Journal Review

Borja Ibanez, Carlos Macaya, Vicente Sanchez-Brunete, Gonzalo Pizzaro, Leticia Fernandez-Friera, Valentin Fuster, et al., Effect of early metoprolol on infarct size in ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention: The effect of metoprolol in cardioprotection during an acute myocardial infarction (METOCARD-CNIC) trial. Circulation 128 (2013) 1495–1503; originally published online September 3, 2013.

Background: The effect of beta-blockers on infarct size when used in conjunction with primary PCI is unknown. We hypothesize that metoprolol reduces infarct size when administered early (intravenously before reperfusion).

Methods and results: Patients with Killip class II or less anterior STEMI undergoing PCI within 6 h of symptoms onset were randomized to receive intravenous metoprolol (n = 131) or not (control, n = 139) before reperfusion. All patients without contraindications received oral metoprolol within 24 h. The predefined primary end point was infarct size on MRI performed 5–7 days after STEMI. MRI was performed in 220 patients (81%). Mean ± SD infarct size by MRI was smaller after intravenous metoprolol compared with control (25.6 ± 15.3 vs 32.0 ± 22.2 g; adjusted difference, −6.52; 95% confidence interval, −11.39 to −1.78; p = 0.012). In patients with pre-PCI TIMI grade 0 to 1 flow, the adjusted treatment difference in infarct size was −8.13% (95% confidence interval, −13.10 to −3.16; p = 0.0024). Infarct size estimated by peak and area under the curve CK release was measured in all study populations and was significantly reduced by intravenous metoprolol. LVEF was higher in the intravenous metoprolol group (adjusted difference, 2.67%; 95% confidence interval, 0.09–5.21; p = 0.045). The composite of death, malignant ventricular arrhythmia, cardiogenic shock, AV block and re-infarction at 24 h in the intravenous metoprolol and control groups was 7.1% and 12.3%, respectively (p = 0.21).

Conclusions: In patients with anterior Killip class II or less STEMI undergoing primary PCI, early intravenous metoprolol before reperfusion reduced infarct size and LVEF with no excess of adverse events during the first 24 h after STEMI.

1. Perspective

1.1. Early intravenous metoprolol in acute STEMI before timely primary PCI—A stitch in time saves nine?

The benefit of oral beta-blockers in STEMI patient is well known and is recommended in all STEMI patients within 24 h unless contraindicated. Beta-blockers have pleiotropic effects on ischemic myocardium and its cardioprotective effect primarily stems from reduction of ischemia reperfusion injury. The literature on acute IV beta-blocker (BB) therapy in STEMI patients before mechanical reperfusion is limited and reveals conflicting results. Hence there is no clear-cut guideline advocating routine use of early intravenous BB (EIVBB) therapy in all STEMI patients.

METOCARD-CNIC is the largest prospective randomized study in the era of mechanical reperfusion clearly showing infarct limiting potential of EIVBB in STE AWMI patients resulting in improved LVEF as compared to control arm. This study forms a landmark because it attempts in a better way in demystifying the fact that EIVBB in STEMI patients is harmful and takes an extra step in proving significant 20% reduction in infarct size above that achieved with mechanical reperfusion with a trend towards reduction in adverse clinical events.

In the era when fibrinolytic therapy was not widely used, trials on IV beta-blockers had shown mixed results. Goteborg metoprolol trial revealed a 17% reduction in infarct size and 36% reduction in mortality with IV metoprolol when it was administered within 7 h of symptom onset. MIAMI trial did show a statistically insignificant 13% reduction in mortality with IV metoprolol in acute MI patients administered within 12 h of symptom onset. ISIS-1 trial on 16,027 patients of suspected myocardial infarction had shown a 15% reduction with IV atenolol therapy. But a meta-regression analysis in the pre-reperfusion era had demonstrated no extra mortality benefit with IV beta-blockers.

In the fibrinolytic reperfusion era, two major trials failed to show any difference in mortality, LVEF or infarct size with EIVBB therapy in STEMI patients reperfused with alteplase. Both GUSTO and COMMIT trials had shown increased rates of CHF and cardiogenic shock with EIVBB in STEMI patients. The COMMIT trial also had shown that EIVBB therapy in STEMI patients in Killip class III increased mortality hence nullifying the benefits like reduced reinfarction rates and ventricular fibrillation. Learning lessons from COMMIT trial, the use of EIVBB was restricted to class I and II patients in the present study.

In the mechanical reperfusion era, again results were mixed on EIVBB. Conflicting reports exist on cardioprotective effect of beta-blocker therapy and post PCI procedural enzyme release. CADILLAC investigators had shown that EIVBB improved 30-day mortality (1.5% vs 2.8%) and LVEF only in those patients who had not received prior beta blocker therapy (3.8% vs 1.3%). Valle et al showed that pre-primary PCI beta blocker use was associated with reduced arrhythmia and mortality without increased rates of cardiogenic shock and congestive cardiac failure.
Majority of the strategies attempting to improve cardioprotection like thrombectomy devices, distal embolization devices, glucose insulin potassium infusion, adenosine, endovascular cooling etc., have yielded equivocal results because of delayed time to reperfusion. In the present study mechanical reperfusion was established within 6 h of symptom onset, hence ensuring reasonable reperfusion window period.

In our opinion this is an important landmark study showing potential cardioprotective benefit of EIVBB in STEMI patients undergoing primary PCI within 6 h and having no contraindications for BB and it may play a vital role in the future in shifting the guideline for IV beta-blocker from class IIa to class I, especially in acute anterior wall MI with sympathetic stimulation and Killip class ≤ II. The 20% greater reduction in infarct size above that was achieved by mechanical reperfusion offers great hope. Hence EIVBB can be regarded as an asset with certainty for cardioprotection. Well-designed RCTs aiming to achieve improvement in hard clinical outcomes with EIVBB in STEMI patients is the need of the hour.

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Dario Sillano, Chiara Resmini, Emanuele Meliga, Giacomo Bocuzzi, Andrea Zuffi, Emanuele Barbato, Julian Gunn, Matthew Price, Fiorenzo Gaita, Imad Sheiban, Retrospective multicenter observational study of the interventional management of coronary disease in the very elderly: The NINETY. Catheter Cardiovasc Interv 82 (2013) 414–421.

OBJECTIVES: The aim of this observational, multicenter study was to describe the outcome of very elderly patients undergoing percutaneous coronary intervention (PCI).

BACKGROUND: There is a paucity of data among nonagenarians undergoing PCI.

METHODS: All consecutive patients 90 years of age or older undergoing PCI with stent implantation between April 2002 and June 2009 were included in the study. The primary endpoint was the long term rate of net adverse cardiac events (NACE), that is, death, myocardial infarction (MI), target lesion revascularization, and life threatening or major bleedings.

RESULTS: One hundred forty-six nonagenarians were divided in three groups according to clinical setting: 27 (group A) stable angina or silent ischemia, 85 (group B) unstable angina or non-ST elevation MI, and 34 (group C) with ST elevation MI (STEMI). At 30 days, the incidence of NACE was significantly lower in patients in Group A vs. B or C (0% vs. 17.3% vs. 31.2%, p = 0.006), and the frequency of definite stent thrombosis was higher in Group C vs. A or B (9.4% vs. 0% vs. 0%, p = 0.007), respectively. Up to a median follow up of 24 months, NACE rate was 33.3% in group A, 49.3% in group B, and 50% in group C (p = 0.32). There were no significant differences between groups in the individual components of the primary endpoint.

CONCLUSIONS: PCI in nonagenarians is safe and feasible with acceptable major bleeding rates. However, long term results show high mortality rates particularly in the STEMI group.

1. Perspective

1.1. NINETY – age not a PENALTY

With an increase in life expectancy, there is a significant increase in the elderly and very elderly population. This trend is expected to increase further in the coming years. CAD is an important cause of mortality in the very elderly age group. Elderly age is an independent risk factor for short term mortality in CAD, especially STEMI patients. Atypical symptoms, late presentation, lack of timely medical advice and transportation to hospitals with critical care units put this population at high risk with increased complications and adverse effects. Elderly and very elderly patients are usually excluded from the major trials of revascularization and optimal treatment strategies and outcomes in this subgroup are less clear.

Thrombolytic therapy was thought to be associated with increased bleeding risks in elderly, especially intracranial bleeding, as compared to primary PCI, but major trials testing this hypothesis had failed to prove it. 1,2 In fact, registry data show that less than 50% of the elderly patients receive any form of revascularization therapy despite suggested mortality benefit. About 20–30% of these patients undergoing PCI...