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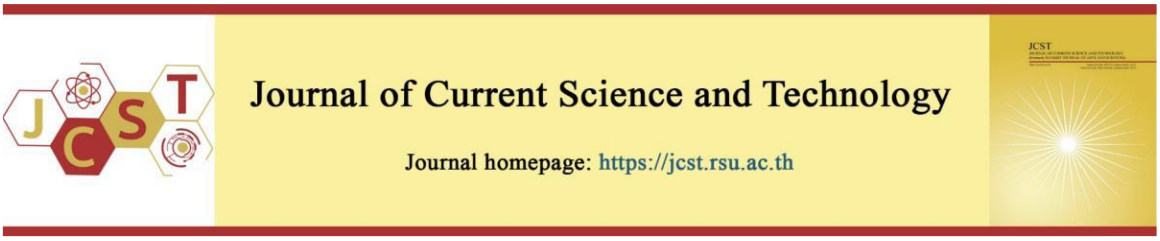

Survival Rates, Quality of Life and Side Effects of Medical Cannabis in Patients with Palliative Cancer in Thailand

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Abstract

This study aimed to compare clinical outcomes and safety in patients with palliative cancer who used cannabis and morphine across dimensions such as survival rate, hospital admission rate, number of hospital days, quality of life, and side effects. A retrospective cohort observational study was conducted based on medical records from January 1, 2020 – March 30, 2023. Additionally, a prospective cohort study was conducted using the EQ-5D-5L and Edmonton Symptom Assessment System (ESAS) quality of life scales. The study included 98 cancer patients receiving palliative care in six hospitals. The results showed that the median survival time of the cannabis group (CG) was 0.69 years, and the morphine group (MG) was 0.52 years ($p = 0.168$). The CG had a lower hospital admission rate than the MG, $p>0.05$. The CG had fewer number of hospital days than the MG, $p<0.05$. The quality of life (QOL) assessment by ESAS indicated that the CG had a better QOL than the MG, $p<0.05$. The EQ-5D-5L tool also demonstrated that the QOL score for the CG was higher than that of the MG, $p<0.05$. The MG had higher levels of liver enzymes, including AST and ALT than those who received cannabis, $p<0.05$. These findings suggest that medical cannabis may be beneficial for palliative cancer patients.

Keywords**:** *survival rates; quality of life*; *side effects; medical cannabis; morphine; palliative cancer; EQ-5D-5L; ESAS*

1. Introduction

Cancer became the leading global cause of mortality in 2020, resulting in over 10 million deaths, accounting for one in six of all recorded deaths. The most prevalent cancer types worldwide include breast cancer, lung cancer, colon cancer, rectal cancer, and prostate cancer. Notably, approximately one-third of all cancer-related deaths are attributed to various risk factors, including cigarette smoking, a high body mass index, excessive alcohol consumption, insufficient

fruit and vegetable intake, and a sedentary lifestyle. It's also worth mentioning that in low- and lower-middle-income countries, cancer-causing factors such as human papillomavirus (HPV) infection and hepatitis contribute to approximately 30% of all cancer cases (World Health Organization, 2025).

Thailand, specifically, bears a substantial burden of cancer, with an annual incidence of 185,000 cancer cases (International Agency for Research on Cancer, 2022), positioning it as the fifth most cancer-prevalent country in Southeast Asia. According to the World Health Organization, cancer incidence is projected to increase by 12.6 million cases, with a corresponding rise in cancer-related deaths by 2040 (International Agency for Research on Cancer, 2024).

The most commonly reported signs and symptoms among cancer patients include insomnia (67.5%), dry mouth (66.3%), changes in self-perception or identity (65.1%), pain (61.4%), fatigue, low energy levels, and weight loss (60.2%). Among these, symptoms that significantly contribute to the suffering of cancer patients are pain, insomnia or sleep disturbances, fatigue, weakness, constipation, and a diminished appetite or anorexia (Taweeyanyongkul, 2015).

Pain, in particular, plays a central role in diminishing the quality of life for individuals with cancer. It is a distressing symptom that not only affects the physical aspect but also has a profound impact on one's emotional state, thoughts, ability to work, and daily activities (World Health Organization, 2020). Addressing and managing these symptoms effectively is a crucial aspect of palliative care for cancer patients, aimed at improving their overall well-being and comfort.

Opioids, particularly morphine, are the standard treatment in palliative cancer care. For patients who are intolerant to morphine's side effects, cannabis offers an alternative (Sena et al., 2023). Common morphine side effects include constipation (35%), nausea/vomiting (25%), and somnolence (22%) (Alonso, 2017). A study on stage III patients (58.6% of survivors) found effective pain control and improved quality of life, including mood, function, social interaction, and symptom relief (Alonso, 2017). Cannabis may provide a valuable alternative for some patients in palliative care.

Cannabis sativa L., which originates from Asia, has a 5,000-year history of medicinal use. Traditional Thai medicine texts like "Ya-San-Tha-Khat-Klon-Haeng," "Ya-Tham-Lai-Phra-SuMeru," and "Ya-Suk-Sai-Yat" document the use of cannabis in treating muscle problems, insomnia, and loss of appetite (Ministry of Public Health, 2021).

Cannabis contains approximately 400 therapeutic compounds, including delta-9-tetrahydrocannabinol (THC), cannabidiol (CBD), terpenoids, flavonoids, and alkaloids. THC and CBD influence the nervous system, hormones, and immunity through the endocannabinoid system. Clinical studies, have demonstrated that cannabinoids can effectively reduce neuropathic pain intensity, alleviate allodynia-induced peripheral neuropathy, and improve sleep quality in chronic pain patients (Appendino et al., 2011; Lynch et al., 2014; Serpell et al., 2014; Chompubai et al., 2023; Charoenying et al., 2023; Nimmaanrat, & Maneewat, 2021; Seevathee et al., 2024; Thaenkham et al., 2023).

Sativex is the brand name for a cannabis-based drug called nabiximols and THC aerosol have been shown to be safe for long-term use and effectively alleviate chronic pain in cancer patients (Johnson et al., 2013). Vaporized cannabis with 1.29% or 3.53% THC demonstrated comparable efficacy in reducing neuropathic pain (Wilsey et al., 2013). Combining Sativex with standard opioid therapy significantly reduces chronic pain in cancer patients with secondary pain syndromes (Portenoy et al., 2012). Both Sativex and THC spray, used alongside standard opioid therapy for two weeks, can reduce chronic pain severity in cancer patients (Johnson et al., 2010). Additionally, smoking cannabis has been reported to significantly relieve chronic neuropathic pain, improve sleep, and reduce anxiety (Ware et al., 2010).

In 2020, Thailand's Ministry of Public Health implemented a policy that authorized the use of cannabis oil and traditional Thai medicines containing cannabis for the treatment of palliative cancer patients in hospitals across the country.

According to the report, there was a 28.66% improvement in the quality of life, with 23.93% remaining unchanged, 7.42% deteriorating, and 39.99% unspecified. Treatment outcomes showed a 30.69% improvement, 20.59% remained unchanged, 7.41% deteriorated, and 41.3% were unspecified (Food and Drug Administration Ministry of Public Health, 2023).

The top five reasons for prescribing cannabis to patients include insomnia, pain, malignant tumors (cancer), and migraines. The most common adverse reactions, including dizziness, dry mouth, dry throat, dizziness, and nausea, were not severe and occurred very rarely, affecting only 5% or 434,286 patients (Food and Drug Administration Ministry of Public Health, 2023). Additionally, there was no comparison

between cannabis-using patients and those who didn't use cannabis in the studies reviewed.

A significant dilemma in hospitals is the lack of access to medical cannabis for palliative care patients. Research indicates that most patients obtain their medications outside the public health system (Thaenkham et al., 2023).

Consequently, there's a lack of information regarding the proper use of cannabis, making it crucial to investigate its usage among cancer patients. One knowledge gap pertains to the absence of head-to-head comparative data between cannabis and the standard care involving morphine.

Our research program will also investigate cannabis use outside hospital settings and analyze the number of patient visits to a doctor and hospitalization days, aspects not explored in the previous project. Our study aims to compare clinical outcomes and safety between cancer patients using cannabis and morphine, focusing on survival rates, hospital admission rates, length of hospitalization, quality of life, and side effects, providing a comprehensive comparison of these two treatments.

Cannabis is a relatively new treatment option for cancer, lacking the extensive empirical evidence of morphine. Therefore, a direct comparison with standard opioid therapy is necessary. Pain, the most debilitating symptom in palliative cancer patients, greatly diminishes their quality of life, causing insomnia, stress, anxiety, frequent hospitalizations, and prolonged stays. Effective pain management not only enhances comfort but may also improve overall survival. The expected outcome of this study is to gain insights into the clinical effects of medical cannabis on cancer patients, including survival rate, hospital admissions, duration of hospital stays, quality of life, and side effects. The findings will offer healthcare professionals evidence-based guidance in assessing the viability of cannabis as a complementary or alternative treatment for palliative cancer patients.

2. Objective

To compare clinical outcomes and safety among cancer patients who used cannabis and morphine in dimensions such as survival rate, hospital admission rate, number of hospital days, quality of life, and side effects.

3. Materials and Methods

3.1 Study Design, Study Site and Participants

3.1.1 Participants

Participants were recruited from 6 hospitals in northeastern part of Thailand including Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen Province; Sirindhorn Hospital, Khon Kaen Province; Yangsisurat Hospital, Maha Sarakham Province; Phra Ajarn Fan Acharo Hospital, Sakon Nakhon Province; Phon Hospital, Khon Kaen Province; and Nong Han Hospital, Udon Thani Province.

The sample size was calculated using the application N4studies. The platform provides a variety of features aimed at simplifying the process of determining sample sizes and conducting power calculations for a wide range of epidemiological study designs (Ngamjarus, 2016). When comparing n4Studies to other applications, it covers a wider spectrum of epidemiological study designs. When using identical parameters, n4Studies yields results that are comparable to those obtained with other statistical software tools, including STATA, the epical package in R, PS, G*Power, and OpenEpi (Ngamjarus, 2016). A literature review found that 491 cancer patients were divided into two groups: a group that received standard treatment and a group that received cannabis treatment. The survival rate among cancer patients receiving standard treatment was 20%, and among patients receiving cannabis treatment was 48.63% (Phansila et al., 2022). The probability of survival in the study and control groups was obtained from a previous study. The output of the sample size calculation from n4Studies: For a cohort study with binary outcome P (outcome/ exposure) = 0.200, P (outcome/ un-exposure) = 0.486, Ratio (r) = 1.000, Alpha (α) = 0.05, Z (0.975) = 1.959964, Beta (β) = 0.20, Z (0.800) = 0.841621. Sample size by using a continuity correction: Exposures = 49, Un-exposures = 49 (Bernard, 2000).

The patients were divided into two groups: the cannabis group, consisting of 49 individuals, and the morphine group, also comprising 49 individuals. This refers to a palliative cancer patient receiving treatment either within a hospital or in the community, with the oversight of a medical doctor and a multidisciplinary healthcare team, while specifically selecting a particular sample for study or analysis. The cannabis group encompassed patients who either utilized all forms of cannabis provided by the hospital or independently used cannabis. The morphine group was composed of patients who were exclusively receiving various types of morphine treatments provided by the hospital.

The inclusion criteria for this study stipulated that participants had to meet all of the following

requirements: aged 18 years or older, diagnosed with palliative cancer affecting any body system, undergoing treatment with either cannabis or morphine methods, received treatments between January 1, 2020, and March 30, 2023, possess Thai nationality, Palliative Performance Scale (PPS) of 70% or higher and provide informed consent to participate in the research project.

"Use" means that palliative cancer patients must consistently use either morphine or cannabis throughout the study period. Patients who do not use either cannabis or morphine continuously will be excluded from the study from the outset.

The exclusion criterion for this study was a patient's request to withdraw before the project was completed. During the study, the patient must not participate in any other research projects or receive additional treatments or palliative care, such as surgery, radiation, chemotherapy, herbal therapy, etc. If the patient uses any treatments other than morphine or cannabis provided by the hospital, or uses cannabis independently, they will be immediately excluded from the research project.

3.1.2 Study Design

A retrospective cohort observational study was conducted based on medical records from January 1, 2020 – March 30, 2023. A prospective cohort study was also conducted using the EQ-5D-5L and The Edmonton Symptom Assessment System (ESAS) quality of life scales. The hospitalization outcomes and survival assessments were conducted in retrospective and prospective cohorts.

Secondary data from hospital medical records were used in this study after obtaining approval from the hospital director. To safeguard patient privacy, the database was anonymized, ensuring that the information of individual patients could not be traced. The study's results do not contain direct references to any specific individual. In both the retrospective and prospective cohorts, informed consent was obtained from patients on the first day of the project. Patients were required to be under prospective care for a duration of 30 days. The study concluded on March 30, 2023.

The author began data collection after obtaining consent from the patients, as follows: reviewing medical records; survival rate, number of hospital admissions, and number of days spent in the hospital. Data collection started from the date the patient was diagnosed for palliative care and continued until the patient's death or the last day of the research project, which was March 30, 2023. The ESAS and EQ-5D-5L assessments were conducted twice using questionnaires: the first immediately after the patient provided consent, and the second on the 30th day of participation in the research project. The patients were not required to be admitted to the hospital for 30 days to participate in the study.

The blood test results were retrieved from the hospital's medical records, as ordered by the doctor according to the treatment plan. The study did not collect additional blood samples. the first at the time the patient began using morphine or cannabis, and the second being the most recent test result in the medical record. However, the timing of the first and second blood tests varied for each patient.

3.1.3 Study Materials

The 5-level EQ-5D version (EQ-5D-5L) represents an enhancement in the instrument's sensitivity while reducing ceiling effects. This version consists of two pages: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension offers five levels of response: no problems, slight problems, moderate problems, severe problems, and extreme problems (Euroqol, 2023). Patients are asked to select the statement that best describes their health state for each dimension, resulting in a 1-digit number representing their chosen level for that dimension (Euroqol, 2023). These digits for the five dimensions can then be combined into a 5-digit number that characterizes the patient's health state.

The EQ VAS records a patient's self-rated health on a vertical visual analogue scale, with endpoints labeled as "The best health you can imagine" and "The worst health you can imagine". The VAS serves as a quantitative measure of health outcomes, reflecting the patient's subjective perception (Euroqol, 2023).

The interclass correlation coefficient (ICC) for EQ-5D-5L indexes was reported as 0.85, indicating a good level of agreement, and kappa coefficients for the 5L dimensions ranged from 0.64 to 0.79, indicating substantial agreement (Moradi et al., 2022). These metrics highlight the reliability and consistency of the EQ-5D-5L as a tool for assessing health-related quality of life.

The Edmonton Symptom Assessment System (ESAS) is a self-reporting tool initially designed for advanced cancer patients to gauge the intensity of

their symptoms. It comprises numerical rating scales for nine common symptoms: pain, fatigue, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath. There is also an option to include a tenth symptom (Watanabe et al., 2009; Kingston Health Sciences Centre, 2023). ESAS has demonstrated strong internal reliability (Cronbach alpha 0.79), test-retest reliability (Spearman correlation coefficient 0.86 on day 2 and 0.45 on day 7), and convergent validity (correlation coefficient 0.85 with FACT pain, 0.83 with MSAS pain, 0.56 with BPI worst pain) (Chang et al., 2000; Hui, & Bruera, 2017). Two assessments were conducted: the first on the day of patient consent and the second 30 days after obtaining consent. The assessment form could be completed either by the volunteers themselves or by the researcher, as per the volunteers' instructions. It typically takes 10-15 minutes to fill out the questionnaire.

3.2 Participants Access

After approval of research ethics in humans and procedures for accessing medical records and patient information were started. The researcher sent the hospital director an official letter to request permission to access medical records. After obtaining approval from the hospital directors, data collection was performed. The patients were still following up for treatment at the hospital. After the patients had met and received treatment from the doctor, the researcher asked the physician or nurse who provided care for the patient to notify the patient and ask permission to have the researcher visit to clarify the study objectives and processes and obtain informed consent. If the patient did not come for follow-up treatment, the researcher would send a statement by mail to the address shown in the medical record to clarify the research project and obtain informed consent.

The researcher created a form to notify the patient in the most convenient way for the research team to interview him or her and attached it to the back of the consent form. For example, by providing the patient's telephone number or the location where they agreed to meet and at the most convenient date and time. If the subjects agree to participate in the research, they must return the consent form that the research team has prepared with a postage stamp. With consent, the research team continued.

The Institutional Review Board (IRB) of Khon Kaen University in Thailand (Approval number: HE651077, Date of approval: 6 July 2022) and the Sirindhorn Hospital's Ethics Committee (No. 0033.202.11/48, Date of approval: 14 November 2022) authorized this study.

3.3 Statistics

The authors utilized descriptive statistics, including the mean and standard deviation (SD), to analyze the general characteristics of the patients.

Survival rates and hazard ratios were analyzed using Kaplan-Meier statistics, Log Rank Test and Cox proportional hazards regression. Analyses were conducted using STATA v.10, Khon Kaen University, Thailand.

Hospital admission rate, number of hospital days, quality of life, and side effects between groups were compared using a Wilcoxon signed-rank test. Analyses were carried out using IBM SPSS Statistics v.28, Khon Kaen University, Thailand. The results were statistically significant at a significant level of $p < 0.05$.

4. Results and Discussion

4.1 Results

The clinical characteristics of the patients in both groups included receiving palliative care and having a Palliative care and had a Palliative Performance Scale (PPS) of 70% or higher.

The baseline demographics and cancer characteristics of patients with palliative cancer (n=98). There were 49 males (50%) and 49 females (50%). The overall age range was 27–88 years, the mean age was 62.32 years (S.D., 12.03); The cannabis group aged 27-88 years, the mean age was 62.18 years (S.D., 11.98) and for the morphine group aged 27–84 years, the mean age was 62.57 years (S.D., 12.57). Most patients were married (59.18%) followed by widowed /separated/separated (34.70%). Similar proportions were found in both groups where there were 65.31% and 53.06% of married patients treated with cannabis and morphine, respectively.

The highest educational level was a primary school (70.41%), divided into a group the cannabis group (69.39%) and the morphine group (71.43%). Most patients were unemployed (73.47%), the cannabis group (65.31%), and were morphine group (81.63%). The majority of patients had a monthly income of less than 10,000 baht (89.80%), were cannabis group (83.68%) and were morphine group (95.92%).

Table 1 Dosage forms of cannabis, Number and percentage of patients with palliative cancer in the cannabis group

Treatment	Dosage form	Dosage	Cannabis n (%)
The dosage form of cannabis the patient received (using more than one form of cannabis)			
1. Fresh cannabis (boiled)	Use 3-5 fresh cannabis leaves or 3-5 cannabis inflorescences to boil with 1-2 liters of water	Drink 300 mL – 1 liter per day	12 (24.49%)
2. Fresh cannabis (Cooking)	Use 3-5 fresh cannabis leaves or 2-3 cannabis inflorescences in boiled, curried and fried dishes	Cannot be identified	1 (2.04%)
3. Dried cannabis (boiled)	Use 1 handful of dried cannabis leaves or 2-3 cannabis inflorescences to boil with 1.5 - 2 liters of water	Drink 300 mL – 1 liter per day	3 (6.12%)
4. Dried cannabis (smoke)	Use an inflorescence of Cannabis, about 1 gram, roll it up with paper and smoke	3 cigarettes per day	2 (4.08%)
5. Fresh or dried cannabis (boiled with herbs)	1 handful of fresh or dried cannabis, boiled with other herbs	1-2 glasses in the morning, evening and 7-8 glasses per day	2 (4.08%)
6. Mordecha cannabis oil 5 mL	THC/drop = 0.08 mg CBD/drop = 0.02 mg	3-5 drops 1 time per day before bedtime	21 (42.86%)
7. Khamint thong cannabis oil 10 mL	Contains 100 g/l of mixed cannabis	3-5 drops 1 time per day before bedtime	4 (8.16%)
8. MorDecha cannabis oil 10% 10 mL	Cannabis extract in coconut oil, concentration 10% by weight of dried cannabis inflorescences (THC 2.0 mg/mL)	3-5 drops 1 time per day before bedtime	11 (22.45%)
9. GPO cannabis oil 5 ml	THC: CBD 1:1	1-2 drops 1 time per day before bedtime	1 (2.04%)
10. Cannabis extract THC 1.7% Abhaibhubejhr	THC 1.7%	1-2 drops 1 time per day before bedtime	2 (4.08%)
11. Ya-San-Tha-Kat-klon-hang (Contains cannabis as an ingredient)	1 gram of cannabis in 21 g of medicinal powder	Take 2 capsules before meals, 2 times a day, morning and evening	1 (2.04%)
12. Ya- Tham- Lai-Phra -Sumeru (Contains cannabis as an ingredient)	30 g of cannabis in 1388.75 grams of medicinal powder	Take 2 grams before each meal, 2 times a day (morning and evening) using red sugarcane juice or cow milk as a liquid. or use boiled water instead	1 (2.04%)
13. Ya-Sookh-Sai-Yat (Contains cannabis as an ingredient)	12 g of cannabis in 78 g of medicinal powder	Take 2 capsules 2 times a day before breakfast and dinner	5 (10.20%)
14. Cannabis Oil (Buy Yourself)	Cannot be identified	5 drops 1 time per day before bedtime	2 (4.08%)
15. Cannabis oil capsules (Buy Yourself)	Cannot be identified	1 capsule 1 time per day before bedtime	1 (2.04%)

Table 1 presents palliative cancer patients in the cannabis group, with 49 individuals receiving cannabis treatment. The first uses of Mordecha cannabis oil (THC/drop = 0.08 mg, CBD/drop = 0.02 mg) numbered 21 people (42.86%). The second uses fresh cannabis (boiled) to drink by yourself, numbering 12 people (24.49%), and the third uses 10% Mordecha cannabis oil (cannabis extract in coconut oil, 10% concentration of dried cannabis inflorescence weight (THC 2.0 mg/mL)), numbering 11 people (22.45%).

Table 2 Dosage form of morphine, Number and percentage of patients with palliative cancer in the morphine group

Treatment	Dosage	Morphine n (%)
The dosage form of morphine the patient received (using more than one form of morphine)		
1. Morphine (MST) 30 mg TAB	Take 1 tablet every 4 hours	20 (40.82%)
2. Morphine (MST) 10 mg TAB	Take 1 tablet every 12 hours	15 (30.61%)
3. Morphine (IR) 10 mg TAB	Take 1 tablet every 2 or 4 hours	16 (32.65%)
4. Morphine Sulfate syrup 10 mg/mL	Take 1 teaspoon every 2 hours or take 5 CC every 4 hours	8 (16.33%)
5. Morphine Sulfate Inj 10 mg/mL	No limitation/24 hours (dose titrated to individual patient's needs)	2 (4.08%)

Table 3 Survival rate of patients with palliative cancer (n=98)

Survival time	Cannabis		Morphine	
	Survival rate (%)	95%CI	Survival rate (%)	95%CI
1 month	100	-	100	-
3 months	83.23	69.25-91.24	71.12	56.15-81.78
6 months	71.98	56.63-82.69	62.32	46.97-74.38
9 months	68.85	52.83-80.39	56.77	40.98-69.82
12 months	68.85	52.83-80.39	56.77	40.98-69.82
15 months	64.26	46.60-77.41	56.77	40.98-69.82
18 months	64.26	46.60-77.41	50.46	32.17-66.20
21 months	56.23	34.34-73.34	42.05	21.47-61.40
24 months	56.23	34.34-73.34	42.05	21.47-61.40

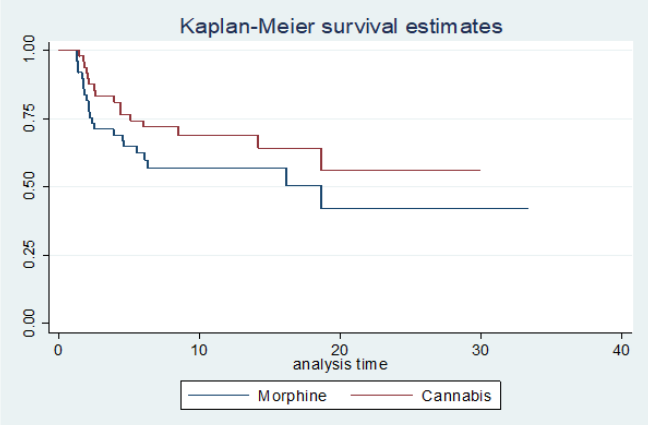

Figure 1 Graph showing the survival time of patients with palliative cancer

Table 2 presents palliative cancer patients in the morphine group, with 49 individuals receiving morphine treatment. The most common were morphine (MST) 30 mg TAB for 20 people (40.82%), followed by morphine (IR) 10 mg TAB for 16 people (32.65%), and morphine (MST) 10 mg TAB for 15 people (30.61%), respectively.

Table 3 presents the survival rates of the cannabis group at intervals of 1, 3, 6, 9, 12, 15, 18, 21, and 24 months, which were as follows: 100% , 83.23%, 71.98%, 68.85%, 68.85%, 64.26%, 64.26%, 56.23%, and 56.23%, respectively. In comparison, the survival rates of the morphine group at the same intervals were: 100%, 71.12%, 62.32%, 56.77%, 56.77%, 56.77%, 50.46%, 42.05%, and 42.05%, respectively.

Figure 1 displays the incident- free curve, illustrating that palliative cancer patients in the cannabis user cohort exhibited a survival rate of over 50% for all durations of survival, as per the Kaplan and Myers method. In contrast, half of the patients who used morphine had passed away after 18 months. This suggests that cancer patients who used cannabis experienced longer survival times compared to those who used morphine.

Table 4 Survival rate of patients with palliative cancer (n=98)

Treatment	Median	Haz. Ratio	Std. Err.	z	P	95% CI
Cannabis	0.69	0.635	0.21	-1.38	0.168	0.333 - 1.210
Morphine	0.52					

*Statistically significant ($p < 0.05$), (log-rank test)

Table 5 hospital admission rate and number of hospital days for patients with palliative cancer (n=98)

Outcomes	Treatment	Minimum	Maximum	Median	S.D.	95% CI		P
						Lower	Upper	
Hospital admission rate	Cannabis	2	34	7	1.12	7.71	12.21	0.54
	Morphine	2	49	5	1.63	7.37	13.94	
Number of hospital days	Cannabis	0	14	0	3.59	0.89	2.95	0.01*
	Morphine	0	64	2	12.33	3.48	10.56	

*Statistically significant ($p < 0.05$), (Wilcoxon signed-rank test)

Table 6 ESAS assessed the quality of life of patients with palliative cancer (n=98)

ESAS	Treatment	Minimum	Maximum	Median	S.D.	95%		p
						Lower	Upper	
Pain	Cannabis	0	8	0	2.07	0.57	1.76	0.04*
	Morphine	0	9	2	2.80	1.38	2.99	
Tiredness	Cannabis	0	10	0	2.74	1.07	2.64	0.09
	Morphine	0	10	5	3.32	2.48	4.38	
Nausea	Cannabis	0	2	0	0.29	-0.04	0.12	1.00
	Morphine	0	6	0	0.86	-0.12	0.37	
Depressed	Cannabis	0	5	0	1.11	0.03	0.67	0.08
	Morphine	0	10	0	2.58	0.50	1.99	
Anxiety	Cannabis	0	5	0	1.21	0.14	0.84	0.19
	Morphine	0	10	0	2.71	0.65	2.21	
Drowsiness	Cannabis	0	8	0	1.73	0.16	1.15	0.03*
	Morphine	0	10	2	3.32	1.07	2.97	
Appetite	Cannabis	0	10	0	2.48	0.76	2.18	0.02*
	Morphine	0	10	4	3.81	2.48	4.67	
Feeling of wellbeing	Cannabis	0	4	0	1.26	0.17	0.89	<0.001*
	Morphine	0	10	2	2.91	1.39	3.06	
Shortness of breath	Cannabis	0	9	0	2.02	-0.05	1.11	0.05*
	Morphine	0	10	0	2.47	0.58	2.00	

*Statistically significant ($p < 0.05$), (Wilcoxon signed-rank test)

Table 4 displays the median survival time for the morphine group was 0.52 years, while for the cannabis group it was 0.69 years. The survival rate based on Cox regression analysis, which indicated that palliative cancer patients in the cannabis group had a 0.635 times higher survival rate compared to the morphine group. However, it's important to note that this difference did not reach statistical significance ($p = 0.168$).

Table 5 presents the hospital admission rates and length of hospital stays in both groups. The cannabis group had a lower hospital admission rate compared to the morphine group; however, this difference was not statistically significant ($p > 0.05$). In contrast, the number of hospital days was significantly lower in the cannabis group than in the morphine group ($p < 0.05$), indicating a shorter duration of hospitalization for cannabis users.

Table 6 presents an evaluation of the quality of life in palliative cancer patients, comparing the cannabis and morphine groups using the ESAS tool. The results indicate that the cannabis group achieved lower scores in categories such as pain, tiredness, nausea, depression, anxiousness, drowsiness, appetite, feeling of well-being, and shortness of breath. This suggests that the cannabis group experienced a better quality of life than the morphine group. Importantly, statistically significant differences ($p < 0.05$) were observed in the categories of pain, drowsiness, loss of appetite, feeling of well-being, and shortness of breath.

Table 7 EQ-5D-5L assessed the quality of life of patients with palliative cancer (n=98)

EQ-5D-5L	Treatment	Minimum	Maximum	Median	S.D.	95%CI		p
						Lower	Upper	
Score	Cannabis	0.27	1.00	0.96	0.18	0.82	0.92	0.005*
	Morphine	-0.13	1.00	0.76	0.34	0.53	0.73	
VAS	Cannabis	60	100	80	10.22	76.56	82.43	0.10
	Morphine	30	100	70	22.69	61.04	74.07	

*Statistically significant ($p < 0.05$), (Wilcoxon signed-rank test)

Table 8 Blood test results of patients with palliative cancer

Blood test	Normal range	Treatment	Minimum	Maximum	Median	S.D.	95% CI		p
							Lower	Upper	
BUN	7-20 mg/dl	Cannabis	5.50	25	11.05	4.76	11.19	14.01	0.30
		Morphine	3	68	12.90	12.09	13.56	20.73	
Cr	M= 0.7 - 1.3 F= 0.5 -1.1 mg/dl	Cannabis	0.50	1.36	0.66	0.24	0.76	0.90	0.66
		Morphine	0.40	2.90	0.92	0.51	0.87	1.17	
AST	8- 33 U/L	Cannabis	10	115	24	24.44	21.65	42.78	0.05*
		Morphine	18	348	35.50	88.50	42.43	118.96	
ALT	4- 36 U/L	Cannabis	6	98	18.50	19.30	17.57	34.26	0.04*
		Morphine	11	231	31.50	52.46	30.14	75.51	
ALP	20- 140 U/L	Cannabis	36	659	66.50	136.57	43.78	171.62	0.71
		Morphine	32	1103	88.50	349.87	122.26	449.75	

*Statistically significant ($p < 0.05$), (Wilcoxon signed-rank test)

Table 7 presents an assessment of the quality of life in patients with palliative cancer, comparing between groups using the EQ-5D-5L tool. The results show that the cannabis group had higher utility scores compared to the morphine group. This indicates that the cannabis group had a better quality of life than the morphine group, and this difference was found to be statistically significant ($p < 0.05$).

Additionally, the cannabis group had a higher VAS (Visual Analog Scale) score compared to the morphine group. This also suggests that the cannabis group had a better quality of life, although the difference was not statistically significant ($p > 0.05$).

Normal range (University of Rochester Medical Center, 2023a, 2023b; The Regents of the University of California, 2023a, 2023b; Sharma et al., 2014)

Table 8 illustrates that cancer patients treated with morphine exhibited higher levels of AST and ALT as compared to patients who received cannabis treatment. Importantly, these differences were statistically significant ($p < 0.05$).

Apart from the laboratory tests, other relevant side effects in the cannabis group included dry throat (1.02%). This was a mild symptom with no serious impact on the patients.

4.2. Discussion

Cancer patients treated with cannabis appeared to have better survival outcomes, although this difference did not reach statistical significance ($p = 0.168$, log-rank test). In line with existing literature, the medicinal cannabis treatment group (CT) exhibited a significantly improved survival rate ($P = 0.001$), with a median survival of 5.66 months or 170 days (95% CI: 1.94–9.38). In contrast, the standard palliative care pain management treatment group (ST) had a median survival time of only 0.83 months or 25 days (95% CI: 0.83–0.93). These findings are consistent with previous research, highlighting the potential benefits of medicinal cannabis treatment in improving survival rates among palliative cancer patients.

As a result, the use of medicinal cannabis (CT) significantly reduced the risk of disease-related mortality, as indicated by a hazard ratio (adj.HR) of 0.28 and a 95% confidence interval (CI) of 0.20–0.37 (Phansila et al., 2022). In the latest survey, it was found that 8% of cancer survivors reported using cannabis within the past year, while this percentage was higher at 15% among individuals without a history of cancer. When comparing across four different time periods, approximately 3.8% of cancer survivors reported cannabis use, as opposed to 6.5% among those without a history of cancer (Do et al., 2021).

These statistics provide insights into the prevalence of cannabis use among cancer survivors and the broader population, suggesting potential differences in usage patterns between the two groups. In patients with advanced malignancies treated with immunotherapy, the overall survival (OS) appears to be notably high. According to Kaplan-Meier estimates based on data from 102 patients, the median OS for cannabis users was 6.4 months (95% CI: 3.2–9.7), while for non-cannabis users, it was significantly longer at 28.5 months (95% CI: 15.6–NA).

These findings suggest that cannabis consumption may have an impact on OS in this context. It's worth noting that cannabis is known to have immunomodulatory effects, which could potentially influence the immune system in cancer patients. Therefore, the use of cannabis should be carefully considered when managing cancer patients, taking into account its potential effects on the immune system (Bar-Sela et al., 2020). This information underscores the importance of evaluating the impact of cannabis on cancer treatment outcomes, particularly in patients undergoing immunotherapy.

Cannabis users are less likely to require hospitalization. Currently, no studies have specifically examined how often cannabis-using cancer patients are admitted to hospitals. A patient told us that “the doctor made an appointment for me in 2-3 months and sent me to the cancer center on the 11th floor. The patient would receive treatment from the foreign pharmaceutical company for 5 years in exchange for 3,000 Baht in travel expenses each time. It has been a few months since my last missed appointment, which I did not attend to”.

“The hospital doctor I went to see said he had given me eight chemotherapy rounds, and he didn't give any more. Go home and take care of yourself. Just treat the symptoms" (Thaenkham et al., 2023). All cancer patients' use of cannabis is self-use (46.93%), such as fresh cannabis (boiled) (24.49%), fresh cannabis (cooked) (2.04%), dried cannabis (boiled) (6.12%), dried cannabis (smoked) (4.08%), fresh or dried cannabis (boiled with herbs) (4.08%), cannabis oil (self-bought) (4.08%), and cannabis oil capsules (self-bought) (2.04%). Therefore, this may be the reason for the low hospitalization rate among patients who use cannabis.

Cannabis users had significantly fewer days of hospital stay than morphine groups. Consistently within this study it was found that the hospital admission rate of cancer patients who used cannabis was lower than that of those who did not use cannabis. Therefore, when palliative cancer patients who use cannabis are not hospitalized, it reduces the number of days they must stay in the hospital. Likewise, cancer patients who do not use cannabis have a higher hospitalization rate. The number of days in the hospital therefore increased.

The quality of life of patients with palliative cancer was compared between the cannabis and morphine groups, assessed by the ESAS and EQ-5D-5L tools. The cannabis user group had a better quality of life for pain, drowsiness and loss of appetite, both physically and mentally, and shortness of breath. Statistically significant differences were consistent with the literature; colon cancer was the most prevalent malignancy. Daily THC use ranged from 0.5 to 5 mg. The severity of pain, tiredness, depression, anxiety, loss of appetite, and insomnia significantly diminished (Srisubat et al., 2021).

A THC concentration of 1.7% w/v can help alleviate pain, anorexia, insomnia and anxiety. These patients' quality of life tended to improve, particularly over the past three months. Before commencing the use of cannabis sublingual oil THC, the median utility score of the EQ-5D-5L questionnaire was 0.767 and increased to 0.928 after six months (Kraikosol et al., 2021). At the eighth visit, quality of life improved considerably from 0.875±0.180 (range 0.016-1.000) at baseline to 0.960± 0.071 (0.928-1.000), $p<0.001$ (Khamjulla, & Thongkun, 2022).

The data collected by the EQ-5D-5L questionnaire revealed that the utility measurement was 0.80±0.19 prior to the intervention and 0.86±0.16 after the 3-month intervention, with the average utility measurement increasing substantially ($p<0.05$) (Silarak, 2022).

The EQ-5D scale Cannabis users had significantly reduced scores in the anxiety/depression and pain/discomfort domains (difference, 0.74; 95% CI, 0.557–0.930; difference, 0.29; 95% CI, 0.037–1.541. The Wilcoxon rank sum test confirmed the EQ-5D's findings of improvements in the pain/discomfort and anxiety/depression domains (z scores of -2.60 and -6.71, respectively). According to the ESAS, cannabis consumers experienced less pain, less fatigue, less depression, less anxiety, a greater appetite, less drowsiness, and a greater sense of well-being overall (Zhang et al., 2018).

They recognized cannabis use as an opportunity to survive (74, 2 %), stimulate appetite (91, 7 %), and enhance slumber comfort (35, 8 %). 49.2% of formerly cannabis-using individuals utilized cannabis oil for convenience. Both the cannabis treatment and standard treatment groups had high PPS scores. The

aggregate global health status (QoL) and quality of life were statistically significantly higher for the cannabis treatment group than for the standard treatment group. Physical functioning and Cognitive functioning were statistically significant measures. Symptom scales were found for Dyspnea and Insomnia, with the standard treatment group having lower average scores for insomnia than the cannabis treatment group (Wongkongdech et al., 2022).

Moreover, according to blood tests, the BUN, Cr, AST, ALT and ALP levels of patients with palliative cancer who used cannabis were lower than those in the morphine groups. In morphine patients, AST and ALT levels increased and differed significantly. Therefore, it indicates that cannabis patients are secure. In line with the research findings, a comparison was conducted involving 13 individuals before and after undergoing treatment with the Suk-sai-yat formula. The evaluation of liver function parameters, including aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and kidney function markers such as blood urea nitrogen (BUN) and creatinine, revealed that there were no significant differences observed between the values before and after treatment.

Additionally, none of these values exceeded the normal reference ranges. These results suggest that the Suk-sai-yat formula and Cannabis did not appear to adversely affect liver or kidney function in the study participants (Tipratchadaporn et al., 2021; Charoenying et al., 2023).

The limitations of this study, including the small sample size, variations in the dosage forms received by each group, and the inability to control the amount of drug used by each individual, may lead to differing survival rates. Therefore, if morphine or cannabis is considered for the treatment of palliative cancer, it should be carefully evaluated and discussed with a specialist doctor.

4.3 Strengths of This Study

This study marked a pioneering effort in Thailand as it was the first to examine and compare survival rates, hospitalization rates, and the duration of hospital stays in palliative cancer patients between those who used cannabis and those who used morphine.

4.4 Limitations

It is impossible to select a group of patients with the same type of cancer because there are a limited number of cancer patients receiving palliative care who are still alive.

5. Conclusion

The findings suggest that palliative cancer patients who incorporated cannabis into their treatment experienced several positive outcomes, including higher survival rates, reduced hospitalizations, shorter hospital stays, and an improved quality of life. Additionally, it's noteworthy that no serious adverse effects from cannabis use were reported in this context.

These results may indicate that cannabis could be a beneficial option for palliative cancer patients who choose to include it as part of their treatment regimen, either in isolation or alongside other therapies. However, it's important to consider that individual responses to cannabis can vary, and its use should be discussed with healthcare professionals who can provide personalized guidance based on a patient's specific medical history and needs.

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7. Conflict of interest:

The authors declare no conflict of interest.

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