ความเหมาะสมในการจัดการความปวดด้วยยา ปัจจัยที่เกี่ยวข้องกับความปวด และอัตราการรอดชีวิตที่ระยะ 5 ปี ของผู้ป่วยมะเร็งปากมดลูกในโรงพยาบาลสระบุรี

Appropriateness of Pain Management with Medications, Factor Associated with Pain and 5-Year Survival Rate of Cervical Cancer Patients at Saraburi Hospital

นิพนธ์ต้นฉบับ **Original Article**

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บทคัดย่อ

วัตถุประสงค์: เพื่อประเมินความเหมาะสมในการจัดการความปวดด้วยยา ปัจจัยที่เกี่ยวข้องกับความปวด และอัตราการรอดชีวิต 5 ปี ในผู้ป่วยมะเร็งปากมดลูกของโรงพยาบาลสระบุรี **วิธีการศึกษา:** ศึกษาข้อมูลย้อนหลังในเวชระเบียนของผู้ป่วยที่รับการรักษาในช่วง 1 ม.ค. ถึง 31 สิงหาคม 2560 แล้วติดตามจนครบ 5 ปี หลังการวินิจฉัย วิเคราะห์ความเหมาะสมในการจัดการความปวดตามคำแนะนำของ WHO Analgesic Ladder ใช้ multiple linear regression ทดสอบปัจจัยที่เกี่ยวข้องกับคะแนนความปวดที่ลดลง ใช้สถิติ Log-rank test และ Kaplan-Meier survival analysis วิเคราะห์อัตราการรอดชีวิตที่ 5 ปี **ผลการศึกษา:** ผู้ป่วยจำนวน 127 คน อายุเฉลี่ย 56.17 ปี ส่วนใหญ่เป็นระยะ IIb (26.0%) เป็นมะเร็งที่ยังไม่ลุกลาม (74.0%) ความปวดปานกลาง (4 – 6 คะแนน) (50.5%) พบความเหมาะสมในการจัดการความปวดด้วยยาที่ 92.91% คะแนนเฉลี่ยความปวดหลังได้รับยา 48 ชั่วโมงลดลง 3.77 คะแนน ซึ่งมีนัยสำคัญทางสถิติ (*P*-value < 0.001) ปัจจัยที่เกี่ยวข้องกับคะแนนความปวดที่ลดลง คือ ระยะของมะเร็ง ขนาดก้อนมะเร็ง จำนวนอวัยวะที่แพร่กระจาย และจำนวนโรคประจำตัว (*P*-value < 0.05) อัตรารอดชีวิตที่ 5 ปี เป็น 65.40% **สรุป:** ความเหมาะสมในการจัดการความปวดด้วยยาของผู้ป่วยมะเร็งปากมดลูกเป็น 92.91% คะแนนความปวดลดลง 3.77 คะแนน ปัจจัยที่เกี่ยวข้องกับคะแนนความปวดที่ลดลง คือ ระยะของมะเร็ง ขนาดก้อนมะเร็ง จำนวนอวัยวะที่แพร่กระจาย และจำนวนโรคประจำตัว อัตราการรอดชีวิต 5 ปีที่ 65.40%

คำสำคัญ: การจัดการความปวด, มะเร็งปากมดลูก, อัตราการรอดชีวิต

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Abstract

Objective: To determine appropriateness of pain management, factors associated with pain and 5-year survival rate of cervical cancer patients at Saraburi Hospital. **Method**: Data of cervical cancer patients receiving treatment between January 1 to August 31, 2017 with 5 years after diagnosis were used for analysis. Appropriateness of pain management was assessed according to the WHO Analgesic Ladder. Factors associated with the decreased pain score were tested using multiple linear regression analysis. 5-year survival rate was analyzed using Log-rank test and Kaplan Meier survival analysis. **Results:** A total of 127 patients were 56.17 years by average. Most patients were with stage IIb (26.0 %) and non-metastasized cancer (74.0%), and with moderate pain (4 – 6 points) (50.5%). Appropriateness of pain management was 92.91%. Pain score within 48 hours after pain medication decreased by 3.77 points with (*P*-value < 0.001). Decreased pain scores were associated with cancer stage, tumor size, number of metastasized organs, and number of underlying diseases (*P*-value < 0.05). 5-year overall survival rate was 65.40 %. **Conclusion**: Appropriateness of pain management was 92.91%. Pain score decreased by 3.77 points. Decreased pain score was associated with cancer stage, tumor size, number of metastasized organs, and number of underlying diseases. 5-year overall survival rate was 65.40%.

Key words: pain management, cervical cancer, 5-year survival rate

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Introduction

The World Health Organization 2020 data revealed 604,000 cervical cancer cases worldwide with 342,000 deaths.[1] In Thailand, cervical cancer has been a major health problem since 1989 as the leading cancer among Thai women. With a nationwide policy to screen for cervical cancer, incident of cervical cancer has been reduced continuously. Cervical cancer is ranked number 5 of all cancers in Thai women with 15 new cases per day, or 5,422 case per year, and 6 deaths per day or 2,238 deaths per year. These statistics were from 2019 data of the Strategy and Planning Division, Ministry of Public Health.[2] Human papillomavirus (HPV) is the main cause of the development of cervical cancer. Screening for cervical cancer and HPV vaccination are effective in preventing cervical cancer.[3] Stage of cervical cancer could be classified by clinical manifestations guided by the International Federation of Gynecology and Obstetrics

(FIGO). This guideline is the standard and applicable for cervical cancer cells at stages of 1A, 1B, 2A, 2B, 3A, 3B, 4A and 4B.[3]

The treatments of cervical cancer range from surgery to radiation, chemotherapy, targeted therapy, and immunotherapy. Physicians choose treatment modalities suitable for stage of cancer. Multiple modalities could be used simultaneously to improve survival. Patients experienced pain after surgery, radiation and chemotherapy. For example, paclitaxel and oxaliplatin could cause burning sensation, muscle pain and numbness. Metastasis of cervical cancer could be directly spreading to other nearby organs such as uterus, vagina, parametrium, peritoneum, urinary bladder and anal sphincter. Cervical cancer can metastasize via lymphatic system and blood system to lung, liver, and bone. The patient experiences pain in the lower stomach, back, coccyx, and upper legs.[3,4]

Cancer pain is found as high as 50.7% in every stage of cervical cancer and 66.4% once entering metastasized stage.[2] This cancer pain needs analgesic drugs. Physicians assess the pain level, cause of pain, and select pain medications according to the cause of pain. For nociceptive pain, which is caused by chemicals, trauma, heat, or physical force, is manifested as dull aching pain in the affected tissues. For neuropathic pain, which is caused by pathologic nervous system, is expressed as shooting, stabbing or burning sensation.

In clinical practice, pain is usually assessed using numerical rating scale (NRS). The patient is instructed to rate their pain from 0 to 10 where 0 is for no pain and 10 is for the worst imaginable pain. Pain medication is chosen according to the WHO analgesic ladder as follows.[5] For mild pain (NRS score of 1 – 3), it is recommended to use paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, mefenamic acid, naproxen sodium and diclofenac sodium which is applicable for all levels of cancer pain. These drugs could be used as monotherapy or in combination with adjuvants such as antidepressants (amitriptyline and nortriptyline), anticonvulsants (gabapentin and pregabaline), muscle relaxants (tolperisisone), antispasmodics (hyoscine butylbromide), and corticosteroids (dexamethasone and prednisolone). If the pain is not relieved within 24 – 48 hours, the next pain remedy for moderate pain should be tried. For moderate pain (NRS score of 4 – 6), weak opioids such as tramadol can be used either as monotherapy or in combination with paracetamol or NSAIDs or with adjuvants. Again, if the pain is not relieved within 24 – 48 hours, analgesic drugs for severe pain could be used. For severe pain (NRS score of 7 – 10), it is recommended to use strong opioids such as morphine and fentanyl either monotherapy or in combination with paracetamol or NSAIDs or with adjuvants. For moderate-to-severe cancer pain in the internal organs, opioid analgesics are recommended.[2] However, since cancer pain is mediated through various receptor stimulations, the use of single analgesic drug is not as effective as combination therapy for different receptors. These additional drugs include paracetamol, NSAIDs, anticholinergics (hyoscine butylbromide, and gabapentin.

In addition to symptomatic relief of pain, survival of cancer patients is of the major concern. In United State, based on the American Cancer Society, first-stage cervical cancer patients had a 92% survival rate in the first 5 years, 59% when cancer metastasizes to nearby organs or lymph node, and 17% when other organs is involved. Overall survival for all stages of cervical cancer was 67%.[4]

In this present study, we aimed to assess appropriateness of pain management using analgesics according to the WHO analgesic ladder and determining pain score within 48 hours after pain medication administration. A previous study suggested that pain was relieved to less than 4 points by average and the patients were satisfied with pain management.[6] A study in India of Goel showed that as high as 95.3% of pain prescriptions was appropriate in cervical cancer patients.[7] However, only diclofenac, tramadol and morphine were studied.[7] Our present study thus aimed to determine benefits of each of all NSAIDs for cervical cancer pain relief. A study of Andres revealed that metastasized cancers caused severe pain in 80% of the patients.[8] However, other factors including patient age, cancer stage, cancer size, number of metastasized organs, and number of underlying illnesses could influence pain and survival[9] and thus are worth investigating. Our present study thus aimed to examine the influence of these factors on survival and pain. Cancer pain could vary in individuals. Factors that aggravate pain should be explored so pain can be managed appropriately by physicians and pharmacists.

A study on 5-year survival showed that age and race resulted in different survival rates in cervical cancer patients.[10] However, survival rate of cervical cancer patients at regional medical centers like Saraburi Hospital has not been

determined. Our present study aimed to determine survival rate of cervical cancer patients under the care of Saraburi Hospital. The survival rate obtained could be compared with the one from the National Cancer Institute to determine performance of care of Saraburi Hospital.

Saraburi Hospital is a 700-bed regional medical center. Despite its medical center status, Saraburi Hospital has only 2 oncologists which might not be adequate to serve a large number of patents. Specifically, two oncologists met 25 – 30 cervical cancer patients per day for two days per week. For the other three days of the week, these two oncologists performed operations. Since oncologists had limited time to talk with the patient about planned management especially medications, pharmacists played a crucial role providing medication use counseling to the patient regarding administration, adverse effects, and drug interactions. Pharmacists also provided consultation of diet and self-care after chemotherapy for these patients. The outcome of pain medication, diet and self-care could also in part be the benefits of pharmacist consultation. If inappropriate pain medication prescription was found in a sizable portion of patient, more contribution of pharmacists in checking pain medication prescription according to the WHO analgesic ladder could be warranted.

This present study aimed to specifically determine appropriateness in pain management with analgesic prescriptions according to the WHO analgesic ladder and comparing pain scores before and 48 hours after pain medication administration. We examined the associations between pain score and independent variables including appropriateness of pain management, age, stage of cervical cancer (i.e., 1 – 4), number of metastasized organs, number of underlying illnesses, and size of the cancer in centimeters. We also determined 5-year survival rate of patients with cervical cancer.

It was hypothesized that (1) pain scores before and within 48 hours after pain medication were different and (2) age, stage of cervical cancer (i.e., 1 – 4), number of metastasized organs, number of underlying illnesses, and size of the cancer in centimeters were associated with the decreased pain score.

Methods

In this retrospective cohort study, computerized and non-computerized databases of medical records of Saraburi Hospital were used. The study was approved for ethics by the Ethics Committee for Human Study of Saraburi Hospital (approval number: EC026/2565; approval date: May 30, 2022).

Study population and sample

Study population was 266 cervical cancer patients receiving cancer treatment at Saraburi Hospital from January 1 to August 31, 2017. Data of 5 years after diagnosis of cervical cancer were obtained for determining 5-year survival rate. The study sample was those in study population who met the inclusion criteria. For inclusion criteria, the patients had to receive cancer treatment (either surgery, radiation or chemotherapy) between January 1 to August 31, 2017, had pain after the cancer treatment (either surgery, radiation or chemotherapy) with NRS pain score of at least 1 point, receiving pain medication, with at least two pain assessments (i.e., before and within 48 hours after pain medication drug was administration) between January 1 to August 31, 2017, with a medical record of at least of 5 years since the diagnosis of cervical cancer for survival study available. A total of 127 cervical cancer patients were eligible as a study subject. For the exclusion criteria, cervical cancer patients who were transferred to other hospitals for care.

Study variables

Appropriate pain management was defined as the prescribed pain medication drug suitable for the pain level according to the WHO analgesic ladder. The pain was assessed using the numerical rating scale (NRS) in clinical practice. The pain management was defined as “appropriate” for prescribing pain medication suitable for the pain level, and “inappropriate” for the one unsuitable for pain level. Appropriateness pain management served as an independent variable to be associated with the dependent variable of the change in pain score. Pain level was also categorized as mild, moderate, and severe in accordance with NRS scores of 1 - 3, 4 – 6, and 7 – 10 points.

The **change in pain score** was defined as the difference between pain score within 48 hours after the pain medication was administered to the patient compared with the pain score before the administration. In clinical practice, the patients were asked by physicians to rate their pain as 0 for no pain to 10 for the worst imaginable pain. The pain levels were documented in the medical record. The pain scores before

and within 48 hours after the pain medication was given were retrieved while the patients were admitted to the in-patient department for in-patient chemotherapy. Difference in pain score before and within 48 hours after pain medication administration was tested for statistical significance. Other independent variables included age, stage of cervical cancer (i.e., 1 – 4), number of metastasized organs, number of underlying illnesses, and size of the cancer in centimeters. For **survival**, it was defined as the last date of being alive either in the medical records, national cancer registry or the government registry. Patients who were alive until the last date of 5-year follow-up since the diagnosis of cervical cancer were censored.

Data collection procedure

Of the 266 cervical cancer patients in the medical records, 75 patients were excluded because of complete pain scores were not documented (before and within 48 hours after the pain medication was administered), 20 transferred to other hospitals, and 44 for no pain medication prescribed resulting in a total of 127 patients eligible as study sample. The living status of the patients were examined from medical records, national cancer registry or the government registry database of the Department of Interior Affairs. All data were verified and inputted to the electronic database for analysis.

Statistical analysis

Descriptive statistics including frequency with percentage and mean with standard deviation were used to summarize demographic and clinical characteristics of the participants, pain scores, and pain management according to the WHO Analgesic Ladder. Pain scores before and within 48 hours after pain medication was administered were compared using paired sample t-test or Wilcoxon signed rank test, as appropriate. Multiple regression analysis was used to examine associations between decreased pain scores (0 – 10 points) and appropriateness of pain management, age, stage of cervical cancer (i.e., 1 – 4), number of metastasized organs, number of underlying illnesses, and size of the cancer in centimeters. No multicollinearity among independent variables was found. Normality of distribution of pain scores was found. Kaplan-Meier plot, 5-year survival rate and median survival time of patients with 4 cancer stages were presented. Log-rank test and cox proportional regression model were used to compare the 5-year survival rate among 4 stages of cancer. Chance of survival in each stage of cancer compared with stage 1 as the reference group was presented as hazard ratio (HR) with 95% confidence interval (CI). All statistical significance was set a type I error of 5% (or *P*-value < 0.05). All statistical analyses were performed using software program SPSS version 20.0.

Results

Of the 127 cervical cancer patients, they were 56.17 ± 12.09 years old by average with the majority in their 50 – 59 years (45 patients or 35.40%). Stage IIb was the most found disease, i.e., in 33 patients or 26.00%. Most tumors were not more than 4 centimeters in size (112 patients or 88.10%) and not in metastasis stage (94 patients or 74.00%). Most patients had pain score before taking pain kill drug of 4 – 6 which was moderate pain (64 patients or 50.50%) (Table 1).

Table 1 Characteristics of the participants (N = 127).

Characteristics	N	%
Age (years)		
20 - 29	2	1.60
30 - 39	9	7.10
40 - 49	22	17.30
50 - 59	45	35.40
60 - 69	33	26.00
70 - 79	11	8.70
80-89	5	3.90
Mean = 56.17 ± 12.0		
Stage of cancer		
Ia	19	15.00
Ib	25	19.70
IIa	11	8.70
IIb	33	26.00
IIIa	4	3.10
IIIb	24	18.90
IVa	3	2.40
IVb	8	6.30
Size of the tumor (cm.)		
≤ 4	112	88.10
> 4	15	11.90
Metastatic disease		
No	94	74.00
Yes	33	26.00
Pain score (level)		
1 – 3 (mild)	12	9.40
4 – 6 (moderate)	64	50.50
7 – 10 (severe)	51	40.10

All patients were provided with every step of pain management according to the WHO analgesic ladder. Specifically, all patients were assessed for pain before prescribing pain medication and assessed for pain every 4 hours after taking pain medication (Table 2). There were only

4 patients that needed management for adverse effects of pain medication.

Table 2 Pain management for participants (N = 127).

Pain management	N	%
1. Assessment of pain using numerical rating scale before prescribing pain medication	127	100
2. Pain medication prescribed according to WHO analgesic ladder	127	100
3. Monitoring of pain every 4 hours after giving pain medication	127	100
4. Management of adverse effects of pain medication	4	3.15

Among patients with mild pain, most were given paracetamol (66.67%) which was appropriate. Other appropriate prescriptions were NSAIDs (8.33%) and paracetamol plus NSAIDs (16.67%). The inappropriate prescription was tramadol (8.33%). For moderate pain, the most appropriate prescribed medication was NSAIDs (21.87%). Collectively, prescriptions with various pain medications were appropriate (95.31%) while the inappropriate one was morphine plus tramadol (4.69%). For severe pain, most appropriate drug prescribed was NSAIDs (13.73%); while inappropriate medications were tramadol (5.88%) and adjuvants (3.92%) (Table 3).

Table 3 Pain medications for each level of pain (N = 127).

Medications	N (%) by level of pain			
	Mild (1 - 3) (n = 11)	Moderate (4 - 6) (n = 64)	Severe (7 - 10) (n = 51)	Total (N = 127)
Paracetamol	8 (66.67)	4 (6.25)	0	12 (9.44)
NSAIDs	1 (8.33)	14 (21.87)	7 (13.73)	22 (17.32)
Tramadol	1 (8.33)	7 (10.93)	3 (5.88)	11 (8.67)
Morphine	0	1 (1.56)	4 (7.84)	5 (3.94)
Adjuvants	0	4 (6.25)	2 (3.92)	6 (4.72)
Paracetamol + NSAIDs	2 (16.67)	4 (6.25)	6 (11.77)	12 (9.43)
Paracetamol + tramadol	0	4 (6.25)	0	4 (3.15)
Tramadol + NSAIDs	0	5 (7.81)	4 (7.84)	9 (7.08)
Morphine + NSAIDs	0	1 (1.56)	2 (3.92)	3 (2.36)
Morphine + tramadol	0	3 (4.69)	0	3 (2.36)
Tramadol + adjuvants	0	2 (3.12)	1 (1.96)	3 (2.36)
Tramadol + NSAIDs + adjuvants	0	6 (9.38)	1 (1.96)	7 (5.52)
Morphine + adjuvants	0	0	1 (1.96)	1 (0.79)
Paracetamol + tramadol + adjuvants	0	9 (14.06)	3 (5.89)	12 (9.43)
Morphine capsule + morphine syrup + fentanyl patch	0	0	17 (33.33)	17 (13.37)
Total	12 (100.00)	64 (100.00)	51 (100.00)	127 (100)

It was found that 92.91% of the patients were prescribed with pain medications that were appropriate for their pain level (Table 4). There were a small number of patients with inappropriate medications, for example tramadol for mild pain (1 patient), tramadol with oral morphine for moderate pain (3 patients), adjuvants or tramadol as monotherapy for severe pain with no NSAIDs, morphine or fentanyl (5 patients) (Table 3).

Table 4 Appropriateness of pain medication (N = 127).

Level of pain (pain score)	N (%)	
	Appropriate	Inappropriate
Mild pain (1 - 3)	11 (8.65)	1 (0.79)
Moderate (4 - 6)	61 (48.04)	3 (2.36)
Severe (7 - 10)	46 (36.22)	5 (3.94)
Total	118 (**92.91**)	9 (7.09)

Pain score before giving pain medication was 6.11 ± 1.89 points. With the pain score of 2.33 ± 1.64 points within 48 hours after pain medication, the decrease of pain was 3.77 ± 0.96 points which was statistically significant (*P*-value < 0.001) (Table 5).

Table 5 Pain scores before and within 48 hours after pain medication (N = 127).

	Pain score
Before pain medication	6.11 ± 1.89
Within 48 hours after pain medication	2.33 ± 1.64
Change of pain score	3.77 ± 0.96 (95% CI = 3.66 - 3.95)
***P*-value for paired t-test**	< 0.001

Multiple linear regression analysis revealed that 4 independent variables including cancer stage, tumor size, number of metastasized organs and number of underlying illnesses were significantly associated with pain score (P-value < 0.001). Pain score increased by 0.491, 0.516, 0.420, and 0.273 points for 1 more cancer stage, 1 more centimeter of the tumor size, 1 more metastasized organ, and 1 more underlying illness, respectively with *P*-values of 0.017, < 0.001, 0.039, and 0.045, respectively. Age was not significantly associated with pain score (*P*-value = 0.733). The equation to predict pain score was as follows:

Pain score = 5.103 + 0.491x(cancer stage) + 0.516x(tumor size) + 0.420x(number of metastasized organs) + 0.273x(number of underlying illnesses).

5-year survival rate

With the 5-year follow-up, since the diagnosis of cervical cancer, 83 out of 127 patients survived (65.40%) with a median survival time of 59.06 ± 02.02 months. Survival rates among patients with 4 stages were significantly different (*P*-value < 0.001, Log-rank test). 5-year survival rates differed by stage of cancer where survival rate was smaller and median

survival time was shorter for patients with later stage. Consequently, patients in stage 1 had the highest 5-yer survival rate of 93.20% and the highest median survival time of 69.00 months (HR = 0.027, 95% CI = 0.006 - 0.083), followed by those in stage 2 (survival rate = 72.70%, median survival time = 63.59 months, HR = 0.121, 95% CI = 0.052-0.275) and stage 3 (survival rate = 35.70%, median survival time = 43.68 months, HR = 0.402, 95% CI = 0.181-0.819). The lowest survival rate was found in patients in stage 4 (survival rate = 27.27%, median survival time = 26.63 months, HR = 1, 95% CI = 0.750-1.682) (Table 6 and Figure 1).

Table 6 Median survival time and chance of survival in patients in 4 cancer stages (N = 127).

Cancer stage	Median survival time (month)	HR (95%CI)
1	69.00 ± 0.00	0.027 (0.006, 0.083)
2	63.59 ± 2.57	0.121 (0.052, 0.275)
3	43.68 ± 5.00	0.402 (0.181, 0.819)
4	43.68 ± 5.00	1 (0.750, 1.682)

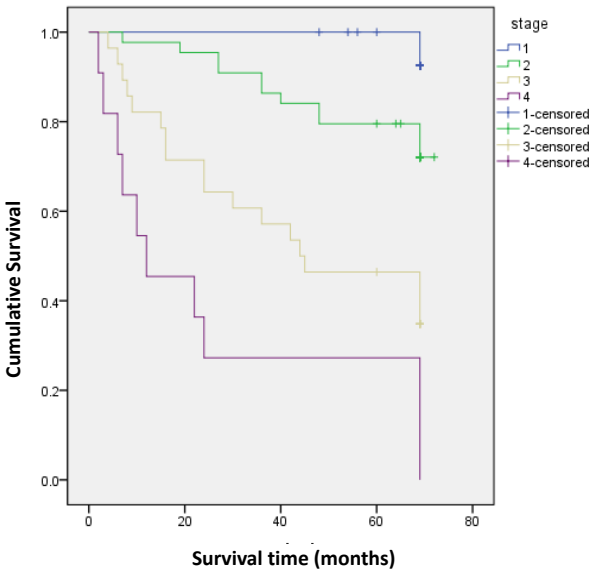

Figure 1 Kaplan-Meier plot of survival of with 4 stages of cervical cancer patients.

Note:

Log—rank test: *P*-value < 0.001.

Cox proportional hazard regression analysis: *P*-value < 0.001.

Discussions and Conclusion

The study for 5-year survival rate in 127 cervical cancer patients of Saraburi Hospital showed different survival rates among stages 1 to 4. Certain findings were discussed as follows. These patients had a mean age of 56.17 ± 12.09 years old which was consistent with 51 ± 12 years old in the work of Pantana which also studied Thai patients.[11] Cervical cancer in Thailand is at the highest prevalence in this age group. We found cervical cancer patients in stage 2b the most (33 patients or 26.0%) which was different from 40.2% of stage 3 patients found in Ethiopia.[12] This could be due to the policy for cervical cancer screening in women 35 years or older which could allow for identifying the cancer at early stage.

Most patients had a tumor with the size of not more than 4 centimeters (112 patients or 88.10%). Another study in Thailand also found 62.30% of cervical cancer patients had a tumor of the same size.[13] The majority had a moderate pain (i.e., pain score of 4 – 6) (50.50%). Our finding is different from the study of Kurl where patients had a mean pain score of 3.6 points.[14] This could be because patients in Kurl's study were treated only with radiation which could cause less pain than other treatments. Since patients in our study were treated with surgery, radiation and chemotherapy, higher level of pain could be expected.

Patients with moderate pain took NSAIDs as monotherapy the most (11.02%) with ibuprofen 400 mg tablets as the most prescribed one. This is consistent with a study revealing that NSAIDs provided safe and effective pain relief in cancer patients.[15] Patients with severe pain in our study were given morphine tablets with morphine syrup and fentanyl patch as high as 13.38%. A study in patients with last stage of cancer showed that fentanyl patch as a monotherapy was used the most for patients with severe pain.[16] The difference could be because patients in our study were with various stages of cervical cancer.

Appropriateness in pain management regarding pain medication was found to be as high as 92.91%. A study revealed that diclofenac relieved moderate pain by 73.63%.[7] In our study, various NSAIDs were used with overt decrease of pain scores to a low level. We found pain scores before pain medication assessed by physicians and appropriate prescription for pain medication according to the WHO analgesic ladder. Pain scores within 48 hours after pain medication decreased significantly, i.e., by 3.77 points. The decrease in pain score is consistent with a previous study of

3.9 points.[17] This could be because there was a large portion of patients with pain after surgery in both studies, pain scores after pain medication could be relatively similar.

There were certain inappropriate pain medications for given pain levels. Tramadol was prescribed for patients with mild pain and it caused nausea. There were 3 patients with moderate pain who were prescribed with tramadol with oral morphine. These patients should be given weak opioid with strong opioid because two drugs exert pain relief by stimulating the same receptor. The competitive binding on mu-receptor by tramadol could hinder pain relief by morphine.[18] This combination therapy could cause constipation, nausea and vomiting. In our study, inappropriate pain medications for severe pain were tramadol or adjuvant (hyoscine n-butylbromide) as monotherapy with no NSAIDs or morphine as recommended.[2] Pain was thus not alleviated. The patients should be given injectable morphine.

Our study found that factors associated with pain scores included cancer stage, tumor size, number of metastasized organs, and number of underlying diseases. This finding is consistent with the work of Andres which showed that metastasized cancer causes severe pain in 80% of the patients.[7] The study did not examine factors other than metastasis status of the cancer and analysis method was different from ours. We used these 4 factors in multiple linear regression analysis to predict pain scores. These four factors simultaneously could explain variance of pain scores by 23.10% (R^2 = 0.231) which has not been reported in any studies predicting pain scores in cervical cancer patient.

The survival rate after 5 years of follow-up was 65.40%. This rate is consistent with a previous study at Vachira Hospital which is a medical center located in Bangkok metropolis where 68.6% survival rate was found.[11] In our study, most patients were in their Ib (19.7%), IIb (26.0%) and IIIb (18.9%) stages which are overtly metastasized. In Vachira Hospital, most patients were in their IIb (36%) and IIIb (35%) stages. Our survival rate was slightly inferior to that of Vachira Hospital. This could be attributable to a fewer number oncologists which is generally found in most regional medical centers. Our finding is consistent with the study in Malaysia which consisted of Malaysian, Indian and Chinese patients showed 5-year survival rates of 59.20%, 69.50% and 73.80%, respectively.[10] Our 5-year survival rate of 65.40% in Thai patients is close to that of Indians (69.50%) but lower than Chineses (73.80%). This could be attributable to that Chinese had a higher survival rate and the fact that a large portion of patients was Chineses (56.30%) made their survival rate even greater.[10] In addition, most Malaysian patients had lower knowledge about cervical cancer screening. They might be diagnosed with cervical cancer at later stages; hence a lower survival rate.[10]

This study has certain limitations. With its retrospective design, a large portion of cervical cancer patients were excluded since no or complete pain scores were available. Hence, a sample size and a potential bias. The representativeness of this sample to the patient population could be somewhat limited. More prospective studies with a larger ample size should be conducted.

Our findings could be useful in practice. The prediction of pain score using the four factors including cancer stage, tumor size, number of metastasized organs, and number of underlying diseases could be useful in patients who are unconscious or incommunicable. The four factors could explain 23.10% of the variance of pain scores.

In conclusion, most cervical cancer patients were managed for pain appropriately (92.91%) according to the WHO analgesic ladder. Pain scores within 48 hours after pain medication decreased by 3.77 points from before the medication with statistical significance (*P*-value < 0.001). Pain score was predicted by cancer stage, tumor size, number of metastasized organs, and number of underlying diseases, with 23.10% variance explained. 5-year survival rate was 65.40% close to that of the study in Malaysia.

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References

1. World Health Organization. Cervical cancer awareness month 2022. 2022. (Accessed on Feb. 1, 2023, at https://www.emro.who.int/fr/noncommunicable-diseases/campaigns/cervical-cancer-awareness-month.html)
2. National Cancer Institute, Department of Medicine and the Thai Association for the Study of Pain. Management for cancer pain. Bangkok. Thanapress, 2022: pp.15-38. (in Thai)
3. Laowahutanont P, Chaiweerawattana A, Imsamran W. Guidelines for cervical cancer screening, diagnosis and treatment. Bangkok. Kosit Printing, 2018: pp.45-52. (in Thai)

4. Cancer.Net. Cervical cancer: Introduction. 2023. (Accessed on Feb. 17, 2023, at https://www.cancer.net/cancer-types/cervical-cancer/introduction)
5. WHO. WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. 2018. Geneva, Switzerland. (Accessed on Feb. 17, 2023, at https://www.who.int/publications/i/item/9789241550390)
6. Jensen MP, Martin SA, Cheung R. The meaning of pain relief in a clinical trial. *J Pain* 2005;6(6):400-406.
7. Goel S, Singh U, Qureshi S, et al. Evaluation of WHO guided pain management protocol in cases of cancer cervix**.** *Indian J Pain* 2015; 29(1):32-35.
8. Missair A, Cata JP, Votta-Velis G, et al. Impact of perioperative pain management on cancer recurrence: an ASRA/ESRA special article. *Reg Anesth Pain Med* 2019;44:13-28. (doi: 10.1136/rapm-2018-000001)
9. Stanca M, Capilna ME. Prognostic factors associated with 5-year overall survival in cervical cancer patients treated with radical hysterectomy followed by adjuvant concurrent chemoradiation therapy at a tertiary care center in Eastern Europe. *Diagnostics (Basel)* 2021; 11(3):570. (doi: 10.3390/diagnostics11030570)
10. Muhammad NA, Kamaluddin MA, Adon MY, et al. Survival rate of cervical cancer in Malaysia. *Asian Pac J Cancer Prev* 2015;16(7): 3067-3072.
11. Bangsomboon P. Survival rate of cervical cancer patients according to the 2018 FIGO staging system: a tertiary hospital based study Vajira Hospital, Bangkok. *Thai J Obstet Gynecol* 2022;30(1):60-67.
12. Kefale B, Engidaw MT, Tesfa D, Molla M, Yismaw MB. Management practice and drug related problems and its contributing factors among cervical patients at oncologic center in Ethiopia: a hospital –based retrospective study. *Ther Clin Risk Manag* 2022;18:643-655.
13. Sheanakul C, Manusirivithaya S, Tantiwattana T, Nakwong L. Results of invasive cervical cancer treatment at BMA medical college and Vajira Hospital. *Vajira Med J* 2003;47(2):93-102. (in Thai)
14. Jamora KE, Castillo MRL, Calagvas MJC. Assessment of the prevalence of pain, adequacy of pain management and influencing factors in patients undergoing radiotherapy. *Ecancermedicalscience* 2019;16: 1483. (doi: 10.3332/ecancer.2022.1483)
15. Mcneill R, Boland JW, Wilcock A, Sinnarajah A, Currow DC. Non-steroidal anti-inflammatory drugs for pain in hospice/palliative care: an International Pharmacovigilance study. *BMJ Support Palliat Care* 2023. (doi: 10.1136/spcare-2022-004154)
16. Shao YY, Lin CP, Chen HM, et al. Fentanyl patch is the most common strong opioids in Taiwan cancer patients. supportive and palliative care. *Ann Oncol* 2015;26(suppl 9):120. (doi: 10.1093/annonc/ mdv531.34)
17. Kumkaew J, Siripun P, Areepium N. Postoperative pain management in adult abdominal surgical patients in general surgical department, Nopparat Rajathanee Hospital. *Thammasart Med J 2015;*15(1):80-90. (in Thai)
18. Dipiro JT, Talbert RL, Yee GC, Matzhe GR, Wells BG, Posey LM. Pharmacotherapy a pathophysiologic approach, 10e (online book). McGraw-Hill Education, 2020. (Accessed on Mar.14, 2023, at https://accesspharmacy.mhmedical.com/book.aspx?bookID=1861)