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RESEARCH LETTER

Association Between Heart Failure Phenotypes and Long Term Mortality After Endovascular Therapy for Symptomatic Peripheral Artery Disease: Insights from a Retrospective Japanese Multicentre Study

Yuki Shima [a,*], Eiji Karashima [b], Shingo Kurimoto [c], Mitsuru Abe [a], SETers investigators [†]

[a] Department of Cardiovascular Medicine, Kurashiki Central Hospital, Kurashiki, Japan
[b] Department of Cardiology, Shimonoseki City Hospital, Shimonoseki, Japan
[c] Department of Cardiology, Tokushima Red Cross Hospital, Tokushima, Japan

Heart failure (HF) frequently co-exists with peripheral artery disease (PAD) and is associated with adverse cardiovascular outcomes. Previous studies have shown that PAD and HF are associated with an increased mortality rate.[1,2] The prognostic impact of HF phenotype after endovascular therapy (EVT) remains insufficiently characterised. Whether heart failure reduced ejection fraction (HFrEF) confers incremental risk compared with heart failure with preserved ejection fraction (HFpEF) in this setting is unclear. Therefore, this study investigated the association between HF phenotype and long term mortality rate in patients, particularly those with chronic limb threatening ischaemia (CLTI).

This multicentre retrospective study included consecutive patients who underwent EVT for symptomatic lower extremity PAD (Rutherford categories 2 − 6) between January 2018 and December 2020 at 13 Japanese centres. Among 1 685 eligible patients, those without available left ventricular ejection fraction (LVEF) data were excluded, leaving 1 585 patients for analysis. A history of HF was determined based on a previously documented clinical diagnosis in medical records. For the purpose of this study, HF definition was retrospectively aligned with the 2021 European Society of Cardiology guideline.[3] As supportive evidence, elevated natriuretic peptide [brain natriuretic peptide (BNP) $\geq$ 100 pg/mL, NT-proBNP $\geq$ 300 pg/mL] levels or LVEF of $<$ 50% were considered indicative of HF. Patients were categorised as non-HF, HFpEF (LVEF $\geq$ 50%) or HFrEF (LVEF $<$ 40%). Patients with midrange LVEF (40 − 49%) were excluded from phenotype specific analysis.

The primary outcome was all cause mortality at three years following EVT. Follow up information was obtained from hospital records and scheduled outpatient visits; vital status was confirmed by telephone when necessary and was available for 88% at three years. Loss to follow up did not differ between groups. Survival was estimated using the Kaplan−Meier method and compared using the log rank test. Cox proportional hazards regression was used to evaluate associations between HF status or phenotype and death, adjusting for clinically relevant covariables including age, sex, diabetes mellitus, CLTI, haemodialysis, serum albumin level, coronary artery disease and use of guideline directed cardiovascular medications including antiplatelet agents, statins, β blockers, renin angiotensin system inhibitors and mineralocorticoid receptor antagonists. This study was approved by the Institutional Review Board of Kurashiki Central Hospital (Reference no. 4622).

Of the one 585 patients, 639 (40.3%) were classified as having HF. Patients with HF were older and had a higher prevalence of diabetes mellitus, haemodialysis, coronary artery disease, atrial fibrillation or flutter, and CLTI than those without HF. During the three year follow up, the all cause mortality rate was significantly higher in patients with HF compared with non-HF (26.8% *vs.* 8.1%, log rank $p < .001$; Fig. 1A). After multivariable adjustment, HF remained strongly associated with the increased mortality rate (HR 2.37, 95% CI 1.76 − 3.18; $p <$ .001). Among the patients with HF, 413 were classified as HFpEF and 75 as HFrEF. Patients with HFrEF were more frequently men and had a higher prevalence of coronary artery disease. Patients with HFrEF exhibited a significantly higher three year all cause mortality rate compared with those with HFpEF (38.5% *vs.* 22.8%, log rank $p = .009$; Fig. 1B). This association persisted after adjustment for baseline differences.

When stratified by PAD severity, HF phenotype had distinct prognostic implications. In patients with intermittent claudication, mortality did not differ between HFpEF and HFrEF (14.3% *vs.* 19.1%, log rank $p = .60$). In contrast, among patients with CLTI, those with HFrEF experienced a markedly higher mortality rate than those with HFpEF (32.4% *vs.* 56.2%, log rank $p = .016$). Given that CLTI itself is associated with poor systemic prognosis,[4] the co-existence of CLTI and HFrEF appears to identify an ultra high risk subgroup even after successful revascularisation.

HF was strongly associated with long term death after EVT for PAD, and HF phenotype provided incremental prognostic information. While the adverse interaction between PAD and HF has been reported previously,[1,2] the present findings extend previous knowledge by highlighting the particularly unfavourable prognosis associated with HFrEF in patients with CLTI undergoing EVT. In such patients, successful limb revascularisation may be insufficient to offset the competing risk imposed by impaired cardiac reserve and systemic vulnerability.

Routine assessment of HF status and LVEF before EVT may improve risk stratification and inform clinical decision

[†] A list of the authors in the SETers Investigators is included in Appendix A.

[*] Corresponding author. Department of Cardiovascular Medicine, Kurashiki Central Hospital, 1-1-1 Miwa, Kurashiki 710-8602, Japan.
E-mail address: yshima518@yahoo.co.jp

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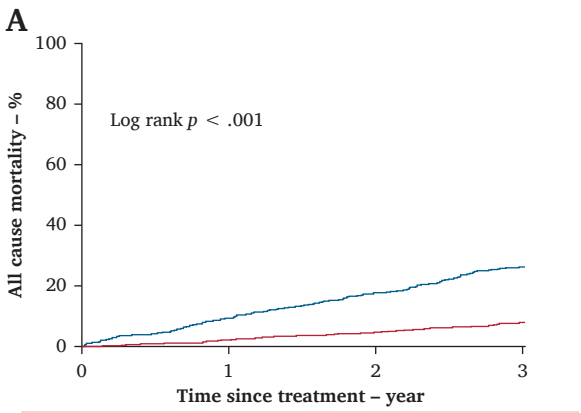
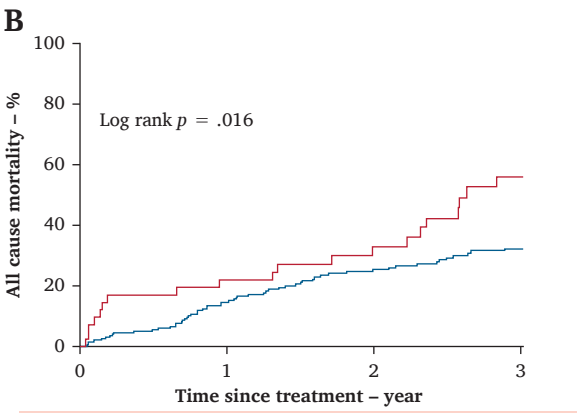


Month	0	6	12	18	24	30	36
HF							
N of patients at risk	639	610	544	496	434	388	308
Cumulative incidence		4.5	9.7	13.8	18.2	22.7	26.8
Non-HF							
N of patients at risk	946	937	895	853	804	747	663
Cumulative incidence		0.1	2.4	3.8	4.8	6.4	8.1



Month	0	6	12	18	24	30	36
HFpEF							
N of patients at risk	197	187	156	139	118	104	87
Cumulative incidence		5.6	15.2	20.7	25.5	29.5	32.4
HFrEF							
N of patients at risk	41	35	31	29	24	18	10
Cumulative incidence		17.1	22.1	27.3	33.1	42.7	56.2

Figure 1. Cumulative Kaplan–Meier estimates of all cause mortality. (A) Comparison between patients with and without HF. (B) Comparison between patients with HFpEF and HFrEF. HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; CLTI = chronic limb threatening ischaemia.

making, particularly in patients with CLTI. According to the 2024 European Society for Vascular Surgery PAD guidelines, risk stratification and optimisation of cardiovascular comorbidities are strongly recommended before revascularisation.[5] The present findings support systematic assessment of HF phenotype as part of this process. Identification of HFrEF may warrant careful peri-procedural management and close post-EVT surveillance.

Several limitations should be acknowledged. This was a retrospective observational study, and residual confounding cannot be excluded. HF diagnosis and phenotyping were based on available clinical data, and patients with midrange LVEF were excluded from phenotype specific analysis. The subgroup of patients with CLTI and HFrEF was small ($n = 41$), and the findings should be interpreted as exploratory. In addition, the study population consisted exclusively of Japanese patients treated with EVT, which may limit generalisability to other populations or revascularisation strategies. No formal sample size calculation was performed, as this was an exploratory retrospective analysis.

In conclusion, HF is strongly associated with increased mortality in patients undergoing EVT for PAD. Among HF phenotypes, HFrEF confers the greatest risk, particularly in patients with CLTI. HF phenotyping may therefore aid risk stratification in patients undergoing EVT for PAD and should be considered in future outcome oriented studies.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2026.04.027.

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Chronic limb threatening ischaemia, Endovascular therapy, Heart failure, Heart failure with reduced ejection fraction, Heart failure with preserved ejection fraction, Peripheral artery disease

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