Epidemiology of Sepsis-3 in a sub-district of Beijing: secondary analysis of a population-based database

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Abstract

Background: With the publication of Sepsis-3 definition, epidemiological data based on Sepsis-3 definition from middle-income countries including China are scarce, which prohibits understanding of the disease burden of this newly defined syndrome in these settings. The purpose of this study was to describe incidence and outcome of Sepsis-3 in Yuetan sub-district of Beijing and to estimate the incidence rate of Sepsis-3 in China.

Methods: The medical records of all adult residents hospitalized from July 1, 2012 to June 30, 2014 in Yuetan sub-district of Beijing were reviewed. Patients with sepsis-3 and severe sepsis/septic shock were identified. The incidence rates and mortality rate of sepsis-3 and sepsis/septic shock were calculated, incidence rates and in-hospital mortality rates were normalized to the population distribution in the 2010 National Census. Population incidence rate and case fatality rate between sexes were compared with the Z test, as the data conformed to Poisson distribution.

Results: Of the 21,191 hospitalized patients, 935 patients were diagnosed with Sepsis-3, and 498 cases met severe sepsis/septic shock criteria. The crude annual incidence rate of Sepsis-3 in Yuetan sub-district was 363 cases per 100,000 population, corresponding to standardized incidence rates of 236 cases per 100,000 population per year, respectively. The overall case fatality rate of Sepsis-3 was 32.0%, the crude population mortality rates of Sepsis-3 was 116 cases per 100,000 population per year, the standardized mortality rate was 67 cases per 100,000 population per year, corresponding to a speculative extrapolation of 700,437 deaths in China. The incidence rate and mortality rate of Sepsis-3 were significantly higher in males, elderly people, and patients with more comorbidities. The 62.1% of patients with Sepsis-3 had community-acquired infections, compared with 75.3% of infected patients without Sepsis-3 ($P < 0.001$). The most common infection in patients with Sepsis-3 was lower respiratory tract infection. When compared with patients with Sepsis-3, patients diagnosed as severe sepsis/septic shock were more likely to have higher case fatality rate (53.4% *vs.* 32.0%, $P < 0.001$)

Conclusions: This study found the standardized incidence rate of 236 cases per 100,000 person-year for Sepsis-3, which was more common in males and elderly population. This corresponded to about 2.5 million new cases of Sepsis-3 per year, resulting in more than 700,000 deaths in China.

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Keywords: Sepsis-3; Severe sepsis; Incidence; Mortality

Introduction

Sepsis, defined as systemic inflammatory response syndrome (SIRS) induced by infection in 1991,[1] is the leading cause of death among critically ill patients in intensive care unit (ICU). Due to multiple factors such as aging population, progress in peri-operative care, advances in invasive diagnostic and therapeutic procedures, and widespread use of chemotherapy and immunosuppression therapy, the morbidity and mortality of sepsis have steadily increased worldwide.[2-4] A systematic review estimated

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the incidence rate of 437 cases per 100,000 person-years for sepsis in high-income countries/regions in the last decade, with case fatality rate of 17%.[5] A tentative extrapolation from these data suggested a global estimate of 31.5 million sepsis cases, with potentially 5.3 million deaths annually.[5]

After more than two decades of widespread use of the original sepsis definition in both clinical practice and research, it is now well understood that both pro- and anti-inflammatory responses are involved in the pathogenesis of sepsis.[6] Moreover, SIRS criteria are too sensitive and insufficiently specific to identify some severe infected patients.[7,8] In 2001, definitions of sepsis and septic shock were revised,[9] incorporating the concept and diagnostic criteria of organ damage. However, owing to its complexity, the revised sepsis definition had not been widely applied in clinical practice. In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock Task Force redefined sepsis (Sepsis-3)[10] as a "life-threatening organ dysfunction caused by a dysregulated host response to infection." Organ dysfunction was defined as an acute increase in total sequential (sepsis-related) organ failure assessment (SOFA) score ≥2 points consequent to the infection.

With the publication of Sepsis-3 definition, multiple studies have reported prevalence of Sepsis-3 among ICU patients, hospitalized patients, and community-dwelling adults.[11,12] However, epidemiological data based on Sepsis-3 definition from middle-income countries including China are scarce, which prohibits understanding of the disease burden of this newly defined syndrome in these settings.

Based on a retrospective study of all hospitalized adult citizens in a sub-district in Beijing during 2-year study period, we speculated the national incidence rate of sepsis as 461 cases per 100,000 person-year, with case fatality rate of 20.6%.[13] As the definition of sepsis changes, the population incidence of sepsis may also require an updated evaluation. In the current study, we estimated the incidence and mortality rates of sepsis in a secondary analysis of the above database using Sepsis-3 definition.

Methods

Ethical approval

This study was approved by the ethics committee of Peking Union Medical College Hospital and informed consent was waived. This study was registered at ClinicalTrials. gov, with registration number as NCT02285257.

Patients and study design

The methods of this study have been described in detail previously.[13] In brief, this study was carried out in Yuetan sub-district of Beijing, China from July 1, 2012 to June 30, 2014. All adults (≥18 years) hospitalized during the study period were identified with the use of the hospital discharge database of Beijing Public Health Information System. All available medical records of enrolled patients were manually reviewed independently by any two of three investigators with more than 5 years of working experience in ICU. Any disagreement was resolved by discussion among the three investigators, and then among the steering committee (XM, YA, and BD) if consensus could not be reached.

Retrieved data included demographic data; admission category (medical, elective surgery, or emergency surgery); comorbidities[14]; and hospital death. Derived from the above data, severity of underlying illness was assessed by McCabe and Jackson classification,[15] while chronic organ dysfunction or immunosuppression was defined based on the criteria in acute physiology and chronic health evaluation II score.[16] In addition, body mass index (BMI) was calculated based on the height and weight on hospital admission.

For patients with infection, we collected data about source of infection and relevant microbiological information, data about SOFA score[17] were also collected.

For the purpose of this study, infection was diagnosed based on clinical manifestations, laboratory tests, and radiographic findings, including microbiologically documented (with definite positive results of microbial culture of body fluids or blood) and clinically documented (with no definite positive culture results but with imaging or pathological evidence of clinical infection) infections.[18] Severe sepsis and septic shock were diagnosed according to the American College of Chest Physicians (ACCP)/Society of Critical Care Medicine (SCCM) consensus definition,[1] whereas Sepsis-3 was diagnosed according to the Third International Consensus Definitions for Sepsis and Septic Shock Task Force,[10] defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, with infection-related organ dysfunction identified as an acute change in total SOFA score ≥2 points in patients with pre-existing organ dysfunction, or total SOFA score ≥2 points in patients not known to have pre-existing organ dysfunction. Patients who developed Sepsis-3 before hospital admission or during hospital stay were both categorized as patients with sepsis. Patients who were readmitted into hospitals during the same study period were regarded as new patients. Only the first incidence of sepsis was counted during this same period of hospitalization. For clinical outcome of sepsis patients, we reported both mortality rate (the number of patients who died from sepsis in the entire population) and case fatality rate (the proportion of patients who died from sepsis among all septic patients).

Statistical analysis

Continuous variables were presented as median (Q1, Q3), and compared using the Wilcoxon rank-sum test. Categorical variables were presented as a percentage of the group from which they were derived, and compared by the use of Chi-square test or Fisher exact test. Incidence rates and in-hospital mortality rates were normalized to the population distribution in the 2010 National Census.[19] The 95% confidence interval (CI) was calculated.[20] Population incidence rate and hospital case fatality

rate between sexes were compared with the Z test, as the data conformed to Poisson distribution. All comparisons were unpaired and all tests of significance were two-tailed. A $P < 0.05$ was considered as statistically significant. All statistical analyses were performed using SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Patient enrollment

During two years study period, a total of 22,552 adult residents in Yuetan sub-district were hospitalized. We were unable to review the medical records of 1361 patients, due to refusal by the hospital ($n = 1084$) and missing records ($n = 277$). Therefore, the medical records of 21,191 patients were manually reviewed and included in the final analysis.

Of the 21,191 adult patients enrolled in this study, median age was 66 (49, 78) years, 9431 patients (44.5%) were male, and median Charlson comorbidity index was 1 (0, 2).

Characteristics of patients with Sepsis-3

A total of 3449 patients with infection were identified, among whom 935 cases (27.1%) met Sepsis-3 criteria (median age: 81 [74, 86] years), and 498 cases (14.4%) met severe sepsis/septic shock criteria (median age: 82 [75, 87] years). When compared with patients suffering from non-septic infection, patients with Sepsis-3 were more likely to be male and older, and have more comorbidities (including cerebrovascular disease, coronary heart disease, chronic lung disease, rheumatic disease, hematologic malignancy, and dementia) and lower BMI [Table 1].

The 62.1% of patients with Sepsis-3 had community-acquired infections, compared with 75.3% of infected patients without Sepsis-3 ($P < 0.001$). The most common infection in patients with Sepsis-3 was lower respiratory tract infection, followed by intra-abdominal infection and urogenital tract infection [Supplemental Tables 1, http://links.lww.com/CM9/A77 and 2, http://links.lww.com/CM9/A77]. A total of 433 bacteria were isolated from 314 patients with sepsis (33.6%), with Acinetobacter baumannii as the most common pathogen, followed by Pseudomonas aeruginosa, Klebsiella pneumoniae, methicillin-resistant Staphylococcus aureus, and Escherichia coli [Supplemental Table 2, http://links.lww.com/CM9/A77].

Patients with Sepsis-3 had worse clinical outcome than infected patients without Sepsis-3, as suggested by higher hospital case fatality rate (32.0% vs. 3.9%, $P < 0.001$) and longer hospital length of stay (20 [11, 39] days vs. 14 [9, 25] days, $P < 0.001$).

When compared with patients with Sepsis-3, patients diagnosed as severe sepsis/septic shock based on ACCP/SCCM consensus definition were more likely to have fewer elective surgeries (6.4% vs. 9.8%, $P = 0.029$), more immunosuppression (21.7% vs. 9.5%, $P < 0.001$), ultimately fatal diseases (20.9% vs. 12.0%, $P < 0.001$), and

ICU admissions (38.8% vs. 24.9%, $P < 0.001$), as well as higher case fatality rate (53.4% vs. 32.0%, $P < 0.001$) [Table 1].

Incidence and mortality rates of Sepsis-3

The crude annual incidence rate of Sepsis-3 was 363 cases per 100,000 population, corresponding to 4.4 (95% CI: 4.1–4.7) cases per 100 hospital admissions. After adjustment for age and sex, the standardized incidence rate was 236 cases per 100,000 population. Generalization of the above-standardized incidence rate to the whole country produced a national estimate of 2,487,949 new cases of Sepsis-3 per year [Table 2].

The crude incidence rate of Sepsis-3 exhibited significant sex difference, with 458 and 274 cases per 100,000 population per year in men and women, respectively [Figure 1 and Table 2]. The incidence rate of Sepsis-3 steadily increased with age, from 20 cases per 100,000 population <50 years to 895 cases per 100,000 population 50 to 89 years, and to 10,305 cases per 100,000 population ≥90 years [Figure 1]. In addition, the incidence rate of Sepsis-3 exhibited significant seasonal variation, being highest in winter (December, January, and February) and lowest in autumn (September, October, and November) [Supplemental Table 3, http://links.lww.com/CM9/A77].

The crude population mortality rate of Sepsis-3 was 116 cases per 100,000 population per year, corresponding to a speculative extrapolation of 700,437 deaths in China. The mortality rate was significantly higher in men than women [Table 2], while case fatality rate showed no sex difference [Figure 2]. Case fatality rate for patients with Sepsis-3 significantly increased with age (from 11.1% in patients <50 years to 40.7% in those ≥90 years) [Figure 2].

Discussion

In a secondary analysis of a database of 21,191 hospitalized patients who were residents in a sub-district of Beijing, we reported standardized incidence and mortality rate of Sepsis-3 as 236 and 67 cases per 100,000 population per year, respectively, corresponding to approximately 2.5 million new cases of Sepsis-3 and 700,437 deaths every year. Moreover, men had a significantly higher incidence and mortality rates of sepsis than women, despite a similar case fatality rate. In addition, patients meeting Sepsis-3 criteria were less severe than traditional severe sepsis/septic shock.

Clinical characteristics of septic patients in our cohort were consistent with previous studies.[12,21] For example, Donnelly et al[12] also reported that patients with Sepsis-3 were more likely to be male and older, to have more comorbidities, lower BMI, and higher case fatality rate. Likewise, lower respiratory tract infection had been consistently reported as the most common infections in sepsis, despite significant variation in the prevalence and ranking of other infections, such as urinary tract infection and intra-abdominal infection.[3,22-24] In addition, Gram-negative bacilli had been reported as the most common pathogens of sepsis,[2,23,25-27] which might be associated with higher case fatality rate than Gram-positive infections.[3]

Table 1: Characteristics of patients with non-infection, infected patients without Sepsis-3, and Sepsis-3 (N = 21,191).

Characteristics	No infection (n = 17,742)	Infected patients without Sepsis-3 (n = 2514)	Sepsis-3 (n = 935)	Sepsis-3 vs. no Sepsis-3		Severe sepsis/septic shock (n = 498)	Sepsis-3 vs. severe sepsis/septic shock	
				Statistical values	P		Statistical values	P
Male sex	7545 (42.5)	1312 (52.3)	574 (61.4)	23.291*	<0.001	311 (62.4)	0.154*	0.694
Age (years)	63 (49, 78)	78 (61, 84)	81 (74, 86)	−8.385†	<0.001	82 (75, 87)	−1.358†	0.174
Body mass index (kg/m²)	24 (22, 27)	24 (21, 26)	23 (20, 26)	−3.291†	0.001	23 (20, 26)	−0.338†	0.736
Type of hospital admission								
Medical	10,235 (57.7)	2245 (89.3)	824 (88.1)	0.954*	0.329	453 (91.0)	2.693*	0.101
Elective surgery	7269 (41.0)	222 (8.8)	92 (9.8)	0.839*	0.360	32 (6.4)	4.791*	0.029
Emergency surgery	238 (1.3)	47 (1.9)	19 (2.0)	0.096*	0.757	13 (2.6)	0.498*	0.480
Smoking	3270 (18.4)	657 (26.1)	283 (30.3)	5.874*	0.015	153 (30.7)	0.032*	0.858
Alcoholism	1334 (7.5)	191 (7.6)	77 (8.2)	0.387*	0.534	44 (8.8)	0.151*	0.697
Comorbidities								
None	4581 (25.8)	289 (11.5)	82 (8.8)	5.274*	0.022	41 (8.2)	0.119*	0.730
Hypertension	7891 (44.5)	1424 (56.6)	555 (59.4)	2.055*	0.152	286 (57.4)	0.498*	0.480
Diabetes	3995 (22.5)	688 (27.4)	248 (26.5)	0.245*	0.621	125 (25.1)	0.342*	0.559
Malignancy	3311 (18.7)	379 (15.1)	150 (16.0)	0.491*	0.483	96 (19.3)	2.390*	0.122
Cerebrovascular disease	2720 (15.3)	815 (32.4)	358 (38.3)	10.465*	0.001	193 (38.8)	0.030*	0.863
Coronary heart disease	3347 (18.9)	755 (30.0)	344 (36.8)	14.343*	<0.001	57 (11.4)	103.579*	<0.001
Chronic lung disease	1165 (6.6)	549 (21.8)	235 (25.1)	4.215*	0.040	126 (25.3)	0.005*	0.945
Peptic ulcer	597 (3.4)	193 (7.7)	61 (6.5)	1.328*	0.249	35 (7.0)	0.132*	0.716
Rheumatic disease	375 (2.1)	71 (2.8)	47 (5.0)	10.006*	0.002	26 (5.2)	0.025*	0.874
Hematologic malignancy	170 (1.0)	23 (0.9)	25 (2.7)	15.364*	<0.001	10 (2.0)	0.604*	0.437
Dementia	207 (1.2)	156 (6.2)	90 (9.6)	12.038*	0.001	41 (8.2)	0.759*	0.384
McCabe and Jackson classification								
Non-fatal	9572 (54.0)	1951 (77.6)	524 (56.0)	156.365*	<0.001	354 (71.1)	30.980*	<0.001
Ultimately fatal	3040 (17.1)	402 (16.0)	112 (12.0)	8.649*	0.003	104 (20.9)	20.128*	<0.001
Rapidly fatal	549 (3.1)	67 (2.7)	22 (2.4)	0.264*	0.607	17 (3.4)	1.381*	0.240
Charlson comorbidity index	1 (0, 2)	1 (0, 3)	2 (1, 3)	−6.248†	<0.001	2 (1, 3)	−0.619†	0.536
Chronic organ dysfunction								
None	14872 (83.8)	2143 (85.2)	707 (75.6)	44.019*	<0.001	345 (69.3)	6.687*	0.010
Cardiovascular	186 (1.0)	46 (1.8)	29 (3.1)	5.182*	0.023	8 (1.6)	2.888*	0.089
Liver	253 (1.4)	62 (2.5)	19 (2.0)	0.560*	0.454	10 (2.0)	0.001*	0.975
Respiratory	64 (0.4)	79 (3.1)	65 (7.0)	25.185*	<0.001	28 (5.6)	0.946*	0.331
Renal	240 (1.4)	53 (2.1)	45 (4.8)	18.059*	<0.001	13 (2.6)	4.058*	0.044
Immunosuppression	2214 (12.5)	177 (7.0)	89 (9.5)	5.880*	0.015	108 (21.7)	40.574*	<0.001
ICU admission	3 (0.0)	5 (0.2)	233 (24.9)	648.308*	<0.001	193 (38.8)	29.773*	<0.001
Hospital length of stay (days)	8 (4, 14)	14 (9, 25)	20 (11, 39)	−8.152†	<0.001	21 (11, 41)	−0.769†	0.442
In-hospital case fatality rate	132 (0.7)	98 (3.9)	299 (32.0)	527.598*	<0.001	266 (53.4)	65.513*	<0.001

The data were shown as median (Q1, Q3) or n (%). * Chi-square values. † Z value of the rank sum test. ICU: Intensive care unit.

Table 2: Crude and standardized incidence rates and mortality rates of Sepsis-3.

Items	Incidence rate			Mortality rate		
	Crude (95% CI)*	Standardized†	National estimate‡	Crude (95% CI)*	Standardized†	National estimate‡
Sepsis-3	363 (326–400)	236	2,487,949	116 (95–137)	67	700,437
Men	458 (416–500)§	290	1,543,334	143 (120–166)‖	77	403,961
Women	274 (241–306)	181	944,615	90 (71–109)	57	296,476
Severe sepsis/septic shock	193 (169–217)	120	1,265,007	103 (86–121)	57	603,276
Men	248 (209–287)§	147	783,327	131 (102–159)§	67	355,290
Women	142 (113–170)	92	481,680	77 (56–99)	48	247,986

*The incidence and mortality rates of Sepsis-3 in Yuetan sub-district of Beijing (per 100,000 population per year). †The national-estimated incidence and mortality rates of Sepsis-3 which was calculated by adjusting the corresponding data of Yuetan sub-district for age and sex (per 100,000 population per year). ‡The estimated number of cases and deaths of sepsis-3. §$P < 0.001$. ‖$P < 0.050$ vs. women. CI: Confidence interval.
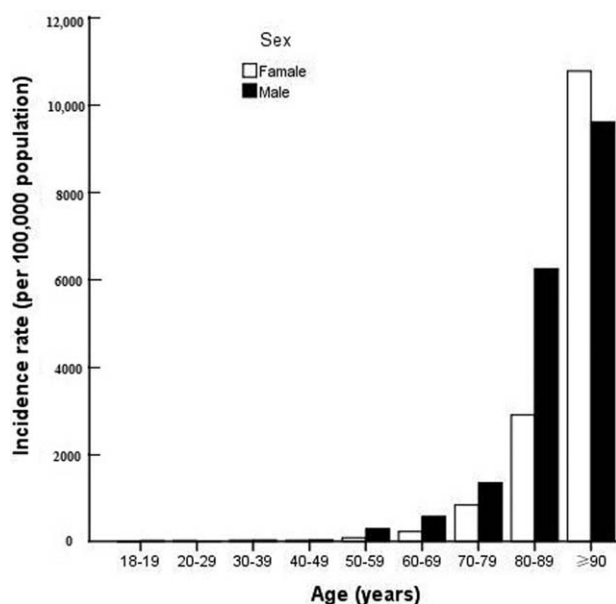
Figure 1: Age-specific incidence rate of Sepsis-3 by sex.
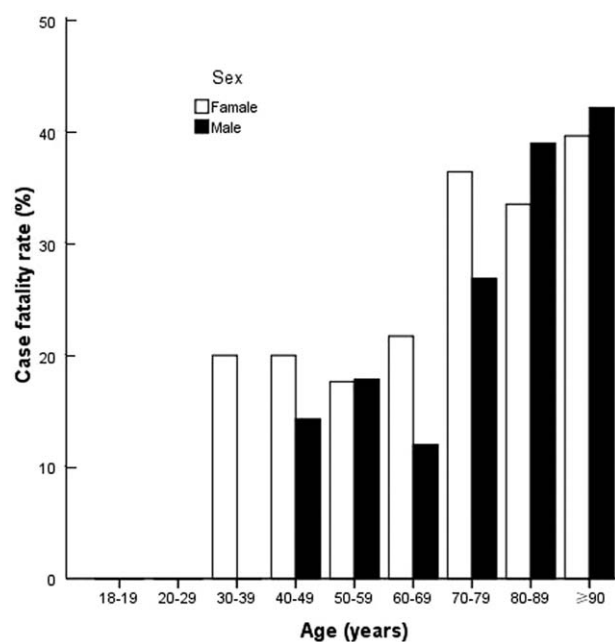
Figure 2: Age-specific fatality rate of Sepsis-3 by sex.

There have been very few studies of population-based epidemiology of Sepsis-3, which reported much higher incidence rates than our study. Mellhammar et al[28] performed a retrospective chart review of 482 adult patients (≥18 years) in two regions in Sweden who started to receive intra-venous antibiotics on four dates which were evenly distributed over the year of 2015. A total of 109 patients met Sepsis-3 criteria, corresponding to an annual incidence of 780 cases of Sepsis-3 per 100,000 population. In addition, in a retrospective analysis of data from 30,239 American adults aged ≥45 years, Donnelly et al reported an incidence of 580 cases per 100,000 person-years for Sepsis-3.[12] Apart from different demographics, socioeconomic characteristics, and case mix among these studies, other potential reasons for conflicting results between these studies and ours might be related to different methodology, such as study population (≥18 years[28] vs. ≥45 years[12]), study dates (randomly selected dates[28] vs. whole year[12]), time window for data extraction (entire hospitalization[28] vs. first 28 h after admission[12]), and descriptive variables (crude[12,28] vs. standardized incidence). Moreover, it is noteworthy that Donnelly et al[12] and Mellhammar et al[28] also reported an

incidence rate of 820 cases per 100,000 person-years for Sepsis-1, and 687 cases per 100,000 person-years for traditional severe sepsis, respectively. Both were much higher than those in the study by Fleischmann et al, which reported the incidence rates of 437 for sepsis and 270 for severe sepsis per 100,000 person-years.[5] In comparison, based on the same database as in the current study, we estimated the population-based annual incidence of 461 cases per 100,000 population for Sepsis-1.[13]

Sex-specific differences in sepsis epidemiology have been extensively studied in experimental and clinical studies. Since the first report by McGowan et al,[29] it has been consistently reported by large epidemiologic studies that incidence of sepsis was 20% to 28% higher in men than women.[2,30] Similar to our previous study of Sepsis-1,[13] we also noticed a significantly higher standardized incidence of Sepsis-3 among men than women (290 vs. 181 cases per 100,000 person-years) in the current study. Such disparities in the incidence of sepsis are likely to be explained by a variety of factors, including demographics, comorbidities, high-risk behaviors (such as smoking),

infection source, different microbes, sex hormones, and differential immune response to infection.[31] Despite agreement over the higher incidence of sepsis in men, there is controversy regarding whether this translates into a higher case fatality rate.[2,32-36] In the current study, case fatality rates did not differ significantly according to sex. However, the higher incidence of sepsis in men resulted in more than 1/3 increase of the number of hospital deaths related to sepsis.

Changes in the definition of sepsis might exert a remarkable impact on future clinical trials. The diagnostic criteria of Sepsis-3 might capture patients with less severity of illness, such as mild thrombocytopenia (1 point for $<150 \times 10^9$/L) and/or hypoxemia (1 point for PaO_2/FiO_2 300–400 mmHg), which was not regarded as organ dysfunction based on diagnostic criteria of severe sepsis.[1,10] As a result, in the current study, the new Sepsis-3 criteria identified a group of patients with less severe clinical syndrome than traditional severe sepsis/septic shock, as suggested by more elective surgeries, fewer comorbidities (including immunocompromise and ultimately fatal comorbidities) and fewer ICU admissions, as well as lower case fatality rates. This was consistent with that of Williams et al,[37] which reported a significantly lower 30-day case fatality rate of Sepsis-3 than traditional severe sepsis (11.4% vs. 13.6%). Sample size calculations might be affected by enrolling septic patients with lower case fatality rate. For example, a sample size of 1232 patients with Sepsis-3, compared with 1388 patients with traditional severe sepsis/septic shock, would provide the study with 80% power to detect an absolute between-group difference of 7.5 percentage points in 28-day case fatality rate,[38] with a two-sided $P < 0.05$ indicating statistical significance. Although the impact of such a reduction of sample size on patient recruitment rate remains to be elucidated, it was noteworthy that enrollment of less severe septic patients in clinical trials might lead to more negative results,[39] since the efficacy of anti-inflammatory therapies during sepsis was dependent on the risk of death.[40]

The projected national estimates of Sepsis-3 burden merited cautious interpretation. In the United States, remarkable variations in economic development and availability of medical service had been associated with significant geographic differences in both incidence and mortality rates of sepsis.[41,42] As the capital city of China, data from a sub-district of Beijing could not be generalized to other provinces. Therefore, our findings with regards to standardized incidence and mortality rates of sepsis required validation by further prospective, large-scale cohort studies.

Our study had some strengths. This was the population-based epidemiological study of hospitalized patients with Sepsis-3 in the mainland of China. All hospitalized patients who were residents of Yuetan sub-district were identified through the hospital discharge database of Beijing Public Health Information System, and cases of sepsis were diagnosed based on manual review of individual medical record. This approach, although labor-intensive, might

provide accurate diagnosis of sepsis while avoiding the unreliability of administrative data.[43]

Our study was also subject to some limitations. First, this was a retrospective study which was not originally designed for the purpose to illustrate the demographic characteristics of Sepsis-3. Second, we did not report epidemiology of septic shock because lactate level was seldom measured in general wards whereas only one out of four patients with Sepsis-3 was admitted to ICUs. Third, the national estimates of Sepsis-3 epidemiology required cautious interpretation and future validation.

In conclusions, in a secondary analysis of a population-based database of hospitalized residents in a sub-district in Beijing, we reported the standardized incidence rate of 236 cases per 100,000 person-years for Sepsis-3, which was more common in males and elderly population. This corresponded to about 2.5 million new cases of Sepsis-3 per year, resulting in more than 700,000 deaths, indicating the national burden of this devastating clinical syndrome which merited further studies to improve better health care policy, rational allocation of resources, and funding for sepsis research.

Funding

Conflicts of interest

None.

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