UPDATE IN CARDIAC RISK EVALUATION

Erik Stilp, MD

Week 24

Educational Objectives:

1. Identify the major modifiable risk factors for cardiovascular disease (CVD) and understand how to assess cardiovascular risk
2. Review the revised United States Preventive Services Task Force (USPSTF) recommendations for the use of aspirin (ASA) for the prevention of CVD and know which groups might potentially benefit from aspirin use
3. Discuss the role of high sensitivity C-reactive protein (hs-CRP) in CVD risk stratification and pharmacotherapy for primary prevention

CASE ONE:

Mr. Ross U. Vastatin, a 48-year-old Caucasian male presents to your clinic to initiate care. He has no specific complaints, except for being annoyed with his significant other for making him schedule the appointment. His past medical history includes only seasonal allergies and an appendectomy at age 18. He takes no medications, works as a commuter rail conductor, and has smoked half a pack of cigarettes per day for the last 10 years. His father had "triple bypass" after an MI at age 56.

Questions:

1. **What are 9 modifiable risk factors for cardiovascular disease (CVD) you might address during this visit?**
   CVD [coronary heart disease (CHD), cerebrovascular disease, peripheral vascular disease (PVD), and aortic atherosclerosis] is the leading cause of death in the United States. The Framingham Heart Study demonstrated a lifetime risk of CHD alone at 49% for asymptomatic 40-year-old men. More than 90% of the risk of a first myocardial infarction (MI) is derived from nine modifiable risk factors that can guide your new patient visit (Yusuf et al, 2004).
   - *Smoking*
   - *Hyperlipidemia*
   - *Hypertension*
   - *Diabetes*
   - *Obesity*
   - *Psychosocial factors like stress/depression*
   - *Inadequate dietary intake of fruits and vegetables*
   - *Lack of moderate alcohol intake*
   - *Absence of regular exercise*

Additionally, your patient has the UNmodifiable risk factors of male sex and a family history of premature CHD (less than 60 in men or any maternal history), further increasing his risk of developing CVD.

CASE ONE:

Mr. Vastatin has never had his cholesterol checked, is not exercising due to time constraints levied by work and his three young children at home, and he has "a few" beers on weekends only. His diet includes fruits and vegetables "daily", and he doesn't consider himself stressed or depressed. His BP is 124/85 and his BMI is 27. You soon find his fasting total cholesterol is 198 with an HDL of 39 and an LDL of 131.

2. **Adult Treatment Panel III (ATPIII) guidelines suggest an assessment of his 10-year risk of developing CHD, given his 2 major risk factors. What are these two major risk factors? How do you assess his risk? What are some limitations to the currently recommended risk assessment model?**
   His two major risk factors, by ATPIII guidelines, are cigarette smoking and low HDL. The Framingham formulation for predicting CHD was incorporated into ATPIII (NCEP, 2003) and has been validated in whites and blacks in the United States. An easy to use calculator can be found at http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof and within many commercially available pocket PC programs. Based on current ATPIII and USPSTF guidelines, the Framingham risk assessment tool should be used to guide further care of this patient. [Take a moment to calculate his 10-year risk via the website above.]

   <10% risk of developing CHD in 10 years = low risk
   10-20% = intermediate risk
   >20% = high risk (considered a CHD equivalent)

   Mr. Vastatin's score = 10% (or intermediate risk)

   Use of the Framingham score has lagged in primary care settings (D'Agostino, 2008), due to the absence of early family history and obesity in the formula, questions about its validity in groups other than U.S. whites and African-Americans, and more recently, due to the emergence of inflammatory markers as independent predictors of CVD. Moreover, it does not predict all-cause CVD risk, but only CHD. It can also falsely reassure those at low risk with multiple marginal risk factor values. The JUPITER trial investigators had previously developed a prediction model that incorporates hs-CRP and family history into its risk assessment, in efforts to improve global CVD risk prediction (Ridker, 2008). This Reynolds Risk Score can be found at www.reynoldsriskscore.org and newer prediction models may be incorporated in ATPIV and/or USPSTF guidelines currently undergoing revision.

CASE ONE CONTINUED:

Based on intermediate Framingham risk, you initiate therapeutic lifestyle changes in hopes of reducing Mr. Vastatin's LDL to <130, while counseling him regarding smoking cessation and moderate exercise. At a follow-up appointment three months later, his LDL is 138. Since he is not "at goal" after a reasonable trial of lifestyle modification you initiate Atorvastatin 10mg daily.

3. **Based on new USPSTF guidelines, should you also initiate ASA therapy? When is ASA recommended for primary prevention in women?**
   In 2002, the USPSTF strongly recommended that clinicians discuss ASA with adults at risk for CHD. Since that time, new studies of ASA vs. controls for primary prevention of CVD have emerged, prompting the release of revised recommendations in 2009.

   Although ASA is still not proven to affect CVD mortality in either men or women, and though its use for primary prevention increases the risk of GI bleeding events, Mr. Vastatin meets the criteria for ASA therapy by falling within the new guidelines (USPTF, 2009):

   The USPSTF recommends:
   - *Use of ASA for men ages 45-79 when benefit from reduction in MIs outweighs harm due to increased GI bleeding (see Figure 1 Annals, 2002)*
   - *Use of ASA for women ages 55-79 when benefit from reduction in ischemic strokes outweighs harm due to increased GI bleeding*
   - *Against use of ASA for primary stroke prevention in women younger than 55*
   - *Against use of ASA for primary MI prevention in men younger than 45*

   Take note of the grades on each of these recommendations, and the insufficient evidence for comment on ASA for primary prevention in men and women over the age of 80.

CASE ONE CONTINUED:

Mr. Vastatin returns again in six months. His LDL is 105 and he is compliant with daily Atorvastatin and baby ASA. Despite multiple attempts to quit, he continues to smoke 5-10 cigarettes daily. He heard about "some planet study on Dateline" and wants to know about additional blood tests to clarify his risk of CHD.

4. **What is the current recommendation from the AHA/CDC regarding measurement of hs-CRP for assessment of CHD risk? Should this additional bloodwork be ordered?**
   The current guideline was released in 2003, and suggests that it is reasonable to measure hs-CRP as an adjunct to the major risk factors, to further assess absolute risk for CHD primary prevention. It appears to be best employed when risk factor scoring projects 10-year CHD risk in the range of 10-20%, when a finding of hs-CRP >3.0 mg/L may allow for intensification of medical therapy beyond current guidelines. Screening the entire adult population is not recommended (Pearson et al, 2003).

   His risk WITHOUT considering early family history is 10%. The Reynold's score incorporates this additional element, calculating his 10-year risk at 16%. hs-CRP measurement may therefore be reasonable, despite reaching his ATPIII-outlined LDL goal.

CASE ONE CONTINUED:

Mr. Vastatin's hs-CRP = 2.5 mg/L.

5. **<u>Briefly</u> discuss the JUPITER trial and how it may change practice. Should this patient's Atorvastatin be increased?**
   JUPITER was a randomized, double-blinded, placebo-controlled, multicenter trial of healthy subjects with "normal" cholesterol (LDL<130) and elevated hs-CRP (>2.0 mg/L). Subjects received either Rosuvastatin or placebo. The trial was stopped after 1.9 of 4 proposed years due to significant reductions in MI, stroke, arterial revascularization, hospitalization for unstable angina, and death from CVD causes in the Rosuvastatin group. The investigators have suggested that Rosuvastatin reduces major CVD events in healthy subjects without hyperlipidemia, but with elevated hs-CRP (Ridker et al, 2008). Critics have highlighted significantly higher levels of new diabetes in the Rosuvastatin group, potentially hazardous effects of lowering LDL beneath 55, conflicts of interest amongst the investigators, and the need for a trial of hs-CRP screening vs. no screening to accurately assess its value as an effective CHD screening tool (Hlatky, 2008). JUPITER does seem to demonstrate that LDL levels beneath current recommendations are protective of future CV events in patients with an elevated CRP. If caution regarding statin side-effects is carefully monitored, Mr. Vastatin's early family history of MI and already intermediate risk of developing CHD may warrant an increase in his statin dose to further decrease his LDL. An alternative would be to await future guideline updates regarding LDL goals and the appropriate use of hs-CRP for primary prevention of CVD.

Primary References:

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Additional References:

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5. D'Agostino, RB, et al. General Cardiovascular Risk Profile for Use in Primary Care: The Framingham Heart Study. *Circulation*. 2008; 117(6):743-753.

Erik Stilp attended The George Washington University School of Medicine and completed his Internal Medicine residency in the traditional program at Yale University. His areas of interest include cardiac critical care and noninvasive bedside assessment of cardiac output. He plans a fellowship in Cardiovascular Medicine following his Chief Residency at Yale.