Special ESC report

Hotline sessions of the 25th European Congress of Cardiology

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Of the 12 presentations at the two Hotline sessions of the 25th European Congress of Cardiology, held in Vienna, Austria, 30 August – 3 September 2003, six are summarized, since the other half of the presentations have been published recently (CHARM studies: *Lancet* 2003; 362:759–781, the EUROPA study: *Lancet* 2003;362:782–788 and the ESTEEM trial: *Lancet* 2003;362:789–797). The authors of this summary collected the information given during the presentations of the studies, as well as from press releases prepared by most speakers. This report only shows preliminary results.

During the first Hotline Session, studies on the medical treatment of heart failure were presented. Of the six presented studies, five have already been published.

Dr Christian Mueller from Basel, Switzerland presented the BASEL study. In this open single-centre study patients with acute dyspnoea presenting at the emergency room were randomized to be diagnosed and treated according to standard clinical practice or to standard clinical practice with an additional rapid BNP (Brain Natriuretic Peptide) analysis. Hypothetically, additional BNP analysis improves diagnostic speed and accuracy which may reduce admission time, treatment costs and potentially improves outcome. In this study BNP levels were always interpreted in conjunction with clinical information: a BNP level of <100 pg/ml almost certainly ruled out heart failure as the primary cause of dyspnoea, while a level of >500 pg/ml was strongly suggestive of heart failure as the principal cause of dyspnoea. In case of an intermediate BNP value clinical judgement prevailed. The baseline characteristics of the 452 study patients were well balanced, the mean age was 70 years, 50% had a history of coronary artery disease and 50% had known pulmonary disease. The two primary endpoints consisting of admission time and treatment costs were significantly reduced by additional rapid BNP analysis compared to traditional clinical assessment (10.6 days vs 13.7 days \(P=0.009\) and $5410 vs $7264 \(P=0.006\), respectively). The secondary endpoint of admission rate was significantly lower in the BNP group: 75% vs 85%, \(P=0.008\). The pre-defined 30-day mortality and re-admission rate did not differ significantly between both groups. This positive study shows the potential benefit of a rapid BNP analysis in triage in the emergency room, improving overall treatment delay and reducing costs. However, these results should be interpreted with caution because of the open study design. Finally, the cut-off values of BNP are somewhat arbitrarily chosen and the role of intermediate ‘grey-zone’ BNP values remains unclear.

The topics of the second Hotline Session were acute coronary syndromes and percutaneous coronary interventions. Of the six presented studies, one has already been published. Dr Arnoud W. J. van 't Hof from Zwolle, the Netherlands presented a randomized double-blind multicentre trial in patients presenting with acute ST-elevation myocardial infarction in the ambulance or in a referral hospital: the On-TIME trial. In a placebo controlled design pre-transportation initiated tirofiban treatment (early) was compared to cath-lab initiated tirofiban treatment (late) in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. The primary endpoint was TIMI-3 flow at initial coronary angiography. In total, 507 medium risk patients (mean age 62 years, 45% anterior myocardial infarction and 15% Killip 2) were randomized and received standard aspirin and heparin at presentation: 251 patients received pre-transportation tirofiban at a median of 59 min earlier than the 256 patients in whom tirofiban was initiated at the cath-lab. The total ischaemic time was 192 min in both groups. The initial pre-procedural TIMI-3 flow did not differ significantly between the early and late tirofiban group (19% vs 15% respectively, \(P=0.22\)). The combined incidence of thrombus or fresh occlusion at initial angiography was significantly less in the early treated group compared to the late treated group (60% vs 73%, respectively, \(P=0.03\)).
Retrospectively, the combination of initial TIMI 2+3 flow was significantly higher in the early treatment group (43% vs 34%, \( P=0.04 \)). The post-procedural success rate was 90% and did not differ between treatment groups. Clinical outcomes at 30 days were: death 2.2%, reinfarction 1.0%, stroke 0.2% and, unfortunately, were not broken down by treatment allocation. Although this is a negative trial and the clinical relevance of the secondary endpoint thrombus and fresh occlusion is unknown, a strikingly low 30-day rate of adverse outcome is reported. This supports the importance of very early treatment in acute ST-elevation myocardial infarction.

The GRACIA-2 study was presented by Dr Fernando Fernandez-Aviles from Valladolid, Spain. In 212 patients with acute ST-elevation myocardial infarction of less than 12 h of duration, primary angioplasty with stent placement and abciximab within 3 h of randomization was compared to TKN-mediated fibrinolysis followed by a complementary angioplasty within 3–12 h after symptom onset: so called ‘facilitated PCI’. Trials in the mid-eighties proved worse clinical outcome of fibrinolysis followed by early complementary angioplasty compared to fibrinolysis alone. Lack of benefit was believed to be due to a high peri-procedural reinfarction rate. The GRACIA-2 re-evaluates the feasibility of this combined strategy in the era of third generation fibrinolitics and improved mechanical revascularization techniques compared to a primary angioplasty strategy. The primary endpoints consisted of enzymatic infarct size, ST-segment resolution and left ventricular angiographic evolution at 6 weeks. The baseline characteristics were well balanced except for prior percutaneous coronary intervention, which tended to be more prevalent in the primary percutaneous coronary intervention group. Per protocol abciximab was used more often in the primary percutaneous coronary intervention group (87% vs 23%, respectively \( P=0.001 \)). By design mean time from randomization to catheterization was significantly lower in the primary percutaneous coronary intervention group as compared to the facilitated percutaneous coronary intervention group (1.1±3.7 vs 5.9±3.7 h). Infarct size defined as the area under the curve of cTnT and CK-MB mass and left ventricular evolution at 6 weeks did not differ between groups. At 6 h the proportion of patients with complete (>70%) ST-segment resolution was significantly higher in the facilitated percutaneous coronary intervention group (61% vs 43%, respectively \( P=0.03 \)). The difference of the combined clinical endpoint at 6 weeks of death, reinfarction and ischaemia-driven revascularization was non-significant; primary percutaneous coronary intervention 12% (death 6%) versus facilitated percutaneous coronary intervention 9% (death 3%). Major bleeding complications were reported in 2% to 3% and did not differ between the two groups. In the facilitated percutaneous coronary intervention arm one intracranial haemorrhage was reported. In this relatively small pilot study a combined approach of fibrinolysis and a complementary angioplasty performed in a timely fashion seems feasible and not inferior to primary angioplasty. This is the first study in primary percutaneous coronary intervention to use ST-resolution as a primary endpoint. Because the clinical significance of late ST-resolution is not completely understood, long-term clinical follow-up is awaited. Large randomized trials are necessary to confirm effectiveness and safety of this combined early pharmacological late mechanical approach compared to primary percutaneous coronary intervention.

Dr Philippe G. Steg from Paris, France presented the DECOPI trial. This multicentre study randomized 212 patients with a recent (2 to 15 days) first Q-wave myocardial infarction to either an angioplasty of the infarct artery or medical treatment. All patients had an occluded infarct related artery in the absence of spontaneous or low-level ischaemia. The study was stopped prematurely because of slow enrolment. Of the initially planned 720 patients, only 212 were included. Patients were randomized at a median of 6 days after the qualifying myocardial infarction. Of all included patients 12% received fibrinolysis at admission and the mean baseline left ventricular ejection fraction was 37%. In patients randomized to angioplasty post-procedural TIMI-3 flow was 82%, stents were used in 80% and a post-procedural creatine-kinase rise exceeding the upper level of normal occurred in 16.7%. At a median follow-up of 34 months the incidence of the combined primary endpoint of cardiac death, non-fatal myocardial infarction and non-fatal ventricular tachycardia/ventricular fibrillation was low and did not differ significantly between the angioplasty group and the medical group (7.3% vs 8.7%, \( P=0.64 \)). The incidence of arrhythmic events was very low and less than 1% in both groups. The secondary endpoint of infarct related artery patency at 6-month angiography was significantly higher in angioplasty group compared to the medical group, 82.7% vs 39.7%, \( P=0.0001 \). Six-month angiographic left ventricular ejection fraction was also significantly higher in the angioplasty group, 43.5% vs 40.0%, \( P=0.025 \). In the angioplasty group the restenosis rate at 6 months was as high as 47.1% with a re-occlusion rate of 12.6%. In the medical group spontaneous recanalization occurred in 32%. The predefined cost analysis was significantly in favour of the medical group (\( \epsilon 12,468 vs \epsilon 13,484 \ P=0.0001 \)). In this prematurely stopped underpowered trial no significant differences were found at the 6-month clinical primary endpoint. Nevertheless, important long-term prognostic risk factors for mortality, such as 6-month infarct artery patency and left ventricular ejection fraction, were significantly higher in the angioplasty group. Long-term results of this trial are eagerly awaited.

Dr Joachim Schofer from Hamburg, Germany presented a sub-study of the multicentre randomized trial E-SIRIUS (sirolimus coated stent versus bare-metal stent in the treatment of patients with de novo native coronary artery lesions). In this sub-study direct stenting was compared with predilatation in patients with single coronary lesions at relatively high risk of restenosis (40% in-stent restenosis at 8 month follow-up in the bare-metal stent control group). QCA data pre- and post-intervention were obtained, as well as 8 months after the initial procedure. For 9 months major adverse cardiac events (MACE), defined as death, myocardial infarction
and target vessel revascularization were collected. In this sub-study of the 352 E-SIRIUS patients 26% (n=92) received direct stenting and 74% (n=260) received predilatation at the operator's discretion. As a consequence of the operator's selection, directly stented lesions on average had a significantly lower pre-procedural diameter stenosis than pre-dilatated lesions. No significant differences in the restenosis rates or MACE rates between direct stenting and predilatation were found. When the comparison between direct stenting and predilatation is restricted to patients who received the sirolimus stent, there was a non-significant trend towards lower rates of restenosis and MACE with direct stenting as compared to the predilatation (respectively 2.4% vs 7.2% for restenosis and 4.4% vs 9.2% for MACE). These retrospective findings in patients with a de novo coronary lesion with angiographic high risk features for restenosis warrant a randomized comparison to elucidate the efficacy and safety of direct stenting with a sirolimus coated stent.

The DELIVER-II study was presented by Dr Eberhard Grube from Siegburg, Germany. The aim of this prospective uncontrolled multicentre trial was to evaluate the paclitaxel eluting coronary stent system in the treatment of lesions with high risk of restenosis at 6 months. DELIVER-II is the largest trial with drug eluting stents so far. The population included chronic total or subtotal occlusions, small vessels, bifurcation lesions, long lesions, multivessel disease and restenotic lesions. As no control group was included, efficacy of the paclitaxel eluting stent could not be assessed. Of the 1533 included patients the target lesion revascularization rate at 6 months was 10.5%, the hierarchical MACE rate (death, Q-wave myocardial infarction, non-Q-wave myocardial infarction and target lesion revascularization rate) was 15.7%. Multivariate analysis identified the following variables to be associated with high risk for 6 month target lesion revascularization: post-procedural minimum lumen diameter, LAD as target vessel, number of diseased vessels, restenotic lesion and total length of all stents. This large multicentre uncontrolled trial identifies independent risk factors for target lesion revascularization after paclitaxel eluting stent placement in a broad spectrum of coronary lesions. Remarkably, the independent risk factors for target lesion revascularization in paclitaxel eluting stents are identical to the risk factors for the uncoated stents. Unfortunately, this trial was performed with a stent withdrawn from the market because of its limited anti-proliferative efficacy.