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Clinical Impact of Worsening Renal Function in Elderly Patients with Acute Decompensated Heart Failure

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ABSTRACT

Background and Objectives: The clinical significance of worsening renal function (WRF) in elderly patients with acute decompensated heart failure (ADHF) is not completely understood. We compared the clinical conditions between younger and elderly patients with ADHF after the appearance of WRF to establish its prognostic influence.

Methods: We included 654 consecutive patients (37% women) admitted for ADHF. We divided the patients into four groups according to their age (<80 years, under-80, n=331; ≥80 years, over-80, n=323) and to their WRF statuses (either WRF or non-WRF group). We defined WRF as an increase in serum creatinine level ≥0.3 mg/dL or ≥150% within 48 hours after hospital arrival (under-80, n=62; over-80, n=75). The primary endpoint was a composite of cardiac events within 1 year.

Results: The survival analyses revealed that the WRF group had significantly more cardiac events than the non-WRF group in patients in the over-80 group (log-rank p=0.025), but not in those of the under-80 group (log-rank p=0.50). The patients in the over-80, WRF group presented more significant mean blood pressure (MBP) drops than those in the over-80 non-WRF group (p=0.003). Logistic regression analyses revealed that higher MBP at admission was a significant predictor of WRF.

Conclusions: WRF is a predictor of poor outcomes in elderly patients with ADHF.

Keywords: Aged; Heart failure; Cardio-Renal syndrome

INTRODUCTION

The population of aging patients with heart failure (HF) is rapidly increasing, especially in developed countries.[1] Aging causes structural and functional changes to the cardiovascular system and organs, including the heart and kidneys.[2] Vascular stiffening and atherosclerosis progression cause cardiac systolic and diastolic dysfunctions. Impaired compensatory mechanisms of the circulatory system lead to acute decompensated heart failure (ADHF). In addition, aging is associated with progressive renal dysfunction that increases the risk of ADHF.[3] Indeed, ADHF is a common cause of hospitalization among elderly patients.[1)4]

Around one third of patients with ADHF experience worsening renal function (WRF) during hospitalizations.[5][6] The mechanism of WRF during the early ADHF phase is considered multifactorial. The increase in the serum creatinine (SCr) level during the early ADHF phase reflects a state of not only renal hypoperfusion and tissue injury[7] but also hemoconcentration due to plasma volume reduction and decongestion.[8] Chronic kidney disease (CKD) has been observed in patients with HF,[9] but the clinical impact of WRF on patients with ADHF is controversial.[8][10] A good effect can be considered when increases in the SCr level reflect reductions in the effective circulating plasma volume and increased hemoconcentration. In contrast, when increases in the SCr level reflect acute kidney injury, it would be a bad effect. Moreover, little is known regarding differences of the prognostic impact of WRF in between younger and older patients with ADHF.

We hypothesized that the clinical significance of WRF in patients with ADHF would be different between younger and elderly patients due to the impaired pathophysiological background of elderly patients compared with that of younger ones. Thus, we aimed to evaluate the association between WRF and the risk of 1-year cardiac events and whether the association varies between younger and elderly patients with ADHF. As a secondary endpoint, we evaluated the clinical determinants of WRF.

METHODS

We conducted a retrospective analysis of a prospectively collected cohort. We enrolled 723 patients aged ≥18 years admitted to our hospital for ADHF between January 2014 and March 2019. The ADHF diagnoses were based on the Framingham criteria. We excluded 18 patients on dialysis or with end-stage renal disease defined by estimated glomerular filtration rates (eGFRs) <15 mL/min/1.73 m^2, 32 with ADHF due to acute myocardial infarction, and 12 with mechanical circulatory support requirements at admission. We also excluded 7 with isolated right ventricular failure (2 idiopathic pulmonary artery hypertension, 2 chronic obstructive pulmonary disease, 2 acute pulmonary embolism, and 1 isolated triceps regurgitation) because hemodynamic status and treatment strategies of them were not similar with left-sided heart failure.

Finally, we analyzed data from 654 patients with ADHF. The clinical research review committee of Ichinomiya Municipal Hospital approved the study protocol (approved No. 1250).

Patients' classification and outcomes

To compare the clinical conditions between younger and elderly patients with ADHF, we divided them into two groups based on the median age (80 years): under-80 group (<80 years) and over-80 group (≥80 years). In addition, we divided the patients according to the development of WRF into WRF and non-WRF groups.

We defined WRF development by modifying the definitions of acute kidney injury of Kidney Disease Improving Global Outcomes (KDIGO) as following; 1) an increase in SCr level ≥0.3 mg/dL or ≥1.5 times within 48 hours from arrival or 2) urine output ≤0.5 mL/kg/h within 48 hours from arrival.[11]

We also recorded 1 year composite cardiac event occurrences, including all-cause mortality, re-hospitalizations caused by decompensated HF, and lethal arrhythmias. We defined lethal

arrhythmias as arrhythmic events requiring urgent defibrillation or adequate shock by an implantable cardiac defibrillator.

Definitions of variables

We defined delta (Δ) as the changes in variables from arrival to 48 hours after admission, as in the following example:

$$\Delta \text{Mean Blood Pressure (MBP) (\%)} = \frac{\text{MBP at 48 Hours} - \text{MBP at Arrival}}{\text{MBP at Arrival}} \times 100.$$

CKD was defined when eGFR was <60 mL/min/1.73 m^2. Regarding the etiology of HF, patients who had moderate or severe heart valve diseases without any other obvious etiologies defined as heart valve diseases.

We converted the loop diuretic dose to furosemide equivalents using 20 mg of oral furosemide, 4 mg of oral torasemide, and 30 mg of oral azosemide. Treatment strategy or drug selection was determined by the attending physicians according to the patients' conditions.

Statistical analysis

We expressed continuous variables as means±standard deviations or medians and interquartile ranges and compared the distributions of these variables between the two groups using 2-sample t-tests or the Wilcoxon rank-sum test. The distribution of data was verified by Shapiro-Wilk test. Categorical variables are expressed as numbers and percentages, and we compared the distributions of these variables between the 2 groups using χ^2 tests. We estimated the event-free survival rates applying the Kaplan-Meier analysis and compared the values between WRF and non-WRF groups using the log-rank test. We calculated the hazard ratio and 95% confidence interval (95% CI) for composite cardiac events after conducting Cox proportional-hazard regression analysis. We conducted univariate logistic analyses to evaluate the odds ratio and 95% CI, and assess the influence of each variable on the development of WRF. We conducted all statistical analyses using the JMP Pro version 13.0 software (SAS Institute, Cary, NC, USA). We considered values of p<0.05 as statistically significant. This investigation was performed according to the latest version (2013) of Declaration of Helsinki.

RESULTS

Table 1 presents the patients' demographics at admission. The patients in the over-80 group were characterized by lower MBP, higher prevalence of CKD, and lower prevalence of diabetes mellitus (DM) than those in the under-80 group (under-80 vs. over-80; MBP, 106±24 mmHg vs. 99±22 mmHg, p=0.0001; CKD, 63% vs. 73%, p=0.006; DM, 37% vs. 25%, p= 0.001, respectively). The prevalence of HF with preserved ejection fraction were 22% in patients in the under-80 group and 25% in those of the over-80 group (p<0.0001). Of all patients, 489 (75%) were first time admissions for ADHF and 162 (25%) were treated with mechanical ventilation. The patients requiring artificial ventilation were significantly more common in the under-80 group (WRF vs. non-WRF, 62 [23%] vs. 22 [35%], p=0.04) than in the over-80 group (WRF vs. non-WRF, 56 [23%] vs. 22 [29%], p=0.23).

Table 1. Patients' characteristics at admission

Characteristics	Under-80			Over-80			
	Non-WRF (n=269)	WRF (n=62)	p	Non-WRF (n=248)	WRF (n=75)	p	p*
Age (years)	72 (63–77)	75 (67–78)	0.07	86 (83–90)	86 (83–90)	0.96	0.95
Male	200 (74)	35 (56)	0.01	120 (48)	35 (47)	0.90	0.90
BMI (kg/m²)	24.8±5.5	23.5±4.6	0.08	21.3±3.7	21.2±4.4	0.86	0.06
NYHA IV	98 (37)	26 (42)	0.82	110 (44)	43 (58)	0.04	0.01
SBP (mmHg)	142±31	150±39	0.08	137±29	151±36	0.0008	0.02
DBP (mmHg)	86±21	89±27	0.36	77±19	85±23	0.004	<0.0001
MBP (mmHg)	105±22	109±29	0.17	97±20	107±25	0.001	0.0002
HR (beats/min)	99±27	102±34	0.47	88±23	95±28	0.052	0.12
Etiology of HF							
Ischemic	76 (28)	17 (27)	1.00	68 (27)	27 (36)	0.39	0.45
VHD	60 (22)	9 (15)	0.29	77 (31)	22 (29)	0.48	0.002
cardiomyopathy	86 (32)	13 (21)	0.12	42 (17)	12 (16)	0.73	0.001
Previous history							
HF	63 (23)	20 (32)	0.35	66 (27)	16 (21)	0.36	1.00
CKD	166 (62)	44 (71)	0.19	188 (76)	47 (63)	0.052	0.01
DM	99 (37)	26 (42)	0.47	62 (25)	20 (27)	0.76	0.01
HT	131 (49)	40 (65)	0.03	143 (58)	47 (63)	0.42	0.06
AF	103 (38)	29 (47)	0.25	102 (41)	26 (35)	0.42	1.00
Laboratory data at admission							
Sodium (mEq/L)	139±4	140±4	0.87	139±5	140±4	0.22	0.32
SCr (mg/dL)	1.12±0.45	1.16±0.58	0.51	1.22±0.59	1.13±0.56	0.25	0.67
TB (mg/dL)	1.0±0.8	0.9±0.5	0.23	0.8±0.6	0.7±0.4	0.03	0.01
Albumin (g/dL)	3.7±0.5	3.6±0.6	0.20	3.5±0.5	3.5±0.5	0.82	0.20
BNP (pg/mL)	638 (362–1,009)	654 (477–1,046)	0.66	730 (457–1,387)	732 (498–1,261)	0.66	0.90
Hb (g/dL)	13.2±2.3	12.4±2.4	0.02	11.2±2.1	11.3±1.8	0.77	0.04
Echocardiogram							
LAD (mm)	44±7	44±8	0.98	41±7	41±8	0.83	0.64
LVEDD (mm)	61±10	57±8	0.003	53±9	53±8	0.66	0.01
LVEF (%)	34±16	37±15	0.13	42±17	44±15	0.41	<0.0001
LVEF ≤40%	184 (68)	35 (56)	0.08	128 (52)	32 (43)	0.19	<0.0001
LVEF ≥50%	53 (20)	17 (27)	0.23	82 (33)	29 (39)	0.41	<0.0001
Medication before admission							
ACEI/ARB	104 (38)	28 (45)	0.39	91 (37)	26 (34)	0.45	0.64
BB	115 (43)	26 (42)	1.00	78 (31)	20 (27)	0.48	0.48
MRA	42 (16)	15 (24)	0.13	43 (17)	12 (16)	0.86	0.86
Loop diuretics	114 (42)	28 (45)	0.78	112 (45)	32 (43)	0.79	0.79

Values are presented as number (%), means±standard deviations, or medians (interquartile ranges).
WRF = worsening renal function; BMI = body mass index; NYHA = New York Heart Association; SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure; HR = heart rate; VHD = valve heart diseases; HF = heart failure; CKD = chronic kidney disease; DM = diabetes mellitus; HT = hypertension; AF = atrial fibrillation; SCr = serum creatinine; TB = total bilirubin; BNP = brain natriuretic peptide; Hb = hemoglobin; LAD = left atrial diameter; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; ACEI/ARB = angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BB = beta-blocker; MRA = mineralocorticoid receptor antagonist.
*p value for under-80 and over-80 groups.

Treatment within 48 hours and parameter changes

Table 2 presents the medications administered intravenously within the first 48 hours. In patients in both the under-80 and over-80 groups, nitrate use was significantly higher in patients with WRF. In addition, patients with WRF were prescribed significantly higher dosage of furosemide. No significant differences were observed in ΔMBP between patients in the under-80 and patients in the over-80 groups (under-80 vs. over-80, –17±15% vs. –15±21%, respectively, p=0.095), but the patients in the over-80 WRF group presented more significant MBP drops than those in the over-80 non-WRF group. Of the 33 patients treated with inotropes, 30 (91%) were administered with dobutamine.

Table 2. Intravenous treatment and parameter changes

Variables	Under-80			Over-80		
	Non-WRF	WRF	p	Non-WRF	WRF	p
Intravenous administration within 48 hours						
Furosemide	299 (85)	58 (94)	0.04	222 (90)	70 (93)	0.26
Furosemide dosage (mg/48 hr)	40 (13–67)	40 (27–80)	0.03	40 (27–67)	53 (40–67)	0.03
Carperitide	39 (14)	12 (19)	0.33	26 (10)	13 (17)	0.11
Nitrate	39 (14)	19 (31)	0.005	30 (12)	23 (31)	0.0003
Inotropes	13 (5)	5 (8)	0.29	12 (5)	3 (4)	0.78
Parameter changes during 48 hours (%)						
ΔMBP	−17±17	−18±22	0.82	−13±21	−21±19	0.003
ΔHR	−17±20	−16±27	0.60	−11±21	−18±22	0.01
ΔSodium,	1.2±2.7	0.6±2.3	0.34	1.1±0.2	0.4±2.2	0.08
ΔHb	−0.6±8.7	−1.8±10.6	0.36	−1.1±12.0	−5.1±9.8	0.01
Urine volume (mL/48 hr)	4,380 (3,270–5,435)	3,700 (2,380–5,155)	0.01	3,775 (2,738–4,860)	3,280 (2,140–4,401)	0.15

Inotropes included dobutamine, dopamine, and milrinone. Values are presented as number (%), means±standard deviations, or medians (interquartile ranges).
WRF = worsening renal function; MBP = mean blood pressure; HR = heart rate; Hb = hemoglobin.

Table 3. Logistic regression analysis for worsening renal function in the over-80 group

Variables	OR (95%CI)	p
Age	1.002 (0.942–1.064)	0.95
MBP	1.020 (1.008–1.032)	0.001
SCr	0.744 (0.437–1.191)	0.23
LVEF	1.007 (0.991–1.023)	0.41
LVEF ≥50%	1.430 (0.981–2.140)	0.058
Sodium	1.039 (0.979–1.106)	0.21
Hb	1.019 (0.895–1.161)	0.77

OR = odds ratio; CI = confidence interval; MBP = mean blood pressure; SCr = serum creatinine; LVEF = left ventricular ejection fraction; Hb = hemoglobin.

Variables associated with WRF in the over-80

We conducted logistic regression analysis to elucidate the association between the occurrence of WRF and being included in the over-80 group using the variables at admission (**Table 3**). Higher MBP at admission had significant predictive value of an occurrence of WRF.

Survival analysis

Figure 1 presents the Kaplan-Meier survival analyses for the composite cardiac events during 1 year. The median follow-up duration was 365 (205–365) days. In total, 188 composite events (63 all-cause death, 115 re-hospitalizations caused by decompensated HF, and 10 lethal arrhythmias) occurred (**Table 4**). The median time of the events was 81 (37–173) days. In the under-80 group, no significant differences were observed between the WRF and non-WRF groups (**Figure 1A**). On the other hand, in the patients in the over-80 group, those with WRF had significantly lower event-free survivals than those without WRF (**Figure 1B**). In detail, WRF group had significantly higher number of all-cause death than non-WRF group (WRF group vs. non-WRF group, 15 [20%] vs. 27 [11%], Log-rank p=0.049), although there was no significant difference in re-hospitalization (WRF group vs. non-WRF group, 15 [21%] and 45 [18%], Log-rank p=0.61).

Table 4. The number of each events

Variables	Under-80		Over-80	
	Non-WRF (n=269)	WRF (n=62)	Non-WRF (n=248)	WRF (n=75)
All events	53 (19.7)	17 (27.4)	75 (30.2)	33 (44.0)
All cause death	16 (5.9)	5 (8.1)	27 (10.9)	15 (20.0)
Re-hospitalization	43 (16.0)	11 (17.7)	45 (18.1)	16 (21.3)
Lethal arrhythmia	4 (1.5)	1 (1.6)	3 (1.2)	3 (4.0)

Re-hospitalization means hospitalization caused by decompensated heart failure. Lethal arrhythmia means arrhythmic events requiring urgent defibrillation or adequate shock by an implantable cardiac defibrillator.
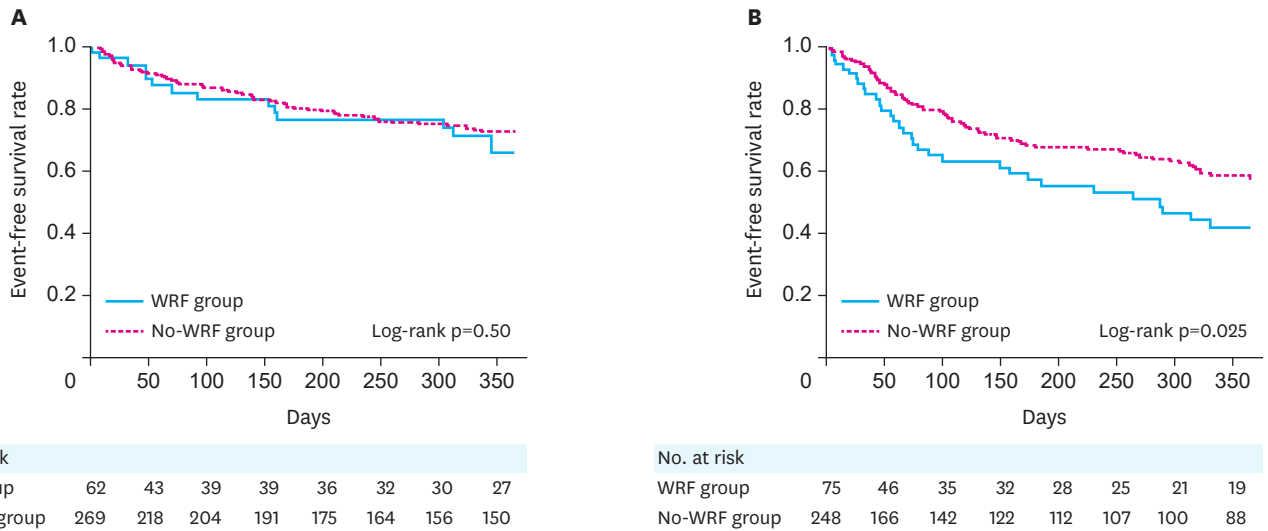WRF = worsening renal function.

Figure 1. Kaplan-Meier survival curves for composite cardiac events during 1 year in the (A) under-80 and (B) over-80 groups.
WRF = worsening renal function.

Our Cox regression analysis was performed using WRF and variables at the time of hospital arrival that revealed that the SCr level at admission was a significant prognostic determinant in both the under-80 and over-80 groups. WRF and MBP were independent prognostic markers in the over-80 group (**Table 5**).

Table 5. Cox regression analyses for composite event determinants

Variables	Univariate		Multivariate	
	HR (95% CI)	p	HR (95% CI)	p
Under-80				
WRF	1.213 (0.691–2.129)	0.50		
NYHA IV	0.996 (0.631–1.575)	0.99		
DM	0.981 (0.621–1.551)	0.94		
HT	0.842 (0.541–1.308)	0.44		
AF	0.907 (0.576–1.429)	0.67		
Age	1.051 (1.023–1.084)	<0.0001	1.032 (1.002–1.063)	0.04
MBP	0.987 (0.977–0.997)	0.01	0.992 (0.982–1.002)	0.10
Sodium	0.962 (0.919–1.013)	0.14		
SCr	2.203 (1.532–3.073)	<0.0001	1.703 (1.156–2.508)	0.01
BNP*	1.034 (1.011–1.012)	0.004	1.023 (1.000–1.047)	0.049
Hb	0.863 (0.784–0.949)	0.002	0.947 (0.853–1.051)	0.31
LVEF	1.000 (0.986–1.013)	0.66		
Over-80				
WRF	1.595 (1.055–2.410)	0.03	1.711 (1.098–2.666)	0.02
NYHA IV	1.587 (1.086–2.320)	0.02	1.753 (1.185–2.595)	0.005
DM	0.971 (0.629–1.501)	0.9		
HT	0.936 (0.640–1.369)	0.73		
AF	0.776 (0.522–1.153)	0.21		
Age	1.040 (0.996–1.085)	0.07	1.049 (1.004–1.095)	0.04
MBP	0.991 (0.982–1.000)	0.04	0.989 (0.980–0.998)	0.02
Sodium	1.026 (0.984–1.073)	0.24		
SCr	1.693 (1.205–2.341)	0.003	1.641 (1.161–2.318)	0.01
BNP*	1.014 (0.999–1.026)	0.07	1.014 (1.001–1.028)	0.05
Hb	0.949 (0.863–1.043)	0.27		
LVEF	0.997 (0.985–1.001)	0.66		

HR = hazard ratio; CI = confidence interval; WRF = worsening renal function; NYHA = New York Heart Association; DM = diabetes mellitus; HT = hypertension; AF = atrial fibrillation; MBP = mean blood pressure; SCr = serum creatinine; BNP = brain natriuretic peptide; Hb = hemoglobin; LVEF = left ventricular ejection fraction. *Per 100 pg/mL increase.

DISCUSSION

For this study, we investigated the clinical impact of WRF on patients with ADHF and found the following 2 important points: First, the patients in the over-80 WRF group presented poor prognoses, but those in the under-80 WRF group did not. Second, the patients in the over-80 WRF group presented large MBP decreases within 48 hours of admission, but those in the over-80 non-WRF group did not. To the best of our knowledge, this is the first report that shows differences of the prognostic impact of WRF between younger and older patients with ADHF.

The development of renal dysfunction in the early ADHF phase is a concern of clinicians. The increases in the SCr level reflect the reductions in the effective circulating plasma volume that is required to ameliorate the symptoms of ADHF.[12)13)] However, the reduction of effective circulating plasma volume and blood pressure drops also cause acute kidney injury.[14)] Determining the clinical impact of WRF during the acute ADHF phase is challenging because multiple factors can affect the renal function.

Some studies have associated WRF with increases in adverse event rates.[5)6)14)] But others have reported the lack of impact on the prognosis of WRF.[15)16)] Therefore, terms such as true-WRF and pseudo-WRF have been proposed.[13)17)] In addition, Metra et al. reported that the persistence of congestion during the hospitalization is the most important prognostic factor and that WRF is clinically significant only when occurring in patients with persistent fluid overloads.[12)] If clinicians consider SCr level increases as true-WRF, they should reconsider the optimal circulatory volume status or reset the target blood pressure level. On the other hand, pseudo-WRF should not determine treatment strategy changes to ameliorate congestion symptoms. Moreover, Nohria et al.[18)] reported that baseline renal function has a higher impact on outcomes than WRF in younger patients with ADHF, but we revealed that the prognostic value of WRF in patients over 80 years was independent of the SCr level upon admission (**Table 5**).

Studies have revealed that age is a predictor of WRF.[19-21)] We showed that the prognostic impact of WRF depends on age, and WRF in patients older than 80 years is probably true-WRF due to normal aging-associated cardiovascular changes.[2)] Vascular stiffening and increased left ventricular wall thickness impair the hemodynamic ability to promptly respond to circulatory dynamic changes (the compensatory mechanisms of the circulatory system are impaired). We showed that the patients in the over-80 group had significantly larger pulse pressures (under-80, 56±23 mmHg; over-80, 61±23 mmHg; p=0.004) and lower diastolic BP than younger patients (**Table 1**). Low urine output was association with the occurrence of WRF in under-80; we consider this as the result rather than the cause of WRF. These data reflect the characteristics of poor compliance vasculatures in the patients in the over-80 group.

In addition, patients older than 80 years had a significantly higher prevalence of heart failure with preserved ejection fraction (HFPEF) than younger ones (**Table 1**), which is in agreement with other reports.[22)] Indeed, HFPEF tended to predict the occurrence of WRF in logistic regression analysis (**Table 3**) according to the previous report.[23)] HFPEF is characterized by cardiac dysfunction and dramatic limitations in systolic reserve capacity and the associated increase in end-diastolic pressure volume.[24)25)] These impaired compensatory mechanisms would easily cause the MBP to drop, leading to renal hypoperfusion, true-WRF, and poor outcomes in patients older than 80 years. It is consistent with the higher prevalence of HFPEF in elder ADHF.[2)]

It is known that renal hypoperfusion does not occur when the MBP is adequate. However, it is also known that the adequate MBP would elevate in specific condition such as chronic hypertension and CKD.[26] Actually, over-80 group had higher number of CKD (p=0.01) and tended to have higher number of HT (p=0.06) than under 80 group (**Table 1**). We showed that the higher MBP at admission as a risk of occurrence of WRF, which might indicate poor compliance of vasculature. In addition, we also presented that, in over-80, MBP drop in patients with WRF was larger than patients without WRF (**Tables 1** and **2**), which might mean poor reserve capacity of their circulatory system.

Diuretics and vasodilators are two common agents for the treatment of ADHF,[27] and they also affect the MBP. In terms of the diuretics and plasma volume reduction in patients older than 80 years, we found no significant differences in urine volumes within 48 hours between patients with WRF and those without WRF (**Table 2**). In addition, there were no significant correlation between MBP drop and urine output (r=−0.12; 95% CI, −0.23 to 0.01; p=0.07). These data indicate that the reduction in the effective circulatory plasma volume caused by the use of diuretic did not have a large impact on the MBP drop. On the other hand, patients in the WRF group were given nitrates more frequently than those in the non-WRF group, regardless of their age (**Table 2**). In addition, MBP drops were associated with WRF only in patients older than 80 years. The hypovolemic state and tissue hypoperfusion reflected by low MBP is two main mechanisms causing WRF; our data suggest that low MBP would have more responsibility for the occurrence of WRF in patients with over-80. In addition, lower MBP at admission was an independent determinant of cardiac event in over-80, although the non-linear association of blood pressure and outcome is known.[28] The safety and efficacy of vasodilators have been confirmed in young patients with ADHF,[29] but clinicians need to pay attention to low MBPs, especially in elderly patients with early ADHF.

We are aware of the following limitations of our study. First, we failed to directly determine causal associations between WRF, MBP drop, and outcomes in the patients in the over-80 group due to the post hoc nature of the study design. Second, we divided the patients into 2 groups based on the median age of 80 years to exclude arbitrariness. In the present study, we intended to explore the impact of aging and prognostic impact of WRF. For that purpose, it would be more appropriate to classify patients into more detailed group. However, it was difficult to analyze the data in this manner because it leads to low statistical power. We consider that the significance of WRF did not change at the age of 80 years. We showed that WRF may adversely affect the prognosis by aging. In the present study, we simply compared prognostic impact of WRF between older and younger patients, which was defined by median age. Third, we defined WRF as a mild SCr level increase within 48 hours after admission, but a standard definition for WRF has not been confirmed. We used SCr level at arrival as baseline. However, SCr level at arrival might already be elevated compare with the SCr level at the previously compensated state, which would lead to underestimation of WRF. We focused on WRF during the early ADHF phase because early SCr level increases or oliguria after hospitalization for ADHF have a large impact on the selection of the treatment strategy. In addition, complications of infectious disease and sepsis would be one of the major causes of WRF in ADHF. However, these factors have not been analyzed in this study.

The occurrence of WRF in patients with ADHF had a poor prognostic impact on elderly patients, but not on younger ones. In the elderly with ADHF, the occurrence of WRF was associated with an MBP drop within the first 48 hours after admission. The hemodynamic statuses of elderly patients with ADHF need to be carefully monitored to avoid the occurrence of WRF.

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