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Is There Any Interaction Between Sex and Renal Function Change During Hospital Stay in Patients Hospitalized With Acute Heart Failure?

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ABSTRACT

Background: Renal dysfunction is a strong predictor of outcomes in patients with acute heart failure (AHF). However, less is known about how sex may influence the prognostic import of renal function in AHF.

Methods and Results: In a post hoc analysis of the ASCEND-HF trial including 5377 patients with AHF (33% female), patients were categorized into 3 groups based on the changes in renal function during their hospital stay. Worsening, stable, and improving renal functions were defined as a ≥20% decrease, a <20% change, and a ≥20% increase in the estimated glomerular filtration rate, respectively. The primary outcome was the composite of 30-day all-cause mortality or HF rehospitalization. The median baseline and discharge estimated glomerular filtration rate were 58.4 and 56.9 mL/min/1.73 m^2, respectively. Worsening, stable, and improving renal function was observed in 31.9%, 63.2, and 4.9% of patients, respectively. Worsening renal function was associated with adverse outcomes at 30 days (adjusted hazard ratio [aHR] 1.47, 95% confidence interval [CI] 1.22−1.76). This association existed in both males and females (aHR 1.42 and aHR 1.56, respectively, both $P < .01$). There was an interaction between renal function changes and sex ($P = .025$), because improving renal function was associated with better outcomes in men (aHR 0.29, 95% CI 0.13−0.66) as compared with women (aHR 1.18, 95% CI 0.59−2.35). There was no interaction between the ejection fraction and renal function in association with subsequent outcomes.

Conclusions: Irrespective of sex, worsening renal function was associated with poorer outcomes at 30 days in patients with AHF. More studies are warranted to further delineate the possible sex differences in this setting. (*J Cardiac Fail 2021;27:934−941*)

Key Words: Acute heart failure, renal function, sex differences, clinical outcomes.

Lay summary

Patients with acute heart failure are at an increased risk of adverse events and, among them, those with impaired kidney function experience poorer outcomes. However, it is not clear how changes in renal function during hospital stay are linked to outcomes and how sex influences that relationship. In the current study, regardless of sex and patient's heart function, worsening renal function was associated with poorer outcomes at 30 days. Also, improved renal function during the hospital stay was associated with better outcomes in men, but not in women. More studies are needed to further explore the possible sex differences in this setting.

One million people develop heart failure (HF) globally each year.[1] Its overall prevalence is estimated to be around 2%−3% and is still increasing because of the aging population and longer life expectancies.[2] Patients with acute HF (AHF) tend to have poor outcomes,[3] especially when accompanied by renal dysfunction, possibly owing to shared cardiovascular risk factors and other factors.

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Previous studies have shown differences in survival between patients with AHF with reduced versus preserved renal function, highlighting the importance of baseline renal function.[4] This difference is present in both HF with preserved ejection fraction (HFpEF) and HF with reduced EF (HFrEF),[5,6] and there are important sex differences that may exist in patients with HFpEF or HFrEF, with women having a higher likelihood of HFpEF, nonischemic etiologies, more severe symptoms, and more comorbidities. Furthermore, during hospitalization for AHF, renal function can improve, remain stable, or worsen, which may affect the subsequent outcomes in these patients.[4] Recently, sex differences have been reported regarding the patient phenotypes and outcomes of patients with HF,[7,8] but it remains unclear whether sex may modify the relationship between renal function changes and outcomes in AHF.

Hence, we investigated the interaction between sex and renal function (and changes in renal function) across the spectrum of EF to explore the relationship to clinical outcomes in patients hospitalized with AHF.

Methods

Study Population

This study is a post hoc secondary analysis of data from the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF; www.clinicaltrials.govNCT00475852). ASCEND-HF was a randomized, double-blind, placebo-controlled trial that enrolled a total of 7141 patients hospitalized for AHF from 398 centers between May 2007 and August 2010 to evaluate the impact of nesiritide infusion in AHF. The rationale and design of this trial have been published previously.[9] Ethics approval was granted by the institutional review board at each participating site, and all participants provided written informed consent. Clinical characteristics and laboratory and echocardiographic data were recorded prospectively at admission and sex status was self-reported. The study groups were similar and balanced in all respects.[10,11] Importantly, ASCEND-HF found that nesiritide did not differ from placebo in terms of death or rehospitalization rates or changes in renal function.

Renal Function Definitions

For this study, patients who had a serum creatinine level measured at baseline (within 2 hours of randomization), and at least once later before discharge, were included. Patients were excluded if creatinine observations were >884 μmol/L (10 mg/dL) or <10 μmol/L (approximately 0.1 mg/dL). The Chronic Kidney Disease Epidemiology Collaboration equation was used to calculate the estimated glomerular filtration rate (eGFR) based on serum creatinine. Using the baseline and peak creatinine measurements, the changes in renal function over hospital stay were categorized into 3 groups. Worsening, improving, and stable renal functions were defined as a ≥20% decrease, a ≥20% increase, and a <20% change in the GFR, respectively.[4] The peak creatinine reflects the worst renal function during the hospital stay.[4]

Other Covariate Definitions

Based on their left ventricular EF (LVEF) at baseline, patients were classified into HFpEF (LVEF of ≥40%) or HFrEF (LVEF of <40%) subgroups. Based on medical history collected through the ASCEND-HF case report forms, we evaluated the Charlson comorbidity index, which is a method of assessing the burden of comorbidities and is shown to be linked to mortality or resource use.

End Points

The primary end point was the composite of 30-day all-cause mortality or HF rehospitalization from randomization. The secondary end point of interest was 180-day mortality.

Statistical Analysis

Patient characteristics, including demographics, comorbidities, baseline renal function, baseline LVEF, and HF therapy were compared between different sexes. For continuous variables, the data were presented as mean and standard deviation if normally distributed, and as median with interquartile range (IQR) if non-normally distributed. The categorical variables were presented as frequencies and percentages. Event rates at 30-day composite end point and 180-days all-cause mortality were presented using percentages. Survival analysis was performed with Kaplan-Meier curves and log-rank tests to compare survival curves across categories of renal function status and HF subtypes. The issue of censoring was dealt with using the Kaplan-Meier curves and Cox proportional hazard models. For the primary analysis, the main variables were grouped and analyzed categorically as worsening, stable, or improving renal function (change in renal function), HFrEF or HFpEF (LVEF), and male or female (sex). For univariate and multivariable analysis, Cox proportional hazard regression modelling was generated to assess the association between main variables and the composite end point of the 30-day mortality or rehospitalization. The multivariable analysis was adjusted for age, baseline eGFR, and Charlson comorbidity index, which had been selected a priori for possible confounding roles. To investigate the association between the main variables for the secondary end point of 180-day mortality, similar tests were performed. To evaluate if the sex and the LVEF modify the association between renal function and adverse outcomes, the Cox proportional hazard regression model was used to assess the 2- and 3-way interactions.

The database was stratified by sex, to further assess the difference between the association of renal function and outcome in the female and male populations separately (ie, to see if sex was an effect modifier). For all outcomes and

covariables, hazard ratios (HR), 95% confidence intervals (CI) and *P* values were determined. To account for the potential confounding effect of congestion, in a sensitivity analysis we also adjusted for the congestion score, which was previously developed using the ASCEND-HF data and incorporates the 3 elements of orthopnea, pedal edema, and N-terminal pro-brain natriuretic peptide levels measured between 48 and 72 hours after admission.[12] As another sensitivity analysis, we assessed the association between the change of renal function from admission to discharge (instead of admission-to-peak changes) and clinical outcomes. Moreover, the association between change in renal function as a continuous variable and clinical outcomes was evaluated. Two-sided α-levels of <0.05 were considered statistically significant. Statistical analysis was performed using R version 4.0.0.[13]

Results

Patient Population

A total of 7141 patients underwent randomization; of these, 7007 received the study drug and were included in the modified intention to treat analysis of the ASCEND-HF study. As shown in Supplementary Fig. 1, 6620 patients had measurements of baseline creatinine plus ≥ 1 other creatinine test before discharge. After removal of the 3 patients with outlier creatinine levels, 6617 patients were left, of whom 5377 patients also had an available LVEF measurement. This cohort consisted of 3607 males (67.1%) and 1770 females (32.9%).

Baseline Characteristics

Men were younger with more coronary artery disease as a comorbidity, and women were older, with more hypertension and diabetes as comorbidities (Table 1). In addition, the median LVEF was higher for the female population (30.5%) than the male population (27.0%) (Fig. 1). Patients had a median number of 4 (IQR 3−4) creatinine measurements during hospital stay. The median time to first creatinine was 3.2 hours (IQR 1.0−16.8) and median time to peak creatinine was 2.3 days (IQR 1.6−4.4). The median eGFR on admission was lower for females (53.4 ml/min/1.73 m^2) than for males (61.0 ml/min/1.73 m^2). There was a greater baseline-to-peak change of eGFR in women than that in men. As shown in Table 2, the majority of patients (63.2%) had stable renal function, whereas 31.9% had worsening renal function and 4.9% had improving renal function.

Clinical Outcomes

The composite end point occurred in 9.7% at 30 days (Table 3): 3.4% all-cause mortality and 6.5% HF rehospitalization. In the worsening renal function group, the composite end point occurred in 11.3% of men and 12.4% of women. In those with stable renal function, the composite end point was 9.1% in males and 8.7% in females. Numerically few composite end points occurred in the improving

Table 1. Patient Characteristics Among Different Sexes

	Male	Female	*P* Value
No. of patients	3607 (67.1%)	1770 (32.9%)	
Median age, years [IQR]	64 [55 to 74]	69 [59 to 78]	<.001
Race, *n* (%)			<.001
American Indian/ Alaska native	92 (2.6)	68 (3.8)	
Asian	1008 (27.9)	488 (27.6)	
Black or African American	507 (14.1)	327 (18.5)	
Multiple	4 (0.1)	4 (0.2)	
Pacific islander	14 (0.4)	5 (0.3)	
White	1981 (54.9)	878 (49.6)	
Missing	1 (0.0)	0 (0.0)	
Medical history			
Hypertension, *n* (%)	2506 (69.5)	1345 (76.0)	<.001
Diabetes mellitus, *n* (%)	1520 (42.1)	824 (46.6)	.002
Hyperlipidemia, *n* (%)	1605 (44.5)	740 (41.8)	.06
Coronary artery disease, *n* (%)	2031 (56.3)	865 (48.9)	<.001
CABG, *n* (%)	823 (22.8)	241 (13.6)	<.001
PCI, *n* (%)	676 (18.7)	278 (15.7)	.007
Peripheral vascular disease, *n* (%)	409 (11.3)	174 (9.8)	.10
Atrial fibrillation, *n* (%)	1340 (37.1)	642 (36.3)	.55
Chronic renal failure, *n* (%)	587 (16.3)	318 (18.0)	.13
Dialysis, *n* (%)	41 (1.1)	18 (1.0)	.79
Cancer, *n* (%)	154 (4.3)	48 (2.7)	.006
Depression, *n* (%)	267 (7.4)	171 (9.7)	.005
Alcohol, *n* (%)	457 (12.7)	35 (2.0)	<.001
Smoking, *n* (%)	611 (16.9)	126 (7.1)	<.001
Median Charlson Comorbidity Index [IQR]	3 [2 to 4]	3 [2 to 4]	<.001
Median Congestion score [IQR]	4 [3 to 5]	4 [3 to 5]	.68
Heart function			
Baseline reduced, *n* EF (%)	3026 (83.9)	1201 (67.9)	<.001
Median baseline EF% [IQR]	27.0 [20.0 to 35.0]	30.5 [25.0 to 45.0]	<.001
Renal function			
Median baseline creatinine, μmol/L [IQR]	114.9 [97.2 to 143.2]	97.2 [79.5 to 130.6]	<.001
Baseline creatinine >176.8 μmol/L (>2 mg/dL), *n* (%)	438 (12.1)	153 (8.6)	<.001
Median baseline eGFR [IQR]	61.0 [45.9 to 76.7]	53.4 [39.3 to 69.5]	<.001
Baseline eGFR <45 mL/min, *n* (%)	852 (23.6)	610 (34.5)	<.001
Baseline eGFR ≥60 mL/ min/1.73 m^2, *n* (%)	1859 (51.5)	679 (38.3)	<.001
Median absolute change in eGFR to discharge [IQR]	0.0 [−9.0 to 6.8]	−2.6 [−10.5 to 4.0]	<.001
Median absolute change in eGFR to peak creatinine [IQR]	−5.7 [−13.8 to 0.0]	−6.9 [−15.0 to −0.2]	<.001
Improved renal function, *n* (%)	185 (5.1)	81 (4.6)	<.001
Stable renal function, *n* (%)	2384 (66.1)	1013 (57.2)	<.001
Worsened renal function, *n* (%)	1038 (28.8)	676 (38.2)	<.001
Median relative baseline to peak change in eGFR % [IQR]	−9.7% (−21.9 to 0)	−14.3% (−27.3 to −0.7)	<.001

CABG, coronary artery bypass graft; EF, ejection fraction; eGFR, estimated glomerular filtration rate; IQR, interquartile range; PCI, percutaneous coronary intervention.

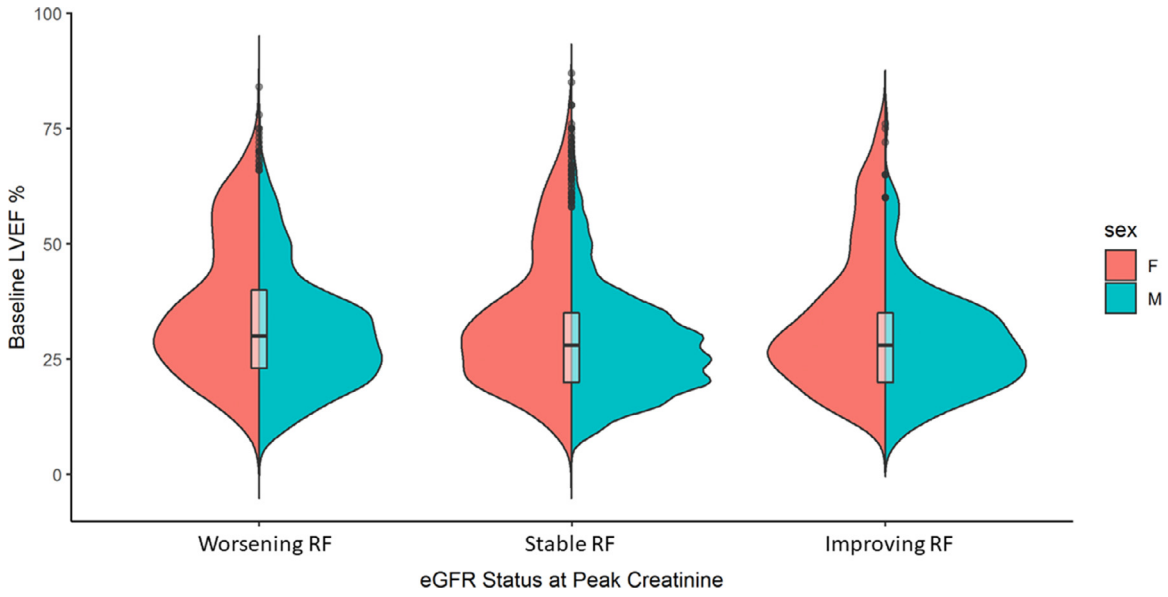

Fig. 1. Distribution of patients based on sex, baseline LVEF, and baseline to peak eGFR change. eGFR, estimated glomerular filtration rate; F, female; IRF, improving renal function; LVEF, left ventricular ejection fraction; M, male; RF, renal function; SRF, stable renal function; WRF, worsening renal function.

renal function group (3.2% of men and 11.1% of women). The 180-day mortality rate was 13.2% in the worsening renal function, 11.8% in the stable renal function, and 10.9% in the improving renal function group.

Compared with those with stable and improving renal function, patients with worsening renal function had higher risk of the primary (Supplementary Fig. 2) and secondary outcomes. Among patients who had worsening renal function, those with HFrEF had a lower survival compared with those with HFpEF. Similar findings were observed between men and women in terms of the higher risk of primary and secondary outcomes in patients with worsening renal function (Fig. 2 and Supplementary Fig. 3).

Table 2. Patient Distribution for Renal Function Status and EF Status Groups

	EF Status				Total	
	Reduced EF		Preserved EF		No. of Patients	
	n	%*	*n*	%*	*n*	%*
Worsened renal function	1250	72.9	464	27.1	1714	31.9†
Male	823	79.3	215	20.7	1038	60.5
Female	427	63.2	249	36.8	676	39.5
Stable renal function	2756	81.1	641	18.9	3397	63.2*
Male	2038	85.5	346	14.5	2384	70.2
Female	718	70.9	295	29.1	1013	29.8
Improved renal function	221	83.1	45	16.9	266	4.9*
Male	165	89.2	20	10.9	185	69.5
Female	56	69.1	25	30.9	81	30.5

Abbreviations as in Table 1.

*Percentages derived from the total number of patients in the renal function status groups.

†Percentages derived from the total number of patients in the cohort (5377).

Multivariable Analyses

Overall, the Cox proportional hazard analyses (Supplementary Table 1) showed higher and lower rates of outcomes, respectively, in patients with worsening and improving renal function, compared with those with stable renal function. In a multivariable analysis, patients with worsening renal function had a higher likelihood for the 30-day composite end point of all-cause mortality and HF rehospitalization with a 47% increased risk (adjusted HR [aHR] 1.47, 95% CI 1.22−1.76), whereas the improving renal function group had a 46% lower likelihood (aHR 0.54, 95% CI 0.32−0.91). For our secondary end point, patients with worsening renal function had a 20% increased risk of 180-day mortality compared with those with stable renal function (aHR 1.20, 95% CI 1.02−1.42).

In the Cox proportional hazard model for the interactions (Supplementary Table 2) between renal function, EF, and sex, a 2-way interaction with clinical outcomes at 30 days was observed for renal function and sex ($P = .025$). The outcomes for males (compared with females) for improving renal function (HR 0.23, 95% CI 0.08−0.69) were better, whereas in the worsening renal function group, men and women had no difference in the composite end point. There were no interactions between either renal function and EF status or EF status and sex and outcomes. Moreover, the 3-way interaction yielded no statistically significant results ($P > .05$ for all).

Stratified Analysis

Because the 2-way interaction was significant for renal function and sex, further analyses stratified by sex (Table 4) were performed. Both males and females with worsening renal function exhibited increased risk of adverse outcomes

Table 3. Number of Events per Renal Function Status Group for the Primary and Secondary End Points

	Worsened Renal Function ($n = 1714$)		Stable Renal Function ($n = 3397$)		Improved Renal Function ($n = 266$)		Total	
	No. of events	%	No. of events	%	No. of events	%	No. of events	%
At 30 days								
Composite end point*	201	11.7	304	8.9	15	5.6	520	9.7
Male†	117	11.3	216	9.1	6	3.2	339	9.4
Female‡	84	12.4	88	8.7	9	11.1	181	10.2
All-cause mortality*	83	4.8	93	2.7	5	1.9	181	3.4
Male†	49	4.7	64	2.3	2	1.1	115	3.4
Female‡	34	5.0	29	2.9	3	3.7	66	3.7
HF Rehospitalization*	120	7.0	217	6.4	11	4.1	348	6.5
Male†	70	6.7	155	6.5	4	2.2	229	6.3
Female‡	50	7.4	62	6.1	7	8.6	119	6.7
At 180 days								
All-cause mortality*	226	13.2	401	11.8	29	10.9	656	12.2
Male†	135	13.0	284	11.9	18	9.7	437	12.1
Female‡	91	13.5	117	11.5	11	13.6	219	12.4

HF, heart failure.

*Percentage derived from the total number of patients in the renal function status and total groups (worsened renal function = 1714, stable renal function = 3397, improved renal function = 266, total = 5377).

†Percentage derived from the total number of male patients in the renal function status and total groups (worsened renal function = 1038, stable renal function = 2384, improved renal function = 185, total = 3607).

‡Percentage derived from the total number of female patients in the renal function status and total groups (worsened renal function = 676, stable renal function = 1013, improved renal function = 81, total = 1770).

at 30 days (aHR 1.42, 95% CI 1.13−1.78] and aHR 1.56, 95% CI 1.15−2.12, respectively). In addition, men with improving renal function exhibited 71% (aHR 0.29, 95% CI 0.13−0.66) fewer adverse outcomes at 30 days ($P = .003$). However, there was no association between the improving renal function and outcomes in female patients (aHR 1.18, 95% CI 0.59−2.35).

Sensitivity Analysis

When adjusting for age, baseline eGFR, Charlson comorbidity index, and the congestion score in a sensitivity analysis, the worsening renal function was still associated with significantly poorer 30-day outcomes among men (aHR 1.39, 95% CI 1−1.93), but the association was not statistically significant in women, although the HR was in the same direction (aHR 1.44, 95% CI 0.92−2.24). Similarly, there was a trend for fewer adverse outcomes with improved renal function among men (aHR 0.39, 95% CI 0.14−1.06) but not in women (aHR 0.97, 95% CI 0.35−2.72) (Supplementary Table 3).

The sensitivity analysis with the change in eGFR as a continuous variable showed similar findings and confirmed the independent association between change in eGFR and clinical outcomes (aHR 0.97, 95% CI 0.97−0.98). No difference in the likelihood of adverse outcomes was observed for patients with a HFrEF compared with HFpEF and the male versus female population ($P > .05$ for all).

In the stratified analysis, similar results were obtained for both male and female subpopulations. When stratified by sex, there was no interaction between the association of EF status and change in renal function with outcome. Similar results were obtained between male and female populations in sensitivity analysis assessing the baseline-to-discharge renal function changes and baseline EF as continuous variables, as shown in Supplementary Table 4.

Discussion

Using data from the ASCEND-HF trial, we identified 2 principal findings in this study. First, worsening renal function during hospitalization was associated with increased risks of adverse outcomes, and this finding was similar in men and women. Second, improved renal function resulted in better outcomes in males, but not in female patients, although this observation could have been due to the small number of events and inadequate power in women's subgroup.

Worsening renal function has been shown previously to be associated independently with increased rehospitalization and mortality in patients with AHF.[4,14] A meta-analysis demonstrated the relationship between worsening renal function and reduced survival, with baseline eGFR and age (but not sex) as strong predictors for the occurrence of worsening renal function.[14] Regarding improving renal function, Reid et al[4] reported that patients with reduced renal function at admission who had an improved renal function during hospital stay had a longer survival compared with patients with stable or worsening renal function during hospitalization. However, this outcome was not consistent across studies and other investigators have reported improving renal function to be associated with increased mortality.[1,15] The paradoxical improvement of renal function despite worsening HF may be explained by interindividual differences in renal function.[1,16] Similarly, the prognostic effect of worsening renal function is postulated to depend on the context as worsened renal function in the context of congestion despite adequate decongestive therapy was purportedly not associated with adverse outcomes.[5] In this study, however, after adjustment for

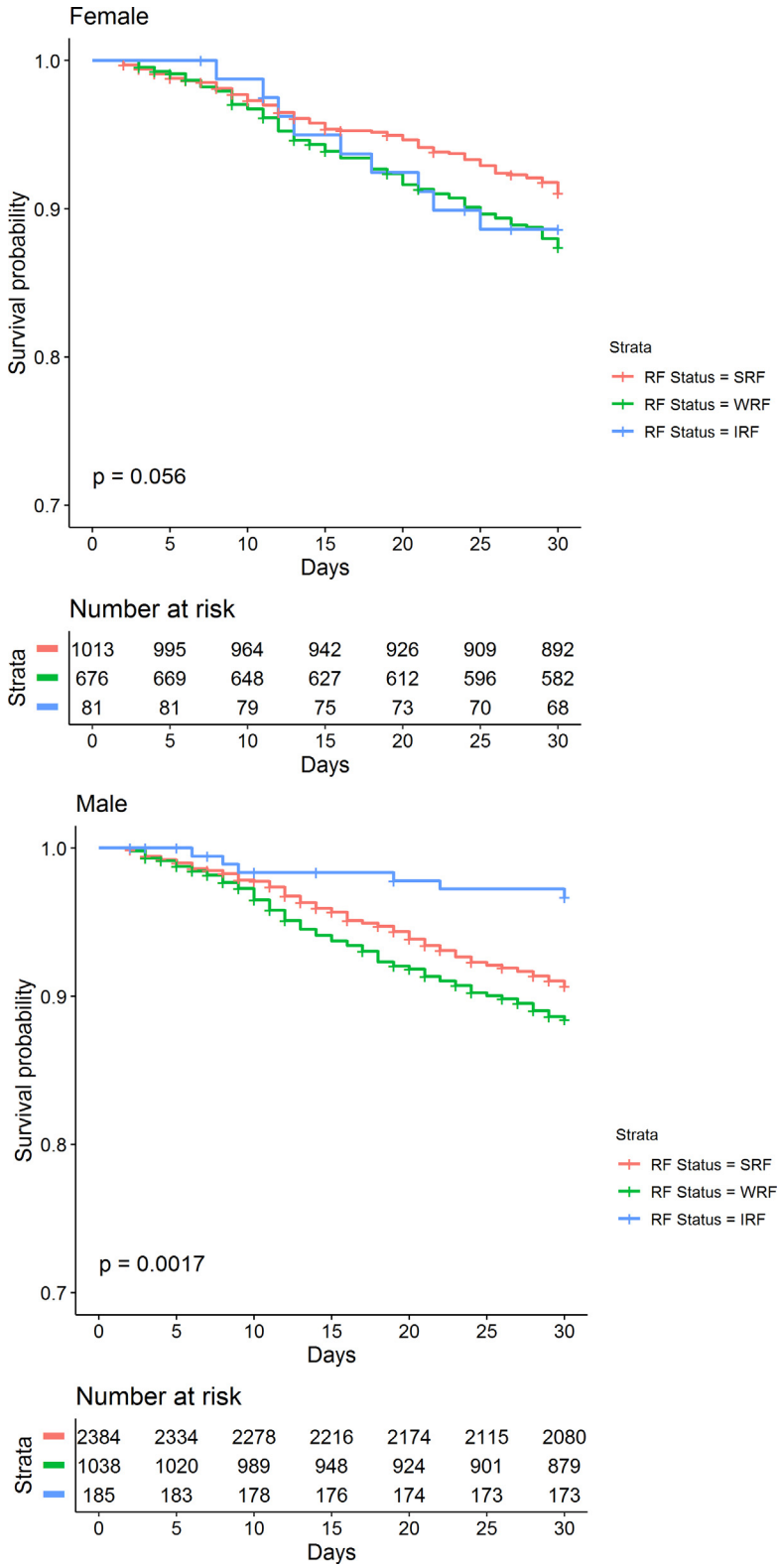

Fig. 2. Kaplan-Meier curves for the composite end point of death and HF rehospitalization at 30 days for renal function status stratified by sex. Abbreviations as in Fig. 1.

congestion score besides other key confounders, the worsening renal function was still associated with poorer 30-day outcomes in both men and women, although the association was not statistically significant in women. These contradictory results underscore the need for future studies to shed more light on the etiology of improving and worsening renal function, because this information may affect treatment strategies.

Table 4. Multivariable Cox Proportional Hazard Model Stratified by Sex for the 30-Day Composite End Point* and the End Point of 180-Day All-cause Mortality

	Renal Function Status (Worsened vs Stable Renal Function)		Renal Function Status (Improved vs Stable Renal Function)		EF (Reduced vs Preserved)	
	aHR† (95% CI)	*P* Value	aHR† (95% CI)	*P* Value	aHR† (95% CI)	*P* Value
30-Day composite end point*						
Male	1.42 (1.13−1.78)	.003	0.29 (0.13−0.66)	.003	1.00 (0.75−1.34)	.984
Female	1.56 (1.15−2.12)	.004	1.18 (0.59−2.35)	.642	1.05 (0.76−1.44)	.789
180-Day all-cause mortality						
Male	1.18 (0.96−1.45)	.120	0.71 (0.44−1.15)	.166	1.29 (0.99−1.67)	.057
Female	1.26 (0.95−1.66)	.109	1.01 (0.54−1.89)	.967	1.12 (0.84−1.49)	.441

aHR, adjusted hazard ratio; CI, confidence interval. Other abbreviations as in Table 1.
*Thirty-day all-cause mortality and HF rehospitalization.
†Adjusted for baseline eGFR, age and Charlson Comorbidity Index score.

There was an interaction between the patient's sex and renal function. The prevalence of chronic kidney disease is generally higher in women compared with men.[17,18] However, renal dysfunction develops faster in males than in females, probably owing to the protective effects of estrogens or the detrimental effect of testosterone and unhealthy lifestyles.[19] Sex hormones have been recognized as modulators of renal function[19] and sex has been included in the estimates of renal function by most eGFR equations. Two prior studies showed that women with AHF were older, more often had HFpEF, had a lower eGFR, and a decreased 1-year mortality risk compared with men.[4,20] In this study, women had a lower baseline eGFR and greater baseline-to-peak eGFR change compared with men. Both men and women with worsened renal function had an increased likelihood of mortality and rehospitalization, although the level of congestion modified the impact of worsening renal function on outcomes and the association disappeared in women after adjustment for the congestion score in the sensitivity analysis. A modest sex difference was observed in the association of improved renal function with outcomes; however, the number of events between male and female patients with improved renal function differed solely by 3 events, with wide CIs in the female population; as such, this finding likely represents an underpowered analysis rather than the presence of a biological difference.

Although this study found only minor differences in baseline renal function between women and men, its change during the hospital stay, and relationship with outcomes between men and women, sex differences, in general, should be further explored through clinical research in this field, and taking those potential differences into account in patient management and providing tailored treatments are advised.

The study has several limitations. First, the recruitment criteria of this trial could have led to a selection bias and may affect the generalizability of our findings since the range of renal function at baseline was narrower than typically seen in clinical practice. Second, several factors including the baseline renal dysfunction and hemoconcentration may modulate the impact of worsening renal function on outcomes. In the current study, we adjusted for a number of covariates, including the baseline eGFR and congestion status, but there is a possibility that other unmeasured confounders remain unaccounted for in this analysis. Third, there is a lack of consensus for the definitions of % change in renal function to be deemed worsened, stable, or improved renal function; however, we used a widely used and studied definition in our study.[4,21−24] Fourth, it should be noted that an eGFR calculated based on formulas such as Chronic Kidney Disease Epidemiology Collaboration is an estimation of the creatinine clearance and that creatinine clearance, itself, might overestimate the GFR owing to the additional tubular secretion of creatinine. Fifth, it should be noted that the congestion score uses a composite of the orthopnea, pedal edema, and N-terminal pro-brain natriuretic peptide levels measured between 48 and 72 hours after admission, and it might not be a true reflective of congestion despite adequate decongestion therapy at discharge. Finally, women were underrepresented (approximately 33%), similar to many other cardiovascular randomized controlled trials.[25]

In conclusion, this study found no major sex differences in the 30-day clinical outcomes of patients hospitalized for AHF with worsening renal function during their hospital stay. However, unlike women, men with improved renal function exhibited better outcomes at 30 days, although this observation was limited by the small number of events and inadequate power. Generally, worsening and improving renal function were associated with, respectively, worse and better clinical outcomes, irrespective of EF. Future studies are warranted to further delineate the possible interactions between sex, change of renal and cardiac functions and their impact on clinical outcomes in patients with AHF.

Disclosures

The authors report no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2021.05.005.

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