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TOP 7 SESSIONS
DAILY COVERAGE
DAY-4

TOPIC OF CONTENT

POST HOC ANALYSIS PROVIDES NEW INSIGHTS ON SACUBITRIL/VALSARTAN IN MYOCARDIAL INFARCTION

Barcelona Monday, August 29th, 2022

Sacubitril/valsartan is superior to ramipril in high-risk survivors of acute myocardial infarction, according to a post hoc win ratio analysis of the PARADISE-MI trial presented in a Hot Line session on August 29th 2022 at ESC Congress 2022.

Study author Dr. Otavio Berwanger of the Academic Research Organization (ARO), Hospital Israelita Albert Einstein, Sao Paulo, Brazil said: "The win ratio was introduced in 2012 as a novel approach for examining composite endpoints in clinical trials. The win ratio accounts for both the clinical relevance and timing of individual components of an endpoint – more serious events are given a higher priority and are analysed first – making it a useful method for analysing composite outcomes in cardiovascular trials. Applying this method to the PARADISE-MI trial extends our understanding of the effects of sacubitril/valsartan in patients with acute myocardial infarction."

The primary results of the PARADISE-MI trial were previously reported. The trial randomly assigned 5,661 patients with acute myocardial infarction complicated by a reduced left ventricular ejection fraction (<40%), pulmonary congestion, or both to receive either the angiotensin receptor–neprilysin inhibitor sacubitril/valsartan (97 mg of sacubitril and 103 mg of valsartan twice daily) or the angiotensin-converting enzyme (ACE) inhibitor ramipril (5 mg twice daily) on top of guideline-recommended therapy. The average age was 64 years and 24% were women. At a median follow up of 22 months, sacubitril/valsartan did not significantly reduce the primary composite outcome of death from cardiovascular causes or incident heart failure. Incident heart failure included hospitalisation for heart failure and outpatient episodes of symptomatic heart failure treated with intravenous or sustained oral diuretic therapy.

A post hoc win ratio analysis of the PARADISE-MI trial is presented today. The principal composite outcome was analysed in the hierarchical order of death due to cardiovascular causes, first hospitalisation for heart failure, and first outpatient episode of symptomatic heart failure. The researchers included events confirmed by the clinical event classification committee and events identified by investigators that did not meet study definitions (and were not included in the previously reported primary analysis), with adjudicated events given a higher priority and computed first. Results were analysed by the unmatched win ratio method, where every patient in the sacubitril/valsartan group is compared with every patient in the ramipril group. The win ratio is the total number of winner pairs divided by the total number of loser pairs. A win ratio that exceeds 1.00 favours sacubitril/valsartan. The analyses included all randomised participants according to the intention-to-treat principle.

In this analysis, sacubitril/valsartan was superior to ramipril. The hierarchical analysis of the principal composite outcome of cardiovascular death, hospitalisation for heart failure, and outpatient heart failure demonstrated a larger number of wins (1,265,767 [15.7%]) than losses (1,079,502 [13.4%]) in the sacubitril/valsartan group, for a win ratio of 1.17 (95% confidence interval 1.03–1.33; p=0.015). The two main contributors to the number of wins were death due to cardiovascular causes (36.9% of wins) and hospitalisation for heart failure (29.8% of wins).

Dr. Berwanger said: "The results suggest that if any two patients are compared, one on sacubitril/valsartan and one on ramipril, and they

are not a tie, then there is a 1.17 odds that the sacubitril/valsartan patient is the winner. These exploratory analyses do not alter the primary neutral results for the drug in acute myocardial infarction, but they do provide supportive evidence to guide decisions to replace ACE inhibitors with sacubitril/valsartan once symptomatic heart failure has developed. The study illustrates how the win ratio approach may be a useful adjunct to the conventional time-to-first event analysis for trials with composite outcomes, especially where ranking the clinical importance of the different types of events is considered relevant."

DRUG COMBINATION MAY DELAY NEED FOR SURGERY IN PATIENTS WITH MARFAN SYNDROME

Barcelona Monday, August 29th, 2022

Angiotensin receptor blockers (ARBs) and beta-blockers have similar and independent effects on reducing aortic root size in patients with Marfan syndrome, suggesting that several years of combined treatment could delay the need for surgery. That's the finding of late breaking research presented in a Hot Line session on August 29th 2022 at ESC Congress 2022.

Marfan syndrome affects approximately one in 5,000 people worldwide and is often caused by a mutation in the FBN1 gene. Nearly all patients experience aortic root enlargement, which increases the risk of potentially life-threatening aortic dissection and rupture, sometimes in early adulthood. To prevent these consequences, elective surgery to replace the aortic root may be performed when dilatation reaches 4.5–5 cm. Beta-blockers are recommended to slow aortic growth based on a single, small, randomised trial.

It has also been suggested that ARBs might slow aortic root growth in Marfan syndrome. Researchers from Oxford Population Health conducted a meta-analysis on behalf of the Marfan Treatment Trialists' (MTT) Collaboration to assess the effects of 1) ARB versus control, 2) ARB versus beta-blocker, and 3) indirectly, beta-blocker versus control, on the rate of change in aortic root size adjusted for age, sex and body surface area. Effects were also examined in subgroups of patients, including those with or without a confirmed FBN1 pathogenic variant. The analysis included individual data on 1,442 patients with no prior aortic surgery from seven randomised trials.

The researchers first analysed four trials involving 676 patients and comparing an ARB with placebo or open control. The average age was 29 years, 54% were women, 75% were receiving a beta-blocker at baseline, and 83% of genotyped patients carried an FBN1 pathogenic variant. During a median follow up of three years, ARBs approximately halved the annual rate of change in the aortic root Z score, a widely used measure of aortic root size. The annual increase was +0.07 with ARBs versus +0.13 with control, for an absolute difference of -0.07 (95% confidence interval [CI] -0.12 to -0.01; p=0.012). Similar effects were observed when absolute aortic dimensions were analysed.

Lead study author Dr. Alex Pitcher, Consultant Cardiologist at Oxford University Hospitals, UK said: "The benefit of ARB therapy was particularly large in patients with an FBN1 mutation at baseline, making it more plausible that the effect is real. There were no other detectable differences in treatment effect depending on other patient characteristics, including age, sex, and blood pressure. The benefit of ARB treatment was similar regardless of whether patients were taking a beta-blocker."

The researchers then analysed the remaining three trials, which involved 766 patients and compared an ARB with a beta-blocker. The

average age was 14 years, 44% were female, none of the patients were receiving a beta-blocker prior to randomisation, and 86% of genotyped patients had an FBN1 pathogenic variant. During a median follow up of three years, the annual change in the aortic root Z score was similar in the two groups (absolute difference ARB minus beta-blocker 0.03; 95% CI -0.05 to 0.10). Results from the two analyses were used to indirectly evaluate the effect of a beta-blocker compared with control. Allocation to a beta-blocker was also estimated to approximately halve the annual change in the aortic root Z score (absolute difference compared with placebo: -0.09; 95% CI -0.18 to -0.0033; p=0.04).

Dr. Pitcher said: "Our results suggest that ARBs and beta-blockers have similar, substantial and independent effects on reducing the aortic root Z score which, if maintained over a period of several years, would be expected to delay the need for elective aortic root surgery. The findings indicate that combination therapy, where tolerable, may benefit patients with Marfan syndrome."

2022 ESC/ERS CLINICAL PRACTICAL GUIDELINES ON PULMONARY HYPERTENSION

Barcelona Monday, August 29th, 2022

The 2022 ESC and European Respiratory Society (ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension (PH) were presented. The Task Force Chairs were Professor Stephan Rosenkranz (University Hospital Cologne - Cologne, Germany; ESC Task Force Chair) and Professor Marion Delcroix (University Hospitals of Leuven - Leuven, Belgium; ERS Task Force Chair).

"In recent years, substantial progress has been made in detecting and managing PH," says Prof. Rosenkranz. "All the new evidence has been integrated into this fourth edition of the ESC/ERS Guidelines, with multidisciplinary input from the Task Force, which included cardiologists and pneumologists, a thoracic surgeon, methodologists and patients among its members." The 2022 guidelines cover the whole spectrum of PH, with an emphasis on diagnosing and treating pulmonary arterial hypertension (PAH) and chronic thrombo-embolic pulmonary hypertension (CTEPH).

So, what's new? The 6th World Symposium on Pulmonary Hypertension in 2019 reconsidered the haemodynamic definition of PH2 and amended PH definitions have been endorsed and expanded in the 2022 ESC/ERS Guidelines. The haemodynamic definition of PH in general has been updated to mean pulmonary arterial pressure (mPAP) >20 mmHg. The definition of PAH also implies a pulmonary vascular resistance (PVR) >2 WU and a pulmonary arterial wedge pressure ≤15 mmHg. "These cut-off values better reflect the limits of normal ranges and are associated with mortality," notes Prof. Delcroix, "but it should be pointed out that they do not yet translate into new therapeutic recommendations in PAH since the efficacy of therapies in patients with pulmonary vascular disease and an mPAP 21–24 mmHg and/or PVR 2–3 WU remain unknown."

The main diagnostic algorithm for PH has been simplified aiming at earlier detection in the community and now follows a three-step approach, from suspicion by first-line physicians, to detection by echocardiography and confirmation with right heart catheterisation in PH centres.

In addition, expedited referral is recommended for high-risk or complex patients. To shorten the time from symptom onset to diagnosis of PAH, screening strategies for PAH in patients with scleroderma and in patients at risk of heritable PAH are proposed based on recent results from cohort studies. To improve underdiagnosis of CTEPH, the new guidelines advocate enhanced

recognition of computed tomography and echocardiographic signs at the time of acute pulmonary embolism (PE), together with a systematic follow-up of patients with acute PE, as indicated in the 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism.

Echocardiographic and cardiac magnetic resonance imaging criteria have been added to the risk-stratification table, refining non-invasive evaluation at diagnosis. Furthermore, a four-strata risk stratification, dividing the large, intermediate-risk group into intermediate-low and intermediate-high risk, is proposed at follow-up.

The PAH treatment algorithm has been simplified, highlighting the importance of cardiopulmonary comorbidities, risk assessment both at diagnosis and at follow-up, and the importance of combination therapies. Treatment strategies during follow-up are based on the four-strata risk model and are intended to facilitate clinical decision-making.

The guidelines emphasise the importance of group 2 PH, i.e., in patients with left heart disease. In group 3 PH, for the first time there is a recommendation for PH medical therapy, based on a single positive randomised trial in patients with interstitial lung disease. In addition, the treatment algorithm for CTEPH has been modified, including multi-modal therapy with surgery, drugs and balloon pulmonary angioplasty. Supervised exercise training is now recommended in patients with PAH under medical therapy.

The Task Force has attempted to close the gap between paediatric and adult PAH care with therapeutic and follow-up strategies based on risk stratification and treatment response, which have been extrapolated from those in adults and adapted for age. There are also updates to the recommendations on sex-related issues in patients with PAH, including pregnancy. The guidelines end with the definition of a PH centre, with new recommendations that PH centres maintain a PH registry and collaborate with patient associations.

P2Y12 INHIBITORS TOP ASPIRIN FOR LONG-TERM SECONDARY PREVENTION: PANTHER

Barcelona **Monday, August 29th, 2022**

Aspirin has long been the antiplatelet of choice for long-term secondary prevention in patients with coronary disease, but a meta-analysis of several trials suggests P2Y12 inhibitor monotherapy has some advantages.

Over a median follow-up of about one-and-a-half years, the risk of CV death, MI, or stroke was lower in patients who were taking a P2Y12 inhibitor alone versus aspirin alone (5.5% vs 6.3%; HR 0.88; 95% CI 0.79-0.97), mostly driven by fewer MIs, Marco Valgimigli, MD, PhD (Cardiocentro Ticino Institute, Lugano, Switzerland), reported here at the European Society of Cardiology Congress 2022.

Though major bleeding overall occurred at similar rates with either approach, risks of GI bleeding and hemorrhagic stroke were lower with P2Y12 inhibitor therapy. No outcomes favored aspirin.

"Based on all available randomized evidence, long-term P2Y12 inhibitor [therapy] may be warranted instead of long-term aspirin monotherapy for secondary prevention in patients with coronary artery disease," Valgimigli concluded at a press conference.

PANTHER META-ANALYSIS

Aspirin has been the mainstay of secondary prevention in patients with established coronary disease for decades, with P2Y12 inhibitors being added as part of dual antiplatelet therapy (DAPT) among patients with ACS and/or after coronary

revascularization. However, the relative efficacy and safety of monotherapy with a P2Y12 inhibitor versus aspirin is not completely understood for patients with established CAD, said Valgimigli, who noted that guidelines currently recommend lifelong aspirin after DAPT is stopped.

To explore the issue, he and his colleagues performed a meta-analysis dubbed PANTHER. It included patient-level data from several randomized trials that at least partly included a comparison of P2Y12 inhibitor or aspirin monotherapy in patients with established coronary disease and no indication for oral anticoagulation. Trials with an initial DAPT phase were included, but data from those studies were limited to the monotherapy phase.

The investigators included seven trials—ASCET, CADET, CAPRIE, DACAB, GLASSY, HOST-EXAM, and TiCAB—with an overall patient population of 35,752 from 492 sites in Asia, Europe, and North America. After excluding patients who did not have established CAD, who left the studies early, who had an event during an initial DAPT phase, or who received DAPT exclusively, there were 24,325 participants (mean age 64 years; 22% women) left for the analysis.

Most patients (60.6%) had presented with ACS, and the remaining had chronic coronary syndromes. More than half (54.9%) had a history of PCI, 10.6% a history of CABG, and 4.4% a history of both; 30.2% had never undergone revascularization.

P2Y12 inhibitor therapy included clopidogrel in 62% and ticagrelor in 38%; there are no trials comparing aspirin and prasugrel monotherapy, Valgimigli said. Median treatment duration was 557 days.

The advantage for P2Y12 inhibitors over aspirin on the primary composite efficacy outcome of CV death, MI, or stroke worked out to a number needed to treat of 123. The better outcomes were mostly related to a lower risk of MI (HR 0.77; 95% CI 0.66-0.90), as there were no significant differences between groups for overall stroke (HR 0.85; 95% CI 0.70-1.02) or CV death (HR 1.02; 95% CI 0.86-1.20).

Major bleeding occurred in 1.2% and 1.4% of patients treated with P2Y12 inhibitors and aspirin, respectively, a nonsignificant difference (HR 0.87; 95% CI 0.70-1.09).

Combining the efficacy outcome and major bleeding, the rate of net adverse clinical events was significantly lower with P2Y12 inhibitors (6.4% vs 7.2%; HR 0.89; 95% CI 0.81-0.98).

Some of the secondary outcomes favored P2Y12 inhibitor therapy as well, including:

- Hemorrhagic stroke (HR 0.32; 95% CI 0.14-0.75)
- Definite stent thrombosis (HR 0.42; 95% CI 0.19-0.97)
- Definite/probable stent thrombosis (HR 0.46; 95% CI 0.23-0.92)
- GI bleeding (HR 0.75; 95% CI 0.57-0.97)

The results were similar across 16 subgroups, with no significant interactions. There was a suggestion of greater benefits associated with P2Y12 inhibitors among patients who had undergone PCI, but Valgimigli cautioned against reading too much into that finding.

END OF ASPIRIN?

Asked during the press conference whether this marks the beginning of the end for aspirin for secondary prevention in CAD, Valgimigli said he doesn't think so: "I think it's the rise of [an] available alternative to aspirin."

Guidelines state that aspirin is the first-line option for long-term antiplatelet therapy, with P2Y12 inhibitors as an option when aspirin is contraindicated, Valgimigli said, indicating that it's unclear how these new data will influence future guidance.

"I think now we have two at least equally effective alternatives. To take aspirin completely out of the

picture, probably that would require additional studies because aspirin has been there for 125 years," he said.

Serving as a discussant following the presentation, Steffen Massberg, MD (Ludwig-Maximilians-Universität München, Germany), also indicated that it's not time to get rid of aspirin, and went through a number of potential issues to consider when interpreting the PANTHER results, including the heavy weight of the CAPRIE trial in the analysis, the relatively young age of the patient cohort, and the small effect size, which plays into discussions of cost-effectiveness.

"The results are definitely very important, and they will have impact on the clinical practice," he said. Nevertheless, he added, "I think that still aspirin is a valid standard because it's associated with less noncompliance, has less variation in treatment response, particularly compared to clopidogrel, and most likely is also more cost-effective, although this has not been formally demonstrated. But this is reasonable considering the low effect size with the P2Y12 inhibitors."

Even so, Massberg said, "I think PANTHER and also HOST-EXAM are giving us good arguments to use P2Y12 inhibitors instead of aspirin monotherapy, particularly in younger patients with a history of revascularization."

Commenting, American College of Cardiology President Edward Fry, MD (St. Vincent Medical Group, Indianapolis, IN), said the PANTHER meta-analysis could have a significant impact on the day-to-day management of patients with coronary disease. "This is bread-and-butter cardiology that you would see in the office every day managing patients' long term," he said.

And, with a large data set, "it helps support what a lot of people are doing in practice already" at the end of a period of DAPT due to concerns about the long-term risks of aspirin, particularly bleeding, Fry said. When a P2Y12 inhibitor is chosen for this purpose, it's mostly clopidogrel due to considerations around the higher cost and twice-daily dosing of ticagrelor and the longer experience clinicians have with using clopidogrel, he added. Moreover, when patients have an indication for adjunctive oral anticoagulation in addition to P2Y12 therapy, most of the existing data addresses use of clopidogrel.

When it comes to use of P2Y12 inhibitor versus aspirin monotherapy, Fry said, "it's sort of the best of both worlds: better efficacy and certainly no increased risk… And in these subsets of GI bleeding and hemorrhagic stroke, there's a definite advantage towards a P2Y12 inhibitor."

Fry said the US guidelines don't specify which antiplatelet agent should be used for long-term secondary prevention in patients with coronary disease. "I suspect in future guidelines this will be a consideration, or at least there will be some suggestion that practitioners consider what antiplatelet therapy they're using long term, looking at both efficacy and risk," he predicted.

CMR, PET SIMILAR FOR IDENTIFYING CORONARY DISEASE AFTER CTA: Dan-NICAD 2

Barcelona Monday, August 29th, 2022

Among patients in whom coronary artery disease cannot be ruled out by coronary CT angiography (CCTA), stress cardiac magnetic resonance (CMR) imaging and positron emission tomography (PET) have comparable accuracy as second-line tests, the Dan-NICAD 2 trial shows.

Though performance is similar between the two, sensitivity is not great for either—ranging from 59% to 64%—when they're being used to uncover hemodynamically obstructive CAD and fractional flow reserve (FFR) is the reference standard, Morten Bøttcher, MD, PhD (Gødstrup

Hospital, Denmark), reported here at the European Society of Cardiology (ESC) Congress 2022.

However, sensitivity improved—ranging from 83% to 90%—when the goal was finding anatomically obstructive CAD, defined as greater than 70% diameter stenosis on 3D quantitative coronary angiography (QCA). Negative predictive value was 95% to 97%.

"There's absolutely no difference between whether you use an MR or whether you use a rubidium PET scan," Bøttcher said at a press conference. "The figures for performance are exactly the same."

The findings demonstrate a continuing dilemma for clinicians, too, as many patients had discrepancies between the results of invasive FFR and noninvasive stress testing. "We now need further studies because we have this group of patients who have a positive perfusion scan and a negative invasive FFR, or vice versa, and we don't really know how we should treat these patients," Bøttcher said.

Dan-NICAD 2

For the study, the investigators focused on a common and challenging clinical scenario - when patients, often with risk factors, bring complaints of dyspnea or angina to their general practitioners, who in turn refer the patients to a cardiologist because of suspected ischemic heart disease. The cardiologists then perform a risk assessment and echocardiogram, which are often followed—at least in Bøttcher's region—by CCTA as the first-line modality for ruling out coronary disease. Danish national databases have shown that in this type of population, CCTA will show that about 50% of patients have normal arteries and another 25% will have suspicious stenoses that require further testing.

It's not clear what should happen with that latter group - whether they should be treated with medical therapy, go to the cath lab for invasive angiography, or undergo noninvasive ischemia testing. The ESC guidelines on chronic coronary syndromes advise the last option both to document ischemia and to guide potential revascularization, but there are no clear recommendations on choice of modality.

"So, we don't know which technique to use and we don't know how they perform," Bøttcher said.

In Dan-NICAD 2, performed across four hospitals in one geographic area, the researchers conducted a head-to-head comparison of rubidium-82 PET and CMR using a 3 Tesla scanner. The study included 1,732 patients (mean age 59; 43% women) with presenting symptoms that were most commonly atypical angina (38.9%), typical angina (20.1%), and nonanginal chest pain (23.4%). All were referred for CCTA, which revealed no lesions or only nonobstructive CAD in about 74%.

The remaining 445 patients were referred for invasive coronary angiography with FFR measurement due to diameter stenosis exceeding 50%, but for the purposes of the study, they first were referred for PET and/or CMR. Ultimately, 372 received all three tests (PET, CMR, and angiography with FFR).

According to FFR, which was used as the reference, 56.1% of patients had nonobstructive disease and the rest had obstructive disease, defined as a high-grade stenosis greater than 90% by visual assessment and an invasive FFR of 0.80 or less. According to anatomically obstructive CAD by QCA, on the other hand, only 19.1% were deemed to have obstructive disease.

Diagnostic performance of PET and CMR were comparable regardless of how obstructive disease was defined. But when they were being used to look for more-severe anatomically obstructive CAD by QCA rather than hemodynamically obstructive disease by FFR, sensitivity and negative predictive value went up, and specificity came down. Of note, among the 164 patients who had an abnormal FFR, 59 had normal PET results and 67 had normal CMR results.

REASSURING FINDINGS

The study "leads us to conclude, first of all, that in a contemporary population of de novo chest pain patients referred to coronary CTA, the incidence of suspected stenosis is very, very low, only about 25%, and only half of these patients actually underwent revascularization and only half of them had a positive FFR," Bøttcher said.

Also, he said, second-line perfusion imaging performs better when looking for more-severe stenoses and frequently yields discrepant results compared with invasive FFR measurements.

Asked about the choice of PET or CMR for the types of patients studied in Dan-NICAD 2, Bøttcher said it differs across centers, adding that many hospitals lack the ability to perform CMR. At his center, CMR is used in select patients for whom they want to avoid radiation but PET is used in most.

The similar performance of the two modalities demonstrated in this study is "good for the doctors so that they can choose the modality that they find feasible for this particular patient," Bøttcher said.

Indeed, "patients can be reassured that whichever they are referred for is going to perform just as well" as the other, commented Colin Berry, MBChB, PhD (British Heart Foundation Glasgow Cardiovascular Research Centre, University of Glasgow), who served as a discussant following the presentation. He noted that centers often only have one of the modalities available, and not both.

Future studies with larger sample sizes, Bøttcher said, will look into how each of the modalities evaluated in Dan-NICAD 2 impact the management of patients when they're used to guide care.

CARDIOVASCULAR PROTECTION FROM STATINS GREATLY OUTWEIGHS THE RISK OF MUSCLE SYMPTOMS

Barcelona **Monday, August 29th, 2022**

The known benefits of statin therapy in preventing cardiovascular disease, including heart attacks and strokes, outweigh the slightly increased risk of muscle symptoms, according to late breaking research presented in a Hot Line session on August 29th 2022 at ESC Congress 2022.

Principal investigator Professor Colin Baigent, Director of the Medical Research Council Population Health Research Unit at the University of Oxford, UK said: "For most people taking a statin, any muscle-related symptoms they experience are not likely to be caused by the drug. The known protective effects of statins against cardiovascular disease greatly exceed the slightly increased risk of muscle symptoms. For example, for every 1,000 people taking a moderate intensity statin, the treatment would cause 11 generally mild episodes of muscle pain or weakness in the first year with no significant excess in subsequent years. Over a five-year period, statins typically prevent 50 major vascular events in those with pre-existing vascular disease, and 25 major vascular events in those with no pre-existing vascular disease, with longer treatment yielding larger benefits."

Statin therapy is effective for the prevention of cardiovascular disease, the world's largest killer, and is widely prescribed. However, there have been concerns that statins may cause muscle pain or weakness, leading some patients to stop taking their treatment. This analysis was conducted to resolve uncertainties around the possible effects of statins on muscle symptoms.

This was an individual participant data meta-analysis of all recorded muscle symptoms in large-scale randomised blinded double-blind trials of statin therapy, led by researchers from Oxford Population Health. The researchers compiled data from 23 trials from the Cholesterol Treatment Trialists' (CTT) Collaboration, with information on nearly 155,000 patients. All trials included at least 1,000 patients and at least two years of scheduled treatment. Adverse event data were collected for all individual participants in 19 large randomised double-blind trials of statin therapy versus placebo (123,940 patients) and in four randomised double-blind trials of more intensive versus less intensive statin therapy (30,724 patients).

The researchers examined all data on adverse effects reported by patients taking part in the clinical trials, as well as data on the timing of and reasons for stopping study treatment, use of other (non-trial) medications, other health conditions, and laboratory results that would help in the interpretation of particular adverse events.

In the 19 trials of any statin regimen versus placebo, during a median follow up of 4.3 years, 16,835 patients (27.1%) in the statin group and 16,446 (26.6%) in the placebo group reported muscle pain or weakness (rate ratio [RR] 1.03 95% confidence interval [CI] 1.01–1.06). In the first year there was a 7% relative increase in reports of muscle pain or weakness among those allocated to a statin (RR 1.07 95% CI 1.04–1.10), which corresponded to an absolute excess rate of 11 (95% CI 6–16) reports per 1,000 person years in the remaining follow up period there was no evidence of any excess risk (RR 0.99; 95% CI 0.96–1.02). During the first year only about 1 in 15 reported cases of muscle pain or weakness were attributable to statin therapy.

In the four trials of more intensive versus less intensive statin therapy, high intensity regimens (e.g. atorvastatin 40 to 80 mg daily or rosuvastatin 20 to 40 mg daily) resulted in a larger relative increase in the rate of muscle pain or weakness than moderate intensity regimens, with rate ratios of 1.08 (95% CI 1.04–1.13) and 1.02 (95% CI 1.00–1.05), respectively.

Professor Baigent said: "Muscle symptoms such as pain or weakness were experienced by similar numbers of people in the statin and placebo groups. 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 small excess risk of muscle symptoms occurred principally during the first year after commencing therapy."

He concluded: "The results should help doctors and patients to make informed decisions about whether to start or remain on statin therapy. Information provided to doctors and patients should be reviewed in light of our findings, including drug labelling and guidelines."

SESSION-1 :
Quality of Life in Patients with Heart Failure

QUALITY OF LIFE IN PATIENTS WITH HEART FAILURE AND IMPROVED EJECTION FRACTION: ONE YEAR CHANGES AND PROGNOSTIC IMPLICATION

Barcelona Monday, August 29th, 2022

A large number of studies were presented on the final day of the European Society of Cardiology Congress 2022 at Barcelona.

This paper was presented by Dr. Beatriz Gonzalez et al., from the Germans Trias i Pujol Hospital - Badalona - Spain, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Quality of Life in Patients with Heart Failure".

Inconsistent and controversial results have been reported about the association of quality of life (QoL) and left ventricular ejection fraction (LVEF) in patients with heart failure (HF). The 2021 universal definition of HF specifically describes the criteria for the patients with HF and improved LVEF (HFimpEF): HF with a baseline LVEF ≤40%, a ≥10 point increase from baseline LVEF, and a second measurement of LVEF >40%.

The purpose of this study was to:

1) To assess whether patients with HF and reduced LVEF (HFrEF) at first visit in an outpatient HF Clinic that fulfil the HFimpEF criteria one year later presented a higher improvement in QoL assessed by the Minnesota Living with Heart Failure Questionnaire (MLWHFQ) than those patients that did not fulfil HFimpEF criteria.
2) To assess the prognostic role of QoL on outcomes in HFimpEF patients.

In a prospective registry of real-life HF outpatients LVEF and QoL evaluated by MLWHFQ were assessed at first visit at the HF Clinic and at one year of follow-up.

From August 2001 to August 2021, baseline and one-year LVEF and MLWFQ scores were available in 1040 patients with an initial LVEF ≤40%. In summary, mean age was 65.2 ± 11.7 years, 75.9% of the patients were men, the main aetiology was ischaemic heart disease (52.9%) and patients were mostly in New York heart Association (NHYA) class II (71.1%) and III (21.6%). Baseline LVEF was 28.5% ± 7.3 and baseline MLWHFQ score was 30.2 ± 19.5. At one year, mean LVEF increased to 38.0 ± 12.2 while MLWHFQ scores improved to 17.4 ± 16.0. There were 361 patients that fulfilled the HFimpEF criteria (34.7%). These patients significantly and markedly improved both LVEF (from 28.7 ± 6.6 to 50.9 ± 7.6, p<0.001) and QoL (from 32.9 ± 20.6 to 16.9 ± 16.0, p<0.001). Although in patients that did not fulfil the criteria of HFimpEF both LVEF (from 28.4 ± 7.6 to 31.1 ± 7.9, p<0.001) and QoL (from 28.7 ± 18.8 to 17.6 ± 15.9, p<0.001) also significantly improved, the improvement in QoL was significantly higher in HFimpEF patients (–16.0 ± 23.8 vs. –11.1 ± 20.3, p=0.001), taking into account that baseline MLWHFQ score was worse in HFimpEF patients (p=0.001). However, at one-year QoL was similar when both groups were compared (p=0.50). MLWHFQ score at one year proved to be superior to QoL improvement (using a cut-off of at least 5 points) from the prognostic point of view.

QoL improved both in patients with and without HFimpEF criteria, and QoL perception at one year was similar in both groups, suggesting the influence of other factors other than LVEF in

QoL perception. QoL at one year revealed to be superior to QoL changes from baseline from the prognostic point of view.

QUALITY OF LIFE (QoL) IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFpEF): A SYSTEMATIC REVIEW

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Jieling Chen et al., from Gaithersburg - United States of America, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Quality of Life in Patients with Heart Failure".

Heart failure with preserved ejection fraction (HFpEF) is associated with significant clinical unmet need as mortality and morbidity rates are high despite current treatments. Patient-reported quality of life (QoL) is an important and clinically relevant endpoint in patients with HF so understanding the impact of HFpEF on QoL is essential.

The aim of this systematic review was to identify and summarize data on QoL in HFpEF.

Systematic searches of Medline, Medline Epub Ahead of Print (In-Process & Other Non-Indexed Citations), Embase, and EBM Reviews were conducted in October 2021. Congress proceedings from the past 3 years and reference lists of included publications were also searched. Publications were screened against eligibility criteria by title/abstract and then by full text. Eligibility criteria included clinical studies of any design reporting baseline QoL in adults with HFpEF published from 2016 onwards.

The electronic database search identified 6,403 articles on HFpEF. After screening, 35 full publications reporting HFpEF and QoL were included. Study designs included observational cohort (n=17), cross-sectional (n=3), and post-hoc analyses of interventional studies (n=15). Tools used to measure QoL included KCCQ (n=17), MLHFQ (n=12), EQ-5D-VAS (n=8), SF-12 (n=2), SF-36 (n=2), and EHFSQ-1 (n=1). Health-state utility values (HSUVs) were captured using EQ-5D in four studies. HSUVs in HFpEF ranged from 0.67-0.74, indicating a substantial QoL burden. Eleven studies using various instruments compared QoL in patients with HFpEF vs non-HFpEF. Of these, five reported statistically significantly poorer QOL in HFpEF vs non-HFpEF, one reported statistically significantly poorer QOL in non-HFpEF vs HFpEF and five found no statistically significant difference between HF subtypes. Four studies compared QoL in men vs women with three reporting statistically significantly worse QoL in women. Three studies examined the impact of comorbidities, and all reported statistically significantly poorer QoL in patients with comorbid atrial fibrillation, diabetes, or metabolic syndrome. Two studies examined the effect of age; one reported that, vs elderly patients (age ≥85 years), younger patients (age ≤55 years) with HFpEF had statistically significantly worse QoL despite having fewer comorbidities; in contrast, the second study reported that younger patients (age ≤55 years) had statistically significantly better QoL than elderly patients (age ≥75 years). Two studies reported on hospitalizations, with one reporting no difference in QoL between patients who had previously been hospitalized and those who had not and the other reporting that readmission for HF correlated with QoL.

QoL burden among HFpEF patients is substantial. QoL may be affected by age, comorbidities, gender, and prior hospitalization, and may be associated with poorer outcomes. QoL in HFpEF is generally poorer than in non-HFpEF.

SESSION-2 :
Acute Coronary Syndromes Nuts and Bolts

REPRODUCIBILITY OF LUNG PERFUSION AND VENTILATION DERIVED USING PHASE-RESOLVED FUNCTIONAL LUNG (PREFUL) MRI IMAGING

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Martynus Bucnius et al. from Lithuanian University of Health Sciences, Department of Cardiology - Kaunas - Lithuania,on 29th August 2022 at the ESC Congress 2022 as a part of the session "Acute Coronary Syndromes Nuts and Bolts".

There is a growing demand for non-invasive imaging biomarkers of lung function, allowing more sensitive and timely decision making to achieve better patient outcomes. Recently developed Fourier decomposition MRI methods enable quantitative assessment of lung performance. The objective of this study was to assess intra- and inter-observer agreement of lung perfusion and ventilation derived using the free-breathing, contrast agent-free, phase-resolved functional lung (PREFUL) imaging. Fifty patients with acute ST-segment elevation myocardial infarction underwent CMR imaging using a 3 T MRI scanner (MAGNETOM Skyra). Coronal images were acquired during free breathing, covering the entire lung using a phase-resolved functional lung 2D FLASH sequence. The main scan parameters were: temporal resolution = 2.1 ms, number of measurements = 250. The lung perfusion and ventilation maps were generated. The analysis of the images was performed using prototype software (MR Lung Prototype version 2.0) by two independent observers. Analysis was repeated after four weeks to assess intra-observer agreement.

PREFUL imaging and analysis were fast with a 35 second scan time and up to one-minute post-processing time for a complete quantitative assessment. The lung perfusion and ventilation demonstrated excellent intra-observer (ICC 0.928 (0.870 to 0.959) and 0.994 (0.990 to 0.997) for mean perfusion and ventilation respectively) and inter-observer agreement (ICC 0.966 (0.940 to 0.981) and 0.992 (0.985 to 0.996) for mean perfusion and ventilation respectively). Bland-Altman plots demonstrate intra- and inter-observer reproducibility for lung perfusion and ventilation. The lung perfusion and ventilation derived using phase-resolved functional lung (PREFUL) MRI imaging are highly reproducible. The Fourier decomposition method may allow fast quantitative evaluation of lung function.

ApoJ-Glyc, AN EARLY MARKER OF MYOCARDIAL ISCHAEMIA, RAPIDLY MAPS IMPROVED MYOCARDIAL PERFUSION IN STEMI PATIENTS UNDERGOING SUCCESSFUL PRIMARY PCI

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Judit Cubido et al. from GlyCardial Diagnostics SL - Barcelona - Spain, on 29th August 2022 at the ESC Congress

2022 as a part of the session "Acute Coronary Syndromes Nuts and Bolts".

Previous studies using experimental models and clinical retrospective samples have pointed to a potential role of glycosylated apolipoprotein J (ApoJ-Glyc) as a marker for the early detection of myocardial ischaemia. Ischaemia induces intracellular accumulation of non-glycosylated ApoJ that mirrors the reduction in ApoJ-Glyc serum levels in patients presenting with ST-segment elevation myocardial infarction (STEMI).

The EDICA (Early Detection of Myocardial Ischaemia in Suspected Acute Coronary Syndromes by Apo J-Glyc as a Novel Pathologically based Ischaemia Biomarker) clinical trial assessed the performance of ApoJ-Glyc as a biomarker for the early detection of myocardial ischaemia in patients attending the A&E department with chest pain suggestive of acute coronary syndrome. Here, we report the observed changes in ApoJ-Glyc concentration in STEMI patients at baseline and after primary percutaneous coronary intervention (PPCI).

The EDICA trial, a multi-centre (10 sites), international, in vitro diagnostic study, assessed 404 patients attending the A&E department with suspected ACS. Of these, 291 patients had a final diagnosis of "non-ischaemic" event and 113 of "ischaemic" event. The main inclusion criterion was chest pain of suspected cardiac origin. Blood samples were obtained for the simultaneous assessment of high sensitivity-troponin and ApoJ-Glyc on admission (time 0) and at 1h and 3h thereafter. Two different glycosylated variants of ApoJ (ApoJ-GlycA2 and ApoJ-GlycA6) were analyzed with a novel ELISA in serum samples. Of the "ischaemic" patients, 33 had STEMI, of whom 85% underwent PPCI. As expected, in the presence of myocardial ischaemia, time 0 ApoJ-GlycA2 and ApoJ-GlycA6 serum levels decreased by 34% and 48%, respectively in STEMI patients, compared with non-ischaemic patients, i.e., ApoJ-GlycA2 in STEMI: 66 [52-95] µg/ml vs. non-ischaemic: 100 [72-131] µg/ml; P=0.0002; ApoJ-GlycA6 STEMI: 38 [34-67] vs. non-ischaemic: 73 [56-95] µg/ml; P<0.0001. ApoJ-GlycA6 showed a discriminating ability for the presence of STEMI with a 67% sensitivity and a 83% specificity (AUC=0.747, cut-off of 50µg/ml). In STEMI patients in whom PPCI successfully restored TIMI 3 flow, ApoJ-Glyc levels increased rapidly and significantly compared with time 0 levels (ApoJ-GlycA2: P=0.02 and P=0.003 for 1h and 3h; ApoJ-GlycA6: P=0.02 and P=0.002 for 1h and 3h) and compared to patients in whom PPCI was not performed.

ApoJ-Glyc concentrations are reduced in STEMI patients on admission and increase rapidly after improved perfusion with PPCI, pointing to a potential role of this biomarker in the early detection of reversible ischaemia and the mapping of reversible changes. The mechanisms whereby ApoJ-Glyc levels rapidly and markedly increase after PPCI are speculative at present and deserve further investigation, together with the potential prognostic value of ApoJ-Glyc in this setting.

0/1H-ALGORITHM USING A NEW HIGH-SENSITIVITY CARDIAC TROPONIN I ASSAY FOR EARLY DIAGNOSIS OF MYOCARDIAL INFARCTION

Barcelona **Monday, August 29th, 2022**

This paper was presented by Dr. Luca Koechlin et al., from University Hospital Basel - Basel - Switzerland, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Acute Coronary Syndromes Nuts and Bolts".

The clinical performance of the novel high-sensitivity cardiac troponin I EXL (hs-cTnI-EXL) assay is unknown so far.

The purpose of this study was aimed to validate the clinical performance of the hs-cTnI-EXL assay and to derive and validate an hs-cTnI-EXL-specific 0/1h-algorithm for the early diagnosis of myocardial infarction (MI).

This multicenter study included patients presenting to the emergency department with symptoms suggestive of myocardial infarction. Central adjudication of final diagnoses was performed by two independent cardiologists using all clinical information including cardiac imaging twice: first, using serial hs-cTnI-Architect (primary analysis) and second, using serial hs-cTnT-Elecsys (secondary analysis) concentrations in addition to those clinically used (hs)-cTn. Hs-cTnI-EXL was measured at presentation and at 1h. The primary objective was to directly compare diagnostic accuracy quantified by the area under the receiver-operating-characteristic curve (AUC) of hs-cTnI-EXL, hs-cTnI-Architect and hs-cTnT-Elecsys. Secondary objectives included the derivation and validation of an hs-cTnI- EXL-specific 0/1h-algorithm.

MI was the adjudicated final diagnosis in 204/1454 (14%) patients. At presentation, the AUC for hs-cTnI-EXL was 0.94 (95%CI, 0.93-0.96), being comparable to hs-cTnI-Architect (0.95; 95%CI, 0.93-0.96) and hs-cTnT-Elecsys (0.93; 95%CI, 0.91-0.95). In the derivation cohort (n=813), an optimal hs-cTnI-EXL-0/1h-algorithm was rule-out of MI with <9ng/L if onset of chest pain >3h or <9ng/L & 0h-1h-change <5ng/L, and rule-in with ≥160ng/L or 0h-1h-change ≥100ng/L. In the validation cohort (n=345), this hs-cTnI-EXL-0/1h-algorithm also performed well: rule-out in 56% of patients, negative predictive value 99.5% (95%CI, 97.1-99.9), sensitivity 97.8% (95%CI, 88.7-99.6), rule-in in 9% of patients, positive predictive value 83.3% (95%CI, 66.4-92.7), specificity 98.3% (95%CI, 96.1-99.3). Secondary analyses confirmed the findings using adjudication including serial measurements of hs-cTnT-Elecsys. Hs-cTnI-EXL has comparable diagnostic performance to the currently best-validated hs-cTnT/I assays.

SESSION-3 :
Cardiovascular Aspects of COVID and Long-COVID

LONG COVID-19 SYNDROME: ASSOCIATION OF CARDIOPULMONARY IMPAIRMENT WITH A PERSISTENT PLATELET ACTIVATION

Barcelona **Monday, August 29th, 2022**

This paper was presented by Dr. Marina Camera et al. from University of Milan, Italy, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Cardiovascular Aspects of COVID and Long-COVID".

A considerable proportion of patients do not fully recover from COVID-19 infection and report symptoms that persist beyond the initial phase of infection: this condition is defined long-COVID-19 syndrome (LCS). LCS can involve lungs as well as several extrapulmonary organs, including the cardiovascular system. The risk and 1-year burden of cardiovascular diseases (CVD) is increased in COVID-19 survivors, even in subjects at low risk of CVD. Recently, we documented that acute COVID-19 infection induces altered platelet activation state characterized by a prothrombotic phenotype and by the formation of platelet-leukocyte aggregates (PLA), that may be involved in the pulmonary microthrombi found in autoptic specimens. No data are yet available on the contribution of platelet activation to residual pulmonary impairment and procoagulant potential in LCS patients.

The purpose was to study platelet activation status, microvesicle (MV) profile, platelet thrombin generation capacity (pTGC) in LCS patients enrolled at 6 months after resolution of the acute phase (6mo-FU), compared to acute COVID-19 infection patients.

6mo-FU COVID-19 patients (n=24) with established LCS were enrolled at Centro Cardiologico Monzino. Residual pulmonary impairment was assessed by Cardiopulmonary Exercise Testing (CPET) and 64-rows-CT scan evaluation. Platelet activation (P-selectin, Tissue Factor [TF] and PLA) and MV profile were assessed by flow cytometry; pTGC by calibrated automated thrombogram. 46 patients enrolled during acute COVID-19 infection and 46 healthy subjects (HS) were used for comparison.

Dyspnea in LCS patients was confirmed by CPET showing compromised alveolus-capillary membrane diffusion and residual pulmonary impairment. TF+-platelet and -MV levels were 3-fold (1.5% [1.2-2.9] vs 2.4% [1.6-5.7]) and 2-fold (217/µl [137-275] vs 435/µl [275-633]) lower at 6mo-FU compared to acute phase, being comparable to HS. pTGC behaved similarly. At 6mo-FU, the MV profile, in terms of total number and cell origin, returned to physiological levels. Conversely, although lower than that measured in acute phase, a 2.5-fold higher platelet P-selectin expression (6.9% [3-13.5] vs 11.7% [5.2-18.9]) and PLA formation (35.5% [27.4-46.8] vs 67.7% [45.7-85.3]) was observed at 6mo-FU compared to HS. Interestingly, a significant correlation between PLA formation and residual pulmonary impairment was observed (r=-0.423; p=0.02).

These data strengthen the hypothesis that the presence of PLA in the bloodstream, and thus also in the pulmonary microcirculation, may contribute to support pulmonary dysfunction still observed in LCS patients.

NON-CONTRAST CARDIAC MAGNETIC RESONANCE IMAGING AFTER SARS-CoV2 INFECTION OR VACCINATION IN ASYMPTOMATIC ADOLESCENTS: INSIGHTS FROM THE EnIGMA STUDY

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Rocio P Guiterrez et al. from Spanish National Centre for Cardiovascular Research - Madrid - Spain, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Cardiovascular Aspects of COVID and Long-COVID".

Myocarditis after SARS-CoV2 infection or vaccination is rare, but seems to be relatively more frequent in young population. Cardiac magnetic resonance (CMR) T2 weighted sequences have the potential to detect subclinical myocarditis. However, there is paucity of data on the potential myocardial involvement after SARS-CoV2 infection or vaccination in asymptomatic adolescents.

The purpose of this study was to evaluate the presence of subclinical myocardial damage in adolescents who were infected with SARS-CoV2 or vaccinated against SARS-CoV2 using non-contrast CMR imaging.

Asymptomatic adolescents enrolled in the "Early ImaginG Markers of unhealthy lifestyles in Adolescents" (EnIGMA) project were scanned using a 3-Tesla CMR scanner between March 2021 and October 2021. CMR scans included CINE imaging and myocardial T2-mapping sequences. SARS-CoV2 IgG antibody testing was performed in capillary blood samples, and date of confirmed SARS-CoV2 infection and/or vaccination if any was collected. Participants were assigned to three different groups according to SARS-CoV2 status: Group 1 (non-infected and non-vaccinated), Group 2 (infected and non-vaccinated), and Group 3 (vaccinated, independently of past infection status). CMR images were analyzed by experienced observers blinded to adolescent's SARS-CoV2 status. ANOVA and multiple regression analysis, together with correlation coefficients, were used to study between-group differences and associations among variables of interest.

A total of 115 adolescents with a mean age of 16.0 years (standard deviation (SD)=0.4), 54% girls, completed the CMR study and SARS-CoV2 data successfully, and were assigned to Group 1 (n=72), Group 2 (n=22), and Group 3 (n=21). Left and right ventricular ejection fraction (LVEF/RVEF) did not significantly differ among groups: mean LVEF was 62.8% (SD=4.1), 63.0% (SD=3.7) and 60.9% (SD=3.9) [p=0.12] and mean RVEF was 56.5% (SD=4.2), 56.5% (SD=5.5) and 54.5% (SD=5.1) [p=0.23] in Groups 1, 2 and 3, respectively. Similarly, there were no between-group significant differences in myocardial T2 relaxation values: mean T2 values were 44.1 ms (SD=2.2), 44.1 ms (SD=1.8) and 44.4 ms (SD=1.9) in Groups 1, 2, and 3, respectively (p=0.63). No differences were found either after adjusting for age and gender. Median time (interquartile range) from date of infection or vaccination to CMR acquisition was 133 (121) days and 28 (38) days in Group 2 and Group 3, respectively. No correlation between time from infection/vaccination to CMR acquisition and T2 values was detected.

This observational study did not find evidence of subclinical myocardial involvement after SARS-CoV2 infection or vaccination in asymptomatic adolescents, as assessed with T2-mapping magnetic resonance imaging.

THE ROLE OF CARDIAC TROPONIN-I AS A PROGNOSTIC TOOL FOR MORTALITY IN PATIENTS HOSPITALIZED WITH COVID-19

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Jeni Quintal et al. from Hospital Center of Setubal - Setubal - Portugal, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Cardiovascular Aspects of COVID and Long-COVID".

Coronavirus disease 2019 (COVID-19) has been associated with significant morbidity and mortality, with cardiovascular involvement being usual. Elevations in cardiac Troponin-I level has proposed as an independent biomarker for mortality among patients with COVID-19.

The aim of this study was to evaluate the role of high sensitivity Troponin-I (hs-TnI) level at hospital admission in predicting 30 day in-hospital mortality and 6-month mortality in patients hospitalized with a COVID-19 diagnosis.

We performed a retrospective single-center cohort study including consecutive patients aged 18 years and older who were admitted for COVID-19, during a 1-year period (n=818). We excluded patients with acute coronary syndrome (n=23), patients with acute heart failure (n=42), and patients in which hs-TnI level was not dosed at admission (n=163). Patients were divided into two groups according to hs-TnI levels: hs-TnI < 19.8 vs hs-TnI ≥ 19.8 pg/mL. Primary outcomes were 30-day in-hospital mortality and 6-months mortality. According to the data distribution, appropriate statistical tests were conducted to compare independent samples. Multivariable logistic regression was used to analyze mortality risk. Receiver operator characteristics (ROC) curve and area under the curve (AUC) were obtained to determine the discriminative power of hs-TnI as a predictor of mortality.

This cohort included 590 patients. Mean age was 71 ≥±15 years and 52.4% were men. Overall, 209 patients (35.4%) had elevated hs-TnI levels and 381 patients had normal hs-TnI levels. Individuals in the hs-TnI ≥ 19.8 pg/mL group were older (80±11 vs 66±14 years, p<0.001) and presented higher prevalence of chronic heart failure (24.9% vs 7.1%, p<0.001), hypertension (77.0% vs 57.5%, p <0.001), atrial fibrillation/flutter (19.1% vs 5.5%, p <0.001), prior stroke (12.4% vs 5.2%, p=0.001) and ischemic heart disease (12.4% vs 3.7%, p < 0.001). There was no difference in length of hospital stay between the groups (8.0 [IQR 9.6] in hs-TnI 19.8 pg/mL group vs 9.0 [IQR 8.0] normal hs-TnI group, p=0.669). Troponin-I was the only independent predictor of in-hospital mortality (OR 3.80, CI 95%: 2.44 – 5.93, p < 0.001). The troponin levels had the highest area under the receiver operating characteristic curve (AUC) with an AUC of 0.705 (95% CI: 0.667 – 0.742, p < 0.001) for association with the in-hospital mortality. There was no difference in 6-months mortality between the two groups.

Acute myocardial injury is common in patients hospitalized with COVID-19. In the present study a TnI level ≥ 19.8 pg/mL was predictor of 30 days in-hospital mortality, suggesting that raised levels of this biomarker is associated with adverse prognosis. This tool might be useful for COVID-19 patient risk stratification. Further studies are needed to provide robust data and reliable recommendations on this theme.

SESSION-4 :
Managing Patients with Multivalvular Disease: Expert Insights

EARLY RESULTS OF RAPID-DEPLOYMENT AORTIC PROSTHESIS IN MULTIVALVULAR SURGERY - A PROPENSITY SCORE MATCHING

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Nuno Carvalho Guerra et al. from University Hospital Santa Maria - CHLN - Lisboa - Portugal, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Managing Patients with Multivalvular Disease: Expert Insights".

Multivalvular surgery (MV) requires prolonged extracorporeal circulation (ECC) and aortic cross-clamp times (X-Ao). Rapid-deployment aortic prosthesis (RD-AV) allow lower ECC and X-Ao times in isolated aortic valve surgery (AVR), but have not been studied in MV surgery.

The purpose of this study was to determine if RD-AV use influences early outcomes when compared to biological stented or mechanical aortic valves in MV surgery.

Retrospectively collected pre, intra and immediate post-operatory data on all MV adult patients with AVR operated on our Department from January 2016 to February 2022. Bentall surgery and aortic dissection patients were excluded. A propensity score matching (PSM) of patients receiving RD-AV (Group A) compared to patients with non-RD-AV (Group B) was performed using sex, age, Euroscore II, type of surgery (involved valves, CABG, ascending aortic replacement), active endocarditis, ventricular function and redo surgery. After PSM, we compared outcomes until death or discharge. Normal distribution of samples was tested using the Kolmogorov-Smirnov test. Normal data was analysed with unpaired t-testing and non-normal data with non-parametric Mann Whitney U test. Categorical data were analysed with Fisher test. A significance level of $p<0.05$ was accepted.

205 patients received non-RD-AV and 58 patients RD-AV. After PSM, 57 pairs of patients were obtained. Sex, BMI, Euroscore II, age, redo surgery, insulin dependent DM, baseline creatinine, left ventricle ejection fraction, right ventricle dysfunction, pulmonary artery systolic pressure, and active endocarditis were similar in both groups. Intra-operatory, RD-AV valves (Group A) were associated with shorter surgery duration (167.3 ± 52 vs 206.6 ± 91 min, p=0.005), shorter ECC duration (89.5 ± 36.5 vs. 118.9 ± 56.5 min, p=0.002), and aortic X-clamp time (71.6 ± 28 vs. 98.9 ± 38.2 min, p<0.001). No differences were found between both groups A vs. B in ventilation time (1270 ± 1911 vs. 2428 ± 5627 min, p=0.59), inotropic support (113 ± 178 h vs. 85 ± 101 h, p=0.38), transfusion of red cells units (1.1 ± 1.6, vs.1.2 ± 1.7, p=0.73), Fresh frozen plasma units (0.86 ±1.9, vs. 0.77 ± 1.8, p= 0.77), platelet pools (0.79 ± 1.0 vs. 0.7 ± 0.9, p= 0.67), fibrinogen (0.77 ± 1.5 vs. 0.75 ± 1.4 g, p= 0.98), intra-aortic balloon pump use (5 vs. 12 patients, p=0.11), chest drain output (804 ± 656 vs. 825 ± 992 ml, p= 0.69), new-onset dialysis (10 vs. 10 patients, p=1.0), new-onset atrial fibrillattion (10 vs 13 patients, p=0.6) and permanent pacemaker implantation (8 vs. 3 patients, p= 0.20). Total ICU stay (9.25 ± 21 vs. 4.5 ± 4 days, p= 0,3), hospital stay (14.4 ± 26 vs. 10.1 ± 13 days, p=0.52) and intra-hospital mortality (7 vs 9 patients, p=0.79) were also similar.

Despite shorter surgery duration, ECC duration and aortic X-clamp duration, RD-AV have similar early outcomes when compared with non-RD-AV in multivalvular surgery.

TRICUSPID REGURGITATION: FREQUENCY, MANAGEMENT AND OUTCOME AMONG PATIENTS WITH SEVERE LEFT-SIDED VALVULAR HEART DISEASE IN EUROPE: INSIGHTS FROM THE ESC-EORP VALVULAR HEART DISEASE II SURVEY

Barcelona **Monday, August 29th, 2022**

This paper was presented by Dr. Julian Dreyfus et al. from Centre Cardiologique du Nord (CCN) - Saint Denis - France, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Managing Patients with Multivalvular Disease: Expert Insights".

Tricuspid regurgitation (TR) is frequent among patients with severe left-sided valvular heart disease (LS-VHD).

This study sought to assess TR frequency, management and outcome in this population. Among 6883 patients with severe LS-VHD or previous valvular intervention in the EURObservational Research Programme prospective VHD II survey, we analyzed frequency and grade of TR according to LS-VHD, and 6-month survival according to TR grade. Among 2081 patients who underwent an intervention for severe LS-VHD, we analyzed frequency and outcome of concomitant TV intervention, and concordance between Class I indications for concomitant TV surgery (patients with severe TR) and real-practice decision-making.

Moderate to severe TR was very frequent among patients with severe mitral VHD (≥30%), especially in patients with secondary mitral regurgitation (46%), and rare among patients with aortic VHD (<5%). Higher TR grade was associated with a poorer 6-month survival (P<0.001). Rates of concomitant tricuspid valve (TV) intervention at the time of left-sided heart valve surgery were high at the time of mitral valve surgery (more than 40%). Concomitant TV intervention at the time of left-sided heart valve surgery (LS-HVS) was not associated with an increase in-hospital mortality (P=0.93). Concordance between Class I indications for concomitant TV surgery at the time of LS-HVS according to guidelines and real-practice decision-making was very good (88% overall).

TR was frequent in patients with mitral VHD and was associated with a poorer outcome as TR grade increased. Compliance to guidelines for Class I indications for concomitant TV surgery at the time of LS-HVS was very good. With the trend toward more transcatheter treatment for left-sided VHD, there is a critical need for safe and efficient tricuspid valve transcatheter treatment for patients with concomitant TR.

SESSION-5 :
Stroke: Diagnosis, Epidemiology, and the Heart-Brain Connection

VALIDITY OF CHA_2DS_2-VASC SCORE IN PATIENTS WITH MALIGNANCIES

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. M Mohammed Alammad et al., from University of Kansas Medical Center - Kansas City, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Stroke: Diagnosis, Epidemiology, and the Heart-Brain Connection."

Anticoagulation for patients with atrial fibrillation/flutter (AF) after risk stratification based on CHA_2DS_2-VASc score (congestive heart failure, hypertension, age group, Diabetes Mellitus, prior stroke, transient ischemic attack or thromboembolism, prior heart attack, peripheral artery disease or aortic plaque and patient's gender) has been the gold standard practice to prevent cerebrovascular accidents (CVA).

Since patients with malignancies are at increased risk of thrombophilia, we tried to study if cancer patients with atrial fibrillation are at increased risk for CVA beyond what should be expected based on their comorbidities.

"We used the Nationwide Readmissions Database (NRD) database for the years 2016-2019. First, we extracted all cases with a diagnosis of atrial fibrillation/flutter. Exclusion criteria included patients younger than 18-year-old. We studied the comorbidities and calculated CHA_2DS_2-VASc score. Then, we compared the risk for admission with an acute CVA in patients with and without any diagnosis of malignancies (solid cancer, leukemia, lymphoma or metastatic disease). Patients with carcinoma in situ were considered non-cancer patients. Corrected logistic regression and Chi-square tests using survey procedures in SAS 8.1 were applied to accommodate for complex sampling (Rao-Scott design)."

We identified 1,748,619 weighted admissions with AF equally distributed across the years. 5% were patients with malignancies. The mean age was 74-year-old for cancer patients and 71-year-old for non-cancer patients with quite equal gender distribution (43-49% were female). Patients with a diagnosis of cancer has high inpatient mortality (13%). Every additional point in CHA_2DS_2-VASc score was associated with increased odds of admission with CVA. Having a diagnosis of cancer was not associated with increased odds of admission with CVA (odd ratio for 95% confidence interval 1.0 [0.95 -1.1]). Patients with history of VTE (assuming they are on anticoagulation) or who are on chronic anticoagulation have lower risk of admission with acute CVA if they have AF.

Although malignancies are associated with hypercoagulable status including higher risk for stroke, deep venous thrombosis and pulmonary embolism, our cross-sectional study indicates that CHA_2DS_2-VASc score is still a reliable tool for risk stratification in patients with atrial fibrillation. More longitudinal studies are needed.

DIFFERENTIAL EFFICACY AND SAFETY OF ORAL ANTICOAGULATION IN ATRIAL FIBRILLATION PATIENTS WITH OR WITHOUT COMORBID VASCULAR DISEASE: INSIGHTS FROM THE GARFIELD-AF REGISTRY

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Freek Verheut et al. from Onze Lieve Vrouwe Gasthuis (OLVG) - Amsterdam - Netherlands, on 29th August 2022 at the ESC Congress 2022 as a part of the session "Stroke: Diagnosis, Epidemiology, and the Heart-Brain Connection."

Many patients with atrial fibrillation (AF) have comorbid vascular disease. The effects of oral anticoagulation (OAC) in AF patients with vascular disease, however, have not been widely studied.

The purpose of this study was to investigate the impact of OAC in AF patients with (Vasc) or without (nVasc) concomitant vascular disease.

GARFIELD-AF is the largest multinational, prospective AF registry. The study comprised 51,574 GARFIELD-AF patients with newly diagnosed AF, 13,365 Vasc and 38,209 nVasc patients. All patients who reported coronary artery disease, aortic or peripheral artery disease, acute coronary syndromes, myocardial infarction, stenting, or coronary artery bypass graft was classified as having vascular disease. Adjusted hazard ratios were obtained via Cox proportional-hazards models to quantify the association of vascular disease with selected endpoints. Comparative effectiveness analyses were restricted to patients enrolled from April 2013-September 2016 (when NOACs became widely available) and who were eligible for anticoagulation (CHA_2DS_2-VASc ≥2 excl. gender). To evaluate the safety and efficacy of different anticoagulation strategies in Vasc and nVasc patients, propensity score using an overlap weighting scheme was applied. Weights were applied to Cox proportional-hazards models to estimate the effects of OAC vs No OAC and NOAC vs VKA.

Vasc patients were older (median (Q1;Q3): 72.0 (65.0;79.0) vs 70.0 (62.0;78.0) and more often male (62.0 vs 53.6%). Vasc patients had a higher rate of comorbidities including heart failure, hypertension, and diabetes. Vasc patients received less OAC (62.8 vs 68.3%). NOACs were less common compared with nVasc patients (23.8% vs 28.7%) but a similar proportion of VKAs was observed in both (39.0% vs 39.6%). Antiplatelet monotherapy was more common in Vasc (31%) than nVasc (18%) patients.

At 2-years, Vasc was associated with a higher risk of all-cause (HR [95% CI]: 1.30 [1.16-1.47]) and cardiovascular mortality (1.59 [1.28-1.97]). OACs significantly lowered the risk of all-cause mortality and stroke in nVasc patients (0.72 [0.63-0.82] and 0.64 [0.49-0.84], respectively), but not in nVasc patients. OACs led to a numerical increase in major bleeding in Vasc patients (1.32 [0.90-1.93]) and a significant increase in major bleeding in nVasc patients (1.40 [1.03-1.90]). Compared with VKAs, NOACs did not significantly improve the risk of outcomes in nVasc patients. In Vasc patients however, NOACs significantly lowered the risk of all-cause mortality (0.74 [0.61-0.90]) and major bleeding (0.45 [0.29-0.70]) compared with VKAs.

AF patients with vascular disease have worse long-term outcomes than those without. They receive less often OAC, specifically NOAC, and more antiplatelet agents. The beneficial effects of NOAC over VKA are much more pronounced in patients with than in those without vascular disease.

THE ASSOCIATION BETWEEN TROPONIN LEVEL AND MORTALITY IN PATIENTS ADMITTED TO HOSPITAL WITH ACUTE STROKE (NIHR HEALTH INFORMATICS COLLABORATIVE TROP-STROKE STUDY)

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Amit Kaura et al. from Imperial College Hospital NHS Healthcare Trust - London - United Kingdom on 29th August 2022 at the ESC Congress 2022 as a part of the session "Stroke: Diagnosis, Epidemiology, and the Heart-Brain Connection."

Acute stroke accounts for significant morbidity and mortality globally. The role of troponin for risk stratification in stroke is unclear.

The aims of this study were to assess the relationship between peak troponin and mortality in patients with ischaemic stroke, haemorrhagic stroke, or subarachnoid haemorrhage and to compare this with the predictive value of first troponin or dynamic troponin change.

A retrospective cohort study was carried out using the National Institute for Health Research Health Informatics Collaborative Cardiovascular dataset of all consecutive patients who had a troponin measured at five hospitals between 2010 and 2017. Patients with at least one troponin measurement and a primary diagnosis of ischaemic stroke, haemorrhagic stroke or subarachnoid haemorrhage during a hospital admission were included. The main exposure variables were first and peak troponin, and dynamic troponin change, and the main outcome was all-cause mortality. Results were analysed using multivariable adjusted restricted cubic spline Cox regression. Survival analyses were adjusted for troponin assay, assay sensitivity (standard or highly sensitive), number of troponin measurements, age, sex, C-reactive protein level, white blood cell count, platelet count, haemoglobin, estimated glomerular filtration rate, angiography during admission, acute coronary syndrome during admission, and cardiovascular history (history of diabetes mellitus, myocardial infarction, heart failure, hypertension, stroke or atrial fibrillation). Receiver Operator Characteristic (ROC) curves were used to assess the predictive value of each exposure variable.

4,712 patients were included in the analysis (ischaemic stroke: 3,346; haemorrhagic stroke: 718; subarachnoid haemorrhage: 648). Peak troponin was above the upper limit of normal in 47.4% of ischaemic stroke patients, 52.8% of haemorrhagic stroke patients, and 57.1% of subarachnoid haemorrhage patients. Patients with elevated peak troponin were older and had more cardiovascular risk factors.

A direct positive relationship was seen between peak troponin level and mortality hazard ratio in all three stroke subtypes. This relationship was consistent when considering dynamic troponin fold change for ischaemic or haemorrhagic stroke. For all three stroke subtypes, there was no added predictive value of peak troponin or dynamic troponin change over first troponin in predicting mortality.

A positive peak troponin was associated with increased mortality in patients presenting with ischaemic stroke, haemorrhagic stroke, or subarachnoid haemorrhage. Overall, serial troponin measurements may not improve mortality prediction beyond a single measurement. These findings may have implications for risk stratification of patients with acute stroke syndromes.

SESSION-6 :
Meet the Experts: How to Lower Cardiovascular Disease Risk in Patients with Diabetes

DOES DULAGLUTIDE IMPACT A COMPOSITE OUTCOME REFLECTING ATHEROSCLEROSIS? A POST-HOC ANALYSIS OF THE REWIND TRIAL

Barcelona **Monday, August 29th, 2022**

This paper was presented by Dr. Guilia Ferannini et al. from Karolinska Institute, Sweden on 29th August 2022 at the ESC Congress 2022 as a part of the session "How to Lower Cardiovascular Disease Risk in Patients with Diabetes."

It has been postulated that the cardioprotective effect of glucagon-like peptide-1 receptor agonists (GLP-1 RA) in patients with type 2 diabetes (T2DM) may retard the progression of atherosclerosis.

The aim of this post-hoc analysis of the REWIND trial was to test the hypothesis that treatment with dulaglutide impacts a clinical outcome that reflects atherosclerosis in patients with type 2 diabetes (T2DM).

In the double-blind, placebo-controlled REWIND trial recruiting 9901 patients (46.3% women, mean age 66 years) with T2DM and cardiovascular disease (CVD) or varying levels of CV risk, a weekly subcutaneous injection of dulaglutide 1.5 mg reduced the hazard of MACE by 12% versus placebo. This post hoc analysis assessed the impact of dulaglutide on atherosclerosis-related outcomes comprising a composite of the first of CV death, nonfatal myocardial infarction, nonfatal ischaemic stroke and any revascularization including coronary, peripheral or carotid. Cox proportional hazards models were used to estimate the effect of randomized treatment. The effect in selected subgroups was estimated by including each subgroup and an interaction term in the model for the primary outcome. The composite of any component of the primary endpoint and non-cardiovascular death was considered as a secondary outcome.

The primary endpoint occurred in 799 (16.1%) patients in the dulaglutide group and 870 (17.6%) patients in the placebo group (incidence rates: 3.25/100 person-years vs 3.58/100 person-years; HR 0.91, 95% CI 0.83 – 1.00; p = 0.05) during a median follow-up of 5.4 years. This finding was consistent regardless of sex, body mass index, previous CVD or not and diabetes duration. The incidence of the secondary outcome was also lower in the dulaglutide group (HR; 95% CI: 0.91; 0.83 – 0.99; p = 0.03).

Dulaglutide was associated with a 9% reduced index of atherosclerosis in patients with T2DM and CVD or high CV risk. This finding supports the hypothesis that dulaglutide may retard progression of atherosclerosis.

EFFECTS OF DAPAGLIFLOZIN ON CARDIOVASCULAR AND KIDNEY EVENTS BY BASELINE EGFR AND UACR IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A PATIENT-LEVEL POOLED ANALYSIS OF DECLARE-TIMI 58 AND DAPA-CKD TRIALS

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Filipe Moura et al. from Brigham and Women's Hospital, Harvard Medical School on 29th August 2022 at the ESC Congress 2022 as a part of the session "How to Lower Cardiovascular Disease Risk in Patients with Diabetes."

The sodium glucose co-transporter 2 (SGLT2) inhibitor dapagliflozin reduced the risk of hospitalization for heart failure (HHF) or cardiovascular death (CVD) and the risk of kidney events in patients type 2 diabetes mellitus (T2DM) and high cardiovascular risk or chronic kidney disease in the DECLARE-TIMI 58 and DAPA-CKD trials. These events are more common at lower levels of kidney function. Combining data from the two trials creates an opportunity to examine the effect of dapagliflozin across the spectrum of baseline kidney function.

The purpose of this study is to determine the effects of dapagliflozin on HHF/CVD and kidney endpoints across a broad range of kidney function in the combined dataset.

"We conducted a post hoc analysis of pooled patient-level data from DECLARE and DAPA-CKD. The effects of dapagliflozin compared with placebo on HHF/CVD and kidney endpoints (defined as sustained eGFR decrease ≥ 40%, end-stage kidney disease, or renal death) were assessed in the combined cohorts and in subgroups of baseline eGFR (<45, 45-<60, 60-<90, ≥90 mL/min/1.73m^2) and urinary albumin: creatinine ratio (UACR) (<30, 30-<300, 300-<1000, ≥1000 mg/g)."

A total of 19,748 patients with T2DM were included. Median (IQR) follow up time was 4.1 (3.7 – 4.4) years. Median eGFR was 85 (65-95) mL/min/1.73m^2 and UACR 18.2 (7-135) mg/g. Overall, dapagliflozin reduced the risk of HHF/CVD by 18% (HR 0.82, 95%CI 0.73-0.92, p<0.001) and kidney endpoints by 40% (HR 0.60, 95%CI 0.52-0.69, p<0.001). Overall rates of HHF/CVD and kidney endpoints were higher with lower eGFR (p<0.001) and with higher UACR (p<0.001). There were consistent relative risk reductions in HHF/CVD and kidney events with dapagliflozin across eGFR (p-interaction 0.25 and 0.32, respectively) and UACR (p-interaction 0.29 and 0.83, respectively) subgroups. The absolute rate difference (ARD) with dapagliflozin for CVD/HHF ranged from 0.1 events per 1000 patient years in patients in normal categories of eGFR and UACR to 1.0-1.7 events in patients in the most abnormal categories. Likewise, the ARD for kidney events ranged from 0.2 events per 1000 patient years in the normal eGFR and UACR groups to 2.5-4.3 events in patients in the most abnormal categories.

In this pooled analysis of pts with T2DM, there was higher risk of HHF/CVD and kidney events with lower eGFR and higher UACR. Dapagliflozin consistently reduced these events regardless of baseline eGFR and UACR, with large absolute risk reductions in patients with lower eGFR and higher UACR.

SESSION-7 :
Blood Pressure Targets: Reasonable and Achievable?

RISK FACTOR RECORDING AND MANAGEMENT IN CORONARY HEART DISEASE PATIENTS FROM 32 COUNTRIES: SURF CHD II

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. A Marza Florenza et al., from University Medical Center Utrecht on 29th August 2022 at the ESC Congress 2022 as a part of the session "Blood Pressure Targets: Reasonable and Achievable?"

Patients with coronary heart disease (CHD) are at high cardiovascular risk, and controlling risk factors in this population is especially important to prevent CHD morbidity and mortality. SURF CHD (Survey of Risk factors in Coronary Heart Disease) II is a clinical audit on secondary prevention of CHD. The goals are to simplify and assess the recording and management of cardiovascular risk factors in patients with CHD.

SURF CHD II consists in a brief online survey conducted during routine outpatient visits in patients with a previous acute coronary syndrome (ACS), stable angina, percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). Information is collected electronically on demographics, risk factor history (smoking history, physical activity), risk factor measurements (blood pressure, BMI, waist circumference), laboratory values and medication.

Risk factor targets were defined as follows: no prior smoking or having stopped smoking, practice of at least 30 minutes of moderate physical activity 3-5 times per week, BMI<25 kg/m^2, waist circumference <94 cm in men and <80 cm in women, blood pressure of <140/90 mmHg (<140/85 mmHg in diabetics), LDL <70 mg/dL, HDL >40 mg/dL in men and>45 mg/dl in women, triglycerides <150 mg/dL, and HbA1c <7% in diabetic participants.

12884 patients from 32 countries participated in SURF CHD in 5 regions: 10195 in Europe, 2048 in South-East Asia (SEA), 415 in the Americas, 210 in North Africa-Eastern Mediterranean (NAEM), and 13 in Western Pacific. All centres participating were located in urban areas and 81.6% were public.

Women represented 24.6% of the participants, mean age 64.1 years (SD 11.2 years). 57.7% of the patients had a previous PCI, 50% ACS, 29.5% stable angina and 16.1% CAGB.

Risk factor recording ranged from 26.8% (waist circumference) to 94.3% for blood pressure. Target attainment varied from 25.8% with a BMI <25 kg/m^2, to 76.3% of participants that had never smoked or had stopped smoking. The South East Asian region presented the highest percentages of risk factor target attainment for smoking, physical activity, BMI, waist circumference and LDL.

92.% of participants used antiplatelet medication, 100% antihypertensive medication and 89.4% lipid-lowering medications. Risk factor recording was reasonable, but poor for some risk factors such as waist circumference and HbA1c. In line with earlier clinical audits, there is still substantial room for improvement in risk factor control in this high cardiovascular risk population. There were regional variations, with the highest level of attainment for most risk factors targets in South East Asia.

SPONTANEOUS, INDEPENDENT, SINGLE-CENTER RENAL DENERVATION REGISTRY OF A RESISTANT HYPERTENSION MULTIDISCIPLINARY TEAM

Barcelona Monday, August 29th, 2022

This paper was presented by Dr. Simone Fezzi et al. from Integrated University Hospital of Verona - Verona - Italy on 29th August 2022 at the ESC Congress 2022 as a part of the session "Blood Pressure Targets: Reasonable and Achievable?"

Uncontrolled resistant hypertension (URH) is defined as PAS ≥ 140mmHg despite the adherence to at least 3 maximally tolerated doses of antihypertensive medications. In the adult population URH is a common condition with a prevalence that ranges between 10-15% and is related with poor prognosis and higher risk of major adverse cardiovascular events.

Renal sympathetic denervation (RDN) has recently proved efficacy in different hypertensive subsets of patients. However, patients with chronic kidney disease (CKD) IIIB-V stages (i.e., glomerular filtrate rate <45 ml/min) have been systematically excluded from randomized clinical trials (RCT).

The purpose of this study was to evaluate the safety and the efficacy of RDN in a daily practice population of patients with URH on top of medical therapy, including patients with renal function impairment (GFR <45 ml/min).

Consecutive unselected patients with URH undergoing RDN were enrolled. Indication of RDN was assessed in a multidisciplinary team involving cardiologist, nephrologist and hypertension specialists, after secondary forms of hypertension had been excluded. Efficacy was defined as the inter-individual change of office (OBP) and ambulatory blood pressure monitoring (ABPM) at 3, 6 and 12 months after RDN. Safety as the absence of any device-related major complication (BARC classification), end-stage renal disease, stroke, acute myocardial infarction and any cause of death within 1 month of the procedure. Safety and efficacy profile was assessed in patients with an estimated GFR below 45 ml/min/1.73m^2.

Seventy-two patients underwent RDN for URH from 2012 to 2022. The population presented with multiple comorbidities and target organ damage: almost 50% were smoker, 43% diabetic, 33% PAD, 25% CAD and 60% CKD. Isolated systolic hypertension prevalence was 53%. The average number of antihypertensive medications at baseline was 5.3±1.1. Baseline OBP and ABPM were 158.8/86.6 ± 23.4/15.3 mmHg and 151.4/87.6 ± 18.8/14.2 mmHg, respectively. The vast majority of the procedures were performed with tetrapolar radio-frequency catheter (91.7%), with 37.3 ± 14.3 number of ablations per procedure. The average amount of contrast medium was 72.1 ± 38.1 ml. At 12-month follow-up a significant reduction of office and ambulatory systolic BP, respectively by -15.66 ± 29.73 mmHg (P<0.01) and by -11.3 ± 23.1mmHg (P<0.05), was noticed. BP reduction at 12-month follow-up among patients with eGFR < 45 ml/min was similar to that obtained in patients with higher eGFR. No major complications were observed and renal function was stable up to 12 months, even in patients with lowest eGFR at baseline.

RDN is safe and feasible in patients with URH on top of medical therapy, even in a high-risk CKD population with multiple comorbidities. Our experience underlines the central role of multidisciplinary team evaluation for the targeted management of uncontrolled resistant hypertension.

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