First printed in Medical Forum WA Magazine, April 2019 Edition.

Assessment of cardiovascular risks in T2DM

By Dr Athula Karu, Cardiologist, Perth

As diabetes increases in Australia (from 1 in 20 adults) it is associated with a two-fold increase in cardiovascular events (CV). Roughly 20% of diabetics are undiagnosed, particularly in indigenous or remote sub groups.

Risk optimisation vs prevention

About 60% have established cardiovascular disease and are in need of secondary risk optimisation rather than prevention. Large studies (e.g. UKPDS) showed optimal T2DM management did not reduce macro vascular CV incidence or death (MACED). Optimisation of concomitant risks remains the corner stone in curbing the CV risks in primary prevention.

Routine treatment with low dose aspirin is not recommended for primary prevention in T2DM though CV risks are high.

ASCEND trial showed that aspirin significantly reduced vascular events but also significantly increased major bleeding in T2DM. Benefits were largely counterbalanced by the increased risk of bleeding. There was no group in which the benefits clearly outweighed the risks in T2DM in the absence of CV disease.

In asymptomatic T2DM, therefore, key strategy in risk stratification should be to prove CV disease if aspirin is to be of any utility.

Using the current American College of Cardiology/ American Heart Association (ACC/AHA) atherosclerotic cardiovascular disease website calculator, a typical T2DM patient with normal coronary arteries has a 5.6% 10-year risk of CV event, with the recommendation for moderate-intensity statin therapy; a typical patient with non-obstructive coronary artery disease (CAD) will have 20% 10-year risk of CV event risk, with the recommendation for high-intensity statin therapy and consideration of aspirin; a typical patient with obstructive CAD has a 23% 10-year risk CV event, with the recommendation for high-intensity statin therapy and a recommendation for aspirin.

KEY MESSAGES

- 1 in 20 Australians have T2DM which brings a two-fold increased risk of CV events.
- Two out of three T2DM already have established CV disease and optimal glucose control alone does not reduce CV morbidity or mortality.
- Routine screening for CVD in asymptomatics with CTCA or a myocardial perfusion study is not recommended with no conclusive RCTs.
- Aspirin without established CV disease is not recommended in primary prevention.
- TMI risk score is useful in established CV with T2DM to risk stratify, based on 10 clinical variables, and may guide treatment intensity.
- New therapeutic agents SGLT2i are recommended in T2DM with heart failure.

To screen or not to screen?

One can hypothesise that by applying above guidelines with a test to confirm asymptomatic CAD would be beneficial. However, a randomized controlled trial (RCT) examining the role coronary CTCA in 900 asymptomatic diabetics with a mean follow-up of 4 years, found no significant difference in MACED. Furthermore, the DIAD study, a RCT with 1,123 asymptomatic T2DM patients, screening for CAD with a myocardial perfusion study did not significantly reduce the MACED.

So far there is no compelling randomised data for screening asymptomatic T2DM for CAD. Primary prevention treatment should target other risk factors in addition to optimal diabetic management with no aspirin unless proven disease.

T2DM with symptomatic CV disease, even if stable, needs thorough testing to confirm established disease so appropriate secondary prevention or invasive treatment is implemented.

ED. **The headline says it all! This is the current situation in the complex world of evidence based medicine.**

Predicting problems

TIMI (Thrombolysis in Myocardial Infarction) risk score in secondary prevention (TRS2P) is a well-established tool in predicting projected event rate of CV morbidity in all patients as well as T2DM patients.

REACH registry data of over 16000 T2DM patients revealed a robust risk gradient for the composite of MACED against TRS2P, with two-year event rates of 0.9% in the lowest and 19.8% in the highest risk groups.

Conventional risk factors displayed a graded risk elevation and hazard ratios for age over 75 (graded risk elevation of 1.6), hypertension (graded risk 1.1), smoking (1.2), ischaemic heart disease (1.7), renal impairment (1.9) and CCF (2.1). The TRS2P predicted a greater absolute benefit with the protease-activated receptor-1 antagonist vorapaxar and the lipid-lowering agent ezetimibe in high-risk subgroups, respectively.

Heart failure events are clinically and prognostically important in patients with T2DM with an odds ratio of 2.1 in CV risks and establishing the degree of LV dysfunction with an echo is recommended. Sodium and Glucose co-transporter 2 inhibitors (SGLT2i) are now a main consideration in this subgroup.

Recently published meta-analysis have concluded that SGLT2i have moderate benefit in CV endpoint events in patients with established atherosclerotic cardiovascular disease. However, they reduce heart failure morbidity including hospital admission and progression of renal disease in T2DM.

The updated Australian heart foundation and Cardiac society of Australia and New Zeeland combine guidelines now recommend SGLT2i and Gliptins in T2DM with CCF.

References available on request.