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Why Optimal Medical Therapy Should Be a Universal Standard of Care

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"A wise man proportions his belief to the evidence".

David Hume—Scottish Philosopher (1711-1776)

Recent randomized controlled trials of management strategies in stable ischemic heart disease (SIHD) have utilized intensive pharmacologic and lifestyle intervention—often referred to as optimal medical therapy (OMT)—with or without initial revascularization (1-3). While critics and supporters alike have attributed the lack of difference in death and myocardial infarction (MI) between treatment groups, in part, to the high quality of OMT employed in all subjects, this has been just an unproven assumption because of the lack of a control group that did *not* receive OMT in these trials. An independent benefit conferred by intensive medical therapy has not, to date, been convincingly established.

In this issue of the *Journal*, Bittner and colleagues report a post hoc analysis from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial that used a creative method to evaluate the relationship between risk factor control, survival, and the composite endpoint of death, MI, or stroke, despite the absence of a no-OMT control group (Bittner et al). As previously reported, not all BARI 2D participants achieved their risk factor goals (5). In fact, it was a small minority of patients who achieved all of their treatment targets. In the present analysis, the authors leveraged this spectrum of risk factor control to assess the relationship between the degree of success with risk factor goal attainment and clinical outcomes by aggregating both treatment groups.

Six risk factors were used in this analysis and were considered "in control" if they achieved the following: no smoking, triglycerides <150 mg/dL, non-HDL cholesterol <130mg/dL, HbA1c <7%, systolic blood pressure <130 mmHg, and diastolic blood pressure <80 mmHg. With the exception of the no smoking goal, these trial definitions go beyond current Class I clinical practice guideline recommendations (6).

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At baseline, only 7% of participants met all 6 risk factor goals. At 5 years, only 15% of individuals achieved control of all 6 risk factors. Nevertheless, about three-quarters of patients had 4 or more risk factors in control during long-term follow-up. There was no relationship between number of risk factors in control at baseline and subsequent death (the BARI 2D primary endpoint). By contrast, risk factor control at year 1 was strongly related to survival and cardiovascular outcomes after adjusting for the number of risk factors in control at baseline. Patients with only 0-2 risk factors in control had twice the risk of death (hazard ratio [95% CI]: 2.0 [1.3 to 3.3], p=0.0031) and 1.7 times the risk of the composite outcome (hazard ratio [95% CI]: 1.7 [1.2 to 2.5], p=0.0043) as compared with patients who were able to achieve all 6 risk factors in control. There was no significant interaction between initial treatment assignment (prompt revascularization or medical therapy) and the number of risk factors in control for either outcome.

This is an important report because it has been assumed that OMT in recent SIHD strategy trials reduced clinical events (assumed because there were no comparison groups that did not receive OMT), but until now the evidence to support this assumption has been lacking,. With this analysis, although post hoc and exploratory, the authors demonstrate the impact of good multiple risk factor control vs. poor or moderate risk factor control in diabetic SIHD patients with adjudicated endpoints. The findings are consistent with what might be expected based on prior studies that compared aggressive multiple risk factor intervention with usual care (7,8). In addition, a recent publication from Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) Trial investigators analyzed the effect of OMT in patients with complex coronary artery disease randomized to PCI or coronary artery bypass grafting (CABG) (9). OMT—not part of the trial intervention—was defined as the combination of at least 1 antiplatelet drug, statin, beta-blocker, and angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, arguably a less stringent definition than reaching 6 risk factor goals. OMT, which was used in 50% or less of patients over 5 years, was associated with a 36% relative reduction in mortality at the 5-year follow-up as compared with those not receiving OMT (9). The 36% relative reduction in mortality over 5 years associated with OMT was greater than the 26% relative reduction in mortality over 5 years associated with the randomized treatment assignment in SYNTAX to CABG versus PCI.

The current analysis demonstrated that when multiple risk factor goals were achieved in diabetics with SIHD, survival was improved and cardiovascular events reduced, but control of all 6 treatment targets was achieved in only a minority of patients. Simultaneous attainment of multiple risk factor goals in patients with SIHD has previously been shown to be infrequent in the REGARDS (REasons for Geographic and Racial Differences in Stroke) prospective cohort study (10) and in a pooled analysis from COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation), BARI 2D, and FREEDOM (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes) (5). The remarkable observation in the present report is the significantly better survival (a 50% lower mortality rate) among patients who achieved good risk factor control in a trial that found no survival benefit from revascularization! Although this was not a randomized comparison of OMT versus no OMT, the conclusions are convincing and entirely consistent with evidence from decades of careful epidemiologic study. Despite the

ongoing uncertainty about the benefit of elective revascularization in patients with SIHD—currently being tested prospectively in the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial (11)—we believe these data are compelling and argue persuasively that all SIHD patients should receive OMT, regardless of whether or not they undergo revascularization. Yet the use of OMT remains disappointingly low in SIHD patients (9,12). The findings of Bittner and coworkers provide powerful evidence that simultaneous multiple risk factor control improves survival and reduces nonfatal MI and stroke. For that singular reason, OMT needs to be more widely embraced and utilized by clinicians as both a best medical practice and a universal standard of care in all patients with coronary artery disease.

References

1. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007; 356:1503–16. [PubMed: 17387127]
2. Frye RL, August P, Brooks MM, et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Engl J Med. 2009; 360:2503–15. [PubMed: 19502645]
3. De Bruyne B, Pijls NH, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. The New England journal of medicine. 2012; 367:991–1001. [PubMed: 22924638]
4. Bittner, et al. (the paper that this editorial accompanies).
5. Farkouh ME, Boden WE, Bittner V, et al. Risk factor control for coronary artery disease secondary prevention in large randomized trials. Journal of the American College of Cardiology. 2013; 61:1607–15. [PubMed: 23500281]
6. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Journal of the American College of Cardiology. 2012; 60:e44–e164. [PubMed: 23182125]
7. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med. 2003; 348:383–93. [PubMed: 12556541]
8. Haskell WL, Alderman EL, Fair JM, et al. Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease. The Stanford Coronary Risk Intervention Project (SCRIP) Circulation. 1994; 89:975–90. [PubMed: 8124838]
9. Iqbal J, Zhang YJ, Holmes DR, et al. Optimal Medical Therapy Improves Clinical Outcomes in Patients Undergoing Revascularization With Percutaneous Coronary Intervention or Coronary Artery Bypass Grafting: Insights From the Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) Trial at the 5-Year Follow-Up. Circulation. 2015; 131:1269–77. [PubMed: 25847979]
10. Brown TM, Voeks JH, Bittner V, et al. Achievement of optimal medical therapy goals for U.S. adults with coronary artery disease: results from the REGARDS Study (REasons for Geographic And Racial Differences in Stroke). J Am Coll Cardiol. 2014; 63:1626–33. [PubMed: 24534599]
11. [Accessed June 2, 2015] International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) home page. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01471522, NIH Grant: 1U01HL105907
12. Borden WB, Redberg RF, Mushlin AI, Dai D, Kaltenbach LA, Spertus JA. Patterns and intensity of medical therapy in patients undergoing percutaneous coronary intervention. JAMA : the journal of the American Medical Association. 2011; 305:1882–9. [PubMed: 21558519]