

BRUNO BUCHHOLZ

Myocardial trabeculae: more than a remnant of myocardial embryological development

Meyer HV, Dawes TJW, Serrani M, Bai W, Tokarczuk P, Cai J, Marvao A, Henry A, Lumbers RT, Gierten J, Thumberger T, Wittbrodt J, Ware JS, Rueckert D, Matthews PM, Prasad SK, Costantino ML, Cook SA, Birney E, O'Regan DP. Genetic and functional insights into the fractal structure of the heart. *Nature*. 2020 Aug 19. doi: 10.1038/s41586-020-2635-8

The internal ventricular surface is markedly irregular due to the presence of a complex meshwork of myocardial trabeculae. The formation of these trabeculae is essential in the early stages of myocardial development, in which, this extensive population of muscular structures that protrude into the cardiac chamber fulfill nutrition and oxygen delivery functions by imbibition from the surrounding blood. Subsequently, cellular proliferation will occupy the intertrabecular spaces, forming vessels and compressing the most superficial myocardial layer. This theory was accepted for many years, but current cellular lineage studies suggest that the adult trabecular myocardium has a different molecular and development profile from compact myocardium.

Myocardial trabecular functions in the postnatal heart are largely unknown. It is evident the insertion support they provide for the chordae tendineae and their relationship with the terminal branches of the conduction system. In addition, current mathematical analyses offer evidence for an important role in ventricular physiology. However, the genetic trabecular architecture, its association with cardiac physiology and its potential pathological role have not been established.

In this work, Meyer et al. performed a genetic study related to the morphological and functional pattern of individuals participating in UK Biobank data. They identified 16 loci containing genes associated with the arborization of the myocardial trabecular cytoskeleton and a defined hemodynamic phenotype. Lack of expression of some of these genes in experimental

models significantly decreased the trabecular meshwork complexity, frequently leading to malformations in the development of the cardiac tube and conduction system. In turn, using theoretical models of magnetic resonance imaging fractal analysis, they observed a causal relationship between myocardial-trabecular complexity and heart performance. Finally, following a Mendelian randomization analysis they found that the reduction in trabecular meshwork complexity is associated with greater risk of heart failure and dilated cardiomyopathy.

The results of this work complement other very recent studies suggesting that a ventricle with an adequate trabecular meshwork can work with less strain to generate the same systolic volume than one with reduced trabecular pattern. This seems to indicate that myocardial trabeculae have a positive effect on diastolic ventricular filling, contractility and cardiac indices. In this sense, the increased cardiac output of athletes and pregnant women might be the result of adaptive myocardial remodeling, increasing the trabecular meshwork. However, hypertrabeculation is a pathological entity manifested in heart failure, arrhythmias and thrombosis, as occurs in non-compaction cardiomyopathy. The results reported by Meyer et al. provide clear indication of the molecular complexity of the pathways participating in cardiac morphogenesis and sarcomere function of the adult heart. On the whole, the evidence suggests that trabeculae of the myocardial deep layer are not simple vestigial remnants of myocardial development. On the contrary, they seem to be decisive for the heart's performance and are genetically codified in specific loci which are expressed in complex trabecular patterns that will condition the heart's normal or pathological functioning. Understanding the pathways that regulate these biological entities will help to better understand the causal mechanisms of heart diseases.

Ethical considerations

Not applicable.