

ESC 2022



Review of the European Society of Cardiology (ESC) Congress 2022

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AFTER 2 years of virtual meetings, the European Society of Cardiology (ESC) adopted a pioneering hybrid format for its 2022 congress, allowing delegates from across the globe to meet onsite in Barcelona, Spain, and also online. Clinicians and academics came together with one common goal: to advance cardiovascular care and improve patient outcomes. This was emphasised by Stephan Achenbach, ESC President, who commented: "At ESC Congress in Barcelona, we discussed the newest science in the light of our collective clinical experience. This is how true progress in cardiovascular medicine is made." Achenbach spoke about the rapid pace of innovation and advancement since the first double-blind randomised trial in cardiovascular medicine was completed in 1971. "Numerous large trials are published every year, often practice-changing, and many are first presented at ESC Congress," he emphasised.

This year's conference was attended by more than 30,270 healthcare professionals from 174 countries, with highly anticipated clinical trial results shared during hotline sessions. Novel and impactful research was also showcased in 3,218 abstracts, presented by scientists from over 80 countries. Several standout abstracts, written by the presenters themselves,

have been summarised in this edition of *EMJ Cardiology*. These cover important topics such as atrial fibrillation and the risk of stroke among veteran athletes, cardiac damage staging in patients undergoing transcatheter aortic valve repair, and artificial intelligence-guided single-lead ECG as a tool to reduce symptom-to-balloon time in ST-elevated myocardial infarction.

Digital health heavily featured at ESC Congress 2022, and EMJ had the privilege of interviewing Nico Bruining, Chair of the ESC Digital Health Committee. At this year's congress, Bruining co-chaired several sessions on e-Cardiology, artificial intelligence, and machine learning, and he provided an overview of the key take-home messages from these. EMJ also had the unique opportunity to speak with Allan Böhm, Chair of the ESC Committee for Young Cardiovascular

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Professionals. Of note, Böhm was one of the first members of the ESC Digital Health Committee, and he talked about the importance of digital health interventions for the prevention of cardiovascular diseases, as well as actions that the ESC can undertake to ensure digital healthcare remains a priority for the cardiology community. Both interviews can be found within this journal, and are not to be missed. These are complemented by our interview with Alexander E. Berezin, a Fellow of the ESC.

Summaries of highly relevant ESC press releases have also been included in this issue of *EMJ Cardiology*, covering radial artery access for coronary angiography or percutaneous coronary intervention, the role of an invasive strategy in patients with advanced chronic kidney disease and chronic coronary disease, and the use of a polypill versus usual care to reduce cardiovascular events after a heart attack.

Looking to the future is important in any field, and Stephan Windecker, Congress Programme Chair, highlighted a particularly noteworthy session from ESC Congress 2022, "in which top experts provided their predictions for the practice of cardiovascular medicine 10 years from now." Specifically,

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this symposium looked at how the screening, prevention, and treatment of atrial fibrillation, coronary artery disease, heart disease, and heart failure might have evolved by 2033. Potential future developments in digital cardiology and artificial intelligence were also considered. This session forms the basis of our compelling in-house congress feature, and is another highlight of our independent congress review.

Whatever the future of cardiovascular medicine holds, the annual ESC Congress will remain crucial for the generation and exchange of scientific knowledge. With this in mind, we look forward to being part of the international cardiology community again at next year's conference in Amsterdam, the Netherlands. Until ESC Congress 2023 opens its doors, read on for our key insights and learnings from ESC Congress 2022. ●



Screening for Signs of Cardiovascular Disease May Reduce Risk of Morbidity and Mortality

NOVEL data has indicated that cardiovascular screening, including cardiac imaging, blood pressure measurement, and blood tests, paired with subsequent treatment when necessary, may reduce risk of heart and stroke, and lower mortality in 65–69-year-olds. The randomised trial, presented at ESC Congress 2022, investigated data from over 45,000 men with an average age of 68.8 years.

The researchers identified a total of 46,526 men between September 2014 and September 2017 from Southern and Central regions of Denmark. These men were divided into two categories: screening and intervention (n=16,736) and no screening (n=29,790), which is the current practice in Denmark. The screening and intervention group were given a cardiac and truncal non-contrast CT to detect coronary artery calcification above the sex- and age-specific medium, aortic and iliac aneurysms, and atrial fibrillation. The programme also included brachial and ankle blood pressure in both arms and legs to diagnose peripheral artery disease, and blood tests to identify high cholesterol and diabetes. When the researchers identified abnormal findings, prophylactic treatments were offered and information on medication, surgery, disease, and mortality was collected for 5 subsequent years.

“Despite remarkable reductions in mortality from cardiovascular disease, it remains the leading cause of death. More than half of cardiovascular disease is avoidable, meaning that successful

prevention has a huge potential to improve public health,” stated Axel Diederichsen, Odense University Hospital, Denmark, explaining the value of this study.

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The primary outcomes from both groups were all-cause mortality, with secondary outcomes including stroke, myocardial infarction, amputation due to vascular disease, aortic dissection, and aortic rupture. When the two groups were compared over a median follow-up of 5.6 years, researchers found that 12.6% of men in the intervention group and 13.1% in the control group had died. Remarkably, the study found that the number of individuals needed to be invited to screening to prevent one death was 155. Analysis demonstrated that though an 11% decreased risk of mortality was found in those aged 65–69 years (p=0.004), no significant difference was found in men aged 70 years and older.

“We observed a substantial reduction in the combined endpoint of death, stroke or myocardial infarction in elderly men by comprehensive cardiovascular screening. Our results point quite firmly at a screening target age below 70 years,” stated Diederichsen.

Superiority of Artificial Intelligence in Assessing Cardiac Function on Echocardiograms

ARTIFICIAL intelligence (AI) technology developed by David Ouyang, Smidt Heart Institute, Cedars-Sinai, Los Angeles, USA, and colleagues, shows superiority at initial echocardiographic assessment of cardiac function compared to initial sonographer assessment.

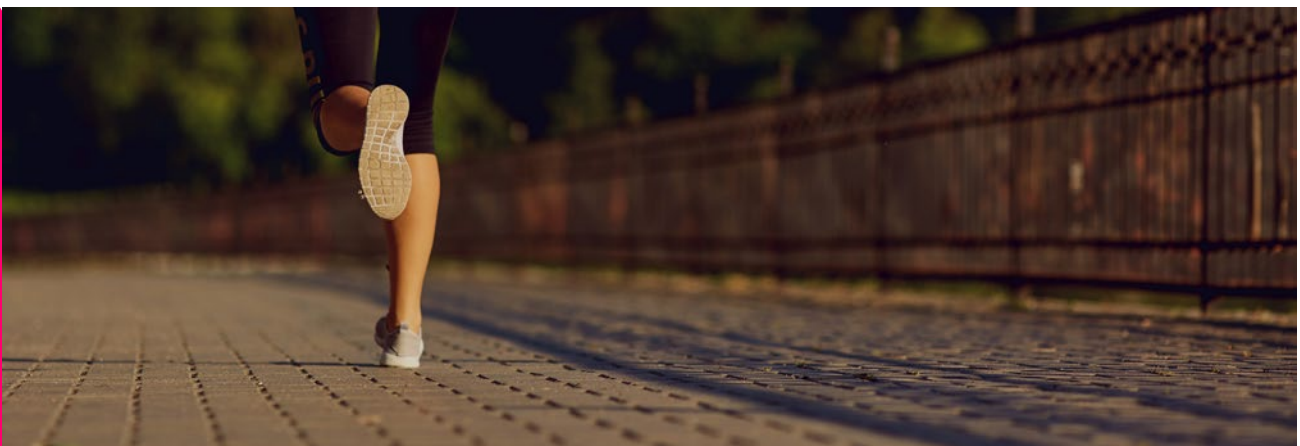
Ouyang presented these findings at ESC Congress 2022 in Barcelona, Spain, on 27th August. Having previously developed the EchoNet-Dynamic deep learning algorithm to assess cardiac function, the authors subsequently performed a randomised controlled trial to assess the algorithm against sonographer echocardiographic examination of left ventricular ejection fraction (LVEF) to determine whether EchoNet-Dynamic was non-inferior in reporting compared to sonographers, validated by a cardiologist. The study was designed to test for non-inferiority, and the primary endpoint was the frequency of a >5% change in the LVEF reporting between the initial assessor and final reporting cardiologist, with a secondary endpoint of testing for AI superiority.

Transthoracic echocardiograms from 3,495 adult patients were randomised to initial assessment by AI or initial assessment by sonographer. These initial assessments were then reviewed by a blinded cardiologist before the final report was confirmed. The percentage

of assessments with >5% change in cardiologist LVEF reporting was 16.8% in the AI group versus 27.2% in the sonographer group (95% confidence interval: -13.2% to -7.7%; $p < 0.001$ for non-inferiority and superiority). The authors further evaluated a safety endpoint, in which they looked at the difference between an historical cardiologist report and the final cardiologist report from the current trial. They found that the mean absolute difference in LVEF reporting was 6.29% for the AI group and 7.23% for the sonographer group.

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These promising findings highlight how AI could be integrated into clinical work to assist with echocardiogram reporting. AI algorithms have the potential to improve the accuracy of reporting, and therefore improve efficiency by reducing the time specialists spend altering reports. However, Ouyang stated that these algorithms will need to be "developed and integrated in the right way" to be beneficial.



Novel Data Assessing the Performance of Invasive Coronary Testing

LATE-breaking research presented at ESC Congress 2022 highlighted the value and the challenges of two myocardial perfusion imaging (MPI) tests for selecting patients with suspected coronary artery disease (CAD) for further invasive testing. Data suggested that the two MPI tests have high specificity but low sensitivity in patients who have undergone a coronary CT angiography (CTA).

Current guidelines suggest that prior to referring patients with suspected obstructive CAD to invasive coronary angiography (ICA), myocardial ischaemia should be confirmed by MPI. There is a lack of evidence about the efficacy and performance of MPI, and whether it is the most accurate choice. In a trial including 1,732 patients with obstructive CAD symptoms, the diagnostic performance of stress MPI by 3T cardiac magnetic resonance (CMR) was compared against rubidium-82 PET (Rb-PET).

The average age of patients recruited was 59 years, and 57% of the cohort was male. Overall, 445 patients had suspected stenosis and were referred for both CMR and Rb-PET. Patients also underwent ICA fractional flow reserve (FFR) as reference, with haemodynamically obstructive CAD identified in 44.1% of patients through ICA FFR.

The sensitivity of CMR was 59% (95% confidence interval [CI]: 51–67%) whereas Rb-PET had a sensitivity of 64% (95% CI: 56–71%). The specificities were 84% (95% CI: 78–89%) and 89% (95% CI: 84–93%), respectively. The overall accuracy of Rb-PET was 78% compared with 73% for CMR. Further, Rb-PET correctly identified more patients as high risk of disease compared with CMR (96.8% and 77.4%, respectively).

“CMR stress and PET stress had comparably moderate sensitivities and high specificities to predict the FFR results. A perfusion test approach therefore seems safe as almost all patients with serious disease (high-grade stenoses, left main, and three-vessel disease) were diagnosed,” explained Morten Botcher, Aarhus University, Denmark.

“The accuracy of coronary CTA needs to improve so that more patients without obstructive CAD avoid further investigations. This might be achieved through better CT image quality and perhaps by more advanced image analyses like non-invasive FFR estimation and photon counting systems.”

Radial Access for Coronary Procedures Improves Mortality?

RANDOMISED controlled trial (RCT) meta-analysis data presented by Giuseppe Gargiulo, Federico II University Hospital, Naples, Italy, at ESC Congress 2022 in Barcelona, Spain, on 29th August, has shown that transradial approach (TRA) for coronary angiography or percutaneous coronary intervention (PCI) resulted in improved 30-day all-cause mortality and major bleeding rates when compared with transfemoral approach (TFA).

Gargiulo stated that the data “provides definitive evidence that TRA should be considered the gold-standard for patients undergoing cardiac catheterisation with or without PCI,” but also commented that the benefits associated with TRA only apply to patients experiencing acute coronary syndrome (ACS), and that the results cannot be generalised to patients undergoing elective cardiac catheterisation with or without PCI.

The meta-analysis reviewed data from seven high-quality RCTs of 21,600 patients undergoing coronary intervention who were randomised to either TRA (n=10,775) or TFA (n=10,825) against the primary outcomes of 30-day all-cause mortality and major bleeding. The median age of participants was 63.9 years, and 68.1% were male. Of the 21,600 enrolled, 95% presented with ACS and PCI was performed in 75.2%. The participants were subcategorised into several cohorts: intention-to-treat, per-protocol, as-treated, PCI, ACS, and myocardial infarction.

Primary analysis of the intention-to-treat cohort showed a 1.6% incidence of all-cause death in the TRA group compared with 2.1% in the TFA group, with a hazard ratio of 0.77 (95% confidence interval: 0.53–0.95; p=0.012). The reduction in all-cause mortality was confirmed across all the subcohorts. In addition to this, the odds of major bleeding were lower in the TRA group, at 1.5%, compared to 2.7% in the TFA group, with an odds ratio of 0.55 (95% confidence interval: 0.45–0.67;

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p<0.001). Moreover, the TRA was independently associated with a relative risk reduction of 24% for 30-day all-cause mortality and 51% for major bleeding, using a multivariable model.

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No Improved Survival Rate for Patients with Kidney Disease and Ischaemia When Using an Invasive Strategy

RESEARCH has discovered that patients diagnosed with advanced chronic kidney disease and chronic coronary disease do not benefit from an invasive strategy compared to a conservative strategy, in terms of the 5-year risk of death outcome.

Late-breaking research presented at ESC Congress 2022 demonstrated that the management of chronic coronary disease has so far excluded those patients who also have advanced chronic kidney disease, or have only included a small number of such patients. Thus, optimal management for this group of patients is currently unknown.

Researchers from the ISCHEMIA-CKD study recruited 777 patients who had advanced chronic kidney disease (estimated glomerular filtration rate <30 ml/min/1.73m², or undergoing dialysis), and who also presented with moderate or severe ischaemia during stress testing. Median age was 63 years, and 31% of patients were female.

Patients were allocated at random to one of two groups. The first involved an initial invasive strategy (cardiac catheterisation and optimal revascularisation with percutaneous coronary intervention, or coronary artery bypass graft surgery if such a treatment proved suitable), as well as guideline-directed medical therapy. The second group consisted of an initial conservative strategy of only guideline-directed medical therapy. Cardiac catheterisation and revascularisation with percutaneous coronary intervention or coronary artery bypass graft surgery were reserved for the failure of the

first-line therapy. During a median follow-up of 2.2 years, researchers discovered that the invasive strategy for patients in the first group did not reduce the outcome of death or non-fatal myocardial infarction.

The trial is following participants for a median period of 9 years. An analysis of all 777 patients after the initial 5-year period had a primary endpoint of all-cause death, and secondary endpoints of cardiovascular and non-cardiovascular death. After the 5-year follow-up, 305 deaths had occurred in the patient cohort (158 in the invasive group; 147 in the conservative group). No significant difference in death between these groups was found.

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Lead study investigator Sripal Bangalore, New York University School of Medicine, USA, stated: "An initial invasive management strategy did not improve survival when added to guideline directed medical therapy in patients [...] of note, the death rate was very high with close to 40% mortality at 5 years indicating a very high-risk group of patients who are in urgent need of therapies to reduce this risk."

Coronary Stenting Not Beneficial for Patients with Severe Left Ventricular Dysfunction

FINDINGS presented at ESC Congress 2022 on 27th August suggest that patients with severe left ventricular dysfunction and extensive coronary artery (CAD) disease do not benefit from percutaneous coronary intervention (PCI). CAD, which is associated with poor survival and low quality of life, is the most common cause of heart failure.

While revascularisation was long considered a treatment option, the STITCH trial showed that only highly selected, young patients showed benefit 10 years after coronary artery bypass surgery. Previously, there was no evidence to support PCI as an alternative to bypass surgery. REVIVED-BCIS2 analysed its efficacy in patients affected by the condition. The study included a total of 700 patients from 40 centres in the UK, with severe left ventricular dysfunction, extensive CAD, and demonstrable viability in at least four dysfunctional myocardial segments that could be revascularised by PCI.

They were randomly assigned to optimal medical therapy, either alone or combined with PCI. The primary outcome (all-cause death or hospitalisation for heart failure) occurred in 134 (38%) of patients in the single therapy group, and 129 (37.2%) of patients in the combined therapy group

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(hazard ratio: 0.99; 95% confidence interval: 0.78–1.27; $p=0.96$). Regarding the secondary outcomes, there was no significant difference in the left ventricular ejection fraction after 6 months and 12 months.

Chief investigator Professor Divaka Perera of King's College London, UK, said: "PCI provided no incremental benefit over optimal medical therapy in this high-risk population, where approximately one in three patients died or were hospitalised with heart failure during follow-up." Furthermore, researchers concluded that PCI should not be offered to stable patients for prognostic benefit. However, PCI is still an option for patients with acute coronary syndromes and limiting angina.



Polypill Reduces Risk of Cardiovascular Events After Heart Attack

NEW research presented at ESC Congress 2022 on 26th August suggests that a polypill, containing aspirin and medication to lower lipids and blood pressure, is more effective in preventing further cardiovascular events after a heart attack than taking the drugs separately. Less than 50% of patients consistently take all of the medications prescribed post-infarction, which include an antiplatelet, lipid lowering medication, and a pressure-lowering and vascular stabilising drug. Therefore, it is suggested that combining the treatments into one polypill would improve adherence to treatment.

The first randomised trial to study the polypill, SECURE, enrolled patients having had a myocardial infarction within 6 months. In total, 2,499 patients were randomly allocated to either usual care or a polypill, which contained 100 mg of aspirin; 2.5, 5, or 10 mg of ramipril; and 20 or 40 mg of atorvastatin. The median follow-up was 3 years, during which the primary composite endpoint of death from cardiovascular causes, nonfatal myocardial infarction, stroke, or urgent revascularisation occurred in 156 (12.7%) of the usual care group and 118 (9.5%) of the polypill group. Cardiovascular death was the most notable event, occurring in 71 (5.8%) patients in the usual care group, and 48 (3.9%) patients in the polypill group. The secondary endpoint of cardiovascular death, nonfatal myocardial infarction, or stroke occurred in 144 (11.7%) patients

in the usual care group and 101 (8.2%) patients in the polypill group. The adherence to treatment in the polypill group was higher than the usual care group.

"The median follow-up was of 3 years, during which the primary composite endpoint of death from cardiovascular causes, nonfatal myocardial infarction, stroke, or urgent revascularisation occurred in 156 (12.7%) of the usual care group and 118 (9.5%) of the polypill group."

Researcher Valentin Fuster from the Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain, and Mount Sinai Health System, New York, USA, said: "The findings suggest that a polypill could become an integral part of strategies to prevent cardiovascular events in post-infarction patients. By simplifying treatment and improving adherence, this approach has the potential to reduce the risk of recurrent disease and cardiovascular death on a global scale."

Improved Decongestion in Patients with Acute Decompensated Heart Failure

ACETAZOLAMIDE decreases congestion in patients with acute decompensated heart failure (ADHF) in 3 days, according to Wilfried Mullins, Hospital Oost-Limburg, Genk, Belgium, who presented the findings of the ADVOR trial at ESC Congress 2022.

Accounting for up to 70% of acute HF presentations, ADHF is the most common form and requires immediate evaluation and treatment. Despite the use of guideline-recommended intravenous (IV) loop diuretics to improve symptoms of fluid overload, residual congestion remains in many patients with the current drug.

Enrolling 519 adults hospitalised with ADHF across 27 centres in Belgium, the primary endpoint of the ADVOR trial was successful decongestion, with no clinical signs of fluid overload except for trace oedema. The trial investigated the use of acetazolamide as an additional drug in IV loop diuretics to improve decongestion in patients with ADHF within 3 days of randomisation, without escalating decongestive therapy. Patients were randomised 1:1, either being administered IV acetazolamide 500 mg once daily or placebo upon randomisation and for 2 days, or until successful decongestion.

In the acetazolamide group, 42.2% of patients achieved the primary outcome compared with 30.5% of patients in

the placebo group (relative risk: 1.46; 95% confidence interval: 1.17–1.82; $p=0.0009$). The acetazolamide group also had shorter hospital stays than the placebo group (8.8 and 9.9 days, respectively; $p=0.02$). However, there was no difference in HF hospitalisation or all-cause mortality at 3 months.

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Finally, of the patients who were alive at discharge, 190 out of 241 patients (78.8%) in the acetazolamide group and 145 out of 232 patients (62.5%) in the placebo group had successful decongestion (relative risk: 1.27; 95% confidence interval: 1.13–1.42; $p=0.0001$).

Mullins, who was also the principal investigator for the ADVOR trial, stated: "Patients treated with acetazolamide had more diuresis and natriuresis, and were more likely to be discharged without residual signs of volume overload. There did not appear to be an increase in adverse events with the drug."





Benefits of Statins Outweigh Risk of Muscle Pain and Weakness

BREAKING research shows that the risk of muscle symptoms related to statin therapy is outweighed by its benefits, which include preventing cardiovascular disease, such as heart attacks and strokes. The research, led by Colin Baigent, Director of the Medical Research Council Population Health Research Unit at the University of Oxford, UK, was presented at ESC Congress 2022 on 29th August.

Statins typically prevent 25 major vascular events in patients with no pre-existing vascular disease, and 50 major vascular events in patients with pre-existing vascular disease; however, there have been concerns that this widely prescribed therapy may cause muscle pain or weakness. A meta-data analysis of the recorded muscle symptoms in 23 randomised, double-blinded trials of statin therapy was completed, compiling information on nearly 155,000 patients. The researchers collected adverse event data from four randomised double-blind trials of more intensive versus less intensive statin therapy, and 19 randomised double-blind trials of statin therapy versus placebo.

In the trials on statins versus placebo, 27.1% of patients reported muscle pain or weakness in the statin group versus

26.6% in the placebo group. There was a 7% relative increase in reports of muscle pain or weakness among the statin group in the first year, corresponding to an absolute excess rate of 11, and no evidence of excess risk in the remaining follow-up period. Only one in 15 of reported cases were attributed to statin therapy.

"The results of this research will help physicians and patients to make more informed decisions when it comes to statin therapy."

The trials on more intensive versus less intensive therapy showed a larger relative increase in muscular pains or weakness compared with the moderate intensity regimens. Baigent said: "Statins were not the cause of muscle pain in more than 93% of patients who reported symptoms. Statin therapy marginally increased the frequency, but not the severity, of muscle-related symptoms." The results of this research will help physicians and patients to make more informed decisions when it comes to statin therapy.