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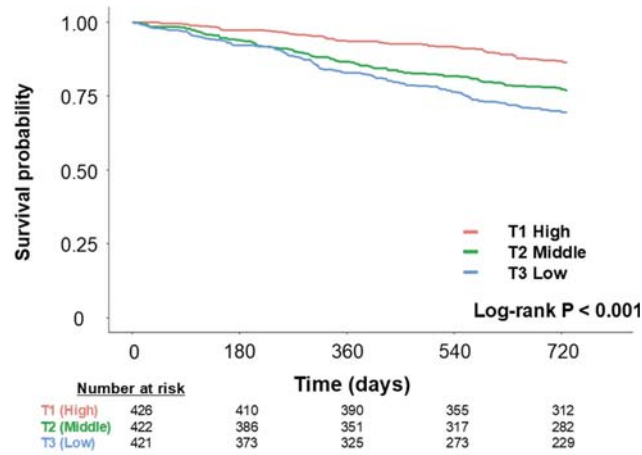
**Funding Acknowledgements:** None.

**Aims:** Handgrip strength, a key marker of sarcopenia known for its simplicity and reliability has uncertain prognostic value in older patients with heart failure. This post-hoc analysis of FRAGILE-HF, a prospective, multicentre cohort study, aimed to evaluate the prognostic value of handgrip strength in hospitalized patients aged  $\geq 65$  years with heart failure.

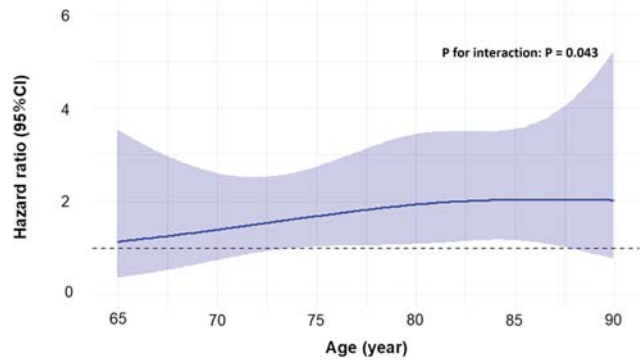
**Methods:** Handgrip strength was measured before discharge using a dynamometer, and the highest value from two trials was recorded. To standardise measurements, handgrip strength was divided by 28 kg for men and 18 kg for women, according to the Asian Working Group for Sarcopenia 2019 criteria. Patients were categorized into tertiles based on the standardised values: T1 (highest), T2 (middle), and T3 (lowest). The primary outcome was 2-year all-cause mortality.

**Results:** Among 1,290 patients (median age 81 years, 57.1% male), 275 deaths occurred during the 2-year follow-up. Kaplan-Meier analysis revealed a significant stepwise increase in mortality in T2 and T3 compared to T1 (Log-rank:  $P < 0.001$ ). Adjusted Cox proportional hazards analysis including MAGGIC risk score and log-transformed BNP as adjustment variables confirmed this trend, with T2 (hazard ratio [HR]: 1.64, 95% confidence interval [CI]: 1.14-2.37,  $P = 0.007$ ) and T3 (HR: 2.03, 95% CI: 1.42-2.90,  $P < 0.001$ ) associated with higher mortality. Furthermore, restricted cubic spline showed that the prognostic impact of reduced handgrip strength increased with advancing age ( $P$  for interaction = 0.043).

**Conclusions:** Lower handgrip strength was independently associated with adverse outcomes in older patients with heart failure, with a stronger association in the oldest patients. This finding provides its additional prognostic value beyond conventional risk factors.



Kaplan-Meier curves



Restricted cubic spline regression

## Heart Failure - Chronic Heart Failure, Clinical, Comorbidities

### Specific antidepressant effects among heart failure patients with depression: real life data

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**On behalf of:** TRENDS-HF

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**Background:** The presence of depression in heart failure (HF) has been linked to increased risk for morbi-mortality. However, the effect of specific antidepressants on prognosis remains unclear.

**Purpose:** In this study, we aimed to investigate the impact of different classes of antidepressants on overall mortality in HF.

**Method:** This subgroup analysis included data from 2,701,099 patients with HF, derived from the Nationwide Electronic Healthcare Database between January 1, 2016 and December 31, 2022. The main outcome was defined as all-cause mortality. Cox regression analysis was employed to assess the impact of specific antidepressants on the main outcome, with adjustments made to mitigate the influence of confounding factors.

**Results:** Overall, there were 348,211 depressed HF patients with prescription data including guideline directed medical therapy (GDMT). Specific antidepressant class effect on all-cause mortality was sought in HF patients with depression. Second line adjunctive medications, which are reserved for more severe and/or resistant cases alone or in combination with other classes were associated with higher mortality (Figure 1A). Herein, not only selective serotonin reuptake inhibitors (SSRIs) but also tricyclic antidepressants (TCA)s alone were associated with better survival. Then, among HF patients with depression, those on quadruple HF related GDMT was separately analyzed (Figure 1B). In the presence of quadruple GDMT, neither TCAs nor Second line adjunctive medications alone or in combination with other antidepressant classes was associated with higher mortality. Of note, herein, SSRIs were linked to improved survival.

**Conclusion:** Second line adjunctive medications alone or in combination with other commonly utilized agents are linked to higher mortality designating severity of treatment resistant depression is linked to excess mortality. However, if depressed HF patients are under quadruple GDMT, there is no hazard related to specific antidepressant medications, even benefit with SSRIs.

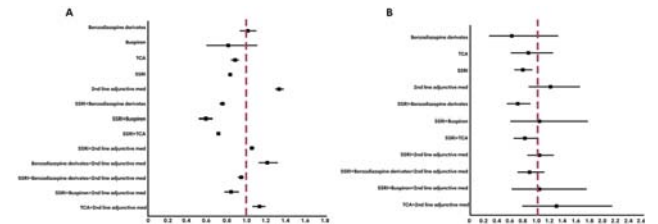


Figure 1A, Figure 1B

## Heart Failure - Chronic Heart Failure, Clinical, Comorbidities

### Therapeutic challenges and mortality outcomes in HFrEF patients with CKD: a multi-centre and multi-ethnic experience

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**Introduction:** The presence of chronic kidney disease (CKD) in patients with heart failure (HF) is associated with increased complications, readmissions, and mortality. CKD can also limit the application of guideline-directed medical therapy (GDMT) for HF in routine clinical practice. The comparative clinical outcomes of HF patients with CKD versus non-CKD patients in dedicated HF clinics remain uncertain.

**Purpose:** To evaluate the characteristics and clinical outcomes of patients with chronic heart failure with reduced ejection fraction (HFrEF) and CKD compared to non-CKD patients.

**Methods:** A retrospective, multi-center cohort study analyzed 465 patients with HFrEF who attended dedicated HF clinics in ten hospitals between January 1, 2021, and June 30, 2023. Clinical records, baseline characteristics, and six-month clinical outcomes were evaluated. CKD is defined as having an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73m<sup>2</sup> according to the 2021 CKD-EPI.

**Results:** Among the 465 patients, 129 (27.7%) had CKD and 336 (72.3%) were non-CKD. CKD patients were significantly older (61 ± 11 years vs. 53 ± 13 years,  $p=0.002$ ), but both groups had a similar male predominance (77% vs. 77%,  $p=0.487$ ). CKD patients exhibited higher rates of hypertension (79% vs. 61%,  $p<0.001$ ), diabetes mellitus (50% vs. 35%,  $p=0.002$ ), dyslipidemia (61% vs. 49%,  $p=0.014$ ), cerebrovascular accidents (12% vs. 6%,  $p=0.033$ ), and anemia (39% vs. 22%,  $p<0.001$ ). However, there were no significant differences in the prevalence of ischemic heart disease (50% vs. 44%,  $p=0.157$ ) or atrial fibrillation (25% vs. 22%,  $p=0.292$ ). The prescription of renin-angiotensin-aldosterone system (RAAS) inhibitors was significantly lower in the CKD group at first clinic visit (69% vs. 88%,  $p<0.001$ ), three months (73% vs. 93%,  $p<0.001$ ), and six months (78% vs. 92%,  $p<0.001$ ). In contrast, prescriptions of beta-blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors were similar across groups at all time points. Both groups demonstrated significant improvement in left ventricular ejection fraction (LVEF) over six months, with no intergroup differences: 29.3 ± 9.8% to 37.2 ± 14.1% (CKD) vs. 26.9 ± 7.8% to 38.3 ± 13.0% (non-CKD,  $p=0.161$ ). Similarly, there was no significant difference in improvement in NYHA functional class ( $p=0.795$ ). However, the CKD group experienced higher six-month all-cause mortality (16.5% vs. 5.6%,  $p<0.001$ ), while the six-month HF readmission rate was comparable (10.9% vs. 6.0%,  $p=0.057$ ).

**Conclusion:** Both CKD and non-CKD patients with HFrEF showed improvement in LVEF and NYHA functional class during follow-up in dedicated HF clinics. However, CKD patients had lower RAAS inhibitor prescriptions and significantly higher six-month all-cause mortality, emphasizing the need for optimized management strategies for this high-risk group.

## Heart Failure - Chronic Heart Failure, Clinical, Comorbidities

**Dynapenia, sarcopenia, hydric alterations and body composition according to the type of heart failure**

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**Background:** Heart Failure (HF) is a syndrome characterized by structural or functional alterations of the heart. Body composition and hydric alterations in HF patients are associated with the worst prognosis. However, the differences in body composition and hydric alterations according to heart failure types have not been studied in depth.

**Objective:** To assess the body composition, determine dynapenia, sarcopenia, and hydric alterations prevalence according to HF type.

**Methods:** Cross-sectional study including patients with confirmed HF according to ESC 2022 guidelines. The diagnosis of sarcopenia was according to EWGSOP2 (Dynapenia: Strength <27 kg in men and <16 kg in women. Sarcopenia: Dynapenia + appendicular skeletal muscle mass (ASMM) <7.0 kg/m<sup>2</sup> in men and <6.0 kg/m<sup>2</sup> in women) and hydric alterations by impedance index >0.83 200kHz/5kHz (BodyStat400).

**Results:** Were evaluated 172 patients which of them, 50% were women. mean age 70.33 ± 11.08. years old. The patients with HFpEF had a higher prevalence of HAS, DM, and nephropathy, and COPD was higher in Right-sided heart failure (RHF). Respect to body composition, more extracellular fluid was observed in HFmrEF, and less skeletal ASMM was observed in HFrEF. The prevalence of dynapenia was 37.93% in HFrEF, 51.35% in HFmrEF, 42.86% in HFpEF, 55.07% in RHF and sarcopenia was 16.13% in HFrEF, 15% in HFmrEF, 28.57% in HFpEF and 22.54% in RHF. The prevalence of hydric alterations was 31.25% in HFrEF, 21.95% in HFmrEF, 23.81% in HFpEF, and 39.74% in RHF.

**Conclusion:** A high prevalence of dynapenia, sarcopenia, and hydric alterations independently of HF type, which is associated with a worse prognosis.

However, a higher prevalence of dynapenia and water disturbances in RHF was observed.

Table 1. General characteristics in each type of HF.

General characteristics	HFrEF	HFmrEF	HFpEF	RHF	p
Age, years	67.09 ± 12.22	70.46 ± 9.42	71.30 ± 14.74	71.30 ± 10.20	0.318
Women, n (%)	20 (62.5)	21 (51.22)	9 (42.86)	36 (46.15)	0.405
SAH, n (%)	13 (40.62)	17 (41.46)	17 (80.95)	38 (48.72)	0.015 *
DM, n (%)	11 (34.38)	14 (34.15)	12 (57.14)	15 (19.23)	0.007 *
COPD, n (%)	10 (31.25)	22 (53.66)	12 (57.14)	49 (62.82)	0.027 *
Nephropathy, n (%)	3 (9.38)	0 (0)	7 (33.33)	2 (2.56)	0.000 *
Asthma, n (%)	4 (12.9)	1 (2.5)	2 (9.52)	12 (15.38)	0.206
Cancer, n (%)	6 (18.75)	1 (2.44)	0 (0)	2 (2.56)	0.002 *
Height, cm	154.65 ± 8.49	158.26 ± 10.30	156.85 ± 6.83	158.42 ± 10.36	0.283
Weight, kg	69.56 ± 17.72	69.53 ± 15.54	76.97 ± 20.03	70.76 ± 15.03	0.337
BMI, kg/m <sup>2</sup>	29.22 ± 8.04	27.63 ± 5.21	31.09 ± 7.03	28.40 ± 6.56	0.250
Right handgrip strength, kg	21.84 ± 7.36	21.52 ± 9.52	23.77 ± 9.6	21.83 ± 8.3	0.793
Waist circumference, cm	97.5 ± 16.6	95.53 ± 12.43	104.43 ± 17.69	101.1 ± 15.61	0.116
Abdominal obesity, n (%)	30 (93.75)	30 (78.95)	16 (76.19)	63 (86.30)	0.229
TBW, lts	48.89 ± 8.41	51.68 ± 7.52	48.61 ± 8.99	51.14 ± 9.28	0.356
ECW, lts	22.36 ± 3.32	25.08 ± 6.63	21.97 ± 3.12	24.66 ± 6.27	0.048 *
ICW, lts	27.61 ± 4.55	28.42 ± 2.78	26.76 ± 4.48	27.63 ± 5.83	0.706
Thoracic impedance index, 200 Hz/5Hz	0.77 ± 0.14	0.81 ± 0.07	0.82 ± 0.05	0.79 ± 0.13	0.591
Trunk impedance index, 200 Hz/5Hz	0.76 ± 0.16	0.82 ± 0.05	0.81 ± 0.09	0.79 ± 0.1	0.225
Abdominal impedance index, 200 Hz/5Hz	0.75 ± 0.18	0.8 ± 0.11	0.81 ± 0.12	0.79 ± 0.13	0.514
Third space fluid, lts	-0.62 ± 1.59	0.14 ± 1.26	-0.66 ± 1.47	-0.03 ± 1.1	0.018 *
Prediction marker, 200 Hz/5Hz	0.82 ± 0.08	0.81 ± 0.05	0.83 ± 0.02	0.84 ± 0.04	0.101
Phase angle, °	5.07 ± 1.03	5.33 ± 1.03	5.16 ± 0.79	4.9 ± 1.02	0.177
ASM, kg	6.79 ± 1.1	6.93 ± 1.11	7.83 ± 2.69	6.9 ± 1.04	0.032 *
Chair test, n (%)	9.85 (8.87)	-	2.85 (4.64)	-	0.636
Prediction marker B3, 200 Hz/5Hz	10 (31.25)	9 (21.95)	5 (23.81)	31 (39.74)	0.194
Dynapenia, n (%)	11 (37.93)	19 (51.35)	9 (42.86)	38 (55.07)	0.419
Sarcopenia, n (%)	5 (16.13)	6 (15)	6 (28.57)	16 (22.54)	0.544

SAH: Systemic Arterial Hypertension. DM: Diabetes Mellitus. COPED: Chronic Obstructive Pulmonary Disease. BMI: Body Mass Index. TBW: Total Body Water. ECW: Extracellular Body Water. ICW: Intracellular Body Water. ASM: Skeletal Appendicular Muscle Mass.  $p<0.05$

## Heart Failure - Chronic Heart Failure, Clinical, Comorbidities

**The role of cystatin c-creatinine eGFR difference in assessing renal function and its correlation with frailty in patients with worsening heart failure: a real-world study**

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**Background:** An accurate assessment of renal function in heart failure (HF) patients is crucial for optimizing pharmacological management and refining prognosis. Although equations combining creatinine and cystatin C provide a more precise estimation of the glomerular filtration rate (eGFR), the creatinine-based equation (eGFRcr) remains the recommended and routinely used method. Nevertheless, eGFRcr often overestimates renal function, and the difference between cystatin C-based eGFR and eGFRcr (eGFRdiff = eGFRcys - eGFRcr) has been associated with poorer outcomes in acute HF. To date, eGFRdiff has not been investigated in worsening HF patients (WHF) with chronic kidney disease (CKD).

**Purpose:** The primary objective was to describe the distribution of eGFRdiff in WHF patients across different CKD stages. Additionally, we aimed to investigate the association between eGFRdiff and frailty.

**Methods:** This observational, single-center pilot study was conducted at the HF outpatients clinic at our Hospital, Italy, enrolling consecutive patients diagnosed with WHF. The eGFRdiff was analyzed both as a continuous and categorical variable using a previously proposed cutoff of -15 ml/min/1.73 m<sup>2</sup>. Frailty was assessed through the Frailty Index (FI), calculated according to the DAPA-HF criteria.

**Results:** A total of 142 patients were included. The median age was 78 years (IQR 69-83), 62% were males. 83.7% were affected by CKD (25.7% with an eGFR < 30 ml/min/1.73 m<sup>2</sup>), 40% had a history of myocardial infarction, and 26.8% of valvular heart disease. The median left ventricular ejection fraction was 42%, and all the patients were treated with loop diuretics. The eGFRcr, eGFRcys, and