Brian maurer young investigator award finalists 2020

1 COVID-19 AND QTC: IS HYDROXYCHLOROQUINE WORTH THE RISK? A REVIEW OF QT PROLONGATION IN HOSPITALISED COVID-19 PATIENTS TREATED WITH HYDROXYCHLOROQUINE AND AZITHROMYCIN

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Background Hydroxychloroquine (HC) and Azithromycin (AZ) is a novel treatment regimen in the management of Coronavirus disease 2019 (COVID-19). Both HC and AZ are associated with QT prolongation, which can precede malignant arrhythmias such as torsade de pointes (TdP) and ventricular fibrillation. Limited literature exists to establish the incidence of QT prolongation with COVID-19 treatment and its relationship with morbidity and mortality. This study was performed to assess the incidence of QT prolongation secondary to HC and AZ, and how it related to morbidity and mortality.

Methods A retrospective chart review was performed of COVID-19 patients treated with HC, with or without concomitant AZ, in our hospital in March and April 2020. Their baseline demographic characteristics and co-morbidities were recorded. The baseline corrected QT interval (QTc) and change in QTc was calculated using Bazett's formula on both electrocardiograms (ECGs) and inpatient cardiac monitors.

Results Out of 62 PCR confirmed COVID-19 patients (34% female; mean age 67), 58 patients (93.5%) received both HC and AZ, while 4 patients (6.5%) received HC alone. Hypertension was the most common co-morbidity (33.5%) followed by diabetes mellitus (16%), known ischaemic heart disease (19.4%) and atrial fibrillation (8%). Twenty-three patients (37.1%) were on ≥ 2 additional QT prolonging medications. Mean baseline QTc was 445.7 msec (SD 30.4). The mean QT peak was 469.3 msec (SD 44.5) with a mean change in QTc of 28.4 msec (SD 31.4). QT prolongation was seen in 62.9% of patients, with increase in QTc ≥ 60 msec or QT peak ≥ 500 msec in 24.2% of patients. The mean length of stay was 19.7 days (SD 15.2) (range 3–57 days). Treatment was stopped in 6 patients (9.7%) due to QT prolongation. There were no cases of torsade de pointes (TdP). Mortality was 22.6%, with 16.1% of patients admitted to an intensive care unit (ICU). Patients with QT prolongation had a significantly higher risk of death (33% vs 4.3%), with an increased likelihood of ICU admission (20.5% vs 8.7%), and increased length of stay (24.7 days vs 18.6 days).

Conclusions In this study, patients who were treated with HC and AZ were at high risk of QT prolongation. QT prolongation was associated with higher mortality, increased ICU admission and longer length of stay. Close cardiac monitoring and rationalisation of additional QT prolonging drugs are essential to prevent adverse cardiac events with this treatment regimen.

2 A HIERARCHAL ANALYSIS OF ELIGIBILITY FOR PCSK9 INHIBITION IN IRELAND: BRIDGING THE DIVIDE BETWEEN THE NCPE MANAGED ACCESS PROTOCOL AND ESC/EAS GUIDELINES

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Introduction In 2019, the national center for pharmacoeconomics (NCPE) released a managed access protocol (MAP) for the prescribing of proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) in Ireland. To be eligible for a PCSK9i, patients must have had a myocardial infarction or coronary artery bypass grafting, LDL of >4.0 mmol/L, treated with high dose statin and ezetimibe. In contrast, the 2019 ESC/EAS guidelines on the management of dyslipidaemias recommend that patients at 'very high risk' with an LDL-C of >1.4 mmol/L on a maximally tolerated dose of a statin and ezetimibe, be considered for PCSK9i. We aimed to define the proportion of patients who are suitable for a PCSK9i following completion of cardiac rehabilitation based on these criteria.

Method We retrospectively analysed data on patients undergoing cardiac rehabilitation in our center from January 2018 to December 2019. We then applied the NCPE MAP and the ESC/EAS criteria to assess eligibility for a PCSK9i in the cohort. 'Very high risk' was defined as documented atherosclerotic coronary artery disease as per ESC dyslipidaemias guidelines.

Results The analysis includes 299 patients, who had complete lipid profiles at baseline and 6 months of follow-up, and who have a history of coronary artery disease. Baseline characteristics, mean age 62.5 years, 76% male. 202 (67.6%) patients had a history of MI or CABG making them eligible for a PCSK9i based on NCPE clinical criteria. Only 1 patient (0.5%) in this group was on a high dose statin, ezetimibe and had a 6 month LDL-C of >4.0 mmol/L making them eligible for a PCSK9i as per NCPE MAP criteria. In contrast to the NCPE MAP criteria all 299 patients were deemed eligible for a PCSK9i based on ESC/EAS clinical criteria of 'very high risk'. 160 patients (53.5%) had an LDL-C level >1.4 mmol/L at 6 months despite maximally tolerated statin therapy, mean LDL-C 2.29 mmol/L. Only a minority of patients in this cohort were on ezetimibe, 30/160 (18.7%), however previous studies have shown that on average ezetimibe reduces LDL-C by 25% in combination with statins. Based on this, we sought to define the cohort who would potentially be eligible if they had been on ezetimibe and experienced a 25% reduction in LDL-C. 81/160 patients had

Abstract 2 Figure 1 Hierarchal application of ESC/EAS guidelines and NCPE criteria to cohort

a 6-monthly LDL-C >1.8 mmol/L and were on high dose statin therapy, we included these patients in our final analysis, resulting in 37.1% (111/299) patients in our cohort being eligible for a PCSK9i based on current ESC guidelines, results are summarized in figure 1.

Discussion Our results highlight the discrepancy between current ESC/EAS guidelines and the reimbursement criteria for PCSK9i in Ireland. This discrepancy results in minimal patients with coronary artery disease being eligible for a PCSK9i in Ireland. The results also highlight that a significant proportion of patients in clinical practice do not meet LDL-C goals post cardiac rehabilitation, these targets should be met in order to reduce future cardiovascular risk and improve outcomes for patients.

3 IMPACT OF MORBID OBESITY AND OBESITY PHENOTYPE ON OUTCOMES POST TRANSCATHETER AORTIC VALVE REPLACEMENT

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Background The obesity epidemic continues to grow and coupled with an ageing population the number of obese patients undergoing transcatheter aortic valve replacement (TAVR) has increased significantly. Morbidly obese (MO) patients however, are underrepresented in trials, and there is conflicting evidence regarding their outcomes post TAVR.

Aim The aim of our study was to compare periprocedural and mid-term outcomes in a matched cohort of MO and non-obese (NO) patients and to determine whether adipose tissue distribution analysis from pre TAVR CT scans can provide prognostic information.

Methods This was a multicentre study involving 18 tertiary referral centres in Europe, Canada, North and South America. Consecutive MO patients (BMI ≥ 40 kg/m², or ≥ 35 kg/m² with obesity related co-morbidities) with severe aortic stenosis (AS) who underwent TAVR were analyzed and compared to a non-obese (NO) cohort (BMI 18.5–29.9 kg/m²). Data on patient characteristics, periprocedural and mid-term outcomes were collected.

A propensity-score matched analysis was performed matching NO and MO patients on a 1:1 basis to assess differences in outcomes between groups. A multivariate analysis was undertaken to determine predictive factors for all-cause mortality at 2 years in the MO group.

Pre-TAVR computed tomography scans were analyzed in a centralized core laboratory to assess adipose tissue distribution based on epicardial fat (EAT), abdominal visceral (VAT) and subcutaneous fat (SAT), and to evaluate its impact on outcomes.

Results A total of 3174 patients undergoing TAVR were included: 2264 in the NO and 910 in the MO groups respectively. After propensity score application, a matched cohort with 770 patients per group was obtained. Groups were well matched although some baseline cardiovascular risk factors, such as hypertension, hyperlipidemia and insulin requiring diabetes mellitus, continued to differ. Major vascular complications (MVC) occurred more commonly (6.6% vs 4.3%, $p=0.043$) and device success was lower (84.4% vs 88.1%, $p=0.038$) in the MO group. After a median follow up of 14.11 months [IQR 6.47–36.01], survival analysis demonstrated similar rates of all-cause and cardiovascular mortality for matched MO and NO groups (79.4 vs 80.6% $p=0.731$ and 88.7 vs 87.4% $p=0.699$ respectively). Decreased baseline hemoglobin, non-transfemoral vascular access, MVC, stage 2–3 acute kidney, and periprocedural stroke were all independent predictors of 2-year mortality.

Adipose tissue distribution analysis identified an adverse MO phenotype whereby abdominal VAT:SAT ratio ≥ 1 was associated with increased 2-year all-cause (HR 3.06, 95%CI 1.20–7.77, $p=0.019$) and cardiovascular (HR 4.11, 95%CI 1.06–15.90, $p=0.041$) mortality, and readmissions (HR 1.81, 95%CI 1.07–3.07, $p=0.027$). Additionally, increased all-cause mortality at 2 years was found for each 10 cm³/m² increment in indexed EAT (HR 1.16, 95% CI 1.03–1.30, $p=0.011$). After multivariable analysis, VAT:SAT ratio ≥ 1 remained a strong predictor of 2-year mortality (HR 2.78, $p=0.035$).

Conclusion MO patients undergoing TAVR demonstrate similar periprocedural and mid-term outcomes to a matched cohort of NO patients. Higher rates of MVC in the MO group highlights the need for vigilance when performing vascular access. VAT:SAT ≥ 1 identifies an obesity phenotype at higher risk of 2-year mortality and readmission.

4 PREDICTORS OF VENTRICULAR ARRHYTHMIA IDENTIFIED FROM FOLLOW UP OF TETRALOGY OF FALLOT

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Introduction Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart defect. Subsequent to the introduction of surgical repair, long-term outcomes for patients with TOF have improved significantly. However right ventricular outflow tract dysfunction and regurgitative volume overload remains a recognised sequelae, often progressing to right ventricular (RV) dilatation and dysfunction, arrhythmia, and premature death. In repaired TOF (rToF), QRS prolongation is a recognised predictor of the development of sustained