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Coronary angiography in heart failure – when and why? Uncertainty reigns.

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Remarkably in 2017 cardiologists do not know when and why patients with heart failure should undergo coronary angiography. This uncertainty is strikingly illustrated in this issue of Heart in a sub-analysis of the BIOSTAT study (69 centres over 11 countries) which reports that only 12% of patients with worsening heart failure underwent coronary angiography. This low rate is similar to that reported in a study of 67,000 patients in the United States(US) in which 16% underwent coronary angiography within 90 days of a new diagnosis of acute decompensated heart failure<sup>1</sup>. Why would a coronary angiogram be recommended for patients with heart failure and when should it be performed?

One clear indication for coronary angiography is to establish which patients are potential candidates for coronary artery bypass grafting (CABG). The STICH trial reported benefit of CABG compared to medical therapy in terms of all-cause mortality, CV mortality and CV hospitalisations after 10 years of follow up<sup>2</sup>. If a patient is a candidate for CABG (from a perspective of functional status and co-morbidity) only coronary angiography can inform the clinician whether or not the patient has coronary artery disease amenable to surgical revascularisation. Some cardiologists are advocates of performing non-invasive testing for ischaemia or viability prior to performing coronary angiography. These modalities have a very weak evidence-base when it comes to deciding whether or not to recommend CABG for heart failure. In the STICH trial, the presence or absence of ischaemia or viability did not identify patients with more or less to gain from CABG<sup>3</sup>. The viability literature is especially poor, relying on data such as a meta-analysis of historical, observational small studies of patients on little medical or device therapy for heart failure<sup>4</sup> or magnetic resonance imaging data recommending cut-offs based on studies of less than 50 patients<sup>5</sup>.

The current BIOSTAT analysis reported that of those who underwent coronary angiography those who had a coronary stenosis had a worse prognosis than those without. While this association does not mean that all those with a stenosis should be revascularised this does remind us that revascularisation in patients with heart failure should be considered. In the previously mentioned study from the US only 4% of patients with newly diagnosed heart failure were revascularised within 3 months<sup>1</sup>.

Should a coronary angiogram be performed to establish whether percutaneous coronary intervention (PCI) should be considered as a treatment for heart failure? This is an easy question to answer as there is absolutely no evidence for percutaneous coronary intervention as a treatment option for heart failure. All of the major trials of PCI versus medical therapy, or PCI versus CABG, have either enrolled very few patients with heart failure or excluded them altogether. For example, the SYNTAX trial recruited only 2% of patients with severe left ventricular dysfunction<sup>6</sup>. Trials in patients with good left ventricular function cannot be used to justify PCI to treat patients with heart failure. Fortunately, the role of PCI as a treatment for heart failure should be at least partially clarified by the BCIS-REVIVED trial

(NCT01920048) which is currently recruiting in the United Kingdom. This trial randomises patients who are not considered to be candidates for CABG, to PCI and optimal medical therapy versus optimal medical therapy alone. No trials are yet underway comparing PCI versus CABG in heart failure.

Should patients with heart failure undergo coronary angiography to clarify the cause of heart failure? One of the major steps in pinning down the cause of heart failure is to decide whether or not the cause is coronary artery disease or not. When unobstructed coronary arteries are observed then the myriad of other causes can be considered. If a diagnosis of “chronic heart failure” is accepted without any more thought, the opportunity to identify potentially reversible, environmental, infectious, genetic and other causes of heart failure is missed. There are reasonable arguments to be made that cardiac magnetic resonance imaging can be used to confirm or refute coronary artery disease as the cause of heart failure. This approach is however, limited by availability and the sparse data validating the technique as a diagnostic modality for heart failure. Guidelines have struggled to make recommendations as to the role of coronary angiography in the diagnosis of heart failure. The 2016 European Society of Cardiology Heart Failure Guidelines<sup>7</sup> state that an angiogram is recommended in those with heart failure either with a) “angina pectoris recalcitrant to pharmacological therapy or symptomatic ventricular arrhythmias or aborted cardiac arrest” (class 1 recommendation C recommendation) or b) in those “with heart failure and intermediate to high pre-test probability of coronary artery disease and the presence of ischaemia in non-invasive stress tests in order to establish the diagnosis of CAD and its severity” (class IIA recommendation level of evidence C). These uncertain recommendations, both based on little or no evidence, highlight the amount of work that the cardiology community has ahead to clarify the role of coronary angiography in the diagnosis and management of patients with heart failure.

Can Computed Tomography (CT) coronary angiography replace invasive coronary angiography in patients with heart failure? The established role of CT coronary angiography is to rule out coronary artery disease in low risk patients. Unfortunately, very few patients with heart failure are at low risk of coronary artery disease. With a high prevalence of diabetes and renal impairment and a predominantly elderly population, CT coronary angiography has a limited discriminatory ability. If CT coronary angiography is used it frequently leads to inconclusive results and the need for other testing such as invasive coronary angiography, subjecting patients to excessive radiation and delayed diagnosis.

More questions arise from the current analysis of BIOSTAT. Low use of coronary angiography was reported in this cohort of outpatients and inpatients. Should a coronary angiogram be performed in all patients presenting both acutely as inpatients and in the outpatient setting? Should patients only undergo angiography when they initially present for diagnostic purposes? Or should coronary angiography be only considered when a patient presents with worsening heart failure to look for therapeutic options? Should patients with acute heart failure be referred for an emergency coronary angiogram on admission or after they are stabilised on medical therapy? Observational studies as to the merits of coronary angiography are necessary.

BIOSTAT included patients with left ventricular dysfunction. What is the role of coronary angiography in the diagnosis and treatment of patients with heart failure and preserved or mid-range ejection fraction?

Another reason why patients with heart failure do not undergo angiography is that patients with heart failure present challenges that are unwelcome in the catheterisation laboratory. They often have comorbidities that complicate angiography and revascularisation. They are often anaemic and bleed more often; they often have renal dysfunction which can worsen with contrast; they often are diabetic

with extensive vascular disease that can make vascular access challenging. Often their coronary anatomy is “unattractive” for revascularisation with chronic total occlusions and diffuse disease. Rarely are type A coronary lesions found that can be tackled with ease.

One development that is bringing patients with heart failure towards the arena of the interventional cardiologist is the growing popularity of mechanical circulatory support techniques in the catheterisation laboratory. Extracorporeal membrane oxygenation and Impella both have an increasing number of proponents and are being used in clinical trials in populations with heart failure or cardiogenic shock. The era of the Complex High Risk and Indicated (CHIP) PCI has invigorated the interventional cardiology community to explore new (and mechanically supported) interventions in patients who may have a lot to gain.

In conclusion, the inescapable truth is that little is known of the role of coronary angiography in the diagnosis and treatment of acute or chronic heart failure. There are currently a few answers, but many more questions. Surprisingly in 2017 this is still an area ripe for a new battery of clinical trials. Funding of these trials is challenging, as there are no major pharmaceutical or device companies with direct interest in the outcomes. The importance of clarifying the role of coronary angiography and coronary artery disease to the diagnosis and treatment of coronary artery disease is undeniable.

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