Effect of sex on clinical outcomes in COVID-19 patients: a population-based study

Seok Hui Kang

Yeungnam University Medical Center   https://orcid.org/0000-0003-1023-0195

Sang Won Kim

Yeungnam University Medical Center

Jong Won Park

Yeungnam University Medical Center

Jun Young Do

Yeungnam University Medical Center

Kyu Hyang Cho (✉ chokh@yu.ac.kr)

https://orcid.org/0000-0003-4969-4245

Research

Abstract

Background

Previous studies have reported the association between sex and clinical outcomes; however, the most relevant results were obtained as part of analyses evaluating other prognostic factors. This study aimed to evaluate the association between sex and clinical outcomes in patinets with COVID-19 using a population-based dataset.

Methods

This retrospective study utilized claims data from the Health Insurance Review & Assessment Service of Korea. Confirmed patients were included among all participants who underwent COVID-19 testing. Diseases including COVID-19 were defined using International Classification of Diseases, 10th revision (ICD-10). During follow-up, clinical outcomes except death were defined using Electronic Data Interchange or ICD-10 codes from the dataset.

Results

A total of 234,427 patients underwent laboratory testing for COVID-19. Finally, 7327 patients were included; of these, 2964 were men and 4363 were women. The proportions of patients with diabetes mellitus or hypertension as major comorbidities were higher among men than among women of the some age groups, but there were no significant differences in the Charlson comorbidity index score between men and women in same age group. Survival and clinical outcomes including acute kidney injury, the use of inotropes, mechanical ventilator, and cardiac events were greater in men than women. The mortality rate was the highest for the populations aged 50–64 or ≥ 65 years. Subgroup analyses for age, diabetes mellitus, or hypertension showed favorable results for patient survival or clinical outcomes in women compared to men.

Conclusion

Our population-based study showed that female patients with COVID-19 were associated with favorable outcomes, including survival. The impact of sex was more evident in population aged 50–64 or ≥ 65 years.

Introduction

Coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global pandemic. An outbreak of COVID-19 was also experienced in South Korea. As of July 8, 2020, 13,244 patients were confirmed to be positive for SARS-COV-2 infection in South Korea [1]. The

number of deaths among the confirmed cases was approximately 285 (2.2%). Although the number of new confirmed cases has decreased compared to that noted in March 2020, new cases are being confirmed to date. Epidemiologic studies have been published from conturies where the outbreak was noted, and these studies have reported various factors associated with the prognosis of COVID-19 patients.

The first epidemiologic study involving 41 COVID-19 patients reported lower rates for intensive care unit (ICU) care for women than for men; however, the difference was not statistically significant [2]. After the first report, clinical studies with large sample sizes reported a positive association between female sex and favorable prognosis for COVID-19 patients [3–5]. Docherty et al. evaluated 20,133 patients with COVID-19 in the UK and reported that the hazard ratio for female patients was 0.81 compared to male patients [5]. The Global Health 50/50 initiative, using data from > 20 countries, recently reported higher mortality among men than among women [6]. Previous studies have suggested that sex differences in the prognosis of COVID-19 patients may be associated with the difference in the expression of angiotensin-converting enzyme-2 (ACE-2), immune responses, comorbidities, socioeconomic factors, or environmental factors, such as smoking or alcohol consumption [6–8]. However, there were no definite conclusions regarding whether sex differences in COVID-19 patients were associated with undefined etiologies or results of statistical probability. Previous studies have reported the association between sex and clinical outcomes; however, the most relevant results were obtained as part of analyses evaluating other prognostic factors or analyses using aggregated data for sex. A few studies have focused on the association between sex and clinical outcomes as the primary objective. Further epidemiologic data regarding sex differences in COVID-19 patients would aid in to identifying the association between sex and clinical outcomes and in further determining the pathogenesis of the disease or optimal treatment strategies for patients with COVID-19. This study aimed to evaluate the association between sex and clinical outcomes in patinets with COVID-19 using a population-based dataset.

Methods

Data source

This retrospective study utilized claims data from the Health Insurance Review & Assessment Service (HIRA) of Korea. The Korean national healthcare system and the Medical Aid program cover nearly all population residing in South Korea. The HIRA, as a government affiliated orgainzation has nearly all the information about patients' diagnosis, past medical or procedural data. The HIRA recently identified all patients that visited for diagnosis of COVID-19 from February 1, 2020 to May 15, 2020. They merged the data with the claims data during the last 3 years from January 1, 2017 to May 15, 2020. They are providing researchers with merged data after anonymization and de-identification [9]. We conducted a retrospective study using these data. The study was approved by the Institutional Review Board of a medical center (IRB No: YUMC 2020-04-128). The board waived the need for obtaining informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Study population and variables

Confirmed patients were included among all participants who underwent COVID-19 testing. Patients aged <18 years or those had undergone maintenance dialysis were excluded. Baseline characteristics included age, sex, time of diagnosis of COVID-19, and comorbidities. The follow-up duration, death at the time of end-point of follow-up, use of inotropes, conventional oxygen therapy, high flow nasal cannula (HFNC), mechanical ventilation (MV), extracorporeal membrane oxygenation (ECMO), and development of acute kidney injury (AKI), cardiac arrest, myocardial infarction (MI), or acute heart failure (AHF) were assessed after the diagnosis of COVID-19.

Diseases including COVID-19 were defined using International Classification of Diseases, 10th revision, Clinical Modification (ICD-10). COVID-19 patients were defined as patients with diagnostic codes for COVID-19 (B342, B972, Z208, Z290, U18, U181, Z038, Z115, U071, or U072) during COVID-19 epidemics. The presence of comorbidities was evaluated during last 1 year prior to diagnosis of COVID-19 and defined as codes from Quan et al. [10,11]. Finally, Charlson comorbidity index (CCI) score was calculated. During follow-up, clinical outcomes except death were defined using Electronic Data Interchange or ICD codes from HIRA. The codes were as follows: M0040 for conventional oxygen therapy, M0046 for HFNC, M5850 or M5857~M5860 for MV, O1901~O1904 for ECMO, O7031~O7035 or O7051~O7055 for RRT, I10, M5873~M5877, or M5880 for cardiac arrest, I21, I22, I252, M655x~M657x, OA631x~OA639x, OB631x–OB639x, OA641x, OA642x, OA647x, O0161x–O0171x, or O1641x–O1647x for MI, and I110, I130, I132, I255, I420, I425, I428, I429, I43, or I50 for AHF. The use of inotropes was defined as the use of norepinephrine, epinephrine, vasopressin, dopamine, or dobutamine after diagnosis of COVID-19. AKI was defined using dialysis after diagnosis of COVID-19.

Statistical analyses

Data were analyzed using SAS Enterprise Guide version 7.1 (SAS Institute, Cary, NC, USA). Categorical variables are expressed as numbers and percentages, and continuous variables are expressed as mean ± standard deviation. The Pearson χ^2 test or Fisher's exact test was used to analyze categorical variables. For continuous variables, the means were compared using the Student's t-test or one-way analysis of variance, followed by Bonferroni's post-hoc comparison. The survival estimates were calculated using Kaplan-Meier curve and Cox regression analyses. *P*-values for the comparison of survival curves were determined by the log-rank test. Multivariate Cox regression analyses were adjusted for age, sex, CCI score, and hypertension. In addition, logistic regression analyses were performed to evaluate the independent variables for clinical outcomes. $P < 0.05$ was considered to be statistically significant.

Results

Clinical characteristics of the participants

A total of 234,427 patients underwent laboratory testing for COVID-19. Among them, 7590 patients (3.2%) were diagnosed with COVID-19. Participants aged <18 years (n = 249) or those who underwent

maintenance dialysis (n = 14) were excluded. Finally, 7327 patients were included; of these, 2964 were men and 4363 were women (Table 1). The mean age of the men and women was 45.7 ± 19.3 and 47.9 ± 18.7 years, respectively ($P = 0.093$). The peripheral vascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, or any malignancy was higher in women than in men. The incidence of hypertension, hemiplegia, or MI was higher in men than in women. The CCI scores among the men and women were 1.3 ± 1.9 and 1.4 ± 1.9, respectively ($P = 0.039$). The CCI score was slightly higher for women than for men.

Differences in clinical outcomes according to sex

Total death during follow-up was 223 (3.0%). The number of deaths during follow-up in men and women was 120 (4.0%) and 103 (2.4%), respectively ($P < 0.001$). Kaplan-Meier curves showed that men were associated with poor survival in COVID-19 patients ($P < 0.001$; Figure 1). Univariate and mutivariate Cox-regression analyses showed that men had higher mortality risk compared to women (Table 2).

There were 17 (0.6%) men and 10 (0.2%) women who developed AKI ($P = 0.017$; Table 3). The rate of use of inotropes, conventional oxygen therapy, HFNC, MV, cardiac arrest, or MI was greater in men than in women. Multivariate logistic regression analyses showed that the use of inotropes, conventional oxygen therapy, HFNC, MV, AKI, cardiac arrest, or MI had greater odds ratio in men than women (Table 4). ECMO and AHF had greater odds ratio in men than women, but statistical significance was not obtained.

Subgroup analyses according to age, diabetes mellitus, or hypertension

The number of men and women aged <35 years, 35–49 years, 50–64 years, and ≥65 years was 1133 and 1282, 486 and 916, 793 and 1354, and 552 and 811, respectively. In patients aged <35 years, mortality was not obtained among both sexes. In patients aged 35–49 years, the 40-days survival rates were 99.2% and 100% for men and women, respectively ($P = 0.284$). In patients aged 50–64 or ≥65 years, the survival rates were greater for women than for men ($P < 0.001$; Figure S1). Multivariate Cox regression analyses showed favorable results for women in the subgroup analysis according to age (50–64 or ≥65 years), diabetes mellitus (DM), or hypertension (Figure S2).

 Table S1 shows the clinical outcomes according to the age groups. We noted favorable results for the use of inotropes, conventional oxygen therapy, HFNC, MV, and cardiac arrest for women in the 50–64- or ≥65-years age groups. Multivariate logistic regression analyses showed favorable results for women with respect to most complications (except AKI, ECMO, and AHF in the two age groups and MI in the 50–64-years age group) in two age groups (Figure S3). Subgroup analysis for DM showed that most complications (except AKI, ECMO, and AHF in groups with and without DM and MI in group without DM) were associated with favorable results for women. Subgroup analysis for hypertension showed that most complications (except ECMO, MI, and AHF in groups with and without hypertension and AKI in the group with hypertension) were associated with favorable results for women.

Comorbidities according to sex and age

Figure S4 shows the rate of DM or hypertension according to sex and age. The rate of DM in the population aged 50−64 years was higher among men than among women. The rate of hypertension in the populations aged <35, 35−49, or 50−64 years was higher among men than among women. The CCI score was 0.4 ± 0.8 and 0.5 ± 0.8, 0.8 ± 1.4 and 0.9 ± 1.4, 1.6 ± 1.9 and 1.6 ± 1.8, and 3.0 ± 2.5 and 2.9 ± 2.4 in men and women aged <35, 35−46, 50−64, and ≥65 years, respectively. The CCI score increased as age increased, but there were no significant differences in the CCI score between men and women in same age group.

Discussion

Our results were analyzed using population-based data in South Korea. The number of COVID-19 patients was greater in women than men. Baseline CCI score was greater in women than men. However, survival and clinical outcomes including AKI, the use of inotropes, conventional oxygen therapy, HFNC, MV, and cardiac events were greater in men than women. The mortality rate was the highest for the populations aged 50−64 or ≥65 years. Subgroup analyses for age, DM, or hypertension showed favorable results for patient survival or clinical outcomes in women compared to men. The proportions of patients with DM or hypertension as major comorbidities were higher among men than among women of the some age groups; however, there were no significant differences in patients aged ≥65 years at a high risk of mortality. In addition, CCI score was similar between two sexes in all age groups.

Previous studies have reported that male patients with COVID-19 had poorer outcomes compared to female patients [3-6]. The favorable outcomes in women would be hypothesized by several issues. First, high expressions of ACE-2 and transmembrane serine protease-2 (TMPRSS2) in men, compared to women, would be associated with poor outcome in COVID-19. The ACE-2 is expressed in various tissues including cardiovascular system, kidney, or lung and SARS-CoV-2 enters the cell through ACE-2. Liu et al. investigated an experimental study using gonadectomized mice with or without estrogen therapy and showed that the expression of renal ACE-2 was decreased by estrogen therapy [12]. Stelzig et al. showed that estrogen was associated with low expression in human bronchial epithelial cells [13]. TMPRSS2 is a critical protease associated with viral spread through cleavage of spike protein of SARS-CoV-2 [14]. Expression of TMPRSS2 would be associated with activity of androgen receptor, which may lead to high expression of TMPRSS2 in men. Therefore, difference in ACE-2 and TMPRSS2 between sexes may be associated with severity or prognosis of COVID-19 patients. However, there were few studies regarding differences in two enzymes by sex and the impact of clinical outcomes.

Second, sex differences in innate or humoral immunities after viral infection may be associated with severity in COVID-19. Although there were few clinical data for sex difference in immunity after COVID-19, previous data for response to other viral infection, vaccines, or autoimmunity suggested that immune responses to COVID-19 may be different between sexes. Women generally have greater antibody production response to viral infection, which is associated with estrogen effect or inherent difference in B cell response after infection [7,15]. In addition, there were evidences for sex differences in cytokine production or gene expression in innate cell subsets [7]. Previous studies showed that women are

associated with more stimulation in toll-like receptor-7 and interferon production after viral infection compared to men [16,17]. These differences may lead to different response for removal of virus, which result in sex difference for severity or mortality in COVID-19 patients.

Third, comorbidities caused by sex or gender related factors may influence the difference. To date, there were few data regarding the different comorbidities according to sex, using disaggregated data of men or women COVID-19 patients. We compared the proportion of patients with DM or hypertension according to sex and age groups. Our study showed higher prevalence in men in DM for 50–64 age group and hypertension for <35, 35–49, or 50–64 age groups than women, but ≥65 age group with highest mortality had no difference in DM and hypertension. In addition, CCI score as merged indicator was not different between two sexes. Both analyses using aggregated data and subgroup analyses for DM, hypertension, or age groups showed mostly favorable results in women. These reveal that comorbidities are associated with clinical outcomes in COVID-19 patients in both sexes, but difference of underlying comorbidities may not lead to sex difference in clinical outcomes in COVID-19 patients.

In our study, clinical outcomes were poor in men, but incidence rate was higher in women than in men. According to Korean Statistical Information Service in May 2020, the numbers of men and women in South Korea were 25,856,030 and 25,985,341, respectively. The incidence rate in men and women was approximately 0.0115% and 0.0168%, respectively [18]. World Health Organization merged each disaggregated data and reported that the distribution of infection between women and men is relatively similar [19]. Global Health 50/50 research initiatives also presented that 55 among 92 countries identifiable with incidence by sex had male predominance [6]. In our study, it is not clear whether female dominance in COVID-19 infection is associated with biological effect or gender-related factors. Considering male predominance from biological data, gender related factors such as life style, socioeconomic status, or religious gathering may have greater influence on female predominance in South Korea. Besides biologic factors, gender related factors were also important to incidence or prognosis in COVID-19 [20]. Alcohol intake or number of cigarettes smoked was generally greater in men than in women, which may be another leading to sex differences the clinical outcomes [21].

Our study has several limitations. First, our study was performed using health insurance claims with procedural or diagnostic codes from HIRA. Therefore, our study did not include laboratory or clinical data. The dataset has the possibility of over or undercoding, which may lead to discrepancies between the relevant code and actual diseaset. Second, our study did not identify the causal relationship by sex. Our study analyzed insurance data alone and did not include data for biologic effects such as ACE2, TMPRSS2 levels, or data for immunologic status. In addition, gender related factors were not included. Therefore, we revealed that men had poor clinical outcomes compared to women, especially elderly. However, we could not identify the cause of sex difference in COVID-19. Third, we did not present sex difference in young population. In our study, the populations aged <35 years or 35–49 years had better outcomes compared to those aged 50–64 years or ≥65 years. We did not perform analyses beyond simple descriptive analysis results for the young population.

In conclusion, our population-based study showed that female patients with COVID-19 were associated with favorable outcomes, including survival. The impact of sex was more evident in population aged 50–64 or ≥65 years. Further studies, including laboratory investigations or evaluation of sex-related factors, are required to identify the causal relationship and impact of sex in the young population.

Perspectives and significance

Previous studies have reported the association between sex and clinical outcomes; however, the most relevant results were obtained as part of analyses evaluating other prognostic factors or analyses using aggregated data for sex. Our population-based study shows that female patients with COVID-19 were associated with favorable outcomes, including survival. The impact of sex was more evident in population aged 50–64 or ≥65 years at a high risk of mortality and two age groups had no difference in comorbidities. Both analyses using aggregated data and subgroup analyses for DM, hypertension, or age groups showed mostly favorable results in women. These reveal that comorbidities are associated with clinical outcomes in COVID-19 patients in both sexes, but difference of underlying comorbidities may not lead to sex difference in clinical outcomes in COVID-19 patients.

Declarations

Ethics approval and consent to participate:

The study was approved by the Institutional Review Board of a medical center (IRB No: YUMC 2020-04-128). The board waived the need for obtaining informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent for publication:

Not applicable

Availability of data and materials:

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests:

The authors have declared that no competing interests exist.

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Authors' contributions:

S.H.K and K.H.C conceived and planned the study. S.H.K and S.W.K identified and obtained the data for this analysis. S.H.K, S.W.K, and J.Y.D extracted, and processed the data. S.W.K and J.W.P carried out the statistical analyses. S.H.K wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline characteristics of the participants

	Total (n = 7327)	Men (n = 2964)	Women (n = 4363)	P-value
Age (years)	47.0 ± 19.0	45.7 ± 19.3	47.9 ± 18.7	0.093
Follow-up duration (days)	20.9 ± 13.1	21.0 ± 13.3	20.7 ± 13.0	0.254
Myocardial infarction	97 (1.32%)	58 (2.2%)	39 (0.9%)	<0.001
Congestive heart failure	292 (3.99%)	128 (4.3%)	164 (3.8%)	0.229
Peripheral vascular disease	570 (7.78%)	206 (7.0%)	364 (8.3%)	0.029
Cerebrovascular disease	518 (7.07%)	218 (7.4%)	300 (6.9%)	0.433
Dementia	443 (6.05%)	151 (5.1%)	292 (6.7%)	0.005
Chronic pulmonary disease	1670 (22.79%)	609 (20.5%)	1061 (24.3%)	<0.001
Connective tissue disease	268 (3.66%)	80 (2.7%)	188 (4.1%)	<0.001
Peptic ulcer disease	1099 (15.00%)	387 (13.1%)	712 (16.3%)	<0.001
Mild liver disease	1540 (21.02%)	606 (20.4%)	934 (21.4%)	0.321
Diabetes mellitus	1223 (16.7%)	515 (17.4%)	708 (16.2%)	0.196
Hemiplegia	99 (1.35%)	50 (1.7%)	49 (1.1%)	0.040
Any malignancy	358 (4.89%)	126 (4.3%)	232 (5.3%)	0.038
Moderate to severe liver disease	9 (0.12%)	5 (0.2%)	4 (0.1%)	0.356
Metastatic tumor	33 (0.45%)	11 (0.4%)	22 (0.5%)	0.404
Acquired immune deficieny syndrome	5 (0.07%)	3 (0.1%)	2 (0.04%)	0.373
Hypertension	1559 (21.28%)	673 (22.7%)	886 (20.3%)	0.014

Data are expressed as number (percentage) for categorical variables and mean ± standard deviation for continuous variables. The P-values for continuous variables were tested with the Student's t-test between men and women, and the Pearson χ^2 test or Fisher exact test was used to analyze categorical variables.

Table 2. Cox regression analysis of survival according to the variables

	Univariate		Multivariate	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age (per increase 1 year)	1.11 (1.10–1.12)	<0.001	1.10 (1.09–1.11)	<0.001
Sex (ref: women)	1.69 (1.30–2.20)	<0.001	2.06 (1.58–2.69)	<0.001
CCI score (per increase 1 score)	1.35 (1.30–1.39)	<0.001	1.14 (1.09–1.20)	<0.001
Hypertension	8.20 (6.11–11.01)	<0.001	1.34 (0.97–1.86)	0.079

The data are expressed as HR (95% CI). Multivariate analysis was adjusted for age, sex, CCI score, and hypertension.

Abbreviations: CCI, Charlson comorbidity index; HR, hazard ratio; CI, confidence interval

Table 3. Clinical outcomes according to sex

	Total	Men	Women	*P*-value
Acute kidney injury	27 (0.4%)	17 (0.6%)	10 (0.2%)	0.017
Inotropics	182 (2.5%)	100 (3.4%)	82 (1.9%)	<0.001
Conventional oxygen therapy	901 (12.3%)	429 (14.5%)	472 (10.8%)	<0.001
High flow nasal cannula	178 (2.4%)	101 (3.8%)	77 (1.8%)	<0.001
Mechanical ventilation	123 (1.7%)	71 (2.4%)	52 (1.2%)	<0.001
Extracorporeal membrane oxygenation	20 (0.3%)	11 (0.4%)	9 (0.2%)	0.184
Cardiac arrest	42 (0.6%)	29 (1.0%)	13 (0.3%)	<0.001
Myocardial infarction	256 (3.5%)	122 (4.1%)	134 (3.1%)	0.017
Acute heart failure	380 (5.2%)	157 (5.3%)	223 (5.1%)	0.725

The data are expressed as number (percentage).

Table 4. Logistic regression analysis of the clinical outcomes according to sex

	Univariate		Multivariate	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Inotropics				
Age (per increase 1 year)	1.08 (1.07–1.09)	<0.001	1.06 (1.05–1.08)	<0.001
Sex (ref: men)	1.82 (1.36–2.46)	<0.001	2.09 (1.53–2.85)	<0.001
CCI score (per increase 1 score)	1.42 (1.35–1.49)	<0.001	1.17 (1.10–1.24)	<0.001
Hypertension	7.68 (5.64–10.54)	<0.001	1.66 (1.15–2.42)	0.007
Conventional oxygen therapy				
Age (per increase 1 year)	1.08 (1.07–1.08)	<0.001	1.07 (1.06–1.07)	<0.001
Sex (ref: men)	1.40 (1.21–1.61)	<0.001	1.67 (1.43–1.96)	<0.001
CCI score (per increase 1 score)	1.41 (1.36–1.45)	<0.001	1.11 (1.07–1.15)	<0.001
Hypertension	5.44 (4.70–6.29)	<0.001	1.31 (1.09–1.57)	0.004
HFNC				
Age (per increase 1 year)	1.08 (1.07–1.10)	<0.001	1.07 (1.06–1.09)	<0.001
Sex (ref: men)	1.96 (1.46–2.66)	<0.001	2.32 (1.70–3.19)	<0.001
CCI score (per increase 1 score)	1.38 (1.32–1.45)	<0.001	1.12 (1.05–1.19)	<0.001
Hypertension	7.40 (5.43–10.18)	<0.001	1.55 (1.08–2.26)	0.020
Mechanical ventilation				
Age (per increase 1 year)	1.07 (1.06–1.08)	<0.001	1.06 (1.04–1.07)	<0.001
Sex (ref: men)	2.04 (1.44–2.93)	<0.001	2.28 (1.57–3.31)	<0.001
CCI score (per increase 1 score)	1.34 (1.27–1.42)	<0.001	1.10 (1.01–1.18)	0.020
Hypertension	7.47 (5.16–10.98)	<0.001	2.01 (1.29–3.17)	0.002
ECMO				
Age (per increase 1 year)	1.05 (1.03–1.08)	<0.001	1.03 (0.98–1.06)	0.083
Sex (ref: men)	1.80 (0.75–4.48)	0.191	1.84 (0.76–4.59)	0.179
CCI score (per increase 1 score)	1.30 (1.13–1.47)	<0.001	1.11 (0.91–1.31)	0.280
Hypertension	6.92 (2.83–18.44)	<0.001	2.89 (0.95–9.50)	0.068
Acute kidney injury				
Age (per increase 1 year)	1.06 (1.04–1.09)	<0.001	1.03 (1.01–1.06)	0.023

Sex (ref: men)	2.51 (1.17–5.70)	0.021	2.58 (1.19–5.89)	0.019
CCI score (per increase 1 score)	1.39 (1.25–1.53)	<0.001	1.21 (1.05–1.37)	0.006
Hypertension	8.88 (4.02–21.57)	<0.001	2.65 (1.01–7.58)	0.057
Cardiac arrest				
Age (per increase 1 year)	1.08 (1.06–1.10)	<0.001	1.06 (1.04–1.09)	<0.001
Sex (ref: men)	3.31 (1.75–6.59)	<0.001	3.66 (1.92–7.35)	<0.001
CCI score (per increase 1 score)	1.43 (1.31–1.55)	<0.001	1.24 (1.11–1.38)	<0.001
Hypertension	6.58 (3.64–13.05)	<0.001	1.21 (0.58–2.61)	0.613
Myocardial infarction				
Age (per increase 1 year)	1.01 (1.00–1.02)	0.013	1.00 (0.99–1.01)	0.535
Sex (ref: men)	1.36 (1.06–1.74)	0.017	1.37 (1.07–1.76)	0.014
CCI score (per increase 1 score)	1.13 (1.07–1.19)	<0.001	1.11 (1.05–1.19)	<0.001
Hypertension	1.38 (1.04–1.82)	0.025	0.98 (0.69–1.39)	0.906
Acute heart failure				
Age (per increase 1 year)	1.04 (1.03–1.04)	<0.001	1.03 (1.03–1.04)	<0.001
Sex (ref: men)	1.04 (0.84–1.28)	0.724	1.10 (0.89–1.36)	0.397
CCI score (per increase 1 score)	1.21 (1.16–1.26)	<0.001	1.05 (0.99–1.10)	0.082
Hypertension	2.82 (2.28–3.48)	<0.001	1.27 (0.98–1.65)	0.075

The data are expressed as OR (95% CI). Multivariate analysis was adjusted for age, sex, CCI score, and hypertension.

Abbreviations: OR, odds ratio; CI, confidence interval; HFNC, high flow nasal cannula; ECMO, extracorporeal membrane oxygenation; CCI, Charlson comorbidity index
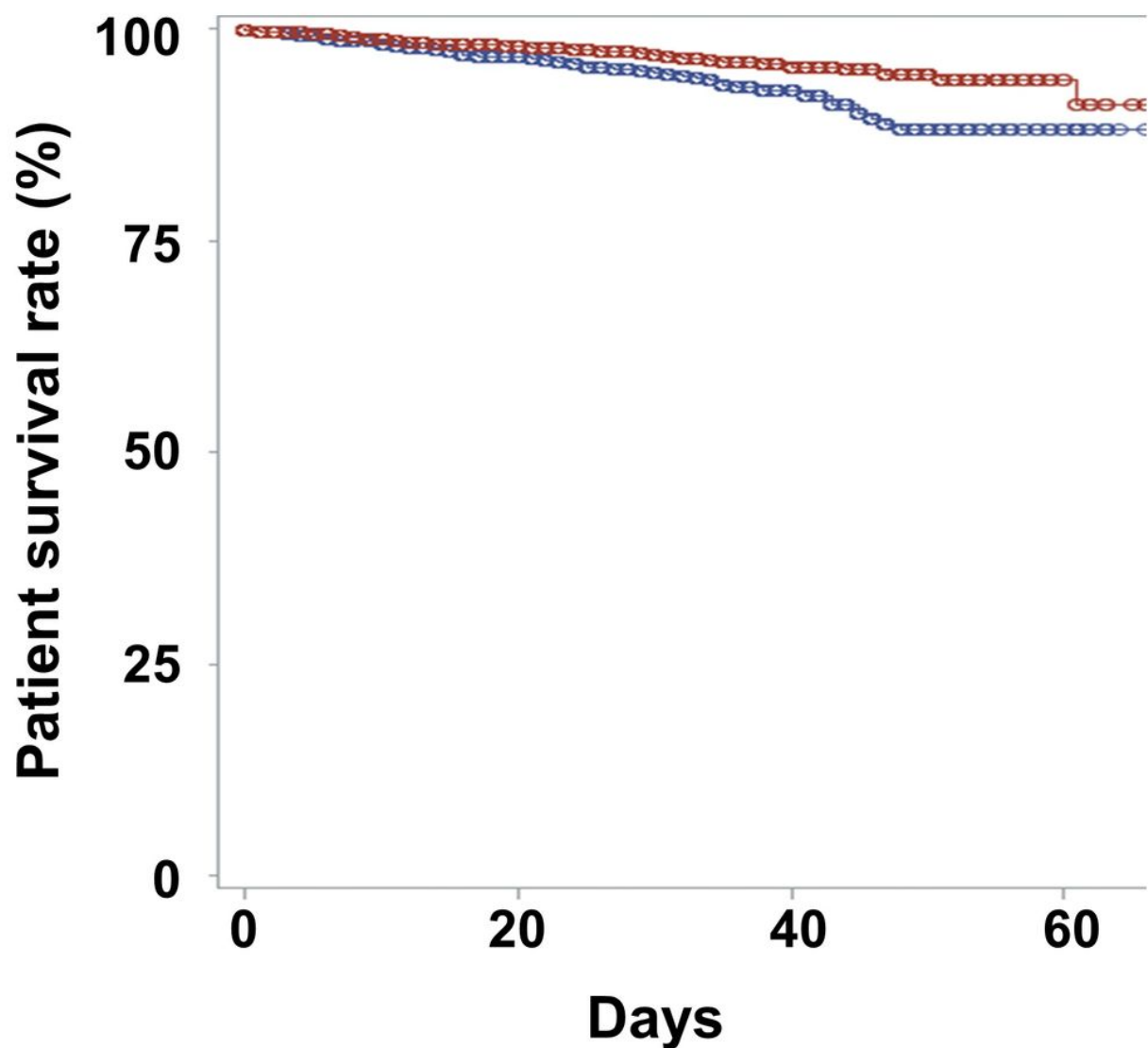
Figures

Figure 1

Kaplan-Meier survival curves according to sex. The blue line shows the 1 survival graph for men and the red line shows the graph for women. The circle reveals the censored point. The 20-day survival rates for men and women were 96.6% and 97.9%, respectively (P < 0.001). The 40-day survival rates for men and women were 92.8% and 95.5%, respectively.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarymaterial.doc