Coronary Functional Abnormalities in Patients With Angina and Nonobstructive Coronary Artery Disease Journal Article Review

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Introduction and Aim

Around 40% of patients undergoing diagnostic coronary angiography for angina have no significant coronary stenosis (1). This prospective observational clinical cohort study was the first to comprehensively evaluate coronary functional abnormalities within this group. It was an exploratory study carried out in a Japanese university hospital which enrolled 187 patients (mean age 63.2 ± 12.3 years) undergoing elective diagnostic coronary angiography for the evaluation of chest pain and/or electrocardiographic abnormalities.

The study looked at the effect of epicardial coronary artery spasm and abnormal microvascular resistance on long-term cardiac outcomes i.e. major adverse cardiac events (MACE). It also evaluated whether the Rho-kinase pathway is implicated in the pathogenesis of these functional coronary abnormalities.

Patient selection

Clinically stable patients with angina-like chest pain and non-obstructive coronary artery disease (CAD) on coronary angiography (defined as luminal narrowing<70% and/or Fractional Flow Reserve >0.8), who successfully underwent both:

1) Coronary artery functional testing of coronary flow reserve (CFR) and index of microcirculatory resistance (IMR). Rho-kinase involvement was evaluated as the percentage change in IMR before and after administration of intracoronary fasudil (a selective Rho-kinase inhibitor).

2) Coronary vasoreactivity testing via the acetylcholine provocation test for epicardial coronary spasm. Microvascular spasm (MVS) was identified based on diagnostic criteria proposed by the COVADIS (Coronary Vasomotor Disorders International Study) group.

Researchers excluded patients with cardiomyopathy, valvular disease, previous coronary stenting, contraindications for provocation test (e.g., bronchial asthma), renal failure, and general poor condition.
Results

187 patients met the inclusion criteria and were followed-up for a median of 893 days. 68.4% of these patients were diagnosed with epicardial coronary spasm (vasospastic angina, VSA) and 12.0% with MVS. Cardiac events occurred in 10 patients (5.3%). High IMR significantly correlated with MACE. IMR cut-off value for developing MACE was 18.0. Additionally, the administration of fasudil significantly ameliorated IMR for patients with VSA and high IMR.

Conclusion

The study demonstrated that in patients with chest pain and non-obstructive CAD, co-existence of epicardial coronary spasm and increased microvascular resistance is associated with worse prognosis, for which Rho-kinase activation may be involved.

Interpretation and Limitations

While this study can be commended for a long follow-up period, it was limited to a single study centre, small sample size and event number. East Asians have higher rates of vasomotor angina compared to Westerners(2). Also, whilst Western studies have reported that non-obstructive CAD is more common in females, 60% of participants that met this study criteria were male. These factors limit its generalisability to an Irish setting.

Although the study found that most patients were on guideline-recommended therapies, no data was collected on changes in treatments or adherence to therapy, which can also impact cardiac outcomes. The study was also notable for finding that an IMR of 18.0 and above was most prognostic of MACE in this group. This is significantly lower than previously reported (IMR ≥25) (3)(4).

Reflection and Future Outlook

Chest pain is a very common complaint managed by physicians. Many doctors may feel challenged when managing patients with ongoing angina despite essentially normal coronaries on angiography. More emphasis needs to be placed on the coronary microcirculation, which despite not being visible on conventional direct angiography, contributes to over 50% of total coronary vascular resistance and helps regulate coronary blood flow (5).

This study highlights the importance of coronary functional abnormalities and microvascular disease as a lesser known cause of angina with significant morbidity and mortality. Coronary microvascular dysfunction (CMD) is known to share similar risk factors to obstructive CAD (e.g smoking, hypertension, hyperlipidemia)(6), and so will benefit from similar treatments. Clinicians may also need to have a lower threshold for treating symptomatic patients with risk factors but normal angiograms, as CMD may be present. More research is also needed on potential therapeutic agents that target CMD and VSA like rho-kinase inhibitors.
References


