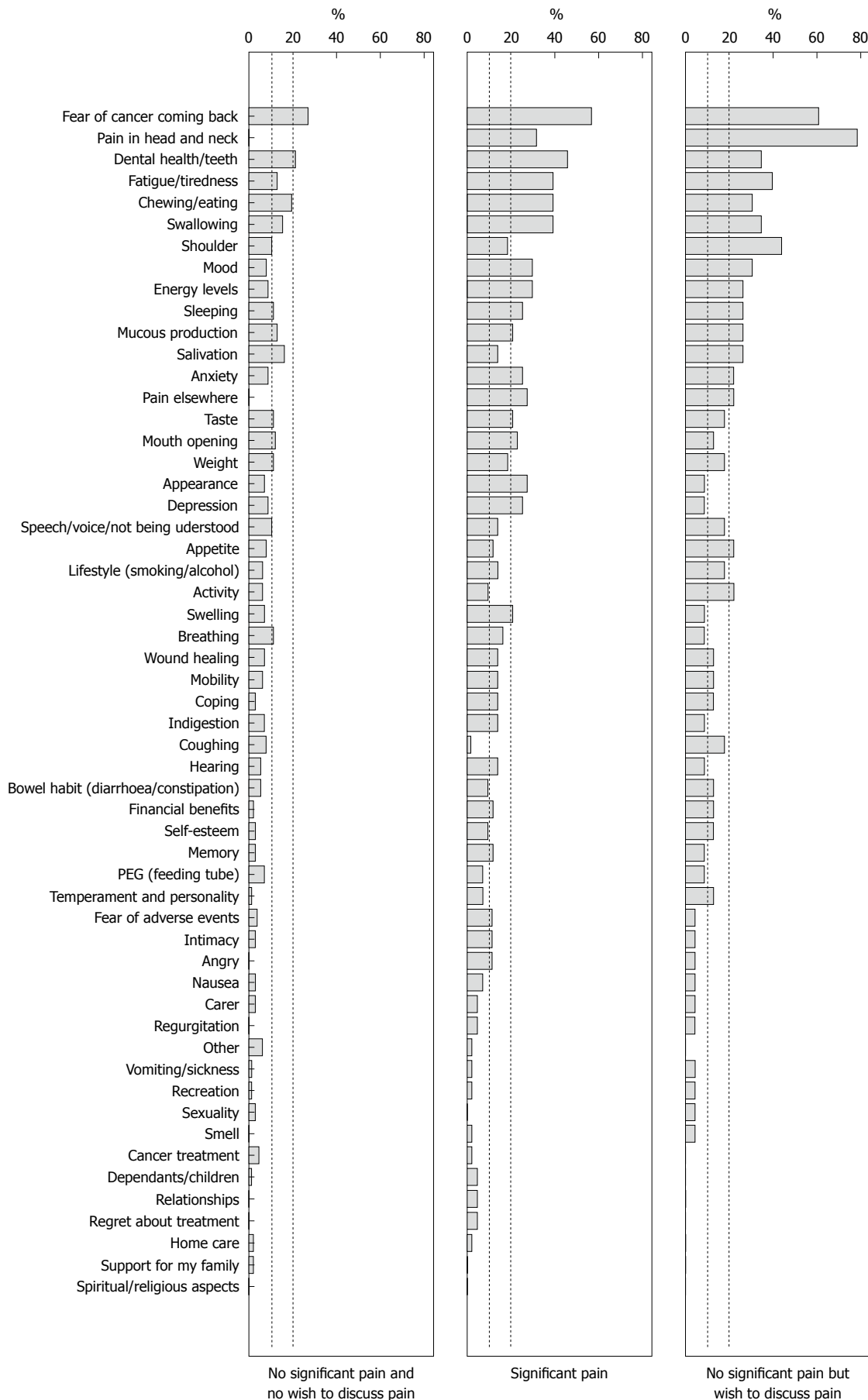
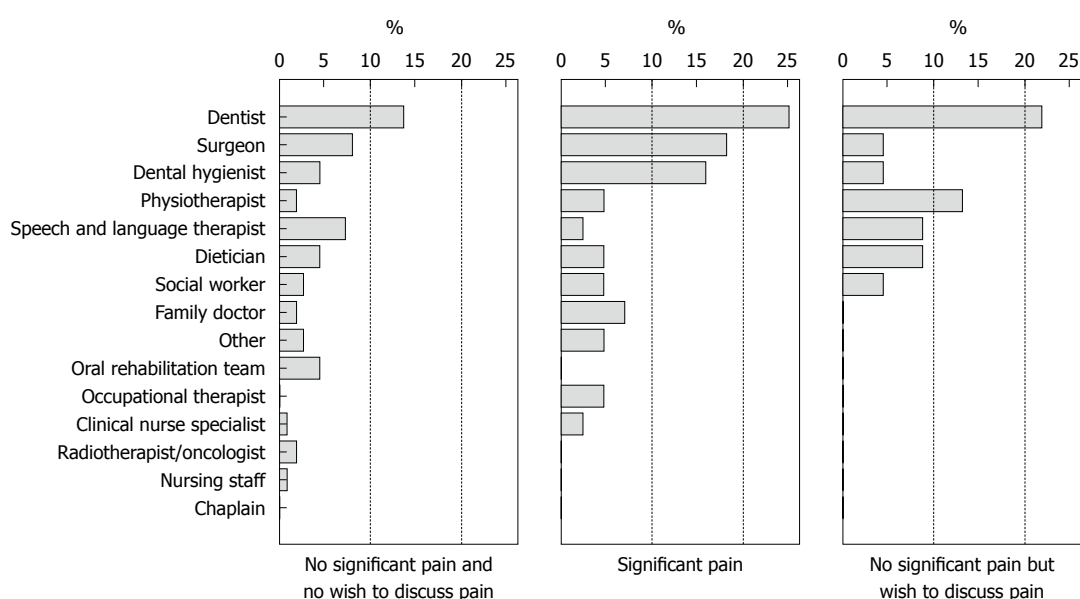


Figure 1 Percentage of Patients Concerns Inventory issues raised before consultation, by whether patients reported significant pain problems on the University of Washington Quality of Life questionnaire and/or wished to discuss pain. $n = 177$ at first study clinic.

Table 5 Longitudinal perspective

	First study clinic		
	No significant pain and no wish to discuss pain	Significant pain	No significant pain but wish to discuss pain
Second study clinic (112 patients)			
No significant pain and no wish to discuss pain	55	5	9
Significant pain	8	16	4
No significant pain but wish to discuss pain	7	-	8
Third study clinic (59 patients)			
No significant pain and no wish to discuss pain	31	5	3
Significant pain	3	9	-
No significant pain but wish to discuss pain	5	-	3
Fourth study clinic (30 patients)			
No significant pain and no wish to discuss pain	20	2	-
Significant pain	3	2	1
No significant pain but wish to discuss pain	1	-	1

**Figure 2** Percentage selecting members of staff to see or be referred on to at clinic, by whether patients report significant pain problems on the University of Washington Quality of Life questionnaire or wished to discuss pain. $n = 177$ at first study clinic.

mentioned and the nature and location of the pain are given in Table 6.

DISCUSSION

This work surveyed self-reported pain in a HNC cohort using the UW-QOL and PCI TST in a routine clinic setting. The main strength of this study lies in the description of self-reported pain in a disease-free, post-treatment group through exclusion of active, residual or recurrent disease because this subgroup may present with a slightly different management approach. The estimated prevalence of self-reported pain issues in this group was 38%, of which 25% had significant pain. Patient who self-report significant pain or others wanting to discuss pain were more likely to have problems in both physical and social-emotional functioning, report suboptimal overall QOL and raise more items other than pain for discussion

on the PCI. Those having treatment with radiotherapy/chemotherapy were more likely to report significant pain or wish to discuss pain. However, just over one-half of those reporting significant problems with pain did not wish to discuss this during their consultation.

There are several issues that may limit this study. Firstly, the sample size ($n = 177$) is relatively small and mainly of patients with oral cancer. A larger cohort could better elicit any other potential trends from the data. The database also lacks sufficient longitudinal data to comment confidently on the stability of pain and the successful management of those patients in significant pain. Following the cohort through future outpatient clinics would achieve this, but the problem of a small study sample would persist. Secondly, this study did not use any specialised self-reported pain questionnaire or clinical examination to qualify the pain experienced by the cohort. This may be relevant from a clinical management perspective.

Table 6 Mention of pain in clinic letters and onward referral

	No significant pain and no wish to discuss pain	Significant pain	No significant pain but wish to discuss pain
Number of clinics (number of patients)	256 (110)	85 (44)	55 (23)
Number of clinics with clinic letters found	240	79	51
Pain mentioned in clinic letter	12% (29/240) from 27 patients (26 patients once, 1 patient 3 times)	56% (44/79) from 29 patients (19 patients once, 7 patients twice, 1 patient three times, 2 patients four times)	47% (24/51) from 19 patients (14 patients once, 5 patients twice)
Onward referral for pain	0.8% (2/240)	11% (9/79) (1 patient once, 2 patients twice, 1 patient 4 times)	8% (4/51)
Who was patient referred to	Consultant gastroenterologist (1) Consultant restorative dentist (1)	Patient 1: first to consultant orthopaedic surgeon then three times to chronic pain team Patient 2: first to senior physiotherapist then to chronic pain management programme Patient 3: first to consultant orthopaedic surgeon then to palliative care Patient 4: to consultant in oral medicine	Senior physiotherapist (2) Consultant in oral medicine (1) Consultant in pain relief (1)
Pain medications mentioned in letter (often in combination)	Gabapentin (1), Oromorph (1), MST (1)	Aciclovir (1), Aspirin (1), Brufen (2), Codeine phosphate (1), Dicoferac (1), Fentanyl patch 25 (1), Gabapentin (7), Morphine patches (2), MST (1), Oromorph (6), Oxynorm (3), Oxycontin (2), Paracetamol (4), Solpadeine (1), Solpadol (1)	None mentioned
Pain as mentioned in letter (number of occasion)	Oral and teeth pain (7) Jaw pain (4) Facial pain (3) Shoulder pain (4) Neck pain (2) Ear pain (2) Stomach pain (2) Back pain (1) Chest wall pain (1)	Single site: Jaw (7); Neck (5); Teeth (1); Face (2); Oral/throat (5); Chest (1); Shoulder (2); Hip (1) Multiple sites: 10 Related to function: 1 Related to fear of cancer recurrence: 3 Related to fear of addition to analgesia: 1	Oral/throat pain (4) Generalised pain in treated area (2) Back pain (2) Shoulder pain (2) Neck (4) Shoulder and neck pain (2) Shoulder pain Jaw pain (1)

Finally, this study did not have a pre-diagnosis baseline of the pain experience, which has been shown to influence the post-treatment experience of pain^[4].

There is a wide range of published prevalence rates (6%-100%) for self-reported pain in HNC patients due to variation in the methodology employed^[2], namely, the time point of the HNC journey selected (e.g., prediagnosis or postdiagnosis; remission or recurrence/active disease), clinical setting surveyed (e.g., oncology outpatients or specialist pain clinics) and treatment received (e.g., unimodality or multimodality). The prevalence of self-reported pain in our cohort was 38% (54% of patients studied were within 24 mo from the completion of treatment). This is higher than that found by Chaplin and Morton^[4], who reported prevalence of 25% and 26% at 12 and 24 mo respectively. The reason for our higher prevalence is unclear although oral and oropharyngeal cancer accounted for only 29% of their sample, which also showed treatment preponderance for radiotherapy.

We found that the clinical factors associated with pain issues were age and primary treatment modality, not seen in the New Zealand cohort^[4]. Those aged 65 years and older reported less significant pain and fewer wished to discuss their pain compared to younger people. This may be due to the possibility that older adults experience lower levels of pain severity and interference from cancer-related pain compared with the younger age group^[34].

However, the contrary was found in the Taiwanese group, where the older group reported more pain and this was attributed to lower pain endurance ability^[6]. In our cohort, patients who received radiotherapy as their primary treatment reported greater levels of significant pain or wanted to discuss pain. Persistent pain after the completion of radiotherapy is commonly reported^[8]. Normal radiotoxicity can result in mucositis, xerostomia, brachial plexopathy and osteoradionecrosis of varying degree, which may cause orofacial pain. Pain secondary to oral mucositis is frequently reported during treatment and the radiation-mediated tissue changes are progressive, suggesting the role of neuropathic mechanisms^[8].

Our cohort was split into three groups to facilitate statistical analysis: A, B and C based on the presence of a significant pain problem and the expression of need to discuss the issue of perceived pain. Group A ($n = 110$) did not have significant pain and did not wish to discuss pain on the PCI. This group includes those with manageable levels of pain as well as those who are pain-free, all of whom perceive pain to be of no concern. Group B ($n = 44$) had significant pain and includes some (just over half) who did not wish to discuss this during consultation. This group may provide a challenge for clinicians because of the unresolved problem of symptom control, the association of pain with physical dysfunction, the increased likelihood of having problems in the social-

emotional areas and that so many of this subgroup do not wish to discuss this in clinic. Group C ($n = 23$) had no significant pain but still wanted to discuss pain in the consultation, indicating that this group may benefit from non-pharmacological interventions for their pain, especially as they were also associated with problems in social-emotional functioning.

Our study found that Groups B and C raised significantly more issues on the PCI than those in Group A (Table 4), where the median number of complaints of patients in Groups B, C and A was 7, 7 and 2, respectively. Interestingly (Tables 3 and 4), Group B and C also seem to struggle with mood, anxiety and depression, far more so than those in Group A. Other studies also report that depression and anxiety contributed to the pain quality ratings in post-treatment HNC patients^[6,16]. Fear of recurrence was a prevalent concern across all groups (Table 4) and this could represent the perception that pain precedes the return of cancer^[12]. Groups B and C had pain mentioned in almost half of their cohort's clinic letters compared to just 12% of clinic letters from Group A (Table 6). Despite this, only 11% of patients from Group B and 8% from Group C were referred onwards for further management of their pain. In Groups B and C, referrals made were to pain specialist professionals (5/12 referrals) and non-pain specialist professionals (7/12 referrals).

Based on the clinic letters, most pain locations were in the head, neck and shoulder region, which compares with another report^[8]. A much smaller proportion was reported at distant sites, including donor site morbidity. Both descriptors of nociceptive and neuropathic pain were used in the clinics letters. However, conclusions regarding the possible mechanisms of pain in this cohort cannot be derived from this list because we are unable to verify if these were the actual terms used by patients in clinic. Nevertheless, the list of medications described in clinic letters used for analgesia in Group B indicates that the range of medication on the WHO pain ladder^[15] have been used, including adjunctive drugs for significant pain.

This may support for a more prominent role for the specialist pain team in the multidisciplinary team management of these patients.

In conclusion, pain remains a significant problem for those with HNC and can arise for many different reasons. Increased levels of pain tend to follow treatment that involves radiotherapy. Those with significant pain and others wanting to discuss pain tend to have multiple other areas of concern, including worries over depression and anxiety. Effective pain management is crucial to ensure a good quality of life and the role of the pain team in HNC is to be evaluated. The PCI approach to help patients highlight issues of concern during routine clinic review is potentially a useful way to help screen oncology patients for pain-related symptoms. Further modular development of the PCI concept in breast cancer and other cancer sites will allow this type of adjunct to be incorporated more widely in oncology.

COMMENTS

Background

Pain is prevalent among head and neck cancer (HNC) survivors. This may be the result of cancer-related pain and also other non-cancer related causes. Its management is complex and challenging due to the multidimensional nature of pain, particularly among the post-treatment, disease-free survivors. Under-reporting of pain by these patients can have damaging impact on their overall quality of life, as it is a source of suffering, distress and anxiety. It can be difficult to identify those who "suffer pain in silence" as some patients may not feel able to vocalize this issue and/or others for many reasons. There is currently no holistic screening tool that can be used in routine clinical practice to help identify HNC patients with concerns, particularly pain.

Research frontiers

The Patients Concerns Inventory (PCI) is a holistic, patient-reported tool that enables patients to highlight items of concerns that they would like addressing during their outpatient visit. In addition, the PCI also allows patients to indicate professionals whom they would like access to. The PCI consists of a 57-item checklist that is administered along with the University of Washington Quality of Life (UW-QOL) using touch-screen computers prior to their consultation. The PCI promotes patient-centred consultations. By highlighting the PCI item "pain", a focused discussion on their pain experience ensues during consultation. The UW-QOL data provides additional data in understanding the severity of their pain. The PCI-UW-QOL tool can potentially empower patients to take a bigger role in their care through self-care, participation in decision-making and by seeking access to specialist expertise for their pain problem.

Innovations and breakthroughs

Previous work on pain in HNC are heterogeneous in design and population characteristics. This study focused on post-treatment, disease-free patients with oral and oropharyngeal cancer. Significant cancer-related pain is prevalent in this group, particularly those who were aged more than 65 years and had received radiotherapy. Patients who opted to discuss pain also indicated other issues of concern. This finding supports the notion of the multidimensional nature of pain. While onward referral to a specialist pain team may be beneficial, the other dimensions of the pain experience must be addressed. The PCI-UW-QOL package is a valuable tool that may routinely screen for significant pain in outpatient clinics.

Applications

The PCI is a holistic, multifunctional patient-reported tool. It can screen for patient concerns by providing a platform for expressing their needs. In addition, the PCI may be regarded as a communication tool to enhance patient-healthcare worker consultations/discussions. Although originally developed in HNC, the PCI concept may be applied to other cancers and also various non-cancer fields. Current developmental work is being carried out to apply the PCI in breast cancer, neuro-oncology, rheumatology and gastroenterology. In addition, expansion of the PCI into a web-based platform for health advice and direct access to healthcare services are being explored.

Peer review

This is a well-written paper dealing with an important issue in the care of HNC patients. The study design is sound and the analysis is straightforward and clear.

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CD26: A prognostic marker of other systemic malignancies besides colo-rectal carcinomas

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Abstract

I read with great interest the recent article by Cordero *et al* in a recent issue of your esteemed journal. Interestingly, the past few years have seen the emergence of CD26 as an important diagnostic and prognostic marker for a number of systemic malignancies besides colo-rectal carcinomas. For instance, serum CD26 levels are an important emerging marker of B-cell chronic lymphocytic leukemia (B-CLL). In fact, Molica *et al* have recently reported shorter time to first treatment in B-CLL which exhibit higher serum CD26 levels and simultaneously demonstrate absence of mutation in *IgV (H)*. Similarly, CD26 serves as a marker of poor prognosis in T cell lymphomas. Simultaneously, a poor response to 2'-deoxycoformycin is seen T cell lymphomas expressing CD26. Similarly, breast carcinomas exhibit decreased CD26 mean fluorescence intensity and a decreased percentage of CD26 positive lymphocytes in comparison to benign breast tumors and healthy individuals.

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Key words: CD26; Cancer; Carcinogenesis; Colon cancer; Marker

Peer reviewers: Jian-Hua Luo, MD, PhD, 3550 Terrace Street, Scaife S-760, Associate Professor of Pathology, Director of Gene

TO THE EDITOR

I read with great interest the recent article by Cordero *et al*^[1] in a recent issue of your esteemed journal. Interestingly, the past few years have seen the emergence of CD26 as an important diagnostic and prognostic marker for a number of systemic malignancies besides colo-rectal carcinomas.

For instance, serum CD26 levels are an important emerging marker of B-cell chronic lymphocytic leukemia (B-CLL)^[2]. In fact, Molica *et al*^[3] have recently reported a shorter time to first treatment in B-CLL which exhibit higher serum CD26 levels and simultaneously demonstrate absence of mutation in *IgV (H)*. Similarly, CD26 serves as a marker of poor prognosis in T cell lymphomas. Simultaneously, a poor response to 2-deoxycoformycin is seen T cell lymphomas expressing CD26^[4]. Similarly, breast carcinomas exhibit decreased CD26 mean fluorescence intensity and a decreased percentage of CD26 positive lymphocytes in comparison to benign breast tumors and healthy individuals^[5].

CD26 is also associated with treatment outcomes. For instance, enhanced sensitivity to paclitaxel is seen in ovarian carcinomas with higher Dipeptidyl peptidase IV (DPPIV/CD26) levels^[6]. Similarly, increased chance of progression to follicular carcinoma is seen in thyroid fol-

licular adenomas with exhibit concurrent PTEN negativity and CD26 positivity^[7]. Similarly, increased expression of CD26 is seen in wound induced skin tumors and this serves as a marker of malignancy^[8]. The anti-diabetic drug stialipin blocks CD26 and thereby reduces proliferation in these skin tumors.

Clearly CD26 is a significant marker of different malignancies. Hopefully, the coming few years will see increased use of CD26 for diagnostic and prognostic purposes in oncology.

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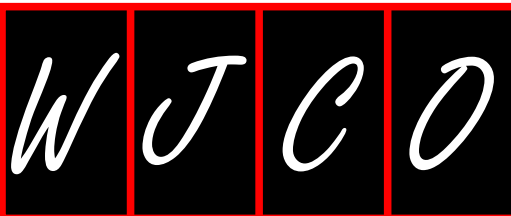
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Events Calendar 2012

January 16-17, 2012
Biomarkers Summit Egypt
London, United Kingdom

January 25-26, 2012
Multi-Disciplinary Approaches to
Cancer Therapy
Dubai, United Arab Emirates

January 26-27, 2012
3rd National Conference: Renal and
Bladder Cancer 2012
London, United Kingdom

January 30-31, 2012
2nd Annual Clinical Trials in
Oncology
Rome, Italy

February 2-3, 2012
Stem Cells 2012 Conference and
Exhibition
San Diego, CA, United States

February 6-8, 2012
Mahidol International Conference
on Infections and Cancers 2012
Bangkok, Thailand

February 12-17, 2012
Keystone Symposia: Cancer and
Metabolism
Alberta, Canada

February 22-25, 2012
Excellence in Oncology
Istanbul, Turkey

March 8-10, 2012
10th International Congress on
Targeted Anticancer Therapies
Amsterdam, Netherlands

March 9-10, 2012
13th European Congress:
Perspectives in Lung Cancer
Amsterdam, Netherlands

March 14-16, 2012
BTOC-11 Biological Therapy of
Cancer
Munich, Germany

March 15-17, 2012
3rd Conference on Therapeutic
Resistance in Cancer
Quebec, Canada

March 29-30, 2012
Modern methods of diagnosis and
treatment of malignant tumors
Kiev, Ukraine

April 13-15, 2012
Asian Oncology Summit 2012
Singapore, Singapore

April 20-21, 2012
Diagnosis and treatment of
advanced forms of prostate cancer,
bladder cancer and kidney cancer
Kiev, Ukraine

April 20-22, 2012
The 9th Meeting of Asian Society for
Neuro-Oncology
Taipei, Taiwan

April 26-28, 2012
3rd International Video
Workshop on Radical Surgery in
Gynaecological Oncology
Prague, Czech Republic

April 28, 2012
Issues in Pediatric Oncology
Kiev, Ukraine

May 5-6, 2012
Radiation Research Methods as A
Diagnostic and Therapeutic Support
in Oncology
Kiev, Ukraine

May 17-18, 2012
Eurasian forum on the management
of patients with tumors of the
gastrointestinal tract
Uman, Ukraine

June 16-17, 2012
Issues of Neurosurgery, vascular
neurosurgery, neurooncology, spinal
surgery and spinal cord
Kiev, Ukraine

July 7-10, 2012
22nd Biennial Congress of the
European Association for Cancer
Research
Barcelona, Spain

July 21-28, 2012
Cancer In Women
Hawaii, HI, United States

July 25-27, 2012
5th Latin American Conference on
Lung Cancer
Rio de Janeiro, Brazil

August 27-30, 2012
UICC World Cancer Congress 2012
Québec, Canada

September 6-8, 2012
The 8th International Jordanian
Oncology Society Conference
Amman, Jordan

September 27-28, 2012
Current issues of diagnosis and

treatment of oncogynecology
diseases
Ivano Frankivsk, Ukraine

September 27-29, 2012
European Conference of Oncology
Pharmacy
Budapest, Hungary

October 5-8, 2012
44th Congress of the International
Society of Paediatric Oncology
London, United Kingdom

October 13-16, 2012
14th Biennial Meeting of the
International Gynecologic Cancer
Society
Vancouver, Canada

October 19, 2012
Modern aspects of diagnosis and
treatment of breast cancer
Kiev, Ukraine

October 23-26, 2012
Sydney International Breast Cancer
Congress 2012
Sydney, Australia

October 27-28, 2012
Optimization methods for radiation
diagnosis in oncology
Odessa, Ukraine

November 6-9, 2012
24th EORTC-NCI-AACR
Symposium on "Molecular Targets
and Cancer Therapeutics"
Dublin, Ireland

November 16-17, 2012
17th Annual Perspectives in Thoracic
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New York, NY, United States



GENERAL INFORMATION

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Statistical review is performed after peer review. We invite an expert in Biomedical Statistics to evaluate the statistical method used in the paper, including *t*-test (group or paired comparisons), chi-squared test, Redit, probit, logit, regression (linear, curvilinear, or stepwise), correlation, analysis of variance, analysis of covariance, *etc.* The reviewing points include: (1) Statistical methods should be described when they are used to verify the results; (2) Whether the statistical techniques are suitable or correct; (3) Only homogeneous data can be averaged. Standard deviations are preferred to standard errors. Give the number of observations and subjects (*n*). Losses in observations, such as drop-outs from the study should be reported; (4) Values such as ED50, LD50, IC50 should have their 95% confidence limits calculated and compared by weighted probit analysis (Bliss and Finney); and (5) The word 'significantly' should be replaced by its synonyms (if it indicates extent) or the *P* value (if it indicates statistical significance).

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Author contributions: The format of this section should be: Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; and Wang CL, Liang L and Fu JF wrote the paper.

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- 3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

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- 4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462

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- 5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

- 6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

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- 7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

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- 8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

- 9 Outreach: Bringing HIV-positive individuals into care. *HRS-A Careaction* 2002; 1-6 [PMID: 12154804]

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- 10 **Sherlock S**, Dooley J. Diseases of the liver and biliary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

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- 11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

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- 12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wiczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

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- 13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

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- 14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

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- 15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: <http://www.cdc.gov/ncidod/eid/index.htm>

Patent (list all authors)

- 16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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Write as mean \pm SD or mean \pm SE.

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