Sepsis is a life-threatening condition that develops because of dysregulation of the host immune response in response to infection. In South Korea, the incidence of sepsis increased from 173.8 per 100,000 population in 2007 to 233.6 per 100,000 population in 2016, whereas the hospital mortality decreased from 30.9% in 2007 to 22.6% in 2016. Globally, an estimated 48.9 million cases of sepsis and 11.0 million sepsis-related deaths were recorded in 2017, suggesting that sepsis is a major health problem worldwide.

Suicide is a major public health issue, accounting for 1.3% of all deaths worldwide in 2019. In South Korea, suicide is a serious public health issue; the prevalence of suicide was 24.6 per 100,000 persons in 2019, which was the highest among the Organization for Economic Cooperation and Development countries. Moreover, the prevalence of death from suicide was 5.26% of total deaths (84,934 deaths by suicide/1,615,288 total deaths) from 2011 to 2016 in South Korea. Suicide might occur in patients with sepsis with several risk factors, worsening conditions, disabilities and psychological deficits that cause patients with sepsis to suffer so much that they no longer want to live. Moreover, patients with sepsis are known to suffer from post-sepsis syndrome, which is characterised by neurocognitive impairment, functional disability, psychological deficits and worsening medical conditions. These worsening conditions after diagnosis of sepsis could increase the rate of suicide mortality among patients with sepsis. Similarly, a recent cohort study by Fernando et al. reported that 0.2% of intensive care unit (ICU) survivors of critical illness died by suicide in the province of Ontario in Canada. They suggested that pre-existing psychiatric illness and receipt of invasive life support were significant risk factors for suicide among ICU survivors. Lund-Sorensen et al. also reported a significant relationship between hospital admission with infection and increased risk of death by suicide among a Danish cohort. This relationship might have occurred because of a biological mechanism – an inflammatory reaction resulting from infection increases risk of suicidal behavior. However, in addition to infection, the information regarding the prevalence of suicide and associated factors in patients with sepsis is still lacking. Considering the global burden of sepsis among critically ill patients, better understanding of the prevalence and associated risk factors for suicide mortality in patients with sepsis is currently needed.

Therefore, using a nationwide cohort database in South Korea, we aimed to investigate the prevalence of suicide and associated factors in patients with sepsis. We included various factors that could be potentially related to the risk of suicide, such as physical characteristics, information related to socioeconomic status, treatment information, medical condition and concurrent psychiatric disorders.

Method

In this population-based cohort study of a nationwide cohort in South Korea, we followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines. The study protocol was approved by the Institutional Review Board of Seoul National University Hospital.

Prevalence and risk factors for suicide in patients with sepsis: nationwide cohort study in South Korea

Tak Kyu Oh, Hye Yoon Park and In-Ae Song

Background

Although a recent study reported that survivors of critical illness have an increased risk of suicide, the suicide rate and factors associated with suicide in patients with sepsis have not yet been investigated.

Aims

We aimed to examine the prevalence and risk factors of suicide among patients with sepsis in South Korea.

Method

All adult patients who were admitted to all hospitals in South Korea with a main diagnosis of sepsis, from 1 January 2010 to 31 December 2018, were included in the study. The primary outcome was suicide within 1 year after sepsis diagnosis.

Results

A total of 251,837 adult patients with sepsis were included, of which 132,691 patients (52.7%) died within 1 year after the diagnosis of sepsis, and death by suicide was the cause in 3903 patients (1.5%). Older age, male gender, living in a rural area, higher Charlson Comorbidity Index and Elixhauser Comorbidity Index scores, invasive treatment (continuous renal replacement therapy and mechanical ventilator support) and admission to a hospital with low annual case volumes were associated with a higher risk of suicide. In addition, concurrent substance misuse, post-traumatic stress disorder, bipolar disorder, dementia and previous attempt of suicide or self-harm were associated with a higher risk of suicide.

Conclusions

During the 1-year follow-up period, 1.5% of patients died by suicide after the diagnosis of sepsis in South Korea. Knowledge of the factors associated with suicide might allow for earlier intervention to potentially reduce the number of suicide attempts in patients with sepsis.

Keywords

Depressive disorders; primary care; post-traumatic stress disorder; risk assessment; suicide.
National University Bundang Hospital (approval number X-1912-580-902), and the National Health Insurance Service (NHIS) permitted data-sharing after approval of the study protocol (approval number NHIS-2020-1-095). The requirement for informed consent was waived because we performed the data analysis retrospectively in an anonymised manner.

**Database (NHIS and Statistics Korea)**

The NHIS database was used for this study. In South Korea, all disease diagnoses and prescription information regarding drugs and/or procedures have to be registered in the NHIS database as the sole public health insurance system. These registrations enable patients to receive government financial support for treatment expenses. The disease diagnoses are registered in the NHIS database, using ICD-10 codes. In addition, we used the Statistics Korea database to extract the death date and main cause of death, up to 31 December 2019. Physicians are required to register the main cause of death (primary disease) in the Statistics Korea database in South Korea. First, we obtained approval from the NHIS for data extraction from the NHIS database, which contains demographic data, socioeconomic status, disease diagnoses and treatment information of the study population. Next, we obtained approval from Statistics Korea for data-sharing regarding death date and main causes of death among the study population. These two databases were linked by the resident registration number, a mandatory identification number issued to residents of South Korea regardless of nationality. The linkage process was performed cooperatively by medical record technicians in the two centres (NHIS and Statistics Korea).

**Patients with sepsis**

We included all adult patients (≥18 years of age) who were admitted to all hospitals in South Korea from 1 January 2010 to 31 December 2018, with a main diagnosis of sepsis (ICD-10 codes A40, A41 and R65.2) based on the ICD-10 codes. The main diagnosis was determined by the NHIS for each patient after hospital discharge or death, as the disease that required the greatest treatment or examination during the patient’s hospital stay. If a patient was admitted to the hospital twice or more with the main diagnosis of sepsis during the study period, only the first episode of hospital admission was considered in this study. In addition, cases with missing date of death were excluded from the analysis because we focused on mortality among patients with sepsis.

**Primary outcome**

The primary outcome of this study was suicide within 1 year after the diagnosis of sepsis among patients with sepsis. Suicide was defined as death by suicide attempt or self-harm (ICD-10 codes X60–X84 and Y870), in accordance with a previous study. Patients who died from suicide were included in the suicide group, whereas patients who died from other causes were included in the non-suicide death group. If patients with sepsis survived over 1 year after diagnosis of sepsis, they were considered as survivors.

**Covariates**

Physical characteristics, socioeconomic status, treatment, medical conditions and concurrent psychiatric disorders were considered as covariates because they might influence risk of death by suicide. Age and gender were the physical covariates. Residence at the time of diagnosis of sepsis and household income level were collected to reflect the socioeconomic status of the patients with sepsis. All patients were classified into two groups according to the residence: urban area (Seoul and other metropolitan cities) and other areas. Classification was based on home postal codes collected upon hospital admission. These data were collected because there might be inequality in the utilisation of health services in rural versus urban areas. Household income level was extracted using insurance premium of all patients as a covariate; it was classified into four groups, using quartile ratios (quartiles 1–4, lowest to highest). All individuals in South Korea are registered in the NHIS and are divided into two groups: employee insured and self-employed insured. The insurance premium for employee-insured individuals was determined according to the income, whereas the insurance premium for self-employed-insured individuals was determined according to the income, property value, living standards and rate of participation in economic activities. To reflect the comorbid status of all patients with sepsis, the Charlson Comorbidity Index (CCI) and Elixhauser Comorbidity Index (ECI) were calculated using ICD-10 codes within 1 year before the diagnosis of sepsis, as shown in Supplementary Tables 1 and 2 available at https://doi.org/10.1192/bjo.2022.19. The annual case volume of hospital admissions for sepsis in South Korea during 2010–2018 was calculated and considered as a covariate. All patients were classified into four groups according to the annual case volume, using the quartile ratio, based on each hospital in which patients with sepsis were admitted: quartile 1, ≤235; quartile 2, 236 to ≤710; quartile 3, 710 to ≤1743 and quartile 4, ≥1743. The admitting department (medical or surgical department) for all of the patients with sepsis was also collected as a covariate. For treatment information, continuous renal replacement therapy (CRRT) use, vasopressor use, extracorporeal membrane oxygenation support and mechanical ventilator support were collected as covariates. Total number of hospital admissions with a main diagnosis of sepsis during the study period was also collected and divided into categorical variables (1, 2–3, 4–5, 6–7 and ≥8). Moreover, ICU admissions with the main diagnosis of sepsis were also collected and considered as a covariate. As mental disorders are well-known risk factors for suicide, concurrent psychiatric illnesses such as depression (ICD-10 codes F32, F33, F34.1), anxiety disorder (ICD-10 codes F40, F41), substance misuse (ICD-10 codes F10–F19), post-traumatic stress disorder (PTSD) (ICD-10 code F43.1), bipolar disorder (ICD-10 code F31), schizophrenia or schizophrenic affective disorder (ICD-10 codes F20, F25), and dementia (ICD-10 codes F00–F03, F05.1, G30–G31) were also included. In addition, history of previous suicide attempt or self-harm (ICD-10 codes X60–X84 and Y870) was extracted using ICD-10 codes within 1 year before and after the diagnosis of sepsis.

**Statistical analysis**

The clinicopathological characteristics of the patients with sepsis were presented as median values with interquartile ranges (IQRs) for continuous variables, because the distribution of continuous variables (age, CCI and ECI) was not normally distributed according to Kolmogorov–Smirnov tests. The categorical variables were presented as numbers with percentages. To compare the clinicopathological characteristics between the three groups (suicide group, non-suicide death group and survivors), we used the Kruskal–Wallis test and chi-squared test for continuous variables and categorical variables, respectively. The proportion of extracorporeal membrane oxygenation support among patients with sepsis was compared with Fisher’s exact test.

We performed competing risk analysis by using the Fine and Gray method to examine associated factors for mortality by suicide and non-suicide mortality, because the Fine and Gray method can be used to assess the deaths from other causes (non-suicide mortality). For example, if a patient died from other causes, they would not die because of suicide, and the death from
Results

Study population
From 1 January 2010 to 31 December 2018, there were 692,932 hospital admissions of 352,823 patients with a main diagnosis of sepsis. The first episode of hospital admission for each patient was included in this study. After excluding 100,976 paediatric patients under 18 years of age and ten cases with incomplete medical records regarding the death date, 251,837 adult patients with sepsis were included in this study. Among them, 132,691 (52.7%) patients died within 1 year after the diagnosis of sepsis, and death by suicide was the cause in 3903 (1.5%) patients, as shown in Figure 1. Among the suicide group, 1512 (0.6%) patients with sepsis died by suicide during their hospital stay. Table 1 shows the clinicopathological characteristics of all patients with sepsis. The median age was 77 years (IQR 64–84 years), and 109,943 (43.7%) patients were male. There were 11,467 (4.6%) patients with substance misuse, and among these patients, the proportion of alcohol misuse was highest (10,194, 4.0%), followed by sedative stance misuse, and among these patients, the proportion of alcohol misuse was highest (10,194, 4.0%). The median values of the CCI and ECI were 6.8 (s.d. 4.5) and 18.5 (s.d. 13.3), respectively. The 30-day and 90-day mortality occurred in 75,736 (30.1%) and 102,560 (40.7%) patients, respectively. Table 2 shows the results of the comparison between the three groups (suicide group, non-suicide death group and survivors). The median age of patients in the suicide group and non-suicide group was 79.0 years (IQR 69.0–86.0 years) and 80.0 years (IQR 73.0–86.0 years), respectively, whereas that of patients in the survivor group was 71.0 years (IQR 53.0–83.0 years).

Competing risk analysis
Table 3 shows the results of the competing risk analyses, using the Fine and Gray model for suicide and non-suicide mortality after the diagnosis of sepsis. Compared with the 18–35 years group (sHR 2.01, 95% CI 1.46–2.76, P < 0.001), 51–65 years group (sHR 2.01, 95% CI 1.46–2.76, P < 0.001), and 66–80 years group (sHR 2.01, 95% CI 1.46–2.76, P < 0.001) were associated with a higher risk of suicide mortality. Male gender (sHR 1.52, 95% CI 1.42–1.66, P < 0.001) and living in a rural area (sHR 1.52, 95% CI 1.42–1.66, P < 0.001) were associated with a higher risk of suicide mortality. Compared with the quartile 1 group of annual case volume of hospital admissions for sepsis, the quartile 3 (sHR 0.87, 95% CI 0.80–0.95, P = 0.002) and quartile 4 (sHR 0.45, 95%
Table 1: Clinicopathological characteristics of the total cohort of 251,837 patients with sepsis

| Variable                                      | N (%) | Median (IQR) |
|-----------------------------------------------|-------|--------------|
| Age, years                                    | 77 (64–84) |             |
| Gender, male                                  | 109,943 (43.7) |             |
| Residence at diagnosis of sepsis              |       |              |
| Urban area                                    | 85,071 (33.8) |             |
| Rural area                                    | 166,766 (66.2) |            |
| Income level at diagnosis of sepsis           |       |              |
| Quartile 1 (lowest)                           | 45,920 (18.2) |         |
| Quartile 2, 236 to < 710                      | 78,023 (31.0) |         |
| Quartile 3, 710 to < 1743                     | 59,804 (23.7) |         |
| Quartile 4, ≥ 1743                            | 39,290 (15.6) |         |
| CRRT use                                      | 69,654 (28.2) |     |
| Vasopressor use                               | 43,787 (17.4) |     |
| ECMO support                                  | 263 (0.1) |             |
| Mechanical ventilator support                 | 34,572 (13.7) |          |
| ICU admission                                 | 60,165 (23.9) |          |
| Total number of hospital admissions for sepsis|       |              |
| 1                                             | 149,520 (59.4) |         |
| 2–3                                           | 73,798 (29.3) |         |
| 4–5                                           | 16,157 (6.4) |             |
| 6–7                                           | 5648 (2.2) |             |
| >8                                            | 6714 (2.7) |             |
| Concurrent psychiatric illness                |       |              |
| Depression                                    | 72,344 (28.7) |         |
| Anxiety disorder                              | 74,731 (29.7) |         |
| Substance misuse                             | 11,467 (4.6) |           |
| PTSD                                          | 100 (0.0) |             |
| Bipolar disorder                              | 35,225 (14.0) |          |
| Schizophrenia or schizophrenic affective disorder | 11,738 (4.7) |         |
| Dementia                                      | 104,175 (41.4) |        |
| History of self-harm or suicidal attempt      | 81 (0.0) |            |
| Year of diagnosis of sepsis                   |       |              |
| 2010                                          | 27,849 (11.1) |          |
| 2011                                          | 23,342 (9.3) |           |
| 2012                                          | 25,057 (9.9) |           |
| 2013                                          | 25,334 (10.1) |         |
| 2014                                          | 27,453 (10.9) |         |
| 2015                                          | 28,711 (11.4) |         |
| 2016                                          | 29,786 (11.8) |       |
| 2017                                          | 30,858 (12.3) |         |
| 2018                                          | 33,447 (13.3) |        |
| Hospital mortality                            | 52,970 (21.0) |         |
| Death by suicide during hospital admission    | 1512 (0.6) |             |
| 30-day mortality                              | 75,736 (30.1) |        |
| 90-day mortality                              | 102,560 (40.7) |        |
| 1-year mortality                              | 132,602 (52.7) |        |

IQR = interquartile range; CRRT = continuous renal replacement therapy; ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit; PTSD = post-traumatic stress disorder.

a. Alcohol, 10 (4.0%); opioids, 6 (0.0%); cannabis, 13 (0.0%); sedatives, 479 (2.2%); cocaine, 12 (0.0%); stimulants, 19 (0.0%); hallucinogens, 9 (0.0%); nicotine, 150 (6.1%); inhalants, 22 (0.0%); and other psychiatric agents, 502 (2.2%).

Among concurrent psychiatric illnesses, substance misuse (sHR 1.25, 95% CI 1.05–1.49, P = 0.012), PTSD (sHR 3.52, 95% CI 1.44–8.58, P = 0.006), bipolar disorder (sHR 1.15, 95% CI 1.05–1.49, P = 0.003) and dementia (sHR 1.31, 95% CI 1.22–1.40, P < 0.001) were associated with a higher risk of suicide mortality. Previous self-harm or suicide attempt (sHR 8.93, 95% CI 4.90–16.30, P < 0.001) was associated with a higher risk of suicide mortality. The cumulative incidence of suicide mortality according to previous self-harm or suicide attempt, living in a rural area, age, bipolar disorder, dementia, substance misuse and PTSD are presented in Supplementary Figures 1–7, respectively.

Other analyses

Supplementary Tables 3 and 4 show the results of the competing risk analyses with the Fine and Gray model for suicide mortality in the male and female groups, respectively. Table 4 shows the results of the competing risk analyses with the Fine and Gray model for suicide mortality after excluding patients with sepsis who had concurrent psychiatric disorders or had a history of self-harm or suicidal attempt. In total, 83,860 patients with sepsis were included in this sensitivity analysis, and 1067 (1.3%) died by suicide. Table 5 shows the results of the competing risk analyses with the Fine and Gray model for suicide mortality in patients with sepsis who were admitted to ICUs. In total, 60,165 patients with sepsis were included in this sensitivity analysis, and 1166 (1.9%) died by suicide.

Discussion

This population-based cohort study showed that 1.5% of patients died by suicide within 1 year after the diagnosis of sepsis in South Korea. Older age, male gender, living in rural areas, comorbid status (higher CCI or ECI score), admission to a hospital with low annual case volumes, invasive treatment (CRRT and mechanical ventilator use), some concurrent psychiatric disorders (substance misuse, PTSD, bipolar disorder and dementia), and history of self-harm or suicide attempt were potential risk factors for suicide among patients with sepsis. Clinically, the knowledge of the factors associated with suicide might allow for earlier intervention to potentially reduce suicide in patients with sepsis. For example, patients with sepsis who have concurrent psychiatric disorders can receive a psychiatric consultation by a psychiatrist, who will prescribe medication for suicide prevention. Moreover, after hospital discharge, the mental health of patients with sepsis who have risk factors for suicide need to be monitored during out-patient visits.

The suicide prevalence in patients with sepsis was 1.5%, which is higher than that reported in a previous study that demonstrated a rate of 0.2% among ICU survivors. A previous study by Fernando et al focused on all ICU survivors, including many cases of postoperative ICU admission after elective surgeries. The disease severity might differ between our study population with sepsis and overall ICU survivors evaluated in the study by Fernando et al. The patients with sepsis in our study may have had more severe conditions because we included all patients with sepsis, regardless of whether they died during their ICU stay or hospital admission. Meanwhile, the study by Fernando et al included ICU survivors. The disease severity during hospital admission might explain the discrepancy in the suicide rates between the two studies.

Various concurrent psychiatric disorders were evaluated as potential risk factors for suicide mortality among patients with sepsis. Among the disorders, substance misuse, PTSD, bipolar disorder and dementia were potential risk factors for suicide, whereas depression, anxiety disorder and schizophrenia were not.
Interestingly, approximately 90% (10 194/11 467) of substance misuse was alcohol misuse among patients with sepsis in this study. Alcohol misuse was a powerful risk factor for suicide, and the relative risk of suicide in patients who misused alcohol was reported as 6.9% in a previous study. Bipolar disorder was also identified as a significant risk factor for suicide in patients with sepsis, regardless of gender, in this study. Bipolar disorder is associated with the highest rate of suicide of all psychiatric disorders, approximately 30 times that of the general population. Fernando et al also reported that concurrent bipolar disorder was a significant risk factor for suicide among ICU survivors. However, an important psychiatric disorder, depression, was not a risk factor for suicide in our study among patients with sepsis. This is the most significant difference between the findings of Fernando et al and our findings. Several factors might affect this finding. The median age of our study population was 69 years, which is younger than the general population. The incidence of depression and other psychiatric disorders may be lower in younger individuals. Furthermore, younger individuals may be more likely to seek treatment for psychiatric disorders, leading to a decrease in the proportion of patients with psychiatric disorders in our study. This may explain why concurrent bipolar disorder was not a risk factor for suicide in this study.

### Table 2: Comparison of the clinicopathological characteristics between the three groups (suicide group, non-suicide death group and survivors)

| Variable                                      | Suicide group, n = 3903 | Non-suicide death group, n = 128 788 | Survivors, n = 119 146 | P-value |
|-----------------------------------------------|-------------------------|--------------------------------------|-------------------------|---------|
| Age, years                                    | 79.0 [69.0–86.0]        | 80.0 [73.0–86.0]                     | 71.0 [53.0–80.0]        | <0.001  |
| Gender, male                                  | 2079 (53.3)             | 60 078 (46.6)                        | 47 786 (40.1)           | <0.001  |
| Residential area                              |                         |                                      |                         | <0.001  |
| Urban                                         | 1126 (28.8)             | 40 955 (31.8)                        | 43 054 (36.1)           |         |
| Rural                                         | 2777 (71.2)             | 87 833 (68.2)                        | 76 092 (63.9)           |         |
| Income level at diagnosis of sepsis           |                         |                                      |                         | <0.001  |
| Quartile 1 (lowest)                           | 725 (18.6)              | 23 757 (18.4)                        | 21 438 (18.0)           | <0.001  |
| Quartile 2                                    | 502 (12.9)              | 16 045 (12.5)                        | 17 354 (14.6)           |         |
| Quartile 3                                    | 703 (18.0)              | 21 768 (16.9)                        | 23 410 (19.6)           |         |
| Quartile 4 (highest)                          | 1263 (32.4)             | 42 840 (33.3)                        | 39 925 (33.5)           |         |
| Unknown                                       | 710 (18.2)              | 24 378 (18.9)                        | 17 019 (14.3)           |         |
| Charlson Comorbidity Index                    | 6 (4–9)                 | 7 (4–11)                             | 5 (4–9)                 | <0.001  |
| Elixhauser Comorbidity Index                  | 19 (10–29)              | 21 (11–30)                           | 14 (6–24)               | <0.001  |
| Admitting department                          |                         |                                      |                         | <0.001  |
| Medical department                            | 3131 (80.2)             | 112 813 (87.6)                       | 108 334 (90.9)          |         |
| Surgical department                           | 772 (19.8)              | 15 975 (12.4)                        | 10 812 (9.1)            |         |
| Total case volume of sepsis treatment         |                         |                                      |                         | <0.001  |
| Quartile 1, ≤ 235                             | 1321 (33.8)             | 43 432 (33.7)                        | 29 967 (25.2)           |         |
| Quartile 2, 236 to < 710                      | 1405 (36.0)             | 45 276 (35.2)                        | 31 342 (26.3)           |         |
| Quartile 3, 710 to < 1743                     | 940 (24.1)              | 30 742 (23.9)                        | 28 122 (23.6)           |         |
| Quartile 4, ≥ 1743                            | 237 (6.1)               | 9338 (7.3)                           | 29 715 (24.9)           |         |
| CRRT use                                      | 168 (4.3)               | 5591 (4.3)                           | 1195 (1.0)              | <0.001  |
| Vasopressor use                               | 849 (21.8)              | 30 934 (24.0)                        | 12 004 (10.1)           | <0.001  |
| ECMO support                                  | 9 (0.2)                 | 217 (0.2)                            | 37 (0.0)                | <0.001  |
| Mechanical ventilator support                 | 988 (25.3)              | 28 795 (22.4)                        | 4785 (4.0)              | <0.001  |
| ICU admission                                 | 1166 (29.9)             | 38 759 (30.1)                        | 20 240 (17.0)           | <0.001  |
| Total number of hospital admissions for sepsis|                         |                                      |                         | <0.001  |
| 1                                            | 2434 (62.4)             | 83 851 (65.1)                        | 63 235 (53.1)           |         |
| 2–3                                          | 1124 (28.8)             | 35 869 (27.9)                        | 36 805 (30.9)           |         |
| 4–5                                          | 222 (5.7)               | 6137 (4.8)                           | 9778 (8.2)              |         |
| 6–7                                          | 65 (1.7)                | 1729 (1.3)                           | 3854 (3.2)              |         |
| ≥ 8                                          | 58 (1.5)                | 1182 (0.9)                           | 5474 (4.6)              |         |
| Concurrent psychiatric illness                |                         |                                      |                         | <0.001  |
| Depression                                    | 1136 (29.1)             | 36 146 (28.1)                        | 35 062 (29.4)           | <0.001  |
| Anxiety disorder                              | 1140 (29.2)             | 36 281 (28.2)                        | 37 310 (31.3)           | <0.001  |
| Substance misuse                              | 241 (6.2)               | 3428 (2.7)                           | 5798 (4.9)              | <0.001  |
| PTSD                                          | 5 (0.1)                 | 28 (0.2)                             | 67 (0.1)                | <0.001  |
| Bipolar disorder                              | 633 (16.2)              | 19 058 (14.8)                        | 15 534 (13.0)           | <0.001  |
| Schizophrenia or schizophrenic affective disorder| 205 (5.3)               | 6701 (5.2)                           | 4832 (4.1)              | <0.001  |
| Dementia                                      | 1992 (51.0)             | 72 393 (56.2)                        | 29 790 (25.3)           | <0.001  |
| History of self-harm or suicidal attempt      | 11 (0.3)                | 35 (0.3)                             | 35 (0.3)                | <0.001  |
| Year of diagnosis of sepsis                   |                         |                                      |                         | <0.001  |
| 2010                                          | 467 (12.0)              | 14 795 (11.5)                        | 12 587 (10.6)           |         |
| 2011                                          | 355 (9.1)               | 12 782 (9.9)                         | 10 205 (8.6)            |         |
| 2012                                          | 470 (12.0)              | 12 629 (10.6)                        | 10 958 (8.2)            |         |
| 2013                                          | 466 (11.9)              | 13 432 (10.4)                        | 11 436 (9.6)            |         |
| 2014                                          | 450 (11.5)              | 13 773 (10.7)                        | 13 227 (11.1)           |         |
| 2015                                          | 419 (10.7)              | 13 978 (10.9)                        | 14 314 (12.0)           |         |
| 2016                                          | 409 (10.5)              | 14 166 (11.0)                        | 15 211 (12.8)           |         |
| 2017                                          | 432 (11.1)              | 15 251 (11.8)                        | 15 175 (12.7)           |         |
| 2018                                          | 435 (11.1)              | 16 979 (13.2)                        | 16 033 (13.5)           |         |

Data are presented as median values with interquartile ranges for continuous variables, and numbers with percentages for categorical variables. The Kruskal–Wallis test and chi-squared test were used for continuous variables and categorical variables, respectively. CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; ICU intensive care unit; PTSD, post-traumatic stress disorder.
population was 77 years (IQR 64–84 years), suggesting that many of the patients with sepsis were elderly patients. Depression in older people can be underdiagnosed and undertreated.22 It is possible that there may have been missed cases of depression in our study because we used a national registration database according to ICD-10 codes. However, in the subgroup analysis, depression was a significant risk factor for suicide in male patients, but was not significant in female patients. A recent study reported that depression in males was significantly associated with suicide risk independent of conventional depression symptoms.23 Moreover, depression
symptoms with the greatest risk in men were emotional suppression, substance misuse, somatic symptoms and risk-taking behaviours. Considering that this is the first study to report the relationship between concurrent depression and suicide in patients with sepsis, further study is needed. Specifically, the association between the timing and occurrence of comorbid psychiatric diseases in patients with sepsis and suicide risk should be clarified in a future study.

Dementia was also a powerful risk factor for suicide and was significant, regardless of gender, ICU admission status or study period (2016–2018). The increased risk of suicide among patients with dementia and its prevention are important public health issues. Moreover, a recent Swedish cohort study reported that dementia

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Table 4 competing risk analyses using the Fine and Gray model for suicide mortality after excluding patients with sepsis who had concurrent psychiatric disorders or had a history of self-harm or suicide attempt

| Variable                                           | Death by suicide, SHR (95% CI) | P-value |
|----------------------------------------------------|--------------------------------|---------|
| Gender, male (versus female)                       | 1.62 (1.43–1.83)               | <0.001  |
| Age, years                                         | 51.65 0.63 (0.41, 0.97)         | 0.034   |
| 36–50                                              | 2.89 (1.79–4.67)               | <0.001  |
| 51–65                                              | 3.15 (1.95–5.08)               | <0.001  |
| 65–80                                              | 3.81 (2.37–6.14)               | <0.001  |
| >81                                                | 4.94 (3.06–7.97)               | <0.001  |
| Residence at diagnosis of sepsis                   | 1.32 (1.15–1.51)               | <0.001  |
| Income level at diagnosis of sepsis                | 0.88 (0.75–1.10)               | 0.144   |
| Quartile 1 [lowest]                                | 1.09 (1.02–1.11)               | 0.013   |
| Quartile 3                                         | 1.27 (1.18–1.39)               | <0.001  |
| Charlson Comorbidity Index                         | 0.88 (0.72–1.08)               | 0.230   |
| Clinical variables                                 | 0.57 (0.41, 0.78)              | 0.002   |
| Total case volume of sepsis treatment              | 0.86 (0.68–1.10)               | 0.166   |
| Admitting department                               | 0.69 (0.50–1.00)               | 0.042   |
| Medical department (versus surgical department)    | 1.02 (0.38–2.74)               | 0.980   |
| Vasopressor use                                    | 0.62 (0.36–1.05)               | 0.073   |
| ECMO support                                       | 0.74 (0.43–1.28)               | 0.280   |
| Mechanical ventilator support                      | 1.11 (0.97–1.28)               | 0.130   |
| ICU admission                                      | 0.74 (0.48–0.79)               | <0.001  |
| Total number of hospital admissions for sepsis     | 0.66 (0.50–0.83)               | 0.001   |
| Year of diagnosis of sepsis                        | 0.66 (0.51–0.86)               | 0.002   |
| 2010                                               | 0.74 (0.57–0.97)               | 0.027   |

SHR, subdistribution hazard ratio; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

Table 5 competing risk analyses using the Fine and Gray model for suicide mortality in patients with sepsis who were admitted to ICUs

| Variable                                           | Death by suicide, SHR (95% CI) | P-value |
|----------------------------------------------------|--------------------------------|---------|
| Sex, male (versus female)                          | 1.37 (1.22, 1.55)              | <0.001  |
| Age, years                                         |                               |         |
| 18-35                                              |                               |         |
| 36-50                                              | 0.84 (0.53, 1.34)              | 0.470   |
| 51-65                                              | 0.63 (0.41, 0.97)              | 0.034   |
| 65-80                                              | 0.61 (0.40, 0.94)              | 0.024   |
| ≥ 81                                               | 0.77 (0.50, 1.18)              | 0.230   |
| Residence at diagnosis of sepsis                   |                               |         |
| Urban                                              | 1.25 (1.10, 1.42)              | 0.001   |
| Rural                                              | 1.15 (1.01, 1.31)              | 0.034   |
| History of Self-harm or suicidal attempt           | 10.34 (3.94, 27.16)            | <0.001  |
| Year of diagnosis of sepsis                        | 1.15 (1.01, 1.31)              | 0.034   |

SHR, subdistribution hazard ratio; CI, confidence interval; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; PTSD, post-traumatic stress disorder.
was more common in individuals diagnosed with sepsis, suggesting that prevention of suicide is clinically important in patients with sepsis and dementia. Previous suicide attempt was an important risk factor for death by suicide, and this also applied in our results. In agreement with the findings by Fernando et al, we suggest that patients with sepsis with a history of suicide attempt are a high-risk population for suicide.

Old age and male gender were potential risk factors for suicide in patients with sepsis in this study. A recent study reported that old age and male gender were risk factors for suicide among Chinese adults, and suicide in elderly people is an important public health issue in many countries. Moreover, urban–rural inequalities in suicide mortality, such as increased risk of suicide in individuals living in rural areas, have also been reported in previous studies. For individuals living in rural areas, social isolation, which results in less intimate face-to-face contact with family and friends, poorer access to mental healthcare facilities and easier access to lethal means, might increase the risk of suicide.

Fernando et al also reported that ICU survivors who experienced invasive treatment, such as mechanical ventilatory support or CRRT, were at a higher risk of suicide. We also found that invasive treatment (CRRT and mechanical ventilator use) was a risk factor for suicide in patients with sepsis. The use of invasive treatments such as CRRT and mechanical ventilation meant that patients experienced major organ failure owing to sepsis. Sepsis survivors who developed major organ failure might have post-sepsis syndrome, resulting in a newly acquired disability, which might be responsible for the increased risk of suicide in our study.

This study has several limitations. First, we did not consider the severity of sepsis by using accurate tools such as the Simplified Acute Physiology Score II or Acute Physiology and Chronic Health Evaluation II. As the severity of sepsis affects the risk of suicide in patients with sepsis, this might have affected our results. Second, some information pertaining to factors such as body mass index, marital status, history of smoking and alcohol consumption was not included in this study because they were unavailable in the NHS database. Third, we used the ICD-10 codes for sepsis to extract the data of the study population from the national registration database in South Korea. However, some cases may have been missed by this method because some patients with sepsis were not registered as sepsis cases based on ICD-10 codes in the NHS database. Fourth, considering the old age and gender imbalance, it is difficult to conclude that our study population was a representative sample of the common population of patients with sepsis in South Korea. For example, elderly people have a high risk of depression because of loneliness and loss of significant others, this affected the prevalence of suicide in this study. Moreover, patients with chronic conditions, such as diabetes mellitus, cancer and other diseases, are more prone to sepsis and might have a lower quality of life before the diagnosis of sepsis. Finally, we used the ICD-10 codes for calculating the CCI and ECI score; however, the actual underlying diseases of patients with sepsis might differ. For example, some patients were not diagnosed in the NHS database because of mild symptoms or poor access to healthcare resources.

In conclusion, during the 1-year follow-up period, 1.5% of patients with a diagnosis of sepsis died by suicide in South Korea. Factors such as old age, male gender, living in rural areas, comorbid status, admission to a hospital with low annual case volumes, invasive treatment, concurrent PTSD, bipolar disorder, substance misuse, dementia and history of self-harm or suicide attempt were potential risk factors for suicide among patients with sepsis. The knowledge of factors associated with suicide could allow for earlier intervention to potentially reduce the number of suicide attempts in patients with sepsis. Future research should identify methods of reducing the number of suicide attempts in patients with sepsis, particularly those with these additional prognostic factors.

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Supplementary material

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Data availability

Data are available upon reasonable request. Anonymous data used in the present study may be available upon reasonable request to the corresponding author, I.-A.S.

Author contributions

T.K.O. designed the study, analysed the data, interpreted the data and drafted the manuscript. I.-A.S. contributed to the study conceptualisation, acquisition of data and review of the manuscript. H.Y.P. contributed to data collection, project administration and review of the manuscript. All authors have given final approval for the final version of the manuscript.

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Declaration of interest

None.

References

1. Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschtman CS, et al. Developing a new definition and assessing new clinical criteria for septic shock: for the third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016; 315(8): 775–87.
2. Oh SY, Cho S, Kim GH, Jang EJ, Choi S, Lee H, et al. Incidence and outcomes of sepsis in Korea: a nationwide cohort study from 2007 to 2016. Crit Care Med 2015; 43(12): e993–8.
3. Rudd KE, Johnson SC, Agessa KM, Shackelford KA, Tsol D, Klevan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the global burden of disease study. Lancet 2020; 395(10219): 200–11.
4. World Health Organization (WHO). Suicide Worldwide in 2019: Global Health Estimates. WHO, 2021. (https://www.who.int/publications/i/item/9789240026643).
5. Organisation for Economic Co-operation and Development (OECD). OECD, Suicide Rates Indicator. OECD, 2022. (https://data.oecd.org/healthstat/suicide-rates.htm).
6. Lee SU, Park JJ, Lee S, Oh H, Choi JM, Oh CM. Changing trends in suicide rates in South Korea from 1993 to 2016: a descriptive study. BMJ Open 2018; 8(9): e023144.
7. Oh TK, Song IA. Quality of life after sepsis and its association with mortality among sepsis survivors in South Korea: a population level cohort study. J Crit Care 2021; 64: 193–8.
8. Mostel Z, Perl A, Marck M, Mehdif SF, Lowell B, Barthija S, et al. Post-sepsis syndrome - an evolving entity that afflicts survivors of sepsis. Mol Med 2019; 25(1): 6.
9. Fernando SM, Qureshi D, Sood MM, Pugliese M, Talarico R, Myran DT, et al. Suicide and self-harm in adult survivors of critical illness: population based cohort study. BMJ 2021; 373: n973.
10. Lund-Sorensen H, Benros ME, Madsen T, Sorensen HJ, Eaton WW, Postolache TT, et al. A nationwide cohort study of the association between hospitalization with infection and risk of death by suicide. JAMA Psychiatry 2016; 73(9): 912–9.
11. Brundin L, Erhardt S, Bryleva EY, Achtenyeed E, Postolache TT. The role of inflammation in suicidal behaviour. Acta Psychiatr Scand 2015; 132(3): 192–203.
12 Turecki G, Brent DA, Gunnell D, O’Connor RC, Oquendo MA, Pirkis J, et al. Suicide and suicide risk. Nat Rev Dis Primers 2019; 5: 74.

13 Guo B, Xie X, Wu Q, Zhang X, Cheng H, Tao S, et al. Inequality in the health services utilization in rural and urban China: a horizontal inequality analysis. Medicine (Baltimore) 2020; 99(2): e18625.

14 Song YJJ. The South Korean health care system. JMAJ 2009; 52(3): 206–9.

15 van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care 2009; 47(6): 626–33.

16 Bradvik L. Suicide risk and mental disorders. Int J Environ Res Public Health 2018; 15(9): 2028.

17 Austin PC, Steyerberg EW, Putter H. Fine-Gray subdistribution hazard models to simultaneously estimate the absolute risk of different event types: cumulative total failure probability may exceed 1. Stat Med 2021; 40(19): 4200–12.

18 Bruceta M, De Souza L, Carr ZJ, Bonavia A, Kunselman AR, Karamchandani K. Post-operative intensive care unit admission after elective non-cardiac surgery: a single-center analysis of the NSQIP database. Acta Anaesthesiol Scand 2020; 64(3): 319–28.

19 Rossow I, Amundsen A. Alcohol abuse and suicide: a 40-year prospective study of Norwegian conscripts. Addiction 1995; 90(5): 685–91.

20 Fox V, Dalm C, Dal H, Hollander AC, Kirkbride JB, Pitman A. Suicide risk in people with post-traumatic stress disorder: a cohort study of 3.1 million people in Sweden. J Affect Disord 2021; 279: 609–16.

21 Miller JN, Black DW. Bipolar disorder and suicide: a review. Curr Psychiatry Rep 2020; 22(2): 6.

22 Allan CE, Valkanova V, Ebmeier KP. Depression in older people is underdiagnosed. Practitioner 2014; 258(1771): 19–22.

23 Cui R, Fiske A. Gender differences in male depression and suicide risk. Violence and Ment Health 2021; 8: 2.

24 Seyfried LS, Kales HC, Ignacio RV, Connell Y, Valenstein M. Predictors of suicide in patients with dementia. Alzheimers Dement 2011; 7(6): 567–73.

25 Ahsstrom B, Larsson IM, Strandberg G, Lipsey M. A nationwide study of the long-term prevalence of dementia and its risk factors in the Swedish intensive care cohort. Crit Care 2020; 4: 548.

26 Bostwick JM, Pabbati C, Geske JR, McKean AJ. Suicide attempt as a risk factor for completed suicide: even more lethal than we knew. Am J Psychiatry 2016; 173(11): 1094–100.

27 Yu R, Chen Y, Li L, Chen J, Guo Y, Bian Z, et al. Factors associated with suicide risk among Chinese adults: a prospective cohort study of 0.5 million individuals. PLoS Med 2021; 18(3): e1003545.

28 Conejero I, Ole E, Courlet P, Calati R. Suicide in older adults: current perspectives. Clin Interv Aging 2018; 13: 691–9.

29 Chan Ot, Caine ED, You S, Yip PS. Changes in South Korean urbanicity and suicide rates, 1992 to 2012. BMJ Open 2015; 5(12): e009451.

30 Heibich M, Plener PL, Hartung S, Blumi V. Spatiotemporal suicide risk in Germany: a longitudinal study 2007–11. Sci Rep 2017; 7: 7673.

31 Kapusta ND, Zorman A, Etzersdorfer E, Ponocny-Selig R, Jandl-Jager E, Sonneck G. Rural-urban differences in Austrian suicides. Soc Psychiatry Psychiatr Epidemiol 2008; 43(4): 311–8.

32 Fontanella CA, Hiance-Steelesmith DL, Phillips GS, Bridge JA, Lester N, Sweeney HA, et al. Widening rural-urban disparities in youth suicides, United States, 1996–2010. JAMA Pediatr 2015; 169(5): 466–73.

33 Lelubre C, Vincent JL. Mechanisms and treatment of organ failure in sepsis. Nat Rev Nephrol 2018; 14(7): 417–27.

34 Singh A, Misra N. Loneliness, depression and sociability in old age. Ind Psychiatry J 2009; 18(1): 51–5.