LETTERS TO THE EDITOR

Assessment and relevance of ventricular wall stress in heart failure

We read with great interest the article by De Simone et al., published in the European Heart Journal. By using M-mode echocardiography, the authors examined the relationship between left ventricular (LV) mass and incident heart failure not attributable to myocardial infarction. LV hypertrophy (LHV) or ‘excess’ of LV mass was found to be an independent predictor of incident heart failure. To quantify this so-called ‘excess’ of LV mass, expected normal values were calculated based on body height, gender, and stroke work. The latter was defined by the authors as systolic blood pressure times Teichholz-based stroke volume. In contrast to the used method, we prefer to assess stroke work in accordance with its physiological definition as the area within the pressure–volume loop, which is the standard method in experimental studies and is also feasible in patients.1 In the present study, systolic cuff blood pressure was obtained,2 which appears to be a further limitation since only LV pressure is decisive for LV wall stress.

In addition, an M-mode-based echocardiographic approach was used to assess LV wall stress. In a recent study on patients with non-ischaemic LV dysfunction, we compared an echocardiography-based method with a thick-walled sphere model,4 using parameters derived from cardiac magnetic resonance (CMR) imaging,5 which is the generally accepted reference method for assessing cardiac volumes and mass. The echocardiography-based method systematically underestimated LV wall stress.6 The extent of underestimation was proportional to the wall stress.7

As regards the present manuscript, a moderately (<5%) increased LV end-systolic wall stress was found in patients with increased ‘excess’ of LV mass as stratified into quartiles. Potentially, the increase in LV wall stress has been underestimated because of the methods used.

Noteworthy, LV dimensions were increased in patients with ‘excess’ of LV mass. LV pressure, volume, and myocardial mass are crucial determinants of wall stress. LV dilatation implies an increase in radius (of the sphere model of the LV) and, therefore, raises LV wall stress by square. An increased wall stress occurs, if the myocardial growth is not adequate for coping with the expanding ventricular volume. It appears likely that calculation of CMR-based wall stress would have revealed greater differences. LV wall stress might thus also emerge as a stronger predictor of incident heart failure. In conclusion, we agree with the authors that it is necessary to assess myocardial mass, a vital parameter in heart failure. However, it also appears crucial to monitor an increased wall stress that has various adverse consequences for energy metabolism, gene expression, and arrhythmia risk. In particular, one should be aware of an increase in myocardial wall stress during progression of heart failure.

References


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Radial artery catheterization and radiological exposure

With interest I reviewed the article recently published by Brasselet et al., showing the data of a higher radiation exposure in the invasive procedures performed by radial artery catheterization (RAC), compared with femoral artery catheterization (FAC).

However, owing to a number of possible biases, I think that their results should be generalized with extreme caution.

First, the study was performed in a moderate volume institution. We recently showed that among experienced operators in RAC, those with the highest volumes of procedures achieved the lowest procedural failure rate in the ‘real world’.2 Therefore, despite their expertise in RAC, the operators in this study might not have performed a sufficient RAC volume to yield the best feasibility. This may explain the longer procedure duration and X-ray exposures reported by the authors in contrast to the aforementioned trial performed in a high volume centre.2 The consequence would be that a more frequent use of RAC could imply safer procedures for both patients and operators.

Secondly, radiation exposure may significantly differ in left vs. right RAC. In fact, performing RAC by the left arm has two main advantages – a shorter distance to the target and its larger table rotation...
Leucocyte activation in coronary heart disease: but how and why?

Leucocytosis, a marker of inflammation, is associated with a greater cardiovascular risk. Thus, leucocyte myeloperoxidase (MPO) could serve as a biomarker of cardiovascular diseases, as shown by Morrow et al. But, they did not study as to why and how leucocyte activation occurs in coronary heart disease (CHD).

Infiltration of intima by leucocytes and macrophages is an early event to occur in atherosclerosis. Elevated low-density lipoprotein (LDL), hypertension, hyperglycaemia, and other systemic factors initiate and accelerate atherosclerosis. Despite the fact that the entire vascular endothelium is exposed to these systemic factors, atherosclerotic lesions occur in a patchy manner and develop preferentially at bifurcations, branch points, and inner curvatures of arteries, suggesting that local factors play a major role in the development of atherosclerosis. Haemodynamic forces induce the expression of pro-inflammatory genes that initiate and accelerate atherosclerosis at these points of shear stress. Normocholesterolemic C57Bl/6 mice and rabbits showed activation of NF-κB and elevated expression of VCAM-1 and ICAM-1, upregulation of pro-inflammatory genes IL-1, IL-6, MCP-1, as well as antioxidant genes glutathione peroxidase and glutathione-S-transferase in endothelial cells in atherosclerosis-susceptible regions of the ascending aorta. Intracellular accumulation of LDL and its oxidation products preceded monocyte recruitment into early atherosclerotic lesions, suggesting that lipid accumulation triggers inflammatory response characterized by upregulation of the expression of chemokines and adhesion molecules in the lesion-prone areas in the intima that contributes to leucocyte accumulation and atherosclerotic lesion formation.

Healthy endothelial cells prevent excess expression of adhesion molecules, resist increases in LDL and cholesterol transport and retention, and abrogate the activation of NF-κB and the induction of expression of pro-inflammatory genes induced by haemodynamic forces at atherosclerosis-prone regions by producing factors that counter pro-atherosclerotic events. The patchy nature of atherosclerosis suggests that arterial walls undergo regional disturbances of metabolism that include the uncoupling of respiration and oxidative phosphorylation, which may be characteristic of blood vessels being predisposed to the development of atherosclerosis. Oxidative stress and abnormalities of uncoupling proteins produce smooth muscle contraction and cause hypertension, and respiratory uncoupling is increased in the aorta of experimental animals that are susceptible to atherosclerosis. Bernal-Mizrachi et al. showed that UCP-1 expression in aortic smooth muscle cells causes hypertension and increases atherosclerosis without affecting the cholesterol levels. This increase in UCP-1 expression enhanced superoxide anion production and decreased the availability of nitric oxide, suggesting that oxidative stress has been elevated. Thus, inefficient metabolism in blood vessels causes atherosclerosis.

One of the earliest signs of atherosclerosis is the development of abnormal mitochondria in smooth muscle cells. Arteries have marginal oxygenation, and hypoxia reduces the respiratory control ratio. Uncoupled respiration precedes atherosclerosis at lesion-prone sites but not at the sites that are resistant to atherosclerosis. Disease-free aortae have abundant concentrations of the essential fatty acid (EFA)-linoleate (LA), whereas fatty streaks are deficient in EFAs. EFA deficiency promotes respiratory uncoupling and atherosclerosis. Hence, local disturbances of EFA metabolism in the arterial wall could be responsible for atherosclerosis and vascular disease.

EFAs-linoleic acid (LA; 18:2 ω-6) and α-linolenic acid (18:3 ω-3) give rise to lipoxins (LXs), resolvins, and protectins in addition to forming precursors to various eicosanoids (reviewed in 3). Aspirin converts arachidonic acid (20:4 ω-6), eicosapentaenoic acid (20:5 ω-3), and docosahexaenoic acid (22:6 ω-3) to form aspirin-triggered 15 epimer LXG (ATLS) that inhibit inflammation on the vessel wall by regulating the motility of polymorphonuclear leucocytes (PMNs), eosinophils, and monocytes. LXs deficiency leads to an interaction between PMN and endothelial cells that result in endothelial damage, initiation, and progression of atherosclerosis. LXs, resolvins, and protectins inhibit cytokine generation, leucocyte recruitment, leucocyte diapedesis, and exude formation, and suppress the production of pro-inflammatory cytokines. Hence, the local deficiency of LXs, resolvins, and NPDP1 could initiate atherosclerosis. Furthermore, lipoxins suppress the production of MPO from activated leucocytes. Increased generation of MPO by leucocytes could be an indication of decreased formation of lipoxins, resolvins, and protectins by endothelial cells. This implies that enhancing the formation of endothelial LXs, resolvins, and protectins may suppress leucocyte activation and MPO generation, and prevent CHD.

References