Beta-blocker use and the development of depression (comment)

van Melle, J.P.; de Jonge, P.

Published in:
American Journal of Cardiology

Publication date:
2009

ternak RC, Smith SC, Stone NJ, for the Coordinating Committee of the National Cholesterol Education Program. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *J Am Coll Cardiol* 2004;44:720–732.
5. Ridker PM, Buring JE, Rifai N, Cook NR. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women. *JAMA* 2007;297:611–619.
6. Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PWF, Wolf PA, Levy D. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006;113:791–798.

doi:10.1016/j.amjcard.2009.02.022

In ST-Elevation Myocardial Infarction Patients Receiving Primary Percutaneous Coronary Intervention, Admission Cardiac Troponin T and Peak Cardiac Troponin T Values Differ in Their Prognostic Properties

We read with interest the study by Hassan et al[1] investigating the ability of peak cardiac troponin T (cTnT) to predict infarct size and long-term outcomes after ST elevation myocardial infarctions in patients treated with primary percutaneous coronary intervention (PCI). Although we do not disagree with the investigators' conclusion that peak cTnT carries substantial predictive value regarding long-term outcome and infarct size, we would like to comment on several points.

We felt that the article lacked a clear articulation of the distinction between cTnT measured before primary PCI (i.e., usually at admission) and after primary PCI. It is well established that cTnT measured almost at any time point after PCI conveys powerful prognostic information regarding impaired left ventricular function and infarct size.[2,3] Although admission cTnT is a predictor of long-term mortality, which appears principally related to the longer delay and recent myocardial damage,[4] the association of admission cTnT and infarct size is weak at best,[4] and several studies have found no such relation.[3,5]

It is unfortunate, therefore, that in conducting their analyses, Hassan et al[1] appear to have mixed pre- and post-PCI samples of cTnT (given that 2% of the study population were reported to have attained peak cTnT values before PCI). It is likely that the inclusion of pre-PCI samples in this report weakened the correlations, although the impact was probably minor given the small fraction of peak cTnT values originating from pre-PCI sampling.

To confuse matters further, in the discussion section, Hassan et al[1] cite ≥4 previous studies as having measured peak cTnT, when in fact closer scrutiny of the reports in question reveals that they all measured admission cTnT values,[6–9] which makes comparison with the present study unhelpful at best.

Last, Hassan et al[1] conclude their report by advocating the use of serial cTnT measurements to derive a peak value for optimal risk stratification after ST elevation myocardial infarction. Several recent investigations have suggested that the prognostic capacity of single-point cTnT measurements, which would constitute a much easier strategy, is comparable with that of peak values.[3,10–12]

Jonas Hallén, MD
Dan Atar, MD
Oslo, Norway
13 February 2009

1. Hassan AKM, Bergheanu SC, Hasan-Ali H, Liem SS, Laarse AVD, Wolterbeek R, Atsma DE, Schalij MJ, Jukema JW. Usefulness of peak troponin T to predict infarct size and long-term outcome in patients with first acute myocardial infarction after primary percutaneous coronary intervention. *Am J Cardiol* 2009;103:779–784.
2. Tzivoni D, Koukoui D, Guetta V, Novack L, Cowing G. Comparison of troponin T to creatine kinase and to radionuclide cardiac imaging infarct size in patients with ST-elevation myocardial infarction undergoing primary angioplasty. *Am J Cardiol* 2008;101:753–757.
3. Giannitsis E, Steen H, Kurz K, Ivandic B, Simon AC, Futterer S, Schild C, Isfort P, Jaffe AS, Katus HA. Cardiac magnetic resonance imaging study for quantification of infarct size comparing directly serial versus single time-point measurements of cardiac troponin T. *J Am Coll Cardiol* 2008;51:307–314.
4. Frostfeldt G, Gustafsson G, Lindahl B, Nygren A, Venge P, Wallentin L. Possible reasons for the prognostic value of troponin T on admission in patients with ST-elevation myocardial infarction. *Coron Artery Dis* 2001; 12:227–237.
5. Ohlmann P, Monassier JP, Michotey MO, Berenger N, Jacquemin L, Laval G, Roul G, Schneider F. Troponin I concentrations following primary percutaneous coronary intervention predict large infarct size and left ventricular dysfunction in patients with ST-segment elevation acute myocardial infarction. *Atherosclerosis* 2003;168:181–189.
6. Rasoul S, Nienhuis MB, Ottervanger JP, Slingerland RJ, de Boer MJ, Dambrink JH, Ernst NM, Hoorntje JC, Gosselink AT, Suryapranata H, Zijlstra F, van 't Hof AW. Predictors of elevated cardiac troponin T on admission in ST-segment elevation myocardial infarction. *Ann Clin Biochem* 2006;43:281–286.
7. Matetzky S, Sharir T, Domingo M, Noc M, Chyu KY, Kaul S, Eigler N, Shah PK, Cercek B. Elevated troponin I level on admission is associated with adverse outcome of primary angioplasty in acute myocardial infarction. *Circulation* 2000;102:1611–1616.
8. Stubbs P, Collinson P, Moseley D, Greenwood T, Noble M. Prognostic significance of admission troponin T concentrations in patients with myocardial infarction. *Circulation* 1996;94:1291–1297.
9. Giannitsis E, Muller-Bardorff M, Lehrke S, Wiegand U, Tolg R, Weidtmann B, Hartmann F, Richardt G, Katus HA. Admission troponin T level predicts clinical outcomes, TIMI flow, and myocardial tissue perfusion after primary percutaneous intervention for acute ST-segment elevation myocardial infarction. *Circulation* 2001;104:630–635.
10. Vasile VC, Babuin L, Giannitsis E, Katus HA, Jaffe AS. Relationship of MRI-determined infarct size and cTnI measurements in patients with ST-elevation myocardial infarction. *Clin Chem* 2008;54:617–619.
11. Steen H, Giannitsis E, Futterer S, Merten C, Juenger C, Katus HA. Cardiac troponin T at 96 hours after acute myocardial infarction correlates with infarct size and cardiac function. *J Am Coll Cardiol* 2006;48:2192–2194.
12. Panteghini M, Bonetti G, Pagani F, Stefini F, Giubbini R, Cuccia C. Measurement of troponin I 48 h after admission as a tool to rule out impaired left ventricular function in patients with a first myocardial infarction. *Clin Chem Lab Med* 2005;43:848–854.

doi:10.1016/j.amjcard.2009.02.032

β-Blocker Use and the Development of Depression

We read with interest the report by Papademetriou[1] in which the investigator reported the effects of nebivolol for the treatment of hypertension in a sample of 845 subjects. Papademetriou observed that depression was not mentioned as an adverse event by subjects receiving nebivolol and used this observation to underline its favorable tolerability. However, we disagree with his suggestion that depression is a typical complaint related to β-blocker use. This is based on old research, often using questionable study designs.

Ko et al[2] clearly demonstrated that depression is not more often mentioned as a side effect after β blockade than after placebo treatment. Using standardized methods of depression, we also found no significant associations between the use of β blockers and the development of depression during the first year after myocardial infarction.[3] After adjustment for baseline depression, β-blocker users even had somewhat lower depression scores than non-β-blocker users at 3 months after myocardial infarction ($p = 0.06$). Despite some old case reports, no empiric support exists for the belief that

depression is a common side effect of β blockade. Unfortunately, this believe once again proves difficult to correct, and an unfortunate side effect of that belief might be a continued reluctance in prescribing β blockers for reasons of putative but unsupported depressant effects.

Joost P. van Melle, PhD, MD
Peter de Jonge, PhD
Groningen, The Netherlands
13 February 2009

1. Papademetriou V. Comparison of nebivolol monotherapy versus nebivolol in combination with other antihypertensive therapies for the treatment of hypertension. *Am J Cardiol* 2009; 103:273–278.
2. Ko DT, Hebert PR, Coffey CS, Sedrakyan A, Curtis JP, Krumholz HM. Beta-blocker therapy and symptoms of depression, fatigue, and sexual dysfunction. *JAMA* 2002;288: 351–357.
3. van Melle JP, Verbeek DE, van den Berg MP, Ormel J, van der Linde MR, de Jonge P. Beta-blockers and depression after myocardial infarction: a multicenter prospective study. *J Am Coll Cardiol* 2006;48:2209–2214.

doi:10.1016/j.amjcard.2009.02.033

The Clinical Dilemma of Positive Results of High-Sensitive Troponin Assays

Since the widespread introduction of highly sensitive assays for troponin testing,[1–3] it is likely that the number of patients presenting with values exceeding the limit of detection and the recommended threshold corresponding to optimal precision (coefficient of variation ≤10%) will increase further, thus raising a dilemma in the appropriate triage of these patients. According to the universal definition of acute myocardial infarction (AMI), elevated value higher than the decision level is required to establish the diagnosis of AMI.[4] However, the demonstration of an increasing and/or decreasing pattern was also clearly highlighted, to help distinguish background elevated troponin levels (e.g., patients with chronic renal failure) from elevations in the same patients that indicate AMI.[4] These indications are strongly supported by the recent findings of Eggers et al,[5] who showed that 0.6% of elderly subjects from a community sample and 6.7% of patients stabilized after acute coronary syndromes would have been labeled has having AMIs according to the universal definition of AMI when diagnostic classification had been based on a single cardiac troponin result.[5] In line with the former recommendations,[4] the investigators also supported the introduction of a degree of troponin change >20% as a diagnostic criterion, which would probably be more appropriate to avoid diagnostic misclassification. Although this conceivably reflects the best practice so far, it raises a further dilemma concerning the appropriate triage of patients presenting with troponin values slightly higher than the diagnostic threshold in the period between the first and the second troponin results, which can be as long as 6 to 9 hours. It is widely acknowledged that time is critical for patients with AMIs, because the clinical outcome is strongly influenced by the early onset of therapy, either pharmacologic or based on percutaneous or surgical revascularisation.[6] Primary percutaneous coronary intervention, for example, appears to be more effective if vessel patency is restored within 120 minutes,[7] whereas anticoagulant or antiplatelet drugs should be initiated as soon as possible to result in significant clinical benefits.[8]

The enhanced sensitivity of the newer troponin assays will inevitably determine substantial increases in case identification, so that physicians will face the new challenge of discriminating between patients who will benefit from more aggressive treatment and those who will not, until AMI is definitely diagnosed or ruled out. Highly sensitive troponin assays offer great diagnostic and clinical opportunities, but guidelines or recommendations are urgently needed for the most appropriate management of patients and to limit the overcrowding of emergency departments.

Giuseppe Lippi, MD
Martina Montagnana, MD
Gian Cesare Guidi, MD
Verona, Italy
24 February 2009

1. Kavsak PA, Macrae AR, Yerna MJ, Jaffe AS. Analytic and clinical utility of a next-generation, highly sensitive cardiac troponin I assay for early detection of myocardial injury. *Clin Chem* 2009;55:573–577.
2. Eggers KM, Jaffe AS, Lind L, Venge P, Lindahl B. Value of cardiac troponin I cutoff concentrations below the 99th percentile for clinical decision-making. *Clin Chem* 2009;55: 85–92.
3. Tate JR. Troponin revisited 2008: assay performance. *Clin Chem Laboratory Med* 2008:46;1489–1500.
4. Thygesen K, Alpert JS, White HD, Jaffe AS, Apple FS, Galvani M, Katus HA, Newby LK, Ravkilde J, Chaitman B; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Circulation* 2007;116: 2634–2653.
4. Thygesen K, Alpert JS, White HD, Jaffe AS, Apple FS, Galvani M, Katus HA, Newby LK, Ravkilde J, Chaitman B; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Circulation* 2007;116: 2634–2653.
5. Eggers KM, Lind L, Venge P, Lindahl B. Will the universal definition of myocardial infarction criteria result in an overdiagnosis of myocardial infarction? *Am J Cardiol* 2009;103: 588–591.
6. Diercks DB, Kontos MC, Weber JE, Amsterdam EA. Management of ST-segment elevation myocardial infarction in EDs. *Am J Emerg Med* 2008;26:91–100.
7. Zimarino M, Sacchetta D, Renda G, De Caterina R, Facilitated PCI. Rationale, current evidence, open questions, and future directions. *J Cardiovasc Pharmacol* 2008;51:3–10.
8. McCann CJ, Menown IB. New anticoagulant strategies in ST elevation myocardial infarction: trials and clinical implications. *Vasc Health Risks Manag* 2008;4:305–313.

doi:10.1016/j.amjcard.2009.02.037

Erratum for Sharma M, et al., "Safety of Cardiac Catheterization in Patients With End-Stage Liver Disease Awaiting Liver Transplantation," Am J Cardiol 2009;103:742–746.

The corresponding author is:
Andrew J. Boyle
505 Parnassus Avenue, Box 0103
San Francisco, California 94143
Tel: 415-514-0827
E-mail address: aboyle@medicine.ucsf.edu

1. In Table 2, the p values have been transcribed incorrectly. The corrected Table 2 appears below.

doi:10.1016/j.amjcard.2009.03.009

Table 2
Clinically evident complications

	Controls	ESLD	p Value
Intracranial bleed	0	0	N/A
Retroperitoneal bleed	0	0	N/A
Pseudoaneurysm	1 (1)	5 (6)	0.119
Complicated pseudoaneurysm:	0	5 (6)	0.029
Arterio-venous fistula	0	0	N/A
Hematoma	6 (7)	6 (7)	0.882
Transfusion-requiring hematoma	0	2 (2)	0.172