ASCEND study results: Definitive data on the use of aspirin and omega-3 fatty acids in diabetic patients

Yesterday, the presentation of Hot Line results from the UK ASCEND (A Study of Cardiovascular Events in Diabetes) study brought us closer to finding out whether aspirin or omega-3 fatty acid supplements are useful for primary prevention of cardiovascular events in individuals with diabetes and no prior history of cardiovascular disease.

Starting in 2005, 15,480 patients with diabetes (94% had type 2) were randomised to receive aspirin 100 mg daily or matching placebo and, separately in a factorial design, omega-3 fatty acid supplements or matching placebo. Participants were followed for a mean of 7.4 years.1 Patients had a mean age of 63.3 years, 63% were male, 83% were overweight and 62% had hypertension. Diabetes was managed with agents other than insulin in most cases (58%) and, in fewer cases, by insulin (alone or with other agents, 25%) or diet alone (16%).1 The composite primary efficacy outcome (shown in 9% of patients overall) was non-fatal myocardial infarction, non-fatal stroke or transient ischaemic attack or vascular death (excluding confirmed intracranial haemorrhage). The primary safety outcome for the aspirin comparison (experienced by 4% of patients overall) was any major bleed.1 Information was available at the end of the study for over 99% of participants.

Professor Jane Armitage (Nuffield Department of Population Health, University of Oxford, Oxford, UK), who presented results of the aspirin analyses reports, “There was a significant 12% reduction in serious vascular events (8.5% vs 9.6%; rate ratio, 0.88; 95% confidence interval [CI], 0.79–0.97; p=0.01). In contrast, major bleeding was increased by 29% (41% with aspirin vs 32% with placebo; rate ratio, 1.29; 95% CI 1.09–1.52; p=0.003), with most of the excess being gastrointestinal (GI) bleeding and other extracranial bleeding.2”

“The benefits from avoiding serious vascular events with aspirin were largely counterbalanced by the excess of major bleeds it caused.”

Continued on page 2...
There was no effect on the composite outcome of a serious vascular event or revascularisation (11.4% vs 11.5% with placebo—)and no suggestion that benefits were beginning to emerge with longer follow-up.

“Average adherence to omega-3 fatty acid capsule was 77%, but this did not impact on how a person does his or her job. Burnout and disaffection can take a heavy toll on workplace challenges for cardiologists and what we can do to overcome them. Our aim was to probe the culture of cardiovascular medicine is a critical element in excellence in research and innovation through grants and fellowships, and by partnering in innovative research programmes that advance cardiovascular health.”

As well as the Research Funding Area, you should also attend today’s symposium on ‘Support for CV research and researchers – where is the funding and how to get it?’ (Monday, 12:45 – 14:00; Agora 2 – Agora), chaired by Axel Pries (Germany) and Gregoraz Gwasian (Belgium). The objective of the session is to facilitate researchers’ access to funding bodies and demystify the people and process behind successful applications for research funding.

“Part of our research strategy is to get young people interested to engage in research and support them through training and by partnering with funding agencies,” says Prof. Casadei. “Every trainee should engage in research if they aspire to become the best cardiologist they can be.”

Don’t miss! Today’s symposium at 12:45 in Agora 2 ‘Support for CV research and researchers – where is the funding and how to get it’.

Prof. Barbara Casadei concluded, “Investing in the people and promoting a supportive culture at work are transformational, low-cost interventions. The ESC will use the findings of the C-Change questionnaire to further develop strategic initiatives that support cardiologists and encourage institutions to create a work environment that allows professionals to aim high and be energised by work.”
Millimetre wave full body scanners do not interfere with cardiac implantable devices

There have been reports in recent years of electromagnetic interference (EMI) from security systems, such as metal detector devices (e.g. walk-through full body scanners) at airports, which could impact on the functioning of cardiac implantable electronic devices (CIEDs). Interference could cause the device to malfunction, potentially leading to spontaneous reprogramming of the device, an unprompted switch to a different mode, administration of inappropriate therapy or failure of therapy. Recently the US FDA called the electromagnetic compatibility of metal detectors with CIEDs into question. However, security checkpoints are changing due to the increasing use of millimetre wave body scanners, which can detect both metal and non-metal threats. Currently, people with CIEDs must be informed of the applied millimetre wave body scanner technique and are asked not to undergo a body scanner check.

Yesterday, a late-breaking study presentation by Doctor Carsten Lennerz (German Heart Center Munich, Department of Electrophysiology, Technical University Munich, Germany) reported that concerns over EMI with an innovative millimetre wave body scanner were unfounded. Dr. Lennerz says, “We wanted to provide reliable evidence on the safety of security body scanners for people with CIEDs to address patient anxieties and prevent unnecessary restrictions on these patients passing through security checkpoints.”

The investigators recruited 302 patients with CIEDs (pacemakers, implantable cardioverter defibrillators and cardiac resynchronisation therapy devices) who attended their routine follow-up appointment at the German Heart Centre Munich between May 2017 and July 2018. The patients were exposed to the electromagnetic fields generated by a millimetre wave body scanner (R&S QPS, Rohde & Schwarz, Germany) and were subsequently analysed for the presence of any EMI events. Once regular scans were completed, patients were positioned in close proximity to, and behind, the scanner itself. Based on the presented study the prevalence of EMI events from a millimetre wave body scanner is 0% (0/302) (95% confidence intervals 0-1.2).

The study found no evidence of electromagnetic interference from millimetre wave body scanners impacting the functioning of CIEDs.

Dr. Lennerz suggests that the findings are in line with what would be expected given the frequency used in the scanning device (70-80 GHz), the low penetration depth of millimetre waves in biological tissue and the very short duration of scans (approximately 100 milliseconds). He adds, “Our study suggests there is no need for specific protocols in the use of millimetre wave body scanners, which are widely used at airports and other security checkpoints, for individuals with CIEDs.”

“We believe that, on the basis of this study, no restrictions for the use of millimetre wave scanners on CIED patients are necessary.”

He thinks that these results could also help to avoid any stigma that individuals with CIEDs may be subjected to while undergoing security checks at airports or elsewhere.

ESC Congress News

ESC Congress News is brought to you by Editors, Steen Dalby Kristensen, Stephan Achenbach, Kurt Huber and Freek W.A. Verheugt. Medical writing assistance was provided by TMC Strategic Communications. We do hope you enjoy these daily contributions showcasing some of the exciting varied content of ESC Congress 2018.
MARINER: Rivaroxaban in patients at high risk of VTE after hospital discharge?

A significant proportion of acutely ill medical patients who are discharged from hospital are at risk of venous thromboembolism (VTE); the greatest risk is found within the first six weeks post-discharge, when the rate of symptomatic VTE more than doubles and the rate of fatal pulmonary embolism (PE) increases five-fold.1,2

The MARINER (Medically ill patient Assessment of Rivaroxaban versus, placebo IN reducing post-discharge venous thromboembolism (VTE) risk) trial investigated the efficacy and safety of extended thromboprophylaxis with rivaroxaban in hospitalised, medically ill patients deemed to be at risk for post-discharge VTE.1,2 The key primary efficacy outcomes (symptomatic VTE and VTE-related death) and safety outcome (major bleeding) were shared for the first time by Professor Alex Spyropoulos (The Donald and Barbara Zucker School of Medicine, Northwell Health System at Lenox Hill Hospital, New York, New York, USA) in a Hot Line session yesterday.3 The findings of this large randomised, double-blind, placebo-controlled study have been awaited with interest as current guidelines suggest against routine extended thromboprophylaxis (beyond the acute hospital stay) in this patient population.4 “This is due to uncertain overall clinical benefit further to experience in clinical trials of extended thromboprophylaxis, with reports of either limited efficacy or efficacy based on mainly reducing asymptomatic deep vein thrombosis or increased rates of major bleeding,” Prof. Spyropoulos explains.

Outlining the study details, Prof. Spyropoulos notes that more than 12,000 patients were randomised at 671 sites across 36 countries. Patients were assessed for risk of VTE based on a validated risk assessment model (International Medical Prevention Registry on Venous Thromboembolism [IMPROVE] score) and elevated plasma levels of a D-dimer biomarker. At hospital discharge they were randomised to either rivaroxaban (10 mg/day if creatinine clearance was 50 mL/min or greater or 7.5 mg/day if creatinine clearance was reduced [30 to <50 mL/min]) or placebo for 45 days.

At baseline, 18.3% of patients had reduced creatinine clearance and the most common diagnoses leading to study entry were heart failure (40.2%), respiratory insufficiency (26.5%), infectious disease (17.4%) and ischaemic stroke (14.4%). Just over half of the patients were taking aspirin and a small proportion (8.5%) had a history of cancer. Also at baseline, more than two-thirds of the population had elevated D-dimer levels and just over one-third had an IMPROVE score ≥4.

The MARINER study results showed that at 45 days, there was no significant difference between rivaroxaban and placebo for the primary efficacy endpoint: a composite of symptomatic VTE and VTE-related death.

The incidence of the primary efficacy endpoint was 0.83% for rivaroxaban compared with 1.1% for placebo (p=0.136).

“However,” says Prof. Spyropoulos, “pre-specified secondary analyses—that should be considered exploratory—examining only symptomatic VTE revealed a significant 56% relative risk reduction with rivaroxaban and with an incidence of 0.18% compared to 0.42% with placebo (p=0.023), as well as a significant 27% relative risk reduction in symptomatic VTE and all-cause mortality, with an incidence of 1.56% in the rivaroxaban group versus 2.00% in the placebo group (p=0.033).” He continues, “There was no significant difference between groups in major bleeding, which occurred at a very low incidence of 0.28% in patients receiving rivaroxaban compared with 0.19% in those receiving placebo (p=0.324). Lastly, the 7.5 mg dose of rivaroxaban did not appear to have a treatment effect in the group of patients with moderate renal insufficiency, with the incidence of the primary efficacy outcome being identical in the rivaroxaban and placebo groups (16.4% in both, p=0.394).”

“MARINER demonstrates that acute medically ill patients discharged from the hospital are at risk of VTE, for up to six weeks post-hospital discharge, even though these events are largely preventable,” says Prof. Spyropoulos. “Exploratory analyses of symptomatic VTE in this study that include non-fatal pulmonary embolism suggest a possible benefit of rivaroxaban. Given the very low rates of major bleeding with rivaroxaban seen in MARINER, these overall findings give us important insights into the optimisation of treatment strategies for preventing VTE in selected acutely ill medical patients once they leave the hospital, with potential to decrease the populational health burden of non-fatal VTE.”

Weight-loss drug does not increase major cardiovascular events in high-risk obese patients

The findings of the landmark randomised controlled trial, CAMELLIA-TIMI 61, to investigate the cardiovascular safety and efficacy of the weight-loss drug lorcaserin, were reported yesterday in a Hot Line session by Doctor Erin Bohula (Brigham and Women’s Hospital, Boston, Massachusetts, USA) from the Thrombolysis In Myocardial Infarction (TIMI) study.¹

The trial involved 12,000 overweight or obese patients with established cardiovascular disease or diabetes and at least one weight-related health condition, such as high blood pressure or high cholesterol, from 473 centres across eight countries.

CAMELLIA-TIMI 61 is the largest cardiovascular outcome trial to date for a weight-loss medication.

With a median follow-up of 3.3 years, lorcaserin did not increase the incidence of major adverse cardiovascular events (MACE)—its primary safety endpoint—compared with placebo (6.1% vs 6.2%, respectively; p=0.0001). “This is the first approved chronic weight-management medication to demonstrate safety for MACE in a dedicated, long-term cardiovascular outcome trial,” comments Dr Bohula. However, the trial did not reach its primary efficacy endpoint, the rate of the composite of MACE/hospitalisation for unstable angina/heart failure/ coronary revascularisation being similar with lorcaserin and placebo (11.8% and 12.1%, respectively; p=0.55).

“Lorcaserin effectively aids weight loss in obese patients at a high risk for cardiovascular events without increasing the rate of MACE.”

“Patients taking lorcaserin lost a greater amount of weight in the first year than those receiving placebo (4.2 kg and 1.4 kg, respectively, p<0.001) and at one year, significantly more of them had lost at least 5% of their body weight (39% vs 17%, p<0.001),” she notes, adding, “We also observed small but significant improvements in multiple cardiovascular risk factors, including triglyceride levels, blood pressure and new onset diabetes.”

Side effects of lorcaserin were consistent with those documented previously—including dizziness, fatigue, headache and nausea—and there was also a higher incidence of serious hypoglycaemia in patients receiving the drug. An echocardiographic substudy revealed a greater incidence of valvular disease at one year with lorcaserin (3.8% vs 1.3% with placebo), but this did not reach statistical significance.

“Whilst education and lifestyle modifications are key for weight management, some overweight or obese patients require additional help to manage their weight over the longer term,” explains Dr Bohula. “It is important for patients and physicians to know that pharmacologic agents that can assist with long-term weight management are not only effective for weight loss, but also safe from a cardiovascular perspective. The CAMELLIA-TIMI 61 trial is the first demonstration of cardiovascular safety for any weight-loss agent. As such, it provides an additional therapeutic option for these patients.”¹


ESC Congress 2018, Munich, Germany

Visit the ACTELION BOOTH D700 (Exhibition 2) to learn more about PAH and to download the Satellite Symposia key slides
Sessions of the day

7:30
Bach
General cardiology crash course - part 2

Beethoven
Blood pressure management in acute stroke

Handel
Join the new world of cardiac telehealthmentation

Schumann
Taking Point-of-Care ultrasound to Centre Stage

8:00
ESC TV Stage
Monday 28 August - Breakfast Buzz

8:30
Abstract-based Programme

Tunis - Library
Heart Failure: new targets for treatment

Science Box 1
Digital Health

Science Box 2
Centre Stage

Cardiac remodelling in athletes

Bratislava
Must hypertension be redefined?

Ljubljana
New frontiers in interventional cardiology

Brussels
What is new in implantable cardiac devices?

Novel approaches to sinus node disease

Yerevan
The Lancet - ESC symposium on heart failure

The European Heart Journal's advances in heart failure


Baku
Coronary CT angiography: a new "crystal ball"?

Vienna
Atrial fibrillation in heart failure

Brussels
Antithrombotic therapy in patients with lower limb chronic wounds: an update on when and how to use antiplatelet and anticoagulant drugs

Copenhagen
Moderating multiple antiplatelet or anti-coagulant therapies

Los Angeles
Aortic stenosis: treatments? I know it all! – You will be surprised... – Satellite Symposium organised by Medtronic

Bach
Atrial fibrillation patients who develop acute coronary syndrome: is there a role for aspirin? – Experts on the Spot organised by Pfizer

Beethoven
Support for CV research and researchers - Where is the funding and how to get it

10:05
Centre Stage

Meet the Task Force of the 2018 ESC/EACTS Guidelines on Myocardial Revascularisation

The European Heart Journal's advances in heart failure and vascular heart disease: the year in cardiology

Digital Health Stage

HF and Digital Health

10:10
ESC TV Stage
Meet the trialist - ARRIVE

10:15

Bach
Echoing approaches to the management of hypertension: combination therapy for all? - Experts on the Spot organised by Servier

Beethoven
Residual cardiac risk after an acute coronary syndrome: identifying, stratifying and managing patients at low risk of arteriogenic cardiovascular events - Experts on the Spot organised by AstraZeneca

Brahms
Atrial fibrillation patients who develop acute coronary syndrome: is there a role for aspirin? – Experts on the Spot organised by Pfizer

Handel
Atrial fibrillation patients who develop acute coronary syndrome: is there a role for aspirin? – Experts on the Spot organised by Bayer

Schumann
Oral anticoagulation in atrial fibrillation - Translating clinical trial data into daily practice - Experts on the Spot organised by Daichi Sankyo Europe GmbH

11:00

Munich
Hot Line Session 3

Centre Stage

Science Box 1

Clinical Importance of quantification in imaging

Science Box 2

Digital Health Stage

Remote monitoring/ECG/Readables

Agora 1

Cardiac anatomy for interventional cardiologists

Agora 2

Cardiac remodelling in athletes

Director of the World Rhythm of Cardiology

12:00

ESC TV Stage
Meet the trialist - ASCEND

12:45

Digital Health Stage

Start-up case studies told by the insider

13:00

Centre Stage

Brahms
Atrial fibrillation patients who develop acute coronary syndrome: is there a role for aspirin? – Experts on the Spot organised by Pfizer

Handel
Atrial fibrillation patients who develop acute coronary syndrome: is there a role for aspirin? – Experts on the Spot organised by Bayer

Schumann
Oral anticoagulation in atrial fibrillation - Translating clinical trial data into daily practice - Experts on the Spot organised by Daichi Sankyo Europe GmbH

Beethoven
Support for CV research and researchers - Where is the funding and how to get it

14:00

ESC TV Stage
Meet the trialist - COMMANDER HF

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Further information is available on the ESC Congress App
Benefit of aspirin for primary prevention of cardiovascular events remains unclear: ARRIVE trial results

Once-daily aspirin failed to reduce the rate of primary cardiovascular events in patients with no known cardiovascular disease and moderate cardiovascular risk, reports Professor J Michael Gaziano (Brigham and Women's Hospital, Boston, Massachusetts, USA) in a Hot Line session yesterday, with simultaneous publication in The Lancet.

The ARRIVE trial involved 12,546 participants with an estimated 10-year cardiovascular disease risk of 20–30% who were allocated daily aspirin vs 4.48% who were taking medications to lower blood pressure and lipids, which protected them from disease,” he adds.

There were considerably fewer events than anticipated (550 participants had a primary endpoint event versus the 1,488 expected), which may have impacted the findings.

The risk of total and non-fatal MI (HR 0.53; 95% CI 0.36–0.79; p=0.0014 and HR 0.55, 95% CI 0.36–0.84; p=0.0056, respectively) was reduced by aspirin in the per-protocol and modified intention-to-treat analysis, and the relative risk reduction of MI in the aspirin group was 82.1% for those aged 50–59 years.

Although mostly mild, gastrointestinal bleeds occurred twice as often in the aspirin group as the placebo group (0.97% vs 0.46%, respectively; HR 2.11; 95% CI 1.36–3.28; p=0.0007).

However, there was an unexpectedly low number of cardiovascular events that occurred overall. “The event rate was more in line with what we would expect to see in a population at low risk of cardiovascular events,” says Prof. Gaziano. “This may have been because some participants were taking medications to lower blood pressure and lipid, which protected them from disease,” he adds.

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Although mostly mild, gastrointestinal bleeds occurred twice as often in the aspirin group as the placebo group (0.97% vs 0.46%, respectively; HR 2.11; 95% CI 1.36–3.28; p=0.0007).
Based on a patient’s home measurement, evidence to suggest that doctors can diagnosis of high blood pressure, as Prof. De Backer highlights. “There is now more control of blood pressure is very, very poor.” The first main change since the previous ESC/ESH Guidelines in 2013 relates to second is that even when it is diagnosed, problems with detection and screening; the is a silent, chronic condition so there are hypertension; definitions are still based on doctors’ office measurements. However, it is accepted that there are more devices around for the measurement of blood pressure that are cheaper and more easily available than they used to be, and that these are being used by patients at home. Diagnosis can therefore now be based on home/ambulatory measurements by the patient, not just at the doctor’s office.”

“New evidence has also come to light,” says Prof. Heagerty, “that suggests the target for acceptable blood pressure control should be lowered, and it is now 130/80 for the majority of patients.” Indeed, the findings from the SPRINT study, which also informed the recent ACC/AHA Guidelines, showed that treating systolic blood pressure to a lower target significantly reduced the rates of cardiovascular events and death.

“Patient follow-up and more attention to treatment compliance will become even more important.”– Prof. De Backer.

Any other significant changes? Prof. De Backer explains, “There is emphasis on the importance of looking at a patient’s total cardiovascular risk, not just blood pressure. Experts advise that we should be measuring hypertension-meditated organ damage; if this is present, then stronger intervention is urged.” Indeed, the updates cover drug therapy extending to additional groups of patients. “There is a section at the end covering important subgroups, such as pregnant women, certain ethnic groups and those with ‘white-coat’ hypertension, in which treatment strategies are different,” says Prof. De Backer.

The new guidelines are planned to replace the 2013 guidelines in 2019 Clinical Practice Guidelines. The guidelines will provide specific recommendations on the management of different clinical scenarios, such as patients with suspected CAD, others with known chronic chest pain, asymptomatic and symptomatic patients with long-standing CAD and patients who have recently undergone successful revascularisation. All these, plus many more clinical scenarios, will be included in this new version of the Clinical Practice Guidelines and will be better classed under the umbrella term of CCS than being reduced to a single condition of ‘stable CAD’ or ‘stable angina’. As with heart failure, clinical presentations will be conveniently categorised as either acute or chronic coronary syndromes, accurately covering the different stages of the disease.

Updated future 2019 ESC Guidelines on the management of ‘chronic coronary syndromes’ to replace prior ESC Guidelines on ‘stable coronary artery disease’

In 2019, new Clinical Practice Guidelines are planned to replace the 2013 recommendations for the management of stable coronary artery disease.

As part of this comprehensive update, the Task Force, led by William Wijns and Juhani Knuuti, have proposed a change in nomenclature from ‘stable coronary artery disease’ to ‘chronic coronary syndromes (CCS). A key rationale is that although coronary artery disease (CAD) often seems ‘stable’ in between acute events, the underlying disease status is anything but ‘stable’. Atherosclerotic plaque accumulation is a dynamic process that can change over time to include growth, stabilisation or regression, as well as changes in plaque composition or thrombosis, depending on lifestyle, risk factor modulation and pharmaceutical therapies. The change to CCS has been proposed to more accurately represent this changing pathophysiology, for the better or the worse, over the continuum of the disease.

2018 ESC/ESH Joint Guidelines for the Management of Arterial Hypertension provide updated recommendations for the diagnosis, risk reduction and treatment of patients with this condition.1 Professor Anthony Heagerty (Division of Cardiovascular Sciences, University of Manchester, Manchester, UK) and Professor Guy De Backer (Department of Public Health, Ghent University, Ghent, Belgium), Review Coordinators for these guidelines, summarise why the new changes are so important and what they will mean for clinical practice.

“There are two key issues,” explains Prof. De Backer. “The first is that hypertension is a silent, chronic condition so there are problems with detection and screening; the second is that even when it is diagnosed, control of blood pressure is very, very poor.”

The first main change since the previous ESC/ESH Guidelines in 2013 relates to diagnosis of high blood pressure, as Prof. Heagerty highlights. “There is now more evidence to suggest that doctors can diagnose hypertension more confidently based on a patient’s home measurement, which reduces the number of people with ‘white-coat syndrome’ who are treated unnecessarily.” Prof. De Backer continues, “It’s important to note that the new guidelines do not change the definition of hypertension categories, as the recent American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines have; the ESC/ESH Guidelines still include well-established categories, such as ‘optimal’, ‘normal’, ‘high-normal’, ‘grade 1, 2 and 3 hypertension’ and ‘isolated systolic hypertension’, definitions which are still based on doctors’ office measurements. However, it is accepted that there are more devices around for the measurement of blood pressure that are cheaper and more easily available than they used to be, and that these are being used by patients at home. Diagnosis can therefore now be based on home/ambulatory measurements by the patient, not just at the doctor’s office.”

“New evidence has also come to light,” says Prof. Heagerty, “that suggests the target for acceptable blood pressure control should be lowered, and it is now 130/80 for the majority of patients.” Indeed, the findings from the SPRINT study, which also informed the recent ACC/AHA Guidelines, showed that treating systolic blood pressure to a lower target significantly reduced the rates of cardiovascular events and death.

“We can now provide increased protection to more patients because the target for blood pressure control has been lowered”–Prof. Heagerty.

Although more patients can now be treated, Prof. Heagerty acknowledges that this change may cause a degree of nervousness among the prescribing community. “Firstly, a larger number of patients will require drug treatment as well as lifestyle advice to achieve the new target for blood pressure control, and secondly, additional patients will need more than one drug. There will be concerns among doctors relating to two areas: the first is the possibility of side effects—although if drug regimens are selected to suit individual patients these will be kept to a minimum—and secondly, some patients will get very low pressures and suffer consequences such as falls, but again, careful monitoring should avoid such issues.”

And what about any changes to drug therapy? “Previously, it was recommended to start with one agent and add others in a step-wise manner,” says Prof. De Backer. “Experience showed, however, that this was insufficient, so the new recommendation is to start with two anti-hypertensive agents in the large majority of patients (those without intolerance or contraindications).” In terms of how this might impact clinical practice, both experts are clear. “There will be an increase in the use of low-dose combination therapy, i.e. fixed dose combinations, which will reduce the pill number,” says Prof. De Backer. Prof. Heagerty agrees. “Patient compliance is increasingly recognised as a big issue and there is a need to minimise the number of pills taken in an effort to improve compliance rates,” he says.

Any other significant changes? Prof. De Backer explains, “There is emphasis on the importance of looking at a patient’s total cardiovascular risk, not just blood pressure. Experts advise that we should be measuring hypertension-meditated organ damage; if this is present, then stronger intervention is urged.” Indeed, the updates cover drug therapy extending to additional groups of patients. “There is a section at the end covering important subgroups, such as pregnant women, certain ethnic groups and those with ‘white-coat’ hypertension, in which treatment strategies are different,” says Prof. De Backer.

The main changes are summarised in a table at the end of the full document and, similarly, there is a table of gaps in the scientific evidence detailing which new studies are required. These new guidelines are therefore more accessible and easier to read for busy clinicians and researchers alike.”

Fourth Universal Definition of Myocardial Infarction, outlines the main take-home points from this latest update.

“The diagnosis of myocardial infarction (MI), once centred around electrocardiographic (ECG) findings, changed markedly with the introduction of biomarkers,” Prof. Hasdai says. “In 2000, the first definition of MI was published, based primarily on circulating levels of cardiac troponin (cTn).” The main principle of the definition was that myocardial injury detected by abnormal biomarkers in the setting of acute myocardial ischaemia should be labelled abnormal biomarkers in the setting of acute myocardial ischaemia, as evidenced by the ECG or by imaging modalities of cardiac function or coronary anatomy, and the criteria for the five MI subcategories remain in place.” The document also attempts to firm up on the identification of type 2 MI, which can be a cause of confusion for some clinicians. “Type 2 MI results from a mismatch between oxygen supply and demand,” Prof. Hasdai recaps. “The update identifies situations associated with myocardial injury that have up until now been loosely labelled as type 2 MI. These include embolism, spontaneous dissection and spasm, along with underlying coronary atherosclerosis without plaque disruption. This may help doctors to more easily distinguish type 2 MI from other injury and to target management accordingly,” he suggests.

“The 2018 update describes in detail the use of high-sensitivity cardiac troponin assays and gives clinicians valuable insights into laboratory and clinical pitfalls.”

“Specifically,” says Prof. Hasdai, “the update discusses the recently introduced rapid rule-out and rule-in high-sensitivity cTn-based protocols for patients presenting with chest pain and identifies situations in which they may be particularly valuable.” Other areas addressed in the update include the intensively debated issue of peri-procedural MI definition and the distinction between peri-procedural myocardial injury and MI. In Prof. Hasdai’s opinion, “The Fourth Universal Definition of MI uses the latest knowledge and analytical tools to provide clinicians with a comprehensive, easy-to-use guide enabling them to accurately diagnose MI in daily practice.”

Eugene Braunwald: Coronary artery disease 10 years from now – my predictions

Prof. Eugene Braunwald

Today, Professor Eugene Braunwald (Distinguished Hersey Professor of Medicine at Harvard University, Boston, Massachusetts, USA) will join other leading lights in a session on the future of cardiology to share his expectations for the management of coronary artery disease (CAD) in the next decade.

Experience Prof. Braunwald live discussing CAD in this afternoon’s session ‘Cardiology 10 years from now – my predictions and how to get yourself ready’ Today, 11:00 – 12:30; Ankara – Spotlight Village

“CAD remains the most important arteriolar disorder, responsible for an enormous number of deaths and morbidity, so it almost goes without saying that efforts to reduce its incidence are incredibly important,” begins Prof. Braunwald. “I can see advances in three main areas – each a soldier in the battle against CAD – that will really improve the way we go about tackling this disorder.”

“The first approach concerns the development of non-invasive coronary artery imaging,” he says. “Up to now, invasive angiography has been the gold standard for assessing coronary arterial lesions. But scientists have been working hard to find accurate non-invasive techniques, such as those combining magnetic resonance imaging with positron emission tomography to detect vulnerable plaques and to distinguish them from those less likely to be of risk.” Prof. Braunwald explains. “These types of diagnostic techniques are a major step forward in more specifically identifying which lesions and which patients we need to focus on.”

“The second area,” continues Prof. Braunwald, “is the use of genomics to ascertain and define the risk of CAD with greater precision. We already have the classical, well-characterised risk factors, including cigarette smoking, diabetes, hypertension and elevated cholesterol, and these remain valid and important in identifying patients at a high risk of CAD. Add to these genomic analyses, which are improving all of the time, and you get another dimension to risk stratification. By combining the classical and the new genomic approaches we can achieve a really exquisite, refined analysis which will enable us to more accurately identify patients at various levels of risk,” he says. “The ability to effectively target medication to those patients with the greatest need – thereby optimising healthcare resource use – will apply precision medicine to CAD.”

“The last approach, which in my opinion is the most interesting,” suggests Prof. Braunwald, “has to do with new drugs developed. In the last few years, the use of monoclonal antibodies to inactivate circulating PCSK9 – and thereby lower low-density lipoprotein cholesterol – has attracted great attention. However, while quite effective, these drugs need to be injected every 2–4 weeks and they are very expensive. Scientists have now developed a new drug, incilisarin, which, rather than blocking the action of PCSK9, inhibits a vital step in its production. The real advantage of this drug is that it needs to be administered only every 6 months or even yearly to lower cholesterol.” Prof. Braunwald goes on to make what he calls “an outrageous suggestion”

“Given that inhibition of PCSK9 production will be able to actually prevent CAD if begun early enough in a person’s life, I would propose that such a drug be administered on a regular once- or twice-yearly basis to everyone over the age of 30 years.”

“This approach would have a profound effect on reducing the development of CAD in populations. The cost of delivering such a drug would be outweighed by the reduction in health care costs associated with treating people with established CAD. However, this approach will have to be shown to be feasible and safe.”

Summing up, Prof. Braunwald is enthusiastic. “With the three-pronged approach of more accurate, non-invasive diagnostic techniques, more accurate risk assessment and new drugs to lower cholesterol, the future for CAD prevention and management is bright.”

European Heart Agency – Creating policies for CVD prevention

The ESC’s European Heart Agency, based in Brussels, is a rather new strategic branch of the society, aiming to cover fast-evolving realities in the cardiovascular domain. It was opened in February of 2013, close to the European Parliament, in order to establish a firm base in the political capital of Europe. It has two distinct components:

The European Heart Health Institute, through four different units, covers ESC activities related to health economics and public policy, CVD prevention, EU research funding, novel technologies, quality assessment and health care management.

The European Heart Academy works to build and strengthen cooperation between ESC’s expert cardiologists and top-tier academic institutions to offer specialised executive programmes that help train future leaders in cardiovascular medicine.

By influencing relevant aspects of policy and shaping new projects and future leaders, the European Heart Agency is a key driver in the ESC’s mission to reduce the burden of CVD.

“It is our belief that public policies must be put in place to encourage CVD prevention but also to reduce the health care gaps between the ESC member countries. The European Heart Agency in Brussels was established so that the ESC could have greater input in these all-important policy decisions.” Professor Panos Vardas, Chief Strategy Officer of the European Heart Agency.

Paving the way for innovation in medical devices

Prof. Alan Fraser

In just two years’ time, significant changes in European regulations for new medical technologies will come into force.

“With over 500,000 medical devices available in Europe, including many high-risk implantable devices that are used in our daily practice, cardiovascular medicine will be impacted enormously,” says Professor Alan Fraser (University Hospital of Wales, Cardiff, UK), Chair of the ESC EU Regulatory Affairs Committee on Medical Devices, following yesterday’s session on innovation in medical devices.

“EU legislation determines the types of medical devices doctors can access and this impacts clinical practice.”

“Medical devices are essential to modern medicine and we couldn’t treat our patients without them,” says Prof. Fraser. “The ESC has been working with EU policymakers since 2010 to clarify and strengthen the existing legal framework which determines what devices are made available on the EU market,” he says. “Today we are pleased to see that the new legislation addresses many of the concerns we raised.”

“For the first time, safety and clinical performance data for each new device obtaining the CE mark will be publicly available.”

Passed in May 2017, the law moves beyond the previous requirements to establish that a medical device is safe and that it performs the task it was designed for: “From 2020, every device used by cardiologists in the diagnosis and treatment of patients will be subject to greater scrutiny and reinforced requirements for clinical evidence,” says Prof. Fraser. “In addition, high-risk devices will now be required to show a positive impact on clinical outcomes.” He thinks these new provisions are extremely good news for clinicians and for patients. “The legislative changes will foster high standards for medical devices. Clinicians will feel more confident in their clinical decisions and choices of device and patient safety will be improved.”

“This new legislation provides doctors with an exciting opportunity to become more actively involved in shaping the regulatory landscape.”

The new regulations will also require greater involvement of health care professionals. For example, expert panels and expert laboratories will be designated to provide scientific, technical and clinical advice. Individuals will also have the opportunity to answer calls for volunteers to participate in ad hoc Expert Working Groups. Prof. Fraser recognises that this is unfamiliar territory for many doctors, which is why he was pleased to be involved in yesterday’s session, where these general elements were explained and concrete examples provided, with reference to electrophysiology and software as a medical device. ESC members wishing to know more may also consult the ESC website and/or contact the ESC Advocacy Team.


www.escardio.org/ESC2018
Having recently retired after 20 years as Director of the Department of Cardiac Surgery at San Raffaele University Hospital, Milan, Italy, Professor Ottavio Alfieri is not one to slow down too much.

He continues to be active in his department—operating, being involved in clinical activities, supervising others—doing what he loves to do, but without the admissions to the ICU that he enjoyed as a younger doctor. It is clear that the passion he has for his work has not dampedened since he graduated from the University of Parma, Italy in 1971. “As a young graduate, I was full of enthusiasm, energy and ideas,” he says. “At that time, cardiac surgery was an incredibly exciting discipline that had just gone through a pioneering phase. We had seen successful treatment of congenital heart disease, valvular disease, coronary heart disease and heart failure; the first heart transplant was in 1967 and the first clinical implementation of a total artificial heart in 1969. It was a very exciting time when anything seemed possible, and that was appealing to me.”

Prof. Alfieri lists three precise principles as the driving force behind his early career. “Firstly, to work and learn in the best centres in the world, should receive clear and full explanation of their diagnosis and the risk of recurrence, hypotension should receive clear and full reassurance and advice on how to avoid triggers. The cornerstone of treatment and have a high impact in reducing the recurrence of syncope,” says Dr. Moreno. The current guidelines also cover some of the non-cardiovascular causes of transient loss of consciousness, which can be very useful for the cardiologist, and include the increased role of prolonged ECG monitoring. A further new aspect is the support of video-recording at home, with mobile phones, of unclear episodes of syncope in order to provide more information to assist with aetiological analysis. The establishment and goals of Syncope Management Units are described in detail, in terms of structure, tests and assessments, access and referrals, the role of the Clinical Nurse Specialist, and outcome and quality indicators. Dr. Moreno adds, “A new chapter is included that provides clear definitions of all the terms that may be related to syncope, in order to avoid frequent confusion–this will be very helpful for cardiologists.”

As to what these changes may mean for clinical practice, Dr. Moreno is clear. “As most episodes of syncope occur away from the hospital and have fully ended by the time of consultation, a significant amount of speculation is always involved in the diagnostic process. Clinicians following the present guidelines should feel reassured in their daily work that they are complying with the highest standards of care according to the ESC.”
Gastrointestinal and genitourinary bleeding in vascular patients treated with antithrombotic drugs should stimulate a search for cancer

Patients were randomised 1:1 to one of three groups: rivaroxaban (2.5 mg twice daily [bid]) plus aspirin (100 mg/day), rivaroxaban alone (5 mg bid), or aspirin alone (100 mg/day). The mean duration of follow-up was 23 months.

“In COMPASS, the most common site of bleeding was the gastrointestinal (GI) tract, and most of the increase in GI tract bleeding with rivaroxaban occurred in the first year after starting treatment.”

Major bleeding (defined according to modified International Society on Thrombosis and Haemostasis criteria) occurred in 3.1% of patients treated with the rivaroxaban plus aspirin combination, compared with 1.9% of patients receiving aspirin alone (hazard ratio [HR] 1.70; 95% confidence intervals [CI] 1.40–2.05; p<0.0001). Compared with aspirin, the combination did not result in a higher incidence of intracranial or fatal bleeding. “Notably, most of the increase in bleeding occurred in the GI tract, and typically during the first year after starting study medication,” Dr. Eikelboom remarks.

New analyses have revealed a strong relationship between GI bleeding and new GI cancer diagnoses, as well as between genitourinary (GU) bleeding and new GU cancer diagnoses.

“GI bleeding was associated with a substantial (12-fold) increase in diagnosis of new GI cancers,” Dr. Eikelboom continues. “Among patients with GI bleeding who had not been previously diagnosed with GI cancer, 7.8% were subsequently found to have a new GI cancer, compared with a 0.9% rate of GI cancer without GI bleeding (HR 12.9; 95% CI 9.77–17.0; p<0.0001).” A similar pattern was evident for GU cancers: among patients with GU bleeding who had not been previously diagnosed with GU cancer, 13.4% were subsequently diagnosed with GU cancer, compared with a 0.3% rate of new GU cancer without GU bleeding (HR 83.4; 95% CI 58.6–118.6; p<0.0001). More than 75% of these cancers diagnosed after bleeding were identified within 6 months.

Dr. Eikelboom concludes, “Although overall cancer rates were similar in the three treatment groups, the early increase in GI bleeding with rivaroxaban-based resulted in earlier diagnosis of GI cancer in these patients. By reducing major cardiovascular events and mortality, the combination of rivaroxaban and aspirin already produces a clear net benefit, and by unmasking GI cancers at an earlier stage, the combination could potentially lead to the added benefit of improved GI cancer outcomes.”