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| Characteristics, treatments, and outcomes of severe sepsis of 3195 ICU-treated adult patients throughout Japan during 2011-2013 |  |
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Characteristics, treatments, and outcomes of severe sepsis of 3195 ICU-treated adult patients throughout Japan during 2011–2013

Mineji Hayakawa¹, Shinjiro Saito², Shigeishi Uchino², Kazuma Yamakawa³, Daisuke Kudo⁴, Yusuke Iizuka⁵, Masamitsu Sanui⁵, Kohei Takimoto⁷, Toshihiro Mayumi⁸, Takeo Azuhata⁹, Fumihito Ito¹⁰, Shodai Yoshihiro¹¹, Katsura Hayakawa¹², Tsuyoshi Nakashima¹³, Takayuki Ogura¹⁴, Eiichiro Noda¹⁵, Yoshihiko Nakamura¹⁶, Ryosuke Sekine¹⁷, Yoshiaki Yoshikawa³, Motohiro Sekino¹⁸, Keiko Ueno¹⁹, Yoko Okuda²⁰, Masayuki Watanabe²¹, Akihito Tampo²², Nobuyuki Saito²³, Yuya Kita²⁴, Hiroyuki Takahashi²⁵, Iwao Kobayashi²⁶, Utaoka Kondo²⁷, Wataru Matsunaga²⁸, Sho Nachi²⁸, Toru Miike²⁹, Hiroshi Takahashi³⁰, Shuhei Takaui³¹, Kenseki Umemori³², Takafumi Todaka³³, Hiroshi Kodaira³⁴, Kohki Andoh³⁵, Takehiko Kasai³⁶, Yoshiaki Iwashita³⁷, Hideaki Arai³⁸, Masato Murata³⁸, Masahiro Yamane³⁹, Kazuhiro Shiga⁴⁰, and Naoto Horie⁴¹

Abstract
Severe sepsis is a major concern in the intensive care unit (ICU), although there is very little epidemiological information regarding severe sepsis in Japan. This study evaluated 3195 patients with severe sepsis in 42 ICUs throughout Japan. The patients with severe sepsis had a mean age of 70 ± 15 years and a mean Acute Physiology and Chronic Health Evaluation II score of 23 ± 9. The estimated survival rates at 28 and 90 days after ICU admission were 73.6 and 56.3 %, respectively.

Keywords: Severe sepsis, Mortality, Epidemiology, Acute respiratory failure, Acute kidney injury, Disseminated intravascular coagulation, Organ failure, Septic shock

Background
Many recent multicenter epidemiological studies have evaluated sepsis [1–7], although there is very little information regarding its epidemiology in Japan [1, 2]. Despite the limited amount of Japanese information, epidemiological data regarding severe sepsis are important for guiding clinical practice and the design of clinical studies. Therefore, the present study aimed to retrospectively evaluate a large population of patients with severe sepsis in intensive care units (ICUs) throughout Japan.

Methods
The present study analyzed the unlinked anonymized database of the Japan Septic Disseminated Intravascular Coagulation (JSEPTIC DIC) study [8]. Cases of shock, respiratory failure, or renal failure were defined as patients with a cardiovascular, respiratory, or renal Sequential Organ Failure Assessment (SOFA) score of ≥4 on day 1 [9]. Cases of disseminated intravascular coagulation (DIC) were defined as patients with a Japanese Association for Acute Medicine DIC score of ≥4 on day 1. All data were expressed as number (percent), mean ± standard deviation, or median (interquartile range), as appropriate. Survival rates were evaluated using the Kaplan-Meier method. All analyses were performed using SPSS software (version 22; SPSS Inc., Chicago, IL).

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Results
The present study included 3195 consecutive patients (2111 patients without shock and 1084 patients with shock). These patients included 1916 men (mean age 68 ± 14 years) and 1279 women (mean age 71 ± 15 years). The mean Acute Physiology and Chronic Health Evaluation II score among all patients was 23 ± 9. The primary infection sites are presented in Table 1. The blood culture results and responsible microorganisms are presented in Table 2. The frequencies of administering various adjunct treatments for severe sepsis during the first 7 days after ICU admission are shown in Table 3. The survival curves for patients with and without various medical conditions are presented in Fig. 1. The estimated survival rates at 28 and 90 days among all patients with severe sepsis after the ICU admission were 73.6 and 56.3 %, respectively.

Discussion
The present study evaluated the characteristics, treatments, and outcomes from 3195 patients with severe sepsis in 42 ICUs throughout Japan. The earlier epidemiological reports from after 2005 are summarized in the Additional file 1: Table S1. Although two previous Japanese studies have reported epidemiological information from 890 Japanese patients with severe sepsis, most of the participating institutions were university hospitals [1, 2]. In contrast, approximately half of the participating institutions in the present study were municipal hospitals. Furthermore, we included both general and emergency ICUs. Nevertheless, the distributions of age, severity, and mortality rates in the present study were similar to the findings from two previous Japanese studies [1, 2].

Patients with severe sepsis in other countries are generally younger than their Japanese counterparts [1–7]. Furthermore, other countries have higher mortality rates for patients with severe sepsis, compared to the rate from the present study, although the Acute Physiology and Chronic Health Evaluation II scores are similar for Japanese patients and other patients with sepsis [1–7]. However, the reports from the other countries evaluated patients with sepsis during an earlier period (2002–2010), compared to the patients from the three Japanese reports (2007–2013) [1–7]. Furthermore, mortality among patients with sepsis has decreased on an annual basis, and these factors may explain the different mortality rates in Japan and other countries.

The present study’s mortality rates for severe sepsis with and without shock are similar to the results from previous Japanese studies [1, 2]. However, severe sepsis is frequently complicated by respiratory failure, renal

| Table 1 Primary infection site responsible for the sepsis |
|---------------------------------------------------------|
| Without shock | With shock | Total |
|---------------|------------|-------|
| n = 2111      | n = 1084   | n = 3195 |
| Abdomen       | 661 (31 %) | 371 (34 %) | 1032 (32 %) |
| Lung/thorax   | 575 (27 %) | 252 (23 %) | 827 (26 %) |
| Urinary tract | 349 (17 %) | 160 (15 %) | 509 (16 %) |
| Bone/soft tissue | 251 (12 %) | 123 (11 %) | 374 (12 %) |
| Cardiovascular system | 54 (3 %) | 14 (1 %) | 68 (2 %) |
| Central nervous system | 44 (2 %) | 19 (2 %) | 63 (2 %) |
| Catheter-related | 23 (1 %) | 21 (2 %) | 44 (1 %) |
| Other         | 37 (2 %) | 23 (2 %) | 60 (2 %) |
| Unknown       | 117 (6 %) | 101 (9 %) | 218 (7 %) |

Data are expressed as number (percent)

| Table 2 Microorganisms responsible for the sepsis and blood culture results |
|--------------------------------------------------------------------------------|
| Without shock | With shock | Total |
|---------------|------------|-------|
| n = 2111      | n = 1084   | n = 3195 |
| Microorganisms responsible for the sepsis | | |
| Gram-negative rod | 774 (35%) | 421 (39%) | 1165 (37%) |
| Gram-positive coccus | 477 (23%) | 261 (24%) | 738 (23%) |
| Fungus | 43 (2%) | 14 (1%) | 57 (2%) |
| Virus | 20 (1%) | 8 (1%) | 28 (1%) |
| Mixed infection | 254 (12%) | 146 (14%) | 400 (13%) |
| Other | 40 (2%) | 18 (2%) | 58 (2%) |
| Unknown | 533 (25%) | 216 (20%) | 749 (23%) |
| Blood culture | | |
| Positive | 866 (41%) | 540 (50%) | 1406 (44%) |
| Negative | 1,083 (51%) | 508 (47%) | 1591 (50%) |
| Not taken | 162 (8%) | 36 (3%) | 198 (6%) |

Data are expressed as number (percent)

| Table 3 Frequencies of various adjunct treatments for severe sepsis during the first 7 days after the ICU admission |
|----------------------------------------------------------------------------------------------------------------|
| Adjunct treatments | | |
| DIC treatments | 1498 (47%) |
| Antithrombin | 990 (31%) |
| Thrombomodulin | 856 (27%) |
| Co-administration of antithrombin and thrombomodulin | 496 (16%) |
| Protease inhibitors | 392 (12%) |
| Heparinoids | 167 (5%) |
| Immunoglobulin | 976 (31%) |
| Low-dose steroids | 777 (24%) |
| Renal replacement therapy | 890 (28%) |
| Non-renal indication renal replacement therapy | 266 (8%) |
| Polymyxin B-direct hemoperfusion | 692 (22%) |

Data are presented as number (percentage)

DIC disseminated intravascular coagulation, ICU intensive care unit
failure, and DIC [10], and the previous studies did not evaluate the mortality rates for severe sepsis in cases with respiratory or renal failure [1, 2]. Thus, the present study provides the first survival curve data for Japanese patients with severe sepsis according to their complications with shock, respiratory failure, renal failure, or DIC.

Additional file

Additional file 1: Table S1. Epidemiological information from previous reports after 2005. (DOC 48 kb)

Abbreviations

DIC, disseminated intravascular coagulation; ICU, intensive care unit; JSEPTIC DIC, Japan Septic Disseminated Intravascular Coagulation; SOFA, Sequential Organ Failure Assessment

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Availability of data and material

The datasets supporting the conclusions of this article are available in the University Hospital Medical Information Network Individual Case Data Repository (UMIN000012543, http://www.umin.ac.jp/icdr/index-j.html). Please contact the corresponding author to access the data.

Authors’ contributions

HM, SS, US, YK, KD, IY, SM, TK, and MT designed the study and reviewed the data set. HM, KD, SS, IY, TK, AT, IF, YS, HK, NT, NE, NY, SR, YY, SM, UK, OY, WM, TA, SN, KY, TH, KI, KY, MW, NS, MT, TH, TS, UK, TT, KH, AK, KT, IY, AH, MM, YM, SK, and HN collected and assessed the data at each institution. HM interpreted the data and drafted the manuscript. All authors also read and approved the final manuscript.

Competing interests

Hayakawa M received a grant for basic research and lecturer’s fees from Asahi Kasei Pharma Co. The other authors declare that they have no competing interests.

Consent for publication

Not applicable.
Ethics approval and consent to participate

The JSEPTIC DIC study reviewed information from consecutive patients who were admitted to 42 ICUs at 40 institutions throughout Japan for treatment of severe sepsis or septic shock between January 2011 and December 2013 [8]. The study’s design was approved by the Institutional Review Board at each hospital, and the requirement for informed consent was waived because of the retrospective design.

Author details

1. Department of Emergency and Critical Care Center, Hokkaido University Hospital, N14W5 Kita-ku, Sapporo 060-8648, Japan. Department of Intensive Care Unit, Department of Anesthesiology, Jikei University School of Medicine, Tokyo, Japan.
2. Department of Emergency and Critical Care, Osaka General Medical Center, Osaka, Japan. 3. Division of Emergency and Critical Care Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan. 4. Department of Anesthesiology and Critical Care Medicine, Jichi Medical University Saitama Medical Center, Saitama, Japan. 5. Department of Critical Care, Shonan Kamakura General Hospital, Kamakura, Japan. 6. Department of Anesthesiology and Intensive Care Medicine, Osaka University Graduate School of Medicine, Suita, Japan. 7. Department of Emergency Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan. 8. Division of Emergency and Critical Care Medicine, Department of Acute Medicine, Nihon University School of Medicine, Tokyo, Japan. 9. Department of Emergency and Critical Care Medicine, Shiga University Hospital, Ohto General Hospital Foundation, Ohta Nishinouchi Hospital, Koriyama, Japan. 10. Pharmaceutical Department, JA Hiroshima General Hospital, Hiroshima, Japan. 11. Department of Emergency and Critical Care Medicine, Saitama Red Cross Hospital, Saitama, Japan. 12. Department of Emergency and Critical Care Medicine, Wakayama Medical University, Wakayama, Japan. 13. Department of Emergency Medicine and Critical Care Medicine, Advanced Medical Emergency Department and Critical Care Center, Japan Red Cross Maebashi Hospital, Maebashi, Japan. 14. Emergency and Critical Care Center, Kyushu University Hospital, Fukuoka, Japan. 15. Department of Emergency and Critical Care Medicine, Faculty of Medicine, Fukuoka University, Fukuoka, Japan. 16. Emergency Department, Ibaraki Prefectural Central Hospital, Kasama, Japan. 17. Department of Intensive Care, Nagasaki University Hospital, Nagasaki, Japan. 18. Department of Emergency and Critical Care Medicine, Tokyo Medical University, Hachioji Medical Center, Tokyo, Japan. 19. Department of Emergency and Critical Care Medicine, Kyoto Daichi Red Cross Hospital, Kyoto, Japan. 20. Intensive Care Unit, Saiseikai Yokohamashi Tobu Hospital, Yokohama, Japan. 21. Department of Emergency Medicine, Asahikawa Medical University, Asahikawa, Japan. 22. Shock and Trauma Center, Nippon Medical School Chiba Hokusoh Hospital, Inzai, Japan. 23. Emergency Medicine, Kameda Medical Center, Kamogawa, Japan. 24. Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School of Medicine, Suita, Japan. 25. Emergency and Critical Care Medicine, Asahikawa Red Cross Hospital, Asahikawa, Japan. 26. Department of Emergency and Critical Care Medicine, Graduate School of Medicine, University of the Ryukyus, Nishihara, Japan. 27. Advanced Critical Care Center, Kyushu University Hospital, Fukuoka, Japan. 28. Emergency and Critical Care Center, Saga University Hospital, Saga, Japan. 29. The Division of Cardiovascular Disease, Steel Memorial Munoran Hospital, Munoran, Japan. 30. Department of Emergency Medicine and Critical Care, Sapporo City General Hospital, Sapporo, Japan. 31. Division of Emergency Medicine, Ehime University Hospital, Toon, Japan. 32. Intensive Care Unit, Tomishiro Central Hospital, Tomishiro, Japan. 33. Department of Emergency Medicine, Akashi City Hospital, Akashi, Japan. 34. Department of Emergency and Critical Care, Sendai City Hospital, Sendai, Japan. 35. Emergency Department, Hakodate Municipal Hospital, Hakodate, Japan. 36. Emergency and Critical Care Center, Mie University Hospital, Tsu, Japan. 37. Department of Emergency Medicine, Gunma University, Maebashi, Japan. 38. Department of Anesthesiology and Intensive Care, KKR Sapporo Medical Center, Sapporo, Japan. 39. Emergency and Critical Care Center, Seirei Mikatahara General Hospital, Hamamatsu, Japan. 40. Intensive Care Unit, Hyogo College of Medicine, Nishinomiya, Japan.

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