Myocardial bridging and sudden death in hypertrophic cardiomyopathy: Salome drops another veil

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This editorial refers to ‘Myocardial bridging, a frequent component of the hypertrophic cardiomyopathy phenotype, lacks systematic association with sudden cardiac death’1, by C. Basso et al., on page 1627

Hypertrophic cardiomyopathy (HCM) is a heterogeneous disease at the clinical, phenotypic, and molecular level.1 In spite of considerable progress in understanding the disease, many issues continue to be shrouded in mystery, with very slow and often incomplete shedding of the veils, reminiscent of Salome’s dance. These issues include the unpredictable occurrence of sudden cardiac death, the clinical relevance of coronary artery bridging, and their possible relationship.1–6

To this day, HCM is among the most common causes of sudden cardiac death in the young, and strategies aimed at improving risk stratification remain less than satisfactory, largely due to the capricious course and individual heterogeneity of the disease.7 Several potential predictors of risk have been identified, each with very low positive predictive accuracy, that may be important in some patients but have little relevance in others.1,7 Symptoms and signs of myocardial ischaemia are often evident in patients with HCM, classically in the absence of epicardial coronary artery disease, and reflect the interplay of structural and functional small-vessel abnormalities, reduced arteriolar density, fibrosis, and elevated left ventricular (LV) end-diastolic pressures.7–9 Occasionally, angina on effort in children or young adults with HCM may be associated with an intramural course of the left anterior descending (LAD) artery, a condition also referred to as myocardial bridging.2–6 In the most severe instances, the artery is embedded in the myocardium for most of its course, and is more appropriately referred to as tunnelled LAD.10 Of note, fibrous bands overlying the LAD may also be found in the context of large myocardial bridges.10 In consecutive series, systolic compression of an epicardial coronary branch as a result of bridging is seen on angiography in ~15% of patients with HCM, and its prevalence is independent of the degree of septal hypertrophy.3–5

Myocardial bridging in adults with HCM is often a benign condition, and in one large cohort it was found to have no impact on overall outcome.5 However, some reports have suggested a distinct association between myocardial bridging and severe symptoms, ventricular arrhythmias, and sudden death in children with HCM.2,6 As yet, the issue remains controversial.3,4 From a pathophysiological standpoint, LAD tunnelling may precipitate severe regional ischaemia on effort, when the adrenergic drive enhances systolic compression of the artery to a sufficient degree to disturb blood flow.3,4 Indeed, impairment of flow due to coronary bridging is not limited to the duration of systole, but extends well into the diastolic phase critical to myocardial perfusion.3,10 Thus, it is not surprising that the recurrence of regional ischaemia upon the complex HCM substrate, with its corollary of hypertrophy, disarray, microvascular dysfunction, and fibrosis,7–9 may precipitate malignant arrhythmias.2,6 As is often the case with HCM, however, all these elements are of uncertain value in the assessment of individual patients at risk.

The study presented by Basso et al.11 represents an important contribution to our understanding of the relationship between myocardial bridging and sudden death. In their report, based on a large series of autopsied hearts, myocardial bridges were more commonly found in deceased HCM patients, irrespective of the cause of death, compared with non-HCM hearts with or without LV hypertrophy. Specifically, deeply embedded LAD segments (with bridges measuring ≥2 mm in thickness) occurred in 23% of HCM patients, vs. ≤5% in the control groups.11 According to a recent hypothesis, the HCM disease process could have a profound influence on the coronary circulation during development.12 In the embryonic heart, following a process called epithelial–mesenchymal transformation, pluripotent epicardium-derived cells (EPDCs) migrate diffusely into the myocardium and differentiate into diverse cell types, including the smooth muscle cells and...
adventitial fibroblasts which give rise to the coronary vasculature.12
At the time of EPDC migration, the heart has already begun to contract, and HCM-causing mutations are expressed in myocardial cells. By a putative mechanism of mechanotransduction, the resulting abnormal contractile status may influence EPDC gene expression, ultimately affecting the development of coronary vessels and their spatial relationship with the myocardium.12 This hypothesis might explain both the increased prevalence of coronary bridging and the striking patterns of microvascular remodelling present in HCM hearts at any age, including infancy.6–11

In their series of HCM hearts, Basso et al. found no difference in prevalence of LAD bridging among patients who died suddenly compared with those who succumbed to progressive heart failure.11 Neither the presence of deep (>2 mm) bridges, nor a scar in the LAD tributary region (presumed to reflect recurrent ischaemia), reliably identified sudden death victims. Furthermore, all these features were comparable in patients who died suddenly before or after 18 years of age. The authors legitimately conclude that there is a lack of association between bridging, regional myocardial scar, and mode of death.11 These findings confirm the generally benign nature of myocardial bridging in adult HCM patients,5 but add to the uncertainty regarding its relevance in children and adolescents.2–4,6 As acknowledged by the authors, their study is limited by the unavoidably retrospective nature of autopsic investigations. Specifically, because systematic risk stratification based on conventional risk factors was not available for all patients,1,7 the individual weight of myocardial bridging relative to other predictors of outcome could not be assessed. Nevertheless, based on the rigorous pathological examination and considerable size of the present series, the findings of the study appear robust.11

Further studies are required to evaluate the impact of myocardial bridging on outcome in HCM patients prospectively, focusing preferentially on younger individuals. Novel opportunities are offered by non-invasive coronary imaging techniques including high-definition CT and magnetic resonance, which now allow accurate anatomic as well as functional assessment of myocardial bridges in vivo.4,10,11 Until further, prospective evidence is available, how can we interpret the evanescent relationship between myocardial bridging and sudden death in HCM?

As a general principle, the need for a personalized approach to each individual should be emphasized.1 In the majority of patients, however, particularly if adult and asymptomatic, myocardial bridging does not seem relevant to clinical course and outcome, even when the artery is deeply embedded in the myocardium.5,11 For example, the incidental detection of LAD bridging on preoperative coronary angiogram in candidates for surgical myectomy often raises the issue of whether to intervene in such an anomaly.5 These data suggest otherwise. Conversely, LAD tunnelling should be specifically sought in HCM children or adolescents with unexplained symptoms on effort,6,10 in whom it may require surgical treatment.10,14 The causal link between LAD tunnelling, arterial compression, and regional ischaemia should be well documented in these patients prior to surgery.10 Moreover, a modern surgical approach should involve a beating-heart technique, significantly reducing operative times and risks, and relieve the lateral as well as the superior aspect of the LAD from myocardial compression.10,17 In this limited subset of paediatric patients, surgery considerably improves symptoms,10,14 and may arguably reduce the risk of sudden death.2,6 Conversely, coronary artery stenting, attempted as an alternative to surgery in non-HCM patients with myocardial bridging, is associated with high rates of periprocedural complications and restenosis, and should therefore be avoided.1,4 Finally, based on existing evidence, myocardial bridging should not be considered relevant in deciding whether an HCM patient should receive an implantable defibrillator for primary prevention of sudden cardiac death.1 A similar potential misconception has recently been confuted with regard to LV outflow obstruction.15

Prevention of sudden cardiac death remains the most complex challenge in HCM.1,5 Endless combinations of different pathophysiological elements underlie the fragility of patients who die prematurely, and teach a sobering lesson to clinicians and researchers alike. On the other hand, a rising proportion of active octogenarians with HCM makes one marvel at the long-lasting mechanical and electrical stability often exhibited by such structurally abnormal hearts. Identifying fragility and protecting stability in our patients will require much further work: Salome continues to intrigue.

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References