Hotline Sessions of the 29th European Congress of Cardiology

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The 29th Congress of the European Society of Cardiology was held from 1 September to 5 September 2007 in Vienna, Austria. During three Hotline sessions, the preliminary results of 15 studies were presented. One trial has been published recently (ADVANCE, Lancet 2007;370:829–840). The results in this overview were collected from the presentations of the speakers, as well as from press handouts.

During the first Hotline Session, several issues were addressed. The first session started with the results of the 3CPO study (Efficacy of non-invasive ventilation in patients with acute Cardiogenic Pulmonary Oedema), presented by David Newby from Edinburgh, UK. This multicentre randomized controlled trial of the early management of patients with acute cardiogenic pulmonary oedema compared continuous positive airway pressure (CPAP) ventilation and non-invasive intermittent positive pressure ventilation (NIPPV) with standard oxygen therapy. In total, 1069 patients were recruited (mean age 78 years, 43% male), CPAP (n = 346), 10 ± 4 cm H2O) or NIPPV (n = 356, 14 ± 5/7 ± 2 cm H2O). At entry, patients were tachycardic (HR 113 ± 22/min), tachypneic (respiration 32 ± 7/min), acidotic (pH 7.22 ± 0.09), and hypoxic (O2 saturation 90 ± 8%). In comparison to standard oxygen therapy non-invasive ventilation was associated with greater improvement in tachycardia (102 ± 23 vs. 96 ± 22 min⁻¹, P < 0.001), tachypnea (26 ± 6 vs. 25 ± 6, P = 0.023), and acidosis (pH 7.30 ± 0.08 vs. 7.32 ± 0.08, P < 0.001) at 1 h. There was no difference between the two treatment modalities. The 7-day and 30-day mortality was similar for standard oxygen therapy and non-invasive ventilation [9.8 vs. 9.5% (P = 0.87) and 16.6 vs. 15.6% (P = 0.69) respectively]. The combined endpoint of 7-day death or intubation rate was similar for both forms of non-invasive ventilation CPAP/NIPPV (11.7 vs. 11.1%, P = 0.81). Thus, in patients with acute cardiogenic pulmonary oedema non-invasive ventilation produces a more rapid resolution of metabolic abnormalities and respiratory distress with both CPAP an NIPPV appearing to be equally efficacious and safe. However, non-invasive ventilation has no major effect on 7-day or 30-day mortality over standard oxygen therapy.

John McMurray from Glasgow, UK presented the ALOFT (Aliskiren Observation of heart Failure Treatment) trial. ALOFT tested the safety and efficacy of adding a direct renin inhibitor (Aliskiren 150 mg once daily) in patients (n = 302) with chronic heart failure already treated with an ACE inhibitor (or angiotensin receptor blocker) and β-blocker. Inclusion criteria were stable NYHA classes II–IV heart failure ≥1 month and past or current diagnosis of hypertension. Aliskiren inhibited plasma renin activity (−0.97 vs. −5.71 ng/mL/h, P < 0.0001) and significantly reduced the BNP levels (−12.2 vs. −61 pg/mL, P = 0.0160) over placebo. There were no difference between the pre-specified safety assessments in Aliskiren and placebo [renal dysfunction (1.9 vs. 1.4%), symptomatic hypotension (3.2 vs. 1.4%), or hyperkalemia (6.4 vs. 4.8%)]. Aliskiren effectively inhibited plasma renin activity, even though most patients were treated with a β-blocker. Adding Aliskerin in patients also treated with an ACE inhibitor (or angiotensin receptor blocker) appeared to be well tolerated. The potential therapeutic role of Aliskiren as alternative or ‘add-on’ therapy to an ACE inhibitor (or angiotensin receptor blocker) in chronic heart failure is worth further investigation.

A comparison of the EUROASPIRE I, II, and III surveys was given by David A. Wood from London, UK. The three EUROASPIRE surveys of coronary patients have been conducted over 12 years in 8 countries. A total of 8547 patients with coronary artery disease have been interviewed and examined over this period. Time trends in the management of lifestyle, other risk factors such as blood pressure, lipids and diabetes, and drugs in the prevention of cardiovascular disease are described. The three surveys show that lifestyle management is a growing cause of concern. The prevalence of
of smoking has not been changed over the three surveys and has in fact increased among younger people (under 50 years) and women. Rates of obesity rose from 25 to 38% between the first and third surveys; rates of central obesity increased from 42 to 55% over the same period. The prevalence of diabetes increased from 17 to 28%. Blood pressure management remains unchanged (41% in the first survey, to 39% in the third), despite a substantial increase in the use of anti-hypertensive medications. Lipid management shows enormous improvement, almost entirely due to the widespread use of statins. The use of cardioprotective medications has increased across all classes with the exception of calcium channel blockers, and the greatest increase is seen for statins (18% in the first survey, to 87% in the third). It is clear from these time trends that drug therapies are simple not sufficient and need to be combined with professional lifestyle and risk factor intervention. These data illustrate the pressing need for professional multidisciplinary ambulatory preventive programmes which should be available for all coronary patients.

Giuseppe Boriani from Bologna, Italy presented SEARCH-MI (Survey to Evaluate Arrhythmia Rate in so-Called High-risk Myocardial Infarction patients). SEARCH-MI is a multicentre registry created in 2002 to prospectively evaluate the arrhythmic rate and ICD interventions in post-infarction patients receiving a prophylactic ICD according to current guidelines. This patient cohort was compared to patients receiving an ICD in the MADIT II trial. The presented data were derived from an interim analysis on 556 patients with a follow-up of more than 70 days. The patients (mean age 66 years) were treated with various types of ICDs (single-chamber in 50%, dual-chamber in 25%, and biventricular in 25%). It is noteworthy that a relevant proportion of enrolled patients (25%) received a device for cardiac resynchronization therapy, in accordance with the scientific contributions of COMPANION and CARE-HF trials. The mean left ventricular ejection fraction was 26 ± 6% (23 ± 5% in MADIT II), and NYHA class distribution was NYHA I in 9%, II in 46%, III in 43%, and IV in 2% indicating more severe symptoms in comparison with MADIT II (NYHA class I in 35%, II in 35%, III in 25%, and IV in 5%, respectively). The results at a mean follow up of 17 months showed that, overall, the incidence of first appropriate ICD therapy was 20%, similar to MADIT II. In detail, 18 and 26% of patients at 1 and 2 years, respectively, received at least an appropriate treatment for ventricular tachyarrhythmia (17 and 27%, respectively, in MADIT II study). Moreover, overall mortality in SEARCH-MI was also similar to MADIT II (7 and 14% of patients at 1 and 2 years in SEARCH-MI, 9 and 16%, respectively, in MADIT II study). Since appropriate shocks and overall mortality observed in SEARCH-MI were comparable with the MADIT II trial, it appears that the benefits of ICD therapy in high-risk patients with a previous myocardial infarction can be replicated in ‘real world’ routine clinical practice.

In the second Hotline Session, trials on coronary and peripheral artery disease were presented. The session started with the results of the RIO trial [Reopro and peripheral arterial intervention to improve clinical Outcome in patients with peripheral arterial disease (PAD)] presented by Iris Baumgartner from Berne, Switzerland. This randomized, double-blind, placebo controlled, multicentre trial evaluate the short- and mid-term safety and efficacy of adjunctive abciximab (bolus 0.25 mg/kg followed by a maintenance infusion of 0.125 μg/kg/min for 12 h) in patients undergoing endovascular revascularization of chronic (>6 weeks) long-segment (>5 cm) femoro-popliteal occlusions. The study randomized 423 patients pretreated with aspirin, clopidogrel, and heparin. The primary endpoint (composite of death, amputation, re-intervention, and target vessel re-occlusion) at 30 days was similar (abciximab 5.1% vs. placebo 5.6%). Intraprocedural peripheral embolism and target vessel occlusion at 6 months was significantly lower in the abciximab group (6.1 vs. 12.3%, P = 0.02 and 22 vs. 39%, P < 0.001, respectively). However, there was a five-fold increase in severe access site bleedings in the abciximab group (5.1 vs. 1.0%, P = 0.020). RIO failed to demonstrate superior of abciximab over placebo to reduce the composite of death, amputation, re-intervention, and target vessel re-occlusion at 30 days and was associated with a significant increase in access site bleeding. Therefore, abciximab seems not to be indicated in elective peripheral interventions.

The next two studies presented the results of studies concerning reperfusion therapy of ST-elevation myocardial infarction. Stephen Ellis from Cleveland, US presented the results of FINESSE (Facilitated INtervention with Enhanced reperfusion Speed to Stop Events) study. This multicentre, randomized, double-blind placebo-controlled study enrolled 2452 patients from 20 countries presenting with acute ST-elevation myocardial infarction (or new left bundle branch block) within 6 h pain onset who had been referred for primary PCI into three groups. The first two groups received two different facilitated PCI treatments regimen: early administration of reduced-dose reteplase and abciximab combination therapy (n = 828) or abciximab alone (n = 818). The third group received primary PCI with abciximab alone administered just prior to PCI in the cath lab (n = 806). Results at 90 days showed that there were no statistically significant differences in the primary endpoint (composite of all cause mortality, rehospitalization for heart failure, revascularized ventricular fibrillation occurring >48 h after randomization, and cardiogenic shock) between the three arms (10.7 vs. 10.5 vs. 9.8%, P = n.s.). There was a significantly higher TIMI 3 flow pre-PCI in the combination therapy arm (36% vs. 15% abciximab facilitated PCI vs. 13% primary PCI). TIMI major bleeding was significantly greatest in the reteplase/abciximab facilitated PCI group followed by the abciximab facilitated PCI group and by the primary PCI with lab abciximab group (4.8 vs. 4.1 vs. 2.6%, respectively). FINESSE showed that neither facilitated PCI strategy tested provided clinical benefit compared with primary PCI with in cath lab abciximab. Reteplase/abciximab facilitation and to a lesser extent abciximab facilitation increased bleeding compared to the cath lab administration of abciximab.

CARESS in AMI (Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction) was presented by Carlo Di Mario from London, UK. This trial was conducted in three European countries (Poland, Italy, and France) involving various networks of community hospitals without primary PCI facilities. In the CARESS in AMI study, 600 patient with acute ST-elevation myocardial infarction ≤ 12 h received combined half-dose reteplase and abciximab and were randomized at the time of admission to immediate transfer for PCI or to transfer for PCI only if they experienced persistent ST-elevation after 90 min of treatment, chest pain, or haemodynamic compromise. The interval
between administration of the thrombolytic drug and angioplasty was 136 min in the immediate transfer group. In the conservative group, rescue PCI was needed in 36% of patients. Results at 30 days showed that 4.1% of the immediate PCI group experienced the combined endpoint of death, re-myocardial infarction, and refractory ischaemia, compared to 11.1% in the conservative group (P = 0.001). Additional findings showed no significant differences in stroke or bleedings requiring transfusion. This trial indicates that immediate transfer of high-risk ST-elevation myocardial infarction patients treated with a combination of half-dose reteplase and abciximab to a PCI centre is highly effective. However, the optimal time of transport for ancillary PCI is still under debate.

Eva Swahn from Linköping, Sweden presented the results of the OASIS-5 women’s substudy. In this study, 184 women with non-ST-elevation acute coronary syndrome were randomised to either an early routine coronary angiography (and, if appropriate, coronary revascularization within 7 days) or to a selective invasive strategy with ischaemia guided coronary angiography. The primary outcome of death/myocardial infarction/stroke between the routine invasive and selective invasive group was not significantly different (21 vs. 15.4%). At 2 years follow-up, eight patients in the routine invasive group had died compared to two patients in the selective invasive group (8.8 vs. 2.2%, HR 4.65, 95% CI 0.97–22.2). There was no significant difference in either of the endpoints myocardial infarction (12.9 vs. 13.3%) or stroke (2.3 vs. 4.4%). Major bleedings were significantly more frequent in the routine invasive group (10.0 vs. 2.2%, HR 6.9, 95% CI 1.48–32.1). In this study, women with non-ST-elevation acute coronary syndrome did not benefit from a routine invasive strategy. However, it should be noted that a much larger sample size of patients was planned. Accordingly, results should be interpreted with caution, particularly with respect to the greater mortality in the routine invasive group. The results taken together with the trend from previous larger trials (FRISC II, RITA 3, TACTICS) suggests that the results from men do not necessarily apply to women and that large randomized trials in women are needed to determine that the optimal strategy in non-ST-elevation acute coronary syndrome.

Petr Widimsky from Prague, Czech Republic presented the PRAGUE-8 study. This multicentre study randomized 1028 patients undergoing elective coronary angiography to group A (‘nonselective’—clopidogrel 600 mg > 6 h before elective coronary angiography; n = 513) or group B (‘selective’—clopidogrel 600 mg in the cath lab after coronary angiography only to patients undergoing subsequent PCI; n = 515). The combined endpoint (death/periprocedural myocardial infarction/stroke or transient ischaemic attack/reintervention within 7 days) occurred in 0.8% in both groups. The secondary endpoint periprocedural troponin elevation (> 3 x ULN) was detected in 2.7% in group A vs. 3.0% in group B (P = n.s.). Bleeding complications occurred in 3.5% of group A patients vs. 1.2% in group B (P = 0.02). When only the patients who underwent PCI were analysed the primary endpoint occurred in 1.3% in group A vs. 2.2% in group B (P = n.s.). Bleeding complications occurred in 7.2% of group A patients vs. 0.7% in group B (P = 0.006). Periprocedural troponin elevation was detected in 8.6% in group A vs. 11.1% in group B (P = n.s.). Routine clopidogrel pretreatment before elective coronary angiography in stable coronary artery disease increases the risk of bleeding complications, whereas there is no clear benefit on periprocedural infarction. This study shows that routine clopidogrel pretreatment is not justified and should be given only to patients with known coronary anatomy who undergo PCI. This can be done safely in the cath lab between the two procedures.

The topics of the third Hotline Session were diverse. The session was opened by Curt Diehm from Karlsbad, Germany, who presented getABI (German Epidemiological Trial on Ankle Brachial Index). The aim of getABI, a prospective observational epidemiological study, was to quantify the excess cardiovascular risk borne by symptomatic and asymptomatic PAD patients compared with those without PAD. A total of 6880 unselected patients from primary care centres were evaluated by an ankle brachial index for the presence of PAD (baseline mean age 72.5 years, 58% female, 46% had formerly smoked or were smokers, 74% hypertension, 24% diabetes, 52% lipid disorders). Of all patients, 12.1% had asymptomatic PAD and 8.7% had symptomatic PAD. The survival data at 5 years based on the status of 97.4% of the initial patient cohort were reported. All-cause mortality was 24.1% in patients with symptomatic PAD, 19.2% with asymptomatic PAD, and 9.5% in patients without PAD. PAD had the best ability to predict future death, stroke, or myocardial infarction. There was a strong association between lower ankle brachial index categories and risk of premature death. Thus, symptomatic as well as asymptomatic PAD patients carry a substantially increased risk for all-cause mortality, compared with individuals without PAD. The data of getABI strongly support the rationale for screening for high-risk PAD patients by determination of the ankle brachial index in the primary care setting.

Francesco Burzotta from Rome, Italy presented the results of OPTIMIST (the Outcome of PCI for stent-Thrombosis Multi-centre Study). This multicentre registry conducted by 11 hospitals located in the urban area of Rome, Italy. During a period of 2 years, all patients with stent thrombosis who were admitted to participating hospitals and treated by PCI were enrolled. Stent thrombosis accounted for 3.6% of the emergency PCI performed in patients with acute myocardial infarction. Thrombosis of drug-eluting stents happened more often after 30 days of implantation, or after 15 days of antiplatelet drug therapy withdrawal than thrombosis of bare-metal stents. However, the type of data collected in the OPTIMIST study did not allow for the clarification of whether risk of thrombosis is higher after drug-eluting stent or bare-metal stent implantation. The procedural and clinical outcomes were not influenced by the type of previously implanted stent. The 6-month clinical outcome of stent thrombosis showed a 16% mortality rate and a 29% rate of major adverse coronary or cerebral events. Further analysis showed that very late thrombosis (1 year after implantation) was associated with higher mortality rates (OR 10.0, 95% CI 1.2–85.7) compared with early thrombosis. Also, when the attempted PCI result was not optimal and when a further stent was implanted during the PCI, the mortality rate was significantly higher (OR 5.4, 95% CI 1.3–22.8). The OPTIMIST study also evaluated the efficacy of thrombectomy (n = 27). Despite sicker patients, no excess of adverse events was observed. Patients without unstable conditions treated by thrombectomy had a
five-fold improved rate of optimal coronary flow restoration. These results show that stent thrombosis is not a benign disease with hospital mortality of 12% and 6-month death of 16%. Emergency PCI in this setting is still associated with unsatisfactory outcome. Finally, the mechanical thrombectomy in PCI for stent thrombosis is feasible but should be reserved to patients without cardiogenic shock.

Philippe Gabriel Steg from Paris, France presented the stent mortality data from the GRACE registry. This analysis used the database from the Global Registry of Acute Coronary syndromes (GRACE), collected in 94 hospitals in 14 countries to compare the survival up to 2 years of patients treated with bare-metal stent (BMS) only or receiving at least one drug-eluting stent (DES). The 6447 patients in the study had at least one stent. Survival appeared similar in the 6-months following discharge (DES 2.3% vs. BMS only 2.2%), but thereafter overall mortality was higher in patients treated with DES (4.6 vs. 2.8%, $P=0.10$). This difference was entirely related to patients treated for ST-elevation myocardial infarction (8.6 vs. 1.6%, $P<0.001$) and was associated with an increased risk of late re-infarction (5.4 vs. 2.9%, $P=0.046$), suggesting that it may indeed be related to late stent thrombosis. Within GRACE patients receiving DES have a lower risk of in-hospital death, but late outcomes are worse, related to ST-elevation myocardial infarction. This registry suggest that DES should be used with caution in patients with ST-elevation myocardial infarction, at least until more evidence is accumulated of their long-term safety from large studies with long-term follow-up.

The WENBIT (Western Norway B-vitamin intervention trial) was presented by Marta Ebbing from Bergen, Norway. From 1999 to 2004, a total of 3090 patients (median age 62 years, 21% women) undergoing coronary angiography for stable angina pectoris (84%), acute coronary syndrome (15%), or aortic valve stenosis (1%) at Bergen or Stavanger University hospitals in Norway were included. A two-by-two factorial design was used. Participants were assigned to four groups receiving daily oral treatment with (i) folic acid (0.8 mg)/vitamin B12 (0.4 mg)/vitamin B6 (40 mg), (ii) folic acid/vitamin B12, (iii) vitamin B6 alone, or (iv) placebo. There were no significant differences in baseline characteristics between the four groups. Almost 60% of participants had 2- or 3-vessel disease. Homocysteine levels were lowered by 28% in groups receiving folic acid/vitamin B12. During a median follow-up of 38 months, 422 (13.7%) of patients experienced an event of the composite primary endpoint (all cause death, AMI, unstable angina pectoris, or stroke). There were no significant differences in outcome when comparing groups receiving homocysteine-lowering folic acid or not, or comparing groups receiving vitamin B6 or not. WENBIT confirms that B-vitamin supplementation is not justified as secondary prevention for coronary artery disease.

The last study of this year’s Hotline Sessions was the PROSPECT (PRedictors Of reSPonsE to Cardiac resynchronisation Therapy) trial presented by Stefano Ghio from Pavia, Italy. This multicentre, observational study of 426 heart failure patients with a classical indication for cardiac resynchronisation therapy (CRT) including a QRS > 130 ms aims to identify echocardiographic measures of dyssynchrony (standard echo and tissue Doppler Imaging measurements) and evaluate their ability to predict response to CRT. The patient characteristics in PROSPECT were similar to classical CRT recipients and clinical and echocardiographic response to CRT were in agreement with previous CRT trials. The yield for echo measures varied between 50 and 92%, the inter core lab variability was relatively great (6.5–72.1%) in view of the expertise of the included centres indicating the need for further simplification of methodology. Presence of single measures of dyssynchrony was linked to 11–13% additional clinical response rate to CRT and 13–23% additional response for reverse remodelling compared absence of measures of dyssynchrony. The results of this study indicate that no single echocardiographic measure of dyssynchrony was reliable and ready for widespread use in the selection of candidates for CRT.

Conflict of interest: none declared.