Neutral results from first prasugrel-clopidogrel test in medically managed ACS

No significant difference in outcomes was found in acute coronary syndrome patients treated with prasugrel and clopidogrel but without revascularisation, according to results of the TRILOGY ACS study reported in yesterday’s Hot Line session. The phase III trial, published simultaneously in the New England Journal of Medicine, was the first comparison of outcomes in patients being medically managed.

“These medically managed patients are at higher risk for repeated cardiovascular-related events,” said study chairman Magnus Ohman at a press conference yesterday, “so optimising medical therapy for them is extremely important.”

Between June 2008 and September 2011 the Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY ACS) study randomised 7243 patients under the age of 75 to prasugrel (10 mg daily) or clopidogrel (75 mg daily).

All subjects were taking aspirin, and the prasugrel dose was reduced to 5 mg daily for those weighing less than 60 kg. In a secondary analysis 2083 patients aged 75 years or older and receiving a reduced dose of 5 mg prasugrel were compared with those receiving 75 mg clopidogrel. The study was performed at 966 sites in 52 countries.

Results showed that for patients aged under 75 years at a median follow-up of 17 months the primary endpoint (a composite of death from cardiovascular causes, MI or stroke) occurred in 13.9% of those treated with prasugrel compared to 16.5% of those treated with clopidogrel (HR 0.81; 95% CI 0.79-1.05; P=0.21). Similar results were observed for the overall patient population of 9326 patients, including the additional 2083 patients aged 75 years or older.

At 30 months, the key bleeding endpoints of non-CABG-related severe or life-threatening events (according to GUSTO criteria) and major bleeding (according to TIMI criteria) occurred with similar frequency among patients under the age of 75 years. No differences in non-benign neoplasms were observed.

“The overall neutral results are surprising and I don’t believe this trial will change the management of patients without revascularisation,” said Ohman, from Duke University Medical Center, Continued on page 2

Encouraging results from phase II trial in HF with preserved ejection fraction

The investigational drug LCZ696 reduced biomarker levels significantly more than the ARB valsartan in patients with heart failure with preserved ejection fraction (HF-PEF), according to the PARAMOUNT study. The phase II study, published simultaneously in the Lancet yesterday, found that LCZ696 also delivered reductions in left atrial size and improvements in NYHA.

“HT-PEF accounts for up to half of heart failure cases, and is associated with substantial morbidity and mortality,” said investigator Scott Solomon from Harvard Medical School, USA. “Yet this is a disorder for which no therapies have been shown to improve clinical outcomes.”

LCZ696 is the first in a new class of dual-action drugs called angiotensin receptor neprilysin inhibitors (ARNIs) which act simultaneously on two pathways involved in development of heart disease. It inhibits both the angiotensin receptor and neprilysin, the enzyme responsible for breakdown of natriuretic peptides.

In the Prospective comparison of ARNI with ARB on the Management Of heart failureUre with preserved ejection fraction (PARAMOUNT) study 301 patients with class II-IV NYHA and LVEF of 45% or higher and documented histories of HF were randomised 1:1 to LCZ696 (n= 149, up to 200 mg twice daily) or to valsartan (n= 152, up to 160 mg twice daily).

The primary study endpoint was change in NT-proBNP (a marker of wall stress and HF severity) assessed at 12 weeks, with an extension phase to 36 weeks. The study, which took place between November 2009 and January 2012, was undertaken in 65 centres and 13 countries.

Results at 12 weeks showed NT-proBNP continued on page 2
Spironolactone improves filling pressure in diastolic HF

Mineralocorticoid receptor blockade with spironolactone improved filling pressure and other measures of structural function in comparison to placebo in patients with diastolic heart failure (DHF), according to the Aldo-DHF study reported in yesterday’s Hot Line session. The phase IIb study found no effect on exercise capacity, NYHA class or quality of life.

Aldosterone has been implicated in the pathogenesis of DHF via aldosterone receptor-mediated myocardial fibrosis, hypertrophy and vascular stiffing. The Aldosterone Receptor Blockade in Diastolic Heart Failure (Aldo-DHF) aimed to test the efficacy and safety of spironolactone in patients with DHF.

The study prospectively randomised 422 patients with symptomatic DHF to receive spironolactone (target dose, 25 mg/day) or placebo for 12 months. The two co-primary endpoints were changes in diastolic function (filling pressure, assessed non-invasively) and changes in maximal exercise capacity.

Results showed a significant decline in filling pressure for patients receiving spironolactone compared to those receiving placebo (P<0.001 at six and 12 months). In contrast, spironolactone did not produce significant effects in exercise capacity at both six and 12 months compared to placebo.

There was also a significant reduction in left ventricular mass index in spironolactone patients at 12 months (P=0.009).

Spironolactone was found to be safe and not associated with severe adverse events.

Heart-healthy living related to gross domestic product

Fruits and vegetables, proteins and non-saturated fats are consumed more often by the wealthy, while poorer people consume more carbohydrates, according to findings reported yesterday. The Prospective Urban Rural Epidemiology (PURE) study found that the greater a country’s gross domestic product (GDP) then the higher the consumption of heart-healthy foods among people.

Commenting on the implications of the results, principal investigator Salim Yusuf from McMaster University, Canada, said: “Policies to prevent cardiovascular disease need to focus on different aspects of lifestyle among the rich versus the poor and between rich and poor countries. In particular, healthy foods need to become more affordable.”

A total of 154,000 people from 628 communities in 17 countries were recruited for the study, which analysed data such as medical history, lifestyle and ECGs. Results from the study found people in poorer countries such as Bangladesh and India derived far less energy from fat, and also consumed less fruit and vegetables. However, poor individuals or those from poorer countries were more active, chiefly because of higher energy expenditure in jobs, at home, and during transportation.

The difference in overall physical activity between the poorest and richest countries in comparison to placebo, Administration of aliskiren on top of standard therapy with renin-angiotensin-aldosterone system (RAAS) blockade in type 2 diabetes at high risk of cardiovascular and renal events is not recommended, according to preliminary trial results. The ALIDIKR study was designed to investigate whether use of aliskiren would improve outcomes by reducing fatal and non-fatal cardiovascular and renal events in type 2 diabetes at high risk of these complications.

Prospects dim for aliskiren in type 2 diabetes

Administration of aliskiren on top of standard therapy with renin-angiotensin-aldosterone system (RAAS) blockade in type 2 diabetes at high risk of cardiovascular and renal events is not recommended, according to preliminary trial results. The ALIDIKR study was designed to investigate whether use of aliskiren would improve outcomes by reducing fatal and non-fatal cardiovascular and renal events in type 2 diabetes at high risk of these complications.

The double-blind study was conducted in 8561 people randomised to aliskiren 300mg once daily on top of single RAAS blockade. The primary outcome measure was time to first event of cardiovascular death, resuscitated death, MI, stroke, unplanned hospitalisation for heart failure, onset of ESRD or doubling of baseline creatinine.

Results from the study showed that, at a median follow-up of 32 months, the primary composite endpoint had occurred in 767 patients (17.9%) assigned to aliskiren and 721 (16.8%) assigned to the placebo, HR for aliskiren vs placebo 1.08 (95% CI 0.98-1.20, p=0.34).

Stroke occurred in 146 (3.4%) of the aliskiren and 118 (2.7%) in placebo, HR 1.25 (95% CI 0.98-1.60, p=0.070).

FFR calculated from computed tomography ‘exciting’ prospect

The non-invasive assessment of fractional flow reserve by computed tomography (FFRct) provides a more accurate determination of which lesions require invasive evaluation than coronary CT angiography alone, according to findings reported in a Hot Line session yesterday.

The report was published simultaneously in the Journal of the American Medical Association.

The DeFacto (Determination of Fractional Flow Reserve by Anatomic Computer Tomographic Angiography) was designed to compare the ability of FFRct with CT alone to identify lesion-specific ischaemia and its physiologic significance.

In what is the first major trial of FFRct, 225 stable patients (n=406) with suspected CAD were enrolled at 17 centres in five countries and all underwent CT, invasive coronary angiography, invasive FFR and subsequent FFRct analysis. Just over half of patients (n=137) had an abnormal invasive FFR.

Results showed that FFRct had a 73% accuracy (95% CI 67.78%) compared with 64% for CT in the diagnosis of patients and vessels with ischaemia. However, this did not meet the trial’s pre-specified primary endpoint of >70% lower bound of 95% CI, which represented a 15% increase for FFRct over traditional methods.

The per-patient sensitivity and specificity of FFRct were higher than with CT alone using an AUC analysis (AUC 0.81 vs 0.68, P=0.0002).

The improvement in diagnostic performance was found greatest in patients with intermediate stenoses, with more than a two-fold increase in test sensitivity from 37% to 82% and no loss of specificity. In these patients, the AUC improved from 0.53 for CT alone to 0.80 for FFRct (P=0.0002).

The trial did not achieve its primary endpoint for diagnostic accuracy, yet principal investigator James Min from Cedars-Sinai Heart Institute in Los Angeles said FFRct could become an important tool for efficiently identifying high-grade stenoses and determining the hemodynamic significance of lesions.

“The results of the DeFacto trial clearly demonstrate that when added to coronary CT angiographic findings, FFRct provides essential physiologic information as to which specific arterial blockages truly restrict blood flow to the heart and heighten patient risk,” he said.

“This is an exciting step forward for cardiology that could significantly improve how we guide patients towards the most effective and efficient care.”

FFRct is currently performed remotely and takes around six hours to complete per patient. Min said the aim was to cut this completion time down to just two hours per patient.
What’s new in the 2012 heart failure guidelines

By Udo Sechtem
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THE NEW ESC GUIDELINES for the diagnosis and treatment of heart failure were released in May at the Heart Failure Congress 2012. The full text of the guideline is available online at http://www.escardio.org/guidelines and with paginated reference in the European Heart Journal (2012; 33: 1787-1847).

The principal changes introduced by John McMurray and his Task Force relate to:

1. An expansion of the indication for mineralocorticoid (aldosterone) receptor antagonists (MRA). MRA such as spironolactone or eplerenone are now recommended for all heart failure patients with persisting symptoms (NYHA Class II-IV) and an ejection fraction ≤35% and persisting symptoms (NYHA Class II-IV) despite optimal medical and device therapy and who have a LBBB QRS morphology, a QRS duration of ≥130 ms, and an ejection fraction ≤35% and if expected to survive ≥1 year, to reduce the risk of heart failure hospitalisation and the risk of premature death. In contrast, in patients who do not have a LBBB QRS morphology, a QRS duration of ≥150 ms is required and the level of recommendation is only IIa-A. The guideline also indicates that the evidence for CRT is uncertain in two commonly encountered clinical situations, in patients with atrial fibrillation and when a patient with a reduced ejection fraction has an indication for conventional pacing and no other indication for CRT.

2. A new indication for the sinus node inhibitor ivabradine. Based on the results of the SHIFT trial, ivabradine should now be considered to reduce the risk of heart failure hospitalisation in patients in sinus rhythm with an ejection fraction ≤35%, a heart rate remaining ≥70 bpm, and persisting symptoms (NYHA Class II-IV) despite treatment with an evidence-based dose of beta-blocker, ACE-inhibitor and a MRA (IIa-B recommendation).

3. An expanded indication for cardiac resynchronisation therapy (CRT). CRT (preferably CRT-D) is now recommended in NYHA class II heart failure patients if they are in sinus rhythm with a QRS duration of ≥130 ms, LBBB QRS morphology and an ejection fraction ≤35% and if expected to survive with good functional status for more than one year, to reduce the risk of heart failure hospitalisation and the risk of premature death. In contrast, in patients who do not have a LBBB QRS morphology, a QRS duration of ≥150 ms is required and the level of recommendation is only IIa-B. The guideline also indicates that the evidence for CRT is uncertain in two commonly encountered clinical situations, in patients with atrial fibrillation and when a patient with a reduced ejection fraction has an indication for conventional pacing and no other indication for CRT.

4. New information on the role of coronary revascularisation in heart failure. The STICH trial led to a I-B recommendation to use CABG in patients with angina and two or three-vessel coronary disease (including a left anterior descending stenosis) who have an LVEF ≤35% and who are otherwise suitable for surgery and expected to survive ≥1 year with good functional status.

5. Recognition of the growing use of ventricular assist devices. Left ventricular or biventricular assist devices are recommended in selected patients with endstage heart failure despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplantation to improve symptoms and reduce the risk of heart failure hospitalisation and to reduce the risk of premature death while awaiting transplantation (I-B recommendation). However, this recommendation is restricted to patients who have severe heart failure symptoms for more than two months despite optimal medical and device therapy and additional clearly defined conditions.

6. The emergence of transcatheter valve interventions. Transcatheter aortic valve replacement should be considered in patients with heart failure and severe aortic stenosis if patients are not medically fit for surgery (in general because of severe pulmonary disease). In patients with secondary mitral regurgitation and judged inoperable or at unacceptably high surgical risk, percutaneous edge-to-edge repair (mitral clip) may be considered in order to improve symptoms.

In contrast to other fields and guidelines, the wealth of evidence in heart failure makes it possible to have the recommendations on chronic heart failure resulting from left ventricular systolic dysfunction focus on mortality and morbidity outcomes. This is a great strength.

A very helpful new feature of the guideline is that practical guidance is provided for the use of the more important disease-modifying drugs and diuretics; this information is only available online because of space restrictions in the printed version. The guideline is very concise and worth reading for everybody treating patients with heart failure.

26 August 16:30 – 18:00
Munich, Central Village
New 2012 ESC acute and chronic heart failure Guidelines
Induced pluripotent stem cells still more a promise than reality in repair medicine

For example, following serious MI the heart muscle will lose cardiomyocytes in sufficient quantity for realistic treatments. reported so far are unable to produce pure enough Second, the differentiation and purification technologies to transport the reprogramming genes to the somatic cells, damaged tissue of heart diseases, particularly heart failure, However, in the promise of iPS cells to repair the single-gene defects. Patient-specific cells carrying the drug therapies for certain cardiac diseases dependent on still a long way to go” for regenerative medicine. She did, however, see more immediate promise in patient-specific therapies. Progress made in understanding single-gene defects. Patient-specific cells carrying the mutation could then be used for drug screening. “That will be the next step,” she said. “It’s where we’re most optimistic.”

However, in the promise of iPS cells to repair the damaged tissue of heart diseases, particularly heart failure, Guan identified three challenges still to be met. First, despite studies of alternatives, retroviruses are still used in the lab to transport the reprogramming genes to the somatic cells, but viral transduction remains unacceptable for treatments. The non-viral reprogramming route is relatively inefficient. There are also doubts over the safety of several transcription factors – notably the C-Myc gene - commonly used in research as far.

Second, the differentiation and purification technologies reported so far are unable to produce pure enough cardiomyocytes in sufficient quantity for realistic treatments. For example, following serious MI the heart muscle will lose between 1 and 2 billion cardiomyocytes in a short space of time, and it is the loss of these cells which prompts the cascade of scar tissue formation, reduced pumping power and left ventricular remodelling consistent with heart failure. That cascade is usually unstoppable, because the heart has no endogenous repair mechanism. To introduce functional cardiomyocytes derived from iPS cells to repopulate the scar tissue and regenerate the heart in such circumstances would require numbers which so far cannot be efficiently produced.

And third, even if we could produce sufficient pure cardiomyocytes, the techniques of reimplantation need to be improved. Efficiency of the injection process - into muscle tissue - is currently very low, said Guan, and would require developments in tissue engineering to make the transplantation process more efficient.

Her talk yesterday reviewed three sources of iPS cells, transplantation process more efficient. Efficiency of the injection process - into muscle tissue - is currently very low, said Guan, and would require developments in tissue engineering to make the transplantation process more efficient.

Female gender reassessed as a risk factor in AF

BEING FEMALE only presents a risk factor for stroke in patients aged over 75 years with non-valvular atrial fibrillation (AF), and obesity offers a powerful predictor of AF in young women, according to two studies featured in a press briefing yesterday. The session, which grouped abstracts exploring the importance of female gender, also included a study suggesting that the greater prevalence of co-morbidities such as diabetes explains why women with acute heart failure receive less treatment than men.

Female gender has already been proposed as a risk factor for stroke/thromboembolism in non-valvular AF, and is included in the CHA2DS2-VASc score. But now a joint Danish and UK study has set out to investigate whether stroke risk was homogenous in women or concentrated in specific age ranges. For the study investigators identified 87,202 patients with AF from a Danish register, 42,458 of whom were women. The AF cohort was then sub-divided into three age bands defined as <65 years, 65-74, and >75 years.

Results showed that for women aged >75 years the stroke rate at one year follow-up was 12.8% in women and 9.76% in men (HR 1.10), but for those aged <65 and 65-74 years no difference was found between the men and the women. “Since the increased stroke risk was concentrated in the oldest age group (>75 years), the study suggests being female shouldn’t automatically be considered a risk factor for stroke,” said Anders Mikkelsen from Copenhagen University Hospital. “AF patients older than 75 years are considered at increased risk of stroke, regardless of gender, he added, women in this age group should already be receiving adequate preventive treatments. Among older patients obesity has been shown to increase AF risk, but the relationship has never been investigated among younger individuals. In a separate study, the same Danish group examined the incidence of AF in relation to body mass index in fertile women. Making use of the unique Danish civil registration numbers given to all citizens, the investigators linked the Danish Birth Registry (which among other information records the mother’s BMI) to hospitalisation for AF.

Subjects were categorised as normal weight (BMI 18.5-25), overweight (BMI 25-30), obese (BMI 30-35) and very obese (BMI >35). Altogether a total of 271,257 women were identified, with a mean age of 30.6 years, and after a follow-up of 4.56 years 110 new-onset cases of AF had been identified.

Results showed that AF incidence rates were 7.4 per 100,000 person years for normal weight individuals; 8.5 per 100,000 person years for overweight; 15.8 per 100,000 person years for obese and 27.3 per 100,000 person years for very obese subjects. Even when known AF risk factors (such as diabetes and ischaemic heart disease) were taken into consideration, obese and very obese individuals had increased risks of AF. “We found very obese women were at three-fold increased incidence when compared to normal weight subjects, suggesting that population level weight loss strategies could decrease the burden of AF,” said investigator Deniz Karasoy. In a secondary analysis of the ALARM study investigators set out to explore the impact of gender on drug prescriptions and mortality in patients with acute heart failure. In the original ALARM study (Acute Heart Failure Global Survey) investigators compared the management of acute HF in 6953 patients admitted to cardiology or intensive care units in 666 hospitals located in nine countries in Europe, Latin America and Australia. In the current secondary analysis study gender differences were explored across the entire ALARM database, where women accounted for 37% of the study population.

Exploring co-morbidities, investigators found that women had a higher prevalence of diabetes (47% vs 43%, p=0.043), obesity (30% vs 22%, p<0.001), anaemia (17% vs 13%, p<0.001), AF/flutter (49% vs 42%, p<0.001), dementia (6% vs 3%, p=0.001), and depression (11% vs 7%, p<0.001). On the other hand men exhibited COPD/asthma more frequently (27% vs 21%, p<0.001) and coronary artery disease (35% vs 24%, p<0.001). On admission, men more frequently received aspirin, clopidogrel and beta blockers (p<0.05), while women more frequently received angiotensin-II receptor blockers and diuretics (p<0.05).

“The presence of co-morbidities has prognostic significance in women affecting the prescription of drugs as well as adherence to medical care and life style modifications,” said study first author John Parissis, a member of the ALARM steering committee.
EKG is ‘cost effective’ in screening young athletes for cardiac problems

ALTHOUGH there were no sporting tragedies reported from this year’s Olympic games, 2012 has already become an infamous year for sudden cardiac death in sports. Several SCDs have been reported in high profile sports players - including a 25-year-old Italian Serie B soccer player, a 26-year-old Norwegian swimmer, a 24-year-old Serbian rower, and a 32-year-old runner in the London marathon in May. Much more fortunately, with a cardiologist in the crowd, was the UK Premier League footballer Fabrice Muamba, whose heart “stopped” for 78 minutes following an on-pitch cardiac arrest in March. Muamba is reportedly back in good shape, having been treated by Pedro Brugada in Belgium, but unlikely to play professional football again.

Even though the incidence of SCD in sports is very low, found to be 1-3 per 100,000 athletes per year in some studies, several countries were still said to have screened all their Olympians before the games - including the UK’s full squad of more than 1000 athletes. The International Olympic Committee recommended but did not insist on screening to reduce the risk of SCD.

The routine screening of sports players has been controversial, largely because of cost concerns. Now, a study from Switzerland supported by the Swiss Heart Foundation and presented here as an abstract has found that cardiovascular screening with EKG in young athletes is a cost effective way of diagnosing cardiac abnormalities - with costs put at around €115 per athlete.

The study, presented by Andrea Menafoglio from Ospedale San Giovanni in Bellinzona, Switzerland, assessed the contribution of ECG (as recommended) to the diagnosis of cardiac abnormalities in young athletes using the latest criteria for interpreting ECG in sports. Competitive athletes aged 14-35 years were assessed based on personal and family history, physical examination and resting ECG. Any abnormal findings prompted further examination, and for each athlete the costs of screening and all subsequent tests were calculated according to Swiss medical rates.

Over a 14-month period 1070 athletes were examined. They had a mean age of 19.7 years, trained for a mean of 7.8 hours per week over 8.9 years, and 75% were male. Football was the most frequently played sport (37%).

Results showed that 6.3% of those screened required further examinations, 3.9% because of abnormal ECGs. A previously unknown cardiac abnormality was finally established in 2.0% of the athletes, and in 0.4% a cardiac abnormality potentially responsible for SCD was established (Wolf-Parkinson-White syndrome and long QT syndrome).

Menafoglio said: “Solid data indicate that cardiovascular screening, including a resting ECG can prevent a substantial proportion of these tragic events, and the ESC and major sports associations recommend such a screening programme. However, ECG has been considered by some to have inherent limitations, meaning that subsequent cardiac examinations are required. This substantially raises the costs of a programme to be implemented on a large scale to prevent these relatively rare fatal events. “However, we found that cardiovascular screening with ECG in young athletes is feasible with few subsequent examinations and, accordingly, at low cost - even in Switzerland where the costs of medical services are rather high.”

Another study presented by Arend Mosterd from the Netherlands showed that people who have a cardiac arrest during or shortly after exercise are three times more likely to survive than those whose arrest was not exercise related. The findings came from the Amsterdam Resuscitation Study.

Meanwhile, a report from the CASPER registry in Canada, presented by Martin Gardiner from Dalhousie University in Halifax, Nova Scotia, found abnormalities in 60 of 221 first-degree relatives of cardiac arrest victims. Most had primary electrical disease (86%) such as LQT syndrome. Systematic screening, which included physical examination, ECG, stress testing, 24-hour ambulatory monitoring and cardiac ultrasound, may prevent sudden death in these family members, said Gardiner.

28 August 11.15
Athens, Village 3
Costs of cardiovascular screening with ECG in young athletes in Switzerland
It is now ten years since Alan Cribier performed the first in-animal implantation of a balloon-expandable valve. In the Cardiologists of tomorrow track this morning, Henning Rud Andersen, a cardiologist at Aarhus University Hospital, takes time and persistence.

Andersen, who eventually developed the valve used by Cribier, says: “Our aim is to increase the quality of procedures.”

“From surveys you get an idea of what people think they’re doing, but for hard data to find out what’s really going on we need prospective registries,” says Blomström-Lundqvist, from Uppsala University Hospital, Sweden.

The European Cardiac and Vascular Association, the European Society of Cardiology, and the European Society for Minimally Invasive Cardiovascular Surgery have launched the European multi-centre registry of transcatheter aortic valve implantation (TAVI).

Andersen, who invented the TAVI device in 1998, use a combined femoral and jugular approach in 2.8% of cases where a combined femoral and jugular approach was needed. Stroke, major vascular complications and post-procedural aortic regurgitation remain the most concerning risks of TAVI. In terms of technology evolution, says Serruys, miniaturisation has been the dominating factor.

Even further into the realms of science fiction, he adds, a future direction might be to use stem cells to grow aortic tissue.”

“Both mechanical tools and new delivery systems have pros and cons,” said Kutarski. “Mechanical tools are cheaper, safer, but more time consuming. The new energy delivery systems separating fibrous adhesions from the cardiac leads are quicker to learn, but have higher risks of serious complications.”

Results showed that clinical success was achieved in 98.1% of patients, with major complications (such as haemopericardium surgery, severe hypotonia and cerebral stroke) in 1.1% and minor complications (such as pulmonary embolism, hemorhoxia, and tricuspid regurgitation) in 1.3%. The mean lead dwelling time prior to the procedure was 82.4 months, and the average procedure time was 112.2 minutes. The standard subclavian venous entry approach was used for 82.8% of leads, a femoral approach in 2.1% of cases, and a combined femoral and jugular approach in 2.8%.

“Results show that mechanical systems remain usable in the era of new, more effective and more expensive systems,” says Kutarski.

IN OCTOBER the first patients will be enrolled into the European Heart Rhythm Association’s (EHRA) lead extraction registry. “Our goal is to increase the quality of procedures, reduce complications and provide educational support,” says Carina Blomström-Lundqvist, the chair of the EHRA Structural Initiatives Committee, which co-ordinates EHRA registries.

Since the first pacemakers were implanted in 1958, use of implantable electronic devices has risen inexorably. But, despite major technology advances, the reliability of leads has not all too often proved a weakness.

It was not until the late 1980s that serious attempts were made to develop tools and technologies to remove problematic leads. First, mechanical extraction systems were used, and more recently laser energy delivery systems have been developed to free the electrodes from the surrounding tissue. Lead extraction today is a specialised procedure, requiring practitioners with a broad understanding of both pathophysiology and mechanical issues. The serious intra-procedural complications that can occur include myocardial avulsion, cardiac tamponade, vascular tear, haemothorax, pneumothorax, and pulmonary embolism.

Infections appear to be the main reason behind lead removal. A recent EHRA survey of 164 centres in 30 countries designed to produce a snapshot of current practice showed that infection accounted for 70% of extractions (European Heart Journal, 2012, 14: 783-86). Other reasons for removal included mechanical malfunction and deterioration over time.

“For surveys you get an idea of what people think they’re doing, but for hard data to find out what’s really going on we need prospective registries,” says Blomström-Lundqvist, from Uppsala University Hospital, Sweden.

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IT IS NOW ten years since Alan Cribier performed the first in-human transcatheter aortic valve implantation (TAVI). In the Cardiologists of tomorrow track this morning, Henning Rud Andersen, the inventor of TAVI, will recall those early days, while Patrick Serruys will outline the developments we can expect to see over the coming years. The bench-to-bedside session has been especially designed to show young cardiologists that achieving real paradigm shifts in medicine takes time and persistence.

Andersen, a cardiologist at Aarhus University Hospital, Denmark, recalls the interventional meeting he attended in Tbilisi, Central Village, Georgia, in February 1989 in the USA. “I was sitting in the auditorium listening to Julio Palmaz describing his experience of using coronary stents in dogs, when I suddenly thought ‘why not make the stents larger and place a biological valve inside?’”

Such an approach, Andersen reasoned, would be useful for patients with symptomatic aortic stenosis who could not undergo surgery due to age or co-morbidities. It would then be possible to introduce the valve percutaneously from the femoral artery.

Back home, Andersen, then training to be an interventional cardiologist, spent his free time building the device from hardware store materials, acquiring porcine valves from his local butchers. And within ten weeks he had performed the first in-animal implantation of a balloon-expandable valve.

Although Andersen obtained a patent on his idea in 1991, the report of his experience implanting the TAVI device in pigs was rejected by many journals, and none of the companies approached had any interest.

The first breakthrough came when Patrick Serruys reviewed the paper. “My immediate thoughts were that the approach could solve the problem of early valvular restenosis that we’d been seeing following balloon valvuloplasty in aortic stenosis,” says Serruys. “Publication swiftly followed in the European Heart Journal (1992: 13: 704-8).

Eventually Andersen licensed the patent to a small American company, who got a team of engineers involved and who eventually developed the valve used by Cribier. The company later sold out to Edwards Lifesciences.

The past and future of TAVI in one congress session

Today, TAVI procedures have been performed in around 50,000 patients, with the longest patient experience now close to seven years. Two different TAVI devices are currently available – the Edwards Sapien valve and Medtronic CoreValve. The Edwards valve is a balloon expandable system with a bovine pericardium valve in a cobalt-chromium stent, while the CoreValve is a self-expandable system with a porcine pericardium valve in a nitinol stent.

Although both devices got European CE marks in 2007, it was not until November 2011 that the Edwards Sapien valve received FDA approval. This followed the PARTNER trial, undertaken in more than 1,000 patients, which showed death from any cause was reduced by 45% for those receiving TAVI compared to balloon aortic valvuloplasty.

Extending TAVI to intermediate risk patients is currently being explored in two ongoing trials – the SURTAVI trial for the CoreValve device and PARTNERS-2 for the Sapien valve. For procedures in younger, lower risk patients to become widely acceptable, says Serruys, further technical improvements and proofs of safety and durability will be needed. Stroke, major vascular complications and post-procedural aortic regurgitation remain the most concerning risks of TAVI. In terms of technology evolution, says Serruys, miniaturisation has been the dominating factor.

New approaches to avoid embolic complications include the introduction of carotid filters and aortic deflectors. But there appear to be two key times for stroke. The first - within 48 hours of the procedure - is likely to involve embolisation, while the second occurs 30 days later and is likely to concern thrombus formation around the valves.

“This raises important questions about whether we should now be routinely offering TAVI patients anticoagulation or antiplatelet treatment,” says Serruys.

Other innovations include use of advanced imaging techniques, such as multi-slice CT scans and 3D Echo, to determine aortic valve anatomy and calcification. The results help multidisciplinary teams determine whether to gain access from the femoral artery, subclavian artery, ascending aorta or directly from the apex of the left ventricle.

Looking long term, says Serruys, it might be possible to use bioresorbable stents in TAVI. Instead of using animal vascular tissues, he adds, a future direction might be to use stem cells seeded on to structural supports.

Even further into the realms of science fiction, he adds, is the idea that mechanical leaflets could be generated by nanotechnology. “One suggestion is a nanotechnology approach where electric fields guide nitinol and titanium molecules to form a valve. This would lead to the creation of thin, flexible valve leaflets that would later be covered by tissue,” says Serruys.

65 year old lady with lead-dependent infective endocarditis. A functional VDD pacing system with very old abandoned ventricular lead with proximal ending in anomalous vein. A rare case for transvenous lead extraction.

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The case for statins in a wider population

Rory Collins to deliver tomorrow’s Geoffrey Rose Lecture on Population Sciences

IT IS NOW ten years since the initial results of the Heart Protection Study were published in the Lancet, and findings from the world’s largest study to investigate statins in the prevention of cardiovascular disease remain as important as ever. In particular, says the study’s principal investigator Sir Rory Collins, it was this trial which unequivocally showed that lowering levels of LDL-cholesterol in a wide range of patients would lower their risk of subsequent cardiovascular events irrespective of their starting cholesterol level.

“The study revolutionised the way cholesterol-lowering drugs are used,” says Collins, who tomorrow will deliver the Geoffrey Rose Lecture on Population Sciences. “Until then, the benefits of cholesterol-lowering drugs were thought only applicable to those at high risk with elevated cholesterol levels. But what the Heart Protection Study showed was a reduction in the risk of coronary heart disease even in those with cholesterol levels in the normal range. That really changed the landscape.”

It was also results from the same study which showed the benefits of lowering LDL-cholesterol levels in those with diabetes. Again, the risk reductions were seen in those with relatively low levels of LDL-cholesterol, as well in many other types of high-risk patients.

Cholesterol and risk is the subject of Collins’s Named Lecture this morning, considered from a past, present and future perspective. The past, he notes, was defined by a misguided view (as has now been shown by the statin trials) that lowering LDL-cholesterol levels was not beneficial for many types of patients and, indeed, might even be hazardous. For example, both the elderly and women were excluded from the benefit roster. But the Heart Protection Study showed unequivocally that statins could produce substantial benefit in a much wider range of subjects than had ever been contemplated. From there on, the mantra became “treat the risk, not the cholesterol”.

As for the present, those findings have been confirmed and extended by meta-analysis of the many different trials of statins, most recently in a huge review performed by Collins’s own group at the Clinical Trial Service Unit (CTSU) of Oxford University, collectively known as the Cholesterol Treatment Trialists collaboration. That study, which included 27 randomised trials, showed that, even in healthy people, reducing blood levels of LDL-cholesterol cut the risk of coronary events (including revascularisation) and ischaemic stroke by around one-third. Healthy people given a statin also had lower overall mortality rates than those given placebo. Since their original 2002 study, the message from Collins and his CTSU colleagues has thus been that CVD prevention guidelines should consider the health benefits of statins in a very much wider range of people.

Today, mortality trends in most developed countries show steep and consistent declines in premature death from heart disease and stroke, and in the UK vascular mortality rates in middle age have, remarkably, fallen by more than half in the past three decades. The CTSU, of which Collins and Sir Richard Peto have been co-directors for more than 20 years, has made substantial contribution to these trends in its major studies of smoking, blood lipids, blood pressure, aspirin and streptokinase.

Collins and his colleagues have emphasised the need for large-scale observational and randomised evidence about the prevention and treatment of major diseases. Indeed, it was the CTSU in the 1970s and 80s which pioneered the use of meta-analysis of trials in vascular disease, and with it the demonstration that even modest effects in a widely prevalent condition could have a dramatic public health impact.

As for the future, Collins’s lecture this morning will hold out the promise of even more rapid demonstration of the benefits of adding newer cholesterol-lowering agents to the statins.

Don’t forget the European Heart for Children project

Since its launch in 2009, funds raised by the EHC have made it possible for 4,144 children to be examined, 38 to be operated on, and nine to be brought to Italy for more complex surgery. There have been missions to Syria, Morocco and Egypt, and ECG machines donated to hospitals in Morocco, Egypt, Kosovo and Romania. The project is still reliant on public support and donation, and estimates that 15 million children die or remain debilitated each year because of a cardiac condition.
As a researcher in cardiovascular prevention I find the time it takes to get research findings out into clinical practice incredibly frustrating. We recently did a study looking at risk factor modification in the workplace and primary care - we have been able to show that over five years 150 life-years could be saved for every thousand subjects in the active arm of the program. But to implement our approach as standard care we need to first convince our minister of health and then educate family doctors. The problem we’re up against in Russia is that family doctors have limited opportunities for continuing education, so it’s hard to keep them up to date with new changes.

In interventional cardiology it’s really important to keep up to date with the latest results about new technologies and to incorporate them into your practice. This year I’ve been particularly impressed by the DeFACTO study exploring the non-invasive assessment of fractional flow by computed tomography. The technology allows you to measure the dynamics of flow inside the artery, and identify those patients who require invasive treatment and those who can get away with conservative management. The technology should be cost effective since it would prevent unnecessary procedures. I want to introduce new technology as quickly as possible to help achieve the best possible outcomes for my patients.

With translational research, you have to try, but once you realize it’s not the right approach then you have to wait for proper data. In the early 90s, we tried all kinds of drugs with restenosis and, in the end, had to stop and wait for the stents. "With rhenium-188-filled balloon catheters, we tried a lot of research and, in a clinical setting, it was about half successful. We’re enthusiastic and it’s vital we keep up with new ideas and try and adapt these ideas. As a doctor though, you don’t want to damage your relationship with patients because they trust you. Once we see it’s not good for a patient, we have to be honest.

I work in an institute where translational medicine is applied. The focus of this congress is important because it brings attention to the difficulties in back-up evidence. It’s a long process from bench to bedside. General clinicians are sceptical, but this is why they must be better aware of what is an unavoidable process - but also the future of how we make things better for patients. One favourable example is the translation of biomarkers, which include a huge number of molecules and which have turned out to be very important in the clinical setting for screening. The reason is they’re simple, as well as very easy and cheap to perform.

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