with established and accepted models of atherosclerosis.

References


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5. Heredity estimates for the existence of additional risk factors, as it is generally well explained. Of interest in this regard might be the heritability of LMD in particular. From our perspective, we kindly invite Dr Patel and coworkers for combining their and our respective analyses for addressing these pertinent questions.

Familial aggregation of left main coronary artery disease and future risk of coronary events in asymptomatic siblings of affected patients: reply

We thank Dr Patel et al. for their kind interest in our manuscript. Indeed, we agree with the authors that manifestation of atherosclerosis is anatomically diffuse and as such modulated by several, including heritable, risk factors. Also, their notion that left main disease (LMD) is rarely an isolated phenomenon but rather occurs in addition to disease manifestation at other branches of the coronary tree is concordant with our results. Based on their clinical observations, Dr Patel et al. argue that the heritability of LMD is a surrogate of heritability of severe coronary artery disease (CAD) rather than a result from distinct heritable predisposition. They further conclude that coincidence of LMD and severe CAD may explain our finding that relatives of LMD patients have a higher risk of developing incident cardiovascular events, as they might have inherited a more severe underlying atherosclerotic process.

In fact, we considered such line of ordinary in our initial analysis. However, in contrast to LMD, we did not find significant heritability estimates for the existence of 1-, 2-, or 3-vessel CAD. Moreover, surrogate phenotypes of CAD severity, like the number of stenoses or the Gensini index seemed not to be markedly influenced by genetic factors. Interestingly, similar observations come from analyses of other traditional risk factors, as it is generally well perceived that they may affect one or the other vascular bed with specific preference. Unfortunately, our subgroup of subjects with LMD is too small to allow meaningful statistical analysis considering further coronary phenotypes as covariates particularly in terms of estimating heritability.

Also, we believe that the mechanism proposed by Dr Patel et al. falls short explaining the higher event rates in relatives of LMD. Indeed, the group used for comparison consisted of individuals who had at least two siblings with evidence of CAD including one with myocardial infarction—but no family history of LMD. Moreover, with the exception of LMD, there was no difference in the distribution of the number of vessels involved in relatives of siblings with known coronary morphology, who experienced myocardial infarctions during follow-up when compared with those relatives of siblings who remained asymptomatic (data not shown). Regrettably, we have no evidence of disease localization in prospectively observed, initially unaffected siblings of CAD patients, of whom many died suddenly.

Finally, Dr Patel et al. consider alternative explanations for the heritability of LMD including flow mechanics in the development of lesions, i.e. arterial wall shear stress. Indeed, it may be plausible that low shear stress in anatomically identical vascular regions would lead to plaque development in such sites. Our previous analysis revealed low if not absent concordance rates for the predominance of coronary blood supply even in monozygotic twins. Thus, as already mentioned by Dr Patel et al., this theory does not explain the relatively high LMD inheritance. Of interest in this regard might be the particular ontogenetic determination of this proximal site that is distinct from more distal parts of the coronary artery.

Future studies including genome-wide associations may shed further light on the inherited factors for CAD in general and LMD in particular. From our perspective, we kindly invite Dr Patel and coworkers for combining their and our respective analyses for addressing these pertinent questions.

References


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doi:10.1093/eurheartj/ehn014
Online publish-ahead-of-print 9 February 2008
D-Dimer in ruling out acute aortic dissection: sensitivity is not 100%

We read with great interest the article by Sodeck et al.1 reporting the negative predictive value of D-Dimer in acute aortic dissection (AAD). Based on a meta-analysis and on a personal series of 65 patients, the authors conclude that current evidence supports a routine measurement of D-Dimer for excluding AAD. Furthermore, a D-Dimer threshold <0.1 μg/mL would exclude AAD in all cases. We previously reported on a 94-case series of patients2 and believe for several reasons that Sodeck’s conclusion could prove misleading.

(1) AAD is the most critical cardiovascular emergency with a mortality risk of 1% for each hour of evolution. Even though D-Dimer testing may be carried out rapidly, it should not delay the imaging diagnostic work-up. The latter is the only procedure that will conduct the patient promptly to the operating room when appropriate, thus saving his life. Consequently, we believe that D-Dimer test should not be considered as a first line and exclusive screening tool in order to rule out the disease, as it is in suspected deep vein thrombosis.

(2) The 0.1 μg/mL threshold proposed is very low and is chosen to obtain the highest sensitivity (100%). However, the authors should also take into account the specificity. On the basis on the ROC curve provided (Figure 2), one can estimate that for a sensitivity of 100% (Y-axis, upper-right of the curve) the corresponding specificity is at best between 10 and 15%. Even though the sensitivity is high, what is the relevance of a 10–15% specificity in terms of medical management of AAD? For 100 patients screened with D-Dimer for suspected AAD, only 10 to 15 will be negative. However, 85 to 90 cases the D-Dimer test will be positive thus necessitating a complementary imaging modality. Yet, these explorations will have been delayed as a consequence of the time needed to obtain the D-Dimer test results. In addition, such a low threshold is not applicable to the majority of D-Dimer tests available on the market since the usual cut-off ranges from 0.3 to 0.5 μg/mL (see Table 3 of the paper1). For example, in our own series, setting a threshold at 0.1 μg/mL would be impossible since the detection limit of the test was 0.2 μg/mL.

(3) Finally, we wish to point out that even by using an usual cut-off (0.3–0.5 μg/mL), D-Dimer test could be negative in acute aortic syndrome due to AAD, especially in patients without a patent false lumen presenting with an aortic intramural haematoma.

References


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Letters to the Editor