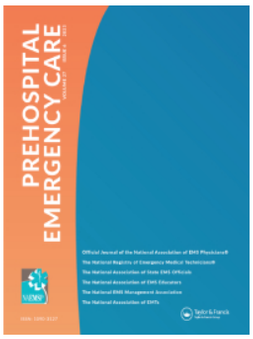

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Evaluation of the PRESEP Score and the Miami Sepsis Score for Prehospital Sepsis Screening

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ABSTRACT

Introduction: Sepsis is a life-threatening organ dysfunction caused by a dysregulated response to an infection that requires early intervention. Prehospital sepsis screening tools have not yet been widely evaluated for their performance in clinical practice.

Objective: To evaluate the ability of the Prehospital Early Sepsis Detection (PRESEP) score and the Miami Sepsis Score to predict sepsis in prehospital settings.

Method: This retrospective analysis included patients with diseases of internal cause who were transported by emergency medical services (EMS) to the hospital and hospitalized between January and June 2020. Data were extracted from the medical and EMS records. The primary outcome was sepsis diagnosis within 48 h of admission. The predictive abilities of the scores were assessed using the area under the receiver operating characteristic curve (AUC). Sensitivity, specificity, and positive and negative likelihood ratios (LRs) were calculated at cutoff values derived using Youden's index.

Results: Data from 354 patients were analyzed. The AUC for the PRESEP score was 0.83 (95% confidence interval [CI] 0.79–0.88) while that for the Miami Sepsis Score was 0.80 (0.75–0.85). The sensitivity, specificity, positive LR, and negative LR for the PRESEP score (cutoff was 5) were 0.83 (0.73–0.90), 0.68 (0.62–0.73), 2.59 (2.12–3.16), and 0.25 (0.15–0.40), respectively, and those for the Miami Sepsis Score (cu-off was 3) were 0.81 (0.71–0.89), 0.65 (0.59–0.71), 2.33 (1.93–2.83), and 0.30 (0.19–0.46), respectively.

Conclusion: Due to their relatively good predictive abilities to detect septic patients and simplicities, the PRESEP and Miami Sepsis Scores could be used for screening patients for sepsis in prehospital settings. Further prospective validation and evaluation of effect on clinical outcomes are needed.

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Introduction

Sepsis is estimated to affect approximately 50 million people and cause or contribute to 11 million deaths every year (1). Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated response to severe infection, causing considerable morbidity and mortality worldwide (2). The delayed recognition of sepsis can lead to multiple organ failure and death. Therefore, early diagnosis of sepsis and timely intervention can improve patient outcomes and reduce disease burden (3–5).

Emergency medical services (EMS) should be used to facilitate the early identification of sepsis. Wang et al. (6) reported that EMS staff provided initial care for over one-third of patients with sepsis, suggesting the potential of EMS to identify and start managing sepsis at an earlier stage. Implementation of EMS sepsis screening tools may help EMS personnel to identify sepsis patients at an early stage, which could improve sepsis management (7). For example, a screening tool could increase compliance with the 3-Hour Surviving Sepsis Campaign Guideline recommendation (blood culture, measuring lactate level, broad-spectrum antibiotics, and fluid resuscitation within 3 h) (8). Although several prehospital sepsis diagnostic tools have been proposed, their performance has not been widely evaluated in clinical practice (9). A recent systematic review reported varied prediction abilities of prehospital sepsis screening tools because of different screening strategies and the lack of high-quality studies (10).

Prehospital screening tools should consist of information readily obtainable at the scene using basic equipment and skills available even in the most basic EMS units, be easily calculable in time-constrained situations, and have diagnostic accuracy. The Prehospital Early Sepsis Detection (PRESEP) score (11) and Miami Sepsis Score (12) meet such requirements. The superiority of the PRESEP score in predicting sepsis diagnosis to other prehospital prediction tools has been demonstrated (10, 11). Although a study evaluated the ability of the PRESEP score to predict admission to intensive care units (ICUs), no external validation study has been performed with the diagnosis of sepsis as the outcome

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(13). Likewise, the Miami Sepsis Score is a newly developed simple tool consisting of variables that have individually been shown to have predictability for ICU admission among sepsis patients. The score as a whole is expected to have a high predictive performance; however, it has not been evaluated for its ability to predict either sepsis diagnosis or ICU admission (12, 14).

The early detection of septic patients in prehospital settings using a simple prediction tool would be vital to improving the overall sepsis care system and patient outcomes because early initiation of treatment is crucial. The PRESEP score and Miami Sepsis Score may serve as such tools if they are shown to have high predictive abilities. Therefore, in this study, we evaluated the PRESEP and Miami Sepsis Scores for their abilities to predict sepsis in prehospital settings.

Methods

Study Design

This was a retrospective observational study to evaluate the diagnostic performance of the PRESEP and Miami Sepsis Scores using prehospital and in-hospital medical records of patients transported by EMS to a single tertiary care hospital. The need for informed consent was waived due to the retrospective nature of the study, and the study design was approved by the appropriate ethics review board.

Study Settings

This study was conducted at Khon Kaen Hospital in Thailand. The hospital is a tertiary-level provincial hospital that receives severe cases including those referred from other hospitals within and surrounding Khon Kaen Province. The hospital has a command-and-control center for the provincial EMS system, which receives emergency calls via the nationally uniform phone number of 1-6-6-9 from the entire province. The personnel in the center perform phone triage, determine patient severity, and dispatch the appropriate level EMS unit from the nearest dispatch station. The Thai EMS system consists of various levels of EMS units dispatched from various organizations. Advance level units staffed with paramedics or nurse practitioners who can perform advance level procedures (e.g., endotracheal intubation) are stationed at hospitals; and basic level units staffed with emergency medical technicians (having 110 hour training) or emergency medical responders (40 hour training) who can perform first aid and basic life support procedures are stationed at local government offices and volunteer organizations (private sectors are involved in the formal EMS system). The basic level units make up the great majority of the EMS units.

Study Participants

This study included patients aged ≥18 years who were transported by EMS directly from the scene and admitted to this hospital between January 2020 and June 2020. Those with traumatic and non-traumatic injuries, incomplete data, hospitalized for palliative care, pregnancy, or cardiac arrest at the scene were excluded from the study. Those with sepsis diagnoses after 48 h of admission were also excluded, assuming that a definitive diagnosis usually occurred within 48 h and delayed diagnosis may have reflected conditions acquired after admission.

Data Collection

We collected data from the EMS and medical records of the hospital. Vital signs at the scene, such as blood pressure, body temperature, respiratory rate, heart rate, and oxygen saturation, were obtained from the first medical contact data in EMS medical records. Sex, age, the Glasgow Coma Scale score on admission, final diagnosis, and underlying diseases such as hypertension, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, cirrhosis, and cardiovascular disease were collected from the hospital medical records.

Outcome Variable

The primary outcome of this study was the final diagnosis of sepsis within 48 h of admission. The diagnosis of sepsis was defined using the International Classification of Diseases 10th Revision (ICD-10) codes A40, A41, R65.1, and R57.2 documented in medical records. The specialist registrars determined the codes based on the descriptions in the records according to the following criteria: clinical symptoms of systemic inflammatory response syndrome (hyperthermia, tachycardia, tachypnea, and leukocytosis) with positive blood culture; alternatively, antibiotic use for 5–7 days or death during treatment of 3–5 days without positive blood culture among those with immunological problems (e.g., cirrhosis, poor control diabetes, splenectomy, or acquired immunodeficiency syndrome). When the ICD-10 codes of sepsis were identified, the researcher reviewed the medical records to determine the timing of the sepsis diagnosis: sepsis within 48 h was defined as septic symptoms appearing and positive blood cultures being taken within 48 h.

Screening Tools

The PRESEP scoring system is based on vital signs, such as body temperature, heart rate, respiratory rate, oxygen saturation, and systolic blood pressure, whereas the Miami Sepsis Score includes body temperature, respiratory rate, and shock index (defined as the heart rate divided by systolic blood pressure) (Table 1). Bayer et al. (11) reported the performance of the PRESEP score: the area under the receiver operating characteristic curve (AUC) was 0.93, a Hosmer-Lemeshow test was not significant, and sensitivity and specificity at the proposed cutoff value of 4 were 0.85, and 0.86 respectively. The Miami Sepsis Score has not yet been

Table 1. Scoring of PRESEP score and Miami Sepsis Score.

	PRESEP score	Miami Sepsis Score
Temperature ≥38 °C	4	1
Temperature <36 °C	1	–
Heart rate >90 bpm	2	–
Respiratory rate ≥22 breaths/min	1	1
Oxygen saturation <92%	2	–
Systolic blood pressure <90 mmHg	2	–
Shock index ≥0.7	–	2

PRESEP, Prehospital Early Sepsis Detection.

evaluated for its predictive abilities, but a cutoff value of 3 to activate sepsis alerts was proposed by its developer (12).

Statistical Analysis

All characteristic data are described using proportions or medians. We calculated the PRESEP and Miami Sepsis Scores for each participant using his or her prehospital data; and determined the AUC together with their 95% confidence intervals (CI) to evaluate their predictive abilities. Additionally, observed proportions of sepsis cases were plotted against the scores to graphically evaluate the calibration. This is a comparison of predicted and observed risks (proportions of cases); in a scoring system, exact predicted values cannot be calculated but scores are considered as simplified proxies for the exact values that are calculable using the predictive regression models, from which the scores are derived.

We then determined the best cutoff values for the scores based on our data using Youden's index, which is "sensitivity + specificity − 1", and the cutoff value that maximize the index is the best. Based on the determined cutoff values and the previously proposed values (4 for the PRESEP score and 3 for the Miami Sepsis Score), the sensitivities, specificities, and likelihood ratios (LRs) with their 95% CIs were calculated. All analyses were performed using SPSS version 26 and MedCalc version 20.118. The sample size calculation assumed that the AUC was 0.85 and the proportion of sepsis was 0.25. To achieve an AUC confidence interval of 10%, the required sample size was 396 (15).

Results

Of the 972 patients transported by EMS directly from the scene and admitted to Khon Kaen Hospital, 567 patients were excluded because of palliative care (n = 38), trauma (n = 402), pregnancy (n = 83), and cardiac arrest at scene (n = 44). Of the remaining 405 patients eligible for the screening, those with incomplete data (n = 45) and those with sepsis diagnosed after 48 h of admission (n = 6) were excluded. Consequently, there were 354 patients left in the analysis; of them, 83 were diagnosed with sepsis within 48 h of admission (Figure 1).

Table 2 shows the characteristics of patients with and without sepsis. The two groups had similar demographic characteristics. However, the sepsis group showed a high proportion of patients with worse vital signs. Of the 83 sepsis patients, 72 (86.7%) and 67 (80.7%) showed higher scores than the previously proposed cutoff values of the PRESEP and Miami Sepsis Scores (4 and 3), respectively; of the 271 non-sepsis patients, 174 (64.2%) and 177 (65.3%) showed lower scores, respectively.

The AUC of the PRESEP score was 0.83 (95% CI 0.79–0.88) while that for the Miami Sepsis Score was 0.80 (95% CI 0.75–0.85) (Figure 2). Figure 3 shows the plots of observed proportions of sepsis cases against the scores. The PRESEP score showed a steady increase of the proportions with an increasing score up to 5, whereas the proportions at scores 6 and 7 were not different from that of 5. The Miami Sepsis Score showed a steady increase with the score in the entire score range.

The best cutoff values based on Youden's index were 5 for the PRESEP score (previously reported value was 4) and 3 for the Miami Sepsis Score (same as the previous one). At these values, both scores showed relatively high sensitivity of over 0.8, low specificity of around 0.65, and low positive LR of around 2.5 (Table 3). The PRESEP score showed slightly lower sensitivity and slightly higher specificity and LRs at a cutoff value of 5 than at 4.

Discussion

This study was the first external validation for the PRESEP score and the first evaluation of Miami Sepsis Score as screening tools to identify patients with sepsis in prehospital settings. This study showed relatively good predictive abilities of PRESEP and Miami Sepsis Scores: the AUCs were over 0.8. At the given cutoff values, their sensitivities were over 0.8, although the specificities were around 0.65, meaning that the scores have a potential as screening tools used by EMS personnel.

The AUC in this study was lower than that of the PRESEP score reported by Bayer et al. (11) (0.83 vs. 0.93). Jouffroy et al. (13) reported an even lower AUC (0.67). These differences were due to the different populations and outcomes. Bayer et al. applied the score for validation to the same population as that used in score derivation, although they used bootstrap sampling, whereas the present study performed an external validation in a different population. Usually, external validation studies show lower abilities than original score derivation studies. Jouffroy et al. evaluated the ability to predict ICU admission among septic patients, which had a different analytical objective than that of Bayer et al. and our study. Therefore, ours is the first external validation study with a diagnosis of sepsis as the outcome.

The Miami Sepsis Score was developed based on study results that investigated predictors of ICU admission among septic patients and found shock index and respiratory rate as significant predictors (14). Although it was developed for a different objective, the Miami Sepsis Score showed a relatively good ability to predict sepsis diagnosis (AUC is over 0.8).

According to the calibration plot, the PRESEP score may overestimate risks (proportions of sepsis cases) in its high value area (6–7 points) given that their observed risks were

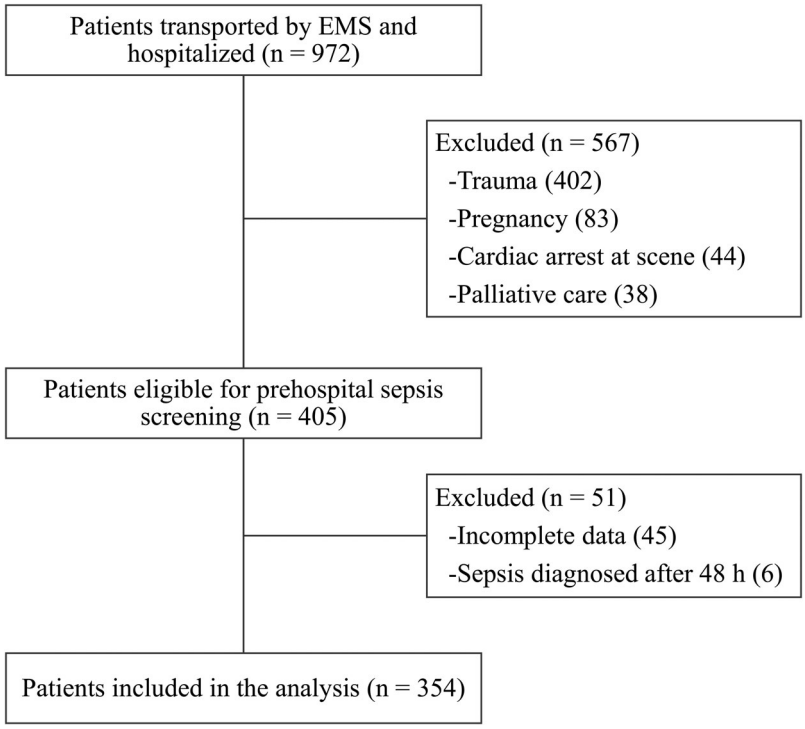

Figure 1. Participant selection procedure. EMS, emergency medical services.

Table 2. Characteristics of the patients (n = 354).

	Sepsis (n = 83) n (%)	Non-sepsis (n = 271) n (%)
Sex, male	52 (62.7)	165 (60.9)
Age (years)		
18–44	11(13.3)	61(22.5)
45–64	35(42.2)	105(38.7)
≥65	37(44.6)	105(38.7)
Pre-existing underlying diseases	66(79.5)	204(75.3)
Body temperature, °C		
<36	5(6)	11(4.1)
≥38	52(62.7)	72(26.6)
Respiratory rate, breaths/min, >22	72(86.7)	131(48.3)
Systolic blood pressure, mmHg, <90	31(37.3)	18(6.6)
Pulse rate, bpm, >90	68(81.9)	177(65.3)
Oxygen saturation, %, <92	32(38.6)	33(12.2)
Glasgow Coma Scale, <15	22(26.5)	37(13.7)
PRESEP score		
≥4	72 (86.7)	97 (35.8)
<4	11 (13.3)	174 (64.2)
Miami Sepsis Score		
≥3	67 (80.7)	94 (34.7)
<3	16 (19.3)	177 (65.3)

PRESEP, Prehospital Early Sepsis Detection.

almost those same as those at 4–5 points. However, this would not be a major problem because it is used to determine if it is greater or less than the cutoff value. In contrast, the Miami Sepsis Score showed a steady increase in all score ranges.

Our findings show that the PRESEP and Miami Sepsis Scores have sufficient abilities for screening in prehospital settings with relatively high sensitivities despite their low specificities at the given cutoff values. The low specificity (i.e., high false-positive rate) is acceptable because the primary objective of sepsis screening is to provide cues for early diagnosis to as many septic patients as possible, and the diagnosing process begins with sepsis in mind immediately after hospital arrival, which may facilitate the definitive diagnosis and early interventions. Although our findings suggest the cutoff value of 5 is the best for the PRESEP score based on Youden's index, its sensitivity is slightly higher at the cutoff of 4, the previously proposed value. The cutoff of 4 may be appropriate for the purpose of screening, in which false negatives should be minimized even at the cost of increased false positives (lower specificity).

Some previous studies aimed to develop or evaluate scores or tools to detect severe sepsis patients requiring ICU admission whereas the present study focused on detection of patients with a high probability of having sepsis. This difference may reflect the different EMS systems. Baez et al. (12) and Jouffroy et al. (13) focused on ICU admission in North American and French systems where well-trained personnel (paramedics and physicians) perform the screening. In contrast, the Thai EMS system mainly consists of basic level personnel with limited skills. In such Thai situations, focusing on detecting sepsis regardless of the severity may be appropriate because severity judgment would require additional skills and resources (e.g., lactate measurement).

In terms of feasibility as EMS tools, the Miami Sepsis Score might be more appropriate than the PRESEP score because of its simplicity with fewer parameters, which makes up for its slightly inferior predictive abilities. Simple scoring is crucial in the prehospital setting because the EMS personnel must perform many tasks while on scene and during transport, including monitoring patients and communicating with the control center and hospitals, in addition to the patients' time-constrained situations. However, both scores can be implemented in EMS because the parameters in both scoring systems are routinely assessed in prehospital settings.

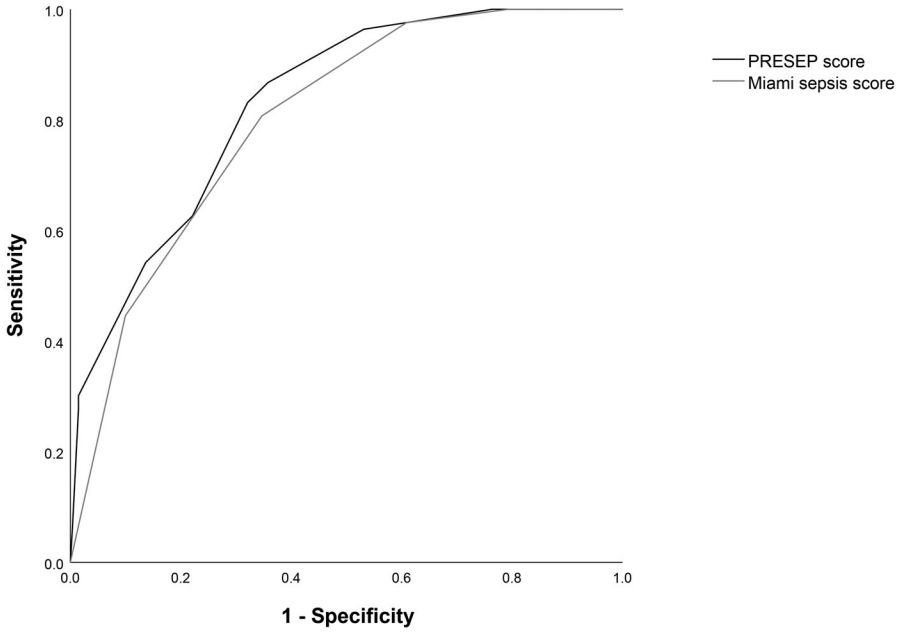

Figure 2. Receiver operating characteristic curve of the PRESEP score and the Miami Sepsis Score. PRESEP, Prehospital Early Sepsis Detection.

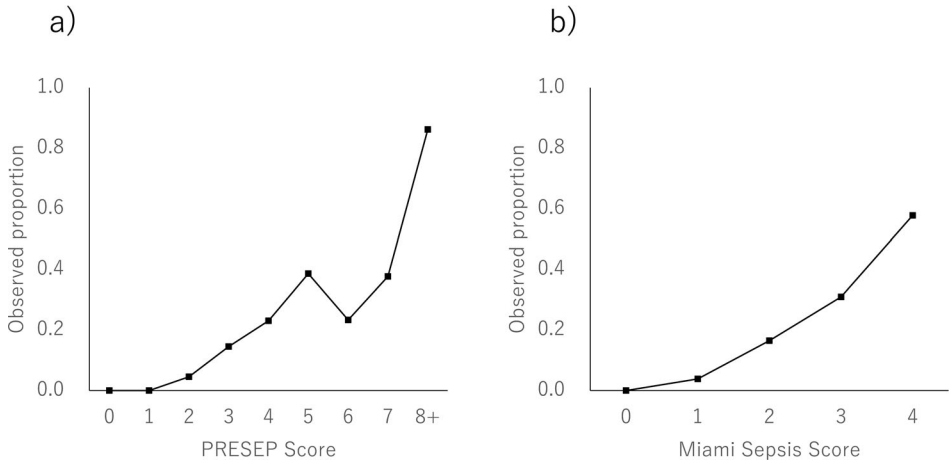

Figure 3. Observed proportions of sepsis cases by score. PRESEP, Prehospital Early Sepsis Detection. (a) PRESEP score and (b) Miami Sepsis Score. The categories of with scores of 8 or higher were merged into one because of the small number of patients included in them.

Table 3. Diagnostic accuracy of PRESEP score and Miami Sepsis Score.

	PRESEP		Miami Sepsis Score
Cutoff value	4	5	3
Sensitivity	0.87 (0.78–0.93)	0.83 (0.73–0.90)	0.81 (0.71–0.89)
Specificity	0.64 (0.58–0.70)	0.68 (0.62–0.73)	0.65 (0.59–0.71)
Positive LR	2.42 (2.02–2.90)	2.59 (2.12–3.16)	2.33 (1.93–2.83)
Negative LR	0.21 (0.12–0.36)	0.25 (0.15–0.40)	0.30 (0.19–0.46)

PRESEP, Prehospital Early Sepsis Detection.

Both the positive and negative LRs of these scores were small, but this is not a significant issue for screening purposes (this is not the case for definitive diagnoses).

EMS is the first contact point for emergency care, which can play a key role in expediting the management of severe sepsis cases by shortening the interval from triage in the emergency department to diagnosis and management for septic patients (8, 16), demonstrating the importance of suspecting sepsis prior to hospital arrival. In addition, a 2018 update of the Surviving Sepsis Campaign guidelines recommend that a bundle of managements should be provided within 1 hour: i.e., lactate measurement, blood culture, broad-spectrum antibiotics, fluid resuscitation using 30 ml/kg of crystalloid, and vasopressor (17). Some of these can be provided in prehospital settings to save time; particularly, the large volume fluid resuscitation may take more time than 1 hour, and preferably may be initiated prior to hospital arrival. Therefore, a reliable sepsis screening tool will help to enhance such roles and contribute to improving the outcomes of patients with sepsis.

This study has several limitations. First, this was a retrospective study, and the final diagnosis of sepsis was made using the ICD-10 codes documented in the medical records. The coding and judgment of the diagnosis timing were based on the unstandardized descriptions of the medical records; however, we standardized the methods of data extraction and judgment wherever possible. Second, this study extracted patient records from a single hospital, which might have caused a selection bias. Even though the study site hospital receives various patients (including severe cases)

from the entire province, there are other hospitals receiving emergency cases in the same area. The potential biases should not distort the results because different patient compositions did not influence the test performance indicators such as AUC.

Conclusion

Due to their relatively high ability to detect sepsis patients, the PRESEP and Miami Sepsis Scores have potential as useful tools to screen septic patients in prehospital settings. Further research, preferably multicenter prospective studies, should be conducted.

Disclosure Statement

The authors declare no conflicts of interest

Ethical Clearance

The ethics committee of Khon Kaen Hospital approved the study protocol and waived informed consent from the participants because of the retrospective nature of this study.

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Data Availability Statement

The research protocol approved by the ethics committee does not allow data sharing.

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