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LETTER TO THE EDITOR

Non-recovery of renal function was correlated with increased mortality in the cancer cohort with septic shock

Dear Editor,

As the overall survival rate of cancer patients has been increasing, an increasing number of patients are experiencing septic shock, and the corresponding mortality rate is becoming unacceptably high [1]. Among cases of organ failure caused by septic shock, the development of acute kidney injury (AKI) is known to be common and correlated with poor outcomes [2]. Moreover, a large Danish cohort study revealed that critically ill patients with cancer had a greater risk of AKI and requirement of renal replacement therapy (RRT) compared to patients without cancer [3]. Adverse outcomes dramatically increase in patients with severe AKI who received RRT, and a recent survey in China reported that the hospital mortality rate for this population was up to 80% [4]. Although the association between septic AKI and mortality has been widely investigated, knowledge about whether patients with recovered renal function have increased long-term risk of end-stage renal disease compared with patients who have not recovered renal function had been scarce, especially in the cancer population [5]. Few studies have tried to reveal the clinical impact of AKI in patients with malignancy, and they included a relatively small sample size or included only certain types of conditions, such as hematologic malignancy [6]. In this study, we tried to determine the relationship between renal function recovery and long-term dialysis dependency among patients with cancer.

We conducted a nationwide population-based study of adult cancer patients who presented to the emergency department with septic shock in South Korea between 2009 and 2017 using data from the Korean National Health Insurance Service (NHIS). The NHIS database contains all of the claim data, including demographics, drug prescriptions, diagnostic codes for the disease coding, the International Classification of Disease 10th edition (ICD-10), insurers' payment coverage, and claimed treatment details [7]. Detailed information about our protocol to select the study population was provided in Supplementary Methods. In brief, we selected all patients admitted to a hospital via the emergency department and who fulfilled the clinical surveillance definition of septic shock according to Sepsis-3, based on concurrent vasopressors, antibiotics, and blood cultures [8]. To identify patients with cancer, we used the cancer diagnosis codes C00-C97 according to ICD-10 (n = 42,477) (Figure 1). Among these patients, we included those who required RRT owing to AKI during admission and excluded those who were already diagnosed with end-stage renal disease and received RRT within 1 year (n = 5,449). Data on demographics, insurance type, religion, underlying disease, chemotherapy, radiotherapy, presence of neutropenia, and cancer type were collected. Renal recovery was defined as discharge from the hospital without further need for RRT within 1 month. We also collected follow-up data of 1 year from the date of hospitalization, including survival and dialysis dependency. In cases where patients had more than one visit because of septic shock, data collected at the first admission was used. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software for Windows, version 26 (IBM Corp., Armonk, NY, USA). Descriptive statistics were stratified by survival within 1 year (i.e., survivor and non-survivor). Univariate logistic regression model was used to compare recovery (within 1 month) and non-recovery groups. Furthermore, the Cox proportional hazard model with multivariable adjustment was used to compare septic shock survivors within 1-year and death. A P value < 0.05 was considered statistically significant.

Of the 5,449 patients receiving dialysis, 1,060 survived at 30 days. Of these, 826 patients were successfully weaned from dialysis after diagnosis of septic shock, and 234 had a continuous need for dialysis within 1 month after discharge (Supplementary Table S1). There were no differences in age, gender, insurance type, and underlying illness between the recovery and non-recovery groups. Moreover, the proportions of cancer types, including

Abbreviations: AKI, acute kidney injury; ICD-10, International Classification of Disease 10th edition; NHIS, National Health Insurance Service; RRT, renal replacement therapy; SPSS, Statistical Package for the Social Sciences

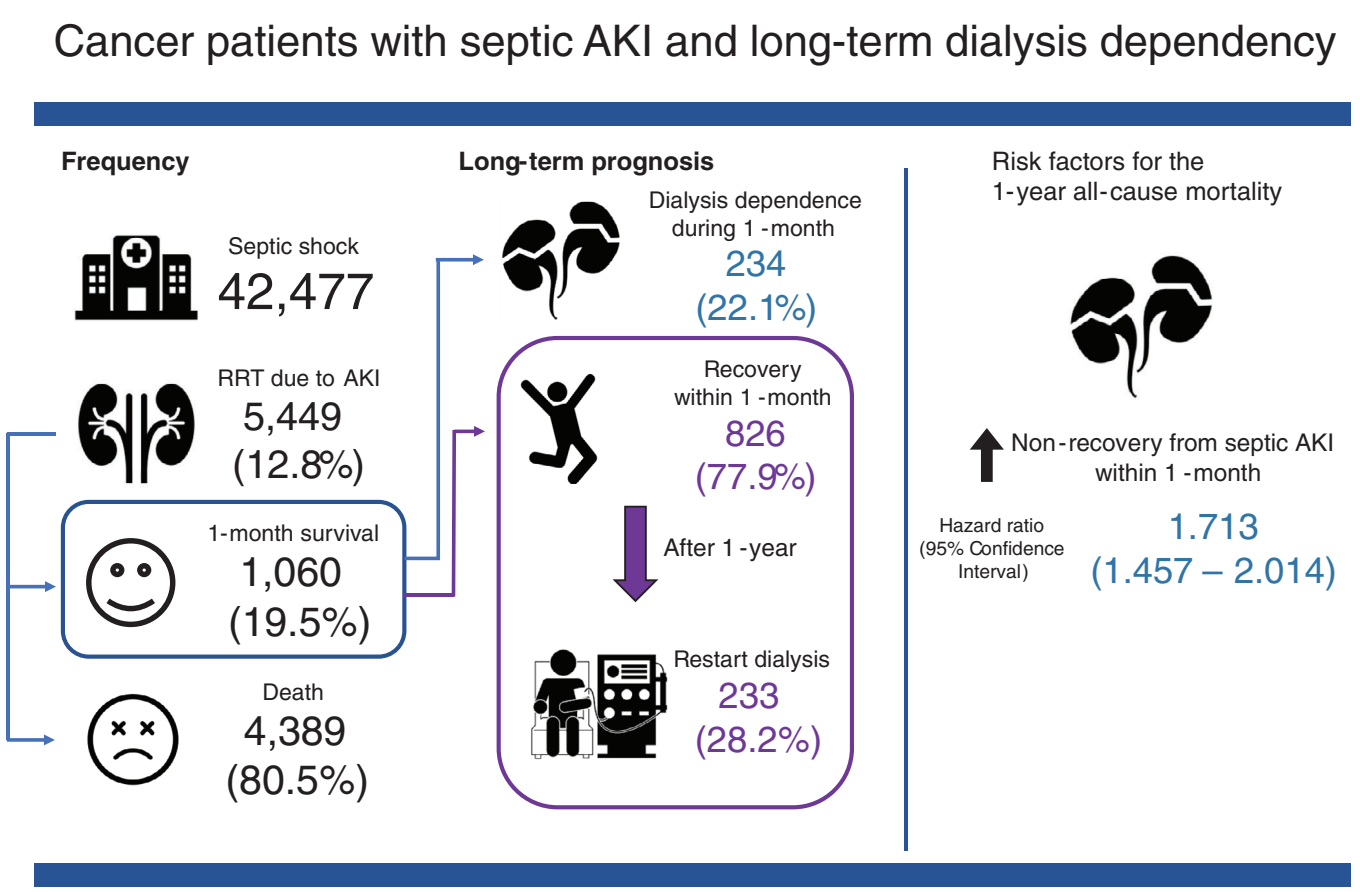

FIGURE 1 Renal recovery, re-dialysis rates, and long-term prognosis of cancer patients with septic shock who received dialysis. AKI, acute kidney injury; RRT, renal replacement therapy

gastric, colorectal, gall bladder, pancreatic, liver, lung cancers, leukemia, and multiple myeloma, were similar between the recovery and non-recovery groups. Meanwhile, receiving chemotherapy was more frequent in patients with renal recovery than in those without recovery (19.6% vs. 12.0%, $P = 0.008$). Among 826 patients who did not require RRT within 1 month, 233 (28.2%) restarted RRT within 1 year (Figure 1).

To compare the potential clinical impacts of each variable, we conducted a multivariate Cox-proportional hazard model. There were no significant differences between 1-year survivors and non-survivors in terms of demographics, underlying disease, presence of neutropenia, chemotherapy, and radiotherapy (Supplementary Table S2). Most types of malignancies, such as gastric, pancreatic, liver, lung cancers, and leukemia showed similar proportions between survivors and non-survivors except colorectal cancer and multiple myeloma. Failure in weaning of dialysis was an independent risk factor for 1-year mortality in the multivariate Cox-proportional hazard model (hazard ratio = 1.713, 95% confidence interval = 1.457–2.014, $P < 0.01$). Among the 826 cancer patients with successful weaning of dialysis, 233 (28.2%) showed dialysis dependency within 1 year.

To our best knowledge, this is the largest study regarding AKI on long-term clinical impact in pooled cancer patients using a nationwide database with high coverage of the Korean population (97%). Our findings could help to give a more comprehensive knowledge of long-term outcomes of septic AKI in cancer patients. However, the Korean NIHS data did not include detailed laboratory data, the cancer stage, performance status, severity of the septic shock, and severity of acute kidney injury. Therefore, it was also not possible to know the cancer stage, baseline performance status, and severity of septic shock. Furthermore, we defined renal recovery by using a 1-month dialysis code, and the recovery rate could have been underestimated because renal function could improve slower than that period.

We found that the non-recovery of renal function was correlated with increased mortality in the cancer cohort with septic shock. Even after recovery from AKI and successful weaning of dialysis at discharge, one-fourth of the patients needed RRT within 1 year. One previous report announced that 82% of critically ill cancer patients with AKI had their renal function recovered and only 6% of patients required long-term RRT [9]. Another study reported chronic RRT dependence in 12.9% of patients with

hematologic malignancies [10]. The different occurrences and outcomes were largely due to the differences in the study population and the proportion of the disease severity.

In conclusion, these findings suggest that physicians should focus on the recovery of renal function during admission, and patients should be followed up carefully even after recovery of AKI.

DECLARATIONS

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This study used data from the NHIS customized health information data (NHIS-2019-1-510), which was provided by the Korean NHIS. The authors alone are responsible for the content and writing of this manuscript.

CONSENT FOR PUBLICATION

Not applicable.

AUTHORS' CONTRIBUTIONS

WYK had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. JSK analyzed the data, wrote and revised the manuscript. YJK collected and analyzed the data.

COMPETING INTERESTS

The authors declare that no competing interests exist.

AVAILABILITY OF DATA

Not applicable.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Institutional Review Board of Asan Medical Center and waived informed consent because of the retrospective study design.

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SUPPORTING INFORMATION

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