

risk-reduction benefits that outweigh the potential for adverse effects and drug-drug interactions, and consider patient preference.” Based on the findings of IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial) (3), ezetimibe would qualify as a nonstatin to be considered with a lower intensity, but tolerated statin in high-risk groups such as those with coronary atherosclerotic disease. Thus, the data from this intravascular ultrasound trial are consistent with what the guidelines recommend if a high-intensity statin cannot be tolerated.

Lastly, there is an implied misconception of the panel’s recommendation regarding lipid targets. The ACC/AHA guidelines stated that “the Expert Panel makes no recommendations for or against specific LDL-C or non-HDL-C targets for the primary or secondary prevention of ASCVD.” The guidelines go beyond stating that lower LDL-C is better; rather they recommend a strategy for achieving a lower LDL-C that can be safely attained with therapies (lifestyle and medication) proven to provide acceptable net benefit. For example, trials of niacin added to statin therapy that achieved lower LDL-C levels by adding Niacin as compared to placebo, did not show net benefit. Thus, the cholesterol guidelines endorse “lower is better, but it matters how you get there and whether the benefit outweighs the risk for that patient” (4).

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## REPLY: Getting What the Guidelines Stated Matters



We have read with great interest the letter by Dr. Stone and colleagues commenting on our recent paper (1), and we greatly appreciate their valuable comments on the interpretation of 2013 American College of Cardiology/American Heart Association (ACC/AHA) cholesterol guideline (2). Especially pertaining to the “Fire and Forget It” concept misleadingly disseminated among the clinicians, it is of clinical importance that the expert panel members clearly recommend in this letter a follow-up lipid panel 4 to 12 weeks after initiation of statin therapy to assess both response to therapy (the anticipated response to high-intensity statin therapy was given as a  $\geq 50\%$  reduction in low-density lipoprotein cholesterol [LDL-C] and as a baseline for adherence. In addition, Drs. Stone, Lloyd-Jones, and Smith emphasized that the ACC/AHA guideline endorse “lower is better, but it matters how you get there and whether the benefit outweighs the risk for that patient.”

In terms of the specific LDL-C treatment goals in secondary prevention, we totally agree with the guideline statement: the expert panel was unable to find robust evidence to support continued use of specific LDL-C treatment targets ( $<100$  mg/dl or  $<70$  mg/dl). In a recent meta-analysis of statin trials (3), however, among 38,153 participants treated with high-dose statin therapy, patients who achieve very low LDL-C levels have a lower risk for major cardiovascular events than do those achieving moderately low levels, and  $>40\%$  did not reach an LDL-C target  $<70$  mg/dl, reaffirming “the lower, the better” and the limitation of statin monotherapy. Furthermore, based on the safety and significant clinical net benefit of combination of statin/ezetimibe evidenced by IMPROVE-IT (Improved Reduction of Outcomes Vytorin Efficacy International Trial) (4) and PRECISE-IVUS (Plaque Regression With Cholesterol Absorption Inhibitor or Synthesis Inhibitor Evaluated by Intravascular Ultrasound) (1) trials in contrast with HPS2-THRIVE (Heart Protection Study 2-Treatment of HDL to Reduce the Incidence of Vascular Events) trial (5), ezetimibe added to statin therapy would qualify as a promising non-statin agent to be considered in high-risk patients such as those with coronary atherosclerotic disease.

Finally, we would like to thank Drs. Stone, Lloyd-Jones, and Smith again for the letter which promoted for us and the readers of our article the accurate interpretation of the 2013 ACC/AHA cholesterol guideline.

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# Reconsidering the Impact of Pre-Operative Malperfusion on Acute Type A Dissection

## The Modified Penn Classification

We read with great interest the recent article reported by Czerny et al. (1) who performed an analysis of a large database to address an important

issue showing that malperfusion remained a severe clinical condition with strong potential for adverse outcomes in patients of acute type A aortic dissection (ATAAD) undergoing surgery while the impact differed substantially in accordance with the number and the type of organ malperfusion involved. Therefore, they proposed a classification system of “complicated” and “uncomplicated” ATAAD to help predict risk of outcomes. We want to congratulate the investigators for shedding light on the important issue of the impact of malperfusion on operative mortality risk for patients with ATAAD. The investigators provided valuable scientific evidences which confirmed and extended the viewpoint of ischemic consequences of organ malperfusion and end-organ dysfunction that compromised survival (2,3), although some investigators still argued that generalized ischemia in ATAAD predicted early surgical outcomes only (4). The issue of generalized ischemia caused by circulatory collapse, distinct from localized organ ischemia, is a very well taken point to be emphasized as the most important predictor of outcome after surgical repair of ATAAD and associated with the highest in-hospital mortality regardless of treatment strategy (3-5). In 2009, Augoustides et al. (2) reported an observational study of mortality risk stratification by ischemic presentation in patients with ATAAD, so-called Penn classification, which has been validated by subsequent investigators (see references 1 and 5 in Chien et al. [5]) and has shown merit to be a useful risk assessment system in predicting ATAAD-related in-hospital mortality (4,5). Nevertheless, Penn classification might still underestimate the surgical risk of ATAAD in the setting with critical organ-specific ischemia (including mesenteric ischemia, sustained major cerebral ischemia, and coronary malperfusion). From this point of view, we have proposed to modify the original Penn classification and suggested to divide the Penn class Ab into subclasses Ab-1 and Ab-2 (Table 1) (5). Based on this consideration, we studied the relationship of ischemic presentations to 30-day mortality after surgical repair in 179 patients from 1997 to 2014 (mean age, 59 ± 12 years; 124 men; classes Aa [n = 60], Ab-1 [n = 44], Ab-2 [n = 27], Ac [n = 10], and Abc [n = 38]). It was found that subclass Ab-2 had much higher mortality rate than that of subclass Ab-1 (22.2% vs. 2.3%), however, without statistical significance (p = 0.175). One possible explanation is the small number of our patients suffered from localized malperfusion (Ab-1 or Ab-2). Nevertheless, we do think that subclass Ab-2 remains a surgical challenge and is

