The predictive value of the Early Warning Scores (EWSs) for admission and in-hospital mortality in elderly patients

（高齢救急患者における早期警戒スコアの入院
ならびに院内死亡の予測値）

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Abstract

The aims of this study are 1) to evaluate the value of pre-hospital National Early Warning Score (pNEWS) and pre-hospital Modified Early Warning Score (pMEWS) for predicting admission and in-hospital mortality in patients older than 65 years who present to the Emergency Department (ED), by comparing the ED National Early Warning Score (eNEWS) and ED Modified Early Warning Score (eMEWS), 2) to clarify the age-associated change in value of the eNEWS for predicting in-hospital mortality in acute medical patients older than 75 years, 80 years, and 85 years, and 3) to evaluate the value of the eNEWS-JmGPS (Japanese modified Glasgow Prognostic Score) for predicting in-hospital mortality in acute medical patients older than 65 years.

This retrospective, single-centre observational study was carried out in the ED of Jikei University Kashiwa Hospital, in Chiba, Japan, from 1 April 2017 to 31 March 2018. All patients aged 65 years or older were included in this study. The NEWS was derived from seven common physiological vital signs: respiratory rate, peripheral oxygen saturation, the presence of inhaled oxygen parameters, body temperature, systolic blood pressure, pulse rate and AVPU (Alert, responds to Voice, responds to Pain, Unresponsive) score, whereas the MEWS was derived from six common physiological vital signs: respiratory rate, peripheral oxygen saturation, body temperature, systolic blood pressure, pulse rate and AVPU score. The JmGPS was derived from two serum biomarkers: C-reactive protein: CRP and albumin. Discrimination was assessed by plotting the receiver operating characteristic (ROC) curve and calculating the area under the ROC curve (AUC).

The AUC for predicting admission was 0.559 for the pNEWS and 0.547 for the pMEWS. The AUCs for predicting in-hospital mortality were 0.678 for the pNEWS and 0.652 for the pMEWS.

The AUC for predicting admission was 0.628 for the eNEWS and 0.591 for the eMEWS. The AUC of the eNEWS was significantly greater than that of the eMEWS for predicting admission ($p < 0.001$). The AUC for predicting in-hospital mortality was 0.789 for the eNEWS and 0.720 for the eMEWS. The AUC of the eNEWS was significantly greater than that of the eMEWS for predicting in-hospital mortality ($p < 0.001$). The AUC of the eNEWS for in-hospital mortality was significantly higher in the group of younger than 85 years than in the group of older than 85 years. On the other hand, the AUC of the eNEWS for in-hospital mortality was significantly lower in the group of younger than 75 years and 80 years than in the group of older than 75 years and 80 years respectively. Furthermore, the AUC for predicting in-hospital mortality was 0.817 for the eNEWS-JmGPS and 0.797 for the eNEWS. The AUC of the eNEWS-JmGPS was significantly higher than that of the eNEWS for predicting in-hospital mortality.

Our single-centre study has demonstrated the low utility of the pNEWS and the pMEWS as predictors of admission and in-hospital mortality in elderly patients, whereas the eNEWS and the eMEWS predicted admission and in-hospital mortality more accurately. In addition to this, in the oldest-old patients older than 85 years, the predictive value of eNEWS for in-hospital mortality is lower than that of the patients younger than 85 years. Furthermore, the eNEWS-JmGPS is a good predictor of in-hospital mortality among elderly patients, whereas the original eNEWS is a moderate predictor of in-hospital mortality. Evidence from multicentre studies is needed for external validation and to remove selection bias.

Introduction

The growing ageing population is a major theme in public health worldwide. Life expectancy is increasing in many countries, and Japanese life expectancies are 81.1 years for men and 87.1 years for women, representing two of the highest in the world[1)]. The proportion of people older than 65 years was 23.0% in 2010—the highest in the world—and is expected to reach 29.1% by 2020[2)], and the number of patients older than 65 years presenting to EDs is increasing in parallel. A study from the United States reported that elderly patients comprised 40% to 50% of all people presenting to the ED[3)].

As improving health care system, most of people orders than 65 years are healthy and people older than 75 years are defined as old people in Japan[4)]. Moreover, one study has shown that the percentage of flail rapidly increase in people older than 80 years[5)]. Overcrowding in emergency departments (EDs) due to the high proportion of late-stage elderly patients has become a serious problem, and there is a critical need to make decisions for the efficient management of EDs as quickly as possible.

Several risk-scoring systems have been established to identify the risk of catastrophic deterioration and death of hospital inpatients.

The National Early Warning Score (NEWS) was developed in 2012 in the United Kingdom by the National Early Warning Score Development and Implementation Group on behalf of the Royal College of Physicians[6)]. The Modified Early Warning Score (MEWS) was validated in 2001 in the United Kingdom as a bedside tool to identify patients at risk for catastrophic events, including death[7)].

Several studies have explored the association between these risk scores and hospital admission or in-hospital mortality. The findings suggest that these risk scores could also be used as triage tools to identify patients requiring admission or the risk of death[7-9)]. Most studies focused on scores that were measured in the hospital or the ED, and only a few studies evaluated the strong relation between pre-hospital NEWS and in-hospital mortality or admission to the critical care unit[10,11)].

There was no study comparing several risk-scoring systems in the pre-hospital setting, and it is still unclear which risk-scoring system is superior as a triage tool for admission and to predict in-hospital mortality of elderly patients who present to the ED by ambulance. Moreover, there was also no study comparing the value of the early warning scores between two different age populations, whose cut-off of age are 75 years, 80 years, and 85 years, and it is still unclear the age-associated changes in value of early warning score for predicting in-hospital mortality in elderly patients.

The Glasgow Prognostic Score (GPS), which is based on inflammation criteria including serum C-reactive protein (CRP) and albumin, is a practical scoring system for the prognosis of patients with advanced cancer[12-16)]. Recently, the studies conducted by Proctor *et al.* [17)] and by Hirashima *et al.* [18)] showed that the modified GPS (mGPS) is superior to GPS as a prognostic factor and that the Japanese-modified GPS (JmGPS), with a CRP cut-off of 0.5mg/dl, also has high value as a prognostic factor. Furthermore, a study conducted by Viviane *et al.* [19)] showed that the mGPS correlates significantly with frailty in elderly patients.

To the best of our knowledge, no study has evaluated the value of the early warning score with the JmGPS (EWS-JmGPS) for predicting in-hospital mortality of elderly patients, and it is still unclear whether the EWS-JmGPS is superior to the original EWS for predicting in-hospital mortality.

The aims of the present study are as below: 1) To evaluate the value of pre-hospital early warning scores (pNEWS / pMEWS) for predicting admission and in-hospital mortality in patients older than 65 years who present to the ED, by comparing the ED early warning scores (eNEWS / eMEWS), 2) To clarify the age-associated change in value of the eNEWS for predicting in-hospital mortality of acute medical patients older than 75 years, 80 years, and 85 years, and 3) To evaluate the value of the eNEWS-JmGPS for predicting in-hospital mortality of acute medical patients older than 65 years who present to EDs.

Materials & Methods

Study design

This retrospective, single-centre observational study was carried out during 1 year in the ED of a university hospital in Japan to evaluate the value of the EWSs for predicting admission and in-hospital mortality in patients older than 65 years who were presented to the ED by ambulance.
The protocol for this research project was approved by a suitably constituted Ethics Committee of the institution and conforms to the provision of the Declaration of Helsinki (Committee of Chiba university, Approval No. 3229/Committee of Jikei university school of medicine, Approval No. 30-094(9115))

Study setting and population

In Japan, EDs are grouped into three categories. Primary emergency medical institutions treat patients with mild conditions and walk-in patients. Secondary emergency medical institutions treat patients with mild or moderate conditions that might require hospitalisation. Tertiary emergency medical institutions treat or resuscitate seriously ill patients who have suffered from multiple trauma, shock or cardiopulmonary arrest[20)]. The present study was carried out between 1 April 2017 and 31 March 2018 at Jikei University Kashiwa Hospital, a tertiary emergency medical institution. The hospital is located in Kashiwa City in Chiba Prefecture. It has 664 beds, and about 8500 patients present to the ED annually. We accept about 5000 patients coming to the ED by ambulance annually. The population of Kashiwa City is about 415,000, and about 105,000 (25.3%) of the population is older than 65 years. People with disease or trauma call the fire department command centre (119), and the centre informs them of the emergency medical services (EMS) that are nearest to them. When the EMS personnel reach the patient, they gather information about the patient, including vital signs, only once, and judge the triage level. The EMS then calls the proper emergency institution and provides all the patient information. In our ED, a chief nurse receives the call and asks the ED doctors to accept the patient. All patients older than 65 years who presented to the ED by ambulance during the study period were included in this study. Patients arrested before arrival at the hospital and patients transferred to other hospitals from the ED were excluded from the study.

Data sources and measurements

When the EMS arrive at our ED, the chief nurse first evaluates the severity of the case. Then, the patient is guided to the appropriate emergency room according to the severity. The junior and senior emergency medicine residents see all the patients who present to our ED, and the emergency physician takes over the patient's treatment and follow-up. During this process, all of the patient's data, including pre-hospital and ED vital signs, are recorded in electrical medical records by the nurses. We obtained the pre-hospital vital signs and the first vital signs just after arrival at the ED. The patients were followed up until discharge or death for a maximum of 28 days. Data on the patient's discharge from the ED, admission to a ward, admission to the intensive care unit (ICU) and in-hospital mortality were recorded. Diagnostic categories were based on the ICD-10 (*International Classification of Diseases-10*) and classified as 1) Trauma, 2) Neurology, 3) Pulmonology, 4) Cardiology, 5) Gastroenterology, 6) Endocrinology, 7) Nephrology/Urology, 8) Haematology, 9) Collagen disease, 10) Otolaryngology, 11) Gynaecology, 12) Dermatology, 13) Ophthalmology, 14) Psychology, 15) Toxicology and 16) Others. We were able to obtain complete information on the patients' age, gender, diagnostic category, length of stay in the ED, disposition and in-hospital mortality, but we could not obtain data on vital signs or serum biomarkers for all of the patients. The reasons for the missing data were that the EMS crew decided to give priority to transportation because the patient's condition was extremely critical; the ED was overcrowded and the nurses were unable to input the patient's information in the medical record, and some patients, such as those directed to otolaryngology, went directly to the treatment room. In the present study, missing values were not excluded, and substitution was made using multiple imputation analysis because transportation was prioritised in only a small number of cases, and most of the missing values occurred because the nurses were unable to input the data for vital signs due to overcrowding of the ED.

The pNEWS/eNEWS and pMEWS/eMEWS were calculated using the recorded physiological parameters of the patients. The pNEWS/eNEWS were derived from seven common physiological vital signs: respiratory rate, peripheral oxygen saturation, the presence of inhaled oxygen parameters, body temperature, systolic blood pressure, pulse rate and AVPU (Alert, responds to Voice, responds to Pain, Unresponsive) score. The scores vary between 0 and 3 for each parameter (Table 1). The pNEWS/eNEWS totals range from 0 to a maximum of 20. The pMEWS/eMEWS were derived from six common physiological vital signs: respiratory rate, peripheral oxygen saturation, body temperature, systolic blood pressure, pulse rate and AVPU score. The scores vary between 0 and 3 for each parameter (Table 2). The pMEWS/eMEWS totals range from 0 to a maximum of 14.

The AVPU score was derived from the GCS as follows: A = 14–15, V = 9–13, P = 4–8, U = 3.

The patients were divided into three groups: those who were discharged from the ED, those who were admitted to a ward and those who were admitted to the ICU. The intergroup differences in all the parameters and the scores during the stay in the ED were also evaluated.

For calculation of value of predicting in-hospital mortality in deferent cut-off of age, the acute medical patients were divided at the age of 75 years, 80 years, and 85 years.

The JmGPS was derived from two serum biomarkers: CRP and albumin. The JmGPS total ranges from 0 to 2 (Table 3), and the eNEWS-JmGPS total ranges from 0 to a maximum of 22.

Statistical analysis

Continuous variables were described as medians and interquartile ranges and were compared by Student's *t*-test and Mann–Whitney *U* test. Categorical variables were described as numbers and percentages and were compared by Pearson's χ^2 test. Analysis of variance (ANOVA) was used to test differences among the three groups. Receiver operating characteristic (ROC) analysis and the AUC were used to evaluate the predictive value of the pNEWS and pMEWS for admission and in-hospital mortality. Confidence intervals (CIs) around the AUC were calculated using bootstrap resampling methods with 1000 repetitions by using R software (R version 3.5.3 binary for OS X 10.11, EI Capitan). The cut-off values for the pNEWS and pMEWS were determined by using Youden's index (sensitivity + specificity – 1). Using these determined cut-off points, the sensitivity, specificity and odds ratio of pNEWS and pMEWS were calculated for the prediction of admission and in-hospital mortality. A p-value of less than 0.05 was considered to indicate statistical significance. Calibration was assessed statistically using the Hosmer–Lemeshow C statistic. A statistically significant result suggests a lack of calibration. Sample size was calculated by EPVs (events per variable). Peduzzi *et al.* **(*Peduzzi P et al., 1996*)** demonstrated that 10 EPVs were required for accurate estimation of regression coefficients in a logistic regression model. We calculated 7 variables for NEWS and 6 variables for MEWS in our study, so we needed more than 70 events. Previous studies reported that mortality rates were 4.7% to 6.9% (***Abbott TE et al., 2016; Abbott TE et al., 2018***), and we assumed the mortality rate to be 5.8%. Finally, we set the sample size at 1210 cases. Data were analysed by the Statistical Package for the Social Sciences, version 16.0 (SPSS, Chicago, IL, USA).

Results

During the study period, 2204 elderly patients presented to the ED by ambulance. Pre-hospital data on vital signs were missing for 916 patients (41.6%), and ED data on vital signs were missing for 595 patients (27.0%). We recovered the data completely by using multiple imputation analysis.
The median age (interquartile range) of the patients was 78 (11) years, and 1188 (53.9%) patients were male. The major diagnostic categories were 373 (16.9%) trauma cases, 492 (22.3%) cardiology cases, 304 (13.8%) neurology cases, 305 (13.8%) gastroenterology cases, 174 (7.9%) pulmonology cases, 132 (6.0%) nephrology/urology cases, 130 (5.9%) otolaryngology cases and 129 (5.9%) other cases (multi-organ failure, severe sepsis, heat stroke, etc.). The median length (interquartile range) of stay in the ED was 125 (114) min. Eight hundred sixty-eight (39.4%) patients were discharged from the ED, 938 (42.6%) patients were admitted to a ward, and 398 (18.1%) patients were admitted to the ICU. One hundred twenty-seven (5.8%) patients died within 28 days of presenting to the ED. Among patients with incomplete pre-hospital or ED data, more patients were discharged from the ED than were admitted to hospital; moreover, this group of patients had a lower mortality rate than did patients with complete pre-hospital and ED data (Table 4).
The median pNEWS/eNEWS and pMEWS/eMEWS of patients admitted to a ward or the ICU were significantly higher than the median pNEWS/eNEWS and pMEWS/eMEWS of patients discharged from the ED. The eNEWS was significantly higher than the pNEWS in patients who were discharged from the ED and admitted to a ward, but there was no significant difference between the eNEWS and the pNEWS in patients who were admitted to the ICU. The eMEWS was significantly higher than the pMEWS in patients who were discharged from the ED and admitted to a ward, but there was no significant difference between the eMEWS and the pMEWS in patients who were admitted to the ICU (Table 5).
The median pNEWS/eNEWS and pMEWS/eMEWS were significantly higher in non-survivors than in survivors. The eNEWS and eMEWS were significantly lower than the pNEWS and pMEWS in survivors. The proportion of patients who had oxygen supplementation or bad consciousness in either the pre-hospital setting or the ED was significantly higher in non-survivors than in survivors (Table 6).
The AUC for predicting admission was 0.559 (95% CI 0.536 to 0.583, $p < 0.001$) for the pNEWS and 0.547 (95% CI 0.525 to 0.572, $p < 0.001$) for the pMEWS. There was no significant difference between the AUC of the pNEWS and the pMEWS for predicting admission ($p = 0.102$). The cut-off values for admission were 5 for the pNEWS and 3 for the pMEWS. A pNEWS of 5 or more had a sensitivity of 54.0%, a specificity of 54.8% and an odds ratio of 1.43 for predicting admission. A pMEWS of 3 or more had a sensitivity of 54.9%, a specificity of 50.6% and an odds ratio of 1.25 for predicting admission (Fig. 1). The AUC for predicting in-hospital mortality was 0.678 (95% CI 0.633 to 0.720, $p < 0.001$) for the pNEWS and 0.652 (95% CI 0.609 to 0.695, $p < 0.001$) for the pMEWS. There was no significant difference between the AUC of the pNEWS and the pMEWS for predicting in-hospital mortality ($p = 0.081$). The cut-off values for in-hospital mortality were 6 for the pNEWS and 4 for the pMEWS. A pNEWS value of 6 or more had a sensitivity of 65.4%, a specificity of 59.7% and an odds ratio of 2.79 for predicting in-hospital mortality. A pMEWS value of 4 or more had a sensitivity of 57.5%, a specificity of 64.5% and an odds ratio of 2.45 for predicting in-hospital mortality (Fig. 2). The AUC for predicting admission was 0.628 (95% CI 0.605 to 0.652, $p < 0.001$) for the eNEWS and 0.591 (95% CI 0.569 to 0.616, $p < 0.001$) for the eMEWS. The cut-off values for admission were 4 for the eNEWS and 3 for the eMEWS. An eNEWS of 4 or more had a sensitivity of 55.3%, a specificity of 63.1% and an odds ratio of 2.12 for predicting admission. An eMEWS of 3 or more had a sensitivity of 41.2%, a specificity of 75.7% and an odds ratio of 2.18 for predicting admission (Fig. 1). The AUC for predicting in-hospital mortality was 0.789 (95% CI 0.747 to 0.829, $p < 0.001$) for the eNEWS and 0.720 (95% CI 0.671 to 0.765, $p < 0.001$) for the eMEWS. The cut-off values for in-hospital mortality were 5

for the eNEWS and 3 for the eMEWS. An eNEWS of 5 or more had a sensitivity of 78.7%, a specificity of 64.0% and an odds ratio of 6.58 for predicting in-hospital mortality. An eMEWS value of 3 or more had a sensitivity of 69.3%, a specificity of 67.6% and an odds ratio of 4.71 for predicting in-hospital mortality (Fig. 2).

For admission and in-hospital mortality, the AUC of the eNEWS was significantly greater than that of the pNEWS **(**$p < 0.001$, $p < 0.001$**)**, and the AUC of the eMEWS was significantly greater than that of the pMEWS **(**$p < 0.01$, $p < 0.05$**)**.

In the acute medical patients younger than 75 years, the AUC for predicting in-hospital mortality was 0.759 [95% CI 0.657 to 0.860, $p < 0.01$] for the eNEWS. The cut-off value for in-hospital mortality was 5 for the eNEWS. The eNEWS of 5 or more had a sensitivity rate of 75.9 %, a specificity rate of 66.7 %, and an odds ratio of 6.29 for predicting in-hospital mortality (Fig. 3A). In the acute medical patients older than 75 years, the AUC for predicting in-hospital mortality was 0.807 [95% CI 0.764 to 0.850, $p < 0.001$] for the eNEWS. The cut-off value for in-hospital mortality was 6 for the eNEWS. The eNEWS of 6 or more had a sensitivity rate of 73.3 %, a specificity rate of 71.9 %, and an odds ratio of 7.04 for predicting in-hospital mortality (Fig. 3B).

In the acute medical patients younger than 80 years, the AUC for predicting in-hospital mortality was 0.787 [95% CI 0.726 to 0.849, $p < 0.001$] for the eNEWS. The cut-off value for in-hospital mortality was 5 for the eNEWS. The eNEWS of 5 or more had a sensitivity rate of 78.6 %, a specificity rate of 65.2 %, and an odds ratio of 6.88 for predicting in-hospital mortality (Fig. 3C). In the acute medical patients older than 80 years, the AUC for predicting in-hospital mortality was 0.803 [95% CI 0.749 to 0.858, $p < 0.001$] for the eNEWS. The cut-off value for in-hospital mortality was 6 for the eNEWS. The eNEWS of 6 or more had a sensitivity rate of 74.6 %, a specificity rate of 71.1 %, and an odds ratio of 7.21 for predicting in-hospital mortality (Fig. 3D).

In the acute medical patients younger than 85 years, the AUC for predicting in-hospital mortality was 0.803 [95% CI 0.757 to 0.849, $p < 0.001$] for the eNEWS. The cut-off value for in-hospital mortality was 7 for the eNEWS. The eNEWS of 7 or more had a sensitivity rate of 67.4 %, a specificity rate of 80.3 %, and an odds ratio of 8.41 for predicting in-hospital mortality (Fig. 3E). In the acute medical patients older than 85 years, the AUC for predicting in-hospital mortality was 0.776 [95% CI 0.687 to 0.864, $p < 0.001$] for the eNEWS. The cut-off value for in-hospital mortality was 6 for the eNEWS. The eNEWS of 6 or more had a sensitivity rate of 70.4 %, a specificity rate of 72.8 %, and an odds ratio of 6.36 for predicting in-hospital mortality (Fig. 3F).

The AUC for predicting in-hospital mortality was 0.817 [95% CI 0.781 to 0.853, $p < 0.001$] for the eNEWS-JmGPS and 0.797 [95% CI 0.756 to 0.837, $p < 0.001$] for the eNEWS. The AUC of the eNEWS-JmGPS was significantly higher than that of the eNEWS for predicting in-hospital mortality ($p < 0.001$). The cut-off values for in-hospital mortality were 7 for the eNEWS-JmGPS and 7 for the eNEWS. The eNEWS-JmGPS value of 7 or more had a sensitivity rate of 75.6%, a specificity rate of 72.6%, and an odds ratio of 8.22 for predicting in-hospital mortality. The eNEWS of 7 or more had a sensitivity rate of 64.7%, a specificity rate of 80.3%, and an odds ratio of 7.47 for predicting in-hospital mortality (Fig. 4).

Discussion

Several studies have evaluated the effectiveness of risk-scoring systems for predicting admission to critical care units from wards or in-hospital mortality in the last decade, but many of them focused on in-hospital management[7,9,23)]. Moreover, previous studies that estimated the prognostic value of risk-scoring systems did not include patients with trauma, but we included such patients in our study because elderly patients frequently have not only endogenous diseases but also traumatic problems in the clinical

setting. Few studies set in the ED have shown the predictive value of the NEWS and MEWS for hospitalisation or in-hospital mortality[3)]. Moreover, few studies from the pre-hospital setting have shown the predictive value of the NEWS for escalation to the critical care unit within 48 hours after hospital admission or death[10,11)].
In a study by Rohr *et al.*[24)], the AUC of the NEWS for ICU admission was 0.73. No study has calculated the AUC of the NEWS for total admissions, which would include patients who were admitted to the ward. In the studies by Subbe *et al.* [7)] and Bulut *et al.* [25)], the AUC of the MEWS for admission to the ward or the ICU was 0.62 to 0.568. Although several studies of the AUC of the NEWS and the MEWS for admission have been carried out, none of them calculated the AUC of the NEWS or the MEWS for admission in elderly patients.
Our study examined the ability of the pNEWS/eNEWS and the pMEWS/eMEWS to predict admission in elderly patients, but none of these scores had excellent (AUC > 0.90) or good (AUC > 0.80) ability to predict admission. We found that the pNEWS/eNEWS and the pMEWS/eMEWS were poorly effective for predicting admission in elderly patients; the AUCs for admission were 0.559/0.628 and 0.547/0.591. There was no significant difference between the AUC of the pNEWS and the pMEWS for predicting admission, whereas the AUC of the eNEWS was significantly greater than that of the eMEWS.
In studies by Smith *et al.* [26)] and Kovacs *et al.* [27)], the predictive value of the NEWS for in-hospital mortality was very high, with an AUC of 0.894 to 0.902. In studies by Bulut *et al.* [25)] and Smith *et al.* [26)], the predictive value of the MEWS for in-hospital mortality was also high, yielding an AUC of 0.630 to 0.865. Although several studies of the NEWS and the MEWS for predicting in-hospital mortality were carried out, none of them calculated the AUC of the NEWS or the MEWS for in-hospital mortality in elderly patients. Only a few studies calculated the predictive value of the pre-hospital NEWS. In the study by Pirneskoski *et al.* [28)], the predictive value of the pre-hospital NEWS for in-hospital mortality within 1 day was high, with an AUC of 0.840, but the study was not based on the elderly population. We found that the pNEWS and the pMEWS had low effectiveness, and the eNEWS and the eMEWS had moderate effectiveness for predicting in-hospital mortality in elderly patients. Our study also found that there was no significant difference between the AUC of the pNEWS and the pMEWS for predicting in-hospital mortality, whereas the AUC of the eNEWS was significantly greater than that of the eMEWS.
The NEWS and MEWS have been introduced to the ED to predict patients' prognosis in the United Kingdom. However, because there is not much evidence for the value of these risk scores in the pre-hospital setting for predicting admission and in-hospital mortality, these risk scores have not been introduced in the pre-hospital setting[10)]. In the past two decades, EMS crews in Japan have used a severity and urgency criterion that is based on physiological evaluation, anatomical evaluation, symptoms and mechanism of injury. This criterion is not based on international triage systems, such as the Canadian Triage and Acuity Scale, and it is not updated regularly[29)].
No study has evaluated the usefulness of pre-hospital risk-scoring systems for predicting patients' prognosis in Japan. Because it is very difficult to predict the severity of illness in elderly patients, we need to accumulate more evidence of the value of pre-hospital clinical risk scores, in order to more clearly anticipate the patient's prognosis and to perform appropriate triage.
Our study has shown that the pNEWS and the pMEWS have low utility as predictors of patient admission and in-hospital mortality. Therefore, it is difficult to use these scores as criteria for judging whether hospitalisation is necessary in the pre-hospital setting or for judging whether the EMS crew should transport the patient to a high-level emergency institution as rapidly as possible.
A study conducted by Zerrin *et al.* [30)] demonstrated that the VitalPac Early Warning Score (VIEWS), which was developed before the NEWS, was a powerful scoring system for use with elderly acute medical patients older than 65 years; the AUC of VIEWS was 0.756 for hospitalisation and 0.900 for in-

hospital mortality. By contrast, one study carried out by Groot *et al.* [23] demonstrated the low prognostic performance of the NEWS for risk stratification in elderly septic patients older than 75 years but a higher prognostic performance in septic patients younger than 75 years. For this reason, in the patients older than 75 years, it might be difficult to expect the elderly patient's prognosis by using these scores. In the subgroup analysis of our study, the AUCs for in-hospital mortality of the patients older than 75 years and 80 years were higher than that of the patients younger than 75 years and 80 years. On contrast, the AUC for in-hospital mortality of the patients older than 85 years was lower than that of the patients younger than 85 years. The reason of these findings is that these oldest-old patients have several factors, such as frailty, dementia, and atypical physiological reaction, which affect the variables that configure the score.

Several studies have evaluated that early warning scores with other biomarkers have strong power for predicting patient's prognosis. A study carried out by Rasmussen et al. [31] evaluated that the NEWS with Soluble Urokinase Plasminogen Activator Receptor (SuPAR) improves risk prediction. Another study carried out by Hasan et al. [32] demonstrated that the Modified Early Warning Score with rapid lactate level was an also powerful scoring system for detecting mortality of 65 years and older patients, and the AUC of the Modified Early Warning Score with rapid lactate level was 0.872 for in-hospital mortality. In the previous study conducted by Anna et al.[33], the GPS showed moderate prognostic accuracy (AUC 0.67) in Emergency Department. Moreover, a study carried out by Rui et al. [34] demonstrated that the GPS is a strong predictor of poor prognosis in elderly patients with acute myocardial infarction.

In our study, we found that the NEWS-JmGPS is highly effective for predicting in-hospital mortality of elderly patients older than 65 years, and the AUC for in-hospital mortality was 0.817. Moreover, the AUC of the NEWS-JmGPS was significantly higher than that of the original NEWS for predicting in-hospital mortality.

In previous studies by Abbott *et al.* [10,22], the mortality rate was 4.7% (15 of 322 patients) to 6.9% (13 of 189 patients). In our study, the in-hospital mortality rate within 28 days after admission was 5.8% (127 of 2204 patients), which is similar to that in the previous study. The EPVs were 18.1, and we secured the number of event cases necessary for accurate estimation.

This study has several limitations. First, it was a retrospective, single-centre study, and we did not evaluate the external validation. Second, discharged patients were not followed up for readmission to the ED and out-of-hospital mortality. Third, the proportion of cases with missing data was relatively high at about 40%. These limitations may reduce the generalizability of the results.

Conclusions

Our single-centre study has demonstrated the low utility of the pNEWS and the pMEWS as predictors of admission and in-hospital mortality in elderly patients, whereas the eNEWS and the eMEWS predicted admission and in-hospital mortality more accurately. In addition to this, in the oldest-old patients older than 85 years, the predictive value of eNEWS for in-hospital mortality is lower than that of the patients younger than 85 years. Furthermore, the eNEWS-JmGPS is a good predictor of in-hospital mortality among elderly patients, whereas the original eNEWS is a moderate predictor of in-hospital mortality. Evidence from multicentre studies is needed for external validation and to remove selection bias.

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Table 1 National Early Warning Score (NEWS)

	3	2	1	0	1	2	3
Respiratory rate (bpm)	≤8		9−11	12−20		21−24	≥25
Oxygen saturation (%)	≤91	92−93	94−95	≥96			
Inhaled oxygen		Yes		No			
Temperature (℃)	≤35.0		35.1−36.0	36.1−38.0	38.1−39.0	≥39.1	
Systolic blood pressure (mmHg)	≤90	91−100	101−110	111−219			≥220
Pulse rate (bpm)	≤40		41−50	51−90	91−110	111−130	≥131
AVPU				A			V, P, or U

AVPU; A, alert; V, to voice; P, to pain; U, to unresponsive; bpm, beats or breaths per minute.

Table 2 Modified Early Warning Score (MEWS)

	3	2	1	0	1	2	3
Respiratory rate (bpm)		≤8	9	10−18	19−20	21−29	≥30
Oxygen saturation (%)	≤91	92−93	94−95	≥96			
Temperature (℃)		≤35.0		35.1−38.4		≥38.5	
Systolic blood pressure (mmHg)	≤70	71−80	81−100	101−199		≥200	
Pulse rate (bpm)		≤39	40−50	51−100	101−110	111−129	≥130
AVPU				A	V	P	U

AVPU; A, alert; V, to voice; P, to pain; U, to unresponsive; bpm, beats or breaths per minute.

Table 3 Japanese modified Glasgow Prognostic Score (JmGPS)

Score	
0	CRP ≤ 0.5mg/dl
1	CRP > 0.5mg/dl and Albumin ≥ 3.5g/dl
2	CRP > 0.5mg/dl and Albumin < 3.5g/dl

CRP, C-reactive protein.

Table 4. Baseline characteristics of the study population

	Total Population (n=2204) Median (interquartile range)	Pre-hospital			Emergency Department		
		Data Complete Group (n=1288) Median (interquartile range)	Data Incomplete Group (n=916) Median (interquartile range)	*p* value	Data Complete Group (n=1609) Median (interquartile range)	Data Incomplete Group (n=595) Median (interquartile range)	*p* value
Age, years	78(11)	78 (11)	78(10)	0.326	78 (11)	78(10)	0.214
Sex [n (%)]				< 0.05			< 0.05
Male	1188(53.9)	719 (55.8)	469(51.2)		896 (55.7)	292(49.1)	
Female	1016(46.1)	569 (44.2)	447(48.8)		713 (44.3)	303(50.9)	
Diagnostic Category [n (%)]				< 0.001			< 0.001
Trauma	373(16.9)	219 (17.0)	154(16.8)		274 (17.0)	99(16.6)	
Cardiology	492(22.3)	391 (30.4)	101(11.0)		440 (27.3)	52(8.7)	
Neurology	304(13.8)	201 (15.6)	103(11.2)		242 (15.0)	62(10.4)	
Gastroenterology	305(13.8)	148 (11.5)	157(17.1)		206 (12.8)	99(16.6)	
Pulmonology	174(7.9)	128 (9.9)	46(5.0)		149 (9.3)	25(4.2)	
Nephrology/Urology	132(6.0)	54 (4.2)	78(8.5)		80 (5.0)	52(8.7)	
Otolaryngology	130(5.9)	15 (1.2)	115(12.6)		37 (2.3)	93(15.6)	
Endocrinology	36(1.6)	19 (1.5)	17(1.9)		24 (1.5)	12(2.0)	
Hematology	36(1.6)	13 (1.0)	23(2.5)		23 (1.4)	13(2.2)	
Dermatology	23(1.0)	10 (0.8)	13(1.4)		13 (0.8)	10(1.7)	
Ophthalmology	22(1.0)	1 (0.1)	21(2.3)		2 (0.1)	20(3.4)	
Gynecology	18(0.8)	8 (0.6)	10(1.1)		10 (0.6)	8(1.3)	
Psychiatry	18(0.8)	5 (0.4)	13(1.4)		7 (0.4)	11(1.8)	
Toxicology	7(0.3)	7 (0.5)	0(0)		7 (0.4)	0(0)	
Collagen disease	5(0.2)	3 (0.2)	2(0.2)		4 (0.2)	1(0.2)	

Others	129(5.9)	66 (5.1)	63(6.9)		89 (5.5)	38(6.4)	
Length of stay in ED [min]	125(114)	132 (113)	113(114)	< 0.001	133 (115)	106(109)	< 0.001
Disposition [n (%)]				< 0.001			< 0.001
Discharge	868(39.4)	359 (27.9)	510(55.7)		469 (29.1)	399(67.1)	
Admission to a ward	938(42.6)	584 (45.3)	353(38.5)		755 (46.9)	183(30.8)	
Admission to ICU	398(18.1)	345 (26.8)	53(5.8)		385 (23.9)	13(2.2)	
Death [n (%)]	127(5.8)	97 (7.5)	30(3.3)	< 0.001	114 (7.1)	13(2.2)	< 0.001

Table 5. Comparison of parameters between the discharged group, the admitted to a ward group, and the admitted to ICU group

	Median (interquartile range)				*p* values of paired comparisons		
	Group1 (Discharged from ED) (n=868)	Group 2 (Admission to a ward) (n=938)	Group 3 (Admission to ICU) (n=398)	*p* value	G1 - G2	G2 - G3	G1 - G3
Age, years	78 (10.0)	79 (10.0)	77 (10.8)	< 0.001	< 0.05	< 0.001	0.440
Sex [n (%)]				< 0.001	< 0.001	< 0.05	< 0.001
Male	411 (47.4)	527 (56.2)	250 (62.8)				
Female	457 (52.6)	411 (43.8)	148 (37.2)				
Category [n (%)]				< 0.01	0.716	< 0.01	< 0.01
Trauma	158 (18.2)	177 (18.9)	48 (12.1)				
Non-trauma	710 (81.8)	761 (81.1)	350 (87.9)				
Length of stay in ED [(min)]	110 (94)	146 (120)	113 (120)	< 0.001	< 0.001	< 0.001	0.418
[Pre-hospital]							
Respiratory rate (bpm)	20 (6.0)	20 (7.0)	24 (9.0)	< 0.001	< 0.001	< 0.001	< 0.001
Oxygen saturation (%)	98 (5.0)	96 (6.0)	97 (6.0)	< 0.001	< 0.001	1.00	< 0.001
Inhaled oxygen				< 0.001	< 0.001	< 0.001	< 0.001
Yes	123 (14.2)	256 (27.3)	253 (63.6)				
No	745 (85.8)	682 (72.7)	145 (36.4)				
Temperature (℃)	36.4 (1.3)	36.7 (1.4)	36.4 (0.9)	< 0.001	< 0.001	< 0.001	0.628

Systolic blood pressure (mmHg)	152 (45.0)	144 (47.0)	140 (57.0)	< 0.001	< 0.001	< 0.05	< 0.001
Pulse rate (bpm)	83 (32.0)	87 (35.0)	89 (37.0)	< 0.001	< 0.001	0.751	< 0.001
AVPU [n (%)}				< 0.001	< 0.01	< 0.001	< 0.001
Alert	640 (73.7)	716 (76.3)	282 (70.9)				
Voice	76 (8.8)	88 (9.4)	70 (17.6)				
Pain	113 (13.0)	77 (8.2)	26 (6.5)				
Unresponsive	39 (4.5)	57 (6.1)	20 (5.0)				
pNEWS	4 (5.0)*	5 (6.0)*	5 (6.0)	< 0.001	< 0.01	< 0.01	< 0.001
pMEWS	2 (3.0)*	3 (4.0)*	3 (3.0)	< 0.001	< 0.01	0.194	< 0.001
[Emergency Department]							
Respiratory rate (bpm)	18 (8.0)	19 (8.0)	20 (9.0)	< 0.001	< 0.01	< 0.001	< 0.001
Oxygen saturation (%)	97 (4.0)	98 (4.0)	98 (4.0)	< 0.001	0.254	< 0.001	< 0.001
Inhaled oxygen				< 0.001	< 0.001	< 0.001	< 0.001
Yes	174 (20.0)	305 (37.3)	263 (66.1)				
No	694 (80.0)	588 (62.7)	135 (33.9)				
Temperature (℃)	36.5 (1.0)	36.8 (1.2)	36.4 (1.0)	< 0.001	< 0.001	< 0.001	0.233
Systolic blood pressure (mmHg)	149 (40.0)	142 (41.0)	139 (52.0)	< 0.001	< 0.001	0.104	< 0.001

Pulse rate (bpm)	81 (26.0)	84 (27.0)	89 (38.0)	< 0.001	< 0.001	< 0.01	< 0.001
AVPU [n (%)}				< 0.001	< 0.001	< 0.001	< 0.001
Alert	803 (92.5)	785 (83.7)	279 (70.1)				
Voice	44 (5.1)	101 (10.8)	75 (18.8)				
Pain	10 (1.2)	32 (3.4)	23 (5.8)				
Unresponsive	11 (1.3)	20 (2.1)	21 (5.3)				
eNEWS	3 (4.0)*	3 (4.0)*	6 (6.0)	< 0.001	< 0.001	< 0.001	< 0.001
eMEWS	2 (2.0)*	2 (3.0)*	3 (4.0)	< 0.001	< 0.001	< 0.001	< 0.001

Data are presented as the median (interquartile range) for continuous variables and the number (%) for categorical variables. pNEWS, pre-hospital National Early Warning Score; pMEWS, pre-hospital Modified Early Warning Score; eNEWS, emergency department National Early Warning Score; eMEWS, emergency department Modified Early Warning Score; bpm, beats or breaths per minute; G1, Group1; G2, Group2, G3; Group3. *:The p value is less than 0.05 between pre-hospital and emergency department.

Table 6. Comparison of parameters between the survivors and non-survivors

	Median (interquartile range)		
	Group1 (Survivors) (n=2077)	Group 2 (Non-survivors) (n=127)	*p* value
Age, years	78 (11.0)	80 (9.5)	0.068
Sex [n (%)]			0.053
Male	1109 (53.4)	79 (62.2)	
Female	968 (46.6)	48 (37.8)	
Category [n (%)]			< 0.001
Trauma	375 (18.1)	8 (6.3)	
Non-trauma	1702 (81.9)	119 (93.7)	
Length of stay in ED [(min)]	122 (112)	159 (112)	< 0.01
[Pre-hospital]			
Respiratory rate (bpm)	20.0 (7.0)	24.0 (10.0)	< 0.001
Oxygen saturation (%)	97.0 (4.0)	95.0 (11.0)	< 0.001
Inhaled oxygen			< 0.01
Yes	479 (23.1)	45 (35.4)	
No	1598 (76.9)	82 (64.6)	
Temperature (℃)	36.5 (1.2)	36.6 (1.3)	0.083
Systolic blood pressure (mmHg)	147 (49.0)	1 36.0 (46.0)	< 0.01
Pulse rate (bpm)	85 (32.0)	96.0 (35.0)	< 0.01
AVPU [n (%)}			< 0.001
Alert	1579 (76.0)	59 (46.5)	
Voice	201 (9.7)	33 (26.0)	

Pain	195 (9.4)	21 (16.5)	
Unresponsive	102 (4.9)	14 (11.0)	
pNEWS	4 (5.0)*	7 (5.0)	< 0.001
pMEWS	3 (3.0)*	4 (2.0)	< 0.001
[Emergency Department]			
Respiratory rate (bpm)	19.0 (7.0)	22.0 (10.0)	< 0.001
Oxygen saturation (%)	97.0 (4.0)	97.0 (5.0)	< 0.001
Inhaled oxygen			< 0.001
Yes	689 (33.2)	98 (77.2)	
No	1388 (66.8)	29 (22.8)	
Temperature (℃)	36.6 (1.1)	36.7 (1.4)	0.196
Systolic blood pressure (mmHg)	145 (40.0)	128.0 (53.0)	< 0.001
Pulse rate (bpm)	83 (28.0)	95.0 (30.0)	< 0.001
AVPU [n (%)}			< 0.001
Alert	1809 (87.1)	58 (45.7)	
Voice	186 (9.0)	34 (26.8)	
Pain	51 (2.5)	14 (11.0)	
Unresponsive	31 (1.5)	21 (16.5)	
eNEWS	3 (5.0)*	8 (5.0)	< 0.001
eMEWS	2 (3.0)*	4 (3.0)	< 0.001

Data are presented as the median (interquartile range) for continuous variables and the number (%) for categorical variables. pNEWS, pre-hospital National Early Warning Score; pMEWS, pre-hospital Modified Early Warning Score; eNEWS, emergency department National Early Warning Score; eMEWS, emergency department Modified Early Warning Score; bpm, beats or breaths per minute. *:The p value is less than 0.05 between pre-hospital and emergency department.

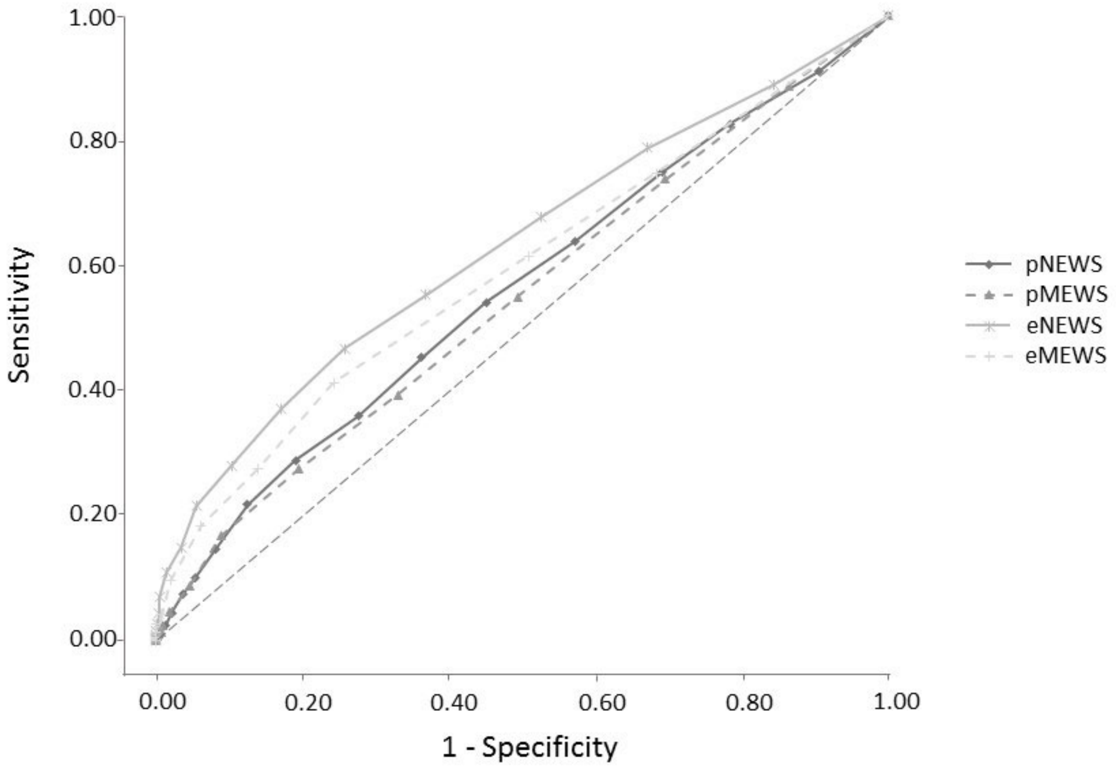

Figure 1. Receiver operator characteristic (ROC) curves for admission comparing the Early Warning Scores in the pre-hospital and in the emergency department.

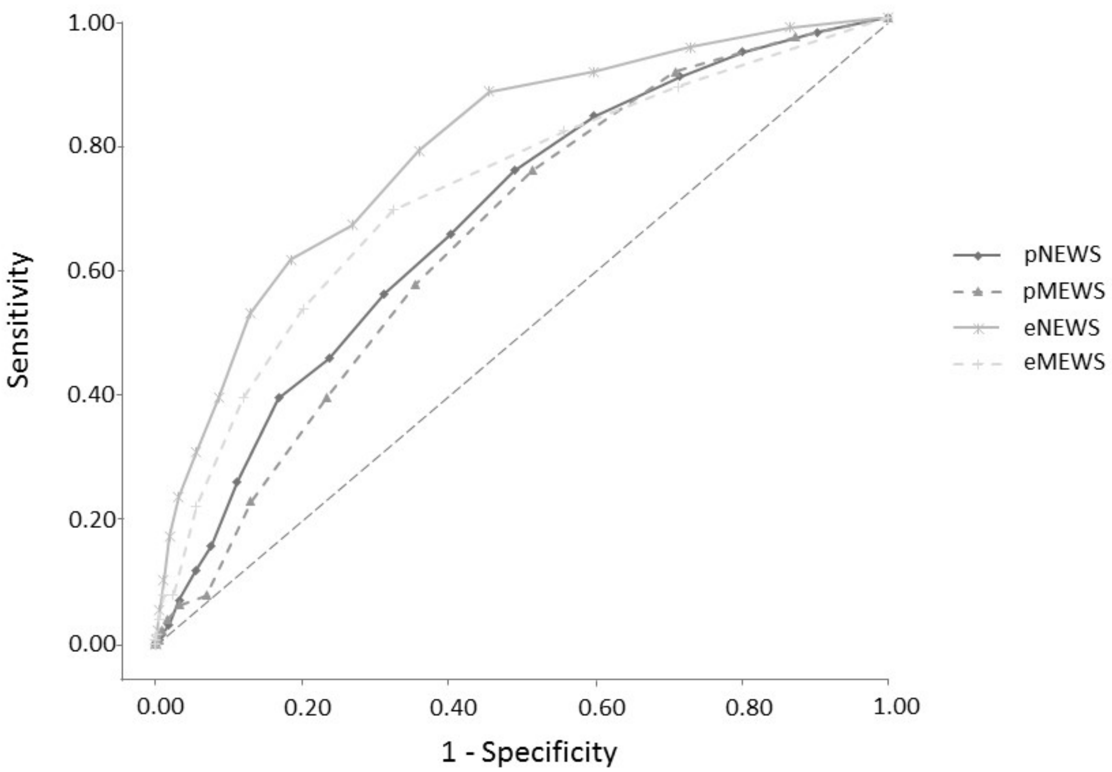

Figure 2. Receiver operator characteristic (ROC) curves for in-hospital mortality comparing the Early Warning Scores in the pre-hospital and in the emergency department.

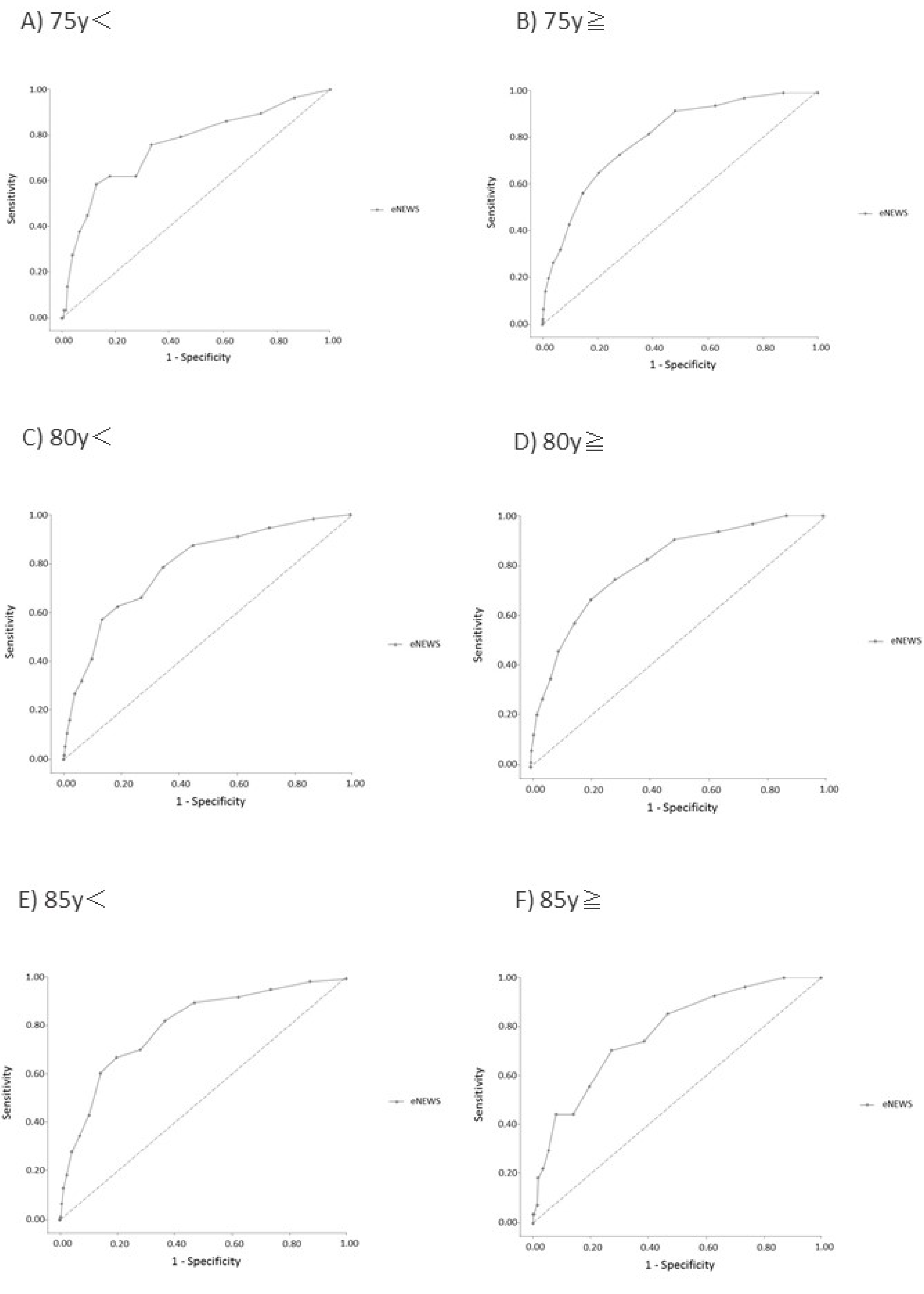

Figure 3. Receiver operator characteristic (ROC) curve of the National Early Warning Score (eNEWS) for in-hospital mortality in different cut-off ages.

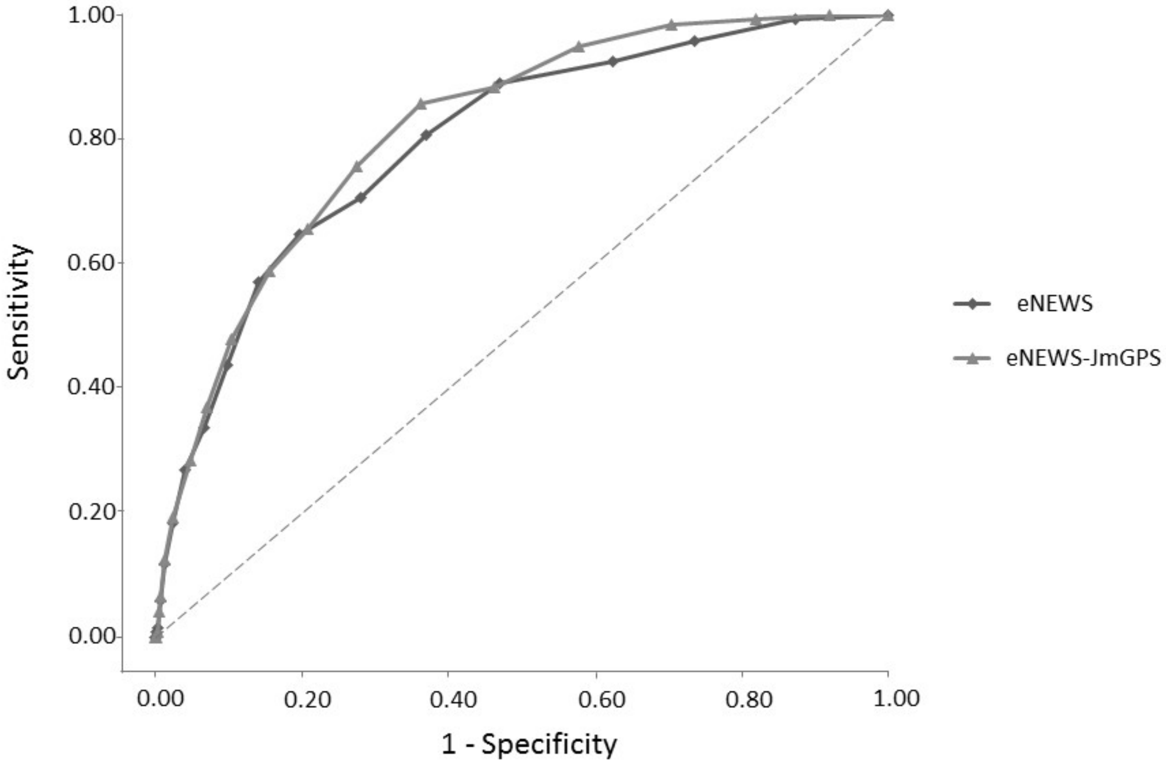

Figure 4. Receiver operator characteristic (ROC) curves for in-hospital mortality comparing the Early Warning Scores in the emergency department.

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