# High-sensitivity troponin in chronic coronary syndromes

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***on behalf of the ORBITA investigators***

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## Background

The diagnosis of angina has changed very little in the past 200 years since William Heberden first described angina pectoris "*Some Disorder of the Breast*".

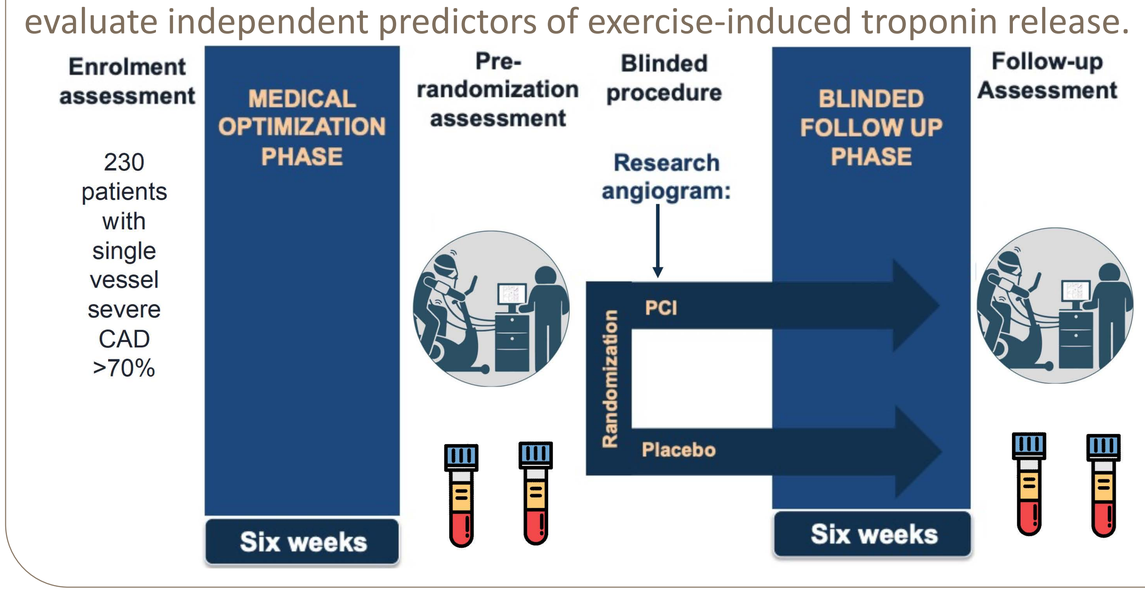
Decision to revascularize patients with stable angina is determined by the presence of **inducible ischemia**, rather than the identification of high-risk patients.

However, there is growing evidence that basing revascularization decisions solely on the presence of ischemia does not accurately discriminate low-risk patients, from the high-risk patients who could benefit from revascularization. The **time course of chronic coronary syndrome** and stable angina is hard to predict and we currently have no robust way of identifying these high risk patients.

We know **troponin** is an excellent **predictor of cardiovascular** risk across the spectrum of acute and chronic disease, however the **mechanism** for troponin release is unclear. In order to provide further insight into the potential role of troponin testing in chronic coronary disease, we first need to establish how levels of this risk-prediction marker are affected by ischemia and its resolution.

## Method

We conducted a substudy of the **ORBITA trial** which was a blinded randomized control trial of 230 patients with known severe single-vessel CAD who were randomized to intervention with **PCI or placebo sham procedure**. Cardiopulmonary exercise testing was performed both before and after intervention (PCI or placebo), and troponin measured at before and after exercise at both time points. Logistic regression was used to evaluate independent predictors of exercise-induced troponin release.




## Results

In total, 198 patients were eligible for inclusion in this substudy. Participants had a median age of 67 (IQR 60 to 73), and had a high prevalence of typical cardiac risk factors including hypertension (n=136, 68.7%), hypercholesterolaemia (n=142, 71.7%), diabetes mellitus (n=36, 18.2%), and previous myocardial infarction (n=12, 10.1%).

Prior to randomisation, 34% of patients had a troponin below the limit of quantification of the assay before exercise. This proportion decreased to 25% after exercise. Similarly the proportion of patients with troponin above the 99$^{th}$-centile upper reference limit (16ng/L in females, 34ng/L in males) increased from 1.6% before exercise, to 2.1% after exercise. (**Figure 1**) In patients randomised to revascularisation, resting hs-cTnI were not altered by PCI (OR 0.78, p=0.375). Revascularisation also did nt alter the exercise induced troponin change. (**Figure 1**)

We constructed logistic regression models to evaluate independent predictors of exercise-induced hs-cTnI change. Following exercise, there was a strong association between exercise-induced hs-cTnI change and exercise time (OR 3.40, p<0.0001), however there was little evidence that revascularisation reduced exercise-induced hs-cTnI increment compared to placebo (OR 1.42, p=0.251).**(Figure 2**) There was also no association between ischemia (p=0.114) or ischaemic-symptom severity (p=0.201).

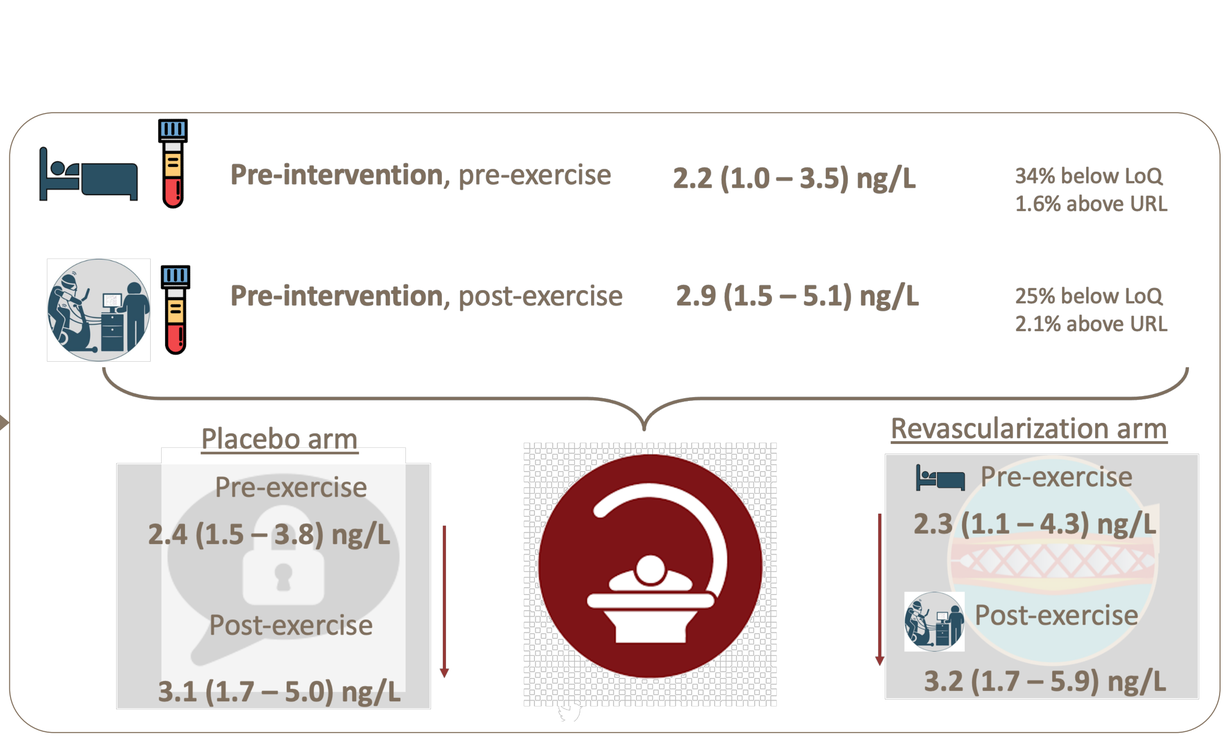



Figure 1: Troponin concentrations pre and post exercise prior to randomisation, and then pre and post exercise after randomisation to either sham/placebo procedure, or revascularisation with PCI

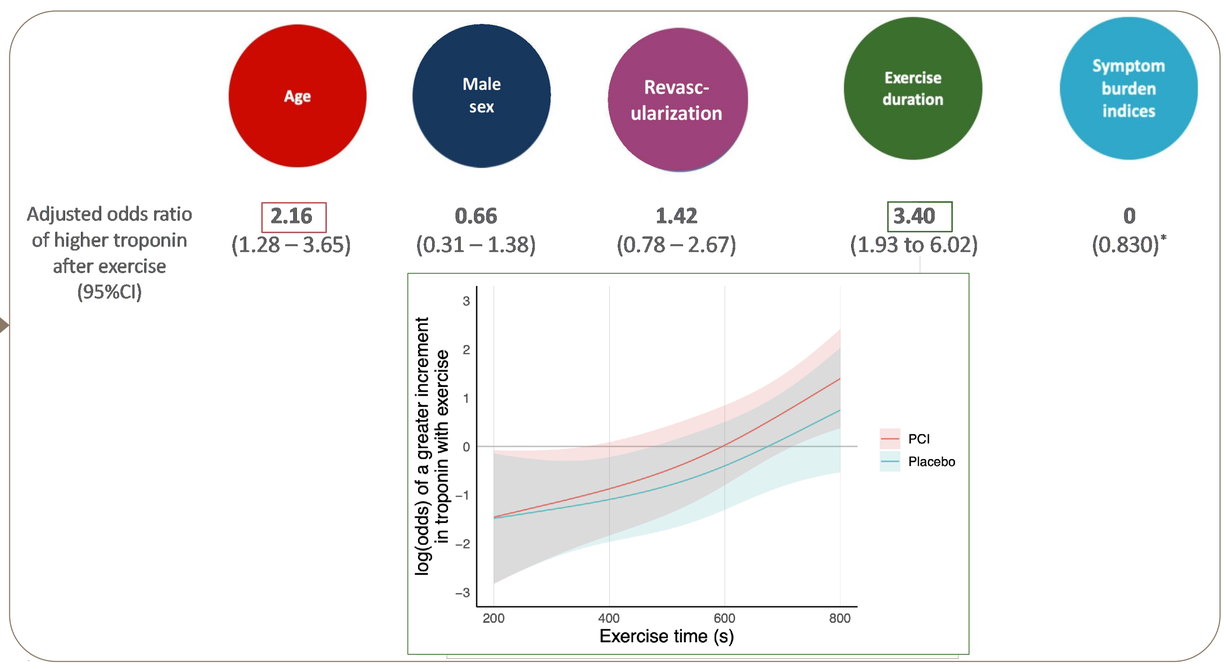



Figure 2: Results of logistic regression models evaluating independent predictors of post-exercise troponin increase

## Conclusion

In patients with stable angina and single vessel coronary disease, revascularization with effective **treatment of myocardial ischemia did not affect resting hs-cTnI or exercise associated hs-cTnI** release over a placebo procedure. Exercise associated hs-cTnI release was not affected by the severity of myocardial ischemia, it was instead, principally **modulated by the intensity of exercise** achieved. Taken together, these data support the conclusion that reversible myocardial ischemia is not the dominant mechanism for resting or exercise associated cardiac troponin release in patients with stable coronary artery disease.

## Potential implications for clinical practice

Ischemia alone is a poor predictor of risk in chronic coronary syndromes, and should have a limited role in revascularization decisions

Troponin could be used in the outpatient clinic to select patients for revascularization who are at the highest risk of acute coronary syndromes

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