REPORT ON THE 59TH SCIENTIFIC SESSIONS OF THE AMERICAN COLLEGE OF CARDIOLOGY ATLANTA, 13-16 MARCH 2010

I was the guest of AstraZeneca at this meeting which generously sponsored my economy class airfare, hotel accommodation and registration.

HEALTH CARE REFORM

The ACC is at present wrestling with the challenges of health care reform in the United States and a significant portion of the meeting was taken up by presentations concerning reform, fee structures and practice management. At the start of the year the ACC had challenged national tariff adjustments in a Florida court. The case was thrown out when the court found it did not have the competence to give a ruling in a federal issue. The tariff adjustment relates to a 20-40% reduction in 2010 fees for cardiologists.

In is opening address, Dr Alfred Bove discussed the disparity in rewards for preventive and long-term care when compared to the returns on procedures. With the increases in obesity, diabetes, hypertension and heart failure, preventive and chronic care are vitally needed. The US medical profession must move away from the current strategy which rewards “keeping America sick”.

One interesting pair of presentations was by two US Congressmen from either side of the floor who discussed their proposals for health care reform. Although the specifics might not apply to the South African situation, it is worthy noting the heads of argument, given our government’s plans to create a National Health Insurance scheme. The Republican speaker spoke of reducing the number of insurers, aligning the aims of insurers with their membership, implementing medical liability reform, ensuring patient’s personal responsibility for their own health care, rewarding innovation and strengthening doctor-patient relationships, increasing incentives to enter the medical profession and guaranteeing quality care. It was not clear to me what plans he had to manage the uninsured group which constitutes some millions of people in the US. The Democrat who replied had less of substance to offer. He cautioned against the influence of fear. He considered the current system unsustainable and suggested basing plans upon available statistics and the findings of registries. Physicians must be encouraged to improve efficiency and to create value within the system. Rewards that accrue from consumption alone will have to be reduced. Suppliers must be subjected to market principles to control their pricing. The aim was to provide universal coverage for which financing was an obstacle to be overcome. The principle of voluntary coverage in the US is ineffective as individuals buy in or buy up only when affected by illness.

PREVENTION STUDIES

The ACCORD Lipid Study compared statin therapy with statin (simvastain 20-40 mg daily) + fibrate (fenofibrate 54-160 mg daily) in 5 518 diabetics and patients at high risk of diabetes. LDL cholesterol was around 2 mmol in both arms at the end of the study. Myalgia was encountered in 40% of subjects though very few had an elevation in CK. The addition of the fibrate made no difference to the outcome. Marginal benefits were observed when triglycerides were **>**2.3 mmol and HDL **<**0.9 mmol.

The ACCORD Blood Pressure Trial compared the effects of controlling the systolic BP in 4 733 diabetics of, on average, 10 years duration, with an HbA1C of 8.3%, at either <140 mm Hg or <120 mm Hg. The result was a 14 mm Hg difference in systolic BP between the two groups (133 mm Hg vs. 119 mm Hg; 3.4 vs. 2.1 antihypertensive agents). This did not influence the primary endpoint although a 40% reduction in stroke (0.5% per year) was observed in the group with the lower BP. The NNT for a reduction of one stroke was 89 over 5 years of treatment.

A follow-up study of the INVEST trial in 6 400 diabetics examined the incidence of death, non-fatal myocardial infarction and non-fatal stroke in groups in which the systolic BP was <130 mm Hg, 130-140 mm Hg and >140 mm Hg. Event rates were highest in the group whose BP was >140 mm Hg. However, the outcomes in the "usual control" and "tight control" groups were similar. All cause mortality was higher in the tight control group after 3 years, led by patients whose systolic BP was <115 mm Hg.

The NAVIGATOR study examined the preventive effects of valsartan and nateglinide on cardiovascular events in a 2X2 factorial design in 9 306 patients with impaired glucose tolerance. In the group receiving nateglinide, cardiovascular outcomes were unaffected when compared to placebo. The incidence of new-onset diabetes was higher and the incidence of hypoglycaemia was greater in the treated group. Cardiovascular outcomes were also not affected in the valsartan arm, although there was a 14% reduction in the incidence of new-onset diabetes in the treated group.

ATRIAL FIBRILLATION

The RACE II study examined lenient vs. strict ventricular rate control in AF. The aim was to compare two groups with rates <110/min and <80/min. There were no detectable differences in outcome. There was no increase in heart failure in the higher rate group. It was stated that the risk of polypharmacy to achieve the lower rate probably outweighs the benefit of tighter rate control.

Amiodarone is the only agent recommended by the guidelines for treatment of AF in the presence of left ventricular hypertrophy. A study from Cleveland evaluated LVH once only at the time of cardioversion and correlated the effect of the anti-arrhythmic agent being given at that time with the subsequent mortality. Those receiving amiodarone were older, had more coronary artery disease, more cardiomyopathy and less valvar disease. Amiodarone was associated with a significantly higher mortality. The effect persisted when propensity matching analysis was performed.

A sub-group analysis of the RELY study of the direct thrombin inhibitor dabigatran looked at outcomes according to the CHADS2 score. The authors reported benefit across the entire range of scores (0-1, 2 and 3-6). There was less bleeding in all groups with dabigatran 110 mg bd. There was a 60-70% reduction in intracranial bleeding in all groups. The net clinical benefit of dabigatran 150 mg bd was greatest in the low to moderate risk groups. The authors suggested that anticoagulation with dabigatran could be expanded to the lowest risk groups with AF. However, the commentators pointed out that the study did not make comparison with aspirin in the lowest risk group, the agent which is currently recommended in the guidelines.

A retrospective analysis of the EURIDIS and ADONIS studies examined the effect of switching from amiodarone to dronedarone treatment within 48 hours. It was found that

efficacy was preserved though heart rate was lower (97/min vs. 102/min), the incidence of QT prolongation was doubled (7.9% vs. 3.6%) and there was a small increase in heart failure events.

Michael Ezekowitz reported results of a dose-ranging Phase 2 trial of the oral anti-Xa agent betrixaban. Its advantages may lie therein that it is not metabolized via CYP450, it is excreted only in the bile and it is being developed in parallel with its antidote. The agent appeared to be safe and will proceed to Phase 3 trials.

Packer of the Mayo Clinic reported on the CABANA trial which compared catheter ablation of AF to anti-arrhythmic drug therapy. Ablation was superior to drug therapy for the prevention of recurrent symptomatic AF. Complications included tamponade, DVT, PFO and late myocardial infarction. Late recurrence of AF was observed.

The STOP-AF study reported a 12 month follow-up of the cryoablation balloon technique. Collateral phrenic nerve damage occurred in 11.9% that was “largely” reversible.

Genotyping in patients on warfarin therapy establishes their sensitivity to warfarin. Knowledge of the sensitivity resulted in a 28% reduction in hospitalisations and a 27% reduction in bleeding and thromboembolism.

ANTI-PLATELET THERAPY

A nested case-control study involving a database of 80 million records examined the impact of NSAID’s on the risk of MI in the elderly. The study matched 65 000 cases to 1.3 million controls. This study could not find a relationship between the intensity of NSAID exposure and MI, apart from the case of naproxen, previously thought to be associated with lower risk than other NSAID’s.

The rate of dyspepsia was no different in individuals using plain or buffered aspirin.

Proton pump inhibitors reduce the effect of aspirin upon whole blood aggregation and platelet activation.

INTENSIVE CARE

A long QT interval occurs in 18% of patients admitted to ICU. Of these 40% receive medications capable of prolonging the QT interval.

QT prolongation occurs in HIV-AIDS. The increment occurs in proportion to increases in viral load and the fall in CD4 count.

MYOCARDIAL INFARCTION

A comparison of outcomes in MI between man and women confirmed again that the women are older, have more co-morbidity and receive less treatment than men. Independent of the type of MI, women have a 70% higher mortality. However when propensity scoring was applied to correct for the patients’ baseline characteristics and treatment, no difference was demonstrable.

The use of high sensitivity troponin measurements used a lower cut-off to identify 25% more patients with ACS who are at higher risk.

In NSTEMI a routine invasive strategy was associated with a 19% better outcome on cardiovascular deaths and MI, with a 23% reduction in MI.

In STEMI, the JETSTENT study evaluated randomised use of the AngioJet ® device and stenting vs. stenting alone on a background of abciximab therapy in 501 patients. Although there was no difference in infarct size, thrombectomy was associated with a longer procedure time (14 minutes), greater ST segment resolution at 30 minutes (86% vs. 79%), and less MACE (3.1% vs. 6.9%) with reductions in death, MI, TVR and stroke. Major bleeding was increased (3.9% vs. 1.6%). There was no increase in the need for pacing or the frequency of coronary perforation. Despite these results, the commentators favoured the use of manual aspiration devices.

HEART FAILURE

The DOSE study was 2x2 blinded study comparing the effect of twice daily IV bolus dosing vs. continuous IV infusion of Lasix ® in acute decompensated heart failure. Patients were given either their usual daily dose or 2.5X their daily dose over 48 hours followed by the option to revert to oral treatment, continue treatment or double the treatment dose. No differences were detected between twice daily bolus dosing and continuous infusion. The changes in renal function were similar. The higher dose regimens were associated with a non-significant lessening of symptoms.

The addition of the renin inhibitor aliskiren to ACE/ARB treatment in patients with LV dysfunction 7-42 days after MI had no influence on LV systolic function and was associated with a non-significant increase in mortality.

A sub-group analysis of the STICH trial showed that the baseline LV systolic volume index did not influence the outcome when left ventricular reconstruction was combined with CABG. There was a trend to improvement in those with smaller LVSVI and a trend to worsening in the group with the largest LVSVI.

VALVE DISEASE

The results of the EVEREST trial evaluated the use of the MitraClip ® device in the treatment of 3-4+ mitral regurgitation in degenerative (75%) and functional (25%) MR. Good results were reported though commentators were unhappy that a number of subjects were left with more than mild regurgitation.

REGENERATIVE MEDICINE

Atala presented an overview of his work in the Simon Dack Lecture during the opening session of the meeting. He discussed the engineering of new organs. The initial difficulty was finding appropriate cells that replicate without inducing tumour formation. Placental and amniotic fluid cells are pluripotential, giving rise to all 3 germ layers without becoming tumourous. These cells can form fat, bone, cardiomyocytes, endothelium, liver, brain, cartilage, kidney, liver, lung, pancreas and haematopoetic cells. 10 years ago, his laboratory engineered the first urinary bladder. Uterus and heart valves have been synthesized since then. One of the difficulties is promoting vascularity

in the cultured organ. He showed how heart cells could be “printed” in layers to create an organ and how the skeletons of decellularised organs might populated with cultured cells eg. liver.