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Interventional cardiology highlights: ESC Vienna 2007

Stefaan Van de Walle*, MD; Christan Roguelov, MD; Andrea Zuffi, MD; Eric Eeckhout, MD, PhD

Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

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Historical Vienna was the scene of this year's annual congress of the European Society of Cardiology and several important issues in interventional cardiology were addressed.

First, one year after the annual congress in Barcelona, new and follow-up data on drug eluting stent (DES) safety were reported. The nation-wide SCAAR registry compiles data on all percutaneous coronary interventions in Sweden (> 37,000 DES implanted) and at this meeting the 4-year clinical outcomes were presented. Contrary to the 3-year clinical outcomes, a difference in mortality and myocardial infarction favouring bare metal stents (BMS) was no longer observed. Patrick Serruys tried to explain these puzzling findings mentioning the heterogeneity of participating centres volume load and looking at the separate landmark analysis suggested that DES were now perhaps better implanted. The Rotterdam and Berne groups presented the 4-year follow up of their DES registry. They kept a permanent track on angiographic stent thrombosis in their patients who were 100% treated with DES (8,146 patients from 2002-2005). At four years the cumulative incidence of angiographic stent thrombosis was 3.3% and the curves showed a continuously rising slope with an annual risk of 0.6%. Interestingly 27% of stent thrombosis occurred on dual antiplatelet therapy. Further follow-up of this patient group is thus warranted. Patrick Serruys also looked at the patient cohort of the Arterial Revascularisation Therapies Study part II (ARTS II) and applied the ARC definitions of stent thrombosis to these multivessel patients treated with sirolimus eluting stents (Cypher®). Stent thrombosis (definite, probable or possible) was 6.4% at three years. The incidence of definite stent thrombosis was 3.3% at three years. The rates of overall death and MI at three years were reassuring when one compared the rates of death (3.0% vs. 4.0%) and MI (3.6% vs. 6.8%) in ARTS-II and ARTS-I PCI, respectively, despite the higher baseline risk profile in ARTS-II. Out of the 127 patients who had a major adverse cardiac event (ARC definitions), 21 had a definite, 11 a probable and seven a possible thrombosis (total 39 or 30.7% of adverse events). The randomised controlled trials of DES versus BMS continue to deny an increased mortality or infarction rate with DES, as also confirmed by the five year follow up of the TAXUS-II data presented by Sigmund Silber. In specific patient groups, a BMS may however still be first choice. Renu Virmani warned against stent malapposition and possible stent thrombosis when DES were implanted in thrombotic lesions, such as during primary PCI. This concept could theoretically explain some of the findings of the GRACE-registry (Global Registry of Acute Coronary Syndromes), presented during ESC, that found an increased mortality associated with DES implantation in STEMI patients (n=569) between six months and two years (8.6% versus 1.6%, p<0.001). Mortality in NSTEMI / unstable angina patients was not different. As William Wijns pointed out this registry is of course prone to confounding factors and the numbers are relatively small. Also these findings contradicted the favourable follow-up of the PASSION trial which randomised STEMI patients to a BMS or DES (Taxus®). In this trial, a total of 619 patients were studied. At two years there was no difference in the primary endpoint of death, myocardial infarction and the need for re-intervention (15.4% BMS – 11.1% DES, p=0.12). At the congress, a global consensus was adapted that presently DES should not routinely be implanted during primary PCI. DES use in general should be dependent on patient and lesion profile contemplating risk of restenosis and possible patient adherence problems with double antiplatelet therapy.

* *Corresponding author: Centre Hospitalier Universitaire Vaudois, 1011 Lausanne, Switzerland*
E-mail: Stefaan.Van-de-Walle@chuv.ch

Exploring treatment options in left main disease, Beatriz Vaquerizo reported the promising results of the French TAXUS left main registry. In 291 patients treated at four centres with a provisional T-stenting technique, 0.7% in-hospital (predicted 6.4% according to the logistic EuroSCORE) and 5.2% cardiac mortality at two years was observed. The need for revascularisation at follow-up was only 7.9%. Another specific lesion subgroup is venous graft disease. The German cypher stent registry analysed the clinical event rates after treatment of stenotic vein grafts using sirolimus-eluting stents on the basis of a large patient registry. Patients treated for vein graft disease (n=344) were compared to patients treated for native vessel disease. During a 6-months follow-up period patients who had a lesion treated in a venous graft had a higher incidence of mortality and myocardial infarction than those patients who had a native vessel treated (3.5% versus 1.7% [p=0.014] and 5.4% versus 2.2% [p<0.001]). Target vessel revascularisation was more than twice as high (18.1% versus 8.2%, p<0.001). Even with active stents venous graft lesions still carry a worse prognosis and the best treatment strategy is not yet clear.

Several presentations also discussed practical issues in interventional cardiology. The Polish PRIMA II trial addressed the issue of immediate total percutaneous revascularisation versus staged intervention (treating the infarct-related artery only in the acute setting) in acute myocardial patients with multivessel disease. In PRIMA II a total of 208 patients were randomised, with at least one significant (>70%) stenosis of a non-infarct related artery amenable to PCI. Haemodynamic instability, renal insufficiency and left main stenosis were among the exclusion criteria. At one year, there was no difference in the primary endpoint (an absolute change in ejection fraction) between both groups but on the other hand, there was no difference in adverse events and a one stage approach appeared more cost-effective. Further clinical research is of course necessary to address this interesting topic. Another practical issue is the question of routing clopidogrel preloading before coronary angiography. The Czech PRAGUE-8 randomised 1,028 patients to routine clopidogrel preloading the day prior to angiography (non-selective group, n=513) or to a selective strategy, in which patients (n=515) received the drug on the table in the lab in case of angioplasty only. The hypothesis was that routine clopidogrel preloading would reduce ischaemic complications of angioplasty because of an optimal antiplatelet effect. However in this study there was no difference in the combined primary endpoint of death, myocardial infarction, stroke and reintervention within seven days between the two strategies: not in the total group and not in the subanalysis of the patients who underwent angioplasty (1.3% for the nonselective PCI patients, loaded with clopidogrel the day before, compared to 2.2% for the selective controls, p=ns). Routine preloading did however increase the number of bleeding complications (3.5% versus 1.2% in the total group, p=0.02 and 7.2% versus 0.7%, p=0.006 in the PCI subgroup). Therefore, routine clopidogrel administration prior to diagnostic angiography cannot be recommended. It increased the bleeding risk without any clear benefit on ischaemic periprocedural complications.

Looking at the problem of concomitant medication during primary angioplasty, Stephen Ellis reported the long awaited results of the FINESSE trial (Facilitated Intervention with Enhanced reperfusion Speed to Stop Events). FINESSE enrolled 2,452 patients with STEMI, symptom onset < 6 h before presentation and expected transfer to the cath lab within 1- 4 hours. Patients were randomised in a 1-1-1 design to three strategies, one group was treated with abciximab and half dose of reteplase before being transferred to the cath lab. The second group was treated with abciximab only, but also before transfer and in the third group abciximab was initiated in the cath lab. The primary endpoint was a combination of death, re-hospitalisation for congestive heart failure, resuscitated ventricular fibrillation occurring > 48 hours after randomisation or cardiogenic shock at 90 days. Despite increased pre-PCI TIMI 3 flow and > 70% ST-segment resolution at 60-90 min in the reteplase / early abciximab group, the primary endpoint did not differ in either group (10.7% with in lab abciximab, 10.5% with abciximab facilitated PCI and 9.8% with reteplase/abciximab facilitated PCI – p=0.55). Significant increases were however observed in TIMI major and minor bleeding in the reteplase/abciximab group compared to the other groups. Frans Van de Werf discussed the data and concluded that these results were compatible with the ASSENT-4 data but also commented on the lack of optimal antithrombotic therapy, such as clopidogrel preloading and the inclusion of STEMI patients up to six hours after symptom onset. A place for facilitated primary PCI (or rather a 'pharmaco-invasive' strategy) may still exist for selected high-risk patients with short duration between symptom onset and medical contact but expected prolonged transfer times to the cath lab. Dealing with the same subject, Dariusz Dudek reported the observational real world data from the Eurotransfer Registry on 1,650 patients from seven countries across Europe. STEMI patients who received abciximab early (median time before balloon 75.5 min) versus those who received it late (median time to balloon 20.5 minutes) had lower incidence of death in hospital (2.8 versus 5.9%, p=0.012) and death at 30 days (3.9 versus 7.5%, p=0.01). Although observational the benefit was maintained after adjustment using traditional covariates and propensity score. Finally, Carlo di Mario presented the data of the CARESS in AMI trial (Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction). This study randomised 600 high risk patients presenting with STEMI (<12 h from symptom onset) in a hospital without cath lab to either reteplase, abciximab and heparin followed by immediate transfer to a PCI centre (facilitated PCI group) or transfer only in case of persistent ST elevation, pain or haemodynamic compromise (rescue PCI group). The primary combined outcome was death, reinfarction and refractory ischaemia at 30 days. This primary endpoint was significantly lower in the facilitated PCI group compared to the rescue PCI group (4.1% versus 11.1%, p=0.001), largely driven by a difference in refractory ischaemia but with favourable trends for death and re-MI. Severe bleeding was low in both treatment groups, with less than 0.8% incidence of intracranial haemorrhage. In their conclusions the authors mentioned that the better outcome strikingly contrasted with results of other facilitated angioplasty trials, and suggested the deleterious effect on platelet aggregation of fibrinolysis was balanced by the simultaneous use of abciximab. They further stated that this trial confirmed and expanded the indication of the ESC guidelines to early PCI after lysis, suggesting that high risk STEMI patients should be immediately

transferred. The optimal time delay in which stable patients without indication for rescue PCI should undergo revascularisation remained however a point of debate.

Finally, very promising innovative technologies were presented at this years ESC. The results of the first-in-man use of a fully bioabsorbable everolimus eluting stent (polylactic acid polymer backbone) were presented (ABSORB). A total of 30 patients with single, *de novo* lesions were treated and followed up by angiography and intravascular ultrasound. Overall, a late luminal loss of 0.44±0.35 mm was reported, resulting in a binary restenosis rate of 11.5%. Only one acute adverse event occurred (partial stent dislodgment). Stent thrombosis was not observed and there was no need for repeat revascularisation. Luminal reduction was due to remodelling and recoil (mean 11.7%) and to discrete neointimal hyperplasia (mean 5.5%). These results have led to current modifications in the design of this stent to improve radial force. We may thus expect future reports on this promising emerging technology.

Another innovative technology is the use of a Endothelial Progenitor Cell (EPC) capture stent in the setting of acute myocardial infarction. Huay Cheem Tan reported retrospective data of 119 STEMI patients treated with the Genous™ stent compared to 116 patients treated with BMS (Liberté™). Classical MACE (death, non-fatal MI and target lesion revascularisation) at one and six months did not differ between the two groups. The TLR at six months was 2.5% in the EPC capture stent group (versus 4.3% in the BMS group, p=0.45) and no patients with late thrombosis were reported in this group, suggesting a good safety profile and warranting further research.

In short, plenty of very interesting topics in interventional cardiology have been addressed in Vienna and we have not even focused on the advances in peripheral and carotid intervention and percutaneous treatment of valvular disease. The next stop for the annual ESC congress will be Munich, where the theme in 2008 will be cardiovascular imaging.