

## Case Report

# Myocardial Bridging Unmasked by High-Sensitivity Cardiac Troponin-I in an Asymptomatic Sportswoman

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New developments in cardiac screening include low-dose coronary CT angiography (CCTA) and high-sensitivity cardiac troponin (hs-cTn). A 38 year-old female had participated in a study on hs-cTn and exercise; hs-cTn-I levels (ng/L) before, immediately after and a day following a 5.4 km run were 6.4, 10.4 and 7.7 respectively (troponin upper reference limit in the local population: all-group = 25.6, women 40-65 years = 17.9, young women with a mean age of 35 years = 4.8). She has hypercholesterolemia but declined medications. Both parents are on statins. Physical examination was normal. Lipids (mmol/L) were elevated - cholesterol 8.2, LDL 5.5. CCTA showed severe myocardial bridging of the mid-LAD associated with 70% stenosis. Use of a single hs-cTn-I cut-off for both sexes or for older women would have masked the fact that her baseline hs-cTn-I values exceeded the female age-specific upper reference interval. Post-exercise hs-cTnI with appropriate age and gender cut-offs may provide additional reasons for further cardiac assessment.

**Keywords:** Exercise; High-Sensitivity Troponin-I; Myocardial Bridging; Screening**Introduction**

The new high-sensitivity cardiac troponin (hs-cTn) assays such as hs-cTnI detects troponin in the majority of normal subjects [1]. Following exercise hs-cTn is released and this phenomenon has been studied in exercise stress testing and sports [2]. The pathophysiology of exercise-induced troponin release has been clarified using new imaging techniques such as coronary CT angiography (CCTA) and hs-cTn assays [2,3]. As more people take up running for health and recreation purposes, front-line physicians may face the issue of screening them for cardiac disease. We report the detection of Myocardial Bridging (MB) using low-dose CCTA in an at-risk asymptomatic sportswoman with increased post-exercise hs-cTn-I. MB, a condition known to cardiologists and radiologists but not the general physicians, may be more prevalent than believed.

**Case Presentation**

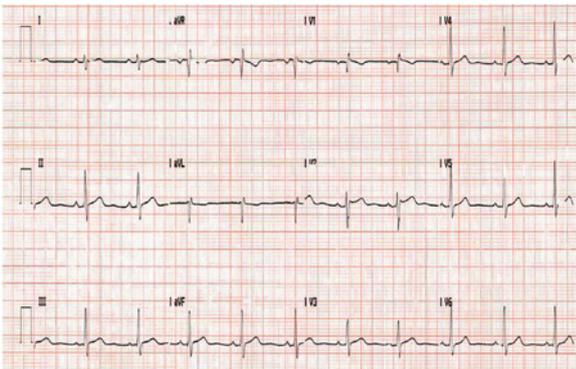
A 38 year-old female runner who had participated in a study on high-sensitivity troponin I (Abbott Diagnostics) and exercise was referred for consultation. After completing a 5.4 km community run in 34minutes, her serum hs-cTn-I results (ng/L) taken before, immediately after and a day later were 6.4, 10.4 and 7.7 respectively (99<sup>th</sup> percentile Upper Reference Interval [URL] for the local population = 25.6 [1], female population 40-65 years = 17.91, young females with a mean age of 35 years = 4.8 [4]). She had been active in various sports (yoga, jogging, rowing, kick boxing, running and swimming) for over 20 years. She has not had chest discomfort, sweating, breathlessness, dizziness, fainting or weakness. She does not smoke cigarettes. Past medical history was significant for high cholesterol (ranging from 5.5-8.0mmol/L) of a few years standing for which she had declined medications. Family history is also significant. Both her parents were on statins for hypercholesterolemia for many

years; in fact, her father had a stent implanted at age 62. Physical examination was normal. BP120/80mm Hg, pulse 60/min and BMI 24.8kg/m<sup>2</sup> [2]. Resting ECG (Figure 1) was borderline abnormal (moderate right axis deviation, incomplete right bundle branch block). This resting ECG finding may in fact reflect exercise-induced cardiac remodeling rather than pathologic changes and is compatible with normal exercise physiology, underscoring the challenge of ECG evaluation in sportspersons [5].

Serum lipids (mmol/L) were abnormal - cholesterol 8.2, HDL 2.5, LDL 5.5. Other blood tests (triglycerides, HbA1c, creatinine, uric acid, liver function, thyroid function) were normal. On the basis of her elevated cholesterol and family history, she is at risk for cardiovascular disease and merited further evaluation. As a “more senior” at-risk sportswoman, she consented to an elective ECG-gated low dose CCTA (GE HD-750 cardiac CT scanner) to detect underlying cardiovascular disease and to guide the need for statins. CCTA showed severe Myocardial Bridging (MB) of the mid-Left Anterior Descending Artery (LAD) associated with 70% stenosis (Figure 2,3) and low density plaque proximally. She was started on atorvastatin 20mg daily and agreed to moderate her exercise regime. Her latest lipids have improved - cholesterol 4.6, LDL 2.2.

**Discussion**

As far as we are aware, this is the first case where MB is discovered fortuitously following evidence of myocardial ischemia from elevated troponin during exercise. MB is a congenital anomaly in which a segment of a coronary artery that normally runs in the epicardial adipose tissue courses through the myocardium beneath a band of muscle i.e. intra-myocardial tunneling [6]. MB frequently occurs in the mid-LAD as in this patient. MB is best detected by CCTA rather than invasive angiography. With better imaging techniques and



**Figure 1:** Resting ECG showing moderate right axis deviation and incomplete right bundle branch block.



**Figure 3:** Low-dose coronary CT angiography showing end on view of mid-LAD with myocardial bridging.



**Figure 2:** Low-dose coronary CT angiography showing profile view of mid-LAD with myocardial bridging.

increased use of CCTA for evaluation of cardiac risk and triage of chest pain in the emergency department the incidence of MB can only rise. The real magnitude of MB is unknown although an incidence of over 50% has been found in autopsy series [6]. MB may be more common than generally appreciated; a prevalence of over 50% in Asians has been reported [7]. While MB is generally benign [6] it can be associated with catastrophic cardiac outcomes [6,8].

The pathophysiology of troponin in exercise has long been an area of interest [3] especially in intensive sports such as marathon running. Prior to the introduction of hs-cTn, studies of troponin release in lower intensity exercise have been hampered by the detection limit of troponin assays. In a recent study using the same Abbott hs-cTnI assay Rosjo et al [9] detected increases in serum hs-cTnI after exercise stress testing. Subjects with reversible ischemia (n=19) showed a 50% increase in median hs-cTnI from 4.4ng/L to 6.9ng/L ( $p < 0.01$ ) 4.5 hours after the exercise stress test. Median hs-cTnI also rose from 2.5ng/L to 5.1ng/L in subjects (n=179) without reversible ischemia. In this case, report the patient's baseline troponin (6.4ng/L) was above the 99<sup>th</sup> percentile URL for healthy young women with a mean age of 35 years in Singapore (4.8ng/L) [4] using the same assay. Applying the all-group URL (25.6ng/L) [1] or female URL (17.9ng/L) [1] for the Abbott assay would have masked the fact that our patient's baseline hs-cTnI was significantly elevated and there was a 62.5% increase in the post-exercise troponin level to 10.4ng/L. From studies on biological variation in healthy subjects and those with stable coronary heart disease, the reference change value

for troponin is 50% [10]. In addition, the 24-hour post-exercise hs-cTnI (7.7ng/L) in this patient was still 20.3% above the baseline level of 6.4ng/L. Did she have a minor silent Type 2 myocardial infarction (MI)? It could also be argued that this could represent reversible myocardial ischemia rather than myocardial injury [11,12]. The precise mechanism is academic as almost all increases of troponin are associated with poorer outcomes in the long-term. More important though is the prevention of repetitive injury from regular strenuous exercise and sports; hence the recommendation of a moderation in the patient's exercise regime. In the Cardiovascular Health Study [13] (n=4221) of older community dwelling subjects, those with a 50% increase troponin T over baseline values had more cardiovascular events (heart failure and deaths) after a median follow-up of 11.8 years. This underscores the need for greater care in the generation of troponin URLs to include sufficient younger subjects (up to 30 years old) and in the interpretation of hs-cTn results. Cognizance must also be given to gender-specific and age-related cut-offs. Besides, the use of the individual's own troponin values in health as baseline may be the appropriate comparator for serial test results. It is noteworthy that in the Scottish MORGAM study (n=15340) of subjects in their 40's followed up for 20 years, a baseline hs-cTnI threshold of 4.7ng/L for women (using the same Abbott troponin assay) was predictive of future cardiovascular events [14]. In the BiomarCaRe study (n=74738, F=44889) subjects with a mean age at baseline of 52.2 years were followed up for cardiovascular events (13.8 yrs) and overall mortality (12.1 yrs) [15]. Those with hsTnI (Abbott) > 6.0ng/L had increased risk of cardiovascular disease (Hazard Ratio HR 1.93) and overall mortality (HR 2.25). The baseline hs-cTnI in our patient (6.4ng/L) exceeds both the MORGAM and BiomaCaRE hs-cTnI risk thresholds.

The exact mechanism of troponin release in exercise remains unclear [2,3]. Besides myocardial injury and myocardial ischemia, elevations in neuro- and sympathetic hormones may be also contributory. As in this patient, an oxygen supply-demand imbalance has been suggested in a recent study in long distance runners where no plaque rupture or coronary thrombosis was detected in subjects with acute exercise-related cardiac events [12,16]. Hs-cTn-I has also been associated with echocardiographic evidence of cardiovascular dysfunction and cardiac risk independent of conventional markers besides being prognostic in patients with stable coronary artery disease [17]. Hs-cTn-T has also been reported as a marker of chronic cardiac injury and hemodynamic stress in the Dallas Heart Study

[18] and sudden cardiac death in the Cardiovascular Health Study [13]. Thus hs-cTn may provide additional information not captured in other screening modalities and serve as a “biochemical” cardiac stress test. Such studies are emerging. In a recent large study (n=229) of myocardial perfusion with Single-Photon Emission Computed Tomography (SPECT), 39.3% had exercise-induced myocardial ischemia accompanied by elevations in both hs-cTnI (Abbott) and hs-cTn-T compared to those without ischemia [19]. Besides, hs-cTn-T levels may also serve as a window to the heart when blood pressure improves with treatment [20]. Hs-cTn has been hailed as an adjunct to cardiac stress testing [21].

The use of CCTA in subjects in the lower intermediate range of pre-test probability for CAD as in this patient has been endorsed in recent guidelines [22]. Moreover, non-invasive imaging modalities such as CCTA may be useful in detecting premature CAD in subjects like this patient and those with familial hypercholesterolemia and/or family history of heart disease. Also illustrated in this patient is the evidence that imaging provides to improve patient compliance and adherence to treatment.

## Conclusions

Young athletes and professional sportsmen are routinely screened for cardiac risk including the use of echocardiography in some European countries. As more adults and senior citizens participate in more strenuous physical activity, they ought to be appropriately screened as well with careful attention paid to eliciting risk factors. Frontline doctors will have to grapple with when, what and how to screen their patients for underlying heart disease. More extensive screening modalities should be reserved for those who are sedentary, with cardiovascular risk factors and who engage in more vigorous exercise. Availability of better predictive biomarkers such as hs-cTn-I and CCTA imaging may optimize clinical decision-making. The use of both biomarkers and CCTA imaging for screening has been suggested [23]. This case illustrates the potential of hs-cTnI in cardiovascular screening. Larger studies are awaited.

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