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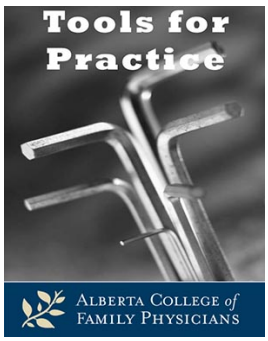

Lipoproteins: The risk of (over)interpreting these risk factors?

Clinical Question: Does lipoprotein testing (like apolipoprotein B) provide meaningful cardiovascular disease (CVD) risk assessment or management information? (For this article, "lipoproteins" do not include LDL or HDL.)

Bottom-line: Lipoproteins (like apolipoprotein B) are associated with CVD but so are ~300 other risk factors. Lipoproteins do not add meaningfully to risk estimation before treatment or prediction of benefit with treatment. Assess risk with CVD risk calculators and treat with proven therapies.

Evidence:

- Primarily systematic reviews of cohort studies examining apolipoprotein B, AI, B/AI ratio, lipoprotein(a) and lipoprotein-associated phospholipase A_2.
  - Are lipoproteins associated with CVD? Yes.
    - Five systematic reviews[1-5] with 23-40 studies: All lipoproteins are associated with CVD.
      - Example: Higher apolipoprotein B, relative risk 1.99 (1.65-2.39).[1]
  - Do lipoproteins add to risk prediction models? No.
    - Systematic review[6] with 37 studies. Taking standard risk prediction tools and:
      - Replacing total cholesterol/HDL with any lipoprotein made prediction worse.
      - Adding any lipoprotein improved overall risk prediction by ≤0.0018 (from 0.7244 area-under-the-curve), a clinically meaningless value.
        - For comparison, leukocyte count improves prediction by 0.0036.[7]
    - Reclassification: Limiting lipoprotein testing to patients at moderate (10%-<20%) 10-year CVD risk and treating those reclassified as high risk would require testing 801-4,541 to prevent one CVD event in 10 years.[6]
  - Do changes in lipoproteins predict benefit? No.
    - One randomized controlled trial of 15,828 CVD patients demonstrated that using darapladib (lipoprotein-associated phospholipase A_2 inhibitor) did not change CVD outcomes.[8]
    - Two systematic reviews[9,10] with 8-25 studies: Apolipoprotein B changes did not predict benefit better than LDL and maybe worse than non-HDL cholesterol.
      - Regardless, monitoring is not required to predict statin benefit.

Context:

- There are ~300 CVD risk factors.[11]
- Many drugs (ezetimibe,[12] torcetrapib,[13] niacin,[14] aleglitazar,[15] rosiglitazone,[16] darapladib,[8] etc.) improve biomarkers but do not change or worsen CVD.
- 2012 Canadian guidelines recommend apolipoprotein B as an alternate biomarker for CVD risk and for treatment target.[17] New US Guidelines do not.[18]

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