

## RESEARCH ARTICLE

## Gender Differences Associated with Pain Characteristics and Treatment in Taiwanese Oncology Outpatients

Shu-Yuan Liang<sup>1\*</sup>, Tsae-Jyy Wang<sup>1</sup>, Shu-Fang Wu<sup>1</sup>, Ta-Chung Chao<sup>2,3</sup>, Yeu-Hui Chuang<sup>4</sup>, Shioh-Luan Tsay<sup>1</sup>, Heng-Hsin Tung<sup>1</sup>, Ming-Der Lee<sup>5</sup>

### Abstract

The purpose of this descriptive and comparative study was to examine gender differences relevant to pain intensity, opioid prescription patterns and opioid consumption in Taiwanese oncology outpatients. The 92 participants had been prescribed opioid analgesics for cancer-related pain at least once in the past week and were asked to complete the Brief Pain Inventory – Chinese questionnaire and to recall the dosage of each opioid analgesic that they had ingested within the previous 24 hours. For opioid prescriptions and consumption, all analgesics were converted to morphine equivalents. The results revealed a significant difference between males and female minimum pain thresholds ( $t = 2.38, p = 0.02$ ) and current pain thresholds ( $t = 2.12, p = 0.04$ ), with males reporting a higher intensity of pain than females. In addition, this study found that males tended to use prescribed opioid analgesics more frequently than females on the bases of both around the clock (ATC) ( $t = 1.90, p = 0.06$ ) and ATC plus as needed (ATC + PRN) ( $t = 2.33, p = 0.02$ ). However, there was no difference between males and females in opioid prescriptions on an ATC basis ( $t = 0.52, p = 0.60$ ) or at an ATC + PRN basis ( $t = 0.40, p = 0.69$ ). The results suggest that there may be a gender bias in the treatment of cancer pain, supporting the proposal of routine examination of the effect of gender on cancer pain management. These findings suggest that clinicians should be particularly aware of potential gender differences during pain monitoring and the consumption of prescribed opioid analgesics.

**Keywords:** Cancer - pain - opioids - gender differences - Taiwan outpatients

*Asian Pac J Cancer Prev*, 14 (7), 4077-4082

### Introduction

Much research has focused on acute pain management, indicating that there may be gender differences in pain perception and responses (Yates, 1998; Keefe et al., 2004; Dao & LeResche, 2000) as well as in analgesic efficacy (Fillingim & Maixner, 1995; Miaskowski et al., 2000; Miaskowski & Levine, 1999). While pain is experienced by approximately 38% to 90% of cancer patients (Grond et al., 1994; Ger et al., 1998), research has suggested the need for better programmatic efforts in providing cancer-pain relief for Taiwanese outpatients (Chang et al., 2002; Lai et al., 2002; Liang et al., 2010). Prior to this study, the role of patient gender in cancer pain perception, analgesic prescription, and analgesic consumption has rarely been examined.

A literature review of pain management reveals disagreement surrounding gender differences. Most studies have reported that females tended to be at greater risk for pain undertreatment (Cleeland et al., 1994; Unruh, 1996; Donovan et al., 2008). For example, Cleeland et al.

(1994) revealed that female cancer patients displayed a 1.5-fold higher chance of inappropriate pain management compared to male cancer patients. Some studies have reported that female experience greater pain intensity than male do (Yates, 1998; Dao & LeResche, 2000), and that females also reported a significantly greater impact from pain compared to males in terms of physical well-being (Yates, 1998). Furthermore, one study reported that compared to males, females reported more frequent analgesic use (Eggen, 1993). In particular, females were significantly less likely than males to have been prescribed high potency opioids by their primary oncology team (Donovan et al., 2008).

However, other studies suggest that males may receive less potent analgesics, placing them at a greater disadvantage than females (Eggen, 1993; McDonald, 1994). For example, when involved in sexual behavior, males reported higher impediments by pain compared to females (Edrington et al., 2004). Researchers suggest that these findings may stem from health care providers' cultural beliefs that males should be able to tolerate more

<sup>1</sup>College of Nursing, National Taipei University of Nursing and Health Sciences, <sup>2</sup>Department of Medicine, School of Medicine, National Yang-Ming University, <sup>3</sup>Division of Hematology-Oncology, Medical Oncology, Department of Medicine, Taipei Veterans General Hospital, <sup>4</sup>School of Nursing, College of Nursing, Taipei Medical University, <sup>5</sup>Graduate Institute of Long-Term Care, National Taipei University of Nursing and Health Sciences, Taipei, Taiwan \*For correspondence: shuyuan@ntunhs.edu.tw

pain than females (Eggen, 1993).

Lastly, a review of the research on gender differences in clinical pain reported no clear pattern of differences in analgesic use (Unruh, 1996) or pain intensity (Turk & Okifuji, 1999; Edrington et al., 2004; Stromgren et al., 2004) by gender.

Although pain control among outpatients is affected by both the prescribed medication and patient self-management behaviors, it is unclear whether male and female Taiwanese oncology outpatients experience similar effects from analgesic prescription/consumption and pain perception.

This study was designed to determine whether (1) there were gender differences in various pain characteristics, including pain intensity; (2) there were gender differences in opioid prescription patterns; and (3) there were gender differences in opioid consumption patterns in Taiwanese oncology outpatients.

## Materials and Methods

### *Study Population, Procedure, and Setting*

The sample population of this study comprised all cancer patients with pain who were admitted to the outpatient oncology units of the two teaching hospitals in the Taipei area of Taiwan. Patients were eligible for enrollment if they met the following inclusion criteria: (1) had a cancer diagnosis; (2) had an average pain intensity score  $\geq 3$  on a 0–10 scale in the past 24 hours; (3) had been prescribed opioid analgesics for cancer-related pain on an around the clock (ATC)  $\pm$  as needed (PRN) basis, and had ingested the analgesics within the previous week; (4) were over 18 years of age; and (5) were conscious and able to sign a consent form. The study was approved by the ethics committees of the institution in which the researcher worked as well as two teaching hospitals.

The data were collected from a convenience sample. Information about patients who had been prescribed opioid analgesics for cancer-related pain, including patient age, was extracted from medical charts. The investigator invited potential participants who had met the eligibility criteria to consider joining the study. Patients who had indicated an interest in the study were screened to assess their average pain levels within the previous 24 hours, and eligible patients were verbally provided further information. If verbal consent was given, the patient information sheet, consent form, and self-administered questionnaire were provided so that the patients could decide whether to participate. After participants had finished the questionnaire, the researcher checked the questionnaire for any missing information. The participants were asked to complete any items they had missed and were then thanked for their valuable contributions. The researcher collected information about relevant medical characteristics from the patients' medical records.

### *Instrument and Study Variables*

For the purposes of this paper, data obtained using the following instruments were analyzed as follows:

### *BPI-Chinese*

Pain experience was measured via the Brief Pain Inventory (BPI, Short Form) Chinese version (Wang et al., 1996). The BPI is a self-reporting instrument used to assess the multidimensional nature of pain, including pain intensity and pain interference on life activities during the preceding 24 hours. Pain intensity is measured according to four variables: "worst pain", "least pain", "average pain", and "current pain"; each variable has a range of 0–10 such that 0 = "no pain" and 10 = "pain as bad as you can imagine." For a total interference score, one variable can be computed by taking the average of 7 items that assess the extent to which pain interferes with the following: general activity, mood, walking, working, relations with others, sleeping, and enjoyment of life. Each of the 7 items has a range of 0–10 (i.e., 0 = "does not interfere" and 10 = "interferes completely").

The developers of the BPI used factor analysis to assess the construct validity of the instrument. The four pain intensity items loaded on one factor, and the seven pain interference items loaded onto the other. The coefficient alphas for the two scales, intensity and interference, were at least 0.80. The test-retest reliability of the pain intensity scale was 0.93 over a 2-day period featuring a sample of 20 cancer inpatients. A significant correlation has been found between pain severity ratings and pain interference ratings (Cleeland & Ryan, 1994). A factor analysis of the Chinese version of the BPI also resulted in two factors. The first factor consisted of the four pain severity scales, while the second factor comprised the seven pain interference scales. The coefficient alphas for pain severity and pain interference items were 0.90 and 0.92, respectively (Wang et al., 1996). The validity and reliability of this instrument are both well-established, with the instrument being applied to numerous studies around the world (Lin, 2001; Reyes-Gibby et al., 2006; Yates et al., 2004).

### *Opioid Prescription and Consumption*

In this study, the researcher extracted the patients' current opioid regimen from the medical charts, and the patients were asked to recall the dosage of each opioid analgesic that they had consumed within the previous 24 hours. This restricted time frame was designed to minimize the risk of recall bias. A chart with the picture and the names of each available medication on the market was provided to help patients recall opioid names.

For prescribed opioid dosages, all analgesics were converted to morphine equivalents. Total daily dosages of opioid analgesics prescribed on an ATC and an ATC+PRN basis were calculated (Nissen et al., 2001; Reynolds et al., 2004; Jarlbaek et al., 2005).

### *Sociodemographic and Medical Variables*

The study questionnaire included key sociodemographic variables: age, gender, education level, marital status and employment status. The medical variables included diagnosis, metastases, time that the patient experienced pain, and opioid administration route. The researcher collected medical variables from the patients' medical charts.

**Table 1. Demographic and Medical Characteristics by Gender**

	Males (n = 54)	Females (n = 38)	t / $\chi^2$ value	p-value
Age (years) [mean (SD)]	58.87(11.26)	54.24(13.24)	1.42	0.16
Education (years) [mean (SD)]	9.50(4.45)	8.76(4.48)	0.78	0.44
Marital status (%)				
Married	77.80	68.40	0.59	0.44
Other	22.20	31.60		
Employment status (%)				
Yes	14.80	7.90	0.46	0.52
No	85.20	92.10		
Time patient has had pain (months) [mean (SD)]	13.55(24.07)	11.24(13.69)	0.53	0.60
Diagnosis (%)				
Head/neck cancer	50.00	15.80	11.35	0.001*
Other	50.00	84.20		
Metastasis (%)				
Yes	61.10	73.70	3.91	0.14
No	20.40	21.10		
Unknown	18.50	5.30		
Opioid administration route (%)				
Oral	68.50	73.70	2.25	0.33
Transdermal	24.10	13.20		
Both oral and transdermal	7.40	13.20		

\* $p < 0.05$  (2-tailed)

### Data Analysis

The Statistical Package for the Social Sciences (SPSS for Windows) Version 17.0 was used to analyze the data. Descriptive statistics (mean and percentages) were used to characterize the sample, pain experience, opioid dosages, and opioid consumption. Potential gender differences in demographics were examined using Chi-square tests for categorical variables (e.g., marital status) and independent-sample t-test analyses for continuous variables (e.g., age). Gender differences for pain experience, opioid dosages, and opioid consumption were analyzed using independent-sample t-tests.

Gender differences for demographic and medical characteristics were considered possible covariates in the analyses, evaluating gender differences in pain intensity and dosages of opioids prescribed and consumed.

## Results

### Demographic and Medical Characteristics

Table 1 lists the demographic and medical characteristics of the male and female patients. The subjects included 54 males (58.7%) and 38 females (41.3%). There were no significant differences between male and female patients in terms of age ( $t = 1.42, p = 0.16$ ), education ( $t = 0.78, p = 0.44$ ), marital status ( $\chi^2 = 0.59, p = 0.44$ ) or employment status ( $\chi^2 = 0.46, p = 0.52$ ). Additionally, there were no significant differences between male and female patients in cancer metastases ( $\chi^2 = 3.91, p = 0.14$ ), time that the patient experienced pain ( $t = 0.53, p = 0.60$ ), and opioid administration route ( $\chi^2 = 2.25, p = 0.33$ ). However, there was a significant gender difference in cancer diagnosis ( $\chi^2 = 11.35, p = 0.001$ ).

In terms of cancer diagnosis, a heterogeneous mix of cancer types was represented; the "other" category in Table 1 includes more than five different cancers. The most common diagnosis among females was breast or genital

**Table 2. Pain and Pain Interference Scores by Gender**

	Males (n = 54)	Females (n = 38)	t-value	p-value
Worst pain	7.13 $\pm$ 2.05	6.61 $\pm$ 2.07	1.20	0.23
Least pain	3.44 $\pm$ 2.49	2.26 $\pm$ 2.14	2.38	0.02*
Average pain	5.30 $\pm$ 1.78	5.08 $\pm$ 1.57	0.61	0.55
Pain right now	4.47 $\pm$ 2.22	3.71 $\pm$ 2.42	2.12	0.04*
Pain relief	65.93 $\pm$ 19.57	57.89 $\pm$ 24.95	1.73	0.09
Total Pain interference	5.55 $\pm$ 2.27	5.89 $\pm$ 2.43	-0.70	0.49
General activity interfered	5.57 $\pm$ 2.88	5.76 $\pm$ 2.90	-0.31	0.76
Mood interfered	5.37 $\pm$ 2.67	6.26 $\pm$ 2.64	-1.59	0.12
Walking ability interfered	4.94 $\pm$ 3.04	5.58 $\pm$ 3.37	-0.94	0.35
Normal work interfered	5.85 $\pm$ 3.17	6.26 $\pm$ 3.49	-0.59	0.56
Relations interfered	5.28 $\pm$ 3.05	5.13 $\pm$ 3.22	0.22	0.83
Sleeping interfered	5.57 $\pm$ 2.80	6.24 $\pm$ 2.91	-1.10	0.27
Enjoyment of life interfered	6.26 $\pm$ 2.93	6.03 $\pm$ 3.08	0.37	0.72

All results are given in mean  $\pm$  standard deviation (SD); \* $p < 0.05$  (2-tailed)

cancer (47.40% of females), whereas the most common diagnosis among males was head and neck cancer (50% of males). To account for the potential confounding effects of the cancer diagnosis, we compared the diagnostic differences in pain intensity and opioid dosages prescribed and consumed. However, cancer diagnoses were unrelated to pain intensity and opioid dosages prescribed or consumed, therefore resulting in little influence on the detection of any gender difference.

### Pain Experiences, Opioid Prescription, and Opioid Consumption

Information on pain was collected using the BPI (Short Form) (Cleeland & Ryan, 1994; Wang et al., 1996). The scale includes subscales for pain intensity and pain interference within the previous 24 hours, with one item assessing pain relief during that period. The pain intensity subscale, which has a score ranging from 0 to 10, was used to measure current pain severity, worst pain, least pain, and average pain during the 24-hour period. The patients in this study reported that in the previous 24 hours, they had experienced a mean least pain level of 3.44 (SD = 2.49) in males and 2.26 (SD = 2.14) in females and a mean worst pain level of 7.13 (SD = 2.05) in males and 6.61 (SD = 2.07) in females. The mean score for average pain level in the last 24 hours was 5.53 (SD = 1.78) in males and 5.08 (SD = 1.57) in females. The mean score for current pain level was 4.47 (SD = 2.22) in males and 3.71 (SD = 2.42) in females.

On a scale ranging from 0 (no interference) to 10 (complete interference), the mean degree of pain interference with the patients' daily activities was 5.55 (SD = 2.27) in males and 5.89 (SD = 2.43) in females. In contrast, in the previous 24 hours, the average pain relief reported by participants was 65.93% (SD = 19.57%, range from 0% -100%) in males and 57.89% (SD = 24.95%, range from 0% -100%) in females.

The results concerning opioid prescriptions included dosages prescribed on both an ATC basis and an ATC+PRN basis. The mean ATC dosage was 142.91 mg/day (SD = 99.09) in males and 131.40 mg/day (SD = 96.37) in females, and the mean ATC+PRN dosage was 149.76 mg/day (SD = 99.25) in males and 141.00 mg/day (SD = 107.61) in females. Table 3 includes a detailed

**Table 3. Opioid Prescription Patterns by Gender**

	Males	Females	t-value	p-value
Dosage prescribed on an ATC basis (n of males = 50, n of females = 33)	142.91± 99.09	131.40±96.37	0.52	0.60
Dosage prescribed on an ATC + PRN basis (n of males = 54, n of females = 38)	149.76±99.25	141.00±107.61	0.40	0.69

All results are given in mean ± standard deviation (SD); The mean dosage expressed as milligrams of oral morphine equivalents per day; \* $p < 0.05$  (2-tailed)

**Table 4. Opioid Consumption Patterns by Gender**

	Males	Females	t-value	p-value
Dosage taken on an ATC basis (n of males = 50, n of females = 33)	105.21 ± 87.45	69.40 ± 78.41	1.90	0.06
Dosage taken on an ATC + PRN basis (n of males = 54, n of females = 38)	104.46 ± 87.28	63.70 ± 75.77	2.33	0.02*

All results are given in mean ± standard deviation (SD); The mean dosage expressed as milligrams of oral morphine equivalents per day; \* $p < 0.05$  (2-tailed)

summary of the findings related to the prescribed opioid dosages.

In addition, the results of opioid consumption included dosages prescribed on both an ATC basis and an ATC+PRN basis. The mean ATC consumption was 105.21 mg/day (SD = 87.45) in males and 69.40 mg/day (SD = 78.41) in females. The mean ATC+PRN consumption was 104.46 mg/day (SD = 87.28) in males and 63.70 mg/day (SD = 75.77) in females. Table 4 provides a detailed summary of the findings related to the consumption of prescribed opioids.

#### *Gender Differences for Pain Experiences, Opioid Prescriptions and Opioid Consumption*

An independent-sample t-test was conducted to compare pain experiences between males and females. There was a significant difference between males and females in terms of least pain ( $t = 2.38, p = 0.02$ ) and current pain ( $t = 2.12, p = 0.04$ ), with males reporting a higher pain intensity than females. Table 2 provides a detailed summary of the findings of these analyses.

In addition, an independent-sample t-test was conducted to compare opioid dosages between males and females. The results indicate that no variable was significantly different by gender. These variables include opioid dosages prescribed on both an ATC basis ( $t = 0.52, p = 0.60$ ) and an ATC+PRN basis ( $t = 0.40, p = 0.69$ ). Table 3 summarizes the findings of these analyses.

Furthermore, an independent-sample t-test was conducted to compare opioid consumption between males and females. There was a significant difference between males and females for ATC+PRN opioid consumption ( $t = 2.33, p = 0.02$ ). Males were more likely to consume their prescribed opioid on an ATC+PRN basis. While not statistically significant, there was also a trend for males to consume more ATC opioid medication ( $t = 1.90, p = 0.06$ ). Table 4 summarizes the findings of these analyses.

## **Discussion**

This study evaluated gender differences in several pain characteristics as well as in opioid prescription patterns and consumption in a heterogeneous sample of oncology outpatients with pain. The results of this study suggest that some significant gender differences exist in both perceived pain severity and opioid intake. The results of

this study indicated that male patients were more likely to report higher levels of least pain and current pain as well as consume more opioid prescriptions. No significant differences were found between male and female patients in terms of opioid prescription patterns.

**Pain Experience by Gender:** In this study, gender was not significantly associated with a worse level of pain. Many studies have explored gender differences in the reporting of pain, finding that females usually have reported more severe pain, a higher frequency of pain, and pain of longer duration than males (Yates et al., 1998; Dao & LeResche, 2000). The absence of a gender difference in the level of worse pain in the current study is consistent with Miaskowski's research; however, the inconsistent findings in the literature suggest that further studies are warranted (Miaskowski, 2004).

Our finding that males reported higher levels of least pain and current pain compared to females is inconsistent with previous research on patients with cancer-related pain (Yates et al., 1998; Dao & LeResche, 2000). Several possible alternatives may explain these findings. For example, in this study, males had a much higher percentage of head/neck cancer than females, potentially influencing their reported pain intensity. On the other hand, the male patients of this study may have experienced more psychosocial distress from cancer pain than female patients (Turk & Okifuji, 1999); within Chinese society, males may play an important role as the primary financial providers for the family (Parker, 1993).

**Opioid Prescription by Gender:** Our findings on opioid prescription patterns contrast with those of Cleeland et al. (1994), who found that female oncology outpatients were more likely than males to experience undertreatment for their pain. Nevertheless, the study results are consistent with those of Edrington et al., who found no significant differences in analgesic prescription patterns between male and female patients (Edrington et al., 2004). The dearth of evidence that gender is relevant to opioid prescriptions may reflect the advancement of prescribing practices of the physicians following the guidelines of cancer pain management as published by the Agency for Health Care Policy and Research (Jacox et al., 1994).

**Opioid Consumption by Gender:** Importantly, this study makes significant contributions toward the understanding of opioid consumption by examining the relationship between gender and opioid intake. Gender

was significantly associated with opioid consumption, with males more likely to use their prescribed opioids on an ATC basis. There are many possible explanations for the current findings. Females may have differed from males in their response to pain such that they were more likely than males to seek a referral for specialized pain management. For example, females may be more likely to prefer alternative approaches (Yu et al., 2011) to relieve cancer-related pain due to a greater likelihood of both worrying about (Wang et al., 1997; Tzeng et al., 2006) and experiencing opioid-related side effects (Cepeda et al., 2003). Research on the effects of gender on opioid consumption has produced mixed results (Eggen, 1993; Edrington et al., 2004). Further research on the relationship between gender and opioid intake is required.

The findings of the current study are important because they suggest gender may influence patients' perceptions of and responses to cancer-related pain. This study is one of the few to examine gender difference in cancer-related pain management in Taiwan; thus, the limitations of the study should be noted. The sample size was small and although the sample was homogenous in terms of demographics and medical characteristics, it was clinically quite diverse. There were many different cancer diagnoses and cancer stages that we could not control for. Finally, although we examined the effects of time that the patient had experienced pain on reported pain, we did not assess whether the reported pain was acute or chronic. Despite the current study's limitations, the findings indicate the need to improve the pain management in oncology outpatients and to more closely examine patient-related factors that may hinder adequate pain management. The findings also support the routine examination of the effects of gender in future cancer pain research.

In conclusion, the study results reveal that males reported a higher intensity of pain compared to females in terms of minimum pain and current pain. In addition, this study found that males tended to use their prescribed opioid analgesics more frequently than females. These findings suggest that clinicians should be particularly aware of potential gender differences in pain perception and the consumption of prescribed opioid analgesics. Further studies are necessary to elucidate the factors that contribute to gender differences in pain perception and prescribed opioid consumption.

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