News

New ESC Guidelines on heart failure and CVD prevention

The European Society of Cardiology (ESC) has published two new guidelines – ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012, and European Guidelines on cardiovascular disease prevention in clinical practice (version 2012).

Heart failure

The recommendations on devices, drugs and diagnosis in heart failure were developed by the ESC in collaboration with a heart failure association of the ESC.

There have been several major updates since the previous guidance published in 2008. The new updates include:

- In devices, left ventricular assist devices (LVADs) have been hailed as a step change in the management of heart failure. LVADs are more reliable and lead to fewer complications than in 2008. Until now, LVADs have been used as a temporary measure in patients awaiting a heart transplant. Professor John McMurray (Glasgow, UK), chairperson of the ESC Clinical Practice Guidelines Task Force, says: "LVADs will increasingly be used as a treatment in their own right, not just as a temporary support while awaiting transplantation". Also in the device arena, new transcatheter valve interventions are discussed. "These interventions offer the possibility of treating aortic stenosis in patients who are unsuitable for surgery," says Professor McMurray.
- A new indication for cardiac resynchronisation therapy (CRT) in patients with mild symptoms. More evidence from new trials and further analysis of existing trials enabled the task force to provide more clarity about the effects of CRT. Patients with left bundle branch block QRS morphology and those who are in sinus rhythm have the greatest benefit from CRT. Conversely, those who have a non-left bundle branch block QRS morphology and patients in atrial fibrillation have less certain benefit.
- In pharmacological treatments, two new indications are highlighted. The guidelines stress that when attempting to reduce heart rate, the dose of beta blocker should be maximised before giving additional medications to reduce heart rate. New evidence has extended the indication for mineralocorticoid receptor antagonists. This means that for many patients, standard therapy should include three neurohumoral antagonists – an angiotensin converting enzyme inhibitor (or angiotensin receptor blocker), a beta blocker and, if symptoms persist, now a mineralocorticoid receptor antagonist as well.
- In the area of diagnostics, a new biomarker called mid-regional pro-A-type natriuretic peptide is mentioned for the first time.

The full guidance is available at http://eurheartj.oxfordjournals.org/content/33/14/1787 (*Eur Heart J* 2012;**33**:1787–847).

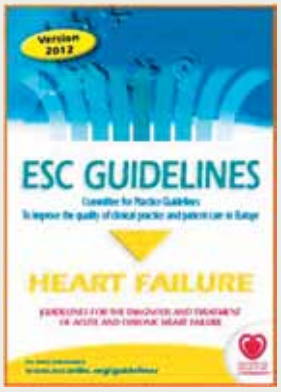
CVD prevention

The cardiovascular disease (CVD) prevention guidelines have been developed by the Fifth Joint Task Force of societies of Cardiovascular Disease Prevention in Clinical Practice, which includes the European Society of Cardiology (ESC) and seven other societies.

Around one third shorter than the 2007 fourth edition, the guidelines have been overhauled to produce a user friendly document with concise messages that awards greater weight than ever before to evidence from clinical trials and observational population studies.

"We've designed the Guidelines in a new format that makes them much more accessible," explained Professor Joep Perk, the chairperson of the Guidelines Task Force. "The change is to help disseminate the information from the Guidelines out to where it's needed".

The Guidelines stress that CVD prevention should be a "lifelong effort". Greater emphasis has been placed on the behavioural aspects of prevention, with discussion of



ways to make it easier for patients to change their lifestyles.

The guidelines highlight the following:

- The urgent need to improve CVD prevention. CVD is still the leading cause of premature death world-wide, the vast majority of which might be prevented through the widespread adoption of simple interventions such as smoking cessation, improved diets and increased exercise.
- Greater emphasis on population studies. For the first time the Grading of Recommendations Assessment Development and Evaluation (GRADE) system has been used to assess medical evidence that gives increased weight to population studies. This is in addition to the traditional assessment, applied by the ESC in all its Guidelines.
- Comprehensive and wide ranging to cover all areas of prevention, including total cardiovascular risk estimation, diseases with increased risk for CVD, methods of CVD prevention, smoking cessation interventions, dietary habits, physical activity, psychosocial factors, body weight, blood pressure, type 2 diabetes, lipids, and antithrombotic therapies.

The full guidance is available at http://eurheartj.oxfordjournals.org/content/33/13/1635 (*Eur Heart J* 2012:**33**;1635–701).

HDL particles may be key to risk

With all the recent controversy about whether raising high-density lipoprotein (HDL) is actually a worthwhile strategy in the battle against heart disease, a new study has suggested that HDL particle concentration may be a better marker of risk.

While the failure of the first cholesterylester transfer protein (CETP) inhibitor, torcetrapib, was blamed on its side effect of raising blood pressure, three more negative trials have also now cast doubt on the value of boosting HDL – AIM-HIGH with niacin, dal-OUTCOMES with dalcetrapib, and a genetic study published earlier this year in *The Lancet*, showing that people carrying gene variants coding for increased HDL levels did not have a reduced risk of heart disease.

However, in a new analysis of the Multi-Ethnic Study of Atherosclerosis (MESA), published on July 11 in the *Journal of the American College of Cardiology* (http://dx.doi.org/10.1016/j.jacc.2012.03.060), the concentration of HDL particles was independently associated with carotid intima-media thickness and coronary heart disease. Unlike HDL cholesterol itself, the association for HDL particles remained when adjusted for other atherogenic measures.

The results suggest that the quantification of HDL cholesterol might not "fully capture the HDL-related risk", according to the researchers. The authors of an accompanying editorial agree that increasing HDL-particle concentrations might prove to be more appropriate than increasing HDL cholesterol for reducing the risk of cardiovascular events.

See also an editorial by Jonathan Morrell (pages 104–05) and a review on CETP inhibitors by Paul Durrington (pages 126–33) in this issue.

Stricter food policies could dramatically cut heart disease deaths

Tougher government policies on diet could prevent 30,000 cardiovascular deaths a year in the UK, according to a new study. Moves suggested include banning the use of industrial trans fats and further reductions in salt and saturated fats while encouraging greater consumption of fruit and vegetables.

The study, published in the *Bulletin of the World Health Organization*, was conducted by a team led by Dr Martin O'Flaherty (University of Liverpool). They note that although the UK has made modest dietary improvements over the past decade, the current goals are "clearly insufficient longer term".

They point out that Denmark banned trans fats in 2004, and many other countries are now also aggressively working to eliminate them. They say that "voluntary agreements" with the processed food industry generally fail, and that further improvements resembling those attained by other countries are

achievable through stricter dietary policies, which will require additional regulatory, legislative, and fiscal initiatives.

The researchers modelled the effects of specific dietary changes on cardiovascular disease (CVD) mortality using data obtained from recent meta-analyses. Potential reductions in mortality between 2006 and 2015 were estimated for two scenarios: modest improvements, simply assuming recent trends will continue until 2015; and more substantial but feasible reductions (already seen in several countries) in saturated fats, trans fats, and salt consumption, together with increased fruit and vegetable intake.

The first scenario would result in around 12,500 fewer CVD deaths per year, the authors say. The more aggressive improvements could save many more lives, ranging from 13,300 to 74,900 fewer CVD deaths per year (average 30,000), they claim.

Lancet highlights damage of physical inactivity

Physical inactivity is responsible for 6% of the worldwide burden of coronary heart disease and 7% of type 2 diabetes cases, as well as 10% of breast and colon cancers, according to a series of papers on lack of exercise recently published in *The Lancet* (**380**:187–306).

"It's no coincidence that we're publishing the series at a time when the country and much of the world is gripped with Olympic fever," stated Dr Pamela Das, executive editor of the *Lancet*, at a press conference.

One paper reported that 9.4% of deaths from any cause are attributable to physical inactivity. Although the host nation of the Olympics, the UK came out particularly badly in the research. In terms of coronary heart disease, lack of exercise was said to account for 5.8% of cases worldwide, but this rises to 10.5% in the UK. If everyone were to engage in just a modest level of physical activity, this would translate into a gain of life expectancy approaching one year, said lead author Dr I-Min Lee (Brigham and Women's Hospital, Boston, US).

In another paper, a global survey showed that 31% of adults failed to meet public health guidelines for physical activity, defined as 150 minutes of moderate physical activity per week. But the figures for adolescents were worse, with more than 80% of individuals aged 13 to 15 years not doing the recommended 60 minutes of moderate to vigorous physical activity per day. Again, UK figures left much to be desired, estimating that 63% of the population were inactive. While 46.1% of Chinese adults walk or cycle to work, this is reduced to 15% in the UK, but is even lower in Australia and some US states.

Other commentators call for better promotion of physical activity by collaborations between schools, businesses, policy makers, advocacy groups, transport agencies, and healthcare groups.

Impressive results for polypill in new UK study

A new study of the polypill has shown large reductions in blood pressure and cholesterol levels, which if maintained long-term could translate into a substantial cut in heart attacks and strokes, the authors claim.

The study, published on July 18 in *PLoS One*, was conducted by Dr David Wald (Wolfson Institute of Preventive Medicine, London) and colleagues. The polypill used contained three antihypertensive medications – the calcium antagonist, amlodipine 2.5 mg; the angiotensin-receptor blocker, losartan 25 mg; and the diuretic, hydrochlorothiazide 12.5 mg – in addition to the cholesterol-lowering agent simvastatin 40 mg. In the study, 86 individuals were randomised to the polypill or placebo for 12 weeks. They then crossed over and took the other treatment.

Mean systolic blood pressure was reduced by 17.9 mmHg, diastolic pressure was reduced by 9.8 mmHg, and low-density lipoprotein (LDL) decreased by 1.4 mmol/L. Although the trial was too short to assess the impact on cardiovascular events, sustained reductions in blood pressure and cholesterol of this magnitude would reduce ischaemic heart disease events by 72% and stroke by 64%, the authors estimate.

Side effects occurred in 29% of those on the polypill compared with 13% on placebo, although none were serious enough to cause discontinuation.

Dr Wald's group are positioning their polypill as a universal medication to be taken by everyone over a certain age – roughly 50 or 55 years. Other groups are developing different formulations for both primary- and secondary-prevention populations.

New data reassures on bleeding risk with dabigatran in surgery patients

New data from the RE-LY trial show that dabigatran is associated with similar rates of bleeding and thrombotic complications to warfarin in patients who have to undergo invasive procedures and surgery.

The study, published in *Circulation* on June 14 (*Circulation* 2012; **126**:343–8. http://dx.doi.org/10.1161/CIRCULATIONAHA.111.090464), reported bleeding rates in RE-LY from seven days before until 30 days following invasive procedures in a total of 4,591 patients. Procedures included pacemaker/defibrillator insertion, dental procedures, diagnostic procedures, cataract removal, colonoscopy, and joint replacement.

Among patients assigned to dabigatran, the last dose of study drug was given an average of 49 hours prior to the procedure, compared with 114 hours in patients receiving warfarin. Bridging anticoagulation with heparin was given in 28% of warfarin patients and 16% of dabigatran patients. Peri-procedural bleeding rates were similar in all three groups.

An accompanying editorial points out that invasive procedures were very common in the two years of this trial, underscoring the clinical importance of this issue. It also highlights the "very low risk of thromboembolic peri-procedural events" – just 0.5% – showing that the risk of briefly interrupting anticoagulation is low.

The editorial notes that these results "should serve as a reassurance to those who are concerned about the lack of a standard way to measure anticoagulant effect and of a specific antidote with dabigatran," and "support the welcome hypothesis that novel shorter-acting oral anticoagulants will simplify the process of interrupting therapy for elective invasive procedures".

NICE – final guidance on rivaroxaban in DVT

The National Institute for Health and Clinical Excellence (NICE) has issued its final appraisal determination (FAD) on the use of rivaroxaban, as an alternative to warfarin, for the treatment of deep vein thrombosis (DVT) and prevention of recurrent DVT.

Estimates suggest there will be more than 46,000 cases of acute DVT in England and Wales during 2012, which will rise to nearly 50,000 cases by 2016, due in part to the ageing population.

Professor Carole Longson, NICE Health Technology Evaluation Centre Director, said: "For many people, using warfarin is difficult because of the need for regular monitoring with blood tests, dosing adjustments, and the need to be careful about their diet because of warfarin's interaction with certain foods. Because rivaroxaban does not require frequent blood tests to monitor treatment it represents a potential benefit for many people who have had a DVT, particularly those who have risk factors for recurrence of venous thromboembolism (VTE) and who therefore need longer term treatment. We are pleased, therefore, to be able to recommend rivaroxaban as a cost-effective option for treating DVT and preventing recurrent VTE in adults".

The EINSTEIN-DVT trial was the key trial supporting the clinical effectiveness of rivaroxaban in this indication. NICE considered the trial to reflect UK clinical practice.

Full guidance is available at http://www.nice.org.uk/nicemedia/live/13332/59383/59383.pdf

…and AF

NICE has also issued an FAD for rivaroxaban in atrial fibrillation (AF) recommending it for NHS use in preventing stroke and systemic embolism in adult patients with non-valvular AF.

The guidance advises that the drug should be considered as a therapeutic option in non-valvular AF patients with one or more stroke risk factors. The published NICE final guidance will require NHS commissioners in England and Wales to list rivaroxaban on hospital formularies within 90 days, making it available for clinicians to prescribe for appropriate patients.

Read the guidance in full at http://www.nice.org.uk/nicemedia/live/13308/58714/58714.pdf