Timing of Antibiotic Treatment in A Swedish Cohort of Septic Intensive Care Patients

Maria Cronhjort, Susanne Rysz, Mattias Sandström, Christer Svensen, Johan Mårtensson, Max Bell, and Eva Joelsson-Alm

ABSTRACT

**Background:** Sepsis is a challenge to healthcare systems, and morbidity and mortality remain high. In the worldwide Surviving Sepsis Campaign, there has been a focus on the timing of antibiotic administration to septic patients. The objective of this study was to describe current practice regarding the timing of antibiotic administration in septic patients admitted to intensive care units (ICUs) in Sweden.

**Methods:** This was an observational cohort study of septic patients in four ICUs in the Stockholm area during 2005-2010. Inclusion criteria were age > 18 years, sepsis upon hospital admission, and a registered time point for the first dose of antibiotic administration. Information on time of arrival at the hospital, physiological parameters within the first hour of arrival, time of administration of antibiotics, results of blood culture, other laboratory results, diagnosis, and medical procedures were retrieved from the medical charts. Patients requiring surgery for source control were labelled as having surgical sepsis.

**Results:** Overall, 64 of 210 septic patients (30%) received antibiotics within one hour of hospital admission. Initiation of antimicrobial therapy was delayed in female patients. Surgical patients received antibiotics later but still had a lower mortality than non-surgical patients.

**Conclusions:** The reason for the delay of antibiotics to female patients and the impact on clinical outcomes of such a gender difference in the treatment of sepsis needs to be further investigated.

Sepsis is a challenge to healthcare systems, and morbidity and mortality remain high (1). Since the early 2000s, several interventions have been implemented in clinical care programs to improve outcomes in patients with sepsis. The Surviving Sepsis Campaign (SSC) Guidelines for Management, first published in 2004, have been revised several times (2-4). Within this framework, there has been an increasing interest regarding the timing of antibiotic administration to septic patients. Early administration is crucial for combating septicaemia but should be weighed against the unnecessary administration of antibiotics that entails the risk of developing resistance. Kumar et al. (5) showed a linear correlation between the time from septic shock to the initiation of antibiotic therapy and in-hospital mortality whereas antibiotic administration might be safely delayed up to six hours after triage in the emergency ward in hemodynamically stable patients (6, 7). Accordingly, the latest SSC Guidelines recommend administration of antibiotics within one hour from rec-
ognition of sepsis for patients suffering from severe sepsis or septic shock (4). The objective of this study was to describe current practice regarding the timing of antibiotic administration in septic patients admitted to intensive care units (ICUs) in the Stockholm area.

**METHODS**

**Ethical approval**

All procedures performed in this study were in accordance with the ethical standards of the national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study was approved by the Regional Ethical Board of Stockholm (No 2010/1780-31-2). For this type of study, formal consent is not required.

**Study Design**

This was an observational cohort study of patients in four Swedish ICUs in the Stockholm area during 2005-2010. The participating ICUs were the mixed general ICU at Karolinska University Hospital Solna, the mixed general ICU at Karolinska University Hospital Huddinge, and the surgical ICU and the medical ICU at Södersjukhuset. An electronic monitoring system was used to retrieve patient data (Clinisoft®, General Electric, Barrington, IL, USA). Clinisoft® was introduced in Stockholm during the years 2005 to 2012, and all ICUs using Clinisoft® during the 2005-2010 study period were selected.

**Data Collection**

Patients were screened for inclusion if a sepsis diagnosis was found in the Clinisoft® system and the patient was treated in the ICU for four days or more. This dataset was taken from a larger dataset where the intention was to study cumulative fluid balance at day four. Inclusion criteria were age > 18 years, sepsis at presentation to the emergency department, and a registered time point for the first dose of antibiotic administration. Information on time of arrival at the hospital, physiological parameters within the first hour of arrival, time of administration of antibiotics, results of blood culture, other laboratory results, diagnosis, and medical procedures were retrieved from the medical charts according to specified definitions (see Appendix A). All sepsis diagnoses were checked and found to be consistent with sepsis as defined according to the Society of Critical Care Medicine/American College of Chest Physicians consensus conference definition (8). Patients requiring surgery for source control were labelled as having surgical sepsis. Classification of co-morbidities and illness severity scoring was performed with the Simplified Acute Physiology Score 3 (SAPS 3) (9). The SAPS 3 score was based on physiological and biochemical parameters recorded within one hour of admission to the hospital. Primary outcome was 90-day mortality.

Data were gathered by two intensive-care consultants and one medical student, and each individual gathered data from at least 50 patients. Data on 90-day mortality were retrieved from the Total Population Register of Statistics Sweden through the Swedish personal identification number (10).

The ICUs started to use Clinisoft® in the following order: the mixed general ICU at Karolinska University Hospital Huddinge in May 2005, the mixed general ICU at Karolinska University Hospital Solna in January 2006, and the surgical and medical ICUs at Södersjukhuset in March 2008. Patients admitted with sepsis before the introduction of Clinisoft® in the respective ICUs were not included in the study. Figure 1 shows the flow chart of patient selection. Patients were divided into two groups, those who received antibiotics within one hour of admission to the hospital (early group) and those who received antibiotics later than one hour after hospital admission (late group), with the intention to evaluate how well the SSC guidelines were followed.

**Statistical Methods**

Categorical data were presented as numbers and percentages. Continuous data were presented as mean with standard deviation (SD) when normally distributed or as median with interquartile range (IQR) when non-normally distributed, and ordinal data were presented as median (IQR). Results were compared by Fisher’s exact test for categorical variables. Continuous variables that were normally distributed were analyzed by Student’s t-test and continuous variables that were non-normally distributed were
analyzed by the Mann-Whitney U-test. In groups with fewer than five observations, no calculation of statistical significance was performed.

The association between late antibiotic administration and 90-day mortality was evaluated by multivariate logistic regression analysis considering the following potential confounding factors: SAPS 3-score, gender, and surgical sepsis. These potential confounders were chosen a priori based on clinical experience.

Statistical analyses were performed using IBM SPSS statistics, version 22 (IBM, Armonk, NY, USA). Results were considered statistically significant at P<0.05.

RESULTS

In total, 627 patients with sepsis were found in Clinisoft® from 2005 to 2010. Of these 627 patients, 299 (48%) were given the sepsis diagnosis at hospital admission. Time of administration of antibiotics was available for 210 patients, and these were included in the study (Figure 1). The other 328 patients developed sepsis during their stay in the hospital and were excluded because of uncertainty of the diagnosis time. Overall, 64 of the 210 septic patients (30%) received antibiotics within one hour of hospital admission. Demographics, source of infection, and outcome in patients who received antibiotics early and late, respectively, were presented in Table 1. Median time to receiving antibiotics was 38 minutes (IQR 23-51 minutes) in the early group and 211 minutes (IQR 124-417 minutes) in the late group. There was a gender difference with a significantly lower proportion of females in the early group (28%) as compared to the late group (47%, P=0.015). There was a higher proportion of patients with surgical sepsis (P=0.004) and unspecified sepsis (P=0.036) in the late group. Ninety-day mortality was 28% in the early group and 31% in the late group (P=0.75). Blood culture results were presented in Table 2: 50% had an initial positive blood culture in the late group compared to 56% in the early group (P=0.43). The first antibiotics administered to the patients were presented in Table 3. A significantly higher proportion of patients in the early group received aminoglycosides as the first antibiotic (19%) compared to the late group (5.5%), (P=0.003). Combinations of antibiotics were presented in Table 4. A total of 63% of the patients received a combination of antibiotics, and the most common combination was an aminoglycoside with a beta-lactam antibiotic (54%).

In univariate logistic regression, the only confounding factor that was statistically significantly correlated to mortality was not having surgical sepsis (odds ratio [OR] 3.1, 95% confidence interval [CI] 1.2-7.8) (Table 5). In multivariate logistic regression analysis adjusting for gender, surgical sepsis and SAPS 3-score, late initiation of antimicrobial therapy was not associated with mortality at 90 days (OR 1.5, 95% CI 0.77-3.1) (Table 6).

DISCUSSION

In this study, it was possible to extract data from 210 patients treated for sepsis in a Swedish ICU cohort from four centers. The main finding was that there was a gender difference between the groups that received antibiotics within one hour and the group that received it later. Male patients received antibiotics within one hour to a higher degree than female patients despite similar illness severity, a finding that was statistically significant. Furthermore, the only confounding
Table 1. Characteristics of the Study Population.

| Characteristic                  | All patients, N=210 | Antibiotics within one hour, N=64 | Antibiotics after one hour, N=146 | P value |
|---------------------------------|---------------------|-----------------------------------|-----------------------------------|---------|
| Time to antibiotics, minutesa  | 132 (54-271)        | 38 (23-51)                        | 211 (124-417)                     |         |
| SAPS 3-scoreb                  | 42 (9.6)            | 44 (7.7)                          | 41 (10)                           | 0.058   |
| Age, yearsb                    | 62 (53-41)          | 62 (52-71)                        | 63 (53-72)                        | 0.46    |
| Female gender                  | 86 (41%)            | 18 (28%)                          | 68 (47%)                          | 0.015   |
| Surgical sepsis                | 41 (20%)            | 5 (8%)                            | 36 (25%)                          | 0.004   |
| 90 day mortality               | 63 (30%)            | 18 (28%)                          | 45 (31%)                          | 0.75    |
| Co-morbidity                   |                     |                                   |                                   |         |
| Renal disease                  | 10 (4.8%)           | 4 (6.3%)                          | 6 (4.1%)                          | N/A     |
| Diabetes                       | 43 (21%)            | 18 (28%)                          | 25 (17%)                          | 0.093   |
| Immunosuppression              | 43 (21%)            | 14 (21%)                          | 29 (20%)                          | 0.71    |
| Cirrhosis                      | 5 (2.4%)            | 1 (1.6%)                          | 4 (2.7%)                          | N/A     |
| Respiratory insufficiency      | 7 (3.3%)            | 5 (7.8%)                          | 2 (1.4%)                          | N/A     |
| Circulatory insufficiency      | 1 (0.5%)            | 0                                 | 1 (0.7%)                          | N/A     |
| Source of infection            |                     |                                   |                                   |         |
| Skin/soft tissue               | 13 (16%)            | 2 (3.1%)                          | 11 (7.5%)                         | N/A     |
| Pneumonia                      | 70 (33%)            | 21 (33%)                          | 49 (34%)                          | 1.0     |
| Gastrointestinal               | 13 (6.2%)           | 0                                 | 13 (8.8%)                         | N/A     |
| CNS                            | 6 (2.9%)            | 2 (3.1%)                          | 4 (2.7%)                          | N/A     |
| Joints                         | 1 (0.5%)            | 0                                 | 1 (0.7%)                          | N/A     |
| Sepsis, unspecified            | 97 (46%)            | 37 (58%)                          | 60 (41%)                          | 0.036   |
| Endocarditis                   | 5 (2.4%)            | 1 (1.6%)                          | 4 (2.7%)                          | N/A     |
| amedian (IQR); bmean (SD).     |                     |                                   |                                   |         |

Table 2. Blood Culture Growth.

| Growth in blood culture          | Late group N=146 | Early Group N=64 | Entire group N=210 |
|----------------------------------|------------------|------------------|--------------------|
| Negative culture                 | 73 (50%)         | 28 (44%)         | 101 (48%)          |
| Gram pos                         |                  |                  |                    |
| Streptococcus, alpha             | 4 (2.7%)         | 1 (1.6%)         | 5 (2.4%)           |
| Streptococcus, beta              | 5 (3.4%)         | 5 (7.8%)         | 10 (4.7%)          |
| Streptococcus pneumonia          | 16 (11%)         | 10 (16%)         | 26 (12%)           |
| Enterococcus                     | 1 (0.7%)         | 0                | 1 (0.5%)           |
| Other Streptococci               | 2 (1.4%)         | 0                | 2 (0.9%)           |
| Staphylococcus aureus            | 15 (10%)         | 4 (6.3%)         | 19 (9.0%)          |
| Staphylococcus epidermidis       | 4 (2.7%)         | 3 (4.7%)         | 7 (3.3%)           |
| Bacillus cereus                  | 1 (0.7%)         | 0                | 1 (0.5%)           |
| Fusobacterium necrophorum        | 2 (1.4%)         | 1 (1.6%)         | 3 (1.4%)           |
| Propionibacterium acnes          | 1 (0.7%)         | 0                | 1 (0.5%)           |
| Gram neg                         |                  |                  |                    |
| Neisseria Meningitidis           | 1 (0.75)         | 0                | 1 (0.5%)           |
| Haemophilus influenzae           | 2 (1.4%)         | 0                | 2 (0.9%)           |
| Escherichia coli                 | 9 (6.2%)         | 6 (9.4%)         | 15 (7.1%)          |
| Klebsiella                      | 2 (1.4%)         | 0                | 2 (0.9%)           |
| Proteus                          | 1 (0.7%)         | 1 (1.6%)         | 2 (0.9%)           |
| Enterobacter species             | 0                | 1 (1.6%)         | 1 (0.5%)           |
| Serratia                         | 0                | 2 (3.1%)         | 2 (0.9%)           |
| Morganella                       | 1 (0.7%)         | 0                | 1 (0.5%)           |
| Pseudomonas species              | 1 (0.7%)         | 1 (1.6%)         | 2 (0.9%)           |
| Bacteroides                      | 1 (0.7%)         | 0                | 1 (0.5%)           |
| Mycoplasma pneumoniae           | 0                | 1 (1.6%)         | 1 (0.5%)           |
| Fungus                           | 1 (0.7%)         | 0                | 1 (0.5%)           |
| Missing data                     | 3 (2.1%)         | 0                | 3 (1.4%)           |
| Patients, total number           | 146 (100%)       | 64 (100%)        | 210 (100%)         |

aMedian (IQR); bMean (SD).
factor that statistically significantly correlated to mortality in the logistic regression analysis was not having surgical sepsis. Thus surgical patients had lower mortality despite receiving antibiotics later. Although there was a trend towards higher mortality among those patients who received antibiotics later, it was not possible to draw any conclusions about the effect of timing of antibiotics on mortality due to the small sample size. To detect a 3% mortality difference, a sample size of 3,600 patients per group would have been required.

The discussion concerning the impact of timing of antibiotics on mortality has been intense. The study by Ferrer et al. (11) including 17,990 septic patients from the SSC database, showed an OR for hospital mortality of 1.5 (95% CI 1.4-1.7) when antibiotics were administered after six hours compared to within one hour when adjusted for sepsis severity score, geographic region, and ICU admission source. When focusing on early administration of antibiotics, they found a trend toward increased mortality from 24.6% when antibiotics were given within one hour compared to 25.9% when antibiotics were given within two hours. This means that 77 patients need to be treated with antibiotics within one hour instead of two hours to save one life. In contrast, Kumar et al. (5) found an increase in mortality from 20% to 30% with antibiotic administration within two hours instead of one hour. The question is whether the statistically significant difference in mortality that Ferrer showed is clinically significant.

Other studies have questioned the importance of early antibiotics. Puskarich et al. (6) showed that delayed antibiotic administration with up to six hours after triage in the emergency room did not increase mortality. Moreover, Gaeski et al. (7) failed to show an association between time from triage to antibiotics and mortality. Early diagnosis and antibiotic treatment is crucial for a patient in septic shock (6), but there are drawbacks with early empiric antibiotic treatment in non-septic patients. If every patient meeting the criteria for systemic inflammatory response (SIRS) were to receive antibiotics, then some patients would receive them unnecessarily. An increased time to decide upon the source of sepsis, and ideally to identify the causative organism, would allow for treatment with proper antibiotics and might reduce the need for broad-spectrum agents. This could lead to less development of resistance (12). Although one must not advocate an intentional delay in administration of antibiotics to a patient in septic shock, the one-hour recommendation for administration might not be clinically crucial for patients with sepsis or even severe sepsis.

Several studies have indicated that there are gender-specific differences regarding infections and sepsis. Female sex hormones exhibit protective effects that might contribute to an advantage during septic conditions (13). However, a large Canadian study with 24,778 patients showed that fewer women were admitted to the ICU, women were less likely to receive invasive treatment, and women were more likely to die after their critical illness (14). Moreover, an Austrian study showed that once in the ICU, men were more likely to receive invasive procedures despite a higher severity of illness score in women. Mortality was the same for both genders (15). Sakr et al. (16) reported higher mortality in female patients with severe sepsis, but no difference in time to antibiotics. In order to understand the reason for gender differences in treatment between male and female septic patients,

### Table 3. First Antibiotic Administered.

| First antibiotic administered | Early group N=64 | Late group N=146 | N (%)        |
|------------------------------|-----------------|------------------|-------------|
| Cefotaxime                   | 20 (31%)        | 37 (25%)         | 57 (27%)    |
| Cefuroxime                   | 7 (11%)         | 33 (23%)         | 40 (19%)    |
| Penicillin                   | 11 (17%)        | 16 (11%)         | 27 (13%)    |
| Aminoglycoside               | 12 (19%)        | 8 (5.5%)         | 20 (9.5%)   |
| Piperacillin-tazobactam      | 3 (4.7%)        | 16 (11%)         | 19 (9.0%)   |
| Meropenem                    | 5 (7.8%)        | 13 (8.9%)        | 18 (8.6%)   |
| Clindamycin                  | 3 (4.7%)        | 4 (2.7%)         | 7 (3.3%)    |
| Imipenem                     | 0               | 3 (2.1%)         | 3 (1.4%)    |
| Ceftazidime                  | 0               | 3 (2.1%)         | 3 (1.4%)    |
| Co-trimoxazole               | 0               | 3 (2.1%)         | 3 (1.4%)    |
| Ampicillin                   | 1 (1.6%)        | 2 (1.4%)         | 3 (1.4%)    |
| Ciprofloxacin                | 0               | 2 (1.4%)         | 2 (1%)      |
| Erythromycin                 | 1 (1.6%)        | 1 (0.7%)         | 2 (1%)      |
| Vancomycin                   | 1 (1.6%)        | 1 (0.7%)         | 2 (1%)      |
| Flucloxacin                  | 0               | 1 (0.7%)         | 1 (0.5%)    |
| Amoxicillin                  | 0               | 1 (0.7%)         | 1 (0.5%)    |
| No antibiotic the first 24 hours | 0        | 2 (2.1%)         | 2 (1%)      |
| Total number                 | 64              | 146              | 210 (100%)  |
more studies with focus on qualitative studies of attitudes and behaviours of health care staff and patients are needed.

We further observed that patients with surgical sepsis received antibiotics later than patients with other causes for sepsis. It is possible that the administration of antibiotics is delayed when the patients have more alarming symptoms such as abdominal pain or fasciitis. Because this study did not include all septic patients in the emergency ward, more studies are needed to describe the flow of septic patients through the emergency ward. In particular, the impact of gender and symptoms on the speed of diagnosis and treatment needs to be explored.

Our study has several strengths. It was performed in four intensive care units. The exact time of arrival at the hospital and administration of antibiotics has been determined by review of medical records. Patients with uncertain registrations have been excluded. Data concerning 90-day mortality was retrieved from the Swedish Total Population Register, which is a reliable measure of mortality status.

This study has limitations. Due to limited sample size, we cannot rule out an association between timing of antibiotics and mortality. Another limitation is that we did not stratify patients according to sepsis severity. However, septic patients requiring intensive care almost always have at least one organ failure and thus, by definition, severe sepsis. The inclusion criterion was sepsis diagnosis in the electronic monitoring system. It is possible that some patients were registered with, for example, pneumonia or meningitis instead of sepsis. It is likely that more patients in our ICUs suffered from sepsis at some point during their ICU stay. However, probably most of the patients who were admitted to the ICU primarily for sepsis would have received the correct diagnosis. This uncertainty, however, holds a risk of selection bias.

Furthermore, the treatment period of four days was chosen because this was part of a larger study where fluid balance data on day 4 was supposed to be retrieved from the continuous electronic monitoring system (Clinisoft®). The limitation that only patients who were treated in the ICU for more than four days were included reduces both the number of patients in the
study and the generalizability of the results. Furthermore, this was an observational study, which means that no standard protocol was used for the treatment of patients and that only patients where sufficient data were available were included. Only a limited number of confounders were adjusted for. Other possible confounders are the level of physical activity before the episode of sepsis, the level of social support, and frailty (17). Only the patients who were admitted to an ICU were included in this study. If early antibiotics would have a protective effect against the deterioration that brings the patients to the ICU, this would not have been detected in this study.

CONCLUSION

This study demonstrated that initiation of antimicrobial therapy was delayed in female patients. The reason for this and the impact on clinical outcomes of such a gender difference in the treatment of sepsis needs to be further investigated. Surgical patients received antibiotics later but still had a lower mortality than non-surgical patients.

Table 5. Univariate Logistic Regression.

| Independent variable | Odds ratio | CI          | Significance level |
|----------------------|------------|-------------|--------------------|
| Antibiotics within 1 hour<sup>a</sup> | 1.14       | 0.60-2.2    | 0.70               |
| SAPS 3 <36<sup>b</sup> |            |             | 0.46               |
| SAPS 3 36-45.33<sup>c</sup> | 1.8        | 0.08-4.0    | 0.15               |
| SAPS 3 45.34-55.67<sup>d</sup> | 1.8        | 0.76-4.3    | 0.18               |
| SAPS 3 ≥55.68<sup>e</sup> | 2.0        | 0.61-6.7    | 0.25               |
| Male gender<sup>f</sup> | 1.30       | 0.71-2.4    | 0.39               |
| Not surgical sepsis<sup>g</sup> | 3.1        | 1.2-7.8     | 0.017              |

<sup>a</sup>Vs. early antibiotics; <sup>b</sup>Vs. lowest SAPS score; <sup>c</sup>Vs. female gender; <sup>d</sup>Vs. surgical sepsis.

Table 6. Multivariate Logistic Regression.

| Independent variables | Odds ratio | CI          | Significance level |
|----------------------|------------|-------------|--------------------|
| Antibiotics within 1 hour<sup>a</sup> | 1.5        | 0.77-3.1    | 0.23               |
| SAPS 3<sup>c</sup> |            |             | 0.44               |
| SAPS 3 36-45.33<sup>c</sup> | 1.8        | 0.80-4.1    | 0.15               |
| SAPS 3 45.34-55.67<sup>d</sup> | 1.8        | 0.73-4.5    | 0.20               |
| SAPS 3 ≥55.68<sup>e</sup> | 2.3        | 0.65-7.8    | 0.20               |
| Male gender<sup>f</sup> | 1.2        | 0.64-2.3    | 0.55               |
| Not surgical sepsis<sup>g</sup> | 3.1        | 1.2-8.1     | 0.018              |

<sup>a</sup>Vs. early antibiotics; <sup>b</sup>Vs. lowest SAPS score; <sup>c</sup>Vs. female gender; <sup>d</sup>Vs. surgical sepsis.

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Appendix A
Definitions of Data to be Retrieved from Patient Records
Primary sepsis: sepsis was the primary diagnosis upon arrival at the hospital or the patient fulfilled the sepsis criteria upon arrival at the hospital although the diagnosis was made later.
Sepsis: suspected infection and at least two of four SIRS criteria fulfilled:
- Respiratory rate >20 breaths/minute or PCO2 < 4.3 kPa;
- White blood cell count >12 or <4 × 109 cells/l;
- Heat rate >90 bpm;
- Temperature >38°C or <36°C.
Arrival time: the arrival time registered in the emergency ward records.
Time point of antibiotic administration: the time of administration of the first dose of antibiotics according to medical records (not prophylaxis administered during previous surgery).
Type of antibiotics: the antibiotic given during the first 24 hours of sepsis.
First blood culture: date and results.
First urinary culture: results.
Other cultures: results.
Diabetes: any kind of diabetes.
Date of source control: the day when the surgeon judges that no further surgery is required for source control and the patient recovers.
Co-morbidities according to APACHE II:
Liver failure: cirrhosis according to biopsy and documented portal hypertension, episodes of upper gastrointestinal bleeding due to portal hypertension, or previous episodes of liver failure/encephalopathy/coma.
Circulatory failure: NYHA class 4; angina or other cardiac symptoms at rest or at minimal exertion.
Respiratory failure: chronic restrictive, obstructive, or vascular disease that leads to serious restriction of working capacity (such as the inability to perform household work or to climb a flight of stairs) or documented chronic hypoxia, hypercapnia, secondary polycytemia, severe pulmonary hypertension (>40 mm Hg), or being on a ventilator.
Kidney failure: chronic dialysis.
Immune system: the patient has received treatment that impairs the immune system (immunosuppression, chemotherapy, radiation, high-dose steroids) or has a disease that impairs the immune system (leukaemia, lymphoma, AIDS).
Medical Records were Checked a Second Time to Calculate the SAPS 3 Scores
Box 1. Patient Characteristics before ICU Admission
Age, co-morbidities, length of stay in hospital before ICU admission, intrahospital location before ICU admission, use of vasoactive drugs before ICU admission.
Box 2. Circumstances of ICU Admission
Planned/unplanned reason for ICU admission, reason(s) for ICU admission, surgery before ICU admission, anatomic site of surgery, presence of infection at ICU admission.
Box 3. Physiologic Derangement at Admission (1 Hour before/after)
Glasgow coma scale (lowest), Total bilirubine (highest), Body temperature (highest), Heart rate (highest), Creatinine (highest), Leukocytes (highest), Hydrogen ion concentration (lowest pH), Platelets (lowest), Systolic blood pressure (lowest), Ventilatory support and oxygenation (lowest).