nature portfolio

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Last updated by author(s): Jul 2, 2025

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	CVI42 (Circle cardiovascular imaging, Calgary, Canada) for cardiovascular magnetic resonance imaging data REDCap was used for data collection
Data analysis	SPSS, version 24 (SPSS; IBM, INC, Armonk, NY) R, version 4.3.3 (R foundation for statistical computing, Vienna, Austria) GraphPad Prism 8.1.2 (GraphPad Software, Inc, San Diego, CA)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

De-identified data will be available upon reasonable request with the corresponding author (cchin03m@gmail.com). Interested researchers should submit proposals

and statistical analysis plans to the corresponding author. Requestors will be required to sign a data use agreement, in compliance with relevant patient confidentiality and privacy regulations.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The study included males and females, of which 41% were males. Post hoc subgroup (including sex) analyses of the primary endpoint were performed to test heterogeneity of treatment effects.
Reporting on race, ethnicity, or other socially relevant groupings	The study included the major races in Singapore (Chinese, Malays and Indians), 91% were Chinese in the study. Information on race of the study participants was self reported. We did not report any stratified analyses on race, ethnicity or other socially relevant groupings because of the small number of patients.
Population characteristics	Eligible participants were adults at least 21 years old with essential hypertension and Stage B HF, defined as having LVH diagnosed based on Asian specific thresholds on cardiovascular magnetic resonance. Essential hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg on at least one medication for BP control. Individuals with known secondary causes of hypertension, inherited cardiomyopathies, atrial fibrillation, and history of cardiovascular complications (such as myocardial infarction, heart failure and stroke) were excluded. Other exclusion criteria included intolerance to ARBs, contraindications for CMR, stage IV or V chronic renal disease, presence of disease with limited life expectancy (< 3 years), pregnancy and/or breast-feeding. The mean age at baseline was 58±11 years, and 32 (41%) were males. The baseline 24h mean systolic and diastolic BP were 137±14 and 81±11 mmHg, respectively.
Recruitment	Potential participants were identified from the REMODEL cohort, an ongoing prospective study that examines the role of CMR in patients with hypertension (ClinicalTrials.gov Identifier: NCT02670031).
Ethics oversight	The trial was reviewed and approved by the SingHealth Centralized Institutional Review Board (CIRB ref: 2018/2182) and the Health Sciences Authority (the local governing body which oversees clinical trials).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	An estimated sample size of 70 (35 per treatment group) would provide effective power of 80% at a 5% significance level (two-sided) to detect superiority of sacubitril/valsartan over valsartan for the primary endpoint, assuming an absolute minimum difference of 3.5 mL/m2 in mean interstitial volume change between the two groups, a standard deviation (SD) of 5.8mL/m2 and a moderate correlation of 0.60 between interstitial volume at baseline and week 52. The effect size was based on an estimate of the magnitude of myocardial fibrosis regression that could be expected to translate into improved cardiac function and clinical outcomes. The study plan was to recruit 80 participants, allowing a withdrawal rate of up to 15%.
Data exclusions	No data was excluded.
Replication	No replication was performed; not applicable in this phase II randomized controlled trial.
Randomization	Participants were randomized to sacubitril/valsartan versus valsartan in a 1:1 fashion for 52 weeks. Randomization was performed using sealed and sequentially numbered envelopes, prepared by the Singapore Clinical Research Institute.
Blinding	This is a prospective, randomized, open-label, blinded endpoint (PROBE). Trained personnel performing image analysis were blinded to the treatment allocation and clinical data. Statistical analyses were performed by team members who were not involved in the image analysis and patient treatment.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJEguidelines for publication of clinical research and a completedCONSORT checklist must be included with all submissions.

Clinical trial registration	NCT03553810
Study protocol	Study protocol has been published (Front. Cardiovasc. Med. 2023;10:1248468) and has been submitted with manuscript
Data collection	Recruitment occurred between June 2019 and June 2023. Study procedures and follow up visits were carried out at a single site (National Heart Centre Singapore). Data were collected using standardized Research Data Collection Forms and entered into an electronic data collection system (REDCap) by the research staff.
Outcomes	The primary endpoint was the difference in absolute change in interstitial volume from baseline and post-treatment between the two groups. Interstitial volume, reflecting diffuse interstitial fibrosis in the absence of infiltrative diseases, was derived as the product of ECV fraction × myocardial volume Secondary endpoints were CMR markers of cardiac remodeling that included LV morphology, function (including multi-directional LV strain) and mechanics. LV concentricity was defined by the ratio between LV mass and end-diastolic volume (EDV).

Plants

Seed stocks	NA
Novel plant genotypes	NA
Authentication	NA