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# Validity of Severity scoring systems in critically ill patients with COVID 19 infection

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**Abstract**

Background In late December 2019, a previous unidentified coronavirus, emerged from Wuhan, the disease is officially named as Coronavirus Disease-2019 (COVID-19, by WHO on February 11, 2020) which led to its declaration as a global pandemic, on 11 March 2020 by the World Health Organization, This study aimed to evaluate some ICU severity scoring systems to predict prognosis, mortality rate and survival rate in critically ill patient with COVID 19 infection. Results: The study was conducted on 100 critically ill patients divided into 2 groups: non survivors group (45 patients), and survivors group (55 patients) showing that the SOFA, qSOFA, APACHE II, MURRAY, 4C mortality and VACO index scores were statistically significant higher in non survivors group. Conclusion: SOFA, qSOFA, APACHE II, MURRAY, 4C Mortality scores and VACO index were statistically significant higher in non survivors groups and significantly can predict mortality in ICU

**Key words:** COVID-19, Scoring systems, SOFA, qSOFA, MURRAY, 4C Mortality, VACO.

## 1. Background

In late December 2019, a previous unidentified coronavirus, emerged from Wuhan, the disease is officially named as Coronavirus Disease-2019 (COVID-19, by WHO on February 11, 2020) which led to its declaration as a global pandemic, on 11 March 2020 by the World Health Organization [1]. Patients with SARS-CoV-2 infection can experience a range of clinical manifestations, from no symptoms to critical illness [2]. Severely ill patients characterized by SpO2<94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%. These patients may experience rapid clinical deterioration. Oxygen therapy should be administered immediately using a nasal cannula or a high-flow oxygen device, while Critically ill Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction [3] Rapid scoring systems for critically ill patients with COVID-19 provide emergency clinicians with an effective adjunct risk stratification tool for critically ill patients with COVID-19 [4]. This study aimed to evaluate some ICU severity scoring systems in critically ill patients with covid-19 infection.

## 2. Patients& METHODS

This was a prospective study conducted on One hundred (100) critically ill patients with covid-19 infection, admitted to ICU in benha and kafrelsheikh, were included and divided into two groups

Survivor group included 55 patients (31 males and 24 females with mean age (54.2±13.55).

Non survivor group included 45 patients ( 21 males and 24 females with mean age (66.8±12.86)

**Inclusion criteria:**

Confirmed cases of COVID 19 by nasopharyngeal PCR swab with severe or critical illness aged above 18 years old according to the egyptian MOHP

**All patients exposed to the following:**

1. Full history taking
2. Assessment of GCS
3. General and local chest examination Oxygen saturation measurement by pulse oximetry
4. Laboratory work up(CBC, Liver function, Kidney function, ABG and inflammatory markers)
5. Plain chest X- ray (posterior-anterior and lateral views) or CT chest.
6. The studied ICU severity scoring systems at admission and after 24 hours

**Measured variables:** Components of each scores SOFA, qSOFA, APACHE II, MURRAY,

4C mortality and VACO index such as age, sex, comorbidity, vital signs and laboratory data.

**Exclusion criteria:** Subjects were excluded from the study if they had any of the following conditions:

- Patients or their relatives refuse to participate.
- Patients with end stage malignancy, end stage liver disease or end stage renal disease which may affect score judgment.
- Patients with history of recurrent ICU admission for other causes which may affect score judgment.

**Ethical approval:** the study was conducted at critical care units of Benha and Kafrelsheikh University Hospitals after approval of the research Ethical committee at faculty of medicine, Benha University (REC-FOMBU).

**Statistical analysis:** The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc. (Chicago, IL, USA).

Probability value (P-value) was interpreted as follow:

- Non-significant if the p value is > 0.05
- Significant if the p value is ≤ 0.05.
- Highly significant if the p value < 0.001.

**The following tests were done**:

1. Data were analyzed using SPSS software, version 22.0 (IBM, Armonk, NY, USA) for Windows. Categorical data were presented as number and percentages.

2. Chi square ($\chi 2$) and Fisher's exact tests were used to analyze them..
3. Degree of agreement between categories were assessed by Kappa test. Quantitative data were tested for normality using Shapiro-Wilks test assuming normality at P>0.05
4. **Receiver operating characteristic (ROC) analysis:**

ROC curves were constructed to assess the validity of cutoff values of the scores with optimum sensitivity and specificity in prediction of mortality. P ≤0.05 was considered significant, P value >0.05 is non-significant (NS), P<0.05 is significant (S), P≤0.001 is highly significant (HS).

## 3. Results

The total number of studied group was one hundred Patients (52 Male، 48Female) with mean age (59.9)، age range (24-92)، (69) Patients with (+ve) comorbidity: (41) diabetic Patients،(38) hypertensive Patients ،(6) COPD Patients ،(5) CKD Patients، (5) Patients Liver cirrhosis and HCV، (+ve) (4) Patients with Dementia or Alzheimer ،(2) Rheumatoid Patients،(1) Patient with history of CABG ،(1) Patient with DVT ،(1) Patient with IHD and (31) Patients without comorbidity. Table (1)

This study showed that SOFA, qSOFA, APACHE II, MURRAY, 4C Mortality scores and VACO index were statistically significant higher in non survivors groups, so significantly are positive predictors of mortality, Comorbidity, increasing age Figure (1) and length of ICU stay associated with increase mortality in ICU.

**Table (1)** Basic characters of the studied sample**.**

| Variable | | No. (n=100) | % (100%) |
|---|---|---|---|
| **Age (years)** | **Mean ±SD (Range)** | 59.9±14.6 (24-92) | |
| **Sex** | **Male** | 52 | 52.0 |
| | **Female** | 48 | 48.0 |
| **comorbidity** | **Negative** | 31 | 31.0 |
| | **Positive** | 69 | 69.0 |
| **Form medical illness** | **DM** | 41 | 41.0 |
| | **HTN** | 38 | 38.0 |
| | **Asthma/COPD** | 6 | 6.0 |
| | **CKD** | 5 | 5.0 |
| | **Liver cirrhosis/HCV** | 5 | 5.0 |
| | **Stroke** | 4 | 4.0 |
| | **Dementia/Alzheimer** | 4 | 4.0 |
| | **Rheumatoid** | 2 | 2.0 |
| | **CABG** | 1 | 1.0 |
| | **DVT** | 1 | 1.0 |
| | **IHD** | 1 | 1.0 |

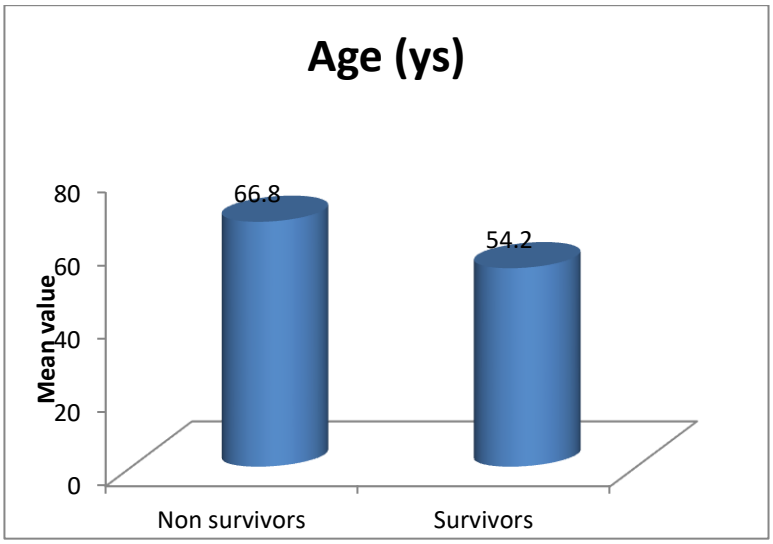


**Fig. (1)** Show mean age among survivors and non survivors

GCS, MAP in survivors were statistically significant higher than non survivors, while HR, RR, Temperature in survivors were statistically significant lower than non survivors Figure (2), also oxygen saturation, hypoxic index and PH are significant lower in non survivors.

WBCs, urea ,creatinine, bilirubin and CRP in non survivors were statistically significant higher than survivors while platelets in non survivors were statistically significant lower than survivors(Table 2), Also pro-calcitonin, IL6, Serum ferritin and D-dimer in non survivors were statistically significant higher than survivors. (Table (3).

There is significant degree of agreement between the predicted mortality by scores and the observed mortality in the study, SOFA (81%, P<0.001) qSOFA (74%, P<0.001), APACHE II (81%, P<0.001), MURRAY (94%, P<0.001), 4C mortality score (81%, P<0.001), VACO score (73%, P<0.001). . (Table 4)

In a statistical comparison between the studied scores showing sensitivity and specificity of those scores،SOFA Score (77.8%,89.1%), qSOFA (55.6%,89.1%), APACHE (84.4%, 70.9), 4C Mortality (77.8%, 83.6%), VACO index ( 80%, 63.6%), Murray Score ( 77.8%,100%) respectively.(Table5).

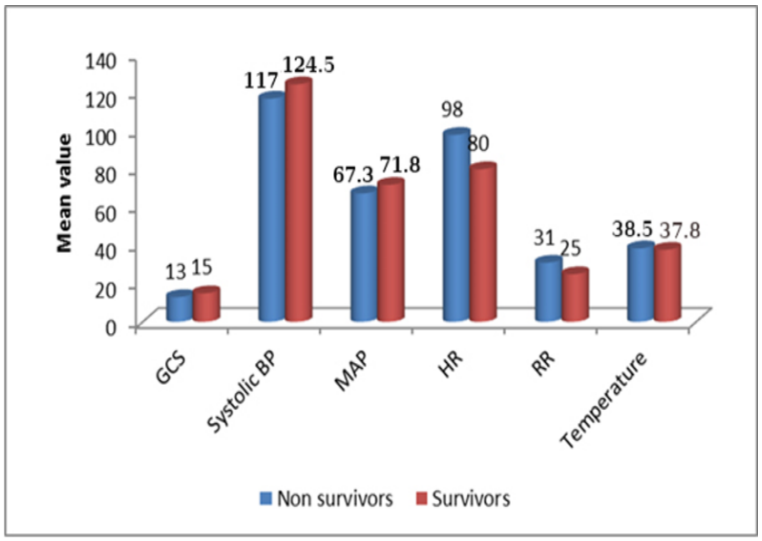


**Fig. (2)** Comparing outcome of survivors and non survivors regarding vital signs

**Table (2)** Comparing outcome of survivors and non survivors regarding routine laboratory data**.**

| Variable | Non survivors (N=45) | | Survivors (N=55) | | $Z_{MWU}$ Test | P |
|---|---|---|---|---|---|---|
| | Median | IQ Range | Median | IQ Range | | |
| **HCT** | 36 | 33-40 | 36 | 33-39 | 0.28 | 0.78 (NS) |
| **WBCs** | 14 | 9.3-18 | 9.0 | 7-12 | 3.12 | 0.002 (S) |
| **PLTs** | 130 | 100-190 | 221 | 195-300 | 5.22 | <0.001 (HS) |
| **Urea** | 60 | 40.5-110 | 35 | 29-41 | 6.03 | <0.001 (HS) |
| **Creatinine** | 1.4 | 0.97-2.0 | 0.94 | 0.86-1 | 4.57 | <0.001 (HS) |
| **Na** | 139 | 131.5-144 | 138 | 136-141 | 0.01 | 0.99 (NS) |
| **K** | 4.9 | 4-5.7 | 4.7 | 4-5.2 | 1.17 | 0.13 (NS) |
| **Bilirubin** | 1.2 | 0.8-1.4 | 0.9 | 0.8-1.0 | 4.18 | <0.001 (HS) |
| **CRP** | 106 | 96-108 | 24 | 12-96 | 5.72 | <0.001 (HS) |

**Table (3)** Comparing outcome of survivors and non survivors regarding inflammatory markers.

| Variable | Non survivors (N=45) | | Survivors (N=55) | | $Z_{MWU}$ Test | P |
|---|---|---|---|---|---|---|
| | Median | IQ Range | Median | IQ Range | | |
| **Procalcitonin** | 0.5 | 0.27-1.0 | 0.3 | 0.19-0.40 | 3.78 | <0.001 (HS) |
| **IL-6** | 77 | 57-160 | 39.0 | 27-57 | 5.17 | <0.001 (HS) |
| **Serum ferretin** | 420 | 305-570 | 320 | 250-420 | 2.89 | 0.004 (S) |
| **D- dimer** | 0.8 | 0.4-1.55 | 0.3 | 0.2-0.4 | 5.39 | <0.001 (HS) |

**Table (4)** Binary logistic regression analysis for predictors of mortality

| Variable | B | OR | 95%CI (β) | P |
|---|---|---|---|---|
| **SOPFA score** | 0.789 | 2.2 | 1.5-3.1 | <0.001 (HS) |
| **qSOFA** | 1.585 | 4.88 | 2.3-10.5 | <0.001 (HS) |
| **APATCHE** | 0.284 | 1.32 | 1.2-1.5 | <0.001 (HS) |
| **Murray score** | 3.56 | 35.2 | 3.4-360.9 | 0.003 (S) |
| **4C mortality score** | 0.441 | 1.55 | 1.3-1.84 | <0.001 (HS) |
| **VACO index** | 0.146 | 1.15 | 1.07-1.25 | <0.001 (HS) |

**Table (5)** Comparing sensitivity and specificity of mortality scores.

| Score (cutoff) | Sens% | Spec% | AUC | SE | 95%CI | P |
|---|---|---|---|---|---|---|
| **SOFA point >3** | 77.8% | 89.1% | 0.889 | 0.034 | 0.82-0.96 | <0.001 (HS) |
| **qSOFA point >1** | 55.6% | 89.1% | 0.732 | 0.052 | 0.63-0.83 | <0.001 (HS) |
| **APATCHE point >8** | 84.4% | 70.9% | 0.877 | 0.033 | 0.81-0.941 | <0.001 (HS) |
| **4 C mortality >12** | 77.8% | 83.6% | 0.876 | 0.034 | 0.81-0.944 | <0.001 (HS) |
| **VACO Index >4** | 80% | 63.6% | 0.753 | 0.049 | 0.66-0.85 | <0.001 (HS) |
| **Murray score >2.5** | 77.8% | 100% | 0.953 | 0.034 | 0.887-1.0 | <0.001 (HS) |

## 4. Discussion

There are many scoring ICU systems that commonly used in their current form grossly underestimate severity of illness and are not associated with mortality in critically unwell COVID-19 patients, we propose that further work is required to generate a COVID-19 specific severity of illness and mortality prediction model [5]. This study showed that Comorbidity is statistically significant higher in non survivors group, in agreement of this study population choice Sanyaolu et al [6] reported that patients with comorbidities should take all necessary precautions to avoid getting infected with SARS CoV-2, as they usually have the worst prognosis.

The current results showed that increasing age of patients is significantly associated with increased mortality in ICU ($p<0.001$), this was in agreement Also, Goodacre et al [7]. reported that increase of mortality rate was associated with increased age among patients ($p<0.001$). ) In this study comparing survivors and non survivors, regarding mechanical ventilation, there was a significant association between the need for MV and mortality, in agreement of this study population choice Li et al. [8] reported that regarding mechanical ventilation, mechanically ventilated patients associated with increase length of ICU stay and high mortalilty. ($p<0.001$)

The present study showed that GCS, MAP and O2 saturation were significant higher in survivors group , while HR, RR, temprature were significant higher in non survivors group, Ende et al [9]. in contrast with this study reported that non survivors had slightly lower mean values for body temperature and in agreement that hemoglobin-O2 saturation had lower mean value, and a slightly higher mean respiratory rate

The current study revealed that inflammatory markers (pro-calcitonin, IL6, ferritin, D-dimer were significantly higher in non survivors group. ($p<0.005$), in agreement of this study Shang et al. [10] reported that among 52 risk factors, The coefficients for each parameter were as follows: 1.371 for PCT >0.15ng/ml, 0.0815 for C-reactive protein (CRP) >55mg/L and 0.5865 for D-Dimer (DD) >0.5ug/ml. Then, by multivariable analysis, PCT and DD remained independent risk factors for mortality

The current study showed that WBCs, urea, creatinine, bilirubin, CRP in non survivors group were significantly than survivors group, However platelets in non survivors were significantly lower than survivor group, these results were similarly to with Li et al. [11] who reported that regarding the blood tests, there was a significant difference between survivors and non-survivors concerning, Creatinine, WBCs, and bilirubin which were higher in non survivors, while platelets was lower in non survivors group.($p<0.05$).

The current study showed that SOFA score, qSOFA score, APACHE II score, Murray, 4C mortality score and VACO index score were statistically significantly higher in non survivors ($P<0.001$), regarding SOFA and qSOFA, our results were following Liu et al. [12] in their study they have reported that there were significant differences between the survivors and non-survivors ($p<0.001$), Vandenbrande et al. [13] agree with this study that the analyses of ROC curves in the subgroup showed that APACHE II had very good discriminative abilities. We found good discrimination for APACHE II (AUC 0.7), In contrast with this study Knight et al.(14) reported that the Murray score showed no significant difference between early and late time points for survivors and non survivors,and in agreement with this study Jones et al. [15] reported that the 4C mortality score for COVID 19 is an valid prognostic tool for use in Canadian hospitals, similarly King et al. [16] reported that the VACO Index demonstrated good discrimination in YNHH data overall (AUC: 0.80, 95% CI 0.77 to 0.83), consistent with that seen in VA overall (AUC: 0.82, 95% CI 0.81 to 0.83).

## 5. Conclusion

SOFA, qSOFA, APACHE, MURRAY, 4C Mortality scores and VACO index were statistically significant higher in non survivors group and significantly can predict mortality in ICU.

## 6. Recommendations

Prognostic Scoring systems as SOFA, qSOFA, MURRAY, 4C Mortality, VACO index should be extensively validated in our ICUs as it may of great helpful in developing ICUs and pay attention for patients to decrease wasted resources.

## Declarations

Ethics approval and consent to participate: yes, research Ethical committee at faculty of medicine, Benha University (REC-FOMBU).

- Consent for publication: Yes all authors approved and sign the copyright form
- Availability of data and material: yes available on request
- Competing interests: The authors declare that they have no conflict of interest.
- Funding :NON
- Authors' contributions:NON
- Acknowledgements :NON

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