CANTOS results show anti-inflammatory therapy lowers future cardiovascular events, reduces cancer incidence and mortality

Yesterday’s ESC Hot Line: Late Breaking Clinical Trials I Session marked a historic turning point in cardiology with a host of seminal, practice-changing data being presented. One of the highlights was the landmark CANTOS study that showed reducing inflammation, even in the absence of significant lipid lowering, significantly reduces recurrent cardiovascular events. Canakinumab, a drug currently indicated for the treatment of interleukin-1B driven inflammatory diseases was used to reduce inflammation. These data, that were the first to test the inflammatory hypothesis of atherosclerosis, could signal a paradigm shift in the core thinking about the treatment of atherosclerosis as they provide evidence that inflammation has a causal role in cardiovascular events. Additional exploratory analyses of the trial data examined whether anti-inflammatory therapy with canakinumab could change the occurrence of cancer and found that targeting the interleukin-1B innate immune response showed a significantly reduced cancer incidence and mortality, particularly in women.

Canakinumab is a high-affinity therapeutic monoclonal anti-human interleukin-1ß antibody that is designed to bind to human interleukin-1ß and functionally neutralise the bioactivity of this pro-inflammatory cytokine.

Professor Paul M Ridker (Brigham and Women’s Hospital, Harvard Medical School, Boston, USA) presented the CANTOS (Canakinumab Anti-Inflammatory Thrombosis Outcomes Study) results, which involved patients from 39 countries. “We conducted a randomised, double-blinded trial of canakinumab involving 10,061 patients with stable coronary artery disease after previous myocardial infarction and a high-risk of cardiovascular events. Canakinumab (150mg every 3 months) was associated with a 15% reduction in major adverse cardiovascular events (MACE), a 4% reduction in cardiovascular death, 15% reduction in myocardial infarction and 17% reduction in stroke. We also looked at non-cardiovascular outcomes—non-cardiovascular death, cancer, and non-cardiovascular death plus cancer—this question: Can inflammation reduction, of atherothrombosis, and asked the question: Can inflammation reduction, in the absence of lipid lowering, reduce cardiovascular events and mortality?”

The primary cardiovascular efficacy endpoint of the study was non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death (MACE). The key secondary cardiovascular endpoint was MACE plus unstable angina requiring unplanned revascularisation (MACE plus). Critical non-cardiovascular safety endpoints included cancer and cancer mortality, infarction and infection mortality. The study was published in the New England Journal of Medicine to coincide with the ESC presentation and the cancer analysis was simultaneously published in The Lancet.

CANTOS results revealed that at 48 months there was an average reduction from baseline of CRP level in all groups receiving canakinumab in comparison to the group receiving placebo. The drug did not reduce lipid levels from baseline. Results showed that a median follow-up of 3.7 years, the incidence rate for the primary endpoint (MACE) was 4.5 events per 100-person years in the placebo group, 4.1 in the 50mg group, 3.9 in the 150mg group and 3.9 in the 300mg group. The 150mg and 300mg groups showed a hazard ratio of 0.85 and 0.86, respectively, for primary endpoint, which was statistically significant when compared to the group receiving placebo (p-trend=0.025). In terms of secondary endpoint (MACE plus), the incident rate per 100-person years in the placebo group was 5.1. It was 4.6 for the 50mg group, 4.3 for the 150mg group and 4.3 for the 300mg group—there was a statistically significant difference between results of patients who received 150mg and 300mg canakinumab and those who received placebo (p-trend=0.043).

The 150mg dose group, but not the other doses, met the multiplicity-adjusted threshold for statistical significance for both the primary and secondary endpoints with a 39% reduction in CRP, no change in LDL cholesterol, 15% reduction in MACE and 17% reduction in MACE plus (HR 0.85 95% CI 0.76-0.96; p=0.007). Prof. Ridker explained. Further data analysis showed that there was a consistency of hazard ratios across all cardiovascular endpoints, consistency of effects across all patients groups, and that there was smaller risk reduction among those with greater hsCRP reduction.

“As shown in these data, inhibition of interleukin-1ß with subcutaneous canakinumab given once every three months among patients with...”

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Will COMPASS point to low-dose rivaroxaban plus aspirin for patients with stable artery disease?

Patients with stable atherosclerotic vascular disease who take rivaroxaban (2.5mg twice daily) plus aspirin (100mg once daily) have better cardiovascular outcomes than those who take aspirin alone, results from the COMPASS trial presented at the ESC Hot Line session yesterday revealed. These results could herald a change in guidelines in this setting, experts opined.

COMPASS results suggested that a patient cohort group that takes the rivaroxaban-plus-aspirin regimen will see fewer cardiovascular deaths, strokes and myocardial infarctions, but more major bleeding events than a group that takes aspirin alone. Yet, there is no significant increase in fatal, intracranial or critical organ bleeding between these two groups and rivaroxaban-plus-aspirin provides a net clinical benefit, delegates heard. They were also told that rivaroxaban monotherapy offers no benefits over rivaroxaban-plus-aspirin or aspirin alone.

Doctor John Eikelboom (Department of Medicine, McMaster University, Hamilton, Canada) presented data from the double-blinded, randomised COMPASS trial (Cardiovascular Outcomes for People Using Anticoagulation Strategies). The trial was designed to determine whether rivaroxaban in combination with aspirin or given alone is more effective than aspirin alone in reducing cardiovascular death, stroke or myocardial infarction, with acceptable safety in patients with around 60 years of age, with the majority being on lipid lowering therapies and taking renin-angiotensin inhibitors,” he said.

The researchers randomly assigned participants with stable atherosclerotic vascular disease to receive rivaroxaban (2.5mg twice daily) plus aspirin (100mg once daily; n=9,126), rivaroxaban (5mg twice daily; n=9,152), aspirin (100mg once daily; n=9,128). The primary efficacy outcome was a composite of cardiovascular death, stroke, or myocardial infarction. The mean age of participants was 68.2 years, and 50.9% were women. Nearly 90% used lipid-lowering agents. A total of 90.6% of the participants had a history of coronary artery disease, and 27.3% had a history of peripheral arterial disease.

The independent data and safety monitoring board recommended early discontinuation of the comparison of rivaroxaban with or without aspirin vs. aspirin alone, for clear evidence of efficacy outcome in favour of rivaroxaban plus aspirin after a mean follow-up of 23 months. A primary outcome event of cardiovascular death, stroke or myocardial infarction occurred in 379 patients (4.1%) who were assigned to rivaroxaban-plus-aspirin, 448 (4.9%) who were assigned to aspirin alone, and 496 (5.4%) who were assigned to aspirin alone. There was a statistically significant difference in primary outcomes between the rivaroxaban-plus-aspirin group and the aspirin-alone group (p=0.0011). However, patients in the rivaroxaban-alone group did not experience significantly fewer cardiac deaths, strokes or myocardial infarctions than those in the aspirin-alone group (p=0.12).

The secondary composite outcome of ischemic stroke, myocardial infarction, acute limb ischemia, or death from coronary heart.dx(156x228 to 321x321)
The incidence of the composite efficacy endpoint—thromboembolic events (myocardial infarction, stroke, or systemic embolism), death, and unplanned revascularization—was significantly lower for canakinumab-dual-therapy groups, combined as with 13.4% in the triple-therapy group (p=0.005 for non-inferiority). The rate of serious adverse events did not differ significantly between groups.

The 110mg and 150mg dabigatran dual-therapy regimens offer all of us two additional options, with evidence, for managing post-PCI AF patients, with both doses approved for stroke prevention, Dr. Cannon told the audience.

**End of post-JMI dabIGR link to further preserve event benefit.**

New subanalysis of the FAME 1 and FAME 2 trials suggests that improvement in fraction reserve reserve FFR in the presence of non-ST elevation myocardial infarction is associated with a lower all-cause mortality one year outcome after PCI according to Dr. Stephanie Fournier (Aix, Belgium). “The higher the post-PCI FFR value, the lower the occurrence of events,” she explained. “The occurrence of events is weak,” Dr. Fournier explained. “The larger the improvement in FFR, the lower the event rate will be.”

Dr. Fournier and colleagues investigated whether the difference between FFR at baseline and post-JMI—AFFR—imparts the two-year year-orientated clinical events (VOCE) rate, irrespective of vessel-related cardiovascular death, vessel-related revascularisation, and vessel-related myocardial infarction.

The FAME 1 and FAME 2 studies provided the raw data for the analysis, in which 1,499 lesions were treated (post-JMI FFR <0.70, FFR range 0.58–0.83 lesion). Of the patients with recorded post-JMI FFR, 277 were in the AFFR lower tertile (FFR <0.18), 282 were in the middle tertile (FFR ≥0.18 and FFR <0.31), and 231 in the upper tertile (FFR ≥0.31). Dr. Fournier and colleagues identified several predictors of AFFR, namely male gender (p=0.003), diabetes (p=0.04), previous PCI (p=0.02), and prior myocardial infarction (p=0.007). The VOCE rate of these patients improved as AFFR increased. For the lower AFFR tertile the rate was 9% (n=25), for the middle tertile 7.1% (n=28), and for the upper tertile was 4.7% (n=13) (all p<0.05). The incidence of the composite efficacy endpoint—thromboembolic events, death, or unplanned revascularisation—was 13.7% in the two-drug therapy group as compared with 13.4% in the triple-therapy group (p=0.001 for non-inferiority and p=0.001 for superiority). The primary endpoint incidence in the 150mg dual-therapy group was 20.2% as compared with 25.7% in the corresponding triple-therapy group, which did not include elderly patients outside of the USA (p=0.001 for non-inferiority).

“The VOCE rate at 2 years will be less,” Dr. Fournier concluded. “The reason for this relationship remains speculative.”
Catheter ablation of atrial fibrillation was associated with improvement in all-cause mortality and fewer hospitalisations in heart failure patients shown to reduce mortality and 

CASTLE AF—presented at yesterday’s Hot Line: Late-Breaking Clinical Trials 1 has found. 

The CASTLE-AF trial is novel because it is the first time mortality and hospitalisation have been used as an endpoint,” Professor Casim Blomstrom-Lundqvist (Uppsala University, Uppsala, Sweden), commented in a discussant review of the study. 

The results, presented yesterday by Doctor Nassir Marrouche (University of Utah Health Care, Salt Lake City, USA), indeed demonstrated a link between catheter ablation of atrial fibrillation (AF) and improved rates of all-cause mortality and worsening heart failure hospitalisation—the combined endpoint of the trial. 

“AF and heart failure are well intertwined,” Dr. Marrouche explained. “Catheter ablation of AF in patients with heart failure has been shown feasible.” Aiming to build on this, the team sought to assess the effectiveness of catheter ablation for AF in heart failure patients. 

Three hundred and ninety-seven patients with symptomatic paroxysmal or persistent AF were enrolled and randomised following eligibility assessment of 3,013 patients. Following exclusions during a five-week run-in period, and patient crossover between the two groups, a final total of 353 patients were treated with catheter ablation and 184 with conventional treatment. In addition to the primary endpoints, the team recorded secondary endpoints including cardiovascular (CV) mortality, and CV-related hospitalisation. Patients were followed-up from three to 60 months. 

The conventional arm was treated according to the ACC/AHA/ESC 2006 guidelines for the treatment of AF in heart failure. The ablation arm underwent pulmonary vein isolation, with additional lesions ablated at the discretion of the operator. Following a blanking period, ablation was repeated. 

When evaluating the effectiveness of catheter ablation according to the composite primary endpoint, the team observed a risk reduction of 38% from baseline at 60 months, statistically significant in comparison to the conventional group (p=0.004; p=0.011, respectively). 

The secondary endpoints of CV mortality and CV hospitalisation also revealed statistically significant risk reductions for catheter ablation in comparison to conventional treatment. Cardiovascular mortality risk was reduced by 51% (p=0.009) and cardiovascular hospitalisation risk by 28% (p=0.03). 

Concluding, Dr. Marrouche explained, “Catheter ablation led to significant improvement in the primary composite endpoint of all-cause mortality and worsening heart failure admissions.” 

“The take-home message of this trial is that it is time to offer catheter ablation procedures at an early stage in heart failure patients with AF,” she added. “But, we must be careful to select patients that reflect the populations included in this trial.”

Will COMPASS point... 

Continued from page 1 

The overall COMPASS trial was an important step in thrombocardiology. “COMPASS has taken a step forward by demonstrating in stable, chronic coronary artery disease that a combination of low dose aspirin and very low dose rivaroxaban is superior to aspirin monotherapy,” Professor Eugene Braunwald (Brigham and Women’s Hospital, Harvard Medical School, Boston, USA) noted that the trial was an important step in thrombocardiology. “COMPASS has a large, rigorously conducted trial with unambiguous results which, I believe, should change guidelines.”

COMPASS-PAD 

Data on peripheral arterial disease patients from the trial (COMPASS-PAD) were presented by Professor Sotiris Anand, McMaster University, Hamilton, Canada, that showed similar benefits with rivaroxaban-plus-aspirin in this subgroup. Consistent with the overall results of COMPASS, in PAD patients the addition of low dose rivaroxaban to aspirin, compared with aspirin alone, reduced cardiovascular death, stroke or heart attack by 28%, and limb-threatening ischaemia, including amputation, by 46%. Considering both outcomes together, rivaroxaban and aspirin lowered major adverse cardiovascular or limb events by 31%.

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ESC Guidelines add “S” to peripheral arterial disease to bring greater clarity

The European Society of Cardiology (ESC) in collaboration with the European Society for Vascular Surgery (ESVS), has produced new Guidelines on the diagnosis and treatment of peripheral arterial diseases. The “S” at the end of the disease is important because it emphasises that the Guideline refers to all atherosclerotic diseases outside of the coronary arteries.

Professor Victor Aboyans (Department of Cardiology, Dupuytren University Hospital, Limoges, France) says that the ESC has always considered that the term “peripheral arterial disease” covers all arterial diseases that are “peripheral to the heart”; but comments that the Task Force behind the new Guidelines have now added the letter “S” to the term because there is a general misconception that “peripheral arterial disease” just refers to the lower extremities. He explains that this confusion may have arisen because several papers cited the previous ESC Guidelines as just focused on lower extremities. Prof. Aboyans explains that the ESC Guidelines review carotid artery disease, upper extremity disease, and mesenteric artery disease among others.

The 2017 Guidelines include chapters on the different antithrombotic therapies available for managing peripheral arterial diseases and on potential concomitant coronary artery disease. According to Prof. Aboyans, a patient with some form of peripheral arterial disease may also have cardiovascular diseases other than coronary artery disease (such as heart failure or atrial fibrillation). So, we have written specific chapters on this.

Given that multiple specialties are involved in managing peripheral arterial diseases, the Guidelines highlight the role of the “Vascular Team”. Similar to the Heart Team concept, the Vascular Teams include a variety of experts. “For example, when you are managing a patient with carotid artery disease, a neurologist’s opinion is also important and should be part of the team because the brain is the target organ to protect,” Prof. Aboyans comments.

The importance of the Vascular Team is why the ESC worked with the ESVS to produce the Guidelines. Past ESVS president Professor Jean-Baptiste Rocco (Department of Vascular Surgery, University Hospital of Poitiers, Poitiers, France) says that both societies highlighted the need for multidisciplinary management of patients with peripheral arterial diseases in earlier individual Guidelines. “When the decision was made to update these ESC Guidelines, it appeared obvious that a combination of efforts from both Societies would provide the most comprehensive single document, providing updated guidelines on PADs for clinicians,” he says and notes that “it is of the utmost importance that every cardiologist should be sensitive in regard to the diagnosis and management of patients with PADs as many of them are seen and managed for concomitant cardiac conditions”.

Valvular Heart Disease Guidelines emphasise Heart Team decisions

The 2017 ESC Guidelines on valvular heart disease have put the heart team firmly at the centre of decision making, noting that heart team collaboration is vital for ensuring optimal outcomes for the patient. They also say that transcatheter aortic valve implantation (TAVI) should be considered, with the consensus of the heart team, for aortic stenosis patients who are at an increased surgical risk for a variety of reasons.

The rationale for the emphasis on the Heart Team—composed of experts including cardiologists, cardiac surgeons, imagers, anaesthesiologists, and even geneticists—is to optimise management of complex patient issues. Decisions around TAVI, which require a risk/benefit analysis for the procedure compared with surgical aortic valve replacement and/or medical therapy, provide a choice example of where the wide ranging knowledge of the heart team is needed. Outside the traditionally used scores for risk stratification, factors such as frailty, the presence of a porcelain aorta or expected patient-prosthesis mismatch must be taken into account. “The message here is that you should decide according to the heart team what’s best for the individual,” explains the co-Chairperson of today’s session, Professor Jose Luis Zamorano Gomez (Hospital Ramon Y Cajal, Madrid, Spain).

The guidelines also include new data demonstrating that neurohormones can be helpful in risk stratifying aortic stenosis patients who may benefit from valve replacement.

“The Task Force authoring the ESC Guidelines acknowledges that current evidence is restricted to elderly patients, since few patients under 70 years have been included in clinical trials. The new guidelines modify the traditional guidelines format and deliver recommendations in a document that is shorter and easier to read. “The summary of key points and existing gaps in evidence at the end of each section have been designed for clarity,” says Professor Volkmar Falk (Department of Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum Berlin), who is co-chairing a session today on the new Guidelines with Professor Zamorano Gomez.

One tip for clinicians wanting to adopt the guidelines is to focus on Class I and Class III indications. “Put simply, you should follow Class I indications for all your patients, and avoid Class III,” explains Prof. Gomez. The jury is still out on Class IIa and IIb indications, which may be changed into Class I or III as more information becomes available. Many Class I recommendations are supported by randomised trials (level of evidence “A” and “B”), but just because a therapy has been awarded a Class I indication with a level of evidence “C” (expert consensus), it does not mean that it is of major importance. “We know that some treatments are valuable without clinical trials. For example using a parachute when jumping out of an aeroplane would have a Class I-C recommendation as you’d obviously never perform trials to test whether it was effective,” he says.

Prof. Falk concludes: “New knowledge in valvular heart disease emerges constantly. While it is not useful to change clinical practice with every new trial, regular updates are considered mandatory.”
40 years of angioplasty, and the man who made it possible

This year marks the 40th anniversary of the first coronary angioplasty, which was performed by Doctor Andreas Roland Grüntzig on 16 September 1977. ESC Congress News charts the evolution of the procedure, and examines the life of the pioneering doctor who created it.

In 1969, Dr. Grüntzig moved to Zurich (Switzerland) to work in internal medicine with Professor Robert Hegglin. Unfortunately, Dr. Hegglin died suddenly shortly afterwards and Dr. Grüntzig was “orphanned”. However, as serendipity would have it, a new division had opened up at Zurich—angiography, focused on treating atherosclerosis in the peripheral arteries—and Professor Alfred Bossinger, the head of the new department, adopted (in a fashion) Dr. Grüntzig. Professor Bernhard Meier (Cardiovascular Department, University Hospital of Bern, Bern, Switzerland), who worked with Dr. Grüntzig, comments: “It meant he got immediate contact with atherosclerosis in the leg arteries, which was excellent training.”

It was during this time that Dr. Grüntzig became aware of the work being done in the USA by Professor Charles Dotter, who was using a crude technique to open up narrowed leg arteries. According to Prof. Meier, Dr. Grüntzig started to use the Dotter technique but, thinking about expanding its use to the coronary arteries, immediately saw it was too primitive and set about improving it. “That is when he thought about using a balloon. And, again, an act of serendipity occurred. Just across the street from the hospital was the Technical University of Switzerland, and there he found a plastics expert who helped him to create the balloon. He wanted one that was cylindrical and could inflate to high pressure—that would get hard without assuming a spherical shape. The engineer suggested polyvinyl chloride,” he continues.

Dr. Grüntzig then worked with a small medical device company in Zurich that specialised in catheters to help him make the balloon. The story that he perfected the balloons at his kitchen table is, in fact, true. Prof. Meier explains: “He got the materials from the plastics industry, and the idea of how to do it from the engineer, but then he had to try it himself. So he used his kitchen—not only the table, but also his kitchen stove to heat the balloons that were subsequently used in legs of patients. Today, that would no longer be possible!”

History was made on 16 September 1977 when, after his successful home experiments, Dr. Grüntzig performed the first-in-human coronary angioplasty procedure. He dilated a short non-branching segment of the left anterior descending (LAD) coronary artery which had a high grade stenosis. The immediate outcome was good, and the patient became and remained angina-free. Grüntzig presented the results of his first four angioplasty cases at the 1977 American Heart Association (AHA) meeting, which led to widespread acknowledgement of his pioneering work. However, despite this success, Dr. Grüntzig recognised that the treatment may not be readily accepted by some physicians—particularly cardiac surgeons but also internists and even fellow cardiologists. Also, he knew that careful patient and lesion selection was required to reduce the risk of poor outcomes as was careful training of operators. His cautious approach paid off as his efforts are now widely credited with being of fundamental importance to the ultimate success of the technique.

Prof. Meier joined Grüntzig’s team in 1976 and says that the father of interventional cardiology was a person of “great charm, eloquence, and wit”. He says: “He knew that he was good. It wasn’t arrogance, but he was sure of himself. Without him, my career would certainly not have been what it was. Those who worked with him were part of an absolutely stunning development in cardiology.”

Dr. Grüntzig did have plans for another innovation but these never came to fruition—his life and career were tragically cut short when he died, aged 46, in a plane crash with his second wife in 1985. Prof. Meier explains: “He always told me ‘this is not the last thing I have developed. I will go on to other ideas.’ He clearly wanted to have at least one more pivotal innovation. But he died too young to prove or disprove it. I have no idea what it would have been, and I think he had no idea himself, but he was looking around for one and then he died.” Even with his first invention, Grüntzig made a major contribution to medicine by demonstrating that doctors could safely work inside arteries, without the need for open surgery. Alas, in a cruel twist of fate, Dr. Grüntzig did not live long enough to see the true impact of his breakthrough procedure. One year after his death, in 1986, Puel implanted the first (self-expanding) coronary stent and one year later, in 1987, Palmaz and Schatz presented the first balloon-expandable stent. Only thereafter did the method initially devised by Andreas Grüntzig develop to its true potential.
New interactive session to explore different PCI strategies

A new type of session—Let’s Talk about Strategy—launches at ESC Congress 2017 today. The aim of the session is to collect opinions from a panel of experts by putting them on the spot, looking at how they would treat a particular case and why they decide in a certain way. In keeping with this year’s Spotlight on 40 years of percutaneous coronary intervention (PCI), the session will focus on different PCI cases ranging from the simple to the more complex.

ESC Congress Programme Committee Chairperson, Professor Stephan Achenbach (Department of Cardiology, Friedrich Alexander Universität Erlangen-Nürnberg, Erlangen, Germany)—who is moderating the session with Professor Spencer King (Emory Heart Center at Saint Joseph’s Hospital, Atlanta, USA)—explains: “The moderators will show a coronary angiogram and will ask the panellists in turn how they would treat the lesion that is shown.” He adds that what will be interesting is to see if the panellists agree about how the lesion should be treated, commenting: “Experts do not always agree and can often have different opinions from each other”.

The experts will not only discuss how they would manage a case but will also explore why they would manage it in a particular way. “It is always good to hear and understand the reasons behind choosing a particular strategy—for example, why one expert would use one stent rather than two or three and in which sequence they would be placed. By listening to their views at this session, you can gain an insight into their thought process,” Prof. Achenbach comments. He adds that those attending the session will be encouraged to interact with the panellists via the ESC Mobile App: “Voting cards in two different colours—for yes and no—will be distributed so that the panel can collect the audience’s opinion on a given case.”

The session is part of the commitment of the ESC Programme Committee to create more interactive formats to disseminate knowledge. “Let’s Talk about Strategy will be a unique learning experience in a new, fast-paced format. So, come and be part of this premier session,” Prof. Achenbach says.

The expert panellists at the session are Professor Antonio Colombo (Unit of Cardiovascular Interventions, Istituto Di Ricovero e Cura a Carattere Scientifico San Raffaele Scientific Institute, Milan, Italy), Doctor Jean Fajadet (Clinique Pasteur, Toulouse, France), Professor Martin B Leon (Center for Interventional Vascular Therapy, Columbia University Medical Center, New York Presbyterian Hospital, New York, USA), Doctor Julinda Mehilli (Department of Cardiology, Munich University Clinic, LMU, Munich, Germany), Professor Helge Möllmann (Department of Cardiology, Johannes Hospital, Dortmund, Germany), and Professor Helge Möllmann (Department of Cardiology, Johannes Hospital, Dortmund, Germany).

Abstract of the day: Study confirms prior infective endocarditis carries greatest risk of the condition

Results from a Danish study support both European and US guidelines by finding that people with a history of infective endocarditis have a significantly greater risk of developing the condition than the general population.

Investigators Doctor Lauge Ostergaard (Rigshospitalet – Copenhagen University Hospital, The Heart Centre, Copenhagen, Denmark) and others observe that both European and US guidelines state that patients with prior infective endocarditis, a prosthetic heart valve or cyanotic congenital heart disease are all at increased risk of developing infective endocarditis. However, in their abstract, they note: “Knowledge is sparse on the relative risk between these three groups and compared with controls”. Therefore, using data from Danish nationwide registries, they sought to identify the incidence of infective endocarditis among these “high-risk” groups and compare this incidence with that of gender-matched controls. Of 24,253 patients, 5,192 had prior endocarditis, 17,241 had a prosthetic heart valve, and 1,820 had cyanotic congenital heart disease. The authors report: “The cumulative risk of infective endocarditis over 10 years was 10.4% for prior endocarditis, 3.4% for a prosthetic heart valve, and 1.1% for those with cyanotic congenital heart disease. All groups carried a significant higher risk of infective endocarditis than matched controls from the general population. These findings justify the European and American guidelines.”

Missed a session?

Review

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Where next for PCI versus CABG?

Saturday and Sunday saw a host of Late-Breaking Science trials that provided further insights into the safety and efficacy of contemporary percutaneous coronary intervention (PCI). For example, on Saturday, results of the SYNTAX II study showed that state-of-the-art PCI yields fewer adverse events in de novo three-vessel disease. However, the question remains—when should PCI be used and when should surgery be preferred? Professor Michael Haude (Medical Clinic I Lukas Hospital, Neuss, Germany) explores recent evidence regarding the use of PCI versus coronary artery bypass grafting (CABG) for coronary revascularisation.

SYNTAX II is a European multicentre single-arm study that compared outcomes of patients (450) with de novo three-vessel disease undergoing PCI with contemporary techniques (such as next-generation drug-eluting stents) with patients who underwent PCI in the first SYNTAX trial. This trial, which compared PCI with a first-generation drug-eluting stent with CABG, found that the more disease present, the greater the benefit of surgery (versus PCI). However, it also showed that left main PCI was associated with similar outcomes to those of surgery.

Following SYNTAX, the EXCEL study found that left main PCI was associated with a similar rate of death, stroke, and myocardial infarction as was surgery at three years. However, another study that was published at the same time as EXCEL—NOBLE—found that PCI was associated with a significantly higher rate of major adverse cardiac and cerebrovascular events at five years compared with CABG. According to Prof. Haude, these apparently opposing results are not as conflicting as they may seem and both support the findings of the original SYNTAX study. He says: “If you have single-vessel left main disease, or limited additional disease, the results between surgery and PCI are equivalent. And, the more distal disease you have to the left main, the more favourable it is to surgery. NOBLE and EXCEL didn’t change that; it was already known from a subgroup analysis of SYNTAX.”

Furthermore, he notes that—compared with CABG—repeat revascularisation is the “Achilles heel” of PCI, stating: “There is no difference in cardiovascular mortality or myocardial infarction between PCI and CABG. And, when you include revascularisation among the endpoints, we always have more reinterventions with PCI.”

Subgroup analyses of PCI versus CABG trials, including SYNTAX, demonstrate that complete revascularisation PCI (both culprit and non-culprit vessels), in the acute setting, has similar rates of revascularisation to surgery. What Prof. Haude calls a “reasonable timeframe, which means two years”, but, he adds: “We need to see what is going to be happening in five and 10 years to find out whether outcomes with PCI are still as good as they are for CABG.”

Also, with PCI, revascularisation may occur because further stenoses can develop in the vessel that has been treated. But, as most of the arterial bed is being bypassed, CABG does not have this issue. “PCI is only treating the tip of the iceberg. Therefore, challenging CABG outcomes in the long term will be extremely difficult. PCI is only treating the emerging stenosis but not the underlying complete atherosclerotic process in the arterial wall especially outside of the stented vessel segment,” he observes. Additionally, the durability of the—nowadays more frequently used—arterial grafts is another factor in favour of CABG.

However, since the original SYNTAX trial, developments in PCI technology—such as next-generation drug-eluting stents that have thinner struts and more flexibility—have enabled lesions that previously would have been too complex for PCI to come within its scope. Also, the SYNTAX score II has optimised decision-making between CABG and PCI. Unlike the anatomical SYNTAX score, it is based on clinical characteristics as well as anatomical characteristics.

Looking to the future, Prof. Haude says that bioresorbable scaffolds still have the potential to improve on existing devices and even possibly be equivalent to surgery. He comments: “There is still hope with the improved technology of the second-generation devices [there have been some limitations with the first-generation devices]. But, these newer devices have to be compared in randomised controlled trials against current drug-eluting stents to show that they, at least, are non-inferior to those devices before they can be evaluated against CABG.”

Prof. Haude is Chairperson, alongside Doctor Marie-Claude Morice (Institut Cardiovasculaire Paris Sud, Paris, France), at today’s 40 years of percutaneous coronary interventions and beyond (16:30-18:00; Bishkek - Village 6).

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Sports cardiology: The conundrum of distinguishing physiological adaptations

In an interactive session yesterday, leading sports cardiologists discussed the challenge of distinguishing “conundrums” facing clinicians who are assessing athletes in distinguishing normal physiological cardiac adaptations to exercise found in athletes from the diseased state. Sports cardiology, defined as a subspecialty of cardiology, takes into account modifications made to the cardiovascular system. “There’s a real danger that cardiologists who aren’t accustomed to seeing sports people can make the mistake of diagnosing these differences as cardiovascular diseases,” says Professor Antonio Pellieca (Institute of Sport Medicine and Science, Italian National Olympic Committee, Rome, Italy). Such physiological changes, he adds, affect not only professional athletes, but also normal individuals engaging regularly in exercise. And with large proportions of the adult population engaging regularly in exercise, such changes may be far more widespread than appreciated.

In the first presentation of yesterday’s session, Professor Stefano Caselli (Department of Cardiology, Institute of Sports Medicine and Science, Rome, Italy) explored whether the presence of pathologic trabeculations fails during early embryogenesis, the remaining trabeculations appear as loose networks of muscle fibres separated by recesses (in imaging studies). In a study published last year, Prof. Caselli showed that out of 2,501 consecutive athletes screened, 1.4% (36) showed prominent trabeculations (LVNC). When the process of “compaction” of normally muscular cardiac adaptations fails during early embryogenesis, the remaining trabeculations appear as loose networks of muscle fibres separated by recesses (in imaging studies). In a study published last year, Prof. Caselli showed that out of 2,501 consecutive athletes screened, 1.4% (36) showed prominent trabeculations suggestive of LVNC. However, on follow-up only 0.1% (three) of these athletes had morphologic and clinical evidence supporting the diagnosis of LVNC (International Journal of Cardiology, 2016; 223: 590-595).

Such data, Prof. Caselli argued in the session, is evidence that “trabeculations are far more widespread than appreciated and that there is a need to give greater weight to clinical information (such as LV dysfunction, family histories and genetic testing) to reach diagnosis of LVNC.”

Doctor Michael Papadakis (Department of Medicine and Clinical Sciences, St. George’s University of London, London, UK) then considered how right ventricle remodelling, as a physiological adaptation to exercise, can overlap with morphologic changes occurring with right ventricular cardiomyopathy.

Finally, Prof. Pellieca drew on his own work screening Olympic athletes in his quest to “put the most extreme “normal” physiological adaptations that can occur with sport. “We want to be able to take into account factors such as the impact of current sports, genders and ethnic origins,” he said.

To provide greater clarity in the field of sports cardiology, a sparse position paper has been published by the European Association of Preventive Cardiology (EAPC) recommended approaches for the diagnostic and management of cardiovascular evaluation; and an international consensus statement has been produced on electrocardiographic changes in athletes. “In the future, these publications should help physicians to identify individuals at risk by reducing at the same time the number of false positives,” says Prof. Pellieca. Thus, the manuscript transfer works for the benefit of the entire ESC Journal Family. Citations are all important for journals because they enhance the visibility of articles, and Altmetric measures the influence Prof. Lüscher mentioned and ORCiD will help our wider community tie together in one place all of their scientific and academic contributions.

In fact, one of the goals of the latest journal in the family (EJH – Case Reports) is to encourage cardiologists at the start of their career to write and submit articles to a journal. Editor-in-chief Professor John Camm (St. George’s University of London, London, UK) explains: “We wanted a journal that would be appropriate for young writers, cardiologists who haven’t had an opportunity of doing extensive research but may have come across an interesting case. Our aim is to encourage them to write about these case reports, particularly as other journals in the family are inundated with case reports that they cannot publish.”

The new journal is online only because authors are charged a nominal fee for publishing their case reports and the Editorial Board wanted to avoid the cost of printing. However, Prof. Camm observes: “All journals are going to be online only eventually, it is only a matter of time.” He adds that, to take full advantage of the online-only status of the journal, the Editorial Board is building a social media profile to help promote those vital citations and downloading.

Therefore, whatever your interest, whether you are a reader or an author, the ESC Journal Family has a journal that suits your needs.
A group of health professionals came together in 2015 to form the AF-SCREEN International Collaboration—a consortium that seeks to promote the case for screening for atrial fibrillation (AF). ESC Congress News reviews the arguments for AF screening and looks at the work of AF-SCREEN, specifically its White Paper recently published in Circulation.

Professor Ben Freedman (Heart Research Institute/the Charles Perkins Centre, Sydney, Australia) formed AF-SCREEN with five other cardiologists to promote discussion and research about AF screening, and to advocate for implementation of country-specific programs. The consortium now has more than 130 members from 33 countries, including many of the foremost names in AF research. It includes many different types of physicians as well as cardiologists, allied health professionals and nurses, epidemiologists and health economists and lay organizations. He sees the consortium as a great opportunity to make a real difference, commenting: “If we went back in time and found asymptomatic AF before an AF-related stroke occurred, you could potentially prevent 10% of all ischemic strokes. This is doubly important because AF-related strokes tend to be at the severe end of the spectrum—people either die or have a severe, disabling stroke. AF represents a rare opportunity in which there is a common condition that causes horrible outcomes that could be prevented if you find it in time and then do something about it.”

AF-SCREEN’s White Paper calls for screening programs aimed at people ≥65 years of age—that could use pulse palpation, oscillometric (blood pressure) or photoplethysmographic (smartphone camera) devices, and handheld ECG devices to diagnose AF. Because an ECG rhythm strip is required to verify the diagnosis, handheld ECG devices are preferred. The paper also recommends more intensive monitoring for some patient groups, such as those with recent embolic stroke of uncertain source (ESUS). Prof. Freedman says: “You need to look for atrial fibrillation in people who are of an age where it’s much more common to get it and, if they have it, the risk of stroke is high enough to warrant treatment. A screening program could be part of a routine health check or chronic care assessment, particularly in the over 65 year olds. Routine checks like these start at age 65 in many countries and, in the USA, Medicare kicks in then. It would work best if you could add screening to an already-established workflow, as it is only a small additional part.”

The White Paper also says AF screening should be individualized according to country and healthcare system-specific requirements and resources, and should also be linked to an effective pathway for appropriate diagnosis and management. The final key point in the paper calls for large randomized controlled studies, using hard endpoints (including stroke, systemic embolism, and death), of strategies for screening that will strengthen the evidence base to inform guidelines and national systematic screening programs.

The White Paper’s publication comes just ahead of a Hot Line session tomorrow at which results will be presented from a late-breaking trial on screening for AF. The senior investigator Professor Julian Halcox (Swansea University Medical School, Swansea, UK) is a member of the AF-SCREEN consortium.

Imaging quiz solution: Patent ductus arteriosus (PDA)

The three-dimensionally reconstructed CT angiogram (left) and a two-dimensional image (right) show a patent ductus arteriosus (PDA, arrows), connecting the aorta (Ao) and pulmonary artery (PA).
Antithrombotic treatment for patients during and after they undergo percutaneous coronary intervention (PCI) has been the subject of much debate and uncertainty. This overview looks at the current status of antithrombotic therapy in this context, and examines data from recent trials and their impact on treatment options.

The PRECISE DAPT score assesses the risk of bleeding, while a second tool, the DAPT score, assesses the global risk of the occurrence of both ischaemic events and bleeding.

The ESC is a proud partner in the development of biomedical code of ethics

In 2014, the DAPT study (published in NEJM) of 99,61 patients demonstrated that extending DAPT beyond one year after the placement of a DES significantly reduced the risks of stent thrombosis and major adverse cardiovascular and cerebrovascular events, compared with aspirin therapy alone, but it was associated with an increased risk of bleeding and no reduction in total death (with even a trend towards increased total mortality). In addition to aspirin, patients were randomly assigned to continue to receive a thienopyridine drug (clopidogrel or prasugrel) or a placebo for 18 months; this followed on from 12 months of treatment with either clopidogrel or prasugrel. The reduction in the risk of ischaemic events was consistent across stent type and specific thienopyridine drug used, and was evident regardless of the risk of stent thrombosis.

But Prof. G Montalescot believes patient characteristics are more important when determining DAPT duration than choice of stents, noting: “A prior history of bleeding, being elderly, being female, and renal insufficiency are major factors that are associated with bleeding risk. In these cases, DAPT should be shortened.”

There are now tools to aid physicians in determining the optimal duration of DAPT. One of these, PRECISE-DAPT, was published earlier this year. The PRECISE-DAPT collaborative study (published in The Lancet) developed a scoring system that can be used to predict the risk of out-of-hospital bleeding in patients receiving DAPT after undergoing PCI. The 14,963 patients who were prescribed DAPT, usually aspirin and clopidogrel. The primary endpoint of out-of-hospital bleeding occurred in 218 patients, of whom 124 had a major bleeding event. Using Cox proportional hazards regression, the investigators identified predictors of out-of-hospital TIMI major or minor bleeding stratified by trial, and devised a simple five-item numerical bleeding risk score based on patients’ age, creatinine clearance, haemoglobin, white cell count at baseline, and previous spontaneous bleeding.

The Barça experience at Camp Nou

D elegates looking to sample the delights of Barcelona would be well advised to take a visit to the iconic Camp Nou, stadium for the city’s premier football team, FC Barcelona.

One of Europe’s largest, the stadium is home to some of the world’s most expensive and celebrated footballers. But Camp Nou (“new place” in Catalan) is more than just a football stadium. It has played an integral part in the city’s history and development, and is held in high regard by Catalonians.

The stadium boasts a tour, and a museum that is one of the most visited in Europe; it is open every day of the year apart from 1 January and 25 December. With tickets available from €20, the tour lasts from 1.5 to two hours and allows visitors to experience the thrill of walking out onto the Camp Nou pitch, exploring the Messi area, and marvelling at the five European cups won by the team, as well as the many domestic trophies.

FC Barcelona is currently placed second in La Liga, the Spanish football league, behind their rivals Real Madrid. For more information, see: www.fcbarcelona.com/tour-buy-tickets

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Debating the role of inflammation in cardiovascular disease

The long-awaited CANTOS study, exploring treatment for cardiac inflammation, was presented in a ESC Hot Line session yesterday (see front page for the full results). The phase III study, which met its primary endpoint, is being heralded as groundbreaking because it provides the first real evidence for the inflammation hypothesis of atherosclerosis.

In the Great Debate this morning Professor Paul M Ridker (Harvard Medical School, Boston, USA), the principal investigator of the CANTOS study, will undoubtedly be drawing heavily upon his latest results to support the motion “Inflammation plays a key role in coronary artery disease.” “The debate should be interesting to attend to because we’re right at the very beginning of a paradigm shift in our core thinking about the treatment of atherosclerosis,” he told ESC Congress News.

It is part of the move towards personalised medicine, which provides the right therapy to the right patient at the right time. “We’re finding that patients with residual inflammatory risk are very common and believe that their treatment should differ from patients with residual cholesterol risk,” Prof. Ridker says.

Some feel the role of inflammation in coronary artery disease (CAD) originally came from observations that up to half of all events occur in apparently healthy individuals with other risk factors, including dyslipidaemia. Studies have suggested inflammation plays a key role in destabilisation and rupture of atherosclerotic plaques, leading to myocardial infarction (MI).

C-reactive protein (CRP), a marker of the inflammatory process, has been a forerunner in the search for inflammatory markers in CAD. Recently, the Physician’s Health study involving 22,071 healthy middle aged men (1997) it has been shown that those in the highest quartile for CRP had three middle aged men (1997) it has been shown that in the search for inflammatory markers. In the leading to myocardial infarction (MI).

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According to Yolande Appelman and Pieter Doevendans, it was a tough ride with about 200km each day, going through the mountains in variable weather conditions. The group started the tour to raise money for inherited cardiac failure caused by a mutation in the phospholamban (PLN) gene. The founder mutation has been identified in the Netherlands, and half of the carriers

In the JUPITER study, it was demonstrated that canakinumab, in comparison with placebo, reduces the rate of recurrent MI stroke and cardiovascular death among MI patients who remain at high risk due to persistent elevation of the inflammatory biomarker CRP (2mg/L) despite receiving the best medical care. Canakinumab, a human monoclonal antibody neutralising interleukin-1β, is already approved for use in several rare heritable paediatric conditions associated with IL-1β over expression.

For the inflammation hypothesis of cardiovascular disease to become widely accepted, further studies will be needed to show that other anti-inflammatory agents have beneficial effects. Further support could come from the National Heart Lung and Blood Institute (NHLBI)-funded CIRT (Cardiovascular Inflammation Reduction Trial) study testing whether low-dose methotrexate reduces MI or death in people with type 2 diabetes or metabolic syndrome that have had a MI or have stable coronary artery disease. These results, however, are not anticipated for several years.

In the debate today Professor Alberico Catapano (University of Milan, Italy), an advocate of aggressive reduction of cholesterol in high-risk patients, will oppose the motion. He may cite the fate of GSK’s darapladib (an inhibitor of an enzyme responsible for pro-inflammatory mediators within the atherosclerotic plaque [lipoprotein-associated phospholipase A2]). The fact that in both SOLID TIMI 52 and STABILITY, darapladib produced negative findings, serves as a reminder of the many challenges facing novel therapies directed towards the inflammatory cascade.

A 1,600km journey for inherited cardiac failure

A group of nine cardiologists and fellows from the Netherlands have completed a cycling journey to ESC in Barcelona. The five men and four women from four hospitals cycled 1,600km in eight days—they left the Netherlands on Saturday 19 August and arrived in Barcelona on Saturday 26 August.

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A comprehensive resource for all professional members of the ESC

An online platform, ESC Cardiovascular Medicine Online, based on the forthcoming third edition of the European Society of Cardiology (ESC) Textbook of Cardiovascular Medicine, is due to be launched early next year exclusively for ESC Professional Members. With third edition available later in print, this multimedia resource will provide you with a thoroughly modern reference work.

Professor John Camm (St George’s University of London, London, UK), an Editor-in-Chief of the textbook, says that the third edition seeks to “join everything from the ESC, from an education perspective, together”. The number of chapters, section editors, and Editors-in-Chief is eight, ten, and four, respectively — proof of just how comprehensive this new work will be. Furthermore, the online edition will include videos and other information that are typically seen in a printed textbook, Professor Thomas F. Lüscher (Zurich Heart House, Careum Campus, Zurich, Switzerland), another of the Editors-in-Chief, comments: “It will be really dynamic. For example, a reader may want to find out more about giant cell myocarditis, because a patient with the condition has presented in their clinic, so they use the online platform. By watching a video, they can see what the histology looks like and what the left ventricular function looks like etc.”

Another important feature of the online version is that it will be regularly updated. Prof. Lüscher observes that a limitation of a print textbook is that it may become outdated — potentially, even by the time it has been printed — because of the lengthy writing, editing, and printing process. He notes that some chapters may have been written a year or two prior to a textbook coming out. Therefore, he says, the aim is to update the online version three times a year to coincide with the dynamic digital version will be available via ESC Congress and other major cardiology conferences.

The online platform shall, thus, be kept fresh with the latest ESC Guidelines. The online platform launches in the first quarter of 2018 and is only available to Professional Members of the ESC. For those who prefer a more traditional textbook, the (printed) third edition of ESC Textbook of Cardiovascular Medicine will be made available for the ESC Congress 2018 in Munich.

Prof. Camm believes that both ESC Cardiovascular Medicine Online and the ESC Textbook of Cardiovascular Medicine are useful resources for all cardiologists — even those who are as experienced as himself. He says: “No one can retain all of the information they receive throughout their career and, therefore, the textbook and online platform can serve as a useful reminder. Furthermore, Prof. Camm states, they can learn new things “because it [the online platform] will continuously be updated with new knowledge.”

Helen Liepman (Senior Publisher, Medicine, Oxford University Press) comments: “Oxford University Press is extremely proud to be publishing the new edition of this innovative project on behalf of the ESC. The publication takes a central position in the ESC publication portfolio and will have dynamic links through to primary research papers and articles especially those from the ESC Journal family such as the leading European Heart Journal. In due course, the fully integrated access to the dynamic digital version will be available via annual subscription and the full launch is planned for July 2018. Professional Members of the Society will be given advance access earlier in 2018 as a member benefit. The publication is being showcased during the Congress at the OUP stand.

The other Editors-in-Chief are Professor Patrick Serruys (National Heart and Lung Institute, Imperial College London, London, UK) and Professor Gerald Maurer (Medical University Vienna, Vienna, Austria).

Social media can make things much easier. For instance, organisations such as the ESC can better reach delegates and help spread more information. I hope that social media will help us in our future day-to-day practice as well. In the Czech Republic, our patients are not used to interacting with physicians through social media, but this is starting to improve. Czech patients are discovering that they can use social media to interact with physicians and learn about cardiovascular health. Doctors need to use social media to connect with these patients and help spread information about cardiology.

I think that we have underestimated the power of social media, in particular how it could help us to interact with our patients. We should try to establish more direct contact; everyone goes online anyway, so why not go online and communicate with your physician? Educating patients is also an obvious use for social media, and I think we could develop much closer interactions so that we can better reach delegates and help spread information about cardiology.