

Can metformin reduce heart muscle thickening and improve exercise capacity in people with heart failure with preserved ejection fraction who are overweight or have insulin resistance?

Submission date 30/06/2026	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 26/07/2026	Overall study status Ongoing	☐ Statistical analysis plan ☐ Results
Last Edited 22/07/2026	Condition category Circulatory System	☐ Individual participant data ☒ Record updated in last year

Plain English summary of protocol

Background and study aims

Heart failure is a condition in which the heart cannot pump blood around the body efficiently. About half of people with heart failure have a type called heart failure with preserved ejection fraction (HFpEF), where the heart muscle still squeezes normally but is stiff and does not relax properly, causing breathlessness, tiredness and reduced ability to exercise. There are very few effective treatments. Many people with HFpEF are overweight or have insulin resistance (where the body cannot use insulin properly), which can thicken the heart muscle (left ventricular hypertrophy) and worsen symptoms. Metformin is a widely used, inexpensive diabetes medicine that can aid weight loss, reduce inflammation and improve insulin sensitivity; in earlier studies it reduced heart muscle thickness and improved exercise ability in heart failure. This study aims to find out whether metformin can reduce heart muscle thickness and improve exercise capacity in people with HFpEF who are overweight or have insulin resistance but do not have diabetes.

Who can participate?

Adults aged 18 years and over with symptomatic HFpEF (NYHA class II–III), evidence of a thickened heart muscle and preserved pumping function on an ultrasound scan, raised levels of a blood marker of heart strain (NT-proBNP) and either obesity or insulin resistance, who do not have diabetes and are taking a water tablet (loop diuretic).

What does the study involve?

Participants are randomly allocated to take either metformin (modified-release) or a matching dummy tablet (placebo) for 12 months; neither the participant nor the study team knows which they receive. The dose starts low and increases after two weeks if tolerated. Over 12 months participants attend visits (with some telephone check-ins) for safety blood tests, an exercise test, heart MRI and ultrasound scans, and a quality-of-life questionnaire. Heart muscle thickness (by MRI) and exercise capacity are compared between the start and end of the study.

What are the possible benefits and risks of participating?

Participants may not benefit directly, but the study may show whether metformin helps people with HFpEF and could lead to a larger trial. Metformin's most common side effects are stomach-related (loss of appetite, nausea, vomiting, diarrhoea, abdominal discomfort, and a metallic taste), usually mild and self-limiting; a very rare side effect is a build-up of acid in the blood (lactic acidosis). People at higher risk are excluded, and participants are monitored with regular blood tests. The heart MRI involves a contrast dye injection and is not suitable for everyone (e.g., certain implants or claustrophobia).

Where is the study run from?

University of Sulaimani (Iraq)

When is the study starting and how long is it expected to run for?

August 2026 to

Who is funding the study?

Who is the main contact?

Contact information

Type(s)

Public, Scientific, Principal investigator

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Study information

Scientific Title

Metformin versus placebo in patients with heart failure with preserved ejection fraction and obesity or insulin resistance (MET-HFpEF)

Acronym

MET-HFpEF

Study objectives

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 13/05/2026, The Ethics Committee of the College of Medicine (University of Sulaimani, Sulaimani, 46001, Iraq; +964 (0)533270924; med.ethics@univsul.edu.iq), ref: 153 (Ethics Committee Meeting No. 17)

Primary study design

Interventional

Allocation

Randomized controlled trial

Masking

Blinded (masking used)

Control

Placebo

Assignment

Parallel

Purpose

Treatment

Study type(s)

Health condition(s) or problem(s) studied

Heart failure with preserved ejection fraction (HFpEF), New York Heart Association (NYHA) Class II-III, insulin resistance, pre-diabetes, obesity

Interventions

Eligible participants will be randomised in a 1:1 ratio to either metformin modified-release or matched placebo. Randomisation will be stratified by the presence of atrial fibrillation and use of SGLT2 inhibitors, and the proportion of participants in atrial fibrillation will be limited to 40% of the total cohort. The randomisation sequence will be generated by an independent statistician using a validated computer-based randomisation system.

Metformin (modified-release) is titrated from 500 mg twice daily to 1000 mg twice daily (2000 mg/day) for 12 months; the comparator is a matching placebo (lactose).

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Metformin

Primary outcome(s)

1. Left ventricular mass index (normalised to height^{1.7}) measured using cardiac MRI at baseline and 12 months

Key secondary outcome(s)

Completion date

01/08/2027

Eligibility

Key inclusion criteria

1. Willing/able to consent
2. Aged ≥ 18 years
3. Symptomatic HFpEF (NYHA II–III)
4. Elevated indexed left ventricular (LV) mass on screening echo (males >81 g/h^{1.7}, females >60 g/h^{1.7})
5. Insulin resistance (Fasting Insulin Resistance Index [FIRI] ≥ 2.7) or pre-diabetes (HbA1c 39–47 mmol/mol) or body mass index (BMI) ≥ 30 kg/m²
6. NT-proBNP >300 pg/mL (sinus rhythm) or >600 pg/mL (AF)
7. Left ventricular ejection fraction (LVEF) $\geq 45\%$
8. On loop diuretics
9. Able/willing to comply

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

18 Years

Upper age limit

98 Years

Sex

All

Total final enrolment

0

Key exclusion criteria

1. Type 1 or 2 diabetes
2. HbA1c >47 mmol/mol
3. SBP >180 mmHg
4. eGFR <30 ml/min/1.73 m²
5. Contraindications to CMR
6. Previous LVEF $<40\%$
7. Metformin hypersensitivity
8. Severe cognitive impairment

9. Active malignancy or other life-threatening disease
10. Hepatic insufficiency or history of alcoholism
11. Acute conditions affecting renal function
12. Pregnancy/lactation
13. Participation in another trial within 30 days
14. Investigator discretion

Date of first enrolment

01/08/2026

Date of final enrolment

31/08/2026

Locations

Countries of recruitment

Iraq

Sponsor information

Organisation

University of Sulaimani

ROR

<https://ror.org/00saanr69>

Funder(s)

Funder type**Funder Name**

Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan**IPD sharing plan summary**

Not expected to be made available