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EUROPEAN SOCIETY OF CARDIOLOGY®

TUESDAY 1 SEPTEMBER

Back to the future in resistant hypertension

Spironolactone 'overwhelmingly' the most effective

HOT LINE SESSION RESULTS

A drug whose history goes back more than 50 years could revolutionise today's treatment of resistant hypertension, a Hot Line session heard yesterday. The PATHWAY-2 study showed that spironolactone, first introduced in 1959 as a diuretic, controlled 60% of previously uncontrolled patients with resistant hypertension and was three times more likely than doxazosin or bisoprolol to exert control.

'Spironolactone is overwhelmingly the most effective drug treatment for resistant hypertension,' said study presenter Bryan Williams, from University College London. 'The result in favour of spironolactone is unequivocal and for the first time establishes a clear hierarchy for drug treatment of resistant hypertension which should influence future guidelines and clinical practice worldwide.'

The study, which has the global potential to influence treatment in 100 million people, offers a 'spectacularly cost-effective' approach, added Williams, since spironolactone is cheap and patients are at very high risk of cardiovascular events.

International guidelines recommend treating resistant hypertension with three BP-lowering agents - ACE inhibitors or ARBs, plus calcium channel blockers plus thiazide-like diuretics. 'However,' said Williams, 'despite 50 years of research the optimal drug treatment is still undefined.'

The PATHWAY-2 study, funded by the British Heart Foundation, randomised 335 patients with resistant hypertension (already treated according to guidelines) to sequentially receive 12 weeks of spironolactone (25-50 mg), bisoprolol (5-10 mg), doxazosin (4-8 mg modified release) and placebo. The study design allowed drug comparisons in each patient, with 230 completing all cycles.

Results showed that spironolactone reduced home systolic BP by 8.70 mmHg more than placebo ($p<0.001$), 4.26 mmHg more than bisoprolol/doxazosin ($p<0.001$), 4.03 mmHg more than doxazosin ($p<0.001$), and by 4.48 mmHG more than bisoprolol ($p<0.001$).

By the end of the trial, said Williams, there would only be 15 patients considered eligible for renal denervation trials in uncontrolled hypertension. 'PATHWAY-2,' he added, will have significant implications for patient recruitment into other trials.'

Bryan Williams, presented 'unequivocal' results from the PATHWAY-2 study of spironolactone in resistant hypertension, and from the PARAMETER study on arterial stiffness in the elderly.

ARNI now tested in elderly hypertension

The recently designated ARNI - angiotensin receptor/neprilysin inhibitor - of sacubitril/valsartan (also known as LCZ696) has already proved its efficacy in heart failure in the PARADIGM trial, reported at last year's ESC Congress. Now, in a bid to extend its indication, the PARAMETER study has shown that this same combination of sacubitril/valsartan significantly reduced central aortic systolic pressure (CASP) and central aortic pulse pressure (CPP) when compared to the standard ARB olmesartan in elderly patients with hypertension.

'An important finding of this trial,' said presenter Bryan Williams from University College, London, 'is that LCZ696 had an especially powerful effect on reducing night-time blood pressure – a strong predictor of cardiovascular risk.'

Following a wash-out period, 454 elderly hypertensive patients (mean age 68 years) were randomised to sacubitril/valsartan 400 mg qd or olmesartan 40 mg qd at 48 study sites in 12 countries.

Results at 12 weeks showed that LCZ696 reduced systolic blood pressure by 12.6 mmHg compared to 8.9 mmHg for olmesartan ($P=0.01$). Data further showed that LCZ696 reduced CPP by 6.4 mmHg, while olmesartan reduced it by 4.0 mmHg ($P=0.012$). The 24-hour ambulatory blood pressure was reduced by an additional 4.1 mmHg for LCZ696 patients, and central systolic blood pressure by an additional 3.3 mmHg ($P<0.001$ for both).

At 52 weeks no difference was found between the two regimens for central and brachial blood pressure, due to the allowance of add-on therapy. However, while 47% of patients taking olmesartan required add-on medication to achieve blood pressure control, only 32 % receiving LCZ696 did so.

Finally LCZ 696 produced a 34% reduction in background NT-pro BNP (the precursor for BNP in the circulation)

Continued on page 2

Don't Miss

- **10:00 & 14:00 - 15:30** — **London (Main Auditorium)**
  ESC Guidelines Sessions - 08:30 -
- **08:30 -18:00** — **Agora**
  Meet in the Agora for Rapid-Fire Sessions
- **10:00 - 11:00 & 15:30-16:30** — **Poster Area**
  Visit the Poster Area to discover new initiatives!
- **08:30 - 10:00** — **Hyde Park (The Hub)**
  Survivor of out-of-hospital cardiac arrest - acute and long-term management
- **10:00 - 11:00** — **San Marino (Village 2)**
  ESC General Assembly
- **10:10 - 10:50** — **St James Park (The Hub)**
  Meet the Editors of the European Heart Journal
- **11:00 - 12:30 & 16:30 - 18:00** — **London (Main Auditorium)**
  Hot Line Sessions
- **16:30-18:00** — **Hyde Park (The Hub)**
  ESC Cardiology Quiz

‘Reassuring’ safety data in two antihyperglycaemics

Patients with type-2 diabetes (T2DM) can safely take two antihyperglycemic drugs without increasing the risk of CVD complications, including heart failure, according to two separate studies presented at a Hot Line session yesterday.

Both the Evaluation of LIXisenatide in Acute Coronary Syndrome (ELIXA) and the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS) found there was no increased risk, even if patients had a history of heart failure.

Prior studies have established an association between anti-diabetic therapy and increased incidence of HF. Indeed, observations from SAVOR-TIMI 53 and also EXAMINE, two recent large trials, suggest an increased risk for hospitalisation for HF with the DPP-4 inhibitors saxagliptin and alogliptin respectively. This has prompted the European Medicines Agency and FDA to establish guidelines for clinical trials to ensure cardiovascular safety in glucose-lowering therapies. Thus, both the TECOS and ELIXA studies had important safety components in their design.

The core data from these two trials were presented at the American Diabetes Association congress in June. ELIXA was powered to establish non-inferiority and superiority of lixisenatide, a glucagon-like peptide-1 receptor agonist, over a minimum of 10 months. The study followed 6068 patients with T2DM and a history of MI (83%) or hospitalisation for unstable angina within the past six months following randomisation to daily injections of lixisenatide (n = 3034) or placebo (n = 3034). The primary endpoint was CV death, MI, stroke or unstable angina with a key secondary endpoint of HF hospitalisation.

The study found that the primary outcome occurred in 13.4% of the lixisenatide group and in 13.2% of the placebo group (HR 1.02; 95% CI 0.89-1.17), prompting study presenter Eldrin Lewis, from Harvard Medical School Brigham and Women’s Hospital, US, to conclude that lixisenatide was ‘a safe way of reducing glucose’. He reminded his audience that lixisenatide’s efficacy in lowering blood glucose had already been clearly demonstrated in earlier ‘metabolic’ studies.

The TECOS trial, said presenter Paul Armstrong from the University of Alberta, Canada, randomised 14,671 patients with T2DM and established CVD to the dipeptidyl peptidase-4 inhibitor sitagliptin (n = 7332) or placebo (n =7 339) in addition in both groups to usual care to achieve glycaemic control.

The primary aim of the study, he explained, was to demonstrate non-inferior cardiovascular risk between patients treated with sitagliptin plus usual care and with usual care alone plus placebo. The prespecified secondary endpoint was to analyse effects on hospitalisation for heart failure and related outcomes.

Results showed that sitagliptin did indeed meet the primary endpoint of non-inferiority to placebo (HR 0.98; 95% CI 0.88-1.09; P=<0.001) after a median follow-up of two years. Hospitalisation for HF was 3.1% for both groups (HR 1.00; 95% CI 0.84-1.20; P=0.95), and hospitalisation for HF or cardiovascular death was 7.3% for the sitagliptin group and 7.2% for the placebo (HR 1.2; 95% CI; P=0.81).

Armstrong described the findings as ‘reassuring’ to patients and prescribers. He said: ‘We can clearly conclude that sitagliptin can be safely used in T2DM patients without concern for worsening heart failure.’

ELIXA investigator Eldrin Lewis, left, described lixisenatide as a ‘safe way’ to reduce glucose, while Paul Armstrong, right, described risk findings from the TECOS study of sitagliptin as ‘reassuring’.

A definite maybe for extended DAPT in low risk bleeding

The controversial extension of DAPT beyond the recommended 12 months after DES implantation appears to confer no added harm in patients at low risk of bleeding, according to the Optimal Duration of Dual Antiplatelet Therapy After Drug-eluting Stent Implantation (OPTIDUAL) trial presented in a Hot Line session yesterday. However, there was no statistically significant reduction in isachaemic outcomes as measured by a primary endpoint of death, MI, stroke and major bleeding.

Presenter Gerard Helft from the Institut de Cardiologie, Pitié-Salpétrière University Hospital, Paris, said the trial findings suggest that the duration of DAPT could be increased in this patient group ‘beyond 12 months’ based on a ‘case-by-case decision’ - so the optimal duration of DAPT after PCI remains a topic of debate.

The aim of the OPTIDUAL study was to investigate whether continuing clopidogrel for up to 48 months would be superior to stopping the drug at 12 months in reducing adverse clinical events following DES implantation.

The study was conducted at 58 sites in France between 2009 and 2013 in a cohort of 1385 patients. All were free of MACCE or bleeding, had been on DAPT for one year, and had undergone PCI with at least one DES for either ACS or stable CAD. They were randomised either to extended DAPT (n = 695) or to remain on aspirin alone (n = 690) for an additional 36 months with follow-up every six months between 12 and 48 months.

Results showed that the primary endpoint of death, MI, stroke and major bleeding was reached in 5.8% of the extended DAPT group and in 7.5% of the aspirin-only group, a non-significant result. However, there was a statistically borderline reduction in post-hoc analysis of ischaemic outcomes of 4.2% in the extended DAPT group and 6.4% in the aspirin group.

Gerard Helft concluded that DAPT beyond 12 months should still be on a case-by-case basis.

Continued from page 1

ARNI in elderly hypertension

compared to 20% for olmesartan. Safety data demonstrated no significant differences in adverse events between the two groups.

The holy grail of systolic hypertension therapy, said Williams, is to achieve a ‘destiffening’ effect. The fact that release of BNP was reduced for LCZ696 provides indirect evidence that this may be occurring. ‘Currently studies are under way using MRI to directly measure changes in arterial distensibility following LCZ696 treatment,’ said Williams.

ARB effects on biomarker change in HT

Treatment with the angiotensin II receptor blocker telmisartan delivered greater beneficial effects on biomarkers than non-ARB therapy in hypertensive patients, according to the ATTEMPT-CVD study yesterday. The Japanese study, also published in the *European Journal of Preventive Cardiology*, showed that telmisartan promoted both smaller increases in plasma brain natriuretic peptide (BNP) and larger decreases in urinary albumin creatinine ratio (UACR).

While it is known that ARBs affect levels of biomarkers such as urinary albumin and BNP, studies measuring biomarkers in hypertensive patients and relating them to cardiovascular events have been rare. In this study Hisao Ogawa and colleagues from Kumamoto University, Japan, investigated the effect of an ARB and non-ARB on biomarker change and the incidence of cardiovascular events in hypertensive patients.

A total of 1228 hypertensive patients aged 40-80 years with at least one other cardiovascular risk factor (diabetes, renal, cerebral or peripheral artery factors) were randomly assigned to receive telmisartan (n = 615) or non-ARB standard treatment (n = 613). Patients were enrolled from 168 institutions throughout Japan.

Hisao Ogawa presented the first evidence that ARB treatment causes a smaller increase in plasma BNP and greater increase in UACR than non-ARB treatment.

Results showed that in comparison to baseline UACR changes in the ARB group were significantly steeper than in the non-ARB group (P<0.0010). The increase of plasma BNP over time in the ARB arm was significantly less than for the non-ARB arm. While fewer cardiovascular events occurred among patients in the ARB group, the difference was not statistically significant.

‘Taken together with the finding that there were no significant differences in blood pressure between the ARB and non-ARB groups throughout the treatment, this study provides the first evidence that ARB treatment suppressed an age-associated increase in plasma BNP independently of blood pressure,’ said the authors.

ESC/ERS guidelines for pulmonary hypertension

By António Vaz Carneiro
University of Lisbon School of Medicine, Portugal

and Victor Aboyans
Dupuytren University Hospital
Limoges, France

THE NEW 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension (PH) are authored by the Joint Task Force of the ESC and of the European Respiratory Society (ERS) and endorsed by the European Paediatric and Congenital Cardiology, the International Society for Heart and Lung Transplantation, the European League Against Rheumatism, and the European Society of Radiology.

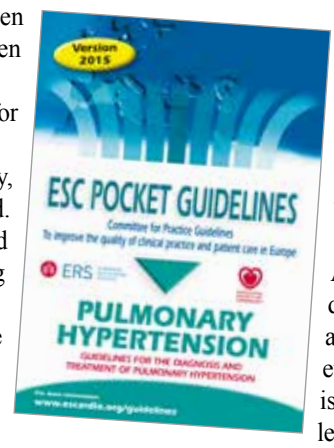
PH is defined as an increase in mean pulmonary arterial pressure (PAPm) ≥25 mmHg at rest as assessed by right heart catheterisation. It is a pathophysiological disorder which may involve multiple clinical conditions and complicate the majority of cardiovascular and respiratory diseases.

This latest edition follows the two previous ESC/ERS guidelines of 2004 and 2009 and is based on systematic literature review to identify new studies published since 2009.

The new clinical classification of PH includes five major types:
1. Pulmonary arterial hypertension (with two subtypes: pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis and persistent PH of the newborn)
2. PH due to left heart disease
3. PH due to lung diseases and/or hypoxia
4. Chronic thromboembolic PH and other pulmonary artery obstructions
5. PH with unclear and/or multifactorial mechanisms.

The main changes from the previous 2009 guidelines are:

- The table of contents has been simplified with three initial general chapters on classifications, basic aspects and differential diagnosis, two chapters on pulmonary arterial hypertension (PAH), and one chapter each for PH due to left heart disease, PH due to lung disease and/or hypoxia, chronic thromboembolic pulmonary hypertension, and PH due to unclear and/or multifactorial mechanisms, respectively.
- New wordings and parameters for the haemodynamic definition of post-capillary PH sub-groups have been adopted. Pulmonary vascular resistance has been included in the haemodynamic definition of PAH.
- An updated common clinical classification for adult and paediatric patients is reported.
- New advances in pathology, pathobiology, genetics, epidemiology and risk factors are reported.
- An updated diagnostic algorithm has been added in an independent chapter, and novel screening strategies are proposed in the web addenda.
- The importance of expert referral centres in the management of PH patients has been highlighted in both the diagnostic and treatment algorithms.
- New developments on PAH severity evaluation and on treatments and treatment goals are reported, including combination therapy and two new drugs recently approved. The treatment algorithm has been updated accordingly.
- New diagnostic and treatment algorithms are added in the chronic thromboembolic PH chapter, including general criteria for operability and for balloon pulmonary angioplasty.



Specifically, in what concerns therapy for PH, there are several recommended approaches:
1. General measures (physical activity and supervised rehabilitation; pregnancy, birth control, and postmenopausal hormonal therapy; elective surgery; infection prevention; psychosocial support; adherence to treatments; travel and genetic counselling).
2. Supportive therapy (oral anticoagulants, diuretics, oxygen, digoxin and other CV drugs and anaemia and iron status).
3. Specific drug therapy with calcium channel blockers (nifedipine, diltiazem and amlodipine), endothelin receptor antagonists (ambrisentan, bosentan, macitentan), phosphodiesterase type-5 inhibitors and guanylate cyclase stimulators (sildenafil, tadalafil, vardenafil, riociguat), prostacyclin analogues and prostacyclin receptors agonists (beraprost, epoprostenol, iloprost, treprostinil, selexipag) and experimental compounds and strategies.
4. Combination therapy.
5. Drug interactions.
6. Balloon atrial septostomy.
7. Advanced right ventricular failure.
8. Transplantation.

A treatment algorithm is also included and the diagnosis and treatment of PH complications are presented. Finally, end-of-life care and ethical issues are discussed. This same approach is followed for specific PH subsets (paediatric, left heart disease or lung diseases/hypoxia, from chronic thromboembolic pulmonary hypertension, etc).

At the end there is a definition of a PH referral centre and a complete online addenda with extra tables, figures and text with the pathology and pathobiology of PH, a proposal for a screening programme and a set of quality of life measurements.

A glass ceiling of careers in cardiology?

A session today aims to encourage greater female leadership

A SESSION this afternoon aims to provide a 'taster' of a unique residential programme for female cardiologists and cardiovascular scientists and the tools they need to find their individual leadership styles. This Special Session is in recognition of the ESC's new commitment to address barriers to female advancement. As a result, five members will be sponsored to attend a leadership programme designed to encourage professional women to develop their unique leadership styles rather than pitting themselves against traditional leadership models. The five were named during this congress as Chiara Bucciarelli-Ducci FESC (UK), Marisa Generosa Crespo-Leiro FESC (Spain), Sigrun Halvorsen FESC (Norway), Nina Johnston FESC (Sweden) and Susanna Price FESC (UK)

The session is the inspiration of Barbara Casadei, the ESC's Vice President for Scientific Affairs, who is on a personal mission to encourage more women from within the ESC to stand for committees and fellowships. 'The ESC is aware that the future will witness a gender flip in the profession, as women now represent more than 50% of medical graduates,' says Casadei. 'But, there is currently a disturbing discrepancy between the number of men and women standing for leadership positions both in the working place and ESC.'

While women now comprise one-third of the ESC membership, only 1.7% of them are ESC fellows compared with 6% of male members. Female professors of cardiology across Europe are scarce and women are similarly under-represented on the ESC Board, with Casadei - from the University of Oxford - being the only elected female voting member alongside 11 men.

Diversity in the leadership of any professional organisation is important, she insists, because it enriches that organisation by creating greater competiveness. 'Having a wider array of people involved allows one to see things from different perspectives, provides organisations with more ammunition in times of crisis and avoids wasting 50% of the talent.'

Barbara Casadei, ESC Vice President for Scientific Affairs and on a mission to encourage more women to take on ESC responsibilities.

There is moreover a general recognition that organisations aiming to survive and thrive need to embrace more women. A report by McKinsey & Co, 'The Business of Empowering Women', published in January 2010, showed that companies with gender-balanced executive committees have 56% higher operating profits than those with male-only committees.

The solution, says Casadei, is not to form women-only splinter groups, but to integrate women firmly into an organisation. 'One needs to equip women with tools that allow them to become confident enough to take some risks and embrace challenges and responsibilities,' she says.

To help promote women the ESC will be sponsoring five female ESC Fellows to attend the Women Transforming Leadership Programme at the Said Business School of the University of Oxford, from 5 to 9 October this year.

In today's session, Kathryn Bishop, the programme director, will provide an overview of the five-day residential programme and an interactive taster of what delegates can expect. The programme, launched in 2012, has been designed to help women reach new levels of personal and professional confidence by transforming their ability to affect organisational and social change. Delegates, who number around 30 women for each programme and come from all over the world, are drawn from a variety of backgrounds, including science, health, engineering, finance, and government. 'What's surprising is that the issues faced are the same,' says Bishop.

Throughout the residential week participants explore different styles of leadership, both traditional and contemporary. 'We aim to encourage women to examine different styles of leadership - to learn a broader set of leadership styles that they feel confident to use in different circumstances.'

All delegates leave Oxford with a personal action plan for their own leadership development and an understanding of their individual skills and strengths. A major bonus is their ready-made network of fellow participants with whom they have shared stories and leadership challenges.

In the interactive Special Session today Bishop plans to take one session from the Women Transforming Leadership programme to help participants explore the leadership challenges they face and how best to rise to those challenges. The highly interactive session will help participants answer the questions: what kind of leader are you and what kind of challenges are you best equipped to face?

Women transforming leadership programme: enabling women's careers in cardiology
1 Sep 12:45-13:45 Regent's Park - The Hub

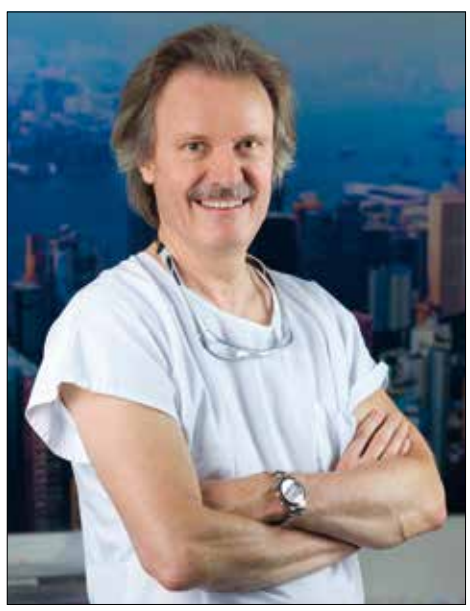
European Heart Journal continues its impact ascent

THE IMPACT FACTOR is not be everyone's favourite metric in medical journal publishing. It is slow, counting citations made more than a year ago, it favours reviews over original articles, and the final assessment may be dominated by just a few highly cited papers. Moreover, 'impact' is measured only by the number of citations in a limited period; what about impact on everyday treatment or on clinical research?

Nevertheless, the impact factor remains the most accessible measure of journal quality and journal success, and it is a tribute to the ESC journals that four of the top 15 journals in this year's Journal Citation Reports for cardiology were titles from the ESC's stable of journals. Moreover, five of the nine ESC titles set new impact factor records and the flagship, the *European Heart Journal*, increased its score from 14.723 to 15.203, another all-time high.

'We're still surprised at how successful we've been' says Editor-in-Chief Thomas F Lüscher (pictured). Having broken through into the exalted realm of double-digit impact factors in 2011, this latest score represents a move of almost five points in just four years and takes the *EHJ* ahead of *Circulation* and only behind *JACC* (with a new impact factor of 16.503) in the cardiology listing.

Lüscher attributes such a huge step forward for the *EHJ* to a greater global - and not just European - appeal. 'More and more



of our manuscripts are coming from US institutions,' he says, 'and we are very happy to attract the top US researchers. We are also increasing our appeal in Asia and Australia, and have strong relationships in Japan.' He adds that innovations like CardioPulse, which provide a forum for international news and comment, and editorials commissioned from international experts have also broadened the *EHJ*'s appeal.

There were several other striking impact factor moves for ESC journals - The *European Journal of Heart Failure* rose to 6.526, the *European Heart Journal Cardiovascular Imaging* from 3.669 to 4.105, and *Cardiovascular Research*, a journal strongly associated with the aims of this congress, from 5.808 to 5.940.

With around 3500 original manuscripts submitted each year and a rejection rate of around 90%, Lüscher is confident that the *EHJ*'s editorial policy of transferring well regarded papers to these more specialist sister journals is helping raise their quality and profile - and protecting the ESC family of journals from other titles. 'But I always feel bad about rejecting good papers,' he says, which is why one session at this congress aims to help investigators better prepare their manuscripts for journal submission. A Special Session this morning will set out 'the editor's criteria for good scientific papers', whose ingredients, says Lüscher, must include clarity, novelty and honesty. 'The statistical analysis is also very important,' he adds, 'and any paper now considered for publication is sent out for statistical review.'

With weekly publication introduced at the start of 2013, the *EHJ* has now joined a select list of high-ranking journals, which includes *JACC* and *Circulation*, but this, admits Lüscher, has surprisingly had no detrimental effect on impact factor. The increased frequency prompted a slight reduction in the size of each issue, which has now settled into a weekly rhythm of four original papers per issue and an additional wealth of news, opinion, invited review, guidelines and correspondence. The journal has also just introduced a novel feature of brief communications (of around 1500 words and one figure) on preliminary but stimulating work. There will also be more papers collected by topic in a single issue.

But perhaps the biggest sign of things to come is the huge role which the digital revolution is having on the *EHJ*. Podcasts of summaries and commentaries of key *EHJ* articles are now available as an 'issue @ a Glance' feature, with associated articles free to access. Downloads are running at about 10,000 per article featured, suggesting that the everyday influence of the *EHJ* may be even greater than its citation impact. 'It's very interesting,' says Lüscher, 'because the downloads are what physicians are reading - and the number of downloads is going up dramatically. I think this is influence . . . mentions on Twitter, blogs and other social networks. The impact factor is science, but it doesn't represent use in everyday practice.' But for the time being at least, it's the metric which matters, and right now a source of pride and satisfaction for the *EHJ*'s editorial team.

What are the editor's criteria for good scientific papers? Meet the editors of the European Heart Journal, 1 Sep
10:10-10:50 St James Park - The Hub

Solving the puzzles of the unstable plaque

DEVELOPING METHODS for risk stratification of vulnerable plaques to identify patients likely to benefit from intensive therapy is 'the holy grail of cardiology', according to a Symposium yesterday. For, following treatment of the initial culprit lesion by PCI, the risk of a coronary event from a further lesion has been estimated at 10% during the following year, and 5% in each of the subsequent four years,

Indeed, said David Erlinge from Skane University Hospital, Lund, Sweden, studies suggest that patients who have had an MI are very likely to have other vulnerable plaques, placing them at high risk of subsequent events.

The term 'vulnerable plaque' refers to a plaque at high risk of disruption leading to thrombosis. Retrospective autopsy studies suggest there are several histological types, one study showing that 55-60% of subjects had underlying plaque rupture as the aetiology; 30-35% erosion; and 2-7% thrombi attributed to calcified nodules. Another autopsy study in patients who had died from cardiac causes found that the most common underlying plaque morphology was a ruptured thin-cap fibroatheroma (TCFA) characterised by an overlying thin fibrous cap (measuring <65 µm) and large necrotic core.

But not all TCFAs will rupture, and neither will all ruptures result in cardiac events - and some vulnerable patients are likely to have vulnerable blood (prone to thrombosis) and a vulnerable myocardium (prone to arrhythmia).

David Erlinge, left, saw a potential benefit of bioresorbable stents in the treatment of vulnerable plaque, while Maria Radu described three imaging technologies for their characterisation.

The three major invasive imaging technologies used for evaluating vulnerable plaques, said Maria Radu, from Herlev Hospital and Rigshospitalet, Copenhagen, include intravascular ultrasound (IVUS), optical coherence tomography (OCT) and near infrared spectroscopy (NIRS).

- IVUS, which has a resolution of 100 to 200 µm, allows measurement of the lumen and external elastic membrane providing information on plaque volumes. The addition of radio-frequency signal analysis provides useful information about plaque composition.
- OCT, based on near-infrared light rather than ultrasound, provides resolutions of 10-20 µm, which is to date the only modality to directly visualise the TCFA in vivo. However, at the expense of increased resolution, it does not penetrate the plaque far enough to provide information of deep morphology or the external elastic membrane in the presence of extensive plaque, and thus is unable to assess plaque burden and remodelling.
- Unlike IVUS and OCT, NIRS does not provide structural information, but rather assesses the chemical composition of a plaque. More specifically, it provides a 'chemogram' of the cholesterol signal, and is thus able to accurately identify large cholesterol accumulations within lipid and necrotic cores.

'Each of these technologies has their pros and cons and so the dream scenario would be to have a catheter combining all three together to increase the accuracy of plaque characterisation,' said Radu.

Secondary prevention of patients who have already suffered an MI currently includes systemic therapy with statins, ACE inhibitors, beta-blockers, aspirin and calcium-channel blockers. But in future, said Erlinge, local therapeutic options might include the deployment of coronary stents to 'seal or stabilise' the plaque and reduce the risk of future events.

'The potential benefits of stent treatment need to be balanced against the risks of procedural complications, re-stenosis and stent thrombosis,' said Erlinge. 'These patients don't have angina or flow-limiting stenosis, which makes their balance of risks different.' The use of biodegradable stents in such circumstances, he added, was likely to be preferable. A recent study showed that implantation of the ABSORB bioresorbable vascular scaffold over vulnerable plaques led to the formation of a neointima layer resembling a thick fibrous cap known for its plaque stability.

In the PROSPECT trial after successful PCI of the target culprit lesions in nearly 700 patients, IVUS was used to examine the proximal 6-8 cm of all three coronary arteries, with patients followed for a median of 3.4 years. Results showed that plaque burden >70% in untreated non-culprit lesions was the most important characteristic associated with future events.

Now, the combined PROSPECT2 and PROSPECT ABSORB studies are building on the PROSPECT study to examine 900 patients with NIRS combined with IVUS and randomise 300 patients with a plaque judged to be at high risk of causing future coronary events to treatment with the Absorb bioresorbable vascular scaffold plus guideline directed medical therapy (GDMT) or GDMT alone. 'We want to see whether MI and sudden death are reduced,' said Erlinge.

Debate: To screen or not to screen for PAD?

No, says Charalambos Vlachopoulos
Athens Medical School, Athens, Greece

SCREENING for occult disease in the general population holds the promise of early detection and therapy. Nonetheless, because no test is perfect, screening is hampered by false-positives, which leads to unwarranted treatment and testing. According to the Bayes' theorem, post-test probability is a function of pretest probability (or disease prevalence) and the likelihood ratio of the test (ie, its diagnostic accuracy). Conceivably, if the disease is very rare or very frequent, and if our diagnostic tools are not accurate, then screening can be misleading.

The prevalence of PAD differs according to the vascular bed. The most common form is lower extremity artery disease (LEAD); its frequency is strongly age-related, being uncommon before 50 years and rising steeply at older ages.

Moreover, women are less likely to have LEAD. In the Framingham Study, the incidence of intermittent claudication was 0.4 per 1000 aged 35-45 years and six per 1000 aged 65 years and older; female incidence was around half that in men, but more similar at other ages. The presence of PAD in renal, mesenteric and upper extremity arteries is similarly low.

The tools for the detection of PAD include the ankle-brachial index (ABI), carotid ultrasonography, CT and MR angiography. ABI is solely used for the detection of LEAD; a threshold of 0.9 is used for diagnosis, but it is unclear if higher thresholds can be used to detect earlier, subclinical disease. Moreover, calcified vessels can lead to falsely high ABI values.

Carotid ultrasonogaphy can be used for the measurement of intima-media thickness (IMT) and the detection of plaques. Meta-analysed data from 45,828 individuals showed that common IMT measurements do not add significantly to the Framingham Risk Score for prediction of first myocardial infarction or stroke. The detection of carotid plaque has a superior diagnostic accuracy, although data are derived from smaller, mostly Caucasian cohorts and should be used with care. CT and MR angiography have a favorable profile for detecting PAD, but are hampered by radiation exposure and limited availability. Taken together, the aforementioned data on disease prevalence and characteristics of available screening modalities speak against the widespread screening for PAD.

An additional argument against screening the general population is that treatments greatly overlap with those for CAD, and are targeted in the modification of the common underlying risk factors with the inclusion of antithrombotic agents. Thus, and because PAD and CAD frequently coexist, a logical inference is that screening for CAD should precede screening for PAD and therapy superseded by treatment for CAD.

In conclusion, screening for PAD should not be performed in the general population, but reserved for selected populations considered at high risk for CVD. Acknowledgment of the strengths and weaknesses of different screening modalities will facilitate the interpretation of results and guide therapy.

YES, says Katerina K Naka
University of Ioannina Medical School, Ioannina, Greece

PAD is a prevalent and serious disease, more commonly found in lower extremity arteries - though carotid and other arteries may also be affected. Up to 10% of people aged <70 years and 15-20% >70 years have PAD.

PAD is a marker of extensive atherosclerosis and is independently associated with increased risks of vascular events and death. Subjects with PAD, even asymptomatic, are at high cardiovascular risk (equivalent to CAD) and are thus recommended for treatment. However, as up to 75% of PAD patients are asymptomatic, PAD is frequently under-diagnosed and under-treated.

In subjects without known CVD, a diagnosis of PAD, regardless of symptoms, requires treatment beyond general advice on lifestyle. This may include statins, antihypertensives and antiplatelet agents in most patients. The diagnosis of PAD is also associated with a poor prognosis in those with other known CVD, both stable and acute.

A careful medical history and detailed physical examination are two important tools in screening for PAD. In addition to CVD risk factors and co-morbidities, all types of symptoms suggesting disease in any vascular bed should be systematically looked for, although these are frequently absent or atypical. The cardiovascular examination should include palpation and auscultation of all relevant arteries, inspection of the feet, and note of the colour, temperature, quality of skin and hair, and presence of ulcerations or poorly healing wounds in the extremities. Carotid, abdominal or femoral bruits, pulse abnormalities in lower extremities, or inter-arm BP difference >20 mmHg are indicative of vascular disease.

A non-invasive screening procedure for PAD is the ankle-brachial index (ABI), calculated as the ratio of the ankle to brachial systolic BP and normal values range from 1.1 to 1.3. ABI values <0.9 indicate the presence of flow-limiting stenosis, while supranormal values (>1.4) are associated with medial calcification, often found in diabetes and chronic kidney disease. ABI is a reliable diagnostic tool for PAD with a 90% sensitivity and specificity compared with angiography and a strong marker for CVD. ABI can be measured easily, rapidly, non-invasively, safely and at very low cost may identify a large number of patients with previously unrecognised PAD.

Although no RCT evidence on screening for PAD exists, several guidelines have endorsed the use of ABI in risk assessment. The European guidelines for CVD prevention recommend ABI for detecting PAD in intermediate risk individuals (class IIa/B), similar to the ESH/ESC guidelines for hypertension. According to the ESC/EASD guidelines for diabetes, ABI may be considered a useful marker that adds predictive value to the usual risk estimate. The latest ACC/AHA guidelines recommend that ABI may be considered if, after quantitative risk assessment, a risk-based treatment decision is uncertain (class IIb/B). In the recent position paper from the ESC Working Group on Peripheral Circulation, ABI is recommended as a useful vascular biomarker for risk stratification in primary and secondary prevention (IIa/A).

The incidence of asymptomatic, under-diagnosed and under-treated PAD is high despite its association with a significantly increased risk for cardiovascular events. Thus, screening for PAD, especially among subjects considered to be at intermediate cardiovascular risk, using the non-invasive, widely available, easy-to-use and low-cost ABI, could have a beneficial impact on public health. The (cost-)effectiveness of such a screening intervention to guide decision-making in the prevention of cardiovascular events needs to be confirmed in the future.

Debates in peripheral artery disease 1 Sep 08:30-10:00 Chisinau - Village 6

European Heart Agency extends its postgraduate education

THE EUROPEAN HEART ACADEMY was established by the ESC two years ago to train future leaders in cardiovascular medicine. It is one of three divisions of the European Heart Agency, the ESC's Brussels bureau. By collaborating with universities in Europe, the Academy provides specialised courses that lead to academic degrees under the European Union Bologna Framework.

Current and upcoming programmes

Current programmes include the Postgraduate Course in Heart Failure which began in 2014 and is set to begin round two in January 2016. It was designed by the Heart Failure Association (HFA) of the ESC in collaboration with Zurich University and the Zurich Heart House in Switzerland, and leads to a Certificate of Advanced Studies.

Future leaders in arrhythmology should check out the Diploma of Advanced Studies in Cardiac Arrhythmia Management, which starts in October 2016 and is a collaboration between the Academy, Maastricht University Medical Centre and the ESC's European Heart Rhythm Association (EHRA).

The Master of Science in Translational Cardiovascular Medicine also launches soon. Designed for cardiovascular clinicians and researchers, it was developed with the German Centre for Cardiovascular Research (DZHK) and the University of Hamburg in Germany.

Master in Health Economics

The Master of Sciences (MSc) in Health Economics, Outcomes and Management in Cardiovascular Sciences begins this year in a course devised by the Academy and the London School of Economics. The programme is the ESC's response to the growth of economic evaluation as a central component of departments and hospitals. The practice of cardiovascular medicine is increasingly shaped by economics yet the relevant skills are not taught at medical school or during specialisation. Students will learn how to use clinical, economic and other types of evidence in decision-making.

The course is targeted at cardiologists and others who focus on CVD in their day to day work including policymakers and those working in the manufacturing industries.

The foundations of health economics and outcomes research will be taught in a number of compulsory courses on quality and outcomes, and students can tailor their choice of modules to their area of interest - and work with an LSE mentor to help meet their aims for the course.

Graduates will emerge with those competencies needed to apply for leadership positions in cardiovascular medicine, both in the traditional sense and in broader roles such as hospital management.

The European Heart Academy is fostering collaborations with selected universities to satisfy the increasing need for continuous medical education. More information on the roles and functions of the Academy can be found at the European Heart Agency stand, located at ESC Plaza P520.

How everyday life affects blood pressure

THERE HAVE BEEN many reminders here in London of the role played by lifestyle in the aetiology and management of hyptertension. Indeed, one widely reported study from Greece presented in a Poster Session on Saturday found that naps taken at midday - a habit favoured in some Mediterranean countries and the Far East but now in decline - are directly associated with reduced blood pressure and prescription of fewer antihypertensive medications. Manolis Kallistratos, a cardiologist at Asklepieion Voula General Hospital in Athens, thus asked if midday sleep is a habit, a privilege (because of the nine-to-five working culture) or an exercise for good health.

A study presented by Manolis Kallistratos, left, found lower systolic BP in those who took a one-hour daily siesta, while Toru Shirakawa raised concerns of pulmonary embolism in those watching more than five hours TV a day.

The study included 386 middle-aged patients with arterial hypertension whose midday sleep time (in minutes), 24-hour ambulatory BP, pulse wave velocity, lifestyle habits, BMI and left atrial size were measured. After adjustments, midday sleepers were found to have 5% lower average 24-hour ambulatory systolic BP (6 mmHg) than those who did not take a midday siesta. The duration of midday sleep was associated with arterial hypertension measures such that those who slept for 60 minutes at midday had 4 mmHg lower average 24-hour systolic BP readings. 'The longer the midday sleep, the lower the systolic BP levels and probably fewer drugs needed to lower BP,' said Kallistratos.

However, a long-term study described in the same Poster Session found that coffee-drinking (maybe as a pick-up after a short-term nap) was associated with an increased risk of cardiovascular events (mainly AMI) in young adults with mild untreated hypertension. The 12-year study in more than 1200 patients found that heavy coffee drinkers had a four-fold increased risk while moderate drinkers tripled their risk.

The study, said investigator Lucio Mos from the Hospital of San Daniele del Friuli in Udine, Italy, adds a little more to the controversial role of coffee consumption in the management of hyptertension. This study, which measured consumption as none (0), moderate (1–3 cups) and heavy (4 or more) in 1201 non-diabetic patients aged 18-45 years, found a linear relationship between coffee and risk of hypertension needing treatment. The association reached statistical significance for heavy coffee drinkers.

Because type-2 diabetes often develops in hypertensive patients at a later stage, the study also examined the long-term effect of coffee drinking on the risk of prediabetes. Again, a linear relationship was found, with a 100% (30-210%) increased risk of prediabetes in the heavy coffee drinkers.

Multivariable analyses over the 12-year showed that both coffee categories were independent predictors of cardiovascular events in these young adults, with hazard ratios of 4.3 (1.3-13.9) for heavy coffee drinkers and 2.9 (1.04-8.2) for moderate drinkers.

There was also a higher risk of fatal pulmonary embolism found in those who spent long hours in front of the television. Toru Shirakawa, a public health research fellow in the Department of Social Medicine at Osaka University in Japan, found that those watching TV for an average of five or more hours a day had twice the risk of fatal pulmonary embolism than those watching less than 2.5 hours daily. The findings come from the Japanese Collaborative Cohort (JACC) Study, a long-term investigation of how individual lifestyle affects disease mortality and cancer morbidity, and is the first prospective assessment of the link between prolonged TV watching and fatal pulmonary embolism. The results, presented in a Poster Session on Sunday, were derived from a study of 86,024 men and women aged 40-79 years who were followed-up for a median of 18.4 years until 2009.

The risk was most prominent in people under 60 watching TV for more than five hours a day - a six-fold greater risk of fatal pulmonary embolism than in those watching less than 2.5 hours (HR 6.49). 'Leg immobility during television viewing may in part explain the finding,' said Shirakawa. 'To prevent the occurrence, we recommend the same preventive behaviour used against economy class syndrome. That is, take a break, stand up, and walk around during the television viewing. Drinking water for preventing dehydration is also important.'

The role of the nurse practitioner?

Tomasz Baron, Non-invasive cardiologist, from Uppsala, Sweden

"In Sweden we use nurse practitioners widely, allowing them to work independently in our outpatient clinics, to look after the rehabilitation of MI patients and those with heart failure, and to check lipid levels. They have great expertise and generally have further degrees. They can offer a different perspective from doctors, because they have more time to understand the impact of disease on people's everyday lives. They can really focus on patient wellbeing and organise labour-intensive activities."

Sergio Bernal, General cardiologist, from Santiago, Chile

"The fact is that cardiologists make mistakes. Some may think they are perfect but it's impossible for us to know about everything. So nurse practitioners are crucial in alerting us when we do get it wrong. Nurses are around the patient the whole time, so they have an instinct if something is wrong. This can mean the difference between death and survival especially in the first 24 hours of treatment. It used to be just women who trained as nurse practitioners, but now we are finding more men too."

faces in the crowd

Theodore Spiro, Clinical research scientist from New Jersey, USA

"In clinical trials and drug discovery we work with many nurses who play an important role in such activities as clinical trial monitoring and drug safety. It is helpful to have people from a variety of backgrounds involved in our studies to provide different perspectives. In clinical trials doctors mainly think from the perspective of study endpoints; while nurses are altogether more patient-centric and likely to consider the impact that trials have on quality of life. They can really help to act as a patient advocate."

Daniel Jesuorobo, General cardiologist from Bayelsa State, Nigeria

"Where I come from there are only around five cardiologists in the entire region. So nurse practitioners are invaluable. Their main role is to educate people about their lifestyles, to reduce their risk of heart problems. This is a crucial job. We can't afford a lot of the equipment, so instead we focus on changing behaviour. Nurses also have a key role to play in clinic, teaching patients with hypertension about home monitoring, and cardiologists also rely on them in rural areas. If they went on strike it would be impossible to cope."

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Patient-centered approach when multiple cardiovascular risks coexist

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