Angina with normal coronary angiogram

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Introduction:
Approximately 20% to 30% of patients undergoing coronary angiography for symptomatic chest pain are found to have normal epicardial coronary arteries. When compared with patients who present with obstructive coronary artery disease, these patients are more likely to be women and tend to be younger. Several conditions can result in chest pain with a normal coronary angiogram (NOCAD) and a proper diagnosis of the etiology is essential in managing these patients.

Pathophysiology:
In the absence of significant coronary artery stenosis, coronary blood flow (CBF) is regulated and limited by two main factors: coronary endothelial function and microvascular function.

Endothelial function:

The endothelial plays an important role in the regulation of vasomotor tone and CBF. This regulation occurs by way of the production and release of vasovative factors. The important vasodilators are:
1) Nitric oxide
2) Prostacyclin I

The most potent vasoconstricting agents produced by the endothelium are:
1) Endothelin-I
2) Thromboxane A_2

If the endothelium does not function properly, NOCAD may occur as a result of a mismatch between myocardial oxygen supply and demand.

An imbalance between these vasoactive substances due to endothelial dysfunction may result in a mismatch between myocardial oxygen supply & demand. Also endothelial dysfunction promotes atherosclerosis & eventual development of coronary artery stenosis.

Microvascular function:

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The coronary arterioles form the resistance vessels in coronary circulation with diameter of 300μm and are the major determinant of coronary blood flow.
Resistance in these vessels is determined by following factors.
1) Myogenic control- Pressure exerted by surrounding myocardium affects cross sectional area of blood vessels.
2) Flow mediated - control
3) Metabolic control- mediated CO_2 by oxygen consumption, adenosine, prostocycline, norepinephrine.
4) Neurohumoral control

The differential diagnosis of NOCAD can be classified anatomically into three categories: (Table I)
1) Epicardial disease
2) Coronary microvascular dysfunction
3) Non coronary disease

Table I
Differential diagnosis of chest pain in the setting of a normal coronary angiogram
I. Coronary disease
A. Epicardial disease
1. Endothelial dysfunction
2. Coronary spasm
3. Coronary bridging
B. Microvascular dysfunction
1. Microvascular endothelial dysfunction
2. Hypertension
3. Cardiomyopathy
4. Infiltrative disease
5. Valvular disease
6. Idiopathic
II. Noncoronary disease
A. Gastrointestinal
B. Pulmonary
C. Musculoskeletal
D. Psychologic
Systematic approach to diagnosing the etiology of normal coronary angiogram: -

Functional angiogram-
Determination of the etiology of NOCAD is essential in its management. A "functional angiogram involving the invasive assessment of coronary physiology allows for a

systematic diagnostic approach to these patients.

Functional angiogram is done to evaluate both the microvascular function and endothelial function. Microvascular function is assessed by coronary flow reserve which is ability of coronary resistance vessels (arterioles) to dilate in response to intra coronary adenosine. Endothelial function is evaluated by intra coronary acetylcholine injection & distal vascular bed is observed for vasoconstriction.

Figure I

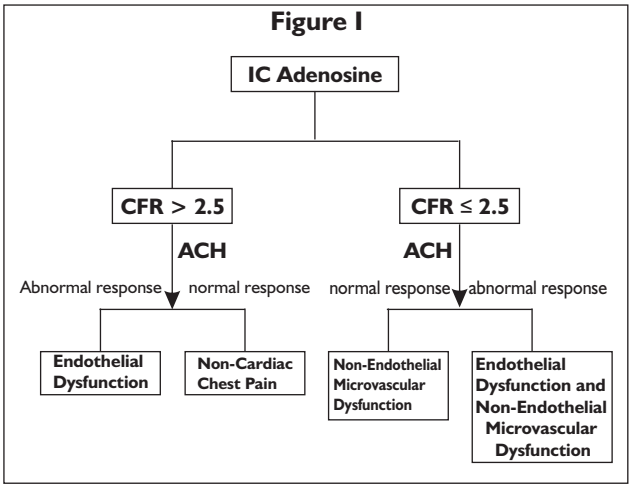

Table II

Treatment strategies for patients with chest pain and a normal coronary angiogram

Etiology	First Line Therapy	Second Line Therapy	Comments
Endothelial Dysfuntion	**Life style modification,** ACIE, Statins	**L-arginine, folate**	**PPAR-γ agents may offer** benefit
Coronary Spasm	Non-dihydropyridine calcium channel blockers, long-acting nitrates	Nifedipine, alpha-blockers, coronary artery stenting, bypass surgery	Non-selective beta blockers should be avoided, aspirin may exacerbate spasm
Myocardial Bridging	Beta-blockers	Coronary artery stenting, surgical myotomy, bypass Surgery	Higher rates of in-stent restenosis occurs in bridging segment
Endothelial-Independent Microvascular Dysfunction	Treatment of underlying etiology of microvascular dysfunction	Beta-blockers, Statins	Imipramine may offer benefits in idiopathic microvascular dysfunction

The management of these patients can be challenging and a correct diagnosis of the etiology is essential. A systematic approach to diagnosing the cause of chest pain can be accomplished with a functional angiogram to assess endothelial and microvascular function. Once the etiology of chest pain is determined, the appropriate therapy can be initiated.

Reference :

Cardiology Clinics – November 2005, Volume 23, Number 4