The Utility of MEWS for Predicting the Mortality in the Elderly Adults with COVID-19: A Retrospective Cohort Study with Comparison to Other Predictive Clinical Scores

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Background: Older adults have been reported to be a population with high-risk of death in the COVID-19 outbreak. Rapid detection of high-risk patients is crucial to reduce mortality in this population. The aim of this study was to evaluate the prognositc accuracy of Modified Early Warning Score (MEWS) for in-hospital mortality in older adults with COVID-19. **Methods** A retrospective cohort study was conducted in Wuhan Hankou Hospital in China from 1 January 2020 to 29 February 2020. Receiver operating characteristic (ROC) analysis was used to evaluate the predictive value of MEWS,Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Function Assessment (SOFA), quick Sequential Organ Function Assessment (qSOFA), Pneumonia Severity Index (PSI), Combination of Confusion, Urea, Respiratory Rate, Blood Pressure, and Age ≥65 (CURB-65), and the Systemic Inflammatory Response Syndrome Criteria (SIRS) for in-hospital mortality. Logistic regression models were performed to detect the high-risk older adults with COVID-19. **Results:** Among the 235 patients included in this study, 37 (15.74%) died and 131 (55.74%) were male, with an average age of 70.61 years (SD 8.02). ROC analysis suggested that the capacity of MEWS in predicting in-hospital mortality was as good as the APACHE ll, SOFA, PSI and qSOFA (Difference in AUROC: MEWS VS APACHE ll, -0.025 [95% CI, (-0.075, 0.026)]; MEWS VS SOFA, -0.013 [95% CI, (-0.049, 0.024)]; MEWS VS PSI, -0.015 [95% CI, (-0.065, 0.035)]; MEWS VS qSOFA, 0.024 [95% CI, (-0.029, 0.076)], all P 0.05), but was significantly higher than SIRS and CURB-65 (Difference in AUROC: MEWS VS SIRS, 0.218 [95% CI, 0.156,0.279)]; MEWS VS CURB-65, 0.064 [95% CI, (0.002, 0.125)], all P 0.05). Logistic regression models implied that the male patients (≥75 years) had higher risk of death than the other older adults (estimated coefficients: 1.16, P=0.044). Our analysis further suggests that the cut-off points of the

MEWS score for the male patients (≥75 years) subpopulation and the other elderly patients should be 2.5 and 3.5, respectively. **Conclusions:** MEWS is an efficient tool for rapid assessment of elderly COVID-19 patients. MEWS has promising performance in predicting in-hospital mortality and identifying the high-risk group in elderly patients with COVID-19.

1   **The Utility of MEWS for Predicting the Mortality in the Elderly Adults with COVID-19: A**

2   **Retrospective Cohort Study with Comparison to Other Predictive Clinical Scores**

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20 **The Utility of MEWS for Predicting the Outcome in the Elderly Adults with COVID-19: A**

21 **Retrospective Cohort Study with Comparison to Other Predictive Clinical Scores**

22 **Background:** Older adults have been reported to be a population with high-risk of death in the

23 COVID-19 outbreak. Rapid detection of high-risk patients is crucial to reduce mortality in this

24 population. The aim of this study was to evaluate the prognostic accuracy of Modified Early

25 Warning Score (MEWS) for in-hospital mortality in older adults with COVID-19.

26 **Methods** A retrospective cohort study was conducted in Wuhan Hankou Hospital in China from

27 1 January 2020 to 29 February 2020. Receiver operating characteristic (ROC) analysis was used

28 to evaluate the predictive value of MEWS, Acute Physiology and Chronic Health Evaluation II

29 (APACHE II), Sequential Organ Function Assessment (SOFA), quick Sequential Organ

30 Function Assessment (qSOFA), Pneumonia Severity Index (PSI), Combination of Confusion,

31 Urea, Respiratory Rate, Blood Pressure, and Age ≥65 (CURB-65), and the Systemic

32 Inflammatory Response Syndrome Criteria (SIRS) for in-hospital mortality. Logistic regression

33 models were performed to detect the high-risk older adults with COVID-19.

34 **Results:** Among the 235 patients included in this study, 37 (15.74%) died and 131 (55.74%)

35 were male, with an average age of 70.61 years (SD 8.02). ROC analysis suggested that the

36 capacity of MEWS in predicting in-hospital mortality was as good as the APACHE Ⅱ, SOFA,

37 PSI and qSOFA (Difference in AUROC: MEWS VS APACHE Ⅱ, -0.025 [95% CI, (-0.075,

38 0.026)]; MEWS VS SOFA, -0.013 [95% CI, (-0.049, 0.024)]; MEWS VS PSI, -0.015 [95% CI,

39 (-0.065, 0.035)]; MEWS VS qSOFA, 0.024 [95% CI, (-0.029, 0.076)], all P□0.05), but was

40 significantly higher than SIRS and CURB-65 (Difference in AUROC: MEWS VS SIRS, 0.218

41   [95% CI, 0.156,0.279)]; MEWS VS CURB-65, 0.064 [95% CI, (0.002, 0.125)], all P□0.05).

42   Logistic regression models implied that the male patients (≥75 years) had higher risk of death

43   than the other older adults (estimated coefficients: 1.16, P=0.044). Our analysis further suggests

44   that the cut-off points of the MEWS score for the male patients (≥75 years) subpopulation and

45   the other elderly patients should be 2.5 and 3.5, respectively.

46   **Conclusions:** MEWS is an efficient tool for rapid assessment of elderly COVID-19 patients.

47   MEWS has promising performance in predicting in-hospital mortality and identifying the high-

48   risk group in elderly patients with COVID-19.

49   **Key words**: COVID-19; Modified Early Warning Score; Older Adults; Outcome.

INTRODUCTION

51

52 The WHO Director-General declared COVID-19 as a pandemic on 11th March, 2020. According

53 to the report of WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)

54 Report,(Wang et al. 2019) the older adults who are above 60 years old are the population with

55 high-risk of death. The crude mortality of the older adults above 80 years old could be as high as

56 21.9%. An epidemiological investigation conducted by the Chinese Center for Disease Control

57 and Prevention found that more than one third of the COVID-19 patients were the older adults

58 aged 60 years and above. (Wu & McGoogan 2020)

59   While older adults have been identified as the main group with COVID-19 infection, the vital

60 signs of these patients could deteriorate very quickly. Hence timely detection of the high-risk

61 group and appropriately-assessed disease severity for the older adults with COVID-19 are

62 practically essential.(Verity et al. 2020) Several disease severity scoring systems are often used

63 to guide the management of patients with pneumonia, such as Acute Physiology and Chronic

64 Health Evaluation II (APACHE II), Sequential Organ Function Assessment (SOFA), quick

65 Sequential Organ Function Assessment (qSOFA), Pneumonia Severity Index (PSI), Combination

66 of Confusion, Urea, Respiratory Rate, Blood Pressure, and Age ≥65 (CURB-65), Modified Early

67 Warning Score (MEWS) and the Systemic Inflammatory Response Syndrome Criteria

68 (SIRS).(Asai et al. 2019; Chalmers et al. 2011; Dremsizov et al. 2006; Goodacre et al. 2010; Kim

69 et al. 2019; Sikka et al. 2000) All these scoring systems have been proven to be useful for

70 predicting the outcome of patient's with pneumonia.

71   Among these scoring systems, MEWS can generally be obtained within minutes after the

72   patient is admitted, providing a rapid assessment result for clinicians and enabling timely

73   treatment to high risk patients.(Churpek et al. 2019; Salottolo et al. 2017; Yu et al. 2019)

74   Although MEWS has been found to be useful for assessment of pneumonia deterioration,(Jo et

75   al. 2016) its utility has not been examined in predicting outcome of the older adults with

76   COVID-19. The aim of this study is to evaluate the prognostic accuracy of MEWS for in-

77   hospital mortality of older adults with with COVID-19.

78

79   **METHODS**

80   **Study Population**

81   This is a retrospective cohort study conducted in the Wuhan Hankou Hospital in China from 1

82   January 2020 to 29 February 2020. It was approved by the Institutional Ethics Committee of

83   Hankou hospital (hkyy2020-014). The Institutional Ethics Committee approved of waiving

84   informed consents by reasons that this study was conducted retrospectively, privacy and

85   personally identifiable information of the patients were protected and data collection would not

86   harm the patient. The data in this study were analyzed anonymously. Inclusion criteria were as

87   follows: (1) (1) Patients diagnosed as COVID-19 (Supplementary Text S1); (2) Patients treated

88   by Guangdong medical team; (3) Older adults aged 60 or above. Exclusion criteria: (1)

89   pneumonia caused by other pathogens; (2) incomplete data.

90

91   **Clinical and Biochemical Data Collection**

92   All the data were obtained from the electronic medical records in the Information System of

93   Wuhan Hankou Hospital. The information of the patients during admission including age,

94   gender, underlying disease, consciousness state, vital signs, physiological and laboratory

95   variables were collected and further used for the calculation of APACH Ⅱ score, PSI score,

96   SOFA score, qSOFA score and MEWS (Supplementary Text S2). All these variables/factors are

97   objective measurable parameters collected by professional medical staff, and the laboratory

98   variables were recorded and double check by two researchers.

99

100   **Outcomes variables**

101   The main outcome of the study was in-hospital mortality. The other issue we tried to address was

102   to identify the group of the high-risk patients based on MEWS. Patients were further categorized

103   into different groups by their gender (male VS female) and age (75 years old or above VS 60-74

104   years old).

105

106   **Statistical Analysis**

107   Statistical analysis was carried out by Microsoft R (version 3.5.3). All the disease severity scores

108   were described as Median (Inter-Quartile Range), while other numerical variables were

109   described as Mean (SD). Categorical variables were reported as percentages and frequencies.

110   Kolmogorov-Smirnov test was used to assess the normality of the numerical variables, and

111   subsequently, we used T-test to compare normally distributed variables and used Mann-Whitney

112   test to test whether the means between two groups are significantly different for non-normally

113   distributed variables. Chi-square test was used to test independence for contingency tables of

114 categorical variables. Receiver Operating Characteristic (ROC) curve was used to evaluate the

115 predictive value of each scoring system for prognosis, and Z-test was used for the Area Under

116 the ROC curve (AUROC). In order to evaluate the accuracy of each scoring system sensitivity,

117 specificity, positive predictive value and negative predictive value were determined. Optimal

118 cut-off value for each score was calculated using Youden's J-statistics. Bootstrapping confidence

119 intervals were calculated to evaluate the difference in the AUROC between MEWS and the other

120 scores. Specifically, by resampling (with replacement) the data for 100 times, we obtained an

121 empirical distribution for the difference of AUROC between MEWS and other scores. The

122 confidence intervals were then obtained using the percentiles of the empirical distribution. In

123 order to detect the high-risk population and understand the risk effect of the MEWS on the

124 mortality rate in different subpopulations, logistic regression models were developed against

125 MEWS, age groups, gender and the interaction between age group and gender. The optimal

126 model was selected by Akaike Information Criterion (AIC). A smaller AIC score indicates a

127 better fit of the corresponding model to the data. All the hypothesis tests were 2-sided with a

128 significance level of 0.05.

129

130 **RESULTS**

131 **Study Population and outcomes**

132 The total number of patients treated by Guangdong medical team was 472, among which 244

133 (51.7%) met the enrollment criteria (patients aged 60 years old or above with a primary diagnosis

134 of COVID-19 disease) from the 1 January 2020 to 29 February 2020. 9 patients were excluded

135 from our study cause 1 patient had been diagnosed with pneumonia caused by other pathogens

136 and 8 patients had incomplete data. Therefore, there were 235 patients included in this analysis.

137   The general information and the clinical characteristics of the patients are listed in Table 1.

138 The mean age was 70.6 years (SD 8.0) and 55.7 % of them were male. 43.8% of these patients

139 had Hypertension, 26.4% of them had Diabetic Mellitus, and 20.9% had history of Coronary

140 Heart Disease. The median values of scores in these patients were as follows: 12 (IQR: 9-17) in

141 APACHE Ⅱ score, 3 (IQR: 2-5) in SOFA score, 82 (IQR: 65-114) in PSI score, 1 (IQR: 1-2) in

142 CURB-65, 2 (IQR: 1-4) in MEWS and 0 (IQR: 0-1) in qSOFA. 56.2% of these patients met

143 SIRS criteria (Table 1).

144   Non-survivors were more likely to be male (27 [73.0%] VS 104 [52.5%]), with higher

145 APACHE Ⅱ score (24 [IQR: 20-27] VS 11 [IQR: 9-14]), SOFA score (7 [IQR: 6-9] VS 3 [IQR:

146 2-4]), PSI score (152 [IQR: 128-166] VS 75[IQR: 63-100]), CURB-65 score (3 [IQR: 2-4] VS

147 1[IQR: 1-2]), MEWS score (5 [IQR: 4-6] VS 2[IQR: 1-3])and qSOFA score (2 [IQR: 1-2] VS 0

148 [IQR: 0-11]) than survivors. In addition, more non-survivors met SIRS criteria (33[89.2%] VS

149 99 [50.0%]).

150   Of the 235 patients during follow-up, 37 (15.8%) died in the hospital and the median

151 duration of hospital stay of the non-survivors were 5.5 days (IQR: 2.0-9.3).

152

153 **Prognostic accuracy of MEWS in predicting the in-hospital mortality rate**

154 The distributions of all the scores were presented at Figure S1, and their relationships with in-

155 hospital mortality in the older adults with COVID-19 were presented in Figure 1. The AUROCs

156   for these scores in predicting in-hospital mortality were as follows: APACHE Ⅱ,0.937 [95% CI,

157   (0.877, 0.995)]; SOFA, 0.926 [95% CI, (0.877, 0.975)]; PSI, 0.927 [95% CI, (0.898, 0.986)];

158   CURB-65, 0.845 [95% CI, (0.740, 0.951)]; MEWS, 0.913 [95% CI, (0.864,0.941)]; SIRS, 0.696

159   [95% CI, (0.616, 0.776)]; and qSOFA, .886 [95% CI, (0.804, 0.969)] (Table 2 and Figure 2).

160   The reliability of MEWS in predicting in-hospital mortality was as good as the APACHE Ⅱ

161   score, SOFA score, PSI score and qSOFA (Difference in AUROC with MEWS: MEWS VS

162   APACHE Ⅱ, -0.025 [95% CI, (-0.075, 0.026), P=0.828]; MEWS VS PSI, -0.013 [95% CI, (-

163   0.049, 0.024), P=0.748]; MEWS VS PSI, -0.015 [95% CI, (-0.065, 0.035), P=0.735]; MEWS VS

164   qSOFA, 0.024 [95% CI, (-0.029, 0.076), P=0.174], but the prognostic accuracy of MEWS was

165   significantly higher as compared with either SIRS criteria or CURB-65 score (Difference in

166   AUROC with MEWS: MEWS VS SIRS, 0.218 [95% CI, (0.156, .279), P<0.001]; MEWS VS

167   CURB-65, 0.064 [95% CI, (0.002, 0.125), P=0.015]).The optimal cutoff value of MEWS for

168   predicting the inpatient mortality in the older adults with COVID-19 was 4.5, with a specificity

169   of 94.5% and a sensitivity of 67.6%.

170   We also analysed the age adjusted ROC curves and AUROCs to evaluate the prognostic

171   accuracy of MEWS).. However, no significant difference was observed from the original

172   analysis without age adjustment (Table 1).

173

174   **Identifying the risk population with high mortality via logistic regression models**

175   In order to identify the high-risk older adults with COVID-19 and understand the prognostic

176   accuracy of the MEWS on the mortality in different subpopulations categorized by gender and

177   age group, logistic regression models were developed. In particular, an interaction term

178   age*gender term was introduced to consider possible interaction effect between age group and

179   gender. The optimal model was selected by AIC. The best model is the one with features

180   age*gender (estimated coefficients: 1.16, P=0.044) +MEWS (estimated coefficients: 1.24,

181   P<0.001) (Table 3). Note that under our notations, the age*gender indicator corresponds to

182   whether the patient is a male patient aged 75 years old or above. The positive coefficient (1.16)

183   thus implies the group of COVID-19 patients who were male and aged 75 years or above had

184   higher risk of death than the other COVID-19 patients in this population. In particular, since the

185   coefficient of age*gender (1.16) is very close to the coefficient of the MEWS (1.24), i.e.,

186   1.16/1.24≈1, the risk of male COVID-19 patients aged 75 years and above for a given MEWS is

187   as high as the risk of other patients with a one mark higher MEWS score. Motivated by this, we

188   further explore the risk effect of the MEWS in the two subpopulations (male patients aged 75

189   years or above VS other patients in this population) separately. Results on the prognostic

190   accuracy of MEWS in predicting the in-hospital mortality of these two subpopulations were

191   showed in Supplementary Table S1 and Figure S2. The optimal cut-off value of MEWS in the

192   male COVID-19 patients aged 75 years or above was 2.5, with 84.3% specificity, 84.6%

193   sensitivity, 57.9% mortality rate for those with MEWS>2.5, and 0.0% mortality rate for those

194   with MEWS<2.5. While for other older adults with COVID-19, the optimal cut-off value of

195   MEWS was 3.5, with 75.0% specificity, 100% sensitivity, 45.8% mortality rate for those with

196   MEWS>3.5, and 2.8% mortality rate for those with MEWS<3.5. We remark that there is a one

197   point difference in the cut-off points of the two subpopulations (2.5 VS 3.5). This is consistent to

198   the results we have discussed for the fitted model.

199

200   **DISCUSSION**

201   In this retrospective cohort study, ROC analysis suggested that prognostic accuracy of MEWS in

202   predicting the inpatient mortality rate is comparable to that of APACHE Ⅱ score, PSI score,

203   SOFA score, and better than the CURB-65, SIRS criteria in older adults with COVID-19. On the

204   other hand, comparing to APACHE Ⅱ, PSI and SOFA, MEWS is much simpler and can be

205   rapidly obtained in clinical practice. Our analysis has also shown MEWS to be a promising tool

206   for risk stratification of these patients. We thus conclude that MEWS is an effective prognostic

207   tool for providing rapid assessment and identifying the high-risk patients among the older adults

208   with COVID-19, so the use of MEWS should be encouraged in this population during this severe

209   plague outbreak.

210   Since the outbreak of COVID-19 has begun, as of July 103, 2020, more than 12 million cases

211   over the world have been confirmed and over half million deaths have occurred. COVID-19 has

212   resulted in considerable morbidity and mortality in more than 200 countries worldwide. There is

213   no specific drug for treating the patients with COVID-19, till mow treatment is mainly

214   symptomatic. Recent literatures have identified older adults group are more prone towards

215   COVID-19 infection, and they might be at higher risk of death than younger patients.(Liu et al.

216   2020; Onder et al. 2020; Verity et al. 2020; Wu & McGoogan 2020) It is reported that the

217   mortality in the patients aged 60 years or above ranged from 5.98% to 12.4%, while the mortality

218   in the younger patients ranged from 1.32% to 0.64%.(Onder et al. 2020; Wu & McGoogan 2020)

219 In our study, mortality in older adults with COVID-19 aged 60 years or above is 15.8%. A recent

220 study demonstrated that older adults aged 65 years or above with COVID-19 are more likely to

221 develop organ injury in a short time, leading to an increased risk of death.(Yang et al. 2020) In

222 our study, we found that the median duration of hospital stay of the non-survivors was 5.5 days

223 (IQR: 2.0-9.3), indicating that the vital signs of these patients could deteriorate very quickly.

224 Early identification of the high-risk patients and timely medical interventions could possibly

225 reduce the high mortality rate among this population. Rapid and effective assessment of these

226 older adults with COVID-19 is thus very crucial. Owning to the rapid spread of COVID-19,

227 there has been a severe shortage of medical resources, so rapid assessment could potentially

228 serve as an essential tool for efficient allocation of these limited resources to those who are

229 indeed at has been high risk of death.

230   PSI score and CURB-65 score have been wildly used for prognostic evaluations and severity

231 assessment of pneumonia, which enables the clinicians to allocate the patients to appropriate

232 level and intensity of care and perform effective medical management in time.(Kim et al. 2019;

233 Ning et al. 2018) It had reported that high PSI score, CURB-65 score, APACHE Ⅱ score and

234 SOFA score were associated with poor outcome in the patients with pneumonia.(Asai et al. 2019;

235 Kao et al. 2018)   Since the outbreak of COVID-19, APACHE Ⅱ score, CURB-65 score, SOFA

236 score and qSOFA score have been used to assess the severity of COVID-19 patients.(Wang et al.

237 2020; Yang et al. 2020; Zhou et al. 2020) In a cohort of 52 patients with COVID 19, non-

238 survivors had higher APACHE Ⅱ score than the survivors (18 [IQR: 16–20] VS 14 [IQR : 12–

239 17]).(Yang et al. 2020) A recent study conducted by Fei Zhou(Zhou et al. 2020) indicated that

240 non-survivors had higher SOFA score (4·5 [IQR: 4.0-6.0] VS 1.0 [IQR: 1.0-2.0], P<·0001),

241 qSOFA score (1 [IQR: 1.0-2.0] VS 0 [IQR: 0.00-1.0], P<.0001), CURB-65 (2.0 [IQR: 1.0-3.0]

242 VS 1.0 [IQR:0.0-1.0], P < 0.0001) than survivors. It is worth mentioning that, non-survivors in

243 the older adult COVID-19 population we studied had higher APACHE Ⅱ score (24 [IQR: 20-

244 27]), SOFA score (7 [IQR: 6.0-9.0]), CURB-65 score (3 [IQR: 2.0-4.0]) and qSOFA score (2

245 [IQR: 1.0-2.0]), compared to previous studies with different populations. Although APACHE Ⅱ,

246 SOFA, PSI and CURB-65 work well in clinical practice, they generally require sophisticated

247 information from the patient and are not suitable for rapid assessment.

248   MEWS consists of 5 physiological parameters, which include systolic blood pressure, pulse

249 rate, respiratory rate, temperature, and level of consciousness. It has been used as an essential

250 tool for early identification of patients who can deteriorate in medical and surgical

251 wards.(Fullerton et al. 2012; Kramer et al. 2019; Salottolo et al. 2017) Some studies have shown

252 that a MEWS score of 5 or above is associated with a high risk of poor outcome in intensive care

253 unit.(Reini et al. 2012) Comparing with other scores, MEWS is much simpler and more

254 importantly allows rapid assessment and dynamic monitoring. However, the capacity of MEWS

255 on COVID-19 patients hasn't been well explored yet. This retrospective cohort study focused on

256 the utility of MEWS in predicting outcome in the older adults with COVID-19. We observed

257 that, for the older adults with COVID-19, the capacity of MEWS to predict in-hospital mortality

258 was significantly higher as compared with SIRS criteria and CURB-65 score, while the

259 prognostic accuracy is comparable to those of APACHE Ⅱ, PSI and SOFA. More importantly,

260 MEWS allows early detection of the high-risk older adults with COVID-19. We found that the

261 cut-off values using MEWS to predict the outcome in COVID-19 is smaller than the 5 points in

262 the guidelines for other disease. In addition, the present study reveals that the male COVID-19

263 patients aged 75 years or above had higher risk of death than the other older adults with COVID-

264 19. In particular, the cut-off points of the MEWS for the male COVID-19 patients aged 75 years

265 or above should be one-point lower than the cut-off for the other older adults with COVID-19

266 (2.5 VS 3.5). It is worth mentioning that when the male patients aged 75 years or above were

267 compared to the rest of the older adults, the true positive rate of MEWS's cut-off points can be as

268 high as 100% for the male aged 75 years or above group, and 84.62% for the other group. This

269 indicates that with our proposed cut-off scores, MEWS works very well in correctly identifying

270 the true high-risk patients. We suggest that these cut-off points could potentially be used as a

271 simple reference to rapidly identify the high-risk older adults in the near future.

272

273 **LIMITATION**

274 There are some limitations in this study. Firstly,, it was a retrospective study conducted in a

275 single center with relatively small sample size. Secondly, this study did not examine the younger

276 population, but it may enable us to generalize the results to the other population. Thirdly, it

277 would be interesting to explore how the heterogeneity in treatments over time would affects the

278 effectiveness of MEWS and other scores. Statistically speaking, if such kind of data is available,

279 more sophisticated models (e.g. logistic regression with mixed effects, or varying coefficient

280 models) can be conducted to take into account possible heterogeneity in the data, and obtain

281 better understandings for the utility of MEWS. Last but not least, although this study revealed

282   that there is a significant association between MEWS and mortality in elderly patients with

283   COVID-19 upon admission, questions such as whether or not subsequent treatments are

284   associated with the reduction of MEWS, and whether or not the reduction of MEWS in

285   subsequent treatments is associated with lower mortality, are yet to be further investigated in

286   future studies.

287

288   **CONCLUSION**

289   Our Retrospective cohort study showed that, in terms of prognostic accuracy, MEWS performed

290   as good as APACHE Ⅱ, PSI and SOFA, and outperformed CURB-65 and SIRS. MEWS has

291   proven to be a promising tool for risk stratifications among the older adults COVID-19

292   population in this study. We have not only found MEWS to be an important variable for the risk,

293   but also identified the subpopulation consists of male COVID-19 patients aged 75 years or above

294   as the group with higher risk of mortality. Our analysis further suggested a cut-off point of

295   MEWS score 2.5 for male COVID-19 patients aged 75 years or above and a cut-off point of

296   MEWS score 3.5 for other older adults with COVID-19.

297   **ADDITIONAL INFORMATION AND DECLARATIONS**

298   **Funding**

299   This research did not receive any specific grant from funding agencies in the public, commercial,

300   or not-for-profit sectors.

301   **Conflict of Interest Disclosures**:

302   All authors have completed the ICMJE Form for Disclosure of Potential Conflicts of Interest.

303   Binyan Jiang was partially supported by an Alibaba (China) - Hong Kong Polytechnic University

304   Collaborative Research project.

305   **Author Contributions**

306   Lei Chen had full access to all of the data in the study and take responsibility for the integrity of

307   the data and the accuracy of the data analysis. Lichun Wang and Qingquan Lv contributed

308   equally and share first authorship. Concept and design: Lei Chen, Lichun Wang, Qingquan Lv,

309   Xiaofei Zhang. Acquisition, analysis, or interpretation of data: Lei Chen, Qingquan Lv, Binyan

310   Jiang, Xiaofei Zhang. Drafting of the manuscript: Lichun Wang, Binyan Jiang, Xiaofei Zhang,

311   En he Liu, Chaoxing Xiao. Critical revision of the manuscript for important intellectual content:

312   Lei Chen, Chunhua Yang. Statistical analysis: Binyan Jiang, Xinyang Yu, Lichun Wang.

313   Administrative, technical, or material support: En he Liu, Chaoxing Xiao. Supervision: Lei

314   Chen.

315   **Data Availability**

316   The following information was supplied regarding data availability:

317   The raw measurements are available in the Supplemental File.

318

319 **REFERENCES**

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406 **LEGENDS**

407 **Figure legends**

408 Figure 1: The Proportion of Survivors and Non- Survivors in Older Adults with COVID-19 by

409 MEWS, APACHE II, SOFA, PSI, CURB-65, qSOFA, SIRS and age.

410 Figure 2: Area Under the Receiver Operating Characteristic Curve to Discriminate in-hospital

411 Mortality for MEWS, APACHE II, SOFA, PSI, CURB-65, SISR, qSOFA.

412 **Supplemental material legends**

413 Supplementary Text S1: Diagnosis and clinical classification of COVID-19-According to the

414 Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment 5th edition

415 Supplementary Text S2: APACHE II score, CURB-65 score, PSI score, SOFA score, MEWS

416 score, qSOFA score, and SIRS Criteria.

417 Supplementary Table S1: AUROC of MEWS in COVID-19 Patients between Male Patients

418 Age≥75 Years and the Others.

419 Supplementary Figure S1: Distribution of patients with COVID-19 in Older Adults by MEWS,

420 APACHE II, SOFA, PSI, CURB-65, qSOFA and SIRS.

421 Supplementary Figure S2: The Age-adjusted Receiver Operating Characteristic Curve by

422 MEWS, APACHE II, SOFA, PSI, CURB-65, SISR, qSOFA.

423

Figure 1

The Proportion of Survivors and Non- Survivors in Older Adults with COVID-19 by MEWS, APACHE II, SOFA, PSI, CURB-65, qSOFA, SIRS and age.

The proportion of survivors and Non- Survivors in older adults with COVID-19 by MEWS (Fig 1.A), APACHE II (Fig 1.B), SOFA (Fig 1.C), PSI (Fig 1.D), CURB-65 (Fig 1.E), qSOFA (Fig 1.F), SIRS (Fig 1.G) and age (Fig 1.H)

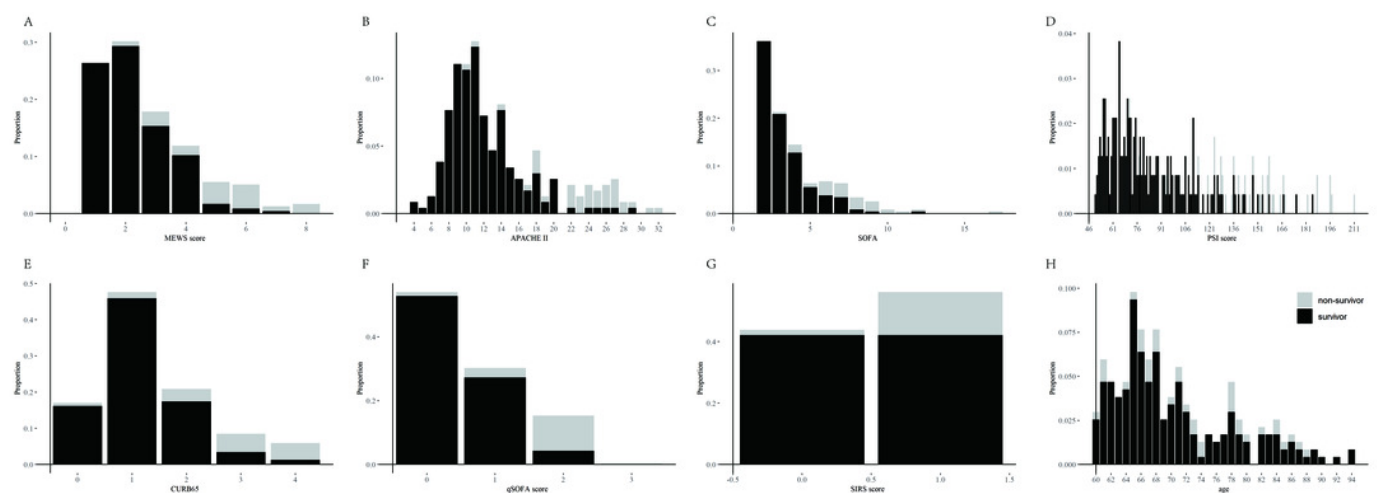
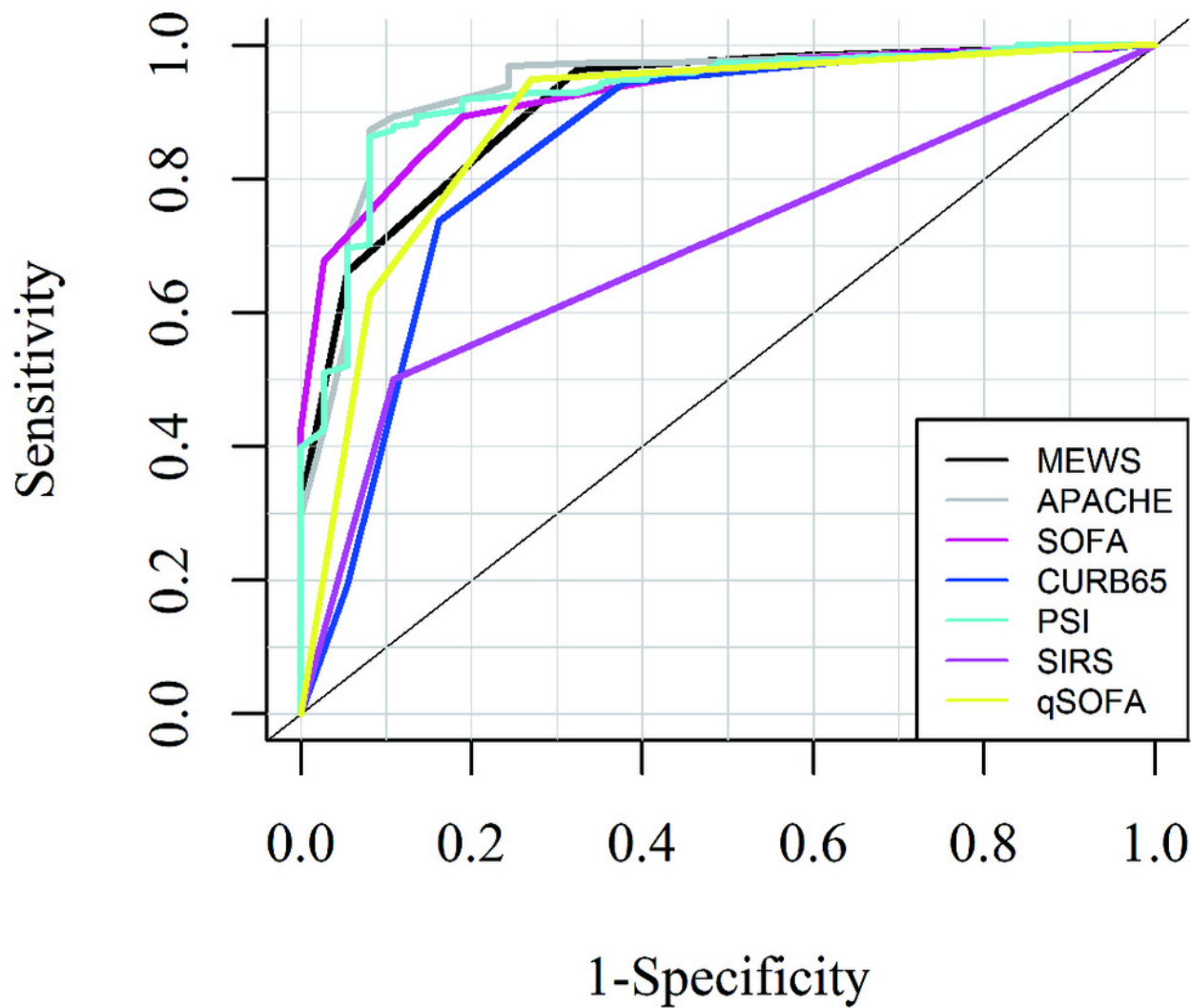



Figure 2

Area Under the Receiver Operating Characteristic Curve to Discriminate in-hospital Mortality for MEWS, APACHE II, SOFA, PSI, CURB-65, SISR, qSOFA.

ROC analysis suggested that the capacity of MEWS in predicting in-hospital mortality was as good as the APACHE II, SOFA, PSI and qSOFA, but was significantly higher than SIRS and CURB-65.

Patient Characteristics and Outcome

APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Function Assessment; qSOFA: quick Sequential Organ Function Assessment; PSI, Pneumonia Severity Index; CURB-65, The Combination of Confusion, Urea, Respiratory Rate, Blood Pressure, and Age ≥65; MEWS, Modified Early Warning Score; SIRS, Systemic Inflammatory Response Syndrome

1   Table 1 Patient Characteristics and Outcome

	All patients	Survivors	Non-survivors	P
Number of patients	235	198	37	
Age, mean (SD), y	70.6 (8.0)	70.17 (9.9)	72.95 (8.1)	0.530
Male, No. (%)	131 (55.7)	104 (52.5)	27 (73.0)	0.030
Co-morbidity No. (%)				
Hypertension	103 (43.8)	89 (45.0)	14 (37.8)	0.474
Coronary heart disease	49 (20.9)	41 (20.7)	8 (21.6)	>.999
Diabetes mellitus	62 (26.4)	52 (26.3)	10 (27.0)	>.999
Chronic obstructive pulmonary	31 (13.2)	29 (14.7)	3 (8.1)	0.433
disease				
Cerebrovascular disease	19 (8.1)	16 (8.0)	3 (8.1)	>.999
Cancer	8 (3.4)	7 (3.5)	1(2.7)	>.999
Others	22 (9.4)	21 (10.6)	1 (2.7)	0.215
None	67 (28.5)	57 (28.8)	12 (32.4)	>.999
Severity of Illness No. (%)				
mild	98 (41.7)	97 (49.0)	1 (2.7)	<0.001
moderate	48 (20.4)	47 (23.7)	1 (2.7)	0.002
severe	89 (37.9)	54 (27.3)	35 (94.6)	<0.001
Scores on Admission, median (IQR),				
APACHE II	12 (9, 17)	11 (9,14)	24 (20, 27)	<0.001
SOFA	3 (2,5)	3 (2,4)	7 (6, 9)	<0.001
PSI	82 (65,114)	75 (63,100)	152 (128, 166)	<0.001
CURB65	1 (1,2)	1 (1,2)	3 (2, 4)	<0.001
MEWS	2 (1, 4)	2 (1,3)	5 (4, 6)	<0.001
qSOFA	0 (0, 1)	0 (0,1)	2 (1,2)	<0.001
SIRS criteria ≥2 No. (%)	132 (56.2)	99 (50)	33 (89.19)	<.0001

Outcome				
Hospital mortality (primary outcome), No. (%)	37 (15.8)	0	37 (100)	＜0.001
Hospital length of stay, median (IQR), d	13 (6,23)	15 (8,24)	5.5 (2.0,9.3)	＜0.001

2   APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Function Assessment;

3   qSOFA: quick Sequential Organ Function Assessment; PSI, Pneumonia Severity Index; CURB-65, The

4   Combination of Confusion, Urea, Respiratory Rate, Blood Pressure, and Age ≥65; MEWS, Modified Early Warning

5   Score; SIRS, Systemic Inflammatory Response Syndrome

Prognostic Accuracy of Difference Score in Predicting the In-Hospital Mortality and the Difference with AUROC of MEWS

APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Function Assessment ; qSOFA: quick Sequential Organ Function Assessment; PSI, Pneumonia Severity Index; CURB-65, The Combination of Confusion, Urea, Respiratory Rate, Blood Pressure, and Age ≥65; MEWS, Modified Early Warning Score; SIRS, Systemic Inflammatory Response Syndrome; AUROC, area under the receiver operating characteristic curve; SEN, sensitivity; SPE, specificity; NPV, negative predictive value; PPV, positive predictive value.

1 Table 2 Prognostic Accuracy of Difference Score in Predicting the In-Hospital Mortality and the Difference with

2 AUROC of MEWS

	AUROC (95% CI)		Age-adjusted AUROC (95% CI)		Cut-off	SEN (%)	SPE (%)	NNPV (%)	PPV (%)	Difference with AUROC of MEWS (95% CI)	P
APACHE II	0.937	(0.877, 0.995)	0.0943	(0.886, 0.984)	16.5	91.9	87.4	98.3	57.6	-0.025 (-0.075, 0.026)	0.828
SOFA	0.926	(0.877, 0.975)	0.927	(0.87, 0.969)	5.5	81.1	89.4	96.2	58.8	-0.013 (-0.049, 0.024)	0.748
PSI	0.927	(0.898, 0.986)	0.934	(0.879, 0.976)	113.5	91.9	86.4	98.3	55.7	-0.015 (-0.065, 0.035)	0.735
CURB-65	0.845	(0.740, 0.951)	0.833	(0.739, 0.912)	1.5	83.8	73.7	96.1	37.4	0.064 (0.002, 0.125)	0.015
MEWS	0.913	(0.864, 0.941)	0.913	(0.853, 0.960)	4.5	67.6	94.5	94.1	78.1	—	
SIRS criteria	0.696	(0.616, 0.776)	0.776	(0.700, 0.842)	0.5	89.9	50.0	96.1	25.0	0.218 (0.156, 0.279)	<0.001
qSOFA	0.886	(0.804, 0.969)	0.899	(0.818, 0.956)	1.5	73.0	95.0	95.0	73.0	0.024 (-0.029, 0.076)	0.174

3 APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Function Assessment;

4 qSOFA: quick Sequential Organ Function Assessment; PSI, Pneumonia Severity Index; CURB-65, The Combination

5 of Confusion, Urea, Respiratory Rate, Blood Pressure, and Age ≥65; MEWS, Modified Early Warning Score; SIRS,

6 Systemic Inflammatory Response Syndrome; AUROC, area under the receiver operating characteristic curve; SEN,

7 sensitivity; SPE, specificity; NPV, negative predictive value; PPV, positive predictive value.

Logistic Regression Models of the Age Group, Gender and MEWS

MEWS, Modified Early Warning Score. Model 1: MEWS; Model 2: Gender*Age +MEWS; Model
3: Age +MEWS; Model 4: Gender +MEWS; Model 5: Age + Gender *Age + MEWS; Model
6:Age + Gender*Age + MEWS + Gender; Model 7□Age + Gender + MEWS; Model 8:
Gender*Age + Gender + MEWS. Logistic regression models were developed against MEWS,
age groups ("1" for 75 years old or above, and "0" for 60-74 years old), gender ("1" for male
and "0" for female), and the interaction between age group and gender (age*gender).

1 Table 3 Logistic Regression Models of the Age Group, Gender and MEWS

Model	AIC	Estimated Coefficients				Standard Error				P			
		Age	Gender	Gender * Age	MEWS	Age	Gender	Gender* Age	MEWS	Age	Gender	Gender* Age	MEWS
1	118.01	-	-	-	1.24	-	-	-	0.18	-	-	-	<0.001
2	116.03	-	-	1.16	1.24	-	-	0.58	0.18	-	-	0.044	<0.001
3	117.68	0.79	-	-	1.23	0.51	-	-	0.18	0.125	-	-	<0.001
4	116.54	-	0.96	-	1.24	-	0.53	-	0.19	-	0.071	-	<0.001
5	118.03	0.04	-	1.13	1.24	0.82	-	0.91	0.18	0.964	-	0.214	<0.001
6	118.52	0.50	0.80	0.34	1.24	0.92	0.66	1.12	0.19	0.584	0.228	0.764	<0.001
7	116.61	0.73	0.91	-	1.24	0.52	0.54	-	0.19	0.163	0.089	-	<0.001
8	116.81	-	0.65	0.84	1.24	-	0.59	0.64	0.19	-	0.272	0.189	<0.001

2   MEWS, Modified Early Warning Score. Model 1: MEWS; Model 2: Gender*Age +MEWS; Model 3: Age +MEWS;

3   Model 4: Gender +MEWS; Model 5: Age + Gender *Age + MEWS; Model 6:Age + Gender*Age + MEWS + Gender;

4   Model 7: Age + Gender + MEWS; Model 8: Gender*Age + Gender + MEWS. Logistic regression models were

5   developed against MEWS, age groups ("1" for 75 years old or above, and "0" for 60-74 years old), gender ("1" for

6   male and "0" for female), and the interaction between age group and gender (age*gender).