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Original Article

Comparing the sensitivity of fatigue and sleep disturbance assessment tools in women with advanced cancer undergoing chemotherapy

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ABSTRACT

Objective: This study aims to investigate the variations in fatigue and sleep disturbances among female patients with advanced lung cancer (ALC) and advanced breast cancer (ABC) during chemotherapy.
Methods: A total of 36 female patients with ALC and 36 with ABC, all of whom had completed their first cycle of chemotherapy, were included. Fatigue was assessed using the General Fatigue Scale (GFS), and sleep disturbances were evaluated using the Pittsburgh Sleep Quality Index (PSQI) at designated time points throughout the chemotherapy process.
Results: Linear regression analysis indicated that variables such as age, education level, employment status, cancer type, clinical stage, and symptom distress had no significant correlation with either fatigue or sleep disturbances. The GFS significantly discriminated fatigue among the ALC, ABC, and combined groups, while the PSQI demonstrated a significant distinction in sleep disturbance only within the ALC and combined groups.
Conclusions: In summary, when considering the findings of both assessments in this study, the GFS score exhibited greater sensitivity in detecting fatigue than the PSQI score did for identifying sleep disturbances in advanced cancer patients undergoing chemotherapy.

Introduction

Lung cancer and breast cancer are two of the most common types of cancer in the world,[1] including Taiwan.[2] In the clinical setting, a series of chemotherapies have been used to prolong the survival of patients with cancer. However, clinical symptoms affect the quality of life of patients with cancer during chemotherapy. Thus, numerous questionnaires have been designed to evaluate the feelings of patients with cancer undergoing chemotherapy, including fatigue, sleep quality,[3] pain, anxiety, psychological distress,[4] and other symptoms.[5]

Regardless of the clinical symptoms, fatigue and sleep disturbance are two commonly used indices in the evaluation of the real feelings of patients with cancer, including lung cancer and breast cancer.[6–9] Both symptoms are caused dynamically by a series of complicated factors, such as the disease itself, clinical treatment, demographics, lifestyle, and psychological factors. Therefore, it is difficult to evaluate the degree of influence of complicated symptoms in patients with cancer, particularly those with advanced cancers.

Among the clinical symptoms, fatigue is considered the most uncomfortable symptom in patients with cancer, particularly during chemotherapy that involves various treatments. Fatigue often manifests dynamically in patients with cancer during treatment and daily activities. Fatigue levels have been assessed in patients with various cancers by using the General Fatigue Scale (GFS)[10] or Brief Fatigue Inventory (BFI).[11] The GFS is a global measure of fatigue patterns, and the BFI can reflect a patient's fatigue level with a recall period. Even though many assessments are performed for patients with advanced cancer, the assessment of fatigue using the GFS has not been explored.

In addition to fatigue, insomnia also causes suffering for almost 10%–15% of the general population of the world.[12] The prevalence of sleep problems varies among different types of cancer, including breast cancer and lung cancer.[13] In addition, disorders of the sleep–wake cycle often lead to insomnia as a common sleep disturbance in patients with cancer.[14,15] Sleep disorders are estimated to have a high occurrence rate in patients with cancer worldwide, such as patients with lung cancer in Japan[16] and patients with breast cancer in the United States.[17] Furthermore, sleep disturbance is

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exacerbated by complicated symptoms in patients with cancer undergoing chemotherapy.[18] A majority (72%) of patients with advanced cancer have sleep disturbances.[19] In addition, a high prevalence of sleep problems was found in patients with primary cancer (breast, bowel, prostate, ovary, gynecological, testicle, etc.) during the active cancer phase and among survivors.[20] Numerous clinical questionnaires have been applied to assess the sleep disturbance of patients with various cancers, such as the Pittsburgh Sleep Quality Index (PSQI) for breast cancer,[21] colorectal cancer,[22] and lung cancer[23]; Insomnia Severity Index for lung cancer[24]; and Epworth Sleepiness Scale for papillary thyroid carcinoma[25] and lung cancer,[26] thus indicating that sleep disturbance is still one of the critical indicators of discomfort levels in patients with cancer.

Reports on the influence of sex on the clinical distress of patients with cancer have been inconsistent. In addition, various treatments for female patients with advanced breast cancer (ABC) always involve hormone ablation, which might cause fatigue[27] and insomnia.[28] Detailed comparisons are needed to determine whether fatigue or sleep disturbance is a better target for most cancer treatments. Therefore, by referencing previous findings in patients with lung cancer[7,8] and by assessing whether clinical symptoms can directly differentiate between various patients with cancer to improve symptoms, we aimed to compare the differences between fatigue and sleep disturbance by using the GFS and PSQI, respectively, in female patients with advanced cancers, including lung cancer, ABC, and a combination of both cancers, during the first cycle of chemotherapy.

Methods

Participants

Female participants with advanced lung cancer (ALC) and ABC were enrolled at two medical centers in Taiwan, namely, Tri-Service General Hospital (TSGH) and Far Eastern Memorial Hospital (FEMH). All enrolled participants were recruited by clinical workers, including attending physicians and nurses. All enrolled participants completed the first cycle of chemotherapy. The clinical stage of the participants was defined according to the sixth edition of the *AJCC Staging Manual*.[29]

Clinical criteria

The inclusion criteria were as follows: (1) female, (2) 18 years or older, (3) diagnosis of lung cancer or breast cancer, (4) patients with advanced cancer undergoing chemotherapy only or postoperative chemotherapy, (5) mentally able to communicate in Mandarin or Taiwanese, (6) performance status score < 2 on the Eastern Cooperative Oncology Group performance status rating, and (7) hemoglobin level >11 g/dL.

The exclusion criteria were as follows: (1) active or chronic infection, (2) previous diagnosis of chronic fatigue syndrome or psychiatric disorder, and (3) previous diagnosis and treatment for cancer with chemotherapy or radiotherapy.

Chemotherapy in participants

Participants with ALC underwent the first cycle of chemotherapy (28 days) with intravenous platinum-based drugs and non-platinum-based drugs (gemcitabine, paclitaxel, or vinorelbine) on day 1. No patient with ALC underwent surgery.

Participants with ABC underwent the first cycle of chemotherapy with intravenous cyclophosphamide, doxorubicin, 5-fluorouracil, cyclophosphamide, methotrexate, and 5-fluorouracil on day 1. All patients with ABC underwent surgery.

Sample size

Limited by the actual inclusion and exclusion conditions, more than the minimum number of participants in either ALC or ABC were enrolled to exceed the minimum and 20% loss to follow-up ($n = 32$), as confirmed by G-Power calculations[30] with an effect size of 0.25, power of 0.8, and significance level of 0.5. A total of 72 participants diagnosed with advanced cancer were included: 36 patients with ALC were enrolled at TSGH,[7] and 36 patients with ABC were recruited from FEMH (Table 1).

Measurements

Symptom distress in participants with ALC or ABC was measured at three time points of the first cycle of chemotherapy: on the day before initiation (T1), on the 8th day (T2), and one day before the next cycle (T3) (28th day for ALC and 21st day for ABC).

Fatigue

Fatigue was measured using the GFS, which is a Likert-type scale with 7 items (1 = no fatigue, 10 = greatest possible fatigue)[10] to measure several aspects of fatigue, including intensity, distress, and effects on daily activities. By averaging the responses to the 7 items, the measure was totaled to generate a score of 0–70 points. The Cronbach's alpha reliability coefficient was 0.92. Acceptable construct validity has been reported for the GFS.

Sleep quality

Sleep quality in patients with advanced cancer was assessed using the PSQI,[31] which is a subjective, self-rated questionnaire with 19 items. The

Table 1
Characteristics of female participants with advanced cancers.

Characteristics	Cancer groups			Combination ($n = 72$)
	ALC ($n = 36$)	ABC ($n = 36$)	*P* value	
Age (years)	59.3 ± 9.4	48.9 ± 9.3	< 0.001	54.1 ± 10.7
Marital status, *n* (%)			0.297	
Married	28 (77.8)	25 (69.4)		53 (73.6)
Single/divorce	8 (22.2)	11 (30.6)		19 (26.4)
Education, *n* (%)			0.005	
High-school or less	30 (83.3)	19 (52.8)		49 (68.1)
Post-high-school	6 (16.7)	17 (47.2)		23 (31.9)
Employment status, *n* (%)			< 0.001	
Employed	4 (11.1)	21 (58.3)		25 (34.7)
Unemployed	32 (88.9)	15 (41.7)		47 (65.3)
Clinical stage, *n* (%)			< 0.001	
Stage III	22 (61.1)	34 (94.4)		56 (77.8)
Stage IV	14 (38.9)	2 (5.6)		16 (22.2)
Comorbid condition, *n* (%)			0.237	
No	23 (63.9)	19 (52.8)		42 (58.3)
Yes	13 (36.1)	17 (47.2)		30 (41.7)

ALC, advanced lung cancer; ABC, advanced breast cancer; SD, standard deviation.

items were grouped into seven components: sleep quality, sleep latency, sleep duration, habitual efficiency, sleep disturbances, medication use, and daytime dysfunction. Each component score was weighted equally on a scale of zero to three. Total scores range from 0 for no disturbance to 21 for more severe complaints and worse sleep quality. Its internal consistency reliability and construct validity were supported by participants with advanced cancer. The Cronbach's alpha for the global PSQI score was 0.75.

Data analysis

The variables were represented as percentages and means ± standard deviations. The categorical variables between the ALC and ABC groups were compared using the chi-square and Fisher's exact tests, and age as a continuous variable was compared using Student's *t*-test. Pearson's correlation coefficient was used to analyze the correlation between multiple variables of symptom distress. Linear regression analysis was applied to the forward conditional methods for the ALC and ABC, including fatigue, pain, poor appetite, cough, dyspnea, age, education level, and employment status. All statistical analyses were performed using SPSS Statistics (version 22.0; IBM Corp., Armonk, NY, USA). A P value < 0.05 was considered statistically significant.

Ethical considerations

The study was conducted under the Declaration of Helsinki and approved by the Institutional Review Board of Tri-Service General Hospital (TSGHIRB No. 095-05-094-A and 099-05-032) and Far Eastern Memorial Hospital (FEMHIRB No. 099038-E). All participants provided written informed consent.

Results

General characteristics of patients with advanced cancer

All participants received the first cycle of chemotherapy, and their general characteristics were described by group alone or in combination (Table 1). The ALC group had a significantly older age ($P < 0.001$), poorer education ($P = 0.005$), no stable employment ($P < 0.001$), and a more severe stage ($P < 0.001$) than the ABC group. However, there were no significant differences in marital status ($P = 0.297$) or comorbidities ($P = 0.237$) between the two groups.

The GFS score in patients with ALC and ABC

To estimate the effect of fatigue in patients with ALC and ABC during the first cycle of chemotherapy, the GFS score was individually applied to the cancer group at the three indicated time points (Table 2). Generally, the average GFS score in the ALC group was significantly higher than that in the ABC group at T2 (41.9 ± 13.8 vs 29.8 ± 14.4, $P = 0.002$) but did not differ at T1 (22.9 ± 11.0 vs 21.3 ± 12.6, $P = 0.996$) or T3 (31.8 ± 14.3 vs 23.3 ± 12.5, $P = 0.071$). In the comparison of the three time points in the cancer group alone, chemotherapy caused sensitive fatigue in the ALC group ($P < 0.001$) and ABC group ($P = 0.019$). In the ALC group, the GFS score at T2 was significantly higher than that at T1 (41.9 ± 13.8 vs 22.9 ± 11.0, $P < 0.001$). Additionally, in the ABC group, the fatigue level at T2 was higher than that at T1 (29.8 ± 14.4 vs 21.3 ± 12.6, $P = 0.019$).

For the ALC and ABC combination group, the statistical results revealed that the GFS score significantly differentiated the effects of chemotherapy on fatigue in patients with ALC and ABC ($P < 0.001$). In the combination group, the GFS score at T1 was lower than that at T2 (22.1 ± 11.8 vs 35.8 ± 15.2, $P < 0.001$). The GFS score at T2 decreased to 27.5 ± 14.0 at T3 ($P = 0.001$). Therefore, the chemotherapy process initially increased the effect of fatigue in participants with advanced cancer and then relieved it at the end.

The PSQI score in patients with ALC and ABC

To estimate sleep quality in the ALC and ABC groups during the first cycle of chemotherapy, the PSQI score was individually applied to the cancer group at the three indicated time points (Table 3). Generally, the average PSQI score in the ALC group was significantly higher than that in the ABC group at T2 (13.3 ± 3.7 vs 10.0 ± 4.6, $P = 0.028$) and T3 (11.4 ± 4.0 vs 8.4 ± 4.1, $P = 0.059$) but did not differ at T1 (10.3 ± 4.9 vs 7.4 ± 5.4, $P = 0.064$). In the comparison of the three time points in the cancer group, chemotherapy significantly affected sleep disturbance in the ALC group ($P = 0.013$) but only had a slight effect in the ABC group ($P = 0.057$). In the ALC group, the PSQI score at T2 was significantly higher than that at T1 (13.3 ± 3.7 vs 10.3 ± 4.9, $P = 0.010$). This was also observed in the ABC group (10.0 ± 4.6 vs 7.4 ± 5.4, $P = 0.047$).

Similar to the ALC and ABC combination group, the statistical results revealed that the PSQI score significantly differentiated the effect of chemotherapy on sleep disturbance in patients with ALC and ABC ($P = 0.002$). In the combination therapy group, the PSQI score at T1 was lower than that at T2 (8.8 ± 5.3 vs 11.7 ± 4.4, $P = 0.001$). The increasing PSQI score at T2 decreased to 9.9 ± 4.3 at T3 ($P = 0.063$). Therefore, chemotherapy leads to poor sleep quality in patients at the beginning but mitigates it at the end.

Correlations between the GFS and PSQI scores in patients with advanced cancer during the first cycle of chemotherapy

Sleep disturbance was significantly correlated with the effect of fatigue in the ALC and ABC combination group (Pearson's correlation coefficients ranged from $r = 0.528$, $P < 0.01$) (Table 4). Regardless of the

Table 2
The GFS scores in females with advanced cancer undergoing first-cycle chemotherapy.

Time point	Cancer groups		Combination ($n = 72$)
	ALC ($n = 36$)	ABC ($n = 36$)	
T1	22.9 ± 11.0	21.3 ± 12.6	22.1 ± 11.8
T2	41.9 ± 13.8	29.8 ± 14.4	35.8 ± 15.2
T3	31.8 ± 14.3	23.3 ± 12.5	27.5 ± 14.0
ANOVA (P value)	< 0.001	0.019	< 0.001
T1 vs T2	< 0.001	0.019	< 0.001
T2 vs T3	0.004	0.095	0.001
T1 vs T3	0.013	0.797	0.047

All quantitative data are expressed as the mean ± SD. One-way ANOVA with Tukey HSD multiple comparison tests was used for statistical analysis among the time points (T1, T2, and T3).
ALC, advanced lung cancer; ABC, advanced breast cancer; SD, standard deviation; GFS, General Fatigue Scale.

Table 3
The PSQI scores in females with advanced cancer undergoing first-cycle chemotherapy.

Time point	Cancer groups		Combination ($n = 72$)
	ALC ($n = 36$)	ABC ($n = 36$)	
T1	10.3 ± 4.9	7.4 ± 5.4	8.8 ± 5.3
T2	13.3 ± 3.7	10.0 ± 4.6	11.7 ± 4.4
T3	11.4 ± 4.0	8.4 ± 4.1	9.9 ± 4.3
ANOVA (P value)	0.013	0.057	0.002
T1 vs T2	0.010	0.047	0.001
T2 vs T3	0.139	0.306	0.063
T1 vs T3	0.544	0.625	0.382

All quantitative data are expressed as the mean ± SD. One-way ANOVA with Tukey HSD multiple comparison tests was used for statistical analysis among the time points (T1, T2, and T3).
ALC, advanced lung cancer; ABC, advanced breast cancer; SD, standard deviation; PSQI, Pittsburgh Sleep Quality Index.

Table 4
The coefficient of determination (R^2) of GFS and PSQI scores with general characteristics in females with advanced cancer undergoing first-cycle chemotherapy.

Index	GFS score			PSQI score		
	T1	T2	T3	T1	T2	T3
ALC ($n = 36$)						
Age	0.006	0.002	0.001	0.043	0.070	0.002
Education	< 0.001	0.019	0.031	0.005	0.001	0.025
Employment	0.028	< 0.001	0.069	< 0.001	0.006	0.006
Clinical stage	0.019	0.105	< 0.001	0.008	0.028	0.002
ABC ($n = 36$)						
Age	0.003	0.014	0.077	0.049	0.078	0.038
Education	< 0.001	0.004	< 0.001	0.007	< 0.001	0.003
Employment	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.003
Clinical stage	< 0.001	0.083	0.033	0.021	< 0.001	0.024
Combination ($n = 72$)						
Age	< 0.001	0.068	0.058	0.023	0.044	0.054
Education	< 0.001	0.004	0.002	0.027	0.018	0.048
Employment	0.009	0.036	0.003	0.019	0.049	0.050
Clinical stage	0.010	0.098	0.021	0.063	0.029	0.057

All the coefficients of determination (R^2) were calculated by the square of the Pearson correlation coefficient between the general characteristics and the questionnaire.
ALC, advanced lung cancer; ABC, advanced breast cancer; GFS, General Fatigue Scale; PSQI, Pittsburgh Sleep Quality Index.

cancer group or combination, all R^2 values were lower than 0.1, thus suggesting that fatigue according to the GFS questionnaire and sleep disturbance according to the PSQI questionnaire were unrelated to the general characteristics at any time point, including age, education, employment, and clinical stage.

Discussion

An increasing number of studies have identified the demographic variables that are significantly related to symptom distress in patients with advanced cancer, including fatigue[32–34] and sleep disturbance.[35] These demographic variables included age,[36,37] sex, cancer type, and treatment type. The severity of the physical and psychological symptoms is related to age and occurrence. Older patients with cancer experience lower or similar levels of fatigue and sleep disturbance during chemotherapy.[36] Therefore, both groups experienced high occurrence rates and moderate-to-severe levels of fatigue and sleep disturbance. However, this finding was inconsistent with the results of the current study, thus suggesting that the general characteristics were unrelated to the GFS or PSQI scores for either ALC or ABC (Table 4). Similarly, there was no significant interaction between sex, age, and insomnia.[38] Therefore, we believe that general characteristics are not the key regulators that dominate symptom distress in patients with advanced cancer, including ALC and ABC.

Fatigue and sleep disturbance are among the most common cancer symptoms and are reported by nearly half of patients with advanced cancer.[39] The most frequently reported symptoms of patients with cancer were fatigue, sleep disturbance, pain, nausea, poor appetite, and constipation. A longitudinal study proved the relationship between fatigue and sleep disorders in patients with breast cancer undergoing chemotherapy.[40] However, fatigue and insomnia were not directly related in men with prostate cancer.[41] Sleep disturbance in patients with cancer is also a result of multiple factors, including the cancer itself or cancer-related symptoms.[42] By contrast, hormone ablation might cause fatigue and insomnia in female patients with ABC.[27,28] Furthermore, psychological factors have been shown to predict sleep disturbance, particularly in patients with ABC.[43] The cluster of fatigue and insomnia was also associated with poor functional status in patients receiving chemotherapy.[44,45] The intercorrelation between fatigue and sleep disturbance is still very close and complicated, thus suggesting that both symptoms could be determined alone or in combination in patients with cancer by using the GSF and PSQI.

Generally, lung cancer is associated with higher levels of symptom distress during chemotherapy than other cancers. Our results indicated that patients with ALC undergoing chemotherapy had higher PSQI scores than patients with ABC (13.3 ± 3.7 vs 10.0 ± 4.6 at T2, $P < 0.001$) (Table 3). A possible reason for this might be the presence of sleep disturbance in female patients with advanced cancer with distant metastasis and hormone ablation.[27,28] Different types of cancer did not show specific influencing factors on sleep disturbance in patients with advanced cancer undergoing chemotherapy. Therefore, the higher sensitivity of the PSQI score in the ALC and ABC combination group suggested that the PSQI might be a useful tool for assessing sleep disorders without confirming the cancer type.

Chemotherapy agents have been frequently reported to induce symptom distress in patients with cancer, including fatigue and sleep disturbance.[46] According to the current study, both the GFS and PSQI scores revealed that the postchemotherapy score (T2) was higher than the prechemotherapy score (T1) in the patients (Tables 2 and 3). This finding was consistent with our previous analysis in patients with lung cancer.[7,8] The fluctuation in symptom distress suggested that the physiological, psychological, and behavioral alterations in patients with ALC were stimulated at T2, decreased considerably at T3 after the first cycle of chemotherapy, and returned to their original scores before the next course of chemotherapy.[7,8] Another study found a significant positive association between symptoms of insomnia during cycles 1 and 2 of chemotherapy.[38] The chemotherapy process resulted in significant fatigue and sleep disturbance in patients with cancer, and inflammatory cytokines might induce symptom distress in these patients. This suggests that chemotherapy might trigger inflammatory responses via excessive cytokine production, thus resulting in cognitive impairment. In the current study, the use of platinum-based drugs in the ALC group and anthracycline-based drugs in the ABC group revealed that different drugs resulted in fatigue and sleep disturbance in patients with advanced cancer undergoing chemotherapy. Further investigations are needed to understand the relationship between chemotherapy agents, fatigue, and sleep disturbance.

The benefits of the GSF for fatigue and the PSQI for sleep disturbance depended on specific items and scale ranges. In this study, the GSF measurement used 7 items to generate a 70-point discriminating difference, whereas the PSQI measurement used 19 items to generate a 21-point discriminating difference. The results revealed that both assessments by the GSF ($P < 0.001$ vs $P = 0.019$) (Table 2) and PSQI ($P = 0.013$ vs $P = 0.057$) (Table 3) had higher identification significance for patients with ALC undergoing chemotherapy than for patients with ABC. Nevertheless, both assessments significantly identified the symptoms in the ALC and ABC combination group (Table 2, $P = 0.002$; Table 3, $P < 0.001$). In addition, the general characteristics of patients with cancer may interfere with clinical distress, including fatigue and sleep disturbance, during chemotherapy.[36] However, none of the general characteristics were unrelated to the GFS or PSQI scores in either the ALC or ABC groups (Table 4). The GSF assessment has high sensitivity for ALC, ABC, or their combination, but the PSQI could be improved by increasing the scores when assessing these types of cancer or by confirming the patient's own physiological condition, such as hormone ablation. Therefore, the assessment of fatigue should be more sensitive than the assessment of sleep disturbance in patients with advanced cancer without confirming the cancer type.

This study showed that fatigue assessment using the GFS and sleep disturbance assessment using the PSQI are two critical methods for treating female patients with advanced cancer undergoing chemotherapy. However, this study had four major limitations. First, the number of patients was small because of the difficulty in collecting questionnaires and clinical indices. Second, the study results, which only included patients with ALC and ABC, did not directly reflect the clinical symptom distress of patients with diverse cancers. Third, these

data were collected only during the first chemotherapy cycle, which may have differed from the data after a full course of chemotherapy. Fourth, differences in Eastern and Western cultures may have affected the study. Therefore, a complete longitudinal study should be performed after the conclusion of all courses of chemotherapy with a larger number of related patients, other cancer types, and patients from different cultures.

Conclusions

Since the analysis of the GFS and PSQI scores, we provided a method for assessing both fatigue and sleep disturbance in female patients with ALC and ABC during chemotherapy by comparing information before (T1), during (T2), and after (T3) a cycle of chemotherapy. Clinicians, including doctors and nurses, can identify patients with advanced cancer who experience fatigue and sleep disturbance as soon as possible. If patients exhibit significant clinical symptom distress, the incidence of fatigue and insomnia is higher than that of other symptoms. Therefore, clinicians can treat patients with ALC and ABC efficiently after improving the symptoms of fatigue and sleep disturbance.

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CRediT authorship contribution statement

Hsiu-Ling Chou: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – Original and Revised draft preparation, and Funding acquisition. **Tsan-Chi Chen:** Validation, Formal analysis, Writing – Original and Revised draft preparation. **Chung-Tay Yao:** Conceptualization, Methodology, Validation, Writing – Reviewing and Editing. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

All authors have none to declare.

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Ethics statement

This study was approved by the Institutional Review Board of Tri-Service General Hospital (TSGHIRB No. 095-05-094-A and 099-05-032) and Far Eastern Memorial Hospital (FEMHIRB No. 099038-E). All participants provided written informed consent.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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