ESC CONGRESS NEWS
ROME 2016
EUROPEAN SOCIETY OF CARDIOLOGY®

MONDAY 29 AUGUST

A rethink for ICDs in non-ischaemic HF

DANISH study's neutral result

Lars Kober, presented results from the DANISH trial.
Survival rates in non-ischaemic HF were no better with ICDs than with usual care.

HOT LINE SESSION RESULTS

USE OF IMPLANTABLE cardioverter-defibrillators in patients with non-ischaemic systolic heart failure did not improve overall survival over usual care, according to results presented a Hot Line study yesterday.

The DANISH trial, published simultaneously in the *New England Journal of Medicine*, did, however, show that the risk of sudden cardiac death in these subjects was halved. There were also findings related to age, with those under 68 showing a lower mortality rate.

The study, which was said to be the first to consider ICDs within the context of 'modern therapy', raised questions about the role and recommendation of ICDs in non-ischaemic HF. Prophylactic ICD implantation currently has a class 1A recommendation in US guidelines and a class IB in Europe for patients with HF and reduced left ventricular systolic function.

'So far, there has only been limited data on ICDs in this population,' said study presenter Lars Kober from Rigshospitalet, University of Copenhagen. 'Our trial fills that gap by now suggesting that ICDs should not be routinely implanted in all patients with systolic heart failure.'

The DANISH trial itself was designed to investigate the usefulness of ICDs in patients with HF not caused by ischaemic heart disease. Guideline indications for primary prophylactic ICD in patients with HF but without CAD have been based on small to medium trials and subgroup analyses, with no large definitive trials showing a benefit for ICDs in these patients. Furthermore, said Kober, medical therapy has improved considerably since the early ICD trials.

In this study 1116 patient with non-ischaemic systolic HF were randomised to receive ICD and usual care (n=556) or to a control group (n=560) of usual care. Notably, all patients were treated well, with around 58% in each group receiving a CRT, 90% ACE inhibitors/ARBSs, and 90% beta blockers.

After a median follow-up of 67.6 months, death occurred in 21.6% of the ICD group and 23.4% of the control group, a non-significant difference (HR 0.87; 95% CI 0.68-1.12). Results also found no difference in rates of cardiovascular mortality.

There was, however, a significant difference in the secondary outcome of SCD, which occurred in 4.3% of ICD patients and 8.2% of controls (HR 0.50; 95% CI 0.31-0.82; P=0.01).

Continued on page 2

Remote ICD monitoring brings no added clinical benefit in HF

TWO CLINICAL trials exploring remote monitoring in HF patients fitted with cardiac implantable electronic devices reported in yesterday's Hot Line session failed to detect improved clinical outcomes over conventional care - although one study did show reductions in office visits and costs.

Despite advances, HF patients remain at high risk of death and hospitalisation. There has thus been much interest in whether the remote transmission of ICD data prompts improved clinical outcomes.

The REM-HF trial randomised 1650 patients from nine English hospitals to usual care and weekly remote monitoring or to usual care alone. The study, which was published simultaneously in *JAMA*, is the largest trial ever of remote monitoring.

Results at a median follow-up of 2.8 years showed that the primary endpoint of all-cause mortality or CV hospitalisation was neutral. Furthermore, no significant differences were found between the two groups in any of the secondary endpoints, and none of the baseline characteristics (age, gender, NYHA Class, type of device, history of coronary artery disease or history of atrial fibrillation) identified any group in which remote monitoring was more effective than usual care alone.

'In the modern era of digital health we could find no evidence of additional benefit from weekly remote monitoring of these devices,' said presenting investigator Martin Cowie from Imperial College London. 'Our

Continued on page 2

Martin Cowie: No gain from weekly remote monitoring in a large randomised trial.

Don't Miss

- **08:30 - 10:00 / 14:00 - 15:30** Rome (Main Auditorium)
  ESC Clinical Practice Guidelines Sessions
- **08:30 - 18:00** Galileo (The Hub)
  Gladiators Arena
- **10:10 - 10:50** Agora (Poster Area)
  Future is in Education
- **10:10 - 10:50 / 15:40 - 16:20** The Hub
  Meet the Guidlelines Task Force &
  Meet the Trialists sessions at coffee breaks
- **11:00 - 12:30 / 16:30 - 18:00** Rome (Main Auditorium)
  Hot Line Sessions
- **12:40 - 13:50** The Hub
  Young Investigators Awards Sessions
- **12:45 - 13:45** Bernini (The Hub)
  Training the future leaders of cardiovascular research - Raising funding in Europe
- **18:00 - 19:00** Agora (Poster Area)
  Awards Ceremony

No cardiovascular benefits of pressure mask in sleep apnea

CONTINUOUS positive airway pressure (CPAP) does not prevent cardiovascular events in patients with moderate-to-severe obstructive sleep apnea (OSA) and established CV disease, according to the population-based SAVE study. Presented as a Hot Line yesterday, the findings were published in the *New England Journal of Medicine.*

The results were not expected. 'Given the level of risk of cardiovascular disease attributed to OSA in previous observational studies, we were surprised not to find a benefit from CPAP,' said presenter Doug McEvoy, from the Adelaide Institute for Sleep Health, Australia.

OSA affects around 40-60% of patients with CVD and has been associated with increased risk of cardiovascular events. It is known to cause episodic hypoxaemia, nocturnal sympathetic activation and elevated blood pressure, and also to influence oxidative stress, inflammation and hypercoagulation. Furthermore, large negative intrathoracic pressure swings impose mechanical stress on the heart and great vessels.

CPAP has become the standard treatment for OSA. Observational studies have shown that CPAP use is associated with lower rates of CV complications and death, especially among patients who are adherent to treatment. However, randomised trial data is lacking for any benefit of OSA treatment for CVD prevention. The Sleep Apnea Cardiovascular Endpoints (SAVE) study was thus designed to explore whether treatment with CPAP does indeed reduce the incidence of future CV events among those with OSA.

Between December 2008 and November 2013, 2717 adults aged between 45 and 75 years with moderate-to-severe OSA and established coronary or cerebrovascular disease were randomised to receive CPAP treatment plus usual care (n=1359) or usual care alone (n=1358).

The patients, who were recruited from 89 clinical centres in seven countries, had a one week run-in with a sham CPAP mask prior to randomisation. They had to demonstrate effective use for a minimum of three hours a night. The investigators excluded those with severe sleepiness, very severe oxygen deprivation, advanced HF, and prior CPAP use. The primary endpoint was a composite of CV death, MI, stroke, hospitalisation for TIA, unstable angina or HF.

Results showed after a mean follow-up of 3.7 years that the primary endpoint occurred in 229 (17.0%) of the CPAP group and 207 (15.4%) of the usual-care group.

Doug McEvoy: A big challenge to use the CPAP mask throughout the night.

However, not all was disappointment. The study also showed that CPAP significantly improved patient well-being. It reduced snoring and daytime sleepiness (P<0.001 vs. controls) and improved health-related quality of life and mood. There was a decrease of 20-30% in episodes of depression among patients, and fewer days were lost due to ill-health.

'It's a big challenge in the field to have people use this treatment throughout the night,' said McEvoy. 'There's some evidence that *when* you use it may be important. There are some studies showing that people who use it only in the first half of the night may not get benefit, particularly as it's the latter part of the night when REM sleep is known to produce more severe OSA.'

Platelet monitoring of little value in the elderly

Gilles Montalescot: Our study does not support platelet monitoring for drug dose in the elderly.

PLATELET MONITORING for dose adjustment of prasugrel is not superior to a conventional fixed dose in elderly patients stented for ACS, according to a Hot Line study yesterday. The results of the ANTARCTIC trial, published simultaneously in *The Lancet*, urge a review of current guidelines, which recommend platelet function testing in high risk patients. Senior investigator Gilles Montalescot said that the trial, the largest randomised PCI study ever performed in the elderly, does not support testing. He expected guidelines and practice to change as a result.

'Platelet function testing is still being used in many centres to measure the effect of antiplatelet drugs and adjust the choice of drugs and their doses,' said Montalescot, from Hopital Pitie-Salpetriere in Paris. 'Our study does not support this practice or the recommendations.'

ANTARCTIC confirms the results of the ARCTIC trial of 2011, which investigated a different patient population (low risk and elective PCI) and a different antiplatelet therapy (clopidogrel). All 877 patients enrolled in the ANTARCTIC study were aged 75 or more and had coronary stenting for ACS.

All were started on prasugrel (5 mg) with 442 randomised to conventional fixed dose therapy and 435 to monitoring and treatment adjustment. Patients in the monitoring arm received the daily 5 mg prasugrel dose for 14 days at which point a platelet function test was used.

If the test showed high platelet reactivity, medication dose was increased - or decreased if reactivity was low. Patients within the therapeutic range remained on the same dose.

The primary endpoint over 12 months was bleeding, SV death, MI, urgent revascularisation, stent thrombosis and stroke. This endpoint occurred at a similar rate in both arms of the study, - 27.6% in the monitoring group and 27.8% in the conventional group.

Similarly, no significant difference was found in rates for the main secondary endpoint, a composite of CV death, MI, stent thrombosis or urgent revascularisation - which occurred in 9.9% and 9.3% of each group.

Overall, platelet function monitoring led to a change of treatment in 44.8% of patients, who were identified as being over or under treated. Yet the strategy did not improve ischaemic or safety outcomes. 'ANTARCTIC after ARCTIC confirms a failure to improve clinical outcomes for patients,' said Montalescot. 'In this case, however, the failure is not related to risk level or the type of P2Y12 antagonist. Although measuring the effect of antiplatelet agents makes some sense, this costly and more complex strategy does not appear to benefit patients.'

Stem cells delivered intravenously for chronic cardiomyopathy

A single dose of mesenchymal stem cells delivered intravenously to patients with chronic non-ischaemic cardiomyopathy resulted in clinically relevant benefits in the CHART-1 study presented in yesterday's Hot Line session.

'Virtually all previous studies of stem cell therapy for heart failure have followed the concept that the cells must be injected directly into the heart to trigger new growth,' said study presenter Javed Butler from Stony Brook University, New York. 'But if stem cells have anti-inflammatory benefits, direct cardiac delivery may not be necessary.'

The study used 'ischaemia tolerant' mesenchymal stem cells (itMSC) donated by healthy volunteers and grown under chronic hypoxic conditions, which are believed to enhance immune modulatory properties. In this single-blind, placebo-controlled, crossover, multicentre study, 20 patients with non-ischaemic cardiomyopathy and left ventricular ejection fraction ≤40% and NYHA class II-III were randomised to receive intravenous itMSC therapy (n=10) or placebo (n=12) for 90 days and then crossed over to the other treatment.

Results at 90 days post itMSC infusion showed there were no major differences in primary safety endpoints of all-cause hospitalisation, and adverse events between the two groups. However, compared to placebo, itMSC therapy resulted in statistically significant improvements in the six-minute walk tests, as well as greater improvements in the Kansas City Cardiomyopathy Questionnaire scores.

'To our knowledge, this trial represents the first experience with intravenously administered itMSCs in patients with any type of chronic cardiomyopathy,' said Butler, adding that further studies should explore the efficacy of serial dosing for more sustained immunomodulatory effects.

Prophylactic ICDs

Continued from page 1

subgroup analysis showed that ICD patients under 68 had a significantly lower mortality rate than controls (HR 0.64, 95% CI 0.46-0.91), a result not found in those over 68.

Commenting on the results, former AHA President Mariell Jessup, an author on both the US and recent European guidelines, said: 'The study showed ICDs work and are especially effective in people who are not going to die from comorbidities. No countries are putting in enough ICDs to prevent sudden death in patients who can expect to live more than a year.'

Remote ICD monitoring

Continued from page 1

'So our conclusion is, do not rush to recommend additional work or a change in the way we deal with data unless you are convinced that you will actually have better outcomes.' Where HF programmes do not exist or there is poor quality treatment, he added, remote monitoring might make a difference. 'But in the context of a randomised trial where patients are well treated, it seems there is not enough scope to improve outcome by forcing people to look at more data.'

In the MORE-CARE study, published yesterday in the *European Journal of Heart Failure*, 917 HF patients implanted with a CRT-D device with wireless transmission capabilities were randomised to remote device checks alternating with in-office visits (n=462) or to a standard arm with all checks in office (n=455). Results at a median follow-up of 24 months showed the rate of mortality and hospitalisations for cardiovascular or device-related reasons was 29.7% in the remote arm and 28.7% in the standard arm (HR 1.02 ; 95% CI 0.80-1.30). However, the study showed reductions in emergency department admissions for any reason, and outpatient visits for those having remote checks. Health care savings were calculated to be €2,899 per 100 patients at two years, and additionally there was a travel cost saving of €145 per patient over two years.

'Our study shows that remote-monitoring avoids patients having to come to hospital, which they really appreciate,' said study presenter Giuseppe Boriani from the University of Modena, Italy.

New practice guidelines in heart failure

By Mitja Lainscak,
General Hospital Celje
Celje, Slovenia

and Gerasimos Filippatos
Athens University Hospital
Athens, Greece

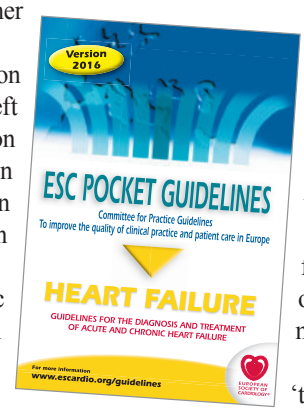
IN THE LATEST ESC guidelines for the diagnosis and treatment of acute and chronic heart failure several new points are emphasised which aim to move HF management into new areas, including prevention.

HF remains an unmet medical challenge worldwide with increasing prevalence despite better management of cardiovascular conditions, including acute coronary events. New guidelines therefore emphasise the potential of ACE inhibitors, beta-blockers and statins to prevent or delay HF and to prolong life in those with arterial hypertension and CAD.

Once a patient presents with suspected HF of non-acute onset, first step should be the assessment of clinical probability before natriuretic peptides and/or echocardiography. Echocardiography remains the central diagnostic tool and, based on left ventricular ejection fraction, HF with mid-range ejection fraction (HFmrEF) has been added to the existing categories of HFrEF and HFpEF (reduced and preserved ejection fraction, respectively). Echocardiography will help evaluate beyond ejection fraction the presence of structural heart disease and diastolic function.

With patients stratified according to the ejection fraction, only those with HFrEF have established therapies to improve prognosis. The 2012 algorithm has been simplified and in the 2016 version some clinical points are emphasised, eg, the patient-adjusted diuretic therapy using the lowest effective dose.

ACE inhibitors, beta-blockers and mineralocorticoid receptor antagonists remain the mainstay of therapy, and ICD is an option for those surviving life-threatening arrhythmia. If after three months of optimal therapy the patient remains symptomatic and with LVEF ≤35%, there are several evidence-based options. In patients who are able to tolerate ACE inhibitors (or ARBs) and based on evidence from the PARADIGM-HF trial, sacubitril/valsartan, a combination of angiotensin receptor neprilysin inhibitor and ARB, is recommended to further reduce morbidity and mortality.



Best candidates for cardiac resynchronisation therapy are those in sinus rhythm, a QRS of left bundle branch block morphology and duration of ≥130 msec; if in sinus rhythm and with an elevated heart rate of ≥70 bpm, ivabradine is an option. More than one of these three options can be implemented in clinical practice.

With persisting symptoms, symptomatic therapy or evaluation for mechanical circulatory support and/or transplantation remains an option. For patients with HFpEF, no major advance has been made since the 2012 guideline, and most of the diagnostic and therapeutic steps remain at the level of expert consensus. Nonetheless, all patients with HF need to be comprehensively managed, preferably in a multidisciplinary care programme, and should be encouraged to exercise regularly.

Being a chronic condition in an elderly population, HF very often coexists with other chronic diseases, a fact that interferes with HF diagnosis and management. It is important to diagnose the comorbidities and to take appropriate action to avoid any drug-drug or drug-disease interactions and to individually optimise the management. In this context, the practical guidance on the use of key pharmacological therapies (published as web addenda) is crucial for adoption and implementation by clinicians.

The field of acute HF has also witnessed some important conceptual changes. Time, as in acute coronary syndromes and in stroke, matters and assessment of cardiac and/or respiratory failure must be performed urgently: if present, the patient must be stabilised (circulatory/ventilator support) and managed in intensive cardiac care units. At the same time, assessment of clinical condition in terms of perfusion and congestion must be performed and the majority of patients will be categorised as 'wet and warm'. This simple assessment will also guide initial therapy and patient management in an early phase.

Within 60-120 minutes other life-threatening syndromes must be evaluated. The acronym CHAMP will help clinicians consider acute Coronary syndromes, Hypertensive crisis, Arrhythmia, acute Mechanical cause, and Pulmonary embolism in these patients and to take immediate action if diagnosed. Most therapies for acute HF, however, remain without robust evidence from randomised trials, which makes the identification of trigger and haemodynamic profile assessment even more important for daily practice.

The 2016 HF guidelines end with the summary of 'to do' and 'not to do' messages, which cover the entire spectrum of HF management. Although the summary is impressive, there remain several gaps in evidence, ranging from diagnosis over acute HF to patient management; these unmet needs should be or are under investigation and the next guideline will hopefully reduce the list of open questions.

Don't miss: The new ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.
29 August 08:30-10:00 Rome - Main Auditorium

Stepping up the run rate: Today's debate asks if more exercise will be better for us or worse?

Yes, better

says Sanjay Sharma
St George's University of London, London

Regular exercise reduces the risk of cardiovascular mortality and all-cause mortality by up to 50% and 30% respectively.[1,2] Several studies show an inverse relationship between physical fitness and relative risk of mortality; in general there is a 10-20% reduction per MET when exercised between 4 and 12 METs. Most studies have assessed relatively few individuals capable of exercising beyond 12 METs and been unable to demonstrate any additional mortality benefit in this small cohort.

Current physical activity guidelines recommend 30 minutes of moderate exercise (4-6 METs) at least five times weekly or 20 minutes of vigorous exercise (>6 METs) at least three times weekly; however, many competitive athletes and individuals engaging in recreational endurance events such as the marathon or triathlon exercise much more intensively than 12 METS and exceed current recommendations by 10-15 times.

The deleterious effects of exercise on a normal heart – A speculative myth

There has been an exponential increase in the number of marathon runners over the past 20 years, with over 2 million marathon runs per year in Europe. In parallel, there has been a plethora of publications alluding to the potential dangers of intensive exercise in athletes with an otherwise normal heart. These concerns are fundamentally based on the detection of high serum concentrations of biomarkers of cardiac damage and decrease in cardiac function following an endurance event. Some researchers have speculated that such episodes could reflect myocardial inflammation and may lead adverse cardiac remodelling and an arrhythmogenic substrate.[3]

But in reality there is no evidence whatsoever linking transient increases in biomarkers of cardiac damage to permanent cardiac inflammation or myocardial fibrosis. On the contrary, all studies have shown that these changes are transient and completely reversible within a few days.

Cardiovascular magnetic resonance (CMR) studies performed immediately after a marathon run in individuals with raised serum cardiac troponin concentrations have not shown any evidence of myocardial inflammation.[4] Furthermore, animals that are sacrificed a few weeks after detraining do not reveal any fibrosis, suggesting that the process is reversible and may represent compensatory remodelling as opposed to pathology.

Only a few studies have reported myocardial fibrosis in veteran marathon runners and these are marred by small sample size and lack of statistical significance in the results. In contrast, others have shown no evidence of fibrosis. There are also small studies demonstrating increased CAC and right ventricular dysfunction in endurance athletes.

The former studies have investigated athletes with established risk factors for atherosclerosis and the latter have reported on a select group of athletes presenting with ominous symptoms or life-threatening arrhythmias. There is some evidence that life-long veteran athletes reveal a higher prevalence of atrial fibrillation, but this has not been confirmed by all studies.

More exercise is better: The numbers say it all

A recent American study of 42,000 sedentary subjects and 13,000 runners reported a very positive impact of jogging on cardiovascular mortality.[5] The benefits were similar in those who exercised moderately and those who exercised more intensively and for a prolonged duration, but there was no upper limit. A recent study of 37,855 middle aged individuals with high fitness levels showed progressive survival benefit with increasing fitness in the 1893 with fitness levels ≥14 METS.[6]

Similarly, a meta-analysis of 628,000 (where the sedentary group alone exceeded the largest number of subjects ever studied in former observational studies investigating the association between exercise and mortality) showed that those who exercised five times above the current recommended levels of exhibited the greatest mortality benefit (HR 0.61). This benefit persisted (with was no harm) in those exercising 10 or more times the recommended level of exercise.

Intuitively, too much of anything may be bad for health; however, there is no convincing data to show any evidence of an upper limit of exercise dose, or that 'more is worse'. Perhaps the best evidence for this could be inferred from studies reporting that former Olympians and Tour de France athletes live considerably longer than the general population.

1. Tanasescu M, Leitzmann MF, Rimm EB, et al. Exercise Type and Intensity in Relation to Coronary Heart Disease in Men. JAMA 2002; 288: 1994–2000.
2. Lee D-C, Pate RR, Lavie CJ, et al. Leisure-time running reduces all-cause and cardiovascular mortality risk. JAMA 2014; 64: 472–481
3. Benito B, Gay-Jordi G, Serrano-Mollar A, et al. Cardiac arrhythmogenic remodeling in a rat model of long-term intensive exercise training. Circulation. 2011 ;123: 13-22.
4. Kirkpatrick ID, Neilan TG, Sharma S, Jassal DS. Relation of biomarkers and cardiac magnetic resonance imaging after marathon running. Am J Cardiol 2009; 103: 1467-1472.
5. Kwok CS, Anderson SG, Myint PK, et al. Physical activity and incidence of atrial fibrillation: a systematic review and meta-analysis. Int J Cardiol 2014; 177: 467–476.
6. Schnohr P, O'Keefe JH, Marott JL, et al. Dose of jogging and long-term mortality. J Am Coll Cardiol 2015; 65: 411–419.

Well...

says Carl Lavie
John Ochsner Heart and Vascular Institute
New Orleans, USA

Certainly, the major problem worldwide is not excessive endurance exercise (EEE), but rather that physical inactivity poses perhaps the century's greatest threat to health. Saying this, however, raises a serious question about the optimal dose of exercise training (ET) and whether EEE could have adverse effects.

In 2014 we studied the effects of running on 55,000 subjects followed for and average of 15 years, comparing 13,000 runners with 42,000 non-running controls.[1] During follow-up, the runners had a 30% reduction in total mortality and a 45% reduction in CVD mortality, with an average life extension of more than three years and CVD life extension of more than four years.

However, we divided the 13,000 runners into quintiles (Q) of dosing based on miles per week, times per week and minutes per week, and found that those low-dose runners in Q1 (<6 miles per week, 1-2 times per week, <52 minutes) had maximal benefits in terms of mortality and CVD mortality; this benefit was equal to Q2-4, with a slightly non-significant trend to better survival than the higher dose runners in Q5. Recently in the Mayo Clinic Proceedings, we divided those in Q5 into tertiles (T) and found that those in Q5 T3 (of the top 7% of runners regarding higher doses) seemed to lose the mortality benefit of running when compared with non-runners. This would certainly suggest that more is not better - and even the possibility that more could be worse.

Data from Wen and colleagues in over 400,000 people from Taiwan also suggest that maximal benefit from vigorous ET seems to occur after 30-40 minutes.[2] Very high doses of EEE, such as marathon running and triathlons, have the potential for cardiotoxicity, including release of troponin, brain natriuretic peptide, and the development of cardiac dilatation and dysfunction, especially of the ventricular septum and the right side of the heart.

Some animal studies have also suggested toxicity of EEE; humans with EEE have increased coronary artery calcification and possibly soft plaque, and, although sedentary lifestyle is associated with increased risk of atrial fibrillation (AF) and low to moderate ET seems to reduce the risk of AF, high ET has been associated with increased AF in many individual studies and meta-analyses.

The conclusion from our own research of is not intended to scare athletes away from participating in marathons or triathlons, because the serious risks from these events are quite low. However, the maximal benefits of ET from a health perspective appear to occur at quite low levels. If an athlete is performing EEE, the reason should not be for health benefits but rather to improve athletic performance, or simply for competition, fun, ego or camararderie. For health, the evidence supports what Hippocrates said centuries ago: If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health.

1. Lee DC, et al. Leisure-time running reduces all-cause and cardiovascular mortality risk. J Am Coll Cardiol 2014;64:472-481.
2. Wen CP, et al. Minimal amount of exercise to prolong life: to walk, to run, or just mix it up? J Am Coll Cardiol 2014;64:482-484.

Don't miss: More exercise: better or worse? 29 August 16:30-18:00 Galileo - The hub

Direct thrombectomy without thrombolysis in acute stroke

A FURTHER REPORT from the ongoing PRAGUE registry studies indicates that direct catheter-based thrombectomy is as effective as bridging thrombolysis in the treatment of acute ischaemic stroke.

As background to the study, which will be presented in a Registry Session this afternoon, Petr Widimsky of Charles University, Prague, explained that, if left untreated, acute ischaemic stroke caused by a major artery occlusion would result in death for up to half of all patients and an additional 40-50% would be left permanently disabled. ' In other words,' he warned, 'without treatment only a few patients with major ischaemic stroke survive without severe sequelae.' Survival increases to around 20-30% with thrombolytic treatment .

In 2015 several randomised trials showed that 45-50% of patients can survive and be functionally independent with endovascular mechanical thrombectomy. If the intervention is performed very early (within three hours from stroke onset), the results are even better – up to 70% of patients may return to normal daily life. As a result of these studies, and updates to some guidelines, mechanical thrombectomy is now recommended for all patients with acute ischaemic stroke caused by a major artery occlusion.

However, Widimsky explained that many questions remain, of which two were investigated in this pilot study. First, whether direct (without thrombolysis) cathether-based thrombectomy (d-CBT) can achieve comparable results to thrombectomy performed after IV ('bridging') thrombolysis. And second, whether d-CBT performed in interventional cardiology departments can achieve results comparable to those in neuroradiology settings.

Petr Widimsky: Catheter-based thrombectomy may be an alternative to thrombectomy after thrombolysis.

'So the study's aim,' said Widimsky, 'was to evaluate the feasibility and safety of d-CBT performed in close cooperation between cardiologists, neurologists and radiologists – a true interdisciplinary approach.'

PRAGUE-16 was a prospective, observational pilot registry study. It included 103 patients who presented within six hours of the onset of moderate to severe acute ischaemic stroke. Patients had an occluded major cerebral artery but no large ischaemia on a CT scan. The attending neurologist decided whether patients received d-CBT or bridging thrombolysis plus CBT depending on the clinical picture and CT scan. The intervention was performed within 60 minutes of the CT scan.

Some 73 patients received d-CBT and 30 had bridging thrombolysis plus CBT. Good functional outcome was achieved in 41% patients overall with similar results between the two groups. 'This compares to 48% given this intervention in seven randomised trials performed in expert neuroradiology units,' said Widimsky.

'Our findings suggest that direct catheter-based thrombectomy performed in a timely manner may be an alternative to thrombectomy after bridging thrombolysis,' said Widimsky. 'Furthermore, in regions with no or limited neuroradiology services, treatment might be offered via interventional cardiology in close cooperation with neurologists and radiologists. However, both of these preliminary conclusions should be confirmed by larger multicentre studies or large international registries.'

Don't miss: Feasibility and safety of direct catheter-based thrombectomy in the treatment of acute ischemic stroke. Prospective registry PRAGUE-16
29 Aug 16:45-17:00 – Sarajevo, Village 2

Alcohol linked to higher stroke risk

ALCOHOL-RELATED hospitalisation is associated with a doubled risk of ischaemic stroke in patients with non-valvular atrial fibrillation, according to a study reported at a press conference by cardiologist Faris Al-Khalili from the Karolinska Institute, Stockholm. This observational population study was performed in more than 25,000 non-valvular atrial fibrillation patients at low risk of stroke identified from 345,123 AF patients in the Swedish national patient register between 2006 and 2012.

The registry data showed that ischaemic stroke occurred at an annual rate of 3.4 per 1000 patient-years. In the multivariable analysis, the only variables that remained significantly associated with an increased risk of ischaemic stroke were age and alcohol related hospitalisation (HR 2.01, p <0.001).

'Doctors should ask their AF patients about alcohol use and advise patients to cut down if they are drinking more than is recommended,' warned Al-Khalili.

HDL: a question of quantity or quality?

Unravelling the conflicting results of HDL's atheroprotective effect

By Johann Wojta
Medical University of Vienna
Austria

UNTIL RECENTLY it was undisputed dogma that high-density lipoprotein cholesterol (HDL-C) has solely atheroprotective properties. This notion was based on population studies and meta-analyses showing an association of high HDL-C plasma levels with a decreased risk for cardiovascular disease.

Recently, however, this view has been challenged, mainly by clinical studies showing that HDL-C levels predicted cardiovascular death only in individuals without CAD. Several lipid-lowering trials showed no or only a weak impact of low HDL-C levels on cardiovascular risk. For example, in the PROVE IT-TIMI 22 trial the levels of HDL-C reached had no predictive value in ACS patients under aggressive atorvastatin therapy. However, in the COURAGE trial an association of cardiovascular risk with HDL-C plasma levels was seen in patients with stable CAD in which target levels of LDL-C of 60-58 mg/dl were reached through intensive lipid lowering therapy.

Further doubts on the exclusively atheroprotective role of HDL-C were raised by trials aiming to raise HDL-C levels. These studies using nicotinic acid or cholesteryl ester transfer protein inhibitors were largely unsuccessful as no additional risk reduction on top of statins could be seen.

These conflicting and controversial results have led to the concept of dysfunctional HDL by which the atheroprotective role of HDL-C does not depend on the transported cholesterol but rather on properties of the HDL particles themselves.

Addressing this concept, recent intensive research has shed some light on the heterogeneity of HDL particles possibly responsible for the contradictory findings. HDL particles can be divided in various sub-fractions or subpopulations depending on their size, composition, density, charge and physiological function. This heterogeneity is a result of the varying contents of lipids and proteins of the respective LDL particles in which size and density show an inverse correlation. According to density, HDL particles can be classified as HDL2, which are large and less dense, and as HDL3, which are small and dense.

Another property of HDL particles is their respective shape. Discoidal HDL particles are poor in lipids and contain mainly apolipoprotein A-1 (apo A-1), whereas spherical HDL particles are larger and contain cholesteryl ester and some triglycerides. The most abundant protein in HDL particles is apo A-1 followed by apo A-II which together make up close to 90% of the total protein content. HDL particles also contain proteins involved in lipid transfer such as cholesteryl ester transfer protein (CTEP) and phospholipid transfer protein (PLTP) and lipolytic proteins such as lecithin cholesteryl acyl transferase (LCAT). The varying content and/or impaired function of these proteins might be related to the anti- or pro-atherogenic effects observed for HDL particles in various setting.

The major atheroprotective effect of HDL is thought to be associated with its function in reverse cholesterol transport. Anti-inflammatory, anticoagulant and antioxidative effects have also been described. The anti-inflammatory and antioxidant effects are brought about by PON-1, whereas the anticoagulant properties of HDL seem to be related to its ability to reduce platelet activation and decrease expression of tissue factor.

These atheroprotective effects are lost in dysfunctional HDL. Current knowledge on the transition from functional to dysfunctional HDL is still fragmentary and mainly based on in vitro findings. However, it is generally believed that systemic inflammation seen in pathologies such as metabolic syndrome, diabetes, CAD and infections contribute to the conversion of HDL-C from an antiatherogenic to a proatherogenic molecule.

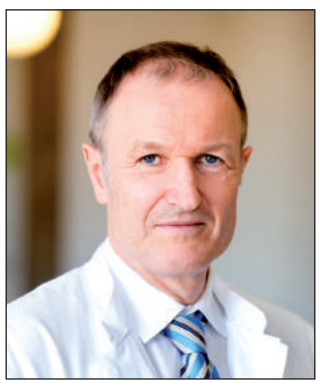
In summary, the controversy of the atheroprotective role of HDL-C fuelled by conflicting clinical data might be explained by the fact that the exact function of HDL-C and thus its role in the development of cardiovascular pathologies depends not so much on its quantity but more on its lipid and protein composition, with the small dense fraction having the highest antiatherogenic activity.

It thus seems likely that the concept of dysfunctional HDL-C will lead to assays with greater sensitivity and specificity and will shape future therapies, which will not only be based on quantitative but more so on qualitative modifications to change or modulate functions of HDL-C.

Don't miss: Is HDL atheroprotective? Current controversies
29 August 08:30-10:00 Baku - Village 1

Technology developments for tomorrow

In a Symposium this morning three experts look ahead to see what the future holds for artificial hearts, TAVI and mobile health technologies. Whatever they see, progress will certainly be swift.



Volkmar Falk, from the Charité University, Berlin, on artificial hearts

Currently, two types of total artificial hearts are available. The SynCardia device, approved by the FDA in 2004 as a bridge to transplant, has been used in over 1400 patients. The longest survived 1374 days before successfully receiving a donor heart. SynCardia has an external pneumatic pump carried in a back pack, and pneumatic tubes passing through the skin delivering pulses of air to two pumping chambers that force the blood into the circulation.

The second device is the Carmat bioprosthetic heart, implanted into the first patient by French surgeon Alain Carpentier in December 2013. Since then it has been used in three other patients. Carmat consists of right and left ventricular cavities, containing two miniaturised motorised pumps that displace the biomembrane and reproduce ventricular wall movement. Notably, surfaces coming into contact with blood are made from bovine tissue, and the device has sensors detecting blood pressure and volume changes to speed up or slow down the pump. The first patient lived for 74 days, the second for nine months, while the third died from renal failure. Carmat are planning the PIVOTAL study in 20 patients with low likelihood of receiving donor hearts.

A great deal of research is ongoing to improve artificial heart design and miniaturise pumps to make percutaneous implant techniques possible. Areas of endeavour focus on improving biocompatibility (by enabling endothelialisation of surfaces in contact with blood), energy transfer (to avoid transcutaneous wires and reduce infections), and feed-back algorithms (to allow pumps to respond to exercise).

Alain Cribier, from the University of Rouen, on transcatheter aortic valve implantation

"TAVI is today indicated for patients who are not good candidates for surgery. But for the future I predict the tables will turn and surgery will only be for patients who are not good candidates for TAVI.

TAVI is already well established for high risk patients, with the five-year analysis from the PARTNER trial showing 'mortality equivalence' between TAVI and surgery. Earlier this year, the PARTNER II trial, presented at the ACC meeting showed equivalence between surgery and the SAPIEN XT valve for intermediate risk patients, with significantly improved mortality for those treated via the transfemoral approach. The superiority of TAVI was even more significant with the last generation of Edwards valve, the SAPIEN 3 (PARTNER IIS3 trial).

In view of these results, we definitely need to rewrite the guidelines for TAVI. The PARTNER III trial, now ongoing, aims to compare TAVI and surgery in all comers older than 65 years. If the results are again equivalent, then surgery might soon be reserved for younger patients (the >5 year durability of TAVI valves remains unknown) or to those with severely calcified or bicuspid valves.

The four-fold predicted expansion of TAVI within the next decade will also be driven by remarkable technological advances, making the procedure simpler, safer and more cost-effective. With the newer devices, it is now possible in nearly 90% of patients to implant the valve like a stent, using a minimalist transfemoral route, under local anaesthesia and with very early discharge (within one to three days), which for patients represents a major advantage for TAVI over open heart surgery.

Partho Sengupata, from Mount Sinai, New York, on 'mobile' health

"In my view there are five classifications of mobile health technologies - smartphone health apps, smart phone connected devices, wearable and wireless devices, hand-held imaging platforms and miniaturised sensor-based technologies.

With over 160,000 smartphone health apps now available there's no doubt that digital medicine is here to stay. According to a law developed by Gordon Moore, one of the inventors of integrated circuits, there's exponential growth in technological progress, with the result we are likely to witness of the order of 20,000 years of 21st century progress in comparison to the hundred years achieved in the 20th century.

With all this data there's a danger clinicians will feel completely swamped and suffer from information overload. Such future scenarios point to the need to develop 'decision support systems' (much like those used today by airline pilots) helping doctors navigate the complex information.

We recently completed follow-up of a study where patients with structural heart diseases were randomised to smart clinics (using smart apps to monitor oxygen saturation, heart rate, blood pressure and pocket ultrasound) or usual clinical assessment. Results showed that those randomised to mHealth had more timely recognition and referral for corrective surgery and interventions with fewer hospital admissions and lower mortality. The implementation of apps and decision supports using machine learning would also lead to a more precise and quicker estimations of the problem and allow us to free up time to take better individualized care of our patients.

Don't miss: Looking at the crystal ball – Be prepared for the revolution! 08:30-10:00 Michelangelo - The Hub

Hypertension in developing countries

Roadmaps for management and roadblocks along the way

OF THE NINE TARGETS and 25 indicators of the Global Monitoring Framework adopted by the UN in 2011 for the control of non-communicable diseases, three were in the specific area of CVD: to reduce the incidence of heart attack and stroke through the wider prescription of drug therapy; to halt the rise in diabetes and obesity; and to bring about a 25% reduction in 'raised blood pressure'. And all before 2025.

As an action plan for these three daunting objectives, the World Heart Federation devised a set of roadmaps whose content not just marked out the rocky road to achievement but also profiled the roadblocks on the way and how they might be faced. And one of these roadmaps - on reducing CVD mortality through the prevention and management of raised BP - will be under the spotlight in a Joint Session this afternoon hosted by the ESC and International Society of Hypertension.

Professor Neil Poulter, who will take over as President of the ISH in September, says the challenge of meeting the hypertension target in developing countries 'is time', and 'what we can practically do before 2025', particularly in the face of the roadblocks he and his fellow authors saw in the WHF roadmap. These, says Poulter, include a widespread unawareness of hypertension risk or status, limited application of guidelines, inadequate resources for screening and medical treatment, and of course prioritisation in a huge catalogue of pressing healthcare needs. But overall, says Poulter, 'it all depends on resources'.

Poulter and his roadmap colleagues accept the widely held guideline definition that the 'normal' BP threshold is 140/90 mmHg, which in an ideal world would be confirmed in several readings. A systolic BP of 140-159 mmHg would be managed with at least dietary and other lifestyle changes, while measurements above 160 mmHg would require antihypertensive agents in addition. Yet even here, in what might be a relatively

Neil Poulter, incoming President of the ISH.
Aiming for a hypertension awareness rate of at least 60%.

straightforward recommendation, the barriers to achievement are huge; a 'care gap' between best practice and usual practice.

In most of the developing regions, and especially in Africa, a clear picture of hypertension is simply not evident. However, Poulter cites the PURE study of 2013 to report that awareness of hypertension in low income countries is no better than 40%, which in turn might lead to a treatment prevalence of 30% and a control rate of 13%. At 46%, 40% and 13% respectively, the equivalent global figures are not much better. 'They're hopeless,' says Poulter. 'We should be aiming for an awareness rate of at least 60%.' For only then, he argues, can the cascade of detection and management even begin.

Indeed, adds Poulter, awareness in low income countries may also be low because of a belief that hypertension is a disease of 'rich countries'. Hence, screening programmes may not even exist. And even if there is limited awareness, health systems may not be equipped for the prevention and management of hypertension.

With such challenges, Poulter and colleagues advocate opportunistic screening, blood pressure measurement at every clinic, pharmacy or doctor visit, which they describe as 'crucial'. In low resource settings, two readings in near sequence are recommended.

The PURE study also found that the lowest uptake of antihypertensive drugs was in low income countries and concluded that cost was still a limiting factor. Poulter, who is Professor of Preventive Cardiovascular Medicine at Imperial College London, and Co-Director of the Imperial Clinical Trials Unit, also notes an absence of clinical trials of antihypertensives in ethnic populations of Africa and South-east Asia. So medical treatment in low income countries will be empirical at best, guided only by reommendations developed for richer countries. It's Poulter's hope that a new trial in an African population can start early next year under his direction.

No-one's holding their breath that the 2025 targets in secondary prevention and hypertension can be universally met, but at least there *are* targets - and an action plan which identifies three key steps for real action: opportunistic screening, improved treatment, and education. With WHO attributing 45% of all CVD deaths to hypertension, even a little progress will have a substantial impact.

Don't miss: Improving hypertension management in low and middle income countries: low hanging fruit for helping reach the 25 x 25 NCD targets
29 August 16:30-18:00 Cairo - Village 3

What in your opinion is the most valuable lifestyle advice?

"From all the epidemiological studies we know that stopping smoking is the most important thing people can do to prevent cardiovascular disease. But there are big problems in that smoking is an addiction, and someone has to really want to stop for it to have any chance of working. There are a lot of psychosocial issues that make people want to smoke, making it important to tackle the problem from the societal perspective. I also believe that physicians need to lead by example. In the US there is a lot less smoking among doctors than in Europe."

Daniel Burkhoff, clinical researcher from New York City

"Exercise is the most important action people can take to improve their cardiovascular health. I advise both my primary and secondary prevention patients to do a minimum of 30 minutes moderate to heavy exercise each day. Exercise delivers a number of clinical benefits - raising HDL levels, improving endothelial function, and encouraging the growth of collateral arteries. In each consultation I share with my patients my own exercise regimen where I make sure to go on a run every day before work. When patients have cardiovascular disease, it's important to individualise their exercise so they can do it safely."

Eduardo Nagib Gaui, clinical cardiologist from Rio de Janeiro, Brazil

faces in the crowd

"Quitting smoking is one of the most important lifestyle changes people can make. That's along with exercise and improving your diet. About 30% of Norwegians were smokers a decade ago - now the figure is more like 13%. Prevention programmes have helped, although in my view smoking cessation clinics are not always necessary. They're only practical in big cities where it's easy for people to access them. And not everyone wants to go to a clinic. Education is a big factor in the likelihood of someone being a smoker or not. The more educated someone is, the less the chance they will smoke."

Maja-Lisa Lochen, professor in preventive medicine in Tromso, Norway

"There's no excuse for people not to be active - everyone can do something. Every movement made expends energy and improves the function of the cardiovascular system. In the Philippines, the Heart Association has launched a campaign to encourage people to take an hour of exercise a day and that includes walking. There are also four minute exercises that people can do in the office such as stretching or lunges. With the older patients we see, we recommend walking to avoid any complications and will monitor their heart rate. It's all about building exercise into your daily regime. The only cautionary advice I'd give is not to over-exercise especially if you're a patient with HF."

Helen Ong-Garcia, cardiologist and rehabilitation specialist, San Juan City, Philippines

ESC CONGRESS NEWS
Rome, Italy
27–31 August 2016

Editors-in-Chief:
Freek W.A. Verheugt, Kurt Huber
Medical writers:
Janet Fricker, Sophie Goodchild

Sub-editor:
Simon Brown
Graphic Design:
Hobby One Multimedia

Printing company:
System Graphic
Photography:
Patrik Engström

Sponsorship:
sponsorship@escardio.org
Project Management:
Ludwig Meert, lmeert@escardio.org

With the support of the
ESC Congress 2016 Press Committee.
Free distribution.