Prognostic factors in the survival of patients with blood disorders recovering from septic shock

Anna Waszczuk-Gajda and Wieslaw Wiktor Jedrzejczak
Department of Hematology, Oncology and Internal Medicine, Warsaw Medical University, Warsaw, Poland

ABSTRACT

Background: Septic shock is one of the major direct causes of death in patients in hematology departments.

Objectives: The knowledge about clinical outcomes and factors associated with negative outcome in these patients can be important and useful for physicians to identify the patients who are most likely to benefit from ICU therapy.

Methods: We retrospectively analyzed records of 214 episodes of septic shock in patients with different blood diseases hospitalized between 1998 and 2011 in the Department of Hematology, Oncology and Internal Medicine, the Medical University of Warsaw, Poland.

Results: Direct survival with resolution of septic shock was 46%. Among these survivors, 75% continued to live at 30 days, 49% at 6 months, and 12% at 5 years after shock resolution. It was found that the most important prognostic factors for direct (short-term) mortality were multiorgan failure, lack of concordance of empiric antibiotic treatment with results of in vitro sensitivity testing, the Karnofsky score below 60%, presence of more than two comorbidities.

Discussion: Septic shock in patients with blood disorders treated in the hematology ward was associated with very high risk of mortality in all periods after its completion. However, although the results of treatment of septic shock in patients with blood diseases are poor, they were comparable to the results of treatment of septic shock in mixed populations treated in intensive care units.

KEYWORDS

Septic shock; blood diseases; prognostic factors; short-term survival; long-term survival

Introduction

Septic shock is one of the major direct causes of death of patients with blood disorders [1,2]. Neutropenic sepsis as a clinical presentation is vastly different, and patients can go into septic shock much more rapidly because of a compromised immune system. Available literature concerns patients treated in intensive care units where only a minor proportion are patients transferred from hematology departments [3–5]. However, there are major differences between general ICU patients in septic shock and hematological patients with this complication because this latter category of patients frequently suffers from underlying immune deficiencies produced by both disease and treatment, such as intensive chemotherapy and hematopoietic transplantation (neutropenia, immunoglobulin deficiency) that predispose them to many more infectious complications [6]. Moreover, if microorganism is acquired in the hospital, it is frequently selected for resistance to major antibiotics.

Therefore, the aim of this retrospective study was to identify factors that have influenced this outcome in hematologic patients.

Materials and methods

Records of 214 cases of septic shock that has occurred in patients with blood diseases were analyzed. They concerned patients with different blood diseases hospitalized between 1998 and 2011 in the Department of Hematology, Oncology and Internal Medicine, The Medical University of Warsaw, Poland. The analyzed group was composed of 97 women and 117 men, aged 20–90 years (59 ± 14), diagnosed with blood diseases as given in Table 1. Only the first episode of septic shock of each patient was included in this study. Fifteen patients had sepsis more than once: two times – six patients, three times – one patient, four times – one patient, five times – one patient.

Septic shock was diagnosed based on the criteria defined by the ACCP/SCCM Consensus Conference Committee (2003) [7]. According to them, septic shock is defined as a severe sepsis with a state of acute circulatory failure characterized by persistent
arterial hypotension unexplained by other causes. Hypotension is generally considered if systolic arterial pressure is 90 mm Hg, mean arterial pressure is less than 60 mm Hg or reduction in systolic blood pressure is more than 40 mm Hg from baseline, despite adequate volume resuscitation, in the absence of other causes for hypotension [7].

Management of septic shock was compatible with the standard of care in septic shock and individual state of the patient [8] also for patients treated before 2008.

Early survival from septic shock was defined as the patient being alive for at least 24 hours after the discontinuation of treatment with pressor amines.

Death in septic shock was defined as death during persistence of symptoms of septic shock, requiring continuous administration of pressor amines or within 24 hours after discontinuation of their administration. Long-term survival of hematological patients was also assessed. Identification of factors influencing short- and long-term mortality was also planned.

Hospital- and healthcare-associated infections were defined when septic shock was diagnosed in the patient hospitalised for more than 48 hours.

**Statistical analysis**

Descriptive analysis was expressed as means ± standard deviation. The primary analysis compared hospital survivors with non-survivors. In testing hypotheses, \( p < 0.05 \) as statistically significant. In order to compare nominal variables, Fisher’s exact test was used. For the scale interval for the independent variables, \( t \)-test (for continuous parameters with normal distribution) or nonparametric test Mann–Whitney \( U \) (if the variables do not meet the criterion of the normal distribution), paired \( t \)-test (for the parameters of normal distribution), or Wilcoxon test (when there is no normal distribution) were applied.

Risk factors for direct mortality were assessed using univariate logistic regression analysis. Binary dependent variable was septic shock-dependent death coded as “1.”

Univariate Cox proportional hazards of regression analysis (PHREG) was used for the analysis of long-term mortality. Survival and mortality after septic shock and time to death in the follow-up in patients with a history of septic shock was estimated using the Kaplan–Meier estimator (SAS, version 8.2).

**Results**

Ninety-nine (46%) patients survived and 115 (54%) died before resolution of this complication from among 214 analyzed cases of hematologic patients with septic shock.

The median duration of septic shock was 2 days in survivors and 1 day in nonsurvivors. The median duration of hospitalization to onset of septic shock was 17 days. Patients with more than two diagnosed comorbidities had 26.39 times higher risk of death due to septic shock in comparison with patients with less than two comorbidities. The worst survival in septic shock was observed in patients in advanced phase of underlying disease: resistance of underlying disease to treatment, lack of response to treatment. Neutropenia with granulocytes lower than or equal to 1.5 G/l was diagnosed in 72% of the patients; agranulocytosis was diagnosed in 59% of the patients. Two weeks before the onset of septic shock, 77% patients were treated with chemotherapy.

The percentage of deaths can be misleading because other factors also played a role in prognosis as type, stage of underlying disease, response to treatment, long-term prognosis connected with underlying hematological disease. About 40% of cases in our group were connected with advanced stages of underlying disease, and the survival possibility resulting from underlying disease was poor. The worst survival was associated with longer time, that is, from the diagnosis of underlying disease to septic shock onset and resistance to chemotherapy and was 41% in comparison to 64% in the rest of the group (\( p < 0.05; \) OR 2.9, PU 1.5–5.65, \( p < 0.05 \)).

Most often, the etiology of septic shock included pneumonia (28.5%), central catheter infection (9%), neutropenic fever (8%), urinary tract infection (6%). In 15% of the patients, fever was not accompanied by neutropenia and no etiology of infection was found. Most patients (91%) were diagnosed with hospital- and healthcare-associated infections.

Septic shock in the analyzed group was associated slightly more often with Gram-positive (the most often cultured: *Staphylococcus aureus*) than Gram-negative bacteria (the most often cultured: *Escherichia coli*).

The mortality due to septic shock caused by Gram-positive and Gram-negative microorganisms was similar. No difference has been found in the mortality between neutropenic and non-neutropenic patients.

Altogether, 35% of patients survived 30 days, 29% survived 60 days, 27% survived 90 days, 23 survived 6

### Table 1. Underlying blood disease.

| Blood disease                        | n (number of patients) |
|--------------------------------------|------------------------|
| Acute myeloid leukemia (AML)         | 64                     |
| Multiple myeloma (MM)                | 49                     |
| Non-Hodgkin lymphoma (NHL)           | 38                     |
| Chronic lymphatic leukemia (CLL)     | 21                     |
| Myelodysplastic syndrome (MDS)       | 9                      |
| Acute lymphoblastic leukemia (ALL)   | 6                      |
| Severe aplastic anemia (SAA)         | 6                      |
| Other: chronic myelogenous leukemia (CML) | 6          |
| amyloidosis – light chains (AL) primary myelofibrosis (PMF) thrombotic thrombocytopenia purpura (TTP) |
months, 17% survived 1 year, 12% survived 2 years, 8% survived 3 years, 6% survived 4 years, 5.6% of all patients survived 5 years from the period of septic shock (Figure 1(a)).

The analysis of 99 patients who survived after resolution of septic shock has shown that 75% of them survived 30 days, 63% survived 60 days, 54% survived 90 days, 49% survived 6 months, 38% survived 1 year, 26% survived 2 years, 18% survived 3 years, 14% survived 4 years and 12% survived 5 years after resolution of septic shock (Figure 1(b)).

Sixty-eight people (32% of the total) were discharged from the hospital after hospitalization associated with the occurrence of septic shock.

Since the analyzed group included patients treated in a wide range of years, we have also attempted to assess whether the results improve over the years. It was found that patients treated in the years 2005–2011 achieved 58% early survival in comparison to patients treated in the years 1999–2004 who achieved 34% (p < 0.0001), while the percentage of patients discharged from the hospital was 44% vs. 19% (p < 0.0001).

**Risk factors of direct mortality from septic shock**

It was found that the most important prognostic factors for early mortality identified in univariate logistic regression analysis in patients with septic shock and blood diseases were multiorgan failure – (failure of four or five organs increased the risk of mortality × 136.8–332.5) or assessed by the organ failure score (APACHE II and APACHE III) (OR (odds ratio) 6.10, CI 3.77–9.89, p < 0.05), lack of concordance of empiric antibiotic treatment with the results of in vitro sensitivity testing (OR 55.84, CI 7.33–426.78, p < 0.05), the Karnofsky score below 60% (OR 43.5, CI 12.5–100, p < 0.05), presence of more than two comorbidities (except for blood disease and septic shock) (OR 26.39, CI 12.13–57.4, p < 0.05), respiratory failure requiring mechanical ventilation (OR 13.58, CI 1.75–1–5.2, p < 0.05). Moreover, the occurrence of septic shock before 2005, i.e. in 1998–2004, was an important risk factor for death due to septic shock (OR 3.44, CI 1.9–6.2, p < 0.05). Other independent risk factors associated with direct mortality are: onset of disseminated intravascular coagulation (OR 6.94, CI 2.58–18.66, p < 0.05), elevated urea concentration (OR 1.91, CI 1.17–2.67, p = 0.0001), decreased serum albumin concentration (OR 1.39, CI 1.03–1.85, p = 0.028), elevated LDH (OR 2.3, CI 1.31–4.06, p = 0.004), primary source of infection prior to the onset of septic shock, which was ileus (OR 4.80, CI 1.35–17.1, p = −0.016), receiving antibiotics before the onset of septic shock (OR 1.80, CI 1.05–3.1, p = 0.034), no modification of antibiotic therapy after the diagnosis of septic shock if the patient received antibiotics before the onset of septic shock (OR 9.1, CI 3.8–12.1, p < 0.05), monotherapy with a narrow-spectrum antibiotic (OR 1.6, CI 1.02–2.31, p = 0.026).

We observed the non-statistically significant trend that inability to identify an etiologic factor of septic shock worsened the survival (OR 1.73, CI 1.01–3.03, p = 0.06).

The prognostic factors influencing direct mortality are listed in Table 2.

**Risk factors for long-term mortality**

Long-term prognosis was affected by multiple factors with the most significant being: patient’s general condition, underlying blood disease, source of infection and antibiotic treatment of septic shock. Moreover, none of them was solely responsible for unfavorable outcome and the factors were varying depending on the time that has passed from septic shock. The following factors associated with patient’s general status and condition were found to be independent risk factors for poor long-term survival (in brackets data for 3-year follow-up are shown): female gender (HR (hazard
Table 2. Factors directly affecting mortality.

| Factors influencing short-term mortality | Survivors | Non-survivors | OR (95% CI) | p     |
|-----------------------------------------|-----------|---------------|-------------|-------|
| KS < 60% vs. KS ≥ 60% (n)               | 46/53     | 112/3         | 43.5 (12.5–126) | 100   |
| 1998–2004 vs. 2005–2011 (n)             | 51/48     | 27/88         | 3.44 (1.9–6.2)  | 0.005 |
| Comorbidities ≥2 vs. ≤1 (n)             | 261/12–42 | 27; 17–42     | 6.1 (3.77–9.89) | 0.0001|
| APACHE II (mean, SD, median, min–max)   | 21 (SD 3.8) | 27 (SD 4.4) | 1.89 (0.98–3.62) | 0.0001|
| Failure of two organs (n = 47) vs. isolated circulatory failure | 42 (89%) | 5 (11%) | 2.26 (0.41–12.35) | 0.346 |
| Failure of three organs (n = 29) vs. isolated circulatory failure | 10 (54%) | 19 (66%) | 3.61 (1.78–7.81) | 0.001 |
| Failure of four organs (n = 41) vs. isolated circulatory failure | 5 (12%) | 36 (98%) | 136.8 (24.04–750.3) | 0.0001|
| Failure of five organs (n = 37) vs. isolated circulatory failure | 2 (5%) | 35 (95%) | 332.5 (44.42–999.9) | 0.0001|
| Failure of six or seven organs (n = 20) vs. isolated circulatory failure | 2 (10%) | 18 (90%) | 114 (14.46–898.5) | 0.0001|
| Respiratory failure requiring mechanical ventilation (n = 15) (+ vs. −) | 1 (7%) | 14 (93%) | 13.58 (1.75–105.2) | 0.013 |
| Hypoalbuminemia (HR 1.62, p < 0.05), as signs of blood disease activity, were also connected with worse long-term prognosis. The next group of factors was related to the origin of infection. When the primary location of infection was pneumonia (HR 1.80, p < 0.05) or ileus (HR 7.94, p < 0.05), the long-term diagnosis was dismal. The last group of factors was associated with antibiotic treatment: when no modification of antibiotic therapy after diagnosis of septic shock was done, the mortality rate was high (HR 12.64, p < 0.05). The long-term prognostic factors are shown in Table 3. Discussion

Septic shock is very severe and relatively common complication of treatment for hematologic patients [1,9]. It was found that hematologic patients, even if they survive septic shock, have poor both short-term (2–3 months) and long-term survival (years). This could be due to either preferential occurrence of septic shock in patients being already in advanced stages of their disorders or to the persistence of the injuries to the function of critical organs produced by the shock. Such injuries subclinical at the time of immediate recovery from the shock may, in the long term, deteriorate function and subsequently produce death by multorgan failure. Moreover, both these mechanisms may contribute to poor outcome.

Since there is paucity of similar studies in the available literature, our results have to be discussed in the...
In this context, the survival after resolution of septic shock in analyzed group is comparable to the survival of patients with blood disorders treated in the ICU, and the results are also comparable to the results of the treatment of septic shock in mixed populations. Thirty-day survival of septic shock patients with cancer treated in intensive care units was almost 36% [5]. The in-hospital survival of patients with hematological disorders (mainly hematologic malignancies) admitted to the ICU for various reasons (septic shock was only one of the many reasons) ranged from 20 to 43% [3,15,16]. The in-hospital survival of mixed populations in septic shock treated in intensive care units from the database CUB-Rea has improved from 37.9 (1993) to 44.1% (2000) (100 554 cases of unselected patients with septic shock treated in intensive care of 22 hospitals in France during the 8 years (1993–2000) [9]. Bousskeley et al. [10] reported 28-day survival of 48.8% in unselected patients treated for septic shock in 2003–2008, which is a better result than in the analyzed group.

Improved results of treatment of septic shock over the years and greater chance of survival in septic patients from general population in the ICU. These studies sometimes included also hematologic patients but mixed with patients with other underlying diseases [3–5,10–13]. The results of short-term analysis of survival in our group of hematologic patients are similar to those of survival of unselected patients with septic shock treated in ICUs, although the patients in mixed populations, by definition, should be in better immune condition than the patients with hematologic disorders. In-hospital survival of unselected patients after treatment of septic shock in ICU ranged from 38.8 [9] to 43.6% [10]. Thirty-day survival of patients with blood diseases and septic shock treated in ICU was 34.5 [5] and 46.6% [4], respectively. The in-ICU combined survival of unselected patients with sepsis. Severe sepsis and septic shock in intensive care based on the “Sepsis Register in Poland” ranged from 46 to 53% [14]. A trend was observed toward improved survival over the years [14]. It should be noted that sepsis and severe sepsis are life-threatening conditions associated with lower risk of death than septic shock.

| Prognostic risk factors | 30-day follow-up | 60-day follow-up | 90-day follow-up | 365-day follow-up | 3-year survival |
|------------------------|-----------------|-----------------|-----------------|-----------------|----------------|
| **HR** | **p** | **HR** | **p** | **HR** | **p** | **HR** | **p** | **HR** | **p** |
| Gender F/M | 2.86 | **< 0.05** | 2.17 | **< 0.05** | 1.86 | **< 0.05** | 1.50 | **< 0.05** | 1.62 | **< 0.05** |
| KS lower than 60% vs. KS higher 60% | 2.84 | **< 0.05** | 3.65 | **< 0.05** | 4.07 | **< 0.05** | 2.93 | **< 0.05** | 3.01 | **< 0.05** |
| Year of septic shock onset: 1998–2004 vs. 2005–2011 | 4.03 | **< 0.05** | 1.97 | **< 0.05** | 1.64 | **< 0.05** | 1.32 | **< 0.05** | 1.16 | **< 0.05** |
| Refractory relapsed HL vs. other blood diseases | 4.16 | **< 0.05** | 5.13 | **< 0.05** | 5.05 | **< 0.05** | 5.05 | 0.05 | 5.05 | **< 0.05** |
| Advanced/fate refractory relapsed phase | 1.06 | **< 0.05** | 1.86 | **< 0.05** | 1.97 | **< 0.05** | 2.44 | **< 0.05** | 2.74 | **< 0.05** |

context of the results of treatment of septic shock in patients from general population in the ICU. These studies sometimes included also hematologic patients but mixed with patients with other underlying diseases [3–5,10–13]. The results of short-term analysis of survival in our group of hematologic patients are similar to those of survival of unselected patients with septic shock treated in ICUs, although the patients in mixed populations, by definition, should be in better immune condition than the patients with hematologic disorders. In-hospital survival of unselected patients after treatment of septic shock in ICU ranged from 38.8 [9] to 43.6% [10]. Thirty-day survival of patients with blood diseases and septic shock treated in ICU was 34.5 [5] and 46.6% [4], respectively. The in-ICU combined survival of unselected patients with sepsis. Severe sepsis and septic shock in intensive care based on the “Sepsis Register in Poland” ranged from 46 to 53% [14]. A trend was observed toward improved survival over the years [14]. It should be noted that sepsis and severe sepsis are life-threatening conditions associated with lower risk of death than septic shock.

In this context, the survival after resolution of septic shock in analyzed group is comparable to the survival of patients with blood disorders treated in the ICU, and the results are also comparable to the results of the treatment of septic shock in mixed populations. Thirty-day survival of septic shock patients with cancer treated in intensive care units was almost 36% [5]. The in-hospital survival of patients with hematological disorders (mainly hematologic malignancies) admitted to the ICU for various reasons (septic shock was only one of the many reasons) ranged from 20 to 43% [3,15,16]. The in-hospital survival of mixed populations in septic shock treated in intensive care units from the database CUB-Rea has improved from 37.9 (1993) to 44.1% (2000) (100 554 cases of unselected patients with septic shock treated in intensive care of 22 hospitals in France during the 8 years (1993–2000) [9]. Bousskeley et al. [10] reported 28-day survival of 48.8% in unselected patients treated for septic shock in 2003–2008, which is a better result than in the analyzed group.

Improved results of treatment of septic shock over the years and greater chance of survival in septic

Table 3. Risk factors for long-term mortality.
shock with each year were observed in analyzed group and confirmed in other studies in mixed populations [10,12,13,17]. Friedman et al. [17] have analyzed the results of treatment of patients with SIRS, bacteremia, sepsis, septic shock over the years 1958–1997 in 10 694 patients from 131 studies (99 prospective and 32 retrospective) [17]. In-hospital survival of patients who are at various stages of systemic inflammatory response at the time of discharge from the ICU was 50.3% [17]. They have also found a trend to improve the results of treatment of septic shock over the years in the period considered (p < 0.05). Similarly, Ferrá et al. [12] showed that patients with hematologic malignancies and life-threatening conditions (33% of patients in septic shock nearly 50% of patients with respiratory failure), treated in the intensive care unit in 2004–2006, had better outcomes than patients treated in 2000–2003 (survival of life-threatening condition in the ICU respectively 51 vs. 31%, p < 0.047) [12].

Two-year survival of all patients after resolution of septic shock was 14% and is comparable with the results obtained in the analyzed group. Pené observed a similar trend in patients with cancer (approximately half of patients with hematologic malignancy) in septic shock: survival after treatment of septic shock in 2002–2005 compared with 1998–2001 was 47% vs. 28%, p < 0.05 (28-day survival) and 32% vs. 16%, p < 0.05 (6-month survival) [13]. The use of 28-day mortality as an end point for studies may lead to inaccurate inferences [18]. Similarly to our results, Leibovici has shown that the diagnosis of multiple myeloma was associated with better prognosis [19]. An increased risk of death in patients where an etiologic agent was not identified was also reported by Degoricija et al. [11], Brun-Buisson et al. [20], Leibovici et al. [21]. The importance of concordance of empiric antibiotic treatment with the results of *in vitro* sensitivity testing was also underlined in the study by Leibovici et al. [22].

Furthermore, the outcome of patients who required a combination of life support techniques was very dismal [16]. In the literature as well as in our study, multiorgan failure is the major risk factor for early and long-term mortality [16].

In the study of Bernal et al. [23], the long-term survival of hematological patients after discharge from the intensive care unit was studied and it was shown that similarly to our group the most important mortality risk factors were an Eastern Cooperative Oncology Group (ECOG) score >2 (we used even more accurate Karnofsky performance score), high APACHE II score, absence of SCT and relapse or resistance to treatment of the underlying disease (HR 5.05, p < 0.05) [23].

There are convincing data that the consequences of severe infections, such as septic shock, extend far beyond the first month of follow-up [19] and we confirmed this hypothesis in our study. During the long-term observation after septic shock/severe sepsis, the survival of patients is worse [18,19]. What is more, their survival is much worse than that of patients without infections [19,22]. In patients with bacteremia, the 1-month mortality rate was 26%, and the 1-year mortality rate was 48% (median survival 16.2 months); in the control group, the mortality rate was 7% at 1 month; 27% at one year, and median survival was >75 months [22]. Factors independently associated with worse survival in long-term observation were the following: inappropriate empiric antibiotic treatment, nosocomial infection, low serum albumin, renal failure (high serum creatine), what is similar in our group. The infections worsen the survival of patients and this was observed not only in studies concerning severe sepsis but also in studies concerning less severe sepsis [19]. The patients with blood disorders in our group have many factors predisposing to infections due to underlying disorder and due to the treatment of the disease (e.g. neutropenia, hypogammaglobulinemia, long duration of hospitalization [carrier of nosocomial infections], foreign bodies, glucocorticosteroids etc.) [6,24]. Our evidence suggests that survivors of septic shock may have lower risk of long-term survival also because their general status can be worse after septic shock and because of this, they can be disqualified from further treatment with chemotherapy. Remission of malignant tumor was significantly connected with better survival and it was also confirmed in other studies [23]. Additional research is required, particularly in regard to the quality of life for patients who survive septic shock.

**Conclusions**

Septic shock in patients with blood disorders was lethal in 50% of patients and was associated with high risk of mortality in all periods after its resolution in the other 50%. The consequences of septic shock in patients with underlying blood disease extend far beyond the first 28 days following sepsis.

However, although the results of treatment of septic shock in patients with blood diseases are poor, they were comparable to the results of treatment of septic shock in mixed populations treated in intensive care units.

The knowledge about clinical outcomes and factors associated with negative outcome in these patients can be important and useful for physicians to identify the patients who are most likely to benefit from ICU therapy and show them possible targets for intervention [2,25].

**Disclosure statement**

No potential conflict of interest was reported by the authors.
Notes on contributors

Anna Waszczuk-Gajda, MD, PhD, is an internist, hematologist in the Department of Hematology, Oncology and Internal Diseases at the Warsaw Medical University. Her research interests include hematopoietic malignancies mainly multiple myeloma, primary amyloidosis, myelodysplastic syndromes but also iron overload and infectious complications in patients with hematological disorders.

Professor Wieslaw Wiktor Jedrzejczak is an internist, hematologist, oncologist and transplantologist with both research and clinical track. His key research achievement was the discovery of inherited hematopoietic growth factor deficiency in the op/op mouse (finally proved to be CSF-1 deficiency). In the clinic, he performed the first allogeneic bone marrow transplantation in Poland in 1984 (patient still alive and well), and first autologous bone marrow transplantation in 1985. He is the chairman of the Department of Hematology, Oncology and Internal Diseases at the Warsaw Medical University. Professor Wieslaw Wiktor Jedrzejczak is the author and coauthor of a wide range of publications in various national and international journals, more than 300 scientific papers and book chapters.

References

[1] Williams MD, Braun LA, Cooper LM, et al. Hospitalized cancer patients with severe sepsis: analysis of incidence, mortality and associated costs of care. Crit Care. 2004;8:291–298.

[2] Torres VB, Azevedo LC, Silva UV, et al. Sepsis-associated outcomes in critically ill patients with malignancies. Ann Thorac Soc. 2015;12(8):1185–1192.

[3] Benoît DD, Vandewoude KH, Decruyenaere JM, et al. Outcome and early prognostic indicators in patients with a hematologic malignancy admitted to the intensive care unit for a life-threatening complication. Crit Care Med. 2003;31(1):104–112.

[4] Regazzoni CJ, Irrazabal C, Luna CM, et al. Cancer patients with septic shock: mortality predictors and neutropenia. Support Care Cancer. 2004;12(12):833–839.

[5] Larché J, Azoulay E, Fieux F, et al. Improved survival of critically ill cancer patients with septic shock. Intensive Care Med. 2003;29(10):1688–1695.

[6] Penack O, Becker C, Buchheidt D, et al. Management of sepsis in neutropenic patients: 2014 updated guidelines from the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology (AGIHO). Ann Hematol. 2014;93(7):1083–1095.

[7] Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. Crit Care Med. 2003;31(4):1250–1256.

[8] Dellinger RP, Levy MM, Carlet JM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock. Intensive Care Med. 2008;34(1):17–60.

[9] Annane D, Aeberter P, Jars-Guincestre MC, et al. Current epidemiology of septic shock: the CUB-Rea network. Am J Respir Crit Care Med. 2003;168:165–172.

[10] Boussekey N, Cantrel J, Dorchin Debrabant L, et al. Epidemiology prognosis and evolution of management of septic shock in a French intensive care unit: a five years survey. Crit Care Res Pract. 2010;2010:436427.

[11] Degoricija V, Sharma M, Legac A, et al. Survival analysis of 314 episodes of sepsis in medical intensive care unit in university hospital: impact of intensive care unit performance and antimicrobial therapy. Croat Med J. 2006;47(3):385–397.

[12] Ferrà C, Marcos P, Misis M, et al. Outcome and prognostic factors in patients with hematologic malignancies admitted to the intensive care unit: a single-center experience. Int J Hematol. 2007;85(3):195–202.

[13] Pène F, Percheron S, Lemiale V, et al. Temporal changes in management and outcome of septic shock in patients with malignancies in the intensive care unit. Crit Care Med. 2008;36(3):690–696.

[14] Kübler A, Durek G, Zamirowska A, et al. Severe sepsis in Poland – results of internet surveillance of 1043 cases. Med Sci Monit. 2004 Nov;10(11):635–641.

[15] Lloyd-Thomas AR, Wright I, Lister TA, et al. Prognosis of patients receiving intensive care for lifethreatening medical complications of haematological malignancy. Br Med J (Clin Res Ed). 1988;296(6628):1025–1029.

[16] Brunet F, Lanet JJ, Dhainaut JF, et al. Is intensive care justified for patients with haematological malignancies? Intensive Care Med. 1990;16(5):291–297.

[17] Friedman G, Silva E, Vincent JL. Has the mortality of septic shock changed with time. Crit Care Med. 1998;12:2078–2086.

[18] Winters BD, Eberlein M, Leung J, et al. Long-term mortality and quality of life in sepsis: a systematic review. Crit Care Med. 2010;38(5):1276–1283.

[19] Leibovici L. Long-term consequences of severe infections. Clin Microbiol Infect. 2013 Jun;19(6):510–512.

[20] Brun-Buisson C, Doyon F, Carlet J, et al. Incidence risk factors and outcome of severe sepsis and septic shock in adults. A multicenter prospective study in intensive care units. French ICU Group for severe sepsis. JAMA. 1995;274(12):968–974.

[21] Leibovici L, Shraga I, Drucker M, et al. The benefit of appropriate empirical antibiotic treatment in patients with bloodstream infection. J Intern Med. 1998;244(5):379–386.

[22] Leibovici L, Samra Z, Königsbärger H, et al. Long-term survival following bacteremia or fungemia. JAMA. 1999;275(10):807–812.

[23] Bernal T, Pardavila EV, Bonastre J, et al. Survival of hematological patients after discharge from the intensive care unit: a prospective observational study. Crit Care. 2013;17(6):R302.

[24] Cohen J, Drage S. How I manage haematology patients with septic shock. Br J Haematol. 2011;152(4):380–391.

[25] Azoulay E, Soares M, Darmon M, et al. Intensive care of the cancer patient: recent achievements and remaining challenges. Ann Intensive Care. 2011;23(1):5.