Simple scoring for acute necrotizing pancreatitis: mortality in acute necrotizing pancreatitis during admission (MANP-A)

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Abstract

Background Acute necrotizing pancreatitis (ANP) can result in a significant healthcare burden. The present study aimed to develop a new scoring system to accurately and promptly identify patients with a high likelihood of mortality to determine the need for aggressive measures.

Methods We retrospectively analyzed patients diagnosed with ANP using the National Inpatient Sample (NIS). The mortality in ANP during admission (MANP-A) scoring system was derived using multivariate Cox regression analysis and validated using receiver operating characteristic (ROC) curves in a validation cohort.

Results A total of 22,980 hospitalizations were identified in the derivation cohort. There was a predominance of males (65%) and white race (73%). Five variables showed significant association with mortality and were selected for developing the MANP-A scoring system: age ≥60 years; acute renal failure/kidney injury; sepsis with shock; vasopressor use; and disseminated intravascular coagulation. The MANP-A score has a maximum of 5 points and the cutoff for predicting mortality was set at 2 points. The area under the curve (AUC) using the ROC curve of the derivation cohort was 0.9195, 95% confidence interval [CI] 0.8838-0.9551 (P<0.001) for 7- and 0.8954, 95%CI 0.8723-0.9185 (P<0.001) for 30-day periods. The AUC of the Validation Cohort was 0.9204, 95%CI 0.8937-0.9469 (P<0.001) for 7- and 0.9059, 95%CI 0.8893-0.9223 (P<0.001) for 30-day periods.

Conclusion We propose a simple and objective score for predicting ANP inpatient mortality at 7- and 30-day intervals with high validity.

Keywords Acute necrotizing pancreatitis, prognostic scoring system, national inpatient sample, mortality predictors

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Introduction

Acute pancreatitis (AP) is the most common gastroenterology-related cause of inpatient admissions in the United States (US) [1]. Each year, the global incidence of AP is 340 cases per one million people and this rate continues to rise [2,3]. AP results from inflammation of the pancreas and is commonly associated with gallstones and alcohol use [4]. Acute pancreatitis severity can be categorized as mild, moderate or severe using the Atlanta classification system, with moderate to severe AP requiring transient or persistent multiple organ dysfunction [5,6]. Acute necrotizing pancreatitis (ANP) is categorized as moderate to severe, as it is often associated with organ failure [7]. In most cases, AP presents with limited symptoms, but occasionally it is accompanied by complications that include peripancreatic fluid collection, pancreatic pseudocysts, pancreatic necrosis, and systemic problems (respiratory, cardiovascular, or acute renal failure) [8,9].
Given AP's variable and often severe presentation when necrosis is present, clinical decisions need to be made urgently. Different scoring systems for the early identification of AP include the Acute Physiology and Chronic Health Evaluation (APACHE-II), Ranson’s score, Modified Computed Tomography Severity Index (MCTSI), and Bedside Index of Severity in Acute Pancreatitis (BISAP) [10]. However, each scoring system has its own distinctive application and limitations. For example, APACHE-II has high predictive accuracy, and it cannot be used exclusively for pancreatic necrosis (infected or noninfected). Likewise, the Ranson score needs exhaustive evaluation on admission and 48 h later. The BISAP score has poor sensitivity for severe AP, limiting its applicability to ANP [11]. MCTSI requires imaging and relies on a radiologist's subjective analysis to measure the area involved in pancreatic necrosis/inflammation. We aimed to develop a simple and effective scoring system to predict the ANP inpatient mortality at 7- and 30-days of admission using the US population.

Materials and methods

Design and data source

For the derivation cohort, we carried out a retrospective analysis using the National Inpatient Sample (NIS) database, evaluating adult (≥18 years) hospitalizations for ANP in the US from January 1 to December 31, 2019 [12]. The NIS was developed as a stratified probability sample to represent all nonfederal hospitals in the US. Detailed information on the design and sampling methods of NIS are available at https://www.hcup-us.ahrq.gov. The NIS database was queried for the principal discharge diagnosis of ANP using ICD-10 codes (Supplementary Table 1) over the study period. Individuals ≤17 years old were excluded from the study.

Outcome measures and statistical analysis

We determined independent predictors that had a >50% increased hazard ratio to develop a risk scoring system for 7- and 30-day inpatient mortality for AP hospitalizations. Additional variables, including acute renal failure, mechanical ventilation, disseminated intravascular coagulopathy, sepsis with shock, acute peritonitis, pseudocyst, paralytic ileus, thromboembolism, respiratory distress syndrome and vasopressor use, were incorporated in the hierarchical multivariate Cox regression analysis. Based on this regression analysis, a specific score was assigned to these variables and the mortality rate for aggregate scores was obtained. Kaplan-Meier curves were generated based on the study findings. We also utilized receiver operating characteristics (ROC) analysis to assess the model’s performance in terms of the area under the curve (AUC) [13]. The models’ predictive performance was assessed using the validation cohort from the NIS study period January 1, 2016, to December 31st, 2017. Any difference between the 2 models was compared using a standard non-parametric test (Delong Test), with statistical significance when P<0.001 [14]. The regression models were tested for over-dispersion using a Pearson goodness-of-fit test before our analysis, and these models were not over dispersed.

Analyses were performed using STATA version 16.0. Hierarchical multivariate Cox regression models were built based on univariate analysis to adjust confounding variables. Only variables associated with the outcome of interest on univariable regression analysis at P<0.2, or known potential confounders despite the P-value indicating no significance, were used in multivariate Cox regression to assess mortality during admission. Our analysis set 0.05 as the threshold for statistical significance and all P-values were 2-sided. All outcomes were adjusted for patient and hospital-level confounders, including age, race, sex, insurance type, residential region, Elixhauser Comorbidity Index comorbidities, hospital teaching status, and hospital size.

The NIS has been used previously to report inpatient outcomes and to derive predictive scoring models [15-17]. Since the NIS contains de-identified patient data, it was deemed exempt from review as per institutional review board guidelines. Patient consent was also waived in view of the public availability of the data.

Results

A total of 22,980 cases were identified in the derivation cohort for the study period, with a mortality of 4.8%. In the mortality cohort, there was a predominance of male sex (65%) and white race (73%). This was followed by African Americans/Blacks (9%), Hispanics (8%), and other races (9%). The mean age was 61.40±1.1 years. The median age of the patients was 52 years (interquartile range 18-90 years). Most hospitalizations were reported at urban teaching hospitals (86%). Medicare was the largest payer (51%), followed by private insurers (30%) and Medicaid (13%) (Table 1). Further demographic characteristics are summarized in Table 1.

Univariate analysis identified several variables associated with an increased risk of inpatient mortality (Supplementary Table 2). The multivariate Cox regression analyses of all common clinical data indicated that 5 variables were significantly associated with patient death at 7- and 30-day intervals during hospitalization (Supplementary Table 3). These variables included age ≥60 years (adjusted hazard ratio [aHR] 2.75, 95% confidence interval [CI] 2.32-5.96; P<0.001), vasopressor use (aHR 1.97, 95%CI 1.29-3.03; P<0.001), sepsis with shock (aHR 3.72, 95%CI 2.32-5.96; P<0.001), sepsis with shock (aHR 3.72, 95%CI 1.34-3.24; P<0.001), sepsis with shock (aHR 3.72, 95%CI 1.34-3.24; P<0.001), and disseminated intravascular coagulation (aHR 1.92, 95%CI 1.01-2.76; P=0.006). These were used to develop the "mortality in acute necrotizing pancreatitis during admission” (MANP-A) scoring system for inpatient mortality at 7- and 30-day intervals for ANP (Table 2). The new scoring system yields a total maximum score of 5 points and is derived from the sum of the variable scores. Based on the calculated highest sensitivity and specificity values from the ROC curves,
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Table 1 Biodemographic characteristics of hospitalizations for ANP in the derivation cohort

| Patient characteristics | ANP-associated survivor cohort | ANP-associated mortality cohort | P-value |
|--------------------------|-------------------------------|--------------------------------|---------|
| Total hospitalizations   | 21875                         | 1105                           | 0.5     |
| Sex                      |                               |                                |         |
| Male                     | 13825 (63%)                   | 720 (65%)                      |         |
| Female                   | 8050 (37%)                    | 385 (35%)                      |         |
| Mean age (years) ± SE    | 51.69±0.27                    | 61.40±1.1                      | <0.001  |
| Race/ethnicity           |                               |                                | 0.06    |
| White                    | 14165 (67%)                   | 785 (73%)                      |         |
| Black                    | 2660 (13%)                    | 100 (9%)                       |         |
| Hispanic                 | 2825 (13%)                    | 90 (8%)                        |         |
| Asian or Pacific Islander| 750 (4%)                      | 60 (6%)                        |         |
| Native American          | 255 (1%)                      | 5 (<1%)                        |         |
| Other                    | 600 (3%)                      | 30 (3%)                        |         |
| Elixhauser comorbidity index score |                   |                                | <0.001  |
| 0                        | 720 (3%)                      | 0 (0%)                         |         |
| 1                        | 2070 (9%)                     | 10 (1%)                        |         |
| 2                        | 3350 (15%)                    | 30 (3%)                        |         |
| ≥3                       | 15735 (72%)                   | 1065 (96%)                     |         |
| Median annual income in patient's zip code, US$ |                   |                                | 0.2     |
| $1-24,999                | 5970 (28%)                    | 355 (33%)                      |         |
| $25,000-34,999           | 5395 (25%)                    | 295 (27%)                      |         |
| $35,000-44,999           | 5615 (26%)                    | 245 (23%)                      |         |
| $45,000 or more          | 4560 (21%)                    | 190 (18%)                      |         |
| Insurance type           |                               |                                | <0.001  |
| Medicare                 | 6200 (30%)                    | 550 (51%)                      |         |
| Medicaid                 | 5080 (24%)                    | 135 (13%)                      |         |
| Private                  | 8065 (39%)                    | 325 (30%)                      |         |
| Uninsured                | 1595 (8%)                     | 60 (6%)                        |         |
| Hospital characteristics |                               |                                | 0.8     |
| Hospital region          |                               |                                |         |
| Northeast                | 3690 (17%)                    | 175 (16%)                      |         |
| Midwest                  | 5300 (24%)                    | 290 (26%)                      |         |
| South                    | 7830 (36%)                    | 370 (33%)                      |         |
| West                     | 5055 (23%)                    | 270 (24%)                      |         |
| Hospital status          |                               |                                | 0.3     |
| Rural                    | 910 (4%)                      | 25 (2%)                        |         |
| Urban non-teaching       | 2880 (13%)                    | 135 (12%)                      |         |
| Urban teaching           | 18085 (83%)                   | 945 (86%)                      |         |
| Vasopressor use          | 470 (2%)                      | 300 (27%)                      | <0.001  |
| Age >60 years            | 7420 (34%)                    | 690 (62%)                      | <0.001  |
| AKI                      | 5500 (25%)                    | 885 (80%)                      | <0.001  |
| DIC                      | 105 (1%)                      | 110 (10%)                      | <0.001  |
| Septic shock             | 1355 (6%)                     | 695 (63%)                      | <0.001  |

ANP, acute necrotizing pancreatitis; SE, standard error; AKI, acute kidney injury; DIC, disseminated intravascular coagulopathy

the determined cutoff value for predicting ANP inpatient mortality over 7- and 30-day periods using the MANP-A scoring system was 2 points using the Liu index, showing sensitivity 78.38%, specificity 92.98%, and sensitivity 76.32%, specificity 88.01%, respectively (Table 3). The ROC curve was used to evaluate the diagnostic efficiency of the MANP-A score. A total of 23,005 patients were included in the derivation cohort. The AUC of the derivation cohort was 0.9195, 95%CI 0.8838-0.9551 (P<0.001) for 7- and 0.9059, 95%CI 0.8893-0.9223 (P<0.001) for 30-day periods (Fig. 1). The validation cohort contained a sample of 38,644 patients. The AUC of the Validation Cohort was 0.9204, 95%CI 0.8937-0.9469 (P<0.001) for 7- and 0.9059, 95%CI 0.8893-0.9223 (P<0.001) for 30-day periods (Fig. 2).

Discussion

Necrosis and multi-organ dysfunction greatly impact inpatient mortality, with severe disease often requiring care
at the Intensive Care Unit (ICU) level [18,19]. ANP can have varying prognoses depending on its severity. No specific score exists for ANP, although the previously described scores are often applied to AP with or without necrosis. Currently, the

Table 2 Seven- and 30-day inpatient mortality for acute necrotizing pancreatitis hospitalizations in the United States using the mortality in acute necrotizing pancreatitis (MANP) during admission scoring system

| MANP score | 7-day mortality rate (%) | 30-day mortality rate (%) |
|------------|--------------------------|---------------------------|
| 0          | 0.29%                    | 0.28%                     |
| 1          | 1.78%                    | 2.64%                     |
| 2          | 5.81%                    | 9.45%                     |
| 3          | 43.05%                   | 55.00%                    |
| 4          | 60.11%                   | 63.16%                    |
| 5          | 88.99%                   | 99.99%                    |

Table 3 Score-specific sensitivities and specificities using the mortality in acute necrotizing pancreatitis scoring system

| Score | 7-day period (cutoff point=2) | 30-day period (cutoff point=2) |
|-------|-------------------------------|-------------------------------|
|       | Sensitivity | Specificity | Sensitivity | Specificity |
| 0     | 100%        | 0%           | 100%        | 0%           |
| 1     | 95.95%      | 59.39%       | 96.84%      | 52.69%       |
| 2     | 78.38%      | 92.98%       | 76.32%      | 88.01%       |
| 3     | 55.41%      | 99.46%       | 53.68%      | 98.11%       |
| 4     | 16.22%      | 99.83%       | 13.16%      | 99.66%       |
| 5     | 0%           | 100%         | 0.53%       | 100%         |

Mortality was estimated for both 7- and 30-day intervals. The MANP-A scoring system is straightforward to use, as it has a maximum score of only 5 points using dichotomous variables (0 or 1 point). All variables are objective clinical measures, allowing the score to be easily obtained during hospitalization. In contrast to previous scoring systems, such as APACHE II and BISAP, the MANP-A scoring system does not include mental status assessment. It also does not include imaging or subjective measures (radiological assessment that can vary

Figure 1 ROC curves for in-hospital mortality over 7- (A) and 30-day (B) periods using the proposed scoring system in the derivation cohort with acute necrotizing pancreatitis

ROC, receiver operating characteristic
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from radiologist to radiologist) to assess inpatient mortality, as the MCTSI system does.

This study has several strengths, with the greatest being the sample size. The study population was obtained from one of the largest inpatient databases available in the US. The weighted counts in the NIS approximate up to 95% of the US population, allowing for generalizable results. Hierarchical regression models allowed for patient and hospital level confounder adjustments, which provided a more accurate and detailed analysis (Supplementary Material). The validation cohort was even larger and had a mix of ICU and general floor patients.

There are several limitations to this study. The database does not report subjective symptoms or AP treatments, nor laboratory values that would be needed to compare our scoring system to other scoring systems. Imaging data, which may offer prognostic value in ANP, were unavailable. The study lacked randomization and blinding, which can impact result interpretation. The scoring system is specific for ANP and not for AP without necrosis, with necrosis confirmation requiring imaging. As the ICD information does not relate to when in the timeline of hospitalization these occurred, it could be that such events only occurred late during hospitalization. Despite these limitations, the large study cohort, unique methodology, and analysis add valuable details to the current literature on ANP.

In conclusion, we report a simple scoring system for predicting inpatient mortality at 7- and 30-day intervals for ANP, based on data from the US population. All variables included in this scoring system can be easily measured during admission. This scoring system would be the first to be specific for ANP. Future research using prospective multicenter studies to compare the MANP-A scoring system to other systems would be beneficial to further support our findings.

Summary Box

What is already known:

- Acute necrotizing pancreatitis (ANP) is a known complication of acute pancreatitis (AP)
- Mild AP is self-limiting; however, ANP leads to significantly higher inpatient mortality rates, up to 30%
- ANP with sepsis has a higher mortality rate than ANP without sepsis

What the new findings are:

- Medicare are the largest payer for ANP hospitalizations, followed by private insurers and Medicaid
- Age ≥60 years, acute renal failure/kidney injury, septic shock, vasopressor use, and disseminated intravascular coagulation significantly increase mortality in ANP hospitalizations
- The mortality in ANP during admission score is a simple mortality scoring system to predict inpatient mortality for ANP hospitalizations

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### Supplementary Table 1 List of ICD-10 codes utilized in the present study

| Condition                                | Codes                                |
|------------------------------------------|--------------------------------------|
| Acute necrotizing pancreatitis           | K8502, K8512, K8522, K8532, K8582,   |
|                                          | K8592, K8501, K8511, K8521, K8531,   |
|                                          | K8581, K8591                          |
| Acute renal failure                      | N170, N171, N172, N178, N179          |
| Disseminated intravascular coagulation   | D65                                  |
| Septic shock                             | R6521                                |
| Vasopressor use                          | 3E030XZ, 3E033XZ, 3E040XZ, 3E043XZ,   |
|                                          | 3E050XZ, 3E053XZ, 3E060XZ, 3E063XZ     |
| Pancreatic pseudocyst                    | K863                                 |
| Peritonitis                              | K650                                 |
| Acute respiratory distress syndrome      | J80                                  |
| Portal vein thrombosis                   | I81                                  |
| Paralytic ileus                          | K560                                 |
| Hyponatremia                             | E871                                 |
| Congestive Heart Failure                 | I09.9, I11.0, I11.3, I12.5, I14.0,    |
|                                          | I14.5–I14.9, I14.9–I14.9, R00.0,     |
|                                          | R00.1, R00.8, T82.1, Z45.0, Z95.0     |
| Cardiac Arrhythmia                       | I44.1–I44.3, I45.6, I45.9, I47–I49,  |
|                                          | R00.0, R00.1, R00.8, T82.1, Z45.0,   |
|                                          | Z95.0                                |
| Valvular Disease                         | A52.0, I05–I08, I09.1, I09.8, I34–I39, |
|                                          | Q23.0–Q23.3, Z95.2–Z95.4              |
| Pulmonary Circulation Disorders          | I26, I27, I28.0, I28.8, I28.9         |
| Peripheral Vascular Disorders            | I70, I71, I73.1, I73.8, I73.9, I77.1,|
|                                          | I79.0, I79.2, K55.1, K55.5, K55.9,   |
|                                          | Z95.8, Z95.9                          |
| Hypertension without Complications       | I10                                  |
| Hypertension with Complications          | I11–I13, I15                         |
| Paralysis                                | G04.1, G11.4, G80.1, G80.2, G81, G82,|
|                                          | G83.0–G83.4, G83.9                   |
| Other Neurological Disorders             | G10–G13, G20–G22, G25.4, G25.5, G31.2,|
|                                          | G31.8, G32, G35–G37, G40, G41, G93.1,|
|                                          | G93.4, R47.0, R56                    |
| Chronic Pulmonary Disease                | I27.8, I27.9, J40–J47, J60–J67, J68.4,|
|                                          | J70.1, J70.3                         |
| Diabetes without Complications           | E10.0, E10.1, E10.9, E11.0, E11.1,   |
|                                          | E11.9, E12.0, E12.1, E12.9, E13.0,   |
|                                          | E13.1, E13.9, E14.0, E14.1, E14.9     |
| Diabetes with Complications              | E10.2–E10.8, E11.2–E11.8, E12.2–E12.8,|
|                                          | E13.2–E13.8, E14.2–E14.8             |
| Hypothyroidism                           | E00–E03, E89.0                       |
| Renal Failure                            | I12.0, I13.1, N18, N19, N25.0, Z49.0–|
|                                          | Z49.2, Z94.0                         |
| Liver Disease                            | B18, I85, I86.4, I98.2, K70, K71.1,  |
|                                          | K71.3–K71.5, K71.7, K72–K74, K76.0,  |
|                                          | K76.2–K76.9, Z94.4                   |
| Peptic Ulcer Disease excluding Bleeding  | K25.7, K25.9, K26.7, K26.9, K27.7,   |
|                                          | K27.9, K28.7, K28.9                  |
| HIV/AIDS                                 | B20–B22, B24                         |
| Lymphoma                                 | C81–C85, C88, C96, C90.0, C90.2       |
| Metastatic Cancer                        | C77–C80                             |

*(Contd...)*
### Supplementary Table 1 (Continued)

| Condition                        | Code          |
|----------------------------------|---------------|
| Solid Tumor without Metastasis   | C00-C26, C30-C34, C37-C41, C43, C45-C58, C60-C76, C97 |
| Rheumatoid Arthritis/Collagen    | L94.0, L94.1, L94.3, M05, M06, M08, M12.0, M12.3, M30, M31.0–M31.3, M32–M35, M45, M46.1, M46.8, M46.9 |
| Coagulopathy                     | D65–D68, D69.1, D69.3–D69.6 |
| Obesity                          | E66           |
| Weight Loss                      | E40–E46, R63.4, R64 |
| Fluid and Electrolyte Disorders  | E22.2, E86, E87 |
| Blood Loss Anemia                | D50.0         |
| Deficiency Anemia                | D50.8, D50.9, D51–D53 |
| Alcohol Abuse                    | F52, F10, G62.1, H2.6, K29.2, K70.0, K70.3, K70.9, T51, Z50.2, Z71.4, Z72.1 |
| Drug Abuse                       | F11 F52, F16, F18, F19, Z71.5, Z72.2 |
| Psychoses                        | F20, F22–F25, F28, F29, F30.2, F31.2, F31.5 |
| Depression                       | F20.4, F31.3–F31.5, F32, F33, F34.1, F41.2, F43.2 |

### Supplementary Table 2
Univariate cox regression for proposed mortality scoring system

| Variables                                      | Hazard Ratio [95%CI] | P-value |
|------------------------------------------------|----------------------|---------|
| Female                                         | 1.01 [0.74–1.36]     | 0.9     |
| Black race vs. white                           | 0.73 [0.44–1.21]     | 0.23    |
| Hispanic race vs. white                        | 0.58 [0.33–1.01]     | 0.7     |
| Asian race vs. white                           | 1.32 [0.71–2.46]     | 0.4     |
| Heart failure                                  | 2.01 [1.48–2.95]     | <0.001  |
| Cardiac arrhythmias                            | 1.78 [1.31–2.42]     | <0.001  |
| Valvular disease                               | 1.59 [0.77–3.25]     | 0.21    |
| Pulmonary embolisms                            | 1.59 [0.96–2.65]     | 0.07    |
| Peripheral vascular disease                    | 2.24 [1.41–3.54]     | <0.001  |
| Hypertension                                   | 0.37 [0.27–0.51]     | <0.001  |
| COPD                                           | 1.14 [0.78–1.66]     | 0.4     |
| Diabetes Mellitus                              | 0.87 [0.61–1.26]     | 0.4     |
| Chronic renal failure                          | 2.19 [1.56–3.1]      | <0.001  |
| Chronic liver disease                          | 1.58 [1.77–2.13]     | <0.001  |
| Peptic ulcer disease excluding bleeding         | 0.72 [0.24–2.15]     | 0.5     |
| Coagulopathy                                   | 2.34 [1.73–3.15]     | <0.001  |
| Obesity                                        | 0.97 [0.66–1.43]     | 0.8     |
| Protein Calorie malnutrition                   | 0.75 [0.56–1.01]     | 0.06    |
| Fluid and electrolyte disorder                 | 2.49 [1.61–3.85]     | <0.001  |
| Iron deficiency Anemia                         | 1.06 [0.59–1.89]     | 0.8     |
| Alcohol abuse                                  | 0.53 [0.37–0.75]     | 0.001   |
| Age >60                                        | 2.99 [2.2–4.10]      | 0.001   |

(Contd...)
### Supplementary Table 2 (Continued)

| Variables                      | Hazard Ratio [95%CI] | P-value |
|--------------------------------|----------------------|---------|
| ARDS                           | 1.65 [0.79-3.42]     | 0.1     |
| AKI                            | 4.91 [3.27-7.38]     | <0.001  |
| Sepsis with shock              | 7.31 [5.20 -10.2]    | <0.001  |
| Intubation                      | 3.44 [2.42-4.89]     | <0.001  |
| Vasopressor use                 | 5.20 [3.55 -7.61]    | <0.001  |
| SIRS                           | 0.59 [0.29 -1.19]    | 0.1     |
| Pancreatic Pseudocyst           | 0.53 [0.37-0.74]     | <0.001  |
| Hyponatremia                    | 0.79 [0.57 -1.11]    | 0.1     |
| Acute Peritonitis               | 0.38 [0.1 -2.56]     | 0.3     |
| DIC                            | 4.59 [2.63-8.00]     | <0.001  |
| Paralytic Ileus                 | 1.74 [0.85 -3.53]    | 0.4     |
| Portal venous thrombosis        | 0.99 [0.61 -1.61]    | 0.9     |
| Hospital region, Teaching       | 1.09 [0.95-1.25]     | 0.9     |
| compared to non-teaching        |                      |         |
| Hospital Bedsize, Large compared to small | 1.17 [0.94 -1.47] | 0.9     |

COPD, chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; SIRS, systemic inflammatory response syndrome; DIC, disseminated intravascular coagulation; 95%CI, 95% confidence interval

### Supplementary Table 3 Multivariate cox regression for proposed mortality scoring system

| Variables                      | Hazard Ratio [95%CI] | P-value |
|--------------------------------|----------------------|---------|
| Heart Failure                  | 1.21 [0.82-1.76]     | 0.3     |
| Cardiac arrythmias             | 1.14 [0.82-1.76]     | 0.4     |
| Peripheral vascular disease    | 1.62 [0.99-2.50]     | 0.09    |
| Chronic renal failure          | 1.43 [0.98-2.07]     | 0.06    |
| Chronic liver disease          | 1.60 [0.83-2.21]     | 0.2     |
| Coagulopathy                   | 1.24 [0.88-1.74]     | 0.2     |
| Fluid and electrolyte disorders | 1.46 [0.95-2.22]   | 0.07    |
| Age >60                        | 2.75 [2.01-3.79]     | <0.001  |
| Acute kidney injury            | 2.10 [1.34-3.24]     | <0.001  |
| Sepsis with shock              | 3.72 [2.32-5.96]     | <0.001  |
| Intubation                     | 0.91 [0.60-1.38]     | 0.7     |
| Vasopressor                    | 1.97 [1.29-3.03]     | <0.001  |
| DIC                            | 1.92 [1.01-2.76]     | <0.001  |
| ARDS                           | 1.31 [0.78-2.67]     | 0.1     |
| Valvular disease               | 1.72 [0.98-1.93]     | 0.5     |
| Pulmonary embolisms            | 1.51 [0.28-3.07]     | 0.09    |
| Peripheral vascular disease    | 1.31 [0.78-2.67]     | 0.2     |

ARDS, acute respiratory distress syndrome; DIC, disseminated intravascular coagulation; 95%CI, 95% confidence interval