

# Congress Review

## Review of the European Society of Cardiology (ESC) Congress 2021

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THE EUROPEAN Society of Cardiology (ESC) Congress 2021 successfully brought together clinicians and researchers from across the globe, working to advance cardiovascular care and medicine and improve patient outcomes. This year, the online meeting attracted more than 39,000 healthcare practitioners from 169 countries. In comparison, the 2019 face-to-face event in Paris, France, was attended by 33,510 delegates from 151 countries. Clearly, the transition to a digital format allowed for greater accessibility, diversity, and inclusivity, enabling the ESC to “provide health professionals working in the field of cardiovascular disease and prevention with information intended to reduce the burden of cardiovascular disease.”

Stephan Achenbach, ESC President, discussed the importance of this year’s event, both directly on cardiologists and indirectly on patients: “Across four days we discovered the latest research findings that will impact cardiovascular practice and improve patient care in a scientific bonanza like no other.”

The spotlight of the ESC Congress 2021 was sudden cardiac death, with presentations highlighting therapeutic interventions and risk of sudden cardiac death in structural heart disease, risk calculators to predict sudden cardiac death in cardiomyopathies, and alternatives to transvenous defibrillators for the prevention of sudden death. Beyond this overarching theme, topics encompassed the consequences of COVID-19 in heart failure, novel approaches to catheter ablation, recent advances in the diagnosis and treatment of hypertension, challenges of cardiovascular pharmacotherapy in the elderly, spiroergometry in clinical practice, insights into metabolic strategies to treat cardiovascular disease, and antithrombotic therapy after transcatheter aortic valve implantation.

Of note were the ‘Guidelines in Practice’ sessions, which examined the management of patients with asymptomatic chronic coronary syndrome, the management of atrial septal defects with pulmonary hypertension, and the ESC and European

Society of Hypertension (ESH) guidelines on the management of arterial hypertension in elderly patients.

Stephan Windecker, Congress Programme Chair, stressed that “sessions were not just one-way presentations. There were plenty of opportunities for scientific exchange between delegates and expert faculty through the discussion chats and live Q&A [question and answer] sessions.” As a result, this year’s event was “a truly interactive congress connecting health professionals around the world.”

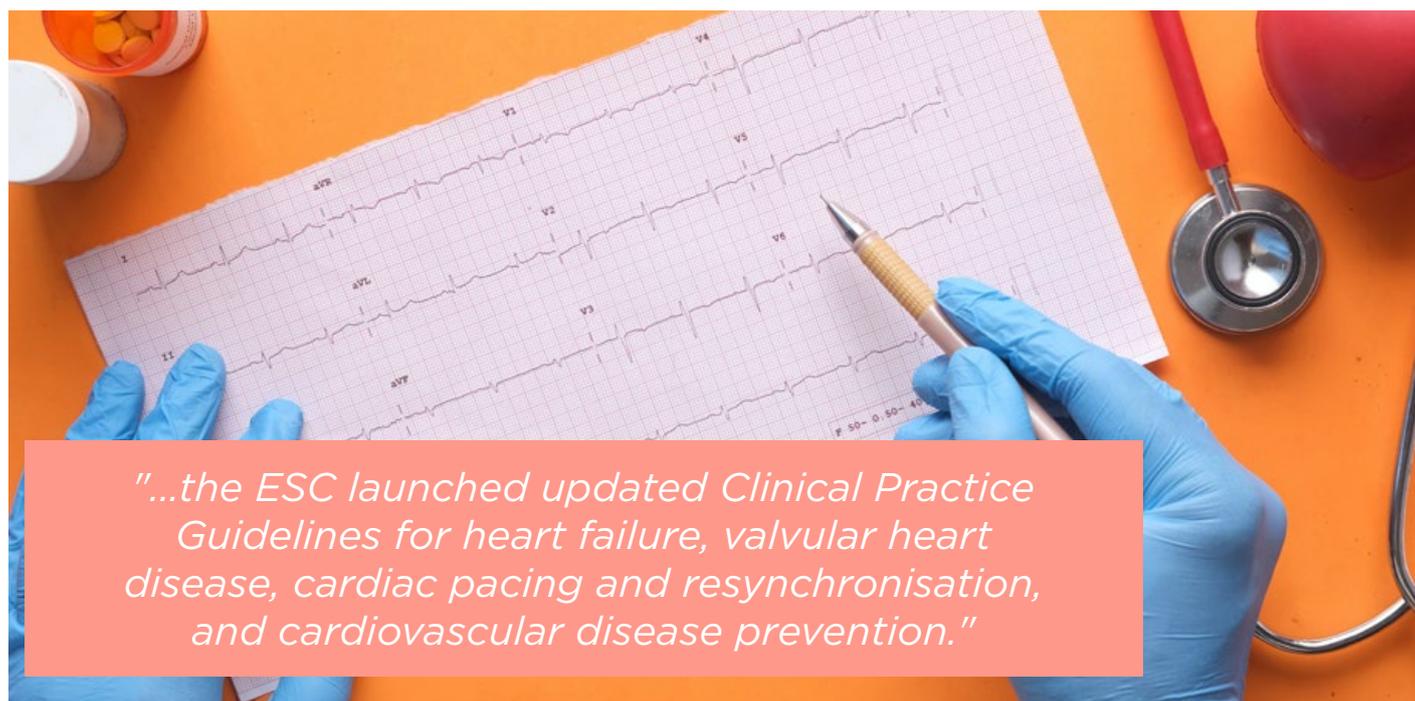
Furthermore, almost 3,700 abstracts were presented over the course of the 4-day conference, providing insights across the various sub-disciplines of cardiology. Several standout abstracts have been summarised in this issue of *EMJ Cardiology*, covering highly relevant topics such as echocardiographic parameters of individuals with COVID-19 pneumonia in hospital and 3 months after discharge, the impact of depression on cardiac autonomic activity, and the effects of elevated circulating levels of TGF- $\beta$  on the progression of valve myxomatosis and leaflets billowing.

In addition, the ESC launched updated Clinical Practice Guidelines for heart failure, valvular heart disease, cardiac pacing and resynchronisation, and cardiovascular disease prevention. Essential

messages were “presented by task force chairs and a panel of experts exploring the implications for clinical practice,” said Windecker. A compelling in-house feature outlining the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure has been included in our independent congress review.

An overview of hot-topic ESC press releases can also be found within these pages, including whether the influenza vaccination should be considered as part of standard hospital care following acute myocardial infarction, the use of ablation and biventricular pacing in people with severely symptomatic permanent atrial fibrillation, and the long-term effects of carotid artery surgery versus stenting on fatal or disabling stroke in patients with asymptomatic carotid stenosis. Each groundbreaking news story featured in this publication was based on research presented during the ESC Congress 2021.

EMJ looks forward to welcoming you all, hopefully in-person, to Barcelona, Spain, next year for the 2022 meeting of the world’s largest cardiology conference. Until then, read on for our key scientific insights from the ESC Congress 2021. ■



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ESC 2021 REVIEWED →

## Stenting and Carotid Artery Surgery Have Similar Effects on Chance of Stroke



*“We have shown that, for patients with a severely narrowed carotid artery, stenting and surgery have similar effects on the chances of having a disabling or fatal stroke. The risk from each procedure is about 1%.”*

**B**REAKING research conducted on patients with asymptomatic severe carotid artery stenosis has discovered comparable long-term effects between stenting and surgery on fatal or disabling stroke, according to research presented during a Hot Line session at the ESC Congress 2021. Both carotid artery stenting (CAS) and carotid endarterectomy (CEA) surgery aim to restore patency and reduce risk of stroke, combatting elevated risk in patients with severe carotid stenosis. The importance of the current ACST-2 trial lies with the provision of comparative data, which is lacking, on the long-term protective effects of both procedures.

ACST-2 was the largest trial to compare CAS and CEA in asymptomatic patients with a severely narrowed carotid artery that had not yet resulted in an ischaemic event, enrolling 3,625 participants from 33 countries. These patients were randomly allocated to CAS or CEA and followed for an average of 5 years. Outcomes measured included procedural risks for both morbidity and mortality within a month of the procedure, as well as non-procedural stroke sub-divided by severity. One percent of patients in both groups had a disabling stroke or died within 30 days (15 allocated to CAS and 18 to CEA), meanwhile 2% had a non-disabling procedural stroke (48 allocated to CAS and 29 to CEA). Alison Halliday, the principal

investigator from the University of Oxford, UK, summarised these findings: “We have shown that, for patients with a severely narrowed carotid artery, stenting and surgery have similar effects on the chances of having a disabling or fatal stroke. The risk from each procedure is about 1%. After that, however, the annual risk over the next 5 or more years is halved, from 1% down to 0.5% per year.” This is clearly reflected in the main outcome, finding that 5-year fatal or disabling non-procedural stroke occurrence was 2.5% in patients of each group, with a rate ratio (RR) of CAS versus CEA of 0.98 (95% confidence interval [CI]: 0.64-1.48;  $p=0.91$ ). Additionally, any non-procedural stroke occurred in 5.3% of the CAS group versus 4.5% of the CEA group (RR: 1.11; 95% CI: 0.86-1.57;  $p=0.33$ ). A meta-analysis of this and all other major trials of a similar design yielded a matching non-significant result for any stroke (RR: 1.11; 95% CI: 0.91-1.32;  $p=0.21$ ).

Evidence this trial brings forward will be esteemed in a field with existing knowledge gaps. Future studies will likely build upon this research to support treatment of the growing number of patients suffering from carotid artery stenosis. ■



## Gum Disease Is Linked with an Elevated Likelihood of Cardiovascular Disease

**I**NCREASED risk of heart disease has been associated with gum disease, according to a study in Sweden, which unravelled a directly proportionate relationship between periodontitis severity and risk of heart attack. Research results were presented during the ESC Congress 2021. Labelled PAROKRANK, the original version of this study presented periodontitis as significantly more common in first-time heart attack patients compared with healthy peers of the same age and sex in the same area. This long-term follow-up described an increased risk of new cardiovascular events over time, both in patients who have had heart attacks and their healthy peers, with the presence of gum disease.

*"This long-term follow-up described an increased risk of new cardiovascular events over time, both in patients who have had heart attacks and their healthy peers, with the presence of gum disease."*

Analysis included 1,587 participants with an average age of 62 years, who underwent a dental exam between 2010 and 2014: 985 were classified healthy, 489 with moderate periodontitis, and 113 with severe periodontitis. The occurrence of cardiovascular events and death were followed

until the end of 2018, with the primary endpoint a composite of all-cause death, non-fatal heart attack or stroke, or severe heart failure. Over an average of 6.2 years, there were 205 primary endpoint events, whereby participants with periodontitis at baseline had 49% higher odds relative to those with healthy gums. In this way, the probability of primary endpoint rose with increasing severity of gum disease.

Giulia Ferrannini, one of the study authors, suggested action based on their findings: "Our study suggests that dental screening programmes, including regular check-ups and education on proper dental hygiene, may help to prevent first and subsequent heart events." This is of particular importance to patients who have experienced a heart attack in the past, where this association of study was discovered to be particularly evident. Ferrannini hypothesised a cause for their discovery: "We postulate that the damage of periodontal tissues in people with gum disease may facilitate the transfer of germs into the bloodstream. This could accelerate harmful changes to the blood vessels and/or enhance systemic inflammation that is harmful to the vessels." Clinicians will second Ferrannini's warning that "the quality of care in Sweden is high, as confirmed by the overall low number of total events during follow-up," and await confirmation or disagreement with contrasting demographics in subsequent studies of a similar design. ■

# Improving and Personalising Prediction of Sudden Cardiac Death

**T**HE LARGEST dataset ever analysed with the purpose of improving understandings of sudden cardiac death risk was presented at the ESC Congress 2021. This is the first phase of the PROFID consortium.

PROFID aims to personalise the prevention of sudden cardiac death after cardiac myocardial infarction. The first phase, presented at the ESC Congress, focused on developing a model to predict the risk of sudden cardiac death in individual post-infarction patients. Sudden cardiac death is the cause of approximately 20% of fatalities, usually resulting from myocardial infarction. Patients with a left ventricular ejection fraction (LVEF) of 35% or lower are recommended a prophylactic cardioverter defibrillator. However, sudden cardiac death occurs most frequently in those with an LVEF of 35% or higher.

The first phase of the PROFID project aimed to develop a model to predict the risk of sudden cardiac arrest in patients post myocardial infarction. Data was pooled for 19 datasets across Europe, Israel, and the USA. Datasets included information on demographics, clinical parameters, medication, ECG, biomarkers, echocardiography, and patient outcomes. Six of the datasets also included cardiac MRI information. In total, approximately 225,000 patients were analysed. Participants were drawn

from a pool of patients who had previously suffered a myocardial infarction regardless of LVEF or ischaemic cardiomyopathy with LVEF below 50%.

Traditional analytical methods and artificial intelligence techniques were used to develop the four models. The models were subsequently tested for their accuracy at predicting primary patient outcomes. The accuracy of the predictions was compared to using LVEF as a predictor. The models were initially developed with the Cardiac MRI data excluded. Researchers found that none of these initial models showed substantial improvement in predicting sudden cardiac events over using LVEF. Researchers are currently in the process of updating the models to include Cardiac MRI data. The preliminary results from these models indicate an improved predictive performance. Nikolaos Dagres, Principal Investigator, explained the importance of these results: “These results contribute substantially to our approach to sudden cardiac death prediction. For the first time it has become obvious that relying on clinical variables alone, we will not be able to achieve significant improvement.” ■

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# Is Difficulty Breathing a More Accurate Predictor of Cardiac Arrest than Chest Pain?

**B**REATHING problems reported prior to cardiac arrest have been identified as an under-rated warning sign, with patients less likely to receive emergency medical help. According to research carried out at the North Zealand Hospital, Hillerod, Denmark, and presented on the 27<sup>th</sup> August at the ESC Congress 2021, difficulty breathing is the most common symptom before cardiac arrest. There is currently limited knowledge about the out-of-hospital early warning signs preceding a cardiac arrest. Increasing knowledge of these signs would improve assessment of cardiac event risk by medical professionals, enabling more effective prevention.

The study drew patients from the Danish Cardiac Arrest Registry and identified those who had contacted emergency services with symptoms 24 hours prior to cardiac arrest. The calls to emergency services were systematically evaluated to identify the symptoms reported by the caller. These patients were subsequently linked to nationwide databases to collect further information, such as survival.

Analysis identified 4,071 patients who had suffered an out-of-hospital cardiac arrest, 481

(11.8%) of whom had made pre-arrest calls. Breathing problems were the most frequently reported pre-arrest symptom, identified by 59.4% of patients, followed by confusion (23.0%), unconsciousness (20.2%), chest pain (19.5%), and paleness (19.1%). Notably, urgent medical response was dispatched to just 68.7% of calls reporting breathing problems compared with 83.0% who reported chest pain.

Furthermore, regarding survival rates, 81% of patients with breathing problems died within 30 days compared with 47% of those with chest pain.

Filip Gnesin, a research scholar at the North Zealand Hospital, explained the findings: “Breathing difficulty was the most common complaint and much more common than chest pain. Despite this, compared to chest pain, patients with breathing issues were less likely to receive emergency medical help and more likely to die within 30 days after arrest. These findings indicate that breathing problems are an under-rated warning sign of cardiac arrest”. He further stated: “We hope our findings will stimulate further research to help emergency medical dispatchers distinguish between symptoms of a pre-arrest condition versus other medical issues.” ■



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## Early Coronary Angiography in Cardiac Arrest Found Not Superior to a Delayed Selective Approach

INVASIVE, immediate strategies towards out-of-hospital cardiac arrest (OHCA) have been classified as not superior to a delayed invasive strategy. The TOMAHAWK trial presented information to clarify this, relating to early coronary angiography for patients without ST-segment elevation. The trial delivers information in a field where the usefulness and timing of coronary angiography for OHCA survivors without ST-segment elevation are uncertain. This can be applied to diagnostic coronary angiography and can guide potential percutaneous interventions, offering a beneficial initiative, where one-third of patients experience acute myocardial infarction as a cause of cardiac arrest.

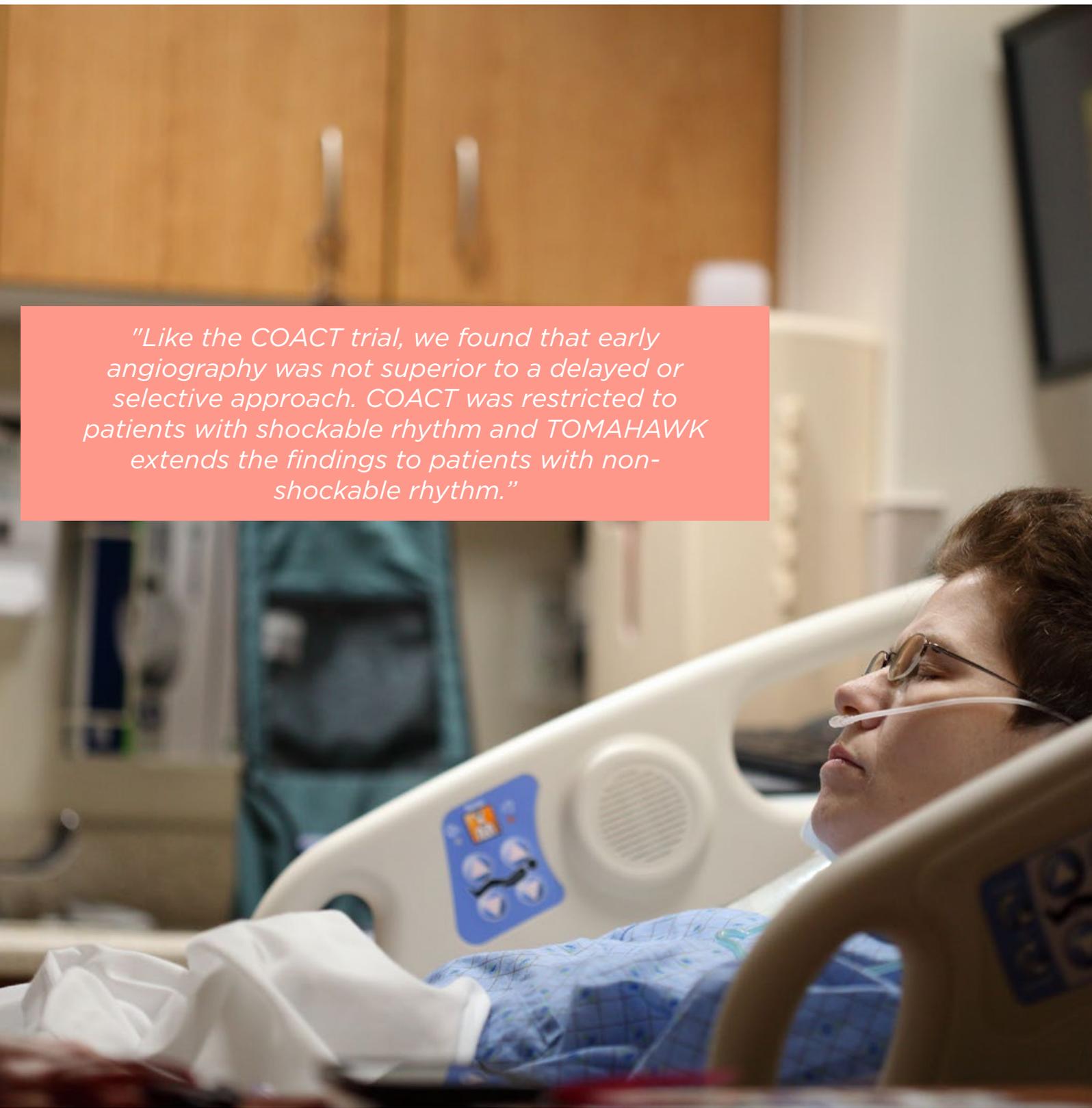
The randomised and open-label TOMAHAWK trial builds on previous guidelines set by the COACT trial, which examined whether immediate coronary angiography for treating or ruling out acute coronary events in OHCA survivors without ST-segment elevation is beneficial for all-cause mortality at 30 days, compared with intensive care unit assessment and delayed selective angiography. The current study enrolled 554 patients aged 30 years or over, all with successful resuscitation after OHCA and including both shockable and non-shockable rhythms, randomised at hospital admission to immediate coronary angiography or initial intensive care unit assessment with delayed angiography, if indicated. The primary endpoint was all-cause mortality at 30 days, occurring in 143 patients (54%) assigned to immediate coronary angiography and 122 patients (46%) in the delayed group. No differences were observed between groups in safety endpoints, including moderate or severe bleeding, stroke, and acute renal failure requiring renal replacement therapy. Other secondary endpoints such as length of intensive care unit stay, peak troponin release, myocardial infarction, or rehospitalisation for congestive heart failure also did not differ between groups. Secondary endpoint of all-cause death or severe neurological deficit at 30 days did occur more frequently in the immediate angiography group (relative risk: 1.16; 95% confidence interval: 1.002-1.340).

Steffen Desch, the Principal Investigator from the Heart Centre Leipzig, Germany, summarised the progress the study has made in the specialty of cardiology: "TOMAHAWK was the second and largest randomised trial addressing the question of early coronary angiography in OHCA

patients without ST-segment elevation. Like the COACT trial, we found that early angiography was not superior to a delayed or selective approach. COACT was restricted to patients with shockable rhythm and TOMAHAWK extends the findings to patients with non-shockable rhythm.” Desch acknowledged limitations: “The higher rate of death or severe neurological deficit in the immediate angiography group is only hypothesis-

generating.” Even so, “the results of the trial suggest that patients without a significant coronary lesion as the trigger of cardiac arrest do not benefit from an invasive approach and might even be harmed.” This study provides an infrastructure for upcoming investigations to take further, as well as useful guidance for the treatment of OHCA in patients without ST-segment elevation. ■

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## Could the Influenza Vaccine Protect Heart Attack Sufferers?

FASCINATING evidence has emerged suggesting that the influenza vaccine may have protective effects combatting adverse cardiovascular events. Presented in a Hot Line Session at ESC Congress 2021 from research in the IAMI randomised trial, this information has prompted the recommendation for flu jabs to become a part of standard care for those who have suffered heart attacks.

During periods of influenza epidemic, there is an observed increase in deaths caused by adverse cardiovascular events, putting many at risk. Previous observational studies have indicated that the influenza vaccine may provide a protective effect against these events. This vaccine, although currently recommended for sufferers of heart disease, is not part of standard care following an acute myocardial infarction.

The IAMI trial aimed to analyse whether the effects improved outcomes in sufferers of myocardial infarction, or percutaneous coronary intervention in high-risk sufferers of coronary artery disease following vaccination. The trial, which is the largest of its kind to date, was carried out at 30 hospitals in 8 countries, over 4 influenza seasons.

Each participant was randomly chosen to receive either the influenza vaccine or a placebo within 72 hours of invasive coronary surgery, or hospitalisation. The primary endpoint of the study was comprised of all-cause death, myocardial infarction, or stent thrombosis at 12 months; a hierarchical testing strategy was also used to assess the key secondary outcomes of these events.

The trial, although prematurely stopped due to the COVID-19 pandemic, enrolled 2,571 patients. The primary composite endpoint was observed in 5.3% of vaccinated patients, and 7.2% of the placebo group. The placebo group also experienced a higher incidence of secondary endpoints, with the exception of myocardial infarction rates which saw no disparity between the two groups.

The results of this study indicated that early administration of the influenza vaccine reduced the incidence of adverse events compared to the placebo group. Ole Fröbert, Örebro University, Sweden, the Principal Investigator of the study explained: “Our findings suggest that influenza vaccination should be considered as part of in-hospital treatment after myocardial infarction.” ■

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# Salt Substitutes as an Affordable Method of Stroke Risk Mitigation

**S**ALT substitutes offer a cheap and simple alternative that can lower risk of high blood pressure, stroke, and cardiovascular disease-caused mortality. These findings have been demonstrated in late-breaking research presented at the ESC Congress 2021.

The SSaSS compared the effect of reduced sodium salt substitutes, made of potassium chloride, against regular salt (sodium chloride). Elevated sodium intake and low potassium have both been previously associated with high blood pressure and an increased risk of cardiovascular disease and premature death. Salt substitutes have been shown to lower blood pressure; however, they have previously drawn concerns about causing hyperkalaemia in patients with chronic kidney disease and their effects on heart disease, stroke, and death have been uncertain. The SSaSS investigated whether reduced sodium salt affected blood pressure, risk of cardiovascular events, mortality, and hyperkalaemia.

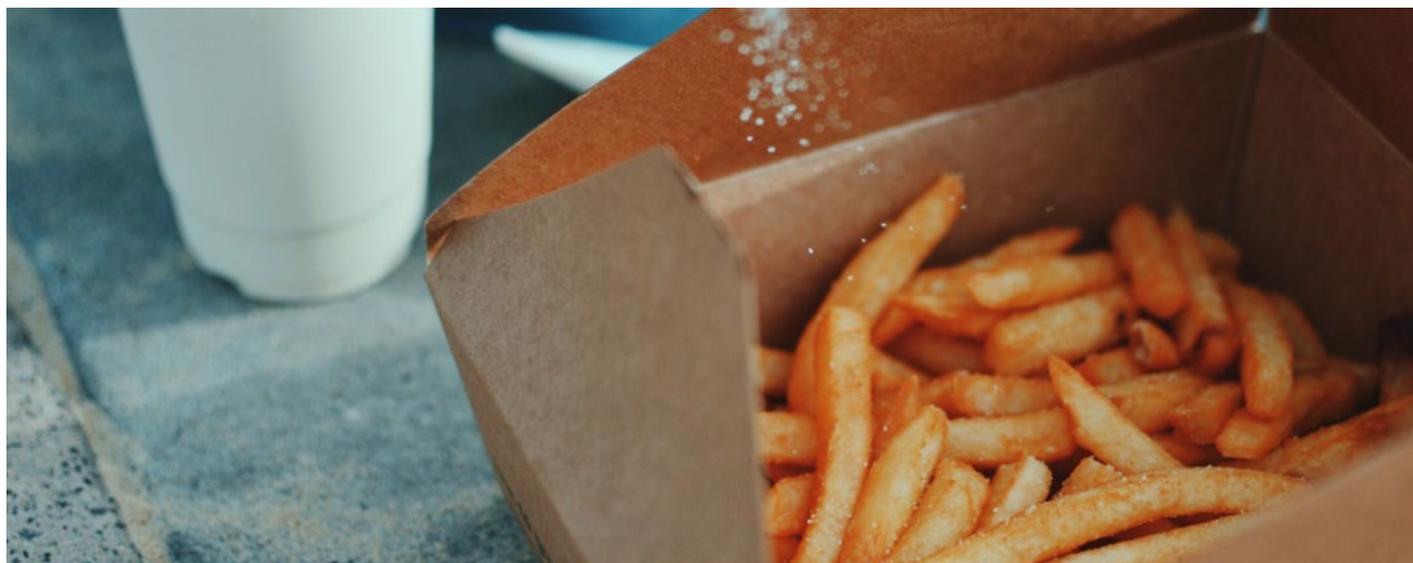
The open, cluster-randomised trial enrolled a total of 20,995 patients between April 2014 and January 2015. Participants were adults who had either suffered a previous stroke or were aged 60 or older with poorly controlled blood pressure and were drawn from 600 villages in 5 rural provinces

of China. Participants were cluster randomised by village in a 1:1 ratio of intervention salt substitute versus continued use of regular salt.

During the 5-year follow up, more than 3,000 participants had a stroke, over 4,000 died, and over 5,000 had a major cardiovascular event. The comparison found that the risk of stroke was reduced in the intervention salt substitute group compared with the regular group (29.14 versus 33.65 per 1,000 patient years, representing a significant reduction at 95% confidence interval as  $p=0.006$ ). Furthermore, risk of major cardiac events was reduced and there was no increased risk of serious adverse events attributed to clinical hyperkalaemia associated with the salt substitute compared to regular salt.

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Principle investigator Bruce Neal of the George Institute for Global Health, Sydney, Australia stated that: “This study provides clear evidence about an intervention that could be taken up very quickly at very low cost.” He further highlighted the significance of the findings: “The trial result is particularly exciting because salt substitution is one of the few practical ways of achieving changes in the salt people eat.” ■



# Ablation and Biventricular Pacing Boosts Survival in Selected Atrial Fibrillation Patients



*"The improvement in survival shown by the APAF-CRT trial supports ablation plus CRT as a first line therapy in patients with permanent AF, narrow QRS, and previous hospitalisation for heart failure."*

**R**EDUCED mortality rates have been observed in severely symptomatic permanent atrial fibrillation (AF), by the use of ablation plus cardiac resynchronisation therapy (CRT) compared to pharmacological therapy, states a new study presented at the ESC Congress on 28<sup>th</sup> August 2021. Research has previously demonstrated, by slowing and regularising the ventricular rate in patients diagnosed with AF, atrioventricular (AV) junction ablation, and right ventricular pacing has led to improved symptoms, quality of life, and cardiac function.

The APAF-CRT trial involved patients diagnosed with severely symptomatic permanent AF and a narrow QRS. Phase I of the study demonstrated that both AV junction ablation and CRT led to reduced hospitalisation compared to the pharmacological therapy. The results of the multicentre, international, prospective, randomised, Phase II trial were presented in the ESC Congress 2021. The criteria of the patients included were severely symptomatic permanent AF (over 6 months) considered unsuitable for AF ablation or in whom AF ablation had failed; narrow QRS (110 msec or below); and at least one hospitalisation for heart failure the previous year. A total of 133 patients were randomised were assigned in a 1:1 ratio to either optimal pharmacological rate control therapy (drug arm) or AV junction ablation and biventricular pacing (ablation+CRT arm). The participants were a mean age of 73 years, and 62 patients (47%) were female.

The primary endpoint of death occurred seven patients (11%) in the ablation+CRT arm and in 20 patients (29%) in the drug arm group (hazard ratio: 0.26; 95% confidence interval: 0.10–0.65;  $p=0.004$ ). The estimated death rates at 4 years were 14% and 41% in the ablation+CRT and drug arms, respectively. Additionally, at 4 years, the relative and absolute risk reductions were 74% in the ablation+CRT arm and 27% in the drug arm group. Furthermore, AV junction ablation and CRT reduced combined risks of death from any cause or hospitalisation for heart failure by 60% (95% confidence interval: 0.22–0.73;  $p=0.002$ ).

Principal Investigator Michele Brignole, Professor of the IRCCS Istituto Auxologico Italiano, San Luca Hospital, Milan, Italy, said: "We hypothesise that the observed benefit was due to the combination of the strict rate control and rate regularisation achieved by AV junction ablation, together with biventricular pacing, which counteracted the adverse effects of right ventricular pacing. The improvement in survival shown by the APAF-CRT trial supports ablation plus CRT as a first line therapy in patients with permanent AF, narrow QRS, and previous hospitalisation for heart failure." ■