Cardiovascular Paradigms: Time for Reappraisal

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Abbreviations
AHA: American Heart Association; CV: Cardiovascular; CVD: Cardiovascular Diseases; LDL: Low-Density Lipoprotein; MI: Myocardial Infarction; NSAID: Non-Steroidal Anti-Inflammatory Drug

While much progress has been made in prevention and treatment over the last 60 years (though not as much as expected), the current paradigm of cardiovascular diseases (CVD) is now facing its most serious challenges.

Have recently been published the results of Fourier Trial [1] whose purpose was to verify if a substantial reduction in cholesterol levels in patients with established CVD, and with LDL cholesterol > 70 mg / dl, through a PCSK9 inhibitor (evolocumab) added to statin therapy would reduce CV events concomitantly. Evolocumab plus statin therapy resulted in significant 59% relative LDL reduction. However, the results also showed a modest reduction in CV events (1.5% as compared with placebo) although notably with a small increase in overall or CV-specific mortality. This is the last episode of many other studies that have been challenging the premise that LDL cholesterol is one of the main drivers of CVD. In fact, as early as 2012, in an editorial in the journal Circulation [2], two prominent cardiologists had already questioned LDL as the target of cardiovascular therapy.

On the other hand, the diet-heart hypothesis (another pillar of the current CVD paradigm) has been the object of heated controversies. In a recent article in Medscape [3] the authors noted that “So much data refute the diet-heart hypothesis that it’s a wonder the AHA can ignore it all”.

Progress happens when the current paradigms are updated or replaced by others with greater scope and explanatory power. It is the time to make a reassessment of the vast literature published in the last 60 years, expand the views and eventually look for new directions to fight cardiovascular disease. In fact, some striking features of CVD hardly find an explanation within the current CVD paradigm: (i) heart attacks, and myocardial infarction (MI) occur even in the absence of thrombus occluding the coronary arteries [4-7]; (ii) acute coronary occlusions may occur without concomitant MI [4]; (iii) the irregular pattern of distribution of atherosclerotic plaques [8]; (iv) the reason why metformin [9] steroids [9,10] and NSAIDs [9,11], proton pump inhibitors [12], calcium supplementation [13], and other common drugs are associated with increased CVD risk.

Alternative views have been put forward over time (e.g. [4,14-17]). A new paradigm should be able to explain the aforementioned aspects, provide a rationale for the major cardiovascular risk factors, and substantially increase the success of clinical practice. This requires a re-analysis of the published biomedical knowledge, recovering the results of previously discarded studies, carrying out new studies, and fundamentally, it requires open minds to change frames of thought and clinical practices.

Conflict of Interest
None.

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Bibliography


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