Less is More Unless it's Sleep or Toilet Paper: Non-traditional lipoproteins for cardiovascular risk

CLINICAL QUESTION

In patients without established cardiovascular disease (CVD), can lipoprotein(a) or apolipoprotein B meaningfully improve standard CVD risk estimation?

BOTTOM LINE

Adding lipoprotein(a) or apolipoprotein B does not meaningfully improve cardiovascular risk prediction above standard risk factors (age, sex, blood pressure, total cholesterol/HDL, diabetes, smoking). Assess risk with CVD risk calculators and offer proven therapies as appropriate.

EVIDENCE

- All evidence from cohort studies and statistically significant unless noted.
- Search focused on lipoproteins additive value above traditional risk factors on CVD risk estimation. C-statistic measures the predictive accuracy of a statistical model to distinguish between individuals with positive outcomes and those with negative outcomes.[1]
  - Changes in C-statistic: ≥ 0.1 is large, 0.05-0.1 is moderate, 0.025-0.05 is small and <0.025 is very small.[2]
- Lipoprotein(a) [Lp(a)]

- o Systematic review of 24 prospective studies (n=133,502, mean follow-up 10.6 years).[3]
    - ▪ C-statistic improvement=0.0016.
- o Evidence since:
    - ▪ UK adults (n=340,339) without CVD not on statins, follow-up 8.9 years.[4]
        - • C-statistic improvement=0.0017.
    - ▪ Swiss adults (n=4829), follow-up 9.9 years.[5]
        - • C-statistic improvement=0.004.
- Apolipoprotein B (apoB)
    - o Systematic review of 26 prospective studies (n=139,581, mean follow-up 10.5 years).[3]
        - ▪ C-statistic improvement=0.0001 (not statistically significant).
    - o Evidence since:
        - ▪ UK adults (346,686) without CVD not on statins, follow-up 8.9 years.[6]
            - • C-statistic improvement=0.0004.
        - ▪ Danish adults (8476) without CVD or diabetes, follow-up 18 years.[7]
            - • C-statistic improvement not statistically different.
    - o Other cohorts found similar results.[8-9]

CONTEXT

- Lp(a) and apoB individually are associated with CVD with relative risks of 1.00-2.21 and 1.03-2.87, respectively. Other non-traditional risk markers have similar associations (relative risk for leucocyte count=1.45; albumin=1.55; pro-insulin=2.23) but provide little additional value when combined with traditional risk factors (e.g., additive value of leukocyte count c-statistic=0.0036).[10]
- Other measures of diagnostic utility, including Net Reclassification Index, suggest Lp(A) and apo(B) generally provide no meaningful value above traditional risk prediction.[3-6]
- Simplified guidelines discourage testing lipoproteins.[10]
- Canadian Cardiovascular Society[11] recommends measuring:
    - o Lp(a) once/lifetime for initial screening.
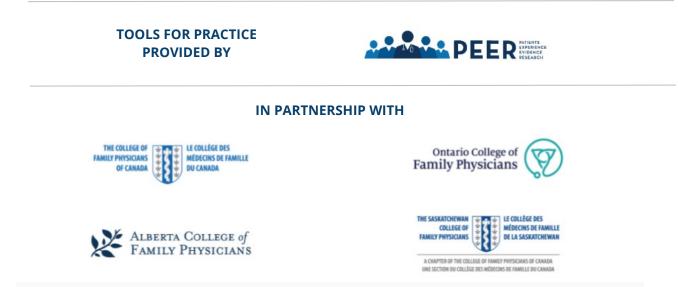   - o ApoB (or non-HDL-C) as preferred screening parameter if triglycerides>1.5mmol/L.

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