THE RELATIONSHIP BETWEEN QRS FRAGMENTATION ON 12-LEAD ELECTROCARDIOGRAPHY AND CORONARY ARTERY ECTASIA

Thesis

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List of Abbreviations

CAE	Coronary artery ectasia
CTO	Chronic total occlusion
CAD	Coronary artery disease
CASS	Coronary Artery Surgery Study
fQRS	Fragmented QRS
IVUS	Intravascular ultrasound
LAD	Left anterior descending
LBBB	Left bundle branch block
LVH	Left ventricular hypertrophy
MRI	Magnetic resonance imaging
NSTEMI	Non ST elevation myocardial infarction
SAECG	Signal averaged electrocardiogram
SPECT	Single photon emission tomography
STEMI	ST elevation myocardial infarction
UAP	Unstable angina pectoris

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Introduction

Cardiovascular diseases (CVD), particularly coronary heart disease (CHD) are the major leading cause of death in developing countries (**Gu et al., 2002**). Mostly, manifestation of coronary artery involvement is stenosis but in some cases, abnormal coronary dilation or ectasia can occur (**Li et al., 2009**).

The term of ectasia was first used by **Bjork in 1966** to identify coronary vasodilatation. Coronary artery ectasia (CAE) is a consequence of atherosclerosis in 50% of cases, whereas 20-30% of subjects have origin of fetus periods. According to the angiographic findings, 3%-8% of atherosclerotic coronary artery patients suffered from ectasia (**Satran et al., 2005**) (**Giannoglou et al., 2006**).

The gold standard investigation for the CAE remains the coronary angiogram (**Sorrell, 1996**). Intravascular ultrasound is an excellent tool to assess luminal size and characterize arterial wall changes and it differentiates correctly a true from a false aneurysm caused by plaque rupture. Recently, MDCT is also used as a non-invasive tool for the diagnosis of CAE (**Ali et al., 2017**).

Fragmentation of QRS complex is an easy and non-invasive electrocardiographic parameter associated with inhomogeneous activation of the ventricles and myocardial conduction delays due to myocardial scar and/or ischaemia, which could predict arrhythmic events as well as death. QRS fragmentation analyzed from surface ECG has appeared as a new risk marker for many diseases such as CAD, nonischemic cardiomyopathy (hypertrophic, dilated, Chagas' disease, arrhythmogenic right ventricular cardiomyopathy, fallot, and sarcoidosis), and ion cannel diseases including Brugada syndrome and long QT syndrome (**Priori et al., 2012**).

Das et al., in 2008 the frst ones who described the presence of fQRS in patients with CAD, have demonstrated its good sensitivity and specifcity for the prediction of myocardial scar in patients with poor prognosis associated with this ECG presentation. The underlying mechanisms of fragmentation have been determiend by autopsy studies of patients with MI. Studies have shown that the presence of fQRS is associated with signifcant myocardial necrosis alternating with viable myocardial tissue and interspersed in abundant fbrous tissue (**Das et al., 2007**) (**Das and Zipes, 2009**).

Individual case reports have shown that isolated CAE alone may be a cause of silent myocardial ischemia and infarction (**Nagata et al., 2001**). It was reported that coronary flow reserve was signifcantly reduced in patients with CAE compared to matched control subjects (**Akyürek et al., 2003**).

Taken together, these results suggest that microvascular dysfunction and/or ischemia might be a reason behind the fragmanted QRS in patients with CAE. It has been shown that CAE could be the cause of transient myocardial hypoperfusion in patients with angina and normal coronary arteries (**Farto e Abreu et al., 1993**).

Aim of the Work

This work aims at studying the relationship between QRS fragmentation on 12-lead electrocardiography and coronary artery ectasia detected by invasive coronary angiography.

Coronary Artery Ectasia

Coronary artery ectasia (CAE) has been observed by pathologists and cardiologists for more than two centuries. As its first description by **Morgagni and De sedlbus in 1761** this not so infrequent form of coronary artery disease has puzzled the clinicians regarding its cause, clinical sequelae and treatment.

With the widespread use of coronary angiography the incidence of CAE in patients undergoing this diagnostic procedure was clearly delineated. Although the incidence may overestimate the true frequency in the general population, CAE has been found in 1–5% during coronary angiography (**Farto–e–Abreu et al., 1993**). In the largest series from the registries, **Swaye et al. in 1983** found CAE in 4.9% of more than 20000 coronary angiograms they reviewed.

The incidence of CAE in an Indian patient cohort with ischemic heart disease has been reported to exceed 10% (**Sharma et al., 1990**). The most commonly used angiographic definition of CAE, albeit arbitrary, is the diameter of the ectatic segment being more than 1.5 times

larger compared with an adjacent healthy reference segment (**Demopoulos et al., 1997**). However, as the distribution of CAE is quite variable and not always focal, normal reference segments may not be readily apparent, and this definition potentially underestimates the true incidence of the disease. More detailed definition characteristics, for example employing larger diameter ratio or incorporating angiographic flow alterations, may enhance detection accuracy during angiography but also may further underestimate the true incidence of the disease.

More than half of CAE are due to coronary atherosclerosis, but occasionally they are related to other pathological entities (**Krueger et al., 1999**). As the first report of coronary dilatation in a patient with syphilitic aortitis (**Morgagni and De sedlbus, 1761**), CAE has been observed in association with connective tissue disorders such as scleroderma (**Chaithiraphan et al., 1973**), Ehlers–Danlos syndrome (**Shiro et al., 1969**) and polyarteritis nodosa (**Tang et al., 1970**) but also with bacterial infections (**Davidson et al., 1990**) and the Kawasaki disease (**Hiraishi et al., 1981**). In a small percentage of patients CAE can be congenital in origin (**Seabra-Gomes et al., 1974**). The differentiation between congenital and

acquired coronary aneurysms may often be difficult, despite the exclusion of other associated diseases (**Krueger et al., 1999**).

Acquired CAE should also be differentiated from coronary aneurysms following coronary interventions. These include true or pseudo-aneurysms during coronary balloon angioplasty, but more importantly following coronary stent placement, atherectomy and brachytherapy (**Bell et al., 1992**). Occasionally large ulcerated coronary plaques can be misinterpreted angiographically as coronary aneurysms. Their true cause can be usually revealed with intravascular ultrasound (IVUS) (**Ge et al., 1995**).

Recent studies have documented the association of CAE with the presence of aneurysms in other vascular beds as well, probably owing to a common underlying pathogenetic mechanism. CAE has been seen more frequently in patients with aneurysms of the abdominal and ascending aorta, the popliteal arteries, veins, and the pulmonary artery (**Befeler et al., 1977**). In a retrospective study by **Stajduhar et al. in 1993**, 20.8% of patients operated on for abdominal aortic aneurysm had CAE, compared with 2.9% of patients who were operated on for

occlusive peripheral vascular disease. Similar findings have been reported (**Lamblin et al., 2002**), but not all investigators (**Hartnell et al., 1985**).

Underlying pathology and causative mechanisms:

The specific causative mechanisms of abnormal luminar dilatation in CAE are essentially unknown. However, as the histo-pathological characteristics are similar to coronary atherosclerosis, it is not surprising that the hypotheses for the origin of CAE revolve around the vascular endothelium and the biological properties of the arterial wall. Virmani and other investigators have provided detailed pathological characterization of CAE, including lipid deposition with foam cells, fibrous caps and significant loss of musculoelastic vascular wall components as main histological abnormalities (**Daoud et al., 1969**).

CAE has to be differentiated from post-stenotic dilatation, in which an increase in wall stress, added to the atherosclerotic destruction of the media, may result in progressive arterial dilatation (**Rodbars et al., 1967**).

In a minority of cases, CAE is observed in the absence of significant atheromatous burden. Despite the