THE AMERICAN JOURNAL of MEDICINE®

The Reply

Jennings et al contend that "pending publication of additional data, we plan to continue to adhere to current guidelines and recommend beta-blocker therapy for clinically stable patients after acute myocardial infarction." The authors cite observational studies and subgroup analysis of a randomized trial (ClOpidogrel and Metoprolol in Myocardial Infarction Trial [COMMIT])[1] as evidence to support the use of beta-blockers after acute myocardial infarction. Observational studies have a number of limitations, including selection and ascertainment bias. In addition, subgroup analyses from randomized trials have limitations, and as Sir Richard Peto aptly stated, "Subgroup analyses are no longer randomized and should be viewed, at best, as hypothesis formulating and, at worst, as rubbish. The biggest danger in interpretation of subgroups is acting as if they provide serious evidence" (Sir Richard Peto, Personal Communication, 2010). This is shown elegantly in a subgroup analysis of the Second International Study of Infarct Survival (ISIS-2) trial in which patients born under Gemini or Libra had a 9% increase in vascular mortality with aspirin when compared with placebo, whereas aspirin reduced the risk for patients with myocardial infarction born under all other birth signs.[2]

In the COMMIT trial, patients with medium to high shock risk index did not benefit (with significant harm) from beta-blockers when considering the overall benefit (reduction in death) to risk (increase in cardiogenic shock) ratio.[1] However, beta-blockers were beneficial in the low shock risk index group, prompting Jennings et al to use this as evidence to continue using beta-blockers despite this being a non-prespecified subgroup analysis. Even if one were to consider this subgroup analysis as providing serious evidence for using beta-blockers, in COMMIT only 54% of patients randomized were in the low shock risk index category.[1] In other words, approximately 1 of every 2 patients with myocardial infarction had medium to high shock risk, and beta-blockers should be avoided. In the United States, beta-blocker use at discharge after myocardial infarction is still considered a quality indicator, and hospitals are judged and compared on the basis of this metric. If the data from COMMIT were to be applied to real-world practice, one would assume beta-blocker use rates to be approximately 50% to 60% if given judiciously to patients with low shock risk index only. However, data from the Joint Commission (for 2012) from an average of 2324 hospitals across the United States show that the average beta-blocker use rate at discharge is a whopping 99.2%! One is left to wonder whether these qualify indicators based on shaky data are placing patients in harm's way. These ethical issues notwithstanding, for beta-blocker use in myocardial infarction, there is evidence of absence or absence of evidence, and neither is a good enough justification to continue current indiscriminate prescription pattern.

Sripal Bangalore, MD, MHA[a]
Franz H. Messerli, MD[b]
[a]*New York University School of Medicine*
New York, NY
[b]*Mt Sinai School of Medicine*
New York, NY

http://dx.doi.org/10.1016/j.amjmed.2014.08.011

References

1. Chen ZM, Pan HC, Chen YP, et al. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet*. 2005;366:1622-1632.
2. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. *Lancet*. 1988;2:349-360.

Funding: None.
Conflict of Interest: None.
Authorship: Both authors had access to the data and played a role in writing this manuscript.