



# Prescribed medications for alleviating suffering symptoms in patients receiving palliative care at a tertiary care hospital

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**Background:** Recognizing and appropriately treating symptoms of suffering in patients receiving palliative care is a means to enhance the quality of life for both the patient and their family. The objective of this study was to determine the proportion of pharmacological treatments for symptoms of suffering and prescribing patterns in hospitalized patients receiving palliative care at a tertiary care government general hospital.

**Methods:** This retrospective study was conducted at the Prachuapkhirikhan Hospital, Thailand. All patients over 18 years old who were admitted to the hospital and received palliative care were included. Data were collected from medical charts and analyzed using descriptive statistics.

**Results:** During the 3-year period of study, 296 admissions were included. Cancer, cardiovascular disease, and infectious disease were the top three primary diseases for which patients received palliative care. Dyspnea was the most reported symptom of suffering (81.08%), followed by fatigue, constipation, and pain (41.89%, 35.14%, and 25.34%, respectively). All cases experienced fatigue, depression, insomnia, and anxiety received pharmacological treatment. Dyspnea, pain, nausea/vomiting, delirium, and malignant bowel obstruction were treated in at least 80% of the cases experiencing suffering. Constipation, diarrhea, and anorexia/cachexia were treated in approximately 66.35%, 78.57%, and 67.86% of the cases, respectively. Strong opioids were the most commonly used medication for the treatment of dyspnea or pain.

**Conclusions:** Our study revealed that suffering symptoms were routinely identified in hospitalized palliative care patients. Pharmacological treatments were prescribed to manage most of these symptoms. However, there is a need to improve the quality of assessing suffering symptoms severity to enhance their effectiveness.

**Keywords:** Palliative care; treatment; suffering symptoms; prescribed pattern

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## Introduction

Palliative care is an interdisciplinary approach to patients with serious illnesses and their family, focusing on improving quality of life through measures including symptom management, quality communication, and assistance navigating complex medical decisions (1). Palliative symptom management addresses not only

the physical aspect of suffering symptoms but also the psychological, social, and spiritual dimensions of suffering for total symptom relief (2). High-quality symptom assessment and management are fundamental to providing positive outcomes for palliative care patients and their families (3).

In Thailand, palliative care has been developing since the late 1990s and increasingly received attention from

government organizations (4). However, palliative care has not been fully integrated into the Thai public health system and has a limited range of services (5). Furthermore, there is a shortage of palliative care specialists, including physicians, nurses, and pharmacists, particularly in tertiary care government hospitals. Additionally, issues such as drug availability and equitable access to treatment remain problematic. A national survey in 2012 revealed that essential drugs for palliative care, particularly opioids, were not appropriately distributed in Thai government hospitals (6). Concerning hospitalized patients in tertiary care government hospitals in Thailand, nearly 20% were palliative care patients (7). Of these, only 20% received a specialist palliative care consult, and one-quarter of patients with pain were not received analgesics. Thus, improvements in palliative care services are still required with regards to structure and access to opioids (5,8). In addition to pain and dyspnea, there is a lack of information about pharmacological treatment for other suffering symptoms.

Therefore, the objective of this study was to determine the proportion of pharmacological treatment of suffering symptoms and prescribing patterns in hospitalized patients who received palliative care at a tertiary care government general hospital in Thailand. We present this article in accordance with the STROBE reporting checklist (available

at <https://apm.amegroups.com/article/view/10.21037/apm-24-52/rc>).

## Methods

The study was a retrospective descriptive study conducted at Prachuapkhirikhan Hospital; one of the tertiary care government general hospitals in Thailand. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethical approval was obtained from the ethics committee of Prachuapkhirikhan Hospital (No. PKHREC 003/62), and the ethics committee of Faculty of Dentistry and Faculty of Pharmacy, Mahidol University (No. MU-DT/PY-IRB 2019/052.1508). Individual consent for this retrospective analysis was waived.

All patients aged over 18 years old who admitted to the hospital between April 1, 2016, and March 31, 2019, and received palliative care (ICD-10 Z515) as determined by their physician were included in the study. Patients were recruited if they met at least one of the following palliative care screening criteria: (I) patients who experienced a decrease in their activity of daily living by more than 50%, as assessed by Palliative Performance Status (PPS), Karnofsky Performance Score (KPS), or Eastern Cooperative Oncology Group (ECOG); (II) patients with multiple comorbidities; (III) patients in advanced stages of disease, with uncontrollable disease and uncomfortable complication; (IV) terminal delirium; (V) cachexia or continuous weight loss of  $\geq 10\%$  during the previous 6 months, or serum albumin levels consistently below 2.5 mg/dL; (VI) persistent hypercalcemia; (VII) unresponsive to treatment for specific diseases; (VIII) patients and/or their family who decided to discontinue full treatment for specific comorbidities; (IX) patients with frequent unexpected admissions; and (X) patients affected by circumstances such as serious falls, situations of functional loss situations, or hospital admissions. Patients were excluded if they died within 24 hours of admission or if their suffering symptoms and/or treatment of these symptoms were not recorded.

All data were extracted from the patients' medical charts, including age, sex, primary diagnosis for receiving palliative care, comorbidities, time since palliative care was provided, and suffering symptoms [which included ten physical symptoms (dyspnea; fatigue; constipation; pain; nausea/vomiting; anorexia/cachexia; sleep wake disturbances; diarrhea; delirium; and malignant bowel obstruction), and two psychological symptoms (depression and anxiety)]. All

### Highlight box

#### Key findings

- Our study revealed that symptoms in hospitalized palliative care patients were routinely identified and treated with medication, but there was still a lack of comprehensive assessment of their severity.

#### What is known and what is new?

- There is abundant data regarding the pharmacological treatment of each symptom in palliative care patients, but limited information on the prescribing patterns of these treatments in our setting.
- This research highlights that all symptoms in palliative care patients are well-recognized and adequately managed with pharmacological treatment by non-palliative care specialist physicians in tertiary care hospitals.

#### What is the implication, and what should change now?

- There is a need to heighten awareness and provide early palliative care to target patients in tertiary care hospitals to achieve better care outcomes.
- Efforts should be directed towards improving the assessment of symptom severity, particularly for dyspnea and pain, to ensure comprehensive and effective management.

**Table 1** Demographic data of 296 hospital admissions

Characteristics	Value (n=296)
Sex (male), n [%]	163 [55]
Age (years), mean $\pm$ SD	67.69 $\pm$ 14.77
Primary disease, n [%]	
Cancer	110 [37.16]
Cardiovascular	64 [21.62]
Infection	56 [18.92]
Respiratory tract	23 [7.77]
Renal	14 [4.73]
Neurological	10 [3.38]
Hepatic	9 [3.04]
Miscellaneous	10 [3.38]
Number of comorbidities per event, mean $\pm$ SD	3.23 $\pm$ 1.98
Number of suffering symptoms per event, mean $\pm$ SD	2.27 $\pm$ 1.34
Intend to receive palliative care, n [%]	
By willingness of patients or primary caregivers	197 [67]
By consent of "do not resuscitate"	99 [33]
Discharge status, n [%]	
Alive	125 [42.2]
Dead	164 [55.4]
Refer	7 [2.4]
Length of stay (days), mean $\pm$ SD	14.32 $\pm$ 13.43
Duration of palliative care per admission (days), mean $\pm$ SD	9.00 $\pm$ 10.54

SD, standard deviation.

suffering symptoms were identified using the definition of the World Health Organization (WHO). Their respective treatment of each suffering symptom was extracted from the medical charts, including type of medication, dosage regimen, route of administration, and medication adjustment. All prescribed medications and their indications for individual suffering symptoms were recorded in the doctor's order sheet. However, if not stated in the doctor's order sheet, the indications could be found in the nurse's note. Treatment was categorized into two groups: causative treatment and symptomatic treatment. Causative treatment was defined as treatment focused on the underlying cause

of each symptom. If the underlying cause could not be indicated, the treatment was classified as symptomatic treatment. Individual data were collected using a code system to prevent identification of individual patients.

### *Measured outcomes and statistical analysis*

The study outcome was the proportion of pharmacological treatment and prescribing patterns for each symptom. The frequency of each suffering symptom, calculated as period prevalence, was also analyzed. Descriptive statistics were employed, and data were expressed as percentages or mean with standard deviation (SD).

## **Results**

The analysis included 296 admission events. The majority of patients were male (55%), with an average age of 67.69 $\pm$ 14.77 years. Approximately 67% of patients or their primary caregivers expressed willingness to receive palliative care upon admission (*Table 1*). The top three primary diseases for which palliative care was sought were cancer (37.16%), cardiovascular disease (21.62%), and infection (18.92%), respectively. A majority of them were admitted to the hospital for the first time following their primary diagnosis. The average hospital stay duration was 14.32 $\pm$ 13.43 days, whereas the average duration of palliative care during admission was 9.00 $\pm$ 10.54 days. Regarding discharge status, 55.4% died during their admission.

Suffering symptoms were reported in 290 admission events (97.97%), and the frequency of each suffering symptom is presented in *Table 2*. Dyspnea was the most commonly reported symptom (81.08%), followed by fatigue, constipation, pain, and nausea/vomiting (41.89%, 35.14%, 25.34%, and 11.49%, respectively). Concerning the treatment of suffering symptoms, all patients who complained with fatigue, insomnia, depression, and anxiety received pharmacological treatment (*Table 2*). Treatment of fatigue focused on correcting underlying causes such as anemia, electrolyte imbalance, and hypoglycemia. Selective serotonin reuptake inhibitors and benzodiazepines were used to treat depression, insomnia, and anxiety. Dyspnea, pain, nausea/vomiting, delirium, and malignant bowel obstruction were treated in at least 80% of each symptom. Remaining suffering symptoms, including constipation, diarrhea, anorexia/cachexia, and sedation, were treated in at least 50% of cases.

Focusing on dyspnea, nearly all patients with dyspnea

**Table 2** Frequency and treatment status of individual suffering symptom (n=296)

Suffering symptom	Frequency (%)	Number of patients received treatment (%)			Number of patients who received treatment (%)
		Total	Causative treatment <sup>†</sup>	Symptomatic treatment <sup>†</sup>	
1. Dyspnea	240 (81.08)	239 (99.58)	104 (43.51)	135 (56.49)	1 (0.42)
2. Fatigue	124 (41.89)	124 (100.00)	124 (100.00)	0	0
3. Constipation	104 (35.14)	69 (66.35)	1 (1.45)	68 (98.55)	35 (33.65)
4. Pain	75 (25.34)	74 (98.67)	3 (4.05)	71 (95.95)	1 (1.33)
5. Nausea/vomiting	34 (11.49)	31 (91.18)	4 (12.90)	27 (87.10)	3 (8.82)
6. Anorexia/cachexia	28 (9.46)	19 (67.86)	15 (78.95)	4 (21.05)	9 (32.14)
7. Sleep wake disturbances	22 (7.43)	21 (95.45)	1 (4.76)	20 (95.24)	1 (4.55)
7.1 Insomnia	20 (6.76)	20 (100.00)	0	20 (100.00)	0
7.2 Sedation	2 (0.68)	1 (50.00)	1 (100.00)	0	1 (50.00)
8. Diarrhea	14 (4.73)	11 (78.57)	11 (100.00)	0	3 (21.43)
9. Delirium	11 (3.72)	9 (81.82)	0	9 (100.00)	2 (18.18)
10. Depression	10 (3.38)	10 (100.00)	0	10 (100.00)	0
11. Malignant bowel obstruction	5 (1.69)	4 (80.00)	0	4 (100.00)	1 (20.00)
12. Anxiety	4 (1.35)	4 (100.00)	0	4 (100.00)	0

<sup>†</sup>, the percentages were calculated based on the total number of cases that received treatment.

(n=239, 99.58%) received pharmacological treatment. Of these, 104 admissions (43.51%) receiving treatment for underlying conditions contributing to dyspnea, such as respiratory tract infection, congestive heart failure, ascites, and acute exacerbation of chronic obstructive pulmonary disease. Meanwhile, 135 admissions (56.49%) received symptomatic treatment specifically targeting dyspnea. In terms of the pharmacological treatment pattern for relieving dyspnea, 14.8% received only an as-needed regimen, while 85.2% received around-the-clock (ATC) regimen (*Figure 1*). Strong opioids, including morphine intravenous infusion (IVIF; 61/135) and midazolam IVIF (21/135), were the most frequent treatments as part of the ATC regimen for dyspnea (45.19%, and 15.56%, respectively). Only 23.7% (32/135) received both the ATC regimen and breakthrough regimen.

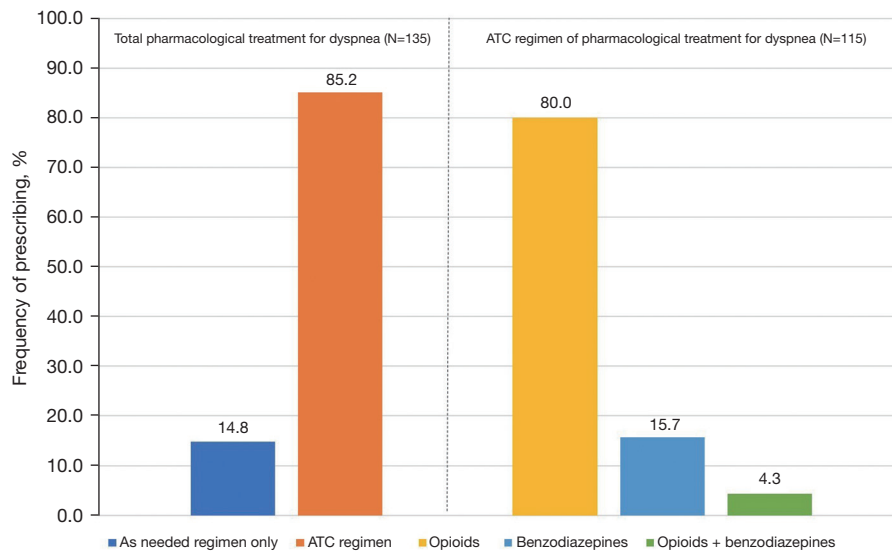
For the treatment of pain, there were 71 admissions that received symptomatic treatment, but only 38 admissions (53.5%) recorded pain score using the numerical rating scale before initiating treatment. Most of these cases involved nociceptive type of cancer pain, with 14 cases experiencing moderate pain and 11 cases experiencing severe pain. Only half of the 38 admissions received ATC

regimens of analgesics (*Figure 2*). Among these, the majority (84.2%) received strong opioids which was morphine IVIF or sustained release tablet. Few received adjuvant analgesics predominantly gabapentin and amitriptyline. Focusing on cases with moderate and severe pain, 50% of patients experiencing moderate pain and 15.8% experiencing severe pain still received only as-needed regimen of opioids.

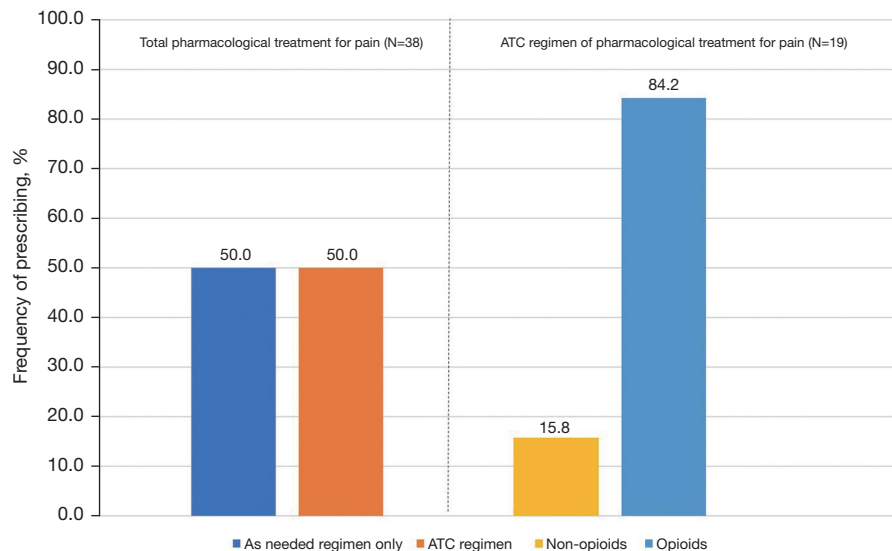
Regarding constipation, it was found that 36 out of 104 cases (34.6%) were caused by opioid use [opioid-induced constipation (OIC)]. Among these, 89% (32 out of 36) received laxatives, predominantly sennosides, magnesium sulfate, and lactulose. Meanwhile, 8.3% (3 out of 36) received ispaghula husk, a bulk-forming laxative.

## Discussion

This retrospective study aimed to assess the prevalence of pharmacological treatment for suffering symptoms in patients admitted to inpatient units at Prachuapkhirikhan Hospital who were diagnosed to receive palliative care by their primary physicians. Since there are no palliative care specialist physicians or other healthcare professionals specializing in palliative care in our hospital, treatment



**Figure 1** Pharmacological treatment pattern for relieving dyspnea (n=135) and medications used as ATC regimen (n=115). ATC, around-the-clock.



**Figure 2** Pharmacological treatment pattern for relieving pain (n=38) and medications used as ATC regimen (n=19). ATC, around-the-clock.

related to suffering symptoms is managed by general physicians or specialists in other areas. The characteristics of our patients, including age, primary diagnosis, and suffering symptoms, are consistent with reports from the WHO (9).

Concerning the prevalence of distinct suffering symptoms, dyspnea or shortness of breath was the most

common complaint in our study, which differs from previous studies in cancer patients where pain and fatigue are commonly reported (10-14). This variation may be attributed to our focus on patients admitted to inpatient units. Therefore, dyspnea, as a debilitating symptom that significantly impacts patients' activities of daily living and quality of life (15), was the primary reason for hospital



admission in our study. However, following dyspnea, other suffering symptoms such as fatigue, constipation, pain, and nausea/vomiting were also observed, which aligns with findings from other studies.

Tragically, most of our patients received palliative care when they were already in the advanced stages of disease. As a result, more than half of them passing away in the hospital, with an average duration of palliative care of about 9 days. This late implementation of palliative care in our patients led to negative outcomes. Current evidence suggests that early palliative care interventions, ideally initiated at least 6 months before death, in advanced cancer patients are associated with more favorable outcomes compared to late implementation (16-18). Given its significance, there is a need for multidisciplinary collaboration in palliative care between non-palliative care physicians and other healthcare specialists such as nurses or pharmacists. This collaboration should involve structured intervention conversation about palliative care (19-24).

With respect to pharmacological treatment for suffering symptoms, it involves addressing the underlying cause(s) and relieving symptom severity to enhance patient comfort. Fatigue, a complex symptom commonly experienced by advanced cancer patients (25), can result from the disease itself, received treatments, and various chronic physical or psychological comorbid conditions, such as anemia, pain, depression, anxiety, cachexia, sleep disturbance, and immobility. These factors lead to biochemical changes in the body, including increased proinflammatory cytokines, growth factors, circadian rhythm modulation, disruption of the hypothalamic-pituitary-adrenal (HPA) axis, serotonin dysregulation, vagal-afferent activation, anemia, and abnormalities in the generation or utilization of adenosine triphosphate (26,27). In our study, patients presenting with fatigue had their underlying causes identified (anemia, electrolyte imbalance, and hypoglycemia), and all received specific treatment targeting these causes. Additionally, regarding depression and anxiety, all our patients received pharmacological treatment. This is because our physicians are experienced in managing these symptoms and frequently prescribe antidepressants and benzodiazepines in their practice.

Concerning treatment of dyspnea, one patient in our study did not receive any treatment for dyspnea due to refusal of all interventions. Dyspnea can stem from various potential causes, which can be categorized into tumor-related and non-tumor causes. For non-tumor causes, patients received specific treatment targeting these underlying causes,

which is the initial step in managing dyspnea. For those whose dyspnea cannot be corrected, oral and parenteral opioids are considered the mainstay of treatment regardless of the cause (28). Opioids act on mu receptors, reducing air hunger discomfort, decreasing spontaneous respiratory drive, and reducing the sensitivity of the central breathing center (29). Effective relief can be achieved with low doses of oral morphine, typically around 10 mg daily. In general, a ceiling effect is typically observed beyond a daily dosage of around 30 mg of oral morphine (30).

In our study, the median dose for ATC regimen of IVIF morphine was 1 mg/hour, equivalent to about 72 mg of oral morphine daily. This dosage may appear higher than recommended, but it is important to note that our patients were in advanced stages of disease and may have been in the end-of-life period. In addition, not all patients with dyspnea received ATC regimens of opioids. A systematic review by Jennings *et al.* revealed that using 24-hour acting oral or parenteral opioids could significantly improve dyspnea intensity both in the morning and evening (31). Hence, the treatment regimen for dyspnea should ideally include both ATC regimen and as-needed regimen, as found in our study at a rate of 23.7%.

However, some dyspnea patients in our study received benzodiazepines, specifically IVIF midazolam, instead of opioids. The role of benzodiazepines in managing dyspnea remains less clear (32). Benzodiazepines should be considered for dyspnea in the presence of clear concomitant anxiety significantly contributing to the patient's experience of dyspnea, or after an opioid has undergone a reasonable therapeutic trial (28). Unfortunately, we could not assess the rationale behind the use of benzodiazepines in these scenarios due to the retrospective nature of our chart review study.

Regarding pain management, it is considered that approximately half of the patients who presented with pain did not receive appropriate pain assessments, especially in terms of identifying the type of pain and assessing pain severity at baseline. This issue persists within the palliative care service of government hospital in Thailand (5,7). Each patient should be treated individually, as their pain management may require different dosages and/or interventions to achieve effective symptom relief. Without this essential information, it is impossible to determine the appropriateness of analgesic prescriptions according to the WHO analgesic concept (33,34).

The primary goal of good pain management is to minimize the patient's pain and the need for breakthrough

medication. However, a similar trend was observed in opioid prescribing for dyspnea. Only half of our patients who presented with pain and had baseline pain assessments received the ATC regimen, while the remainder did not. This latter group included patients who complained of nociceptive pain with moderate and severe intensity. These patients should receive their pain medicines throughout the day through an ATC regimen, either via intravenous administration or sustained release preparations. This approach allows for continuous pain relief and minimizes the episodes of pain the patient may suffer throughout a 24-hour period (35).

Indeed, while opioids are effective in managing dyspnea and pain, they are linked with various adverse events, including OIC. OIC can persist throughout the duration of opioid treatment and significantly impact the quality of life for palliative patients. Opioids contribute to constipation by impairing propulsive and peristalsis movements, inhibiting intestinal mucosal secretion, enhancing intestinal fluid absorption, and impairing anal sphincter function (36). As a result, stimulant laxatives and osmotic laxatives are typically recommended as the first-line treatment for OIC. It is important to note that some of our patients received ispaghula husk, a bulk-forming laxative, is not effective for treating OIC (37). It may exacerbate abdominal pain and potentially contribute to bowel obstruction (38). Therefore, clinicians should exercise caution when prescribing bulk-forming laxatives and consider alternative treatments for OIC in palliative care patients receiving opioids. In addition, treatment for constipation was primarily provided when patients experienced symptoms (68 out of 69 cases received laxatives for symptomatic treatment). However, if the constipation was mild, the treatment did not be initiated even if the patient received opioid. This finding reflects actual clinical practice in our setting. Thus, healthcare providers should be mindful in treating and preventing constipation, especially when opioid have been prescribed.

Our study has some limitations. Firstly, the findings are based on a retrospective study conducted at a single tertiary care hospital in Thailand. This could restrict the generalizability of our results to other regions within Thailand, as well as to countries with different healthcare structures. Secondly, some crucial baseline characteristics of our participants are incomplete due to the retrospective chart review study design. These data, especially severity of each suffering symptoms, could offer valuable insights into the medication patterns used to alleviate suffering symptoms in individual patients. Additionally, clinical outcomes

after receiving pharmacological treatments could not be evaluated due to incomplete and unsystematic records. Accordingly, a prospective study design with multicenter collaboration would be beneficial. Furthermore, our result can inform the development of hospital policies aimed at enhancing palliative care services, specifically in establishing multidisciplinary healthcare teams for palliative care.

## Conclusions

This retrospective study revealed that palliative care in our tertiary care hospital primarily targeted patients with cancer, cardiovascular disease, and infectious disease. Dyspnea emerged as the most frequently reported suffering symptom. While more than 50% of all suffering symptoms received pharmacological treatment, the lack of comprehensive assessment of symptoms severity remained a significant concern.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://apm.amegroups.com/article/view/10.21037/apm-24-52/rc>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (Available at <https://apm.amegroups.com/article/view/10.21037/apm-24-52/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related

to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Prachuapkhirikhan Hospital (No. PKHREC 003/62), and the ethics committee of Faculty of Dentistry and Faculty of Pharmacy, Mahidol University (No. MU-DT/PY-IRB 2019/052.1508). Individual consent for this retrospective analysis was waived.

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