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American College of Cardiology Congress update 2020

28-30 March 2020

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LEARNING OBJECTIVES

You will learn:

- Management of cardiovascular risk factors such as cigarette smoking, hypertension, dyslipidaemia and polygenic risk
- SGLT-2 inhibitors also show benefits in the treatment of heart failure
- The results from the latest studies of valvular heart disease
- The latest data on the use of ticagrelor in both acute coronary syndromes and coronary revascularisation
- The promise of novel agents, vericiguat and mavacamten, in treating heart failure
- The superiority of transcatheter aortic valve replacement over surgery for the treatment of valvular heart disease.

Because of the COVID-19 pandemic, the meeting that was to have been held in Chicago was cancelled and a virtual meeting was held online. A large number of cardiologists from around the world attended the live sessions. The ACC has also made the entire content of the meeting available online for the next three months. The content can be accessed at virtual.acc.org/on-demand at no charge.

Risk factor management

Cigarette smoking

Three hundred and seventy-six active smokers willing to stop were enrolled in a study. These were people smoking an average of 21 cigarettes per day who had smoked for an average of 35 years. They were randomised to the use of nicotine e-cigarettes plus counselling, non-nicotine e-cigarettes plus counselling or just counselling alone. At 12 weeks the rate of abstinence was 22%, 17% and 9%, respectively. Unfortunately, continuous abstinence was only achieved in 5% or less of these smokers.

(Presented by Dr MJ Eisenberg (Canada) at ACC 2020/WCC, March 2020.)

This report was made possible by an unrestricted educational grant from **Cipla**. *The content of the report is independent of the sponsor.*

Cipla

Featuring talks by

Prof Dirk Blom
University of Cape Town Heart Centre and Lipid Clinic
Groote Schuur Hospital

Professor FJ Raal
FRCP, FCP(SA), Cert Endo, MMed, PhD
Director, Carbohydrate & Lipid Metabolism Research Unit
Professor & Head, Division of Endocrinology & Metabolism,
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Hypertension

Previous studies of renal denervation for the treatment of hypertension have compared the procedure with the responses of patients to antihypertensive medication. The SPYRAL HTN-OFF MED[1] Pivotal trial compared renal denervation to sham-operated untreated controls. Three hundred and thirty-three patients with systolic blood pressures between 150mmHg and 180mmHg and diastolic pressures above 90mmHg were enrolled. Patients with an eGFR below 45 and those with type I diabetes or type II diabetes with an HbA_{1c} above 8% were excluded. The denervation group required antihypertensive medication if blood pressure exceeded 180mmHg. At three months the blood pressure had fallen by 4.7/3.7mmHg in the denervation group compared to 0.6/0.8mmHg in those who were sham operated. The researchers anticipate that, as has been observed in previous trials, a further fall in blood pressure will occur after six months of follow-up. During the trial period 10% in the denervation group and 17% in the sham-operated group required the addition of antihypertensive medication for uncontrolled blood pressure. The result establishes renal denervation as an effective means to control hypertension. There is an ongoing trial that will compare denervation to medication, the SPYRAL HTN-ON MED study.

Dyslipidaemia

SA experts present virtually at ACC

Dr Dirk Blom from Cape Town presented the results of the ODYSSEY HoFH trial in 69 patients with homozygous familial hypercholesterolaemia. The 45 patients in the treatment group received alirocumab 150mg subcutaneously every two weeks for 12 weeks while 24 patients received placebo injections. All were maintained on their usual lipid-lowering treatment. The average absolute reduction in LDL cholesterol was 1.6mmol/l in the treated group. LDL levels were 27% lower on alirocumab versus 9% higher in the placebo group at 12 weeks. The treatment was well tolerated. Blom noted that there was a small number of patients with specific mutations who did not respond or responded poorly to alirocumab.

Professor Derick Raal from Johannesburg presented a separate study of homozygous familial hypercholesterolaemia in 65 patients, the majority of whom were already treated with high-intensity statin therapy, a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor and ezetimibe. One-third were receiving regular plasma apheresis. This group was treated with evinacumab, a monoclonal antibody binding to angiopoietin-like protein 3, which reduces LDL cholesterol through a mechanism different from that of any existing agent. Evinacumab was given via intravenous infusion every four weeks at a dose of 15mg/kg for 24 weeks in 43 patients. Twenty-two were randomised to placebo infusions. At 24 weeks, the treated group had reduced their LDL cholesterol by 47% while in those receiving placebo the LDL rate had risen by 2%. No serious treatment-related adverse events were observed. Reductions in LDL cholesterol were achieved in patients with no LDL receptor function as well as in those with some residual receptor function. The former group are the least responsive to currently available agents.

Inclisiran is a small double-strand interfering RNA which inhibits the production of PCSK9 in liver cells. Phase 3 trials have been conducted to examine the effect of inclisiran. Pooled analysis of the ORION-9, ORION-10 and ORION-11 trials, which included heterozygous familial hypercholesterolaemia patients and patients with atherosclerotic cardiovascular disease, was undertaken. In all, 3 660 patients were randomised to twice yearly injections of the active agent or placebo, of whom 93% had completed follow-up of 18 months. Most patients were on treatment with a high-intensity statin and 14% were also receiving ezetimibe. The baseline LDL cholesterol was 2.9mmol/l. Treatment resulted in a highly significant 55% reduction in LDL cholesterol. Reductions in PCSK9, non-HDL cholesterol, apoliproprotein B and

lipoprotein(a) were noted. The effect was consistent across all subpopulations. Treated patients had a 1% excess in arthralgia as compared to those on statins and ezetimibe. Injection site reactions were noted in 5%.

The REDUCE-IT trial examined the effect of icosapent ethyl in patients with cardiovascular disease who had an elevated triglyceride level and were on treatment with a statin. The primary results were reported at the American Heart Association (AHA) in Chicago in 2018. It was shown that cardiovascular death, myocardial infarction, stroke, coronary revascularisation and unstable angina were reduced by 5% over five years, a relative risk reduction of 25%. There was a 4% reduction in the key secondary composite endpoint of cardiovascular death, myocardial infarction and stroke. Over the entire trial there was a 31% reduction in the total cumulative events experienced by the treated group. Dr Deepak Bhatt reported on the results in relation to the baseline serum eicosapentanoic acid (EPA) levels. The treatment was shown to benefit patients across the range of EPA levels. There was a fivefold increase in the level of EPA on treatment. On-treatment EPA levels correlated strongly with cardiovascular death, myocardial infarction, stroke, coronary revascularisation, unstable angina, sudden cardiac death, cardiac arrest, new-onset heart failure and all-cause mortality. These benefits could not be explained by changes in triglycerides or other biomarkers. Bhatt emphasised that these results do not apply to omega-3 fatty acid preparations that also contain docosahexaenoic acid (DHA) and which has many different biological effects.

Polygenic risk

Combining the lifetime exposure to elevated LDL cholesterol and systolic blood pressure with the polygenic score may more accurately estimate an individual's lifetime risk of cardiovascular disease

The lifetime risk of cardiovascular disease was computed at all levels of the polygenic score for coronary artery disease, dependent on differences in the lifetime exposure to elevated LDL cholesterol and systolic blood pressure. This was to obtain an understanding of how the polygenic score could be combined with information about LDL cholesterol and systolic blood pressure, both of which are modifiable and can reduce risk. The results for almost 450 000 individuals were taken into account. Cardiovascular risk, as assessed by the polygenic score, rose in relation to the height of the score and increasing age. The results were then adjusted for minor elevations or decreases in LDL cholesterol (0.25mmol/l) and systolic blood pressure (2mmHg) in relation to the middle quintile of the polygenic score. In both cases there was a proportionate increase or decrease in risk. The authors concluded that the lifetime risk of cardiovascular disease varies substantially at all levels of the polygenic score for coronary artery disease, depending on differences in the lifetime exposure to elevated LDL cholesterol and systolic blood pressure. Combining the lifetime exposure to these risk factors with the polygenic score may more accurately estimate an individual's lifetime risk of cardiovascular disease, more accurately identify individuals who will benefit from early intervention and better estimate the potential benefit of early intervention. This approach has the potential to personalise the prevention of cardiovascular disease by minimising the risk of lifetime exposure to elevated LDL cholesterol and systolic blood pressure.

(Presented by Dr BA Ference (USA) at ACC 2020/WCC, March 2020.)

Chronic coronary syndromes

The ISCHEMIA study[2] was first reported on by Dr Judith Hochman at the AHA meeting in November 2019. Patients were randomised to routine invasive therapy with coronary angiography and percutaneous coronary intervention or coronary bypass surgery as deemed appropriate vesus a medically treated group whose subjects underwent coronary angiography only if medical treatment failed. All patients had moderate to severe ischaemia on non-invasive stress testing – assessed either by nuclear study, echocardiographic stress testing, cardiac MRI or treadmill exercise testing. A large percentage of these patients underwent CT coronary

angiography to exclude those patients with significant left mainstem stenosis. ISCHEMIA showed that routine invasive therapy was not associated with a reduction in adverse ischaemic events when compared to optimal medical therapy. It is important to note that patients with more than 50% left mainstem stenosis, an ejection fraction below 35% and recent myocardial infarction, in NYHA class III or class IV heart failure, who had undergone prior revascularisation within the last 12 months or who had an unacceptable level of angina at baseline, were excluded. During the entire follow-up period of 3.3 years, 96% of the invasive group and 28% of the medical therapy group underwent cardiac catheterisation. Revascularisation was performed in 80% and 23%, respectively. Dr DJ Maron reported on the associations between the degree of ischaemia and the coronary anatomy in respect of the clinical outcome. No association was found between the degree of ischaemia and all-cause mortality, although there was a weak association with myocardial infarction. The extent of coronary disease was related to all-cause mortality and myocardial infarction. However, the outcomes in the invasive versus conservative arms were similar, irrespective of the degree of ischaemia or the extent of coronary disease.

The ISCHEMIA-CKD study[3] evaluated the largest group of patients with chronic kidney injury and chronic coronary syndrome studied to date; 777 patients were enrolled. The trial design was essentially the same as that of the main ISCHEMIA trial. Over the entire follow-up period of 2.3 years, 85% of the invasive group underwent cardiac catheterisation versus 22% in the medical therapy group. Revascularisation was performed in 50% and 12%, respectively. Death or myocardial infarction occurred in 36% of the routine invasive group versus 37% of the medical therapy group. No differences were noted between the revascularised and medically treated groups in respect of the stage of chronic kidney disease. More than one-quarter of patients in each group died during the follow-up period. At 12 and 36 months there was no discernible quality-of-life benefit in either group.

Many patients in the ISCHEMIA study were enrolled after undergoing CT coronary angiography. Among those screened, there was a group in whom no obstructive coronary disease (stenosis less than 50%) was demonstrable. These 208 Ischaemia with Non-Obstructed Coronary Arteries (INOCA) patients were entered into the CIAO-ISCHEMIA study and compared to 1 079 patients in the ISCHEMIA trial, all of whom had had undergone stress echocardiography. At entry both groups had similar levels of ischaemia. The frequency of angina was greater in the INOCA group. Sixty-six percent were women, compared to only 26% in the main trial. At one year, around 50% of INOCA patients had a normal stress echocardiogram. Anginal symptoms improved in 42% and worsened in 14%. No correlation was found between the stress test findings and the change in symptoms.

(Presented by Dr HR Reynolds at ACC 2020/WCC, March 2020.)

Rivaroxaban plus aspirin … The absolute risk reductions were numerically larger in those patients with diabetes

Stable atherosclerotic cardiovascular disease

COMPASS[4] enrolled 27 395 participants with stable coronary disease or peripheral arterial disease, randomising them to either aspirin 100mg daily, rivaroxaban 5mg BD or rivaroxaban 2.5mg BD plus aspirin 100mg daily. The primary result, reported in 2017, was in favour of rivaroxaban plus aspirin, with a significant risk reduction of 24%. This presentation examined the 6 922 patients with diabetes, comparing them to 11 356 patients without diabetes (Figure 1). The overall incidence of cardiovascular death, myocardial infarction or stroke was higher in those patients with diabetes. Rivaroxaban plus aspirin effected a 26% reduction in the composite outcome compared to aspirin alone. All-cause deaths were reduced by 19%. Major adverse limb events or major vascular amputations were also reduced. The absolute risk reductions were numerically larger in those patients with diabetes. The bleeding risk in patients with diabetes was similar to that in those without diabetes. There was no increase in intracranial or fatal bleeding.

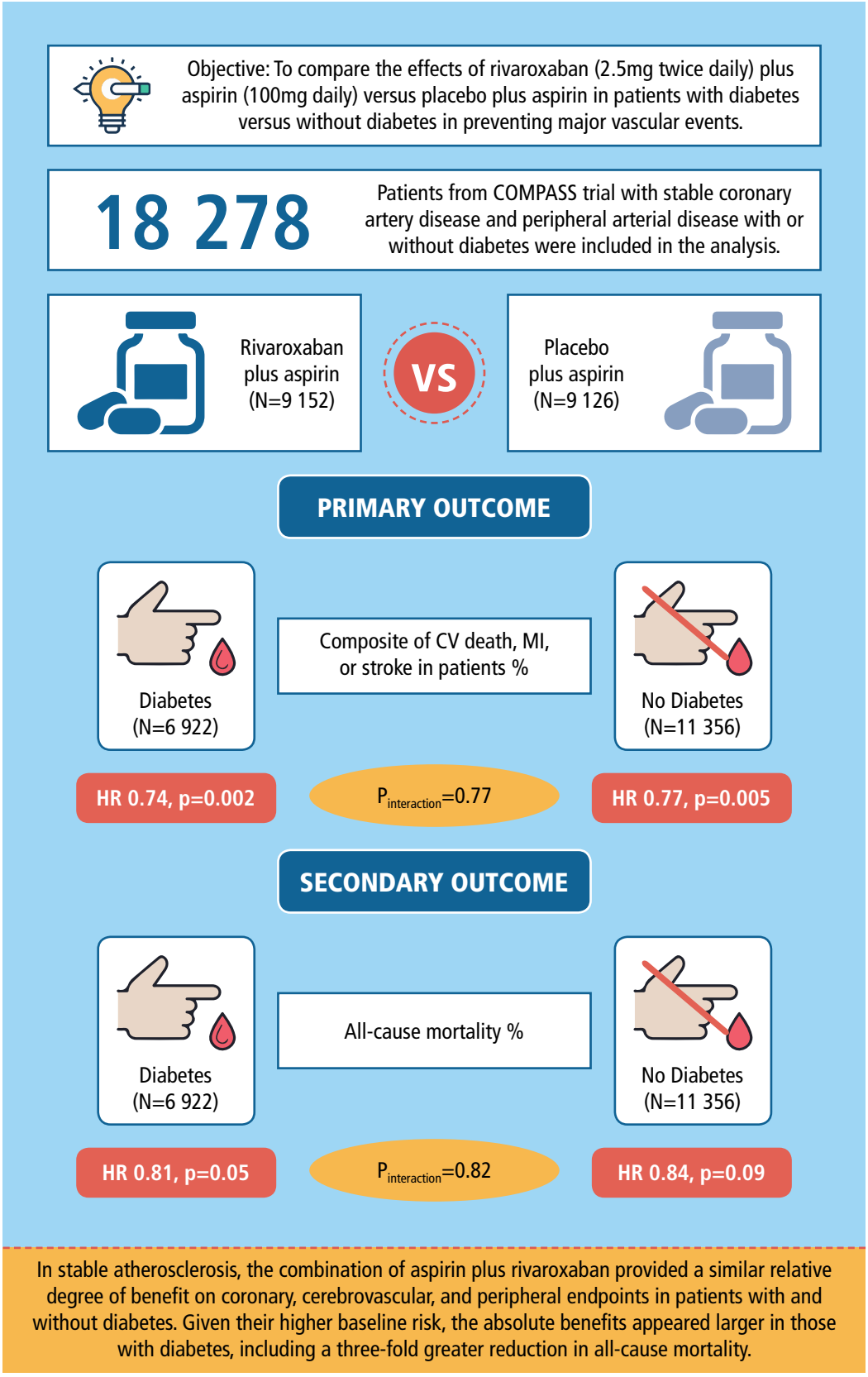

Figure 1. COMPASS Diabetes: Role of combination antiplatelet and anticoagulation therapy in diabetes and cardiovascular disease

After peripheral arterial revascularisation, patients are at high risk of major adverse limb events, major adverse cardiovascular events, prolonged hospital stay, disability and death. To date there is no proven antithrombotic strategy that will reduce the risk of these events.

The VOYAGER PAD trial[5] enrolled 6 564 patients with lower-extremity peripheral arterial disease who were undergoing acute peripheral revascularisation for ischaemia (Figure 2). All patients were treated with aspirin 100mg daily and, at the investigator's discretion, clopidogrel. The patients were randomised to receive rivaroxaban 2.5mg BD or placebo and followed up for a median of 28 months. The primary efficacy endpoint was a composite of acute limb ischaemia, major amputation of vascular aetiology, myocardial infarction, ischaemic stroke or cardiovascular death. The principal safety endpoint was TIMI major bleeding. Fifty-one percent of patients in both groups received clopidogrel during the trial. At 36 months the primary endpoint was significantly reduced from 20% to 17%, with a hazard

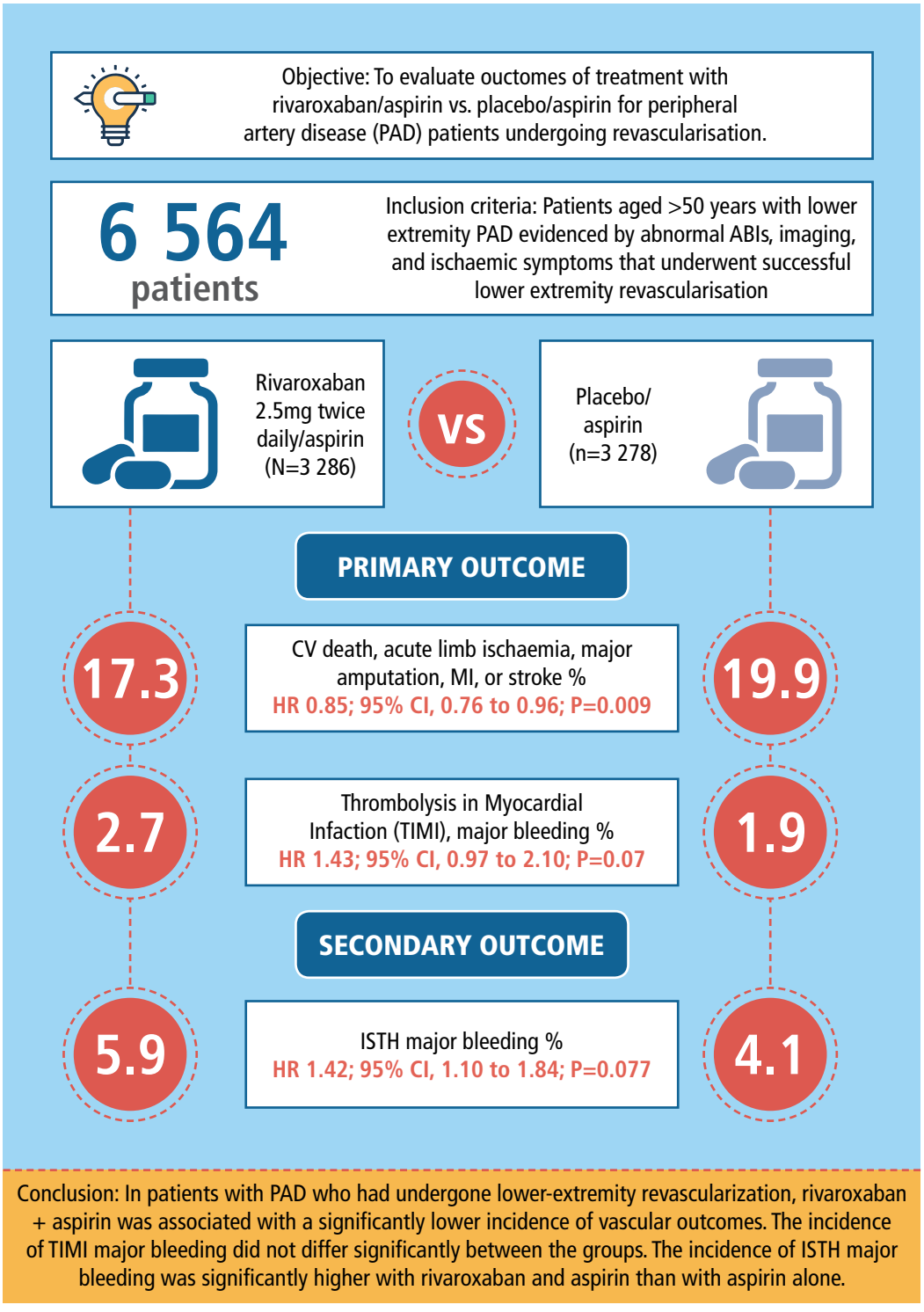

Figure 2. VOYAGER PAD: Rivaroxaban in peripheral artery disease after revascularisation

ratio of 0.85. The benefit was consistent across all subgroups examined. A continuous incremental benefit was noted over the trial duration. There was a 43% increase in TIMI major bleeding (2.7% versus 1.9%) with rivaroxaban plus aspirin but no increase in intracranial haemorrhage or fatal bleeding. The results for patients on and off clopidogrel were not shown.

Acute coronary syndromes

The TICO study enrolled 3 056 patients who had undergone percutaneous intervention for acute coronary syndrome (unstable angina 29%, NSTEMI 35% and STEMI 36%). All patients had received ultra-thin bioresorbable polymer sirolimus-eluting stents. They were randomised to either standard dual antiplatelet therapy with aspirin and ticagrelor for 12 months or aspirin and ticagrelor for three months followed by ticagrelor monotherapy for up to 12 months. The primary outcome was the net adverse clinical event rate, which included ischaemic events and bleeding. The primary outcome occurred in 3.9% of the ticagrelor monotherapy group as opposed to 5.9% in the standard therapy group. In the absence of multivessel disease there was a 59% reduction in the endpoint whereas the reduction was 14% when multivessel disease was present. Major bleeding at 12 months was reduced by almost 50%, whereas there was no difference in the rate of stent thrombosis that occurred in 0.4% and 0.3%, respectively.

(Presented by Dr B-K Kim at ACC 2020/WCC, March 2020.)

Colchicine... demonstrated cost-effectiveness with cost reduced by 47% for the trial period and by 69% over the patient's lifetime

Last year the COLCOT trial randomised 4 745 patients following myocardial infarction to colchicine 0.5mg per day or placebo within 30 days. The primary composite endpoint showed a 23% reduction in the risk of a major adverse cardiac event (MACE). The secondary analysis presented at ACC 2020 demonstrated cost-effectiveness with cost reduced by 47% for the trial period and by 69% over the patient's lifetime. In addition, the quality adjusted life-years increased.

(Presented by Dr M Samuel at ACC2020/WCC, March 2020.)

Coronary revascularisation

The TWILIGHT study, which was published in 2019, showed that percutaneous intervention with ticagrelor monotherapy after three months of dual antiplatelet therapy was associated with a lower incidence of clinically relevant bleeding without an increase in the risk of ischaemic events, when compared to continuing dual antiplatelet therapy. A *post hoc* analysis of the trial presented by Dr DG Dangas. looking only at those patients undergoing complex intervention, included 2 620 patients who had completed three months of dual antiplatelet therapy. Around two-thirds of these patients had presented with acute coronary syndrome. Fifty-two percent had a stent length greater than 60mm, 30% required treatment of more than three lesions and chronic total occlusion was treated in 19%. Patients treated with ticagrelor monotherapy after three months had a lower bleeding risk and no increase in death, myocardial infarction or stroke.

PRECOMBAT[6] is a Korean study comparing revascularisation with a sirolimus-eluting stent to coronary bypass surgery for severe left main stem stenosis. Six hundred patients were enrolled in this trial. After 10 years of follow-up there was no overall difference in the primary outcome (major adverse cardiac or cerebrovascular events): 30% in patients treated with stenting versus 25% in those who underwent coronary bypass surgery. There were no significant differences in deaths, myocardial infarction or stroke. Target vessel revascularisation occurred in 16% of the stented patients, versus 8% in those who had had coronary bypass surgery. Patients with left main stem stenosis and triple vessel coronary artery disease fared less well with coronary stenting than those with isolated left main stem stenosis.

In a trial including 142 patients who were followed up for five years, bypass surgery employing a radial artery graft to the circumflex coronary artery was superior to

saphenous vein grafting. The radial artery graft patency was 98.3%, as opposed to 86.4% with a saphenous vein graft. The Radial Artery Database International Alliance (RADIAL) includes 1 036 patients followed for 10 years and shows reductions in death or myocardial infarction, and the need for revascularisation in favour of radial artery grafting.

(Presented by Dr MFL Gaudino at ACC 2020/WCC, March 2020.)

Cardiomyopathy and heart failure

Dapagliflozin, a sodium-glucose co-transporter 2 (SGLT-2) inhibitor initially developed for the treatment of diabetes, has been shown to be highly effective in the treatment of heart failure. The DAPA-HF trial[7] compared dapagliflozin to placebo in patients with heart failure with a reduced ejection fraction. The trial enrolled 4 744 patients irrespective of their diabetes status. These patients had symptomatic heart failure, an ejection fraction below 40% and an elevated natriuretic peptide level. The principal finding was a reduction in the combination of cardiovascular death, hospitalisation for heart failure or urgent heart failure visit. Treatment reduced the endpoint by an absolute 5%. This was seen irrespective of diabetes status, age, health status and baseline medication use. The use of sacubitril-valsartan at baseline was low. Dapagliflozin reduced the time to first events and to recurrent events equally.

Dapagliflozin has been shown to be highly effective in the treatment of heart failure

(Presented by Dr P Ponikowski at ACC 2020/WCC, March 30 2020.)

The PARAGON-HF trial[8] randomised 2 730 patients with heart failure with preserved ejection fraction to 27 months of treatment with sacubitril-valsartan 97/103mg BD versus valsartan 160mg BD. The level of NT-proBNP strongly predicted rates of total heart failure hospitalisation and cardiovascular death during the trial. Prediction was modified by the presence of atrial fibrillation and also obesity. NT-proBNP was reduced by 19% by sacubitril-valsartan in comparison to valsartan alone. Though decreases in NT-proBNP were associated with a lower event rate, the level of NT-proBNP did not modify the treatment effect of sacubitril-valsartan.

Vericiguat increases soluble guanylate cyclase activity. In the VICTORIA trial,[9] 5 050 patients with congestive heart failure with recent decompensation were randomised to vericiguat in a dose up to 10mg daily or placebo. These patients were in NYHA class II to IV, had an ejection fraction below 45% and were on guideline-directed heart failure therapy. All had recently been hospitalised for heart failure or received intravenous diuretic therapy. All had elevated natriuretic peptide levels. Patients were followed for 12 months. The treatment was safe and well tolerated. The composite of cardiovascular death or hospitalisation for heart failure was reduced by 3%, p=0.019. The primary outcome was more favourable in those below 75 years of age. All-cause mortality was not affected.

The MAVERICK-HCM trial evaluated a novel cardiac myosin inhibitor, mavacamten, in a small group of patients with nonobstructive hypertrophic cardiomyopathy. Many of the trial subjects were on treatment with a beta-blocker or calcium channel blocker. The left ventricular ejection fraction decreased by 4.1% in the treated group and by 2.3% in the placebo-treated group. Reductions in NT-proBNP and troponin levels were noted in the mavacamten group. The composite functional endpoint, comprising peak oxygen uptake and NYHA class, improved in 35 of 40 patients in the treated group. There was a high incidence of adverse events. despite which the investigators considered that the medication was well tolerated.

(Presented by Dr C Ho at ACC 2020/WCC, March 30, 2020.)

Atrial fibrillation

AUGUSTUS[10] was a 2×2 factorial study in atrial fibrillation patients with recent acute coronary syndrome or percutaneous intervention. All patients were treated with a P2Y12 inhibitor; 4 614 patients were randomised to apixaban or warfarin and to aspirin or placebo, and were followed for six months. The primary safety outcome of major or clinically relevant nonmajor bleeding (ISTH definition) was 10.5% with apixaban versus 14.7% with warfarin. In the aspirin versus placebo arms, the rates of bleeding were 16% versus 9%. When compared to warfarin, death or hospitalisation was significantly reduced with apixaban. The rates of intracranial haemorrhage were low and not significantly different among the groups. A number of trial results (WOEST, PIONEER AF-PCI, RE-DUAL PCI and AUGUSTUS) now support the use of anticoagulation with P2Y12 monotherapy in patients with atrial fibrillation following acute coronary syndrome or percutaneous intervention.

Reductions in NT-proBNP and troponin levels were noted in the mavacamten group

The vein of Marshall is a small vessel that descends obliquely across the back of the left atrium and ends in the coronary sinus near its left extremity. The single-centre VENUS study in 343 patients showed that concomitant alcohol ablation of the vein of Marshall in patients with persistent atrial fibrillation undergoing catheter ablation is superior to standard ablation alone. The atrial tachycardia/atrial fibrillation burden and recurrences were reduced. Freedom from arrhythmia at three months increased from 38% to 49%, and recurrences were reduced from 37% to 31%.

(Presented by Dr M Valderrábano at ACC 2020/WCC, March 2020.)

The National Cardiovascular Data Registry (NCDR) left atrial appendage occluder registry commenced following the approval of the Watchman device in March 2015. The registry began enrolling in January 2016. Approximately 90% of hospitals in the United States using this device have participated. By December 2018, 38 158 of these devices had been implanted in 495 hospitals by 1 318 physicians. Patients in the registry have a mean age of 76 years and 41% are women. There is a high incidence of prior ischaemic stroke or transient ischaemic attack, congestive heart failure, diabetes and hypertension. Twelve percent had previously had an intracranial bleed and previous clinical bleeding had occurred in 69%. The median CHA_2DS_2-VASc score was 4.6 with a median HAS-BLED score of 3. The device was deployed in 93% of the procedures attempted. Half of the cancelled procedures were due to left atrial appendage thrombus detected on the day of the procedure. Procedural success was 98%. Major in-hospital complications occurred in 2.2%. Though the frequency was less than 1% in all instances, the most frequent adverse events were ischaemic stroke, transient ischaemic attack, device embolisation and myocardial infarction. Despite the registry patients being at higher risk for stroke and bleeding than in the initial studies, procedural characteristics and safety compared favourably with those trials.

(Presented by Dr JW Freeman at AAC 2020/WCC, March 2020.)

Valvular heart disease

Transcatheter mitral valve repair

The EXPAND study investigators reported on the results of the MitraClip NTR and XTR systems in patients with significant primary mitral regurgitation. This observational study was conducted in the United States, Europe and the Middle East. One thousand and forty-one subjects underwent implantation of the MitraClip, of whom 422 were considered to have primary mitral regurgitation or a mixed aetiology and were the substance of this report. The mean age of patients was 79 years; 93% had atrial fibrillation, 28% chronic kidney injury, 19% diabetes and 80% hypertension. Forty-three percent had been hospitalised within the last year for heart failure. The acute procedural success rate was 95%, with a fluoroscopy time of 18 minutes and procedure time of 82 minutes. The hospital stay was one day. The mean mitral gradient at 30 days was 3.7mmHg. All-cause death had occurred in 2.4% at 30 days, stroke occurred in 1.2% and non-elective cardiovascular surgery for device-related complications in 0.9%. No or only mild mitral regurgitation was present in 86.9% of patients at 30 days. Gross mitral regurgitation was present in only 0.5%.

(Presented by Dr DS Lim at ACC 2020/WCC, March 30, 2020.)

Transcatheter aortic valve replacement (TAVR)

TAVR resulted in a shorter hospital stay and more rapid improvement in functional capacity and quality of life

PARTNER 3 was a study of low-risk patients and demonstrated the superiority of TAVR versus surgery for the primary endpoint of death, stroke or re-hospitalisation at one year. This report concerned the two-year follow-up of this group; 1 000 patients had been randomised and 96.5% of them were available for primary endpoint analysis at two years. From year 1 to year 2 more deaths and stroke events were noted in the TAVR patients, resulting in no significant difference from the surgical group at that juncture. Reduced cardiovascular rehospitalisations were noted in favour of TAVR. Valve thrombosis events increased between 12 and 24 months in the TAVR group. The frequency of moderate or mild paravalvular aortic regurgitation did not change.

(Presented by Dr MJ Mack at ACC 2020/WCC, March 30, 2020.)

The PARTNER 3 study excluded patients with bicuspid valves. The Evolut Low Risk Bicuspid Study was designed to assess the safety and efficacy of TAVR in patients with bicuspid aortic valve stenosis at low surgical risk. Symptomatic and asymptomatic patients with severe aortic stenosis were included. After screening of 222 patients, the procedure was attempted in 150. The valve was implanted in 149 patients, one of whom required conversion to surgery. Therefore 148 patients were discharged with the implant *in situ*. Device success rate was 95%. The rate of paravalvular leakage was low. There was one death and one stroke during the 30 days of follow-up, a frequency of 1.3%. Permanent pacemaker implantation was required in 15%. These patients will be followed up for 10 years.

(Presented by Dr B Ramlawi at ACC 2020/WCC, March 30, 2020.)

A 'real-world' trial of TAVR in the United Kingdom enrolled patients aged above 70 years with severe symptomatic aortic stenosis at intermediate or high operative risk, who then underwent TAVR. They had similar stroke, major bleeding and all-cause mortality at one year compared with patients who underwent surgical AVR. Nine hundred and thirteen patients were randomised to TAVR or conventional surgery. Transfemoral access was employed in 92% of patients and a wide range of valves was used. At one year death from any cause had occurred in 4.6% of TAVR patients and 6.6% of those who had undergone conventional surgery. Aortic valve gradients and effective orifice areas were comparable. TAVR was associated with an increase in mild and moderate aortic regurgitation. Functional outcomes and quality of life did not

differ. TAVR was judged to be noninferior to conventional surgery in respect of death from any cause at one year. TAVR was associated with less major bleeding, but with increased vascular complications, pacemaker implantation and mild or moderate aortic regurgitation. TAVR resulted in a shorter hospital stay and more rapid improvement in functional capacity and quality of life.

(Presented by Professor WD Toff at ACC 2020/WCC, March 30, 2020.)

In patients undergoing TAVR who had an indication for long-term oral anticoagulation, 326 patients were enrolled in the POPular-TAVI study[11] and followed for three months. They were randomised to oral anticoagulation alone or anticoagulation plus clopidogrel; 96% of these patients had atrial fibrillation. Bleeding (based on the VARC-2 definition) occurred in 22% of those on oral anticoagulation alone compared to 35% in those receiving the combination of oral anticoagulation and clopidogrel. The reduction in bleeding risk for those receiving warfarin was 25% versus 72% with direct oral anticoagulants when compared to the combination treatment. The rate of cardiovascular death, non-procedural bleeding, myocardial infarction or stroke was 31% with oral anticoagulation alone versus 46% in those on combination treatment. It should be noted that only 24% of patients were treated with a direct oral anticoagulant in the trial.

Venous thromboembolism

In patients deemed at risk, rivaroxaban might replace low-molecular-weight heparin to prevent venous thromboembolism during the period of postoperative reduced mobility following non-major orthopaedic surgery

The Caravaggio trial[12] compared oral apixaban (10mg BD for seven days, then 5mg BD for six months) to subcutaneous dalteparin (200IU/kg subcutaneously for seven days, then 150IU/kg subcutaneously for six months) in cancer patients with deep vein thrombosis or pulmonary embolism. Some 580 patients were randomised in each group. Follow-up was for six months. The oral agent was noninferior to the parenteral agent. There was no increase in gastrointestinal bleeding, unlike that seen with rivaroxaban or edoxaban.

Professional society guidelines vary in their recommendations regarding prophylaxis for deep vein thrombosis in patients with isolated lower leg injuries requiring immobilisation. Some have recommended low-molecular-weight heparin or fondaparinux after assessing the risk factors for venous thromboembolism and considering the potential for bleeding. The PRONOMOS study compared the effect of rivaroxaban to that of enoxaparin in preventing major venous thromboembolism during immobilisation after lower limb non-major orthopaedic surgery. Patients received either rivaroxaban 10mg daily and placebo or enoxaparin 4000IU daily subcutaneously and placebo; 3 604 patients with an average age of 41 years were randomised. There was a very low incidence of symptomatic venous thromboembolism and major bleeding. The net clinical benefit was in favour of rivaroxaban. The authors concluded that in patients deemed at risk, rivaroxaban might replace low-molecular-weight heparin to prevent venous thromboembolism during the period of postoperative reduced mobility following non-major orthopaedic surgery.

(Presented by Dr N Rosencher at AAC 2020/WCC, March 2020. Publication online at nejm.org)

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Reg: 2012/216456/07

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