



# Patients with head and neck cancer may need more intensive pain management to maintain daily functioning: a multi-center study

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## Abstract

**Purpose** The purpose of this study is to investigate the prevalence of pain, pain management, and impact of recent pain on daily functioning in patients with head and neck cancer (HNC) and patients with other cancers.

**Methods** This multi-center survey was conducted by using Brief Pain Inventory questionnaire to evaluate pain status and its impact on daily functioning.

**Results** A total of 3289 patients were analyzed including 708 HNC patients and 2581 patients with other cancers. The overall pain prevalence was 69.17%. A higher percentage of HNC patients had recent pain (60.59 vs. 44.01%,  $P < 0.001$ ), required pain management (86.29 vs. 72.03%,  $P < 0.001$ ), and used any analgesics (53.81 vs. 34.52%,  $P < 0.001$ ). HNC patients with pain management had a higher prevalence of recent pain (85.83 vs. 81.14%,  $P = 0.044$ ) and a slightly lower satisfaction rate (74.00 vs. 79.70%,  $P = 0.070$ ). Regarding the impact of pain on daily functioning, HNC patients had a lower mean interference score for general activity such as walking, normal work, sleep, and life enjoyment.

**Conclusions** The HNC patients may need more intensive pain management to achieve optimal pain control and maintain daily functioning.

**Keywords** Head and neck cancer · Prevalence of pain · Pain management · Daily functioning · Multi-center study

## Introduction

Pain has been a major healthcare issue for cancer patients for several decades. Despite advances in cancer treatment and supportive care, many cancer patients still experience pain. Patients experience diverse types of pain caused by cancer or therapeutic intervention during the disease course. In one survey, among patients who received curative cancer treatment, 33% of them experienced pain [5]. In addition, a meta-analysis showed that up to 64% of cancer patients with advanced disease status experienced pain [14]. Importantly,

high prevalence of pain in cancer patients is significantly related to poorer quality of life and overall survival [27].

Many therapeutic strategies and medications for pain management are based on the World Health Organization (WHO) recommendations, which provide a “3-step analgesic ladder” for cancer pain management in adult cancer patients [21]. However, many cancer patients still have suboptimal pain management. One of the key factors is insufficient treatment intensity. Previous studies indicated that about half of patients with pain were undertreated [13, 18]. To effectively manage pain in cancer patients, it is critical for healthcare professionals to have comprehensive knowledge of every available analgesic, including the effectiveness and safety profiles, and the management of treatment-related side effects. Moreover, healthcare professionals should understand the diverse clinical manifestations of each cancer type to be able to tailor pain management and its education for each cancer patient [39].

Head and neck cancer (HNC) is a heterogeneous group of malignant tumors that develop from the nasal cavity, oral cavity, oropharynx, hypopharynx, and larynx. It is ranked as the

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sixth most common cancer in Taiwan [8]. A majority of new cases of HNC were diagnosed as localized or locally advanced disease [4, 36]. In addition, the percentage of distal metastasis in HNC patients is relatively low in comparison with patients with other malignancies [17, 20, 25, 30]. Treatment for HNC is primarily localized, involving surgical resection, radiotherapy, or concurrent chemoradiation. Therefore, HNC patients may face disease-related and treatment-related complications, making the nature of pain multifaceted and complex in mechanism [6, 10]. For example, the local destruction of soft tissue and bone from invasion of cancer or treatment such as tumor resection would result in somatic pain. Invasion of tumor cells to nerve or local inflammatory reaction caused by treatment are associated with development of neuropathic pain [19]. During systemic chemotherapy and regional radiotherapy, painful oral mucositis due to damage to oral mucosa is a common complication [16, 32]. Regarding incidence of pain in HNC patients, previous studies revealed that 40 to 84% of patients had pain at diagnosis and about 40% of them still suffered from pain after treatment [7, 22, 26, 33]. Hence, there is still an unmet need for ideal pain management in HNC patients since quality of life or daily functioning can be adversely affected by pain at diagnosis or during or after treatment.

We conducted this multi-institute study to explore the prevalence of pain, management of pain, and the impact of pain on daily functioning in patients with HNC and other cancers. The study also examined whether HNC patients had unique pain issues and aimed to provide additional information to physicians to tailor a pain control plan when treating pain for this group of patients.

## Participants and methods

### Patient population and study design

This multi-center survey for pain management was conducted at 16 hospitals across Taiwan from November 2013 to June 2014. Patients with cancer aged 20 years and older were enrolled after they provided written informed consent. Exclusion criteria included unconscious patients and patients with known or suspected psychotic disease or intellectual disability. All participants were divided into two groups: patients with HNC and those with other cancers.

This non-interventional survey was conducted by completing a paper questionnaire to collect information on patient demographics, current disease status, pain characteristics, and management of pain. The questions were answered by patients and physicians (medical oncologists) separately. For the patients, they completed the survey in clinics with the assistance of study coordinators. The patients answered questions related to personal information, recent or current pain

status (pain intensity), the impact degree of pain on their daily functioning, and the rating of satisfaction of current pain management. At the same time, the physicians answered questions related to the diagnosis for their patients, their current disease status, the causes of pain, and medication for pain management. The patients and physicians answered their respective questions separately without the knowledge of the other's responses. For the purpose of gathering clinical data, the associated medical record of each patient was also reviewed. Disease status was categorized as no evidence of disease, stable/static disease, partial response, progression, and not yet assessed. The disease status of "not yet assessed" indicated the patient were under anti-cancer treatment when they answered the questions.

### Investigation of pain severity and impact on daily functioning

The questionnaire for this investigation were based on the Brief Pain Inventory (BPI) (Short Form) [11], which has been recommended as a tool for cancer pain assessment by the Expert Working Group of the European Association for Palliative Care. For this study, patients were asked to rate their current pain intensity at its worst, least, and average on a numeric scale ranging from 0 to 10, with 0 representing "no pain" and 10 representing "pain as bad as you can imagine." A cut-off value of 4 was used for this analysis, with scores 0 to 3 representing none to mild pain and 4 to 10 representing moderate to severe pain [41]. For evaluation of recent pain, patients were asked to rate their pain intensity on a similar numeric scale if they experienced any pain in the past 7 days.

To evaluate the impact of pain on daily functioning, a similar scale was used, with a score of 0 representing "not interfered by pain at all" and 10 representing "interfered by pain completely." Patients rated the extent of pain interference with seven associated domains, including physical function (general activity, walking, and normal work) and psychological function (mood, relationships, life enjoyment, and sleep). A cut-off value of 4 was used for this analysis, with 0 to 3 representing none to mild interference and 4 to 10 representing moderate to severe interference.

### Statistical analysis

The data analysis included all eligible data. Descriptive statistics were used to summarize the results. All continuous variables including the number, mean, standard deviation, minimum, median, and maximum were presented. Categorical variables included the number and percentages of subjects in each class. The independent two-sample *t* test was used to compare continuous variables, and the  $\chi^2$  test was used to compare the frequencies of each categorical variable. The statistical

analyses in the present study were based on two-sided hypothesis tests with a significance level of  $P$  value  $< 0.05$ .

To assess the association between pain intensity and the score of pain interference with daily functioning, the scatter plots were presented by using the Loess regression curve [37, 40].

## Ethical approval

This study was conducted in accordance with the Declaration of Helsinki. The protocol, amendments, informed consent form, and all other forms of patient information related to the study were reviewed and approved by the independent ethics committee or institutional review board for each participating site. All enrolled patients provided written informed consent before participation.

## Results

### Characteristics of participants

Of the 3289 patients enrolled in this study, 708 had HNC and 2581 had other cancers (detailed subtypes and patient numbers in Supplemental Table S1). A higher percentage of patients with HNC lived in central and southern Taiwan compared to those with other cancers. Additionally, HNC patients were predominantly male and younger than those with other cancers. Regarding sites of metastasis, HNC patients had a significantly higher percentage of regional lymph node invasion, but a significantly lower percentage of distant metastases. Detailed demographic data are shown in Table 1.

### Prevalence of pain and pain management

Pain was documented by physicians in 586 patients in HNC group and 1689 patients in other cancer group (82.76 vs. 65.44%, respectively), with an overall prevalence of 69.17%. HNC patients had a higher percentage of cancer-related (50.42 vs. 39.13%,  $P < 0.001$ ) or cancer treatment-related pain (23.45 vs. 9.1%,  $P < 0.001$ ) but a lower percentage of non-cancer-related pain (11.72 vs. 17.59%,  $P < 0.001$ ) (Table 2). A higher percentage of patients with HNC reported the need for pain management during their disease course (86.29 vs. 72.03%,  $P < 0.001$ ). With respect to pain management, a higher percentage of HNC patients used any analgesic (oral or non-oral) (53.81 vs. 34.52%,  $P < 0.001$ ) but a lower percentage used non-pharmacological adjuvant therapy (6.36 vs. 14.41%,  $P < 0.001$ ). In terms of the WHO stratification of medications for pain management, a higher percentage of HNC patients used non-opioid, weak opioid, and strong opioid

analgesics (Table 2). There was no difference in the satisfaction rate (very satisfied and satisfied) between patients with HNC and those with other cancers (80.79 vs. 84.66%,  $P = 0.139$ ).

### Recent pain in patients with cancer

A total of 1565 patients, including 429 HNC patients and 1136 patients with other cancers, experienced any pain (score of 1 or greater on a 0–10 scale) in the past 7 days. A higher percentage of HNC patients experienced any pain in the past 7 days (60.59 vs. 44.01%,  $P < 0.001$ ) (Table 2). Among the 1272 patients who were currently receiving any pain management (381 with HNC and 891 with other cancers), 1050 patients, including 327 HNC patients and 723 patients with other cancers, experienced recent pain (85.83 vs. 81.14%,  $P = 0.044$ ). In analyzing the pain management of these 1050 patients, a higher percentage of HNC patients tended to take any oral analgesics ( $P = 0.090$ ), and a significantly higher percentage took non-opioid analgesics ( $P < 0.001$ ) (Supplemental Table S2).

As mentioned previously, the 1050 patients were further categorized based on their pain status; patients with HNC had a higher mean pain score when they experienced least pain and current pain. In contrast, HNC patients had a lower mean pain score when they felt worse pain (Table 3). Additionally, patients with HNC had a slightly lower satisfaction rate than those with other cancers (74.00 vs. 79.70%,  $P = 0.070$ ).

### Impact of recent pain on daily functioning

To investigate the impact of recent pain on daily functioning, we analyzed patients undergoing any pain management and who experienced any pain in the past 7 days. The pain interference score correlated with disease status. Lower interference scores were noted when the disease was responsive to treatment (partial response, stable disease, or disease free), and higher scores were noted when the disease progressed. Compared to patients with other cancers, those with HNC had lower interference scores on physical function when the disease was stable/static or they had partial response to treatment (Table 4).

In terms of impact of recent pain on daily functioning, the results revealed that a higher pain intensity score was associated with greater interference on physical and psychological function (Fig. 1). The degree of interference was then compared between HNC patients to those with other cancers, and patients with HNC were found to have lower mean interference scores overall ( $3.68 \pm 2.49$  vs.  $4.18 \pm 2.62$ ,  $P = 0.003$ ) and in physical function ( $3.38 \pm 2.67$  vs.  $4.19 \pm 2.89$ ,  $P < 0.001$ ). When analyzed for impact of pain on the seven associated domains, HNC patients had lower mean interference

**Table 1** General information of the study population

	All enrolled patients ( <i>n</i> = 3289)		<i>P</i> value
	HNC patients ( <i>n</i> = 708)	Patients with other cancers ( <i>n</i> = 2581)	
Residential area ( <i>n</i> , %)			
Northern Taiwan	240 (33.9%)	1161 (44.98%)	< 0.001
Central Taiwan	174 (24.58%)	448 (17.36%)	
Southern Taiwan	294 (41.53%)	972 (37.66%)	
Gender ( <i>n</i> , %)			< 0.001
Male	613 (86.58%)	1278 (49.52%)	
Female	95 (13.42%)	1303 (50.48%)	
Age (years, mean ± SD)	53.7 ± 10.02	58.02 ± 12.81	< 0.001
Subgroups of age, years ( <i>n</i> , %)			
≤ 40	77 (10.88%)	249 (9.65%)	< 0.001
41–50	186 (26.27%)	411 (15.92%)	
51–60	275 (38.84%)	777 (30.1%)	
61–70	134 (18.93%)	709 (27.47%)	
≥ 71	36 (5.08%)	435 (16.85%)	
Disease status ( <i>n</i> , %)			< 0.001
No evidence of disease	129 (18.22%)	553 (21.42%)	
Stable/static	195 (27.54%)	865 (33.51%)	
Partial response	134 (18.93%)	409 (15.85%)	
Progression	92 (12.99%)	468 (18.13%)	
Not yet assessed	158 (22.32%)	286 (11.08%)	
Sites of metastasis ( <i>n</i> , %)			
Any sites	258 (36.44%)	1356 (52.54%)	< 0.001
Lymph node	173 (24.44%)	451 (17.47%)	< 0.001
Lung	39 (5.51%)	340 (13.17%)	< 0.001
Liver	19 (2.68%)	380 (14.72%)	< 0.001
Bone	29 (4.1%)	378 (14.65%)	< 0.001
Soft tissue	14 (1.98%)	81 (3.14%)	0.1020
Brain	2 (0.28%)	85 (3.29%)	< 0.001
Others	22 (3.11%)	261 (10.11%)	< 0.001

HNC head and neck cancer, SD standard deviation

scores for general activity, walking, normal work sleep, and life enjoyment (Table 5).

## Discussion

In this study, we analyzed the prevalence of pain, pain management, and impact of recent pain on daily functioning in patients with HNC and those with other cancers. HNC patients had a significantly higher prevalence of pain including cancer pain and treatment-related pain documented by physicians. Patients with HNC also had a higher demand for pain management. These findings revealed high prevalence rate of pain and reflects the complex nature of pain in HNC patients, suggesting the necessity for a more intensive pain management.

Our questionnaire was answered by both cancer patients and physicians, and we found that a difference may exist in their perceptions of pain severity, as observed in previous studies [28, 35]. Indirect comparison of pain documented by physicians with the need for pain management answered in the questionnaire by patients showed the percentage of former was slightly lower than later. Although pain is a subjective feeling, not all pain occurrences were recorded by physicians. A possible explanation for this finding is that pain in some patients is underestimated or under-treated. Another explanation is that some cancer patients may express other cancer-related symptoms or discomfort as pain to physicians. These finding indicates that careful evaluation of cancer symptoms and good communication between patients and their physicians are important.

**Table 2** Pain status and pain management of the study population

	All enrolled patients (n = 3289)		P value
	HNC patients (n = 708)	Patients with other cancers (n = 2581)	
<b>Pain status</b>			
Pain documented by physician (n, %)	586 (82.76%)	1689 (65.44%)	< 0.001
Cancer-related pain (n, %)	357 (50.42%)	1010 (39.13%)	< 0.001
Non-cancer-related pain (n, %)	83 (11.72%)	454 (17.59%)	< 0.001
Cancer treatment-related pain (n, %)	166 (23.45%)	235 (9.10%)	< 0.001
**Need pain treatment (n, %)	611 (86.29%)	1859 (72.03%)	< 0.001
**Any pain in the past 7 days (n, %)	429 (60.59%)	1136 (44.01%)	< 0.001
<b>Pain management</b>			
Currently taking any analgesics (n, %)	381 (53.81%)	891 (34.52%)	< 0.001
#Currently taking any oral analgesics (n, %)	369 (52.19%)	870 (33.71%)	< 0.001
Currently using non-oral analgesics (n, %)	77 (10.88%)	153 (5.93%)	< 0.001
Currently using non-opioid analgesics (n, %)	210 (29.66%)	404 (15.65%)	< 0.001
Currently using weak opioid analgesics (n, %)	181 (25.56%)	405 (15.69%)	< 0.001
Currently using strong opioid analgesics (n, %)	132 (18.64%)	275 (10.65%)	< 0.001
**#Any other non-pharmacological therapy (n, %)	45 (6.36%)	372 (14.41%)	< 0.001

The non-oral analgesics included transdermal analgesics. The non-pharmacological adjuvant therapy included massage, acupuncture, exercise, rehabilitation, Qigong herbal medicine, and aromatherapy

\* With at least two causes of pain

\*\* These questions were answered by patients

# One patient with head and neck cancer did not answer these two questions

This study also showed that a higher percentage of HNC patients received pain management, including oral or non-oral analgesics and non-opioid, weak opioid, or strong opioid analgesics. The high prevalence of pain and demand for pain management may be due to a high pain sensitivity caused by the many anatomical structures in a small space [10]. In addition, patients with HNC may have pain caused by direct tumor

effect or anti-cancer treatment-related pain, such as radiotherapy or surgery.

The prevalence of recent pain and its impact on daily functioning were investigated in patients receiving pain management. The results showed that more than 80% of patients with pain management still experienced any pain in the past 7 days. Of these, about 55% had average pain scores between 4 and

**Table 3** Pain severity scores at different pain intensities in patients with pain management who experienced any pain (score of 1 or greater on a 0–10 scale) in the past 7 days

	HNC patients (n = 327)	Patients with other cancers (n = 723)	P value
Worst pain intensity (mean ± SD)	5.48 ± 2.43	5.81 ± 2.44	0.042
< 4 (n, %)	74 (22.63%)	133 (18.40%)	0.110
≥ 4–10 (n, %)	253 (77.37%)	590 (81.6%)	
Least pain intensity (mean ± SD)	2.59 ± 1.98	2.20 ± 1.96	0.003
< 4 (n, %)	229 (70.03%)	543 (75.1%)	0.084
≥ 4–10 (n, %)	98 (29.97%)	180 (24.9%)	
Average pain intensity (mean ± SD)	3.93 ± 1.95	3.85 ± 1.99	0.557
< 4 (n, %)	147 (44.95%)	326 (45.09%)	0.967
≥ 4–10 (n, %)	180 (55.05%)	397 (54.91%)	
Current pain intensity (mean ± SD)	3.29 ± 2.38	2.98 ± 2.39	0.050
< 4 (n, %)	189 (57.8%)	443 (61.27%)	0.287
≥ 4–10 (n, %)	138 (42.2%)	280 (38.73%)	

SD standard deviation

**Table 4** Impact of pain on physical and psychological functions stratified by disease status in patients with pain management who experienced any pain (score of 1 or greater on a 0–10 scale) in the past 7 days

Disease status and interference scores (mean ± SD)	Physical interference		<i>P</i> value	Psychological interference		<i>P</i> value
	HNC	Other cancers		HNC	Other cancers	
No evidence of disease	3.85 ± 2.63	3.33 ± 2.7	0.552	3.67 ± 2.22	3.85 ± 2.65	0.829
Stable/static	3.12 ± 2.42	3.81 ± 2.62	0.025	3.57 ± 2.38	3.56 ± 2.42	0.959
Partial response	3.12 ± 2.86	3.98 ± 2.96	0.038	3.9 ± 2.79	4.24 ± 2.77	0.380
Progression	4.57 ± 2.63	4.83 ± 3.02	0.539	4.91 ± 2.48	4.79 ± 2.79	0.768
Not yet assessed	2.93 ± 2.55	4.02 ± 2.86	0.015	3.55 ± 2.53	4.07 ± 2.46	0.200

The case numbers in different disease status:

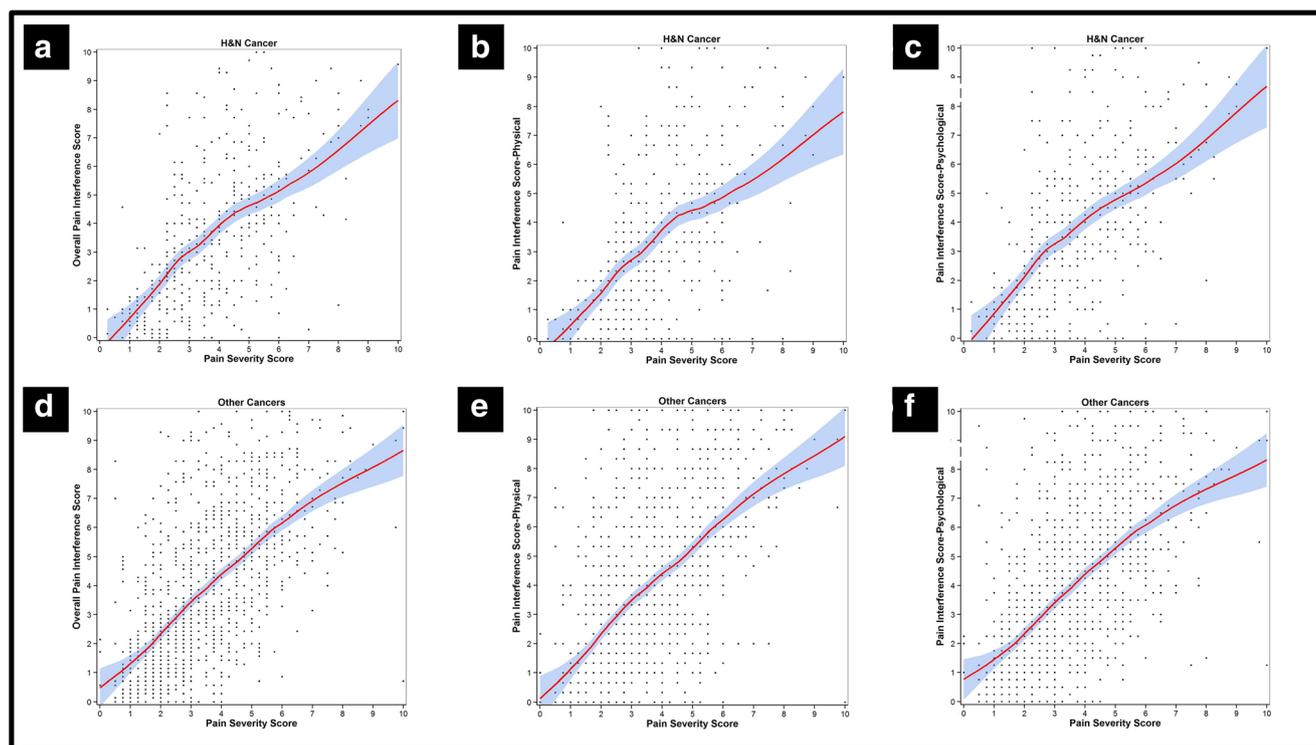
1. Head and neck cancer ( $n = 327$ ): no evidence of disease ( $n = 13$ ), stable/static ( $n = 97$ ), partial response ( $n = 83$ ), progression ( $n = 62$ ), not yet assessed ( $n = 72$ )

2. Patients with other cancers ( $n = 723$ ): no evidence of disease ( $n = 40$ ), stable/static ( $n = 227$ ), partial response ( $n = 133$ ), progression ( $n = 247$ ), not yet assessed ( $n = 76$ )

10, in the range of moderate to severe pain (Table 4). This finding suggests that some patients do not achieve sufficient pain control. Furthermore, we found that the rate of satisfaction in patients with HNC was slightly lower than patients with other cancers. Since treatment adequacy was associated with patient satisfaction, these findings suggest some patients with HNC may not have received adequate pain assessment or management [1, 2].

Regarding the impact of recent pain on daily functioning, about 40 to 50% of this subgroup of participants had overall scores of moderate to severe pain interference (Table 5).

Patients with HNC had similar or even lower interference scores than those with other cancers for the seven domains of daily functioning. A possible explanation is that HNC patients are younger and are better to tolerate pain than are patients with other cancers. Moreover, patients with HNC tend to have localized lesions than those with other cancers. With less distant metastatic lesions, the cancer pain is mainly confined to its primary site or nearby organs. With similar or less interference but slightly lower satisfaction compared to patients with other cancers, those with HNC may need more intensive pain control to maintain daily functioning.



**Fig. 1** The severity of pain and its impact on daily functioning. Panels (a), (b), and (c) show the association between pain severity score and interference score on overall, physical, and psychological function, respectively, in patients with head and neck cancer. Panels (d), (e), and

(f) show the association between pain severity score and interference score on overall, physical, and psychological function, respectively, in patients with other cancers. Red line represents fitted LOESS curve; light blue area represents 1 standard deviation. H&N, head and neck

**Table 5** Impact of pain on daily functioning in patients with pain control who experienced any pain (score of 1 or greater on a 0–10 scale) in the past 7 days

	Patients with any pain management who experienced pain in the past 7 days ( <i>n</i> = 1050)		<i>P</i> value
	HNC patients ( <i>n</i> = 327)	Patients with other cancers ( <i>n</i> = 723)	
Physical function (mean ± SD)	3.38 ± 2.67	4.19 ± 2.89	< 0.001
< 4 ( <i>n</i> , %)	203 (62.08%)	355 (49.1%)	< 0.001
≥ 4–10 ( <i>n</i> , %)	124 (37.92%)	368 (50.9%)	
General activity (mean ± SD)	3.6 ± 2.83	4.13 ± 2.98	0.007
< 4 ( <i>n</i> , %)	174 (53.21%)	331 (45.78%)	0.026
≥ 4–10 ( <i>n</i> , %)	153 (46.79%)	392 (54.22%)	
Walking (mean ± SD)	2.8 ± 2.97	4.04 ± 3.17	< 0.001
< 4 ( <i>n</i> , %)	213 (65.14%)	339 (46.95%)	< 0.001
≥ 4–10 ( <i>n</i> , %)	114 (34.86%)	383 (53.05%)	
Normal work (mean ± SD)	3.74 ± 3.36	4.39 ± 3.5	0.005
< 4 ( <i>n</i> , %)	181 (55.35%)	334 (46.2%)	0.006
≥ 4–10 ( <i>n</i> , %)	146 (44.65%)	389 (53.8%)	
Psychological function	3.91 ± 2.57	4.18 ± 2.68	0.127
< 4 ( <i>n</i> , %)	174 (53.21%)	367 (50.76%)	0.462
≥ 4–10 ( <i>n</i> , %)	153 (46.79%)	356 (49.24%)	
Mood (mean ± SD)	3.98 ± 2.71	4.27 ± 2.99	0.116
< 4 ( <i>n</i> , %)	155 (47.4%)	318 (43.98%)	0.303
≥ 4–10 ( <i>n</i> , %)	172 (52.6%)	405 (56.02%)	
Relations with people (mean ± SD)	3.34 ± 2.95	3.23 ± 3.22	0.583
< 4 ( <i>n</i> , %)	189 (57.8%)	421 (58.23%)	0.896
≥ 4–10 ( <i>n</i> , %)	138 (42.2%)	302 (41.77%)	
Sleep (mean ± SD)	4.38 ± 3.15	4.81 ± 3.15	0.040
< 4 ( <i>n</i> , %)	144 (44.04%)	286 (39.56%)	0.172
≥ 4–10 ( <i>n</i> , %)	183 (55.96%)	437 (60.44%)	
Life enjoyment (mean ± SD)	3.93 ± 3.15	4.39 ± 3.36	0.032
< 4 ( <i>n</i> , %)	159 (48.62%)	320 (44.26%)	0.189
≥ 4–10 ( <i>n</i> , %)	168 (51.38%)	403 (55.74%)	
Overall pain interference score (mean ± SD)	3.68 ± 2.49	4.18 ± 2.62	0.003
< 4 ( <i>n</i> , %)	191 (58.41%)	367 (50.76%)	0.021
≥ 4–10 ( <i>n</i> , %)	136 (41.59%)	356 (49.24%)	

The physical parameters included general activity, walking, and work. The psychological parameters included mood, relations with other persons, sleep, and life enjoyment

*SD* standard deviation

Strengths of this study include the substantial number of enrolled cases, which are highly representative of cancer patients across Taiwan. Additionally, pain assessment and pain management of all participants were performed by medical oncologists only, which may reduce the possible bias from physicians of different specialties. However, some limitations of this study are also noted. First, the baseline characteristics of the patients with diverse cancers are different. Demographic data showed a higher percentage of HNC in central and southern Taiwan, which may be attributed to higher rate of alcohol consumption and smoking in above areas [9, 23]. The differences of these baseline characteristics

may reflect the distinct organ involvement or biological behavior of each cancer, suggesting the importance of individualized treatment plan. Besides, the information of each patient, such as clinical stage and treatment strategy, were highly heterogeneous. To minimize this effect on subsequent analysis, we used disease status in this study. Second, the type of pain (e.g., visceral or neurologic pain) and detailed dosage information of analgesics used in every patient was not available in this study. In addition, pain-related clinical manifestation like depressive symptoms were not investigated by depression scale. However, some parameters of daily functioning like mood, sleep, and life enjoyment may be associated with

depressive symptom and were evaluated in patients with recent pain. Third, patients with different cancers have different cancer-related symptoms that may interfere with their daily functioning in diverse ways. Fourth, the component of the patients with other cancer types may affect the result of the analysis. However, most of the patients in this group were composed of the most common cancer types in Taiwan (Supplemental Table S1). Also, each patient was only surveyed once; this made lack of data for longitudinal analysis.

The management of pain in HNC patients remains a challenge for cancer care physicians in real-world clinical practice. To achieve an ideal pain control, effective communication between patients and physicians is critical to assess pain and make pain management plan. Additionally, accumulating data have revealed that caring cancer patients merely by their primary care physician is insufficient, suggesting the necessity of a more intensive and comprehensive approach in term of cancer-related treatment and supportive care to improve clinical outcome and quality of life [3, 24]. Since the pain nature of HNC patient is multidimensional, a multidisciplinary team composed of medical or surgical oncologist, pain management specialist, pharmacist, psychologist, or physical therapist should work together and use an interdisciplinary pain approach to provide best care quality to the cancer patient. For patients receiving curative treatment like radiotherapy or chemoradiation, interventions like oral or dental assessment and management before treatment, and patient education for good oral hygiene are related with better control of treatment-related complication like painful mucositis and quality of life [12, 29, 31, 34]. In parallel, the primary care physician should carefully evaluate the disease and pain status, and adjust medical treatment accordingly. The development of pain treatment protocol and patient education program, and incorporation of other non-pharmacologic intervention therapies like speech and swallowing training, along with physical or psychiatric treatment can further improve pain and daily functioning in HNC patients [15, 38]. Conclusively, this study provides valuable information on pain prevalence, pain status, pain management, and impact of pain on daily functioning in cancer patients. For patients with HNC, a significant effort is still to be made to achieve an ideal pain control and better daily functioning.

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K.M.R., Y.Y.S., C.J.Y., M.F.W., J.S.C., C.S.C., Y.M.L., T.J.C., R.K.H., M.Y.L., Y.C.S., K.D.L., P.Y.L., M.S.Y., W.L.H., and T.C.L. collected clinical data.

S.F.C. and T.C.L. conducted the database interpretation and statistical analysis.

S.F.C. wrote the manuscript.

T.C.L. approved of the last version of the manuscript.

All the authors read and approved the final manuscript.

## Compliance with ethical standards

**Conflict of interest statement** We have read and understood the policy of *Supportive Care in Cancer* on disclosing conflicts of interest. The authors of this manuscript do not have any financial relationship with the organization that sponsored the research. The authors have full control of all primary data and agree to allow the journal to review study-related data if requested.

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