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ORIGINAL ARTICLE

A nationwide survey of adherence to analgesic drugs among cancer patients in Taiwan: prevalence, determinants, and impact on quality of life

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Abstract

Purpose Poor adherence to analgesic drugs is one of the most common barriers to adequate pain management. This prospective, cross-sectional, patient-oriented observational study aimed to explore the adherence rate, clinical factors, and impact of adherence to analgesic drugs on the quality of life (QoL) among cancer outpatients in Taiwan.

Methods Eight hundred ninety-seven consecutive adult outpatients with cancer who had reported tumor pain and received regular analgesic drug treatment were enrolled from 16 medical centers across Taiwan. The Brief Pain Inventory was used to assess pain intensity and QoL. Morisky's four-item medication adherence scale was used to assess adherence to analgesic drugs. Clinical factors possibly associated with good adherence to analgesic drugs were analyzed using multivariate logistic regression analyses.

Results Of the 897 patients, 26.9% met criteria for the good, 35.5% for the moderate, and 37.6% for the poor adherence groups. The good adherence group had significantly better QoL outcomes than the moderate and poor adherence groups (all $p < 0.05$). Age ≥ 50 years, head and neck or hematological malignancies, cancer-related pain, patients who agreed or strongly agreed that

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the side effects of analgesic drugs were tolerable, and patients who disagreed or strongly disagreed that the dosing schedule could be flexibly self-adjusted to deal with the actual pain were predictors of good adherence to analgesic drugs.
Conclusions Awareness of the clinical factors associated with adherence to analgesic drugs may help clinicians to identify cancer patients at a greater risk of non-adherence, reinforce optimal pain management, and improve the QoL by enhancing adherence to pain medications.

Keywords Cancer · Pain · Adherence · Predictive factor · Quality of life

Introduction

Pain is one of the most common devastating symptoms for cancer patients. The prevalence of pain is reported to be 30–50% for patients when cancer is diagnosed [1, 2] and up to 75–90% for patients with advanced stage [3]. Although many clinical guidelines have been developed to provide adequate pain relief for cancer patients [4, 5], a large number of patients still suffer from inadequate pain management [6–8]. A recent systemic review based on 20 articles published from 2007 to 2013 reported that approximately one third of cancer patients did not achieve adequate pain relief [6]. In Taiwan, the national healthcare system has devoted a lot of resources to improve the quality of pain management and palliative care services for cancer patients over the last several decades. However, three nationwide surveys of pain conducted from 1994 to 2014 identified pain as a consistent symptom causing distress among cancer patients in Taiwan, with prevalence rates of 54% of patients in 1994 [9], 51% in 2009 [10], and 63% in 2014 [11].

The reasons for under-treating pain in cancer patients are multifactorial and include the clinicians' attitude with prescribing analgesics [12, 13], patients' perception of their analgesic drugs [14–17], caregiver's attitude toward analgesic drugs [17, 18], and the availability or accessibility of analgesic drugs [19]. Among the patient-related factors, one of the biggest barriers to adequate cancer pain management is poor adherence to analgesic drugs [20, 21]. Previous studies have reported that only 9–20% of cancer outpatients adhere well to pain medications [20–22]. Low adherence to analgesic drugs has been reported to compromise the patients' QoL and increase health care burden due to more frequent hospital visits and unnecessary examinations [22].

Various factors affect a patient's adherence to medications, including fear of side effects, addiction, and tolerance [17]. Due to the high prevalence of inadequate cancer pain control [9–11], we believe that awareness and identification of the clinical factors associated with the adherence to analgesic drugs and the impact on QoL may help to enhance patient care and achieve better QoL outcomes in Taiwan. Few reports have explored the issue of adherence to analgesic drugs in cancer patients in Taiwan, and they have either been conducted at a single center or included a small number of patients. Therefore, it remains unclear how many cancer patients adhere to analgesic drugs and whether the impact of adherence to analgesic drugs is associated with the patients' QoL in Taiwan. As a first step toward improving pain management for cancer patients in Taiwan, this study aimed to: (a) determine the adherence to analgesic drugs, (b) identify the clinical factors associated with adherence to analgesic drugs, and (c) correlate adherence to analgesic drugs and QoL at outpatient oncologic clinics in Taiwan.

Methods

Patient selection

This study was part of a large study conducted by the Taiwan Cancer Palliative Care Society as a nationwide survey of pain in cancer patients in Taiwan [11]. This was a prospective, cross-sectional, patient-oriented observational study including a total of 2652 consecutive patients with cancer who visited the outpatient oncologic clinics at 16 participating medical centers across Taiwan in 2014. Patients who fulfilled all of the following inclusion criteria were recruited: age ≥ 20 years, diagnosis of cancer, and providing written informed consent. The exclusion criteria were: known or suspected psychotic disease, mental retardation, and unconsciousness. The study design is presented in Fig. 1. The study protocol was approved by the Institutional Review Board of all the participating centers.

Data collection and management

A trained research assistant would approach an eligible patient and explain about the study. Patients were asked to complete the questionnaires by themselves. If a patient was unable to read, the research assistant would read and explain the questionnaires to the patient and recorded the answer. The survey was performed once during a clinic visit. Patient characteristics (including gender, age, primary cancer site, present disease status, previous/current anti-tumor therapy, possible cause of pain, and type, dosage, and interval of analgesic drugs prescribed in the last week) were obtained from the patients' records. The Brief Pain Inventory (BPI) was used to assess pain intensity and QoL in the last 7 days [23]. The

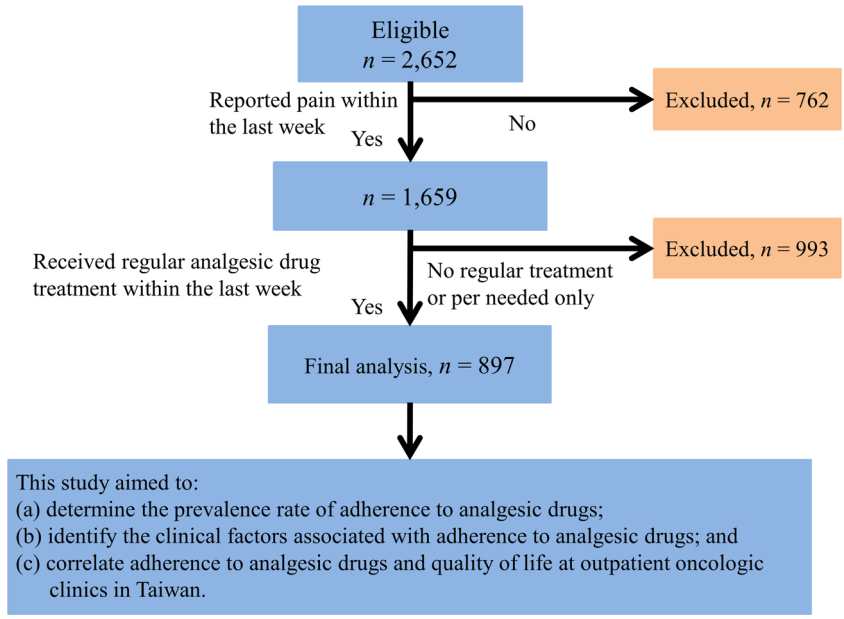

Fig. 1 Study flowchart

patient's pain intensity was defined as mild pain if numerical rating scale (NRS) ranged from 1 to 3, moderate pain if NRS ranged from 4 to 7, and severe pain if NRS ranged from 8 to 10. Using a scale of 0 (does not interfere) to 10 (interferes completely), patients were asked to rate the extent to which their pain interfered with their QoL domains. The QoL domains were then grouped into two subscales: pain interfering with physical functions (general activity, walking ability, and normal work) and psychological functions (mood, relationships with others, enjoyment of life, and sleep), in addition to the more widely used total interference index. The possible cause of pain was further categorized as cancer or non-cancer related based on the clinician's discretion. We used questionnaires to evaluate the patients' satisfaction with the pain control provided by the physician and the effectiveness of the analgesics. Choices of "very satisfied," "satisfied," "neutral," "dissatisfied," and "very dissatisfied" were then converted to a scale of 1 to 5, with 1 being the least satisfied and 5 the most satisfied, as previously described in detail [10]. Satisfaction with the pain control is defined as either "very satisfied" or "satisfied." In our previous study [11], it was found that pain control satisfaction significantly associated with positive pain management index (PMI). The PMI was used to measure whether a patient was being adequately treated for pain (a positive PMI value) or not (a negative PMI value) [24].

Morisky's four-item medication adherence scale (MMAS-4) [25] was used to assess adherence to the analgesic drugs. The MMAS-4, which is a simple four-item questionnaire, has been used to assess adherence to cancer pain medications and has been validated in Taiwan [26]. A "yes" or "no" answer to any question was scored as one point and zero point, respectively, for that item, with a maximum score of 4. We used the same categories of the previous study to defined drug compliance, as a score of 0 was indicative of good adherence, 1–2 of moderate adherence, and 3–4 of poor adherence [26]. The rationale behind such conversion is exactly that there is no precise measurement on a patient's perception about pain management, to broaden the coverage, not only to better representing the true landscape of each group but also simplify the statistical analysis to reach a clearer conclusion.

The patients' perception of their pain medications was investigated via a five-item questionnaire, in which patients were asked to answer whether they "strongly agree," "agree," "disagree," or "strongly disagree" with the following statements: (1) the analgesic drugs are effective in relieving pain, (2) the side effects of the analgesic drugs are tolerable, (3) the analgesic drugs are convenient and easy to use, (4) a frequent and/or irregular dosing schedule has a negative influence on drug adherence, and (5) the dosing schedule can be flexibly self-adjusted to deal with the actual pain. To the best of our knowledge, there was no definitive tool to evaluate a patient's perception on pain medication. Previous studies had reported using pertinent factors to represent medication adherence [27, 28]. We used the same stratification strategy reported to further analyze the associations between the quality of pain control and drug compliance.

Statistical analysis

Basic demographic data were summarized as *n* (%) for categorical variables, and mean with range, standard error (SE), or 95% confidence interval (CI) for continuous variables. The patients who reported pain within the last week and received treatment with regular analgesics were further stratified into "good," "moderate," and "poor" adherence groups for the analysis of pain-induced interference with QoL domains.

Possible clinical variables associated with good adherence to analgesic drugs were examined using univariate and multivariate logistic regression analyses. We selected these variables primarily to cover a broad range of clinical factors that were readily available in the medical records. Moreover, we designed this cross-sectional study with the goal to find out what clinical variables may be related to analgesics adherence. Significant variables identified in the multivariate mode were further analyzed by recursive partitioning analysis (RPA), a decision tree method used to identify specific groups of patients with a greater probability of a specific outcome, to identify optimal patient classification for having good adherence to analgesic drugs [29]. Differences in interference with QoL domains among the three adherence groups and patients based on RPA classification were analyzed using one-way ANOVA. The SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All statistical assessments were two-sided, and a p value ≤ 0.05 was considered to be statistically significant.

Results

Patient characteristics

There were 2652 consecutive cancer patients who completed the pain survey questionnaires from the 16 participating medical centers in this study. Exactly 1755 patients (67.2%) who did not complete questionnaires or did not receive any analgesics were excluded from the study. Overall, 897 of the 2652 patients (33.8%) who had reported pain and received regular analgesic drug treatment within the last week were included for final analysis. The demographic data of the 897 patients are shown in Table 1. The mean age of the patients was 56.7 (range 22–92) years, and 64% were male. The most common primary cancer site was the head and neck (30.4%), followed by the gastrointestinal tract (28.7%), breast (14.5%), and thorax (10.3%). Approximately 89.4% of the patients had active cancer, and 10.4% of the patients were cancer-free at the time of assessment. Six hundred and twenty-five patients (69.7%) had pain related to cancer. Of all patients, 29.3% had mild pain, 47.3% had moderate pain, and 23.4% had severe pain. Regarding kinds of analgesic drugs used, 12.5% of the patients took one kind, 61.0% took two kinds, 23.3% took three kinds, and 3.2% took more than three kinds. With regard to PMI, 72.9% of the patients had a positive PMI, and 28.1% had a negative PMI.

Distribution, consistency, and validity of MMAS-4 score

Of all patients, 26.9, 15.3, 20.2, 18.3, and 19.3% had total adherence MMAS-4 scores of 0, 1, 2, 3, and 4, respectively. Accordingly, 26.9% of the patients were categorized as having good adherence (total adherence score 0), 35.5% as moderate adherence (total score 1–2), and 37.6% as poor adherence (total score 3–4). The Cronbach alpha coefficient for the four items was 0.73, suggesting fair internal consistency of the MMAS-4 items. In addition, the item-to-item correlation coefficients ranged from 0.27 to 0.56 for the four items (Supplementary Table 1). Factor analysis was used to determine the underlying constructs measured by the items in the MMAS-4. The factor loading was high and ranged from 0.43 to 0.63, indicating the association of the four measured items with a single factor (Supplementary Table 2).

Degree of pain-induced interference with quality-of-life domains among the different adherence groups

The degree of pain-induced interference with QoL domains according to different MMAS-4 adherence groups is shown in Fig. 2. The patients with good adherence had significantly better outcomes of the QoL domains in terms of low values of mean degrees of pain-induced interference with physical, psychological, and total function than the patients with moderate or poor adherence (all $p < 0.05$).

Clinical predictive factors of good adherence to analgesic drugs

Univariate and multivariate analyses of the clinical variables to predict good adherence are presented in Table 2. Univariate analysis showed that an age ≥ 50 years (vs. 20–49 years), male gender (vs. female), primary tumor site in the head and neck or hematological malignancies (vs. breast), pain caused by cancer (vs. non-cancer related), having received alternative therapy for pain management (vs. those never having received alternative therapy for pain management), those who agreed or strongly agreed that the side effects of the analgesic drugs were tolerable (vs. those who disagreed or strongly disagreed), those who agreed or strongly agreed that a frequent and/or irregular dosing schedule had a negative influence on drug adherence (vs. those who disagreed or strongly disagreed), and those who agreed or strongly agreed that the dosing schedule could be flexibly self-adjusted to deal with the actual pain (vs. those who disagreed or strongly disagreed) were significant factors for good adherence. Age, primary tumor site, cancer-related pain, those who agreed or strongly agreed that the side effects of analgesic drugs were tolerable, and those who agreed or strongly agreed that the dosing schedule could be flexibly self-adjusted to deal with the actual pain were independent variables that predicted good adherence to pain medications.

Table 1 Basic demographic data of the patients ($n = 897$)

Variable	Category	Number (%)
Age, years	20–49	204 (22.7)
	50–59	314 (35.0)
	60–69	225 (25.1)
	≥ 70	154 (17.2)
Sex	Male	571 (63.7)
	Female	326 (36.3)
Primary cancer site	Head and neck	273 (30.4)
	Gastrointestinal tract	257 (28.7)
	Breast	130 (14.5)
	Thorax	92 (10.3)
	Hematology	70 (7.8)
	Genitourinary tract	44 (4.9)
	Others	31 (3.5)
Disease status	Disease free	93 (10.4)
	Presence with active tumor	804 (89.6)
	Locally advanced disease	266 (29.7)
	Metastatic disease	538 (59.9)
Metastatic site	Distant lymph nodes	217 (24.2)
	Bone	186 (20.7)
	Lung	116 (12.9)
	Liver	115 (12.8)
	Brain	34 (3.8)
	Others	27 (3.0)
Number of metastatic organs	0	325 (36.2)
	1	363 (40.5)
	2	134 (14.9)
	≥ 3	48 (5.4)
Cause of pain	Cancer related	625 (69.7)
	Non-cancer related	272 (30.3)
Pain intensity (numeric rating scale)	Mild (1–3)	263 (29.3)
	Moderate (4–7)	424 (47.3)
	Severe (8–10)	210 (23.4)
Kinds of analgesic drugs currently taking	1	112 (12.5)
	2	547 (61.0)
	3	209 (23.3)
	> 3	29 (3.2)
Pain management index	Negative	243 (27.1)
	Positive	654 (72.9)
Received alternative therapy for pain management	No	759 (84.6)
	Yes	138 (15.4)

Recursive partitioning analysis classification to predict the probability of good adherence to analgesic drugs

The results of the RPA model are illustrated in Fig. 3**.** The patients were categorized into five classifications ranging from the lowest (4.8%) to the highest (53.6%) probability of having good adherence to the analgesic drugs, based on the decision tree method. The patients who (a) agreed or strongly agreed that the dosing schedule could be flexibly self-adjusted to deal with the actual pain, and (b) disagreed or strongly disagreed that the analgesic drugs were effective in relieving pain had the lowest probability of having good adherence to the analgesic drugs (classification I, defined as the reference group). The highest probability of having good adherence was found in the patients who (a) disagreed or strongly disagreed

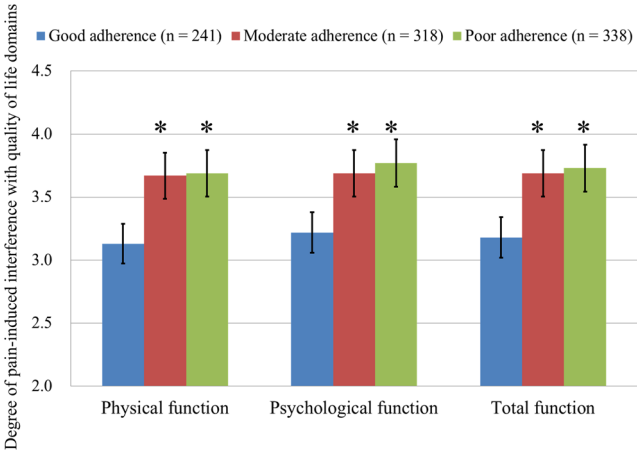

Fig. 2 Degree of pain-induced interference with quality-of-life domains among different adherence groups. (*p values < 0.05 compared to the good adherence group)

that the dosing schedule could be flexibly self-adjusted to deal with the actual pain, and (b) had a primary tumor site in the head and neck or hematological malignancies. According to RPA, significant differences were observed between the reference group and the other groups, with odds ratios ranging from 2.64 to 22.7 (Supplementary Table 3).

Analysis of the degree of pain-induced interference with quality-of-life domains among the different RPA classifications

Figure 4 shows the degree of pain-induced interference with QoL domains among the different RPA classifications. The patients with the highest probability of having good adherence to analgesic drugs (classification IV and V groups) had significantly better outcomes of the QoL domains in terms of low values of mean degrees of pain-induced interference with physical, psychological, and total function than the patients with the lowest probability of having good adherence (classification I group) (all $p < 0.05$).

Discussion

Our results showed that 26.9% of the cancer outpatients had good adherence to analgesic drugs, whereas 35.5 and 37.6% of the patients had moderate or poor adherence, respectively. Non-adherence to analgesic drugs significantly interfered with the QoL of the cancer patients in terms of poor physical functions, psychological functions, and total functions. In addition, old age (≥ 50 years), primary tumor site in the head and neck or hematological malignancies, cancer-related pain, and the patients' perception of their pain medications for those who agreed or strongly agreed that the side effects of the analgesic drugs were tolerable, and those who disagreed or strongly disagreed that the dosing schedule could be flexibly self-adjusted to deal with the actual pain, were independent predictors of good adherence to analgesic drugs.

Using the same adherence questionnaire with the MMAS-4, an early study in Taiwan reported that 51.1% of the cancer outpatients poorly adhered to their pain medications, and that only 8.9% of the patients completely complied with the analgesic regimens [26]. Similar to the current study, Valeberg et al. reported that 21% of the cancer patients fully adhered to their pain medication regimen [21], whereas Miakowski's group reported that up to 90.8% of their cancer outpatients adhered to pain medication regimens [20]. The wide variation in the adherence rate to analgesic regimens in cancer patients among different study cohorts and countries reflect that the determinants relevant to adherence to analgesic regimens are multifactorial. Several factors for poor adherence have been reported in the literature, including underlying psychological problems [30], lack of trust in the medication [17, 30], low intensity of pain [21, 30], intolerable side effects of the medications [15, 31], poor patient-physician relationship [30], complex treatment [30], and financial concerns [30]. Our data showed that the primary tumor site, cause of pain, and patients' perception of the pain medications were the most important predictive factors for adherence to pain medications in our Taiwanese cancer patients, whereas the kind of medication, satisfaction of pain control by the physicians or analgesic drugs, pain intensity, and PMI were insignificant factors. Most importantly, we previously found that non-cancer-related pain was an independent variable in predicting patients who were under-treated for cancer pain in Taiwan [11]. Taken together with the findings of the present study, we believe that non-cancer-related pain is under-evaluated, under-treated, and under-valued by both physicians and patients in Taiwan.

Information regarding the influence of age on adherence to pain medications is inconsistent in the literature. For example, an age > 50 years was a predictor of good adherence in our study, and similar observations that older patients had better compliance with treatment than younger patients have also been reported in other studies [26, 32, 33]. It has also been suggested that older patients tend to be more satisfied with pain management by clinicians, and that this may contribute to better compliance among older patients relative to younger patients [32]. In contrast, another study reported that older patients had more concerns regarding the use of analgesics and had a higher percentage of side effects from analgesics [34]. Given these inconsistent results, the influence of age on adherence to pain medication is still uncertain, and further studies are needed to elucidate this issue.

The strengths of this study include the large number of patients from multiple centers in Taiwan. To the best of our knowledge, this study is the first nationwide survey conducted to evaluate the predictive variables influencing adherence to analgesic drugs among outpatients with cancer in Taiwan. Most importantly, we presented differences in QoL

Table 2 Univariate and multivariate analyses of the clinical variables associated with good adherence to analgesic drugs ($n = 897$)

Variable	Category	No. of patients with good adherence/total no. of patients (%)	Univariate analysis			Multivariate analysis		
			Odds ratio	95% CI	*p*	Adjusted odds ratio	95% CI	*p*
Age, years	20–49	28/204 (13.7)	1			1		
	50–59	94/314 (29.9)	2.69	1.69–4.28	< 0.001	3.01	1.86–4.86	< 0.001
	60–69	70/225 (31.1)	2.84	1.74–4.63	< 0.001	3.27	1.96–5.44	< 0.001
	≥70	49/151 (31.8)	2.93	1.74–4.95	< 0.001	3.40	1.96–5.90	< 0.001
Sex	Male	168/571 (29.4)	1			1		
	Female	73/326 (22.4)	0.69	0.50–0.95	0.023	0.90	0.59–1.37	0.63
Disease status	Disease free	24/93 (25.8)	1					
	Presence with active tumor	217/804 (27.0)	1.06	0.65–1.74	0.81			
Presence of lung metastases	Yes	33/116 (28.4)	1					
	No	208/781 (26.6)	0.84	0.69–1.47	0.88			
Presence of liver metastases	Yes	25/115 (21.7)	1					
	No	216/566 (27.6)	1.37	0.86–2.20	0.19			
Presence of distal lymph node metastases	Yes	50/217 (23.0)	1					
	No	191/680 (28.1)	1.31	0.91–1.87				
Presence of bone metastases	Yes	41/186 (22.0)	1					
	No	200/711 (28.1)	1.38	0.94–2.03	0.10			
Pain management index	Negative	54/243 (22.2)	1			1		
	Positive	187/654 (28.6)	1.4	0.99–1.98	0.056	1.19	0.81–1.76	0.37
Pain intensity (numeric rating scale)	Mild (1–3)	69/263 (26.2)	1					
	Moderate (4–7)	114/424(26.9)	0.97	0.55–1.72	0.92			
	Severe (8–10)	58/210 (27.6)	1.02	0.61–1.68	0.95			
Primary cancer site	Breast	26/130 (20.0)	1			1		
	Head and neck	92/273 (33.7)	2.03	1.24–3.34	0.005	1.83	1.26–2.65	0.002
	Hematology	22/70 (31.4)	1.83	1.15–3.56	0.013	1.78	1.05–2.51	0.029
	Others	101/424 (23.8)	1.42	0.75–2.66	0.29	1.41	0.77–2.57	0.26
Cause of pain	Cancer related	181/625 (29.0)	1			1		
	Non-cancer related	60/272 (22.1)	0.69	0.50–0.97	0.033	0.62	0.43–0.89	0.010
Kinds of analgesic drugs currently taking	1	21/112 (18.8)	1					
	2	154/547 (28.2)	1.59	0.88–2.85	0.12			
	≥ 3	66/238 (27.7)	1.42	0.83–2.42	0.21			
Received alternative therapy for pain management	No	215/759 (28.3)	1			1		
	Yes	26/138 (18.8)	0.59	0.37–0.93	0.022	0.67	0.41–1.09	0.11
Satisfaction of pain control by the physicians	Very satisfied or satisfied	195/751 (26.0)	1.00					
	Neutral or dissatisfied	46/146 (31.5)	1.09	0.89–1.32	0.41			

Table 2 (continued)

Variable	Category	No. of patients with good adherence/total no. of patients (%)	Univariate analysis			Multivariate analysis		
			Odds ratio	95% CI	*p*	Adjusted odds ratio	95% CI	*p*
Satisfaction of pain control by the analgesic drugs	Very satisfied or satisfied	193/729 (26.5)	1					
	Neutral or dissatisfied	48/168 (28.6)	1.03	0.85–1.26	0.76			
Analgesic drugs are effective in relieving pain	Strongly agree or agree	216/800 (27.0)	1.065	0.66–1.72	0.80			
	Strongly disagree or disagree	25/97 (25.8)	1					
Side effects of analgesic drugs are tolerable	Strongly agree or agree	229/814 (28.1)	2.32	1.23–4.35	0.009	2.56	1.30–5.04	0.007
	Strongly disagree or disagree	12/83 (14.5)	1			1		
Analgesic drugs are convenient and easy to use	Strongly agree or agree	234/867 (27.0)	1.22	0.51–2.87	0.66			
	Strongly disagree or disagree	7/30 (23.3)	1					
A frequent and/or irregular dosing schedule has a negative influence on drug adherence	Strongly agree or agree	97/427 (22.7)	0.665	0.49–0.90	0.008	0.77	0.55–1.06	0.11
	Strongly disagree or disagree	114/470 (30.6)	1			1		
The dosing schedule can be flexibly self-adjusted to deal with the actual pain	Strongly agree or agree	170/720 (23.6)	0.46	0.33–0.65	< 0.001	0.49	0.34–0.72	< 0.001
	Strongly disagree or disagree	71/177 (40.1)	1			1		

parameters between patients with adherence and non-adherence. However, there are several limitations to this study. First, head and neck cancer were the most common cancer type in our study because it is an endemic cancer in Taiwan and these patient groups were with high prevalence of tumor pain, which were more likely to be included in our study. Second, we used the MMAS-4 as an assessment tool to evaluate adherence to pain medications. The MMAS-4 was designed to describe the medication-taking behavior of patients; however, it cannot be used to identify reasons for non-adherence [25]. As a result, the degree of the MMAS-4 scale does not correlate well with clinical outcomes. For example, Cohen et al. reported a significant correlation between medication adherence and MMAS-4 score in diabetic patients; however, the MMAS-4 score was not significantly associated with glycated hemoglobin level [35]. In contrast, we found a good relationship between the MMAS-4 and QoL of the cancer patients. Pain is one of the most incapacitating symptoms of cancer that is often severe enough to impair a patient's daily function [11], and non-adherence inevitably hinders adequate pain management thereby resulting in a poor QoL. Based on RPA classification, we identified patients with a high probability of having good adherence to analgesic drugs, and these patients had better outcomes of QoL domains than the patients with a low probability having good adherence to analgesic drugs. Our data support the clinical value of the MMAS-4 in screening adherence to pain medications and predicting the QoL for patients receiving regular analgesic drug treatment. Finally, 89% of our patients with poor adherence agreed that "analgesic drugs are effective in relieving pain", and 96.5% of the patients with poor adherence agreed that "the side effects of analgesic drugs are tolerable." However, these patients were still unwilling to take the drugs regularly. As a result, multiple factors seem to influence adherence to analgesic drugs in cancer patients, and we were unable to identify the reasons using the variables we analyzed.

In conclusion, this prospective nationwide survey showed that cancer patients who had better analgesics compliance also had better QoL. However, only one fourth of those prescribed with analgesics showed good compliance. We identified that age, primary tumor site, cancer-related pain, and patients' perceptions about pain medications were independent predictors of good compliance. We urge health care professionals to recognize that good pain control equals to good quality of life and can since optimize pain managements in cancer patients. Moreover, with the factors identified in our study, they should be used to identify patients who may have poorer compliance to spend more time on improving their compliance. They can also be used to reinforce patients may have better compliance ensuring them a better QoL. Finally, we would like to design a future case-controlled study to further validate the factors identified in the current study.

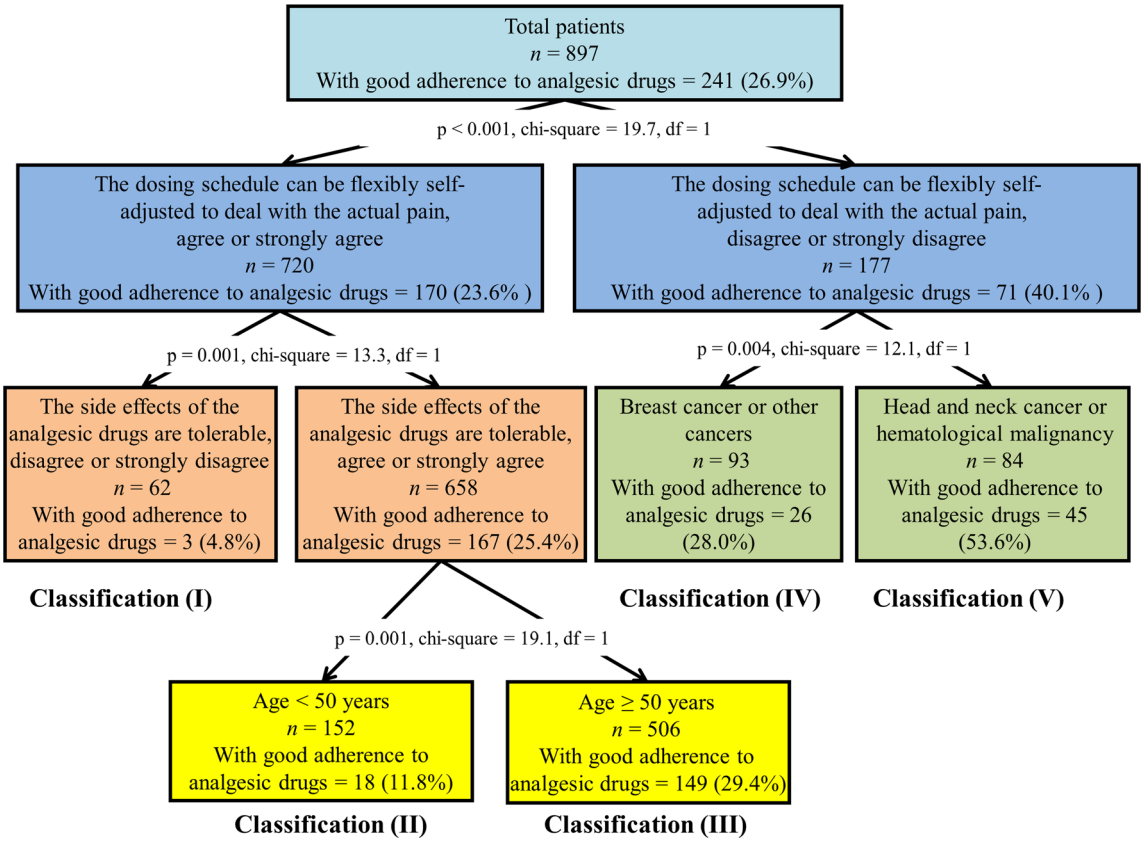

Fig. 3 Recursive partitioning analysis of all study patients ($n = 897$). The classification mode, which was used for univariate logistic regression analysis in Supplementary Table 3, is presented as the number below the node of the decision tree

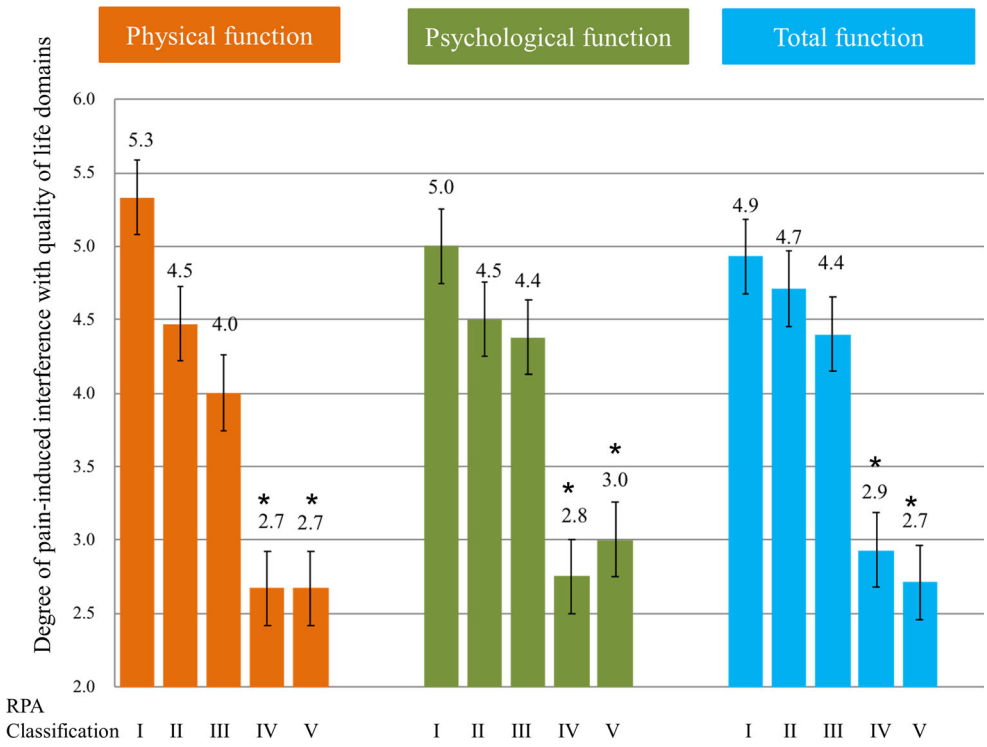

Fig. 4 Degree of pain-induced interference with quality-of-life domains among different recursive partitioning analysis classifications. (*p values < 0.05 compared to the classification I group)

Compliance with ethical standards

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Conflicts of interest The authors declare that they have no competing interests.

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