References

1. Masulli M, Vaccaro O: Association between cigarette smoking and metabolic syndrome (Letter). *Diabetes Care* 29:482, 2006
2. Oh SW, Yoon YS, Lee ES, Kim WK, Park C, Lee S, Jeong EK, Yoo T: Association between cigarette smoking and metabolic syndrome: the Korea National Health and Nutrition Examination Survey (Brief Report). *Diabetes Care* 28:2064–2066, 2005
3. Foy CG, Bell RA, Farmer DF, Goff DC Jr, Wagenknecht LE: Smoking and incidence of diabetes among U.S. adults: findings from the Insulin Resistance Atherosclerosis Study. *Diabetes Care* 28:2501–2507, 2005
4. Sairenchi T, Iso H, Nishimura A, Hosoda T, Irie F, Saito Y, Murakami A, Fukutomi H: Cigarette smoking and risk of type 2 diabetes mellitus among middle-aged and elderly Japanese men and women. *Am J Epidemiol* 160:158–162, 2004

The Effectiveness of β-Blockers After Myocardial Infarction in Patients With Type 2 Diabetes

Response to McDonald et al.

In the September 2005 issue of *Diabetes Care*, McDonald et al. (1) showed that β-blocker therapy after myocardial infarction (MI) was not associated with reduced mortality or fewer recurrent events in people with type 2 diabetes in routine practice. This contrasted with studies performed before intervention with drugs such as ACE inhibitors and statins were available. These studies showed a significant decrease in mortality and reinfarction post-MI in diabetic subjects (2,3). The authors conclude that the benefits of β-blockers are attenuated in the era of multiple interventions.

I believe that there is another reason for the decreased effectiveness of β-blockers in the modern era. When the older studies were preformed, the majority of β-blockers used were nonselective β-blockers that blocked both the β_1 and the β_2 receptors. Selective β_1 blockers, unless used intravenously at the time of the MI, have never been shown to decrease reinfarction or mortality post-MI (4). In contrast, nonselective β-blockers (propranolol and pindolol) with normal ventricular function, as well as carvedilol with decreased ventricular function, have been shown to decrease cardiac events and mortality post-MI.

Therefore, I believe that the shift in effectiveness of β-blockers post-MI is not due to multiple other interventions but to utilization of β_1-blockers, which—especially at lower doses—have not been shown to decrease mortality or reinfarction. A reanalysis based on the use of β_1 selective and nonselective β-blockers could prove or disprove this theory.

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References

1. McDonald CG, Majumdar SR, Mahon JL, Johnson JA: The effectiveness of β-blockers after myocardial infarction in patients with type 2 diabetes. *Diabetes Care* 28: 2113–2117, 2005
2. Kjekshus J, Gilpin E, Cali G, Blackey AR, Henning H, Ross J Jr.: Diabetic patients and beta-blockers after acute myocardial infarction. *Eur Heart J* 11:43–50, 1990
3. Jonas M, Reicher-Reiss H, Boyko V, Shotan A, Mandelzweig L, Goldbourt U, Behar S: Usefulness of beta-blocker therapy in patients with non-insulin dependent diabetes mellitus and coronary artery disease: Bezafibrate Infarction Prevention (BIP) Study Group. *Am J Cardiol* 77:1273–1277, 1996
4. Freemantle N, Cleland J, Young P, Mason J, Harrison J: Beta blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ* 18:1730–1737, 1999

The Effectiveness of β-Blockers After Myocardial Infarction in Patients With Type 2 Diabetes

Response to Bell

We thank Dr. Bell (1) for his interest in and insightful comments about our study. Dr. Bell proposes that the use of lower doses of cardioselective β-blockers could have reduced the effectiveness of this class of agents after myocardial infarction (MI) in diabetic subjects, a reasonable hypothesis. Another hypothesis is that short-acting cardioselective β-blockers lead to periods of withdrawal and decreased efficacy (2).

As in previous studies (3,4), we assumed a class effect among β-blockers. Unfortunately, we could not differentiate the type of β-blockers that were prescribed, although our sample size would have been precipitously reduced if we had done so. However, atenolol and metoprolol are the most commonly prescribed β-blockers in Canada (5).

Dr. Bell asserts that cardioselective β-blockers have never been shown to reduce mortality post-MI unless used intravenously. However, meta-analyses have demonstrated a 25% reduction in mortality with long-term β-blockade after MI (including cardioselective agents) (6,7); cardioselectivity or membrane-stabilizing activity did not predict mortality. Rather, Yusuf et al. (6) demonstrated decreased effectiveness when trials using agents with intrinsic sympathomimetic activity (ISA) were pooled (odds ratio [OR] for agents with ISA 0.90 [0.77–1.05]; OR without ISA 0.69 [0.61–0.79]). Freemantle et al. (7) also failed to demonstrate a significant effect of cardioselectivity, although the OR for the protective effect of β-blockers with ISA was 1.19 (0.96–1.47). Moreover, older observational studies of β-blockers (as a class) post-MI, conducted in an era when metoprolol and atenolol were frequently prescribed, have found no effect of cardioselectivity (3,4,8). For example, in the Bezafibrate Infarction Prevention (BIP) study, mortality was similar in patients who received propranolol or a cardioselective β-blocker (4), and in the Diabetes Insulin-Glucose in Acute Myocardial Infarction (DIGAMI) study, metoprolol was an independent predictor of reduced mortality after MI (relative risk ratio 47%) (8). If Dr. Bell's hypothesis is correct, it seems unlikely that these earlier studies would have shown mortality benefit.

Therefore, we believe that the putative benefits of β-blockade were less in our study because of cointerventions that also reduce mortality. Future studies should include the type of β-blocker as a covariate rather than assuming a class effect, as we and others have done. The answer to this question is clinically