Early Intravenous Beta-Blockade Before Primary Percutaneous Coronary Intervention Gives Major Benefits, Apparently Without Side Effects

The paper by Pizarro et al. (1) gives strong support to the concept of very early low-cost intravenous beta-blockade for primary percutaneous coronary intervention (pPCI) and makes metoprolol the agent of choice. When metoprolol was given to patients with acute myocardial infarction (AMI) in Killip class ≤II ST-segment elevation myocardial infarction undergoing pPCI, there were fewer heart failure admissions. The number needed to treat to avoid 1 implantable cardioverter-defibrillator was only 8. Unexpectedly, there was no indication of any side effects of beta-blockade. Were there really none?

In the COMMIT (Clopidogrel and Metoprolol in Myocardial Infarction Trial) study of 45,852 patients admitted to 1,250 hospitals within 24 h of suspected AMI, patients were randomly allocated metoprolol (up to 15 mg intravenous, then 200 mg oral daily; n = 22,929) or matching placebo (n = 22,923) (2). The use of early beta-blocker therapy in AMI reduced the risks of reinfarction and ventricular fibrillation, yet cardiogenic shock was a major side effect. Pizarro et al. (1) suggested starting beta-blocker therapy only when the hemodynamic condition had stabilized.

Yusuf (3) analyzed 28 trials involving approximately 27,500 patients during suspected early AMI. Overall, he concluded that intravenous plus oral beta-blockade reduced the risk for early death, reinfarction, and ventricular fibrillation by approximately 15% (3). He suggested that the reduction in mortality was greatest for those treated within 2 h of pain. The treated group had few side effects, namely reversible and nonfatal heart block and hypotension.

Thus in 2 large studies, beta-blockade had side-effects to which clinicians should be alerted when considering the use of beta-blockers for early AMI.

REFERENCES


REPLY: Early Intravenous Beta-Blockade Before Primary Percutaneous Coronary Intervention Gives Major Benefits Apparently Without Side Effects

We appreciate the comment by our admired Professor Opie regarding the potential side effects of early intravenous (IV) beta-blockers in patients with ST-segment elevation myocardial infarction (STEMI). Our paper described the long-term follow-up of patients in the METOCARD-CNIC (Effect of Metoprolol in Cardioprotection During an Acute Myocardial Infarction) trial (1). The acute effects of IV metoprolol in this trial were reported in a previous publication (2). In the first publication, we described the incidence of adverse events during admission (those that can be ascribed to an acute single administration of IV metoprolol before primary angioplasty); death during admission (2.1% vs. 2.3% in IV metoprolol vs. control, respectively), advanced atrioventricular block (0.7% vs. 1.5%), cardiogenic shock (4.3% vs. 5.4%), and ventricular tachycardia/fibrillation (3.6% vs. 7.7%). Thus, it is not correct that there were no side effects of beta-blockade in our study; rather, we presented that metoprolol was not associated with an excess number of these side effects.

The role of early IV beta-blockade in STEMI was mostly evaluated long ago, and the side effect profile has been dramatically changed within the last few years. The METOCARD-CNIC trial was the first randomized trial performed in patients with STEMI undergoing reperfusion by primary angioplasty. One of Dr. Opie’s references to support the potential increase in side effect frequency is from Yusuf reporting a
meta-analysis of 27 trials, all performed in the pre-reperfusion era. Any comparison of the side effect profile between patients with STEMI not reperfused by any means and those undergoing early primary angioplasty is futile. Conversely, we agree with Dr. Opie that the results of the COMMIT (Clopidogrel and Metoprolol in Myocardial Infarction Trial) (3) should be placed in perspective. We commented extensively on the COMMIT results in our 2 previous publications, and we refer the readers to the original publications (1, 2). To summarize, the side effects in the COMMIT study were concentrated in patients at the highest risk for shock: Killip class III and/or systolic hypotension on presentation. We learned lessons from the COMMIT study, and in the METOCARD-CNIC trial, patients presenting with Killip class III and/or systolic blood pressure below 120 mm Hg were contraindicated for enrollment. Altogether, the COMMIT and METOCARD-CNIC trials suggest that a comprehensive selection of patients for early IV metoprolol treatment might result in a significant benefit, with no increase in the frequency of side effects. The ongoing EARLY-BAMI (Early Beta-Blocker Administration Before Primary PCI in Patients With ST-Elevation Myocardial Infarction) trial (Zwolle, the Netherlands) should confirm the infarct size reduction and increased long-term ventricular function observed in the METOCARD-CNIC trial. Even if confirmed, infarct size and ventricular function are surrogate markers, and a large randomized clinical trial with hard clinical endpoints should be performed. The MOVE ON! (Impact of Pre-Reperfusion Metoprolol on Clinical Events After Myocardial Infarction) trial will recruit more than 3,500 patients with STEMI in 8 European countries, randomize them to IV metoprolol or placebo during transfer to primary angioplasty, and quantify the incidence of death or heart failure admission over a median follow-up of 3 years. This trial will answer whether early IV metoprolol is the first therapy used in conjunction with primary angioplasty to improve clinical outcomes (4).

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REFERENCES


Zero-Hour Aortic Sclerosis: Auscultatory Biomarker or Imaging Biomarker?

We read with interest the paper by Coffey et al. (1) reporting the results of a meta-analysis on the prevalence, incidence, and risks of aortic valve sclerosis (ASc). In this review, the authors demonstrated that ASc is common in the general population and is independently associated with an increased frequency of major adverse cardiovascular and cerebrovascular events (MACCE), as well as all-cause mortality, making it a powerful “imaging biomarker.”

The researchers analyzed studies that defined ASc as any thickening or calcification of the aortic valve—detectable by any means, such as transthoracic or transesophageal echocardiogram or computed tomography—without any significant hemodynamic effect. Although not directly addressing the results of this meta-analysis, we want to take this opportunity to address that mindful auscultation can lead one in the right direction hours, days, and even weeks before the same results can be achieved by those who rely solely on modern technology.

We have a wonderfully rich tradition of physical diagnostic signs in cardiology. However, in contemporary medicine, many have come to rely solely on clinical imaging and laboratory testing, looking at physical diagnostic signs askance and thus neglecting or even discarding knowledge acquired during clinical training. Disregard for physical diagnostic methods now pervades clinical training in the United States, and the art of physical diagnosis has been reduced to a mere vestige, with several experts contending that physical diagnosis has little to offer the modern clinician. This is particularly true of the stethoscope, which some believe should be exiled to the archives of medical history.

Without distracting the readers from the results of this meta-analysis (1), it is important to note