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Early initiation of SGLT2 inhibitor therapy following an acute cardiac event in people with diabetes.

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Background

The early benefits of sodium-glucose cotransporter 2 inhibitors (SGLT2i) in preventing heart failure and kidney disease are well described.

However, evidence for safely initiating SGLT2i immediately following a cardiac event is limited due to exclusion of recent acute coronary syndrome (ACS) or coronary artery bypass graft (CABG) surgery from trials.

Trials evaluating SGLT2i use early after ACS (EMPACT-MI, DAPA-MI and EMMY) are awaiting publication. No trials in CABG surgery are known.

Aims

1. To explore the clinical outcomes in patients prescribed SGLT2i early after ACS or CABG surgery.
2. Evaluate real-world barriers to initiating SGLT2i therapy.

Methods

Data from two prospective observational studies in patients with type 2 diabetes admitted with ACS (March-September 2018) and CABG surgery (October 2018-June 2020) was evaluated.

Cardiologists and cardiothoracic surgeons were educated and encouraged to prescribe SGLT2i in appropriate patients before hospital discharge.

Results

A total of 391 patients were included in the study; 41 of 196 patients (20.9%) with ACS and 69 of 195 patients (35.4%) who underwent CABG surgery were discharged on an SGLT2i (see characteristics in table 1).

SGLT2i therapy was initiated a median of:

- **3 days (IQR 1-4; minimum 1, maximum 11) following an ACS and,**
- **7 days (IQR 5-11.5; minimum 3, maximum 42) following CABG surgery.**

Inpatient adverse reactions to SGLT2i therapy were reported for two patients following CABG surgery:

☒ One patient experienced perioperative euglycaemic diabetic ketoacidosis (pH 7.3, capillary ketones 4.8 mmol/L and blood glucose 9.9 mmol/L) secondary to not withholding an SGLT2i as advised. This was treated with an insulin-dextrose infusion and the patient re-commenced on the SGLT2i nine days post-surgery.

☒ The second patient developed hypoglycaemia and fasting ketosis three days after initiating a new SGLT2i (pH 7.41, capillary ketones 1.3 and blood glucose level 3.8-9.4 mmol/L). The SGLT2i was ceased and not recommenced.

☑ No patients prescribed SGLT2i therapy were re-admitted with diabetic ketoacidosis within one month.

Rationale for not initiating SGLT2i therapy was explored in 127 patients (see table 2)

Table 1: Characteristics of patients discharged on SGLT2 inhibitor.

Characteristic *n*(%) or *mean(SD)	ACS (*n* = 41)	CABG surgery (*n* = 69)	Total (*n* = 110)
Age (years)*	56.3 (9.8)	62.8 (9.9)	60.4 (10.3)
Male gender	34 (82.9%)	55 (79.7%)	89 (80.9%)
Indigenous Australian	9 (22.0%)	16 (23.2%)	25 (22.7%)
HbA1c (%)*	9.1 (2.1)	8.7 (1.5)	8.9 (1.8)
SGLT2 inhibitor on admission	20 (48.8%)	47 (68.1%)	67 (60.9%)
Dyslipidaemia or prescribed a statin	27 (65.9%)	63 (91.3%)	90 (81.8%)
Hypertension	23 (56.1%)	57 (82.6%)	80 (72.7%)
TIA/stroke	4 (9.8%)	6 (8.7%)	10 (9.1%)
PAD/AAA	4 (9.8%)	7 (10.1%)	11 (10%)
Prior MI or PCI	16 (39.0%)	43 (62.3%)	59 (53.6%)
Prior CCF	7 (17.1%)	16 (23.2%)	23 (20.9%)
Current smoker	14 (34.1%)	17 (24.6%)	31 (28.2%)
BMI (kg/m^2)*	31.9 (5.9)	30.1 (5.5)	30.8 (5.7)
Discharge SBP (mmHg)	119.9 (13.6)	127.0 (14.7)	124.3 (14.6)
Discharge DBP (mmHg)	70.4 (10.7)	68.9 (10.5)	69.5 (10.5)
eGFR ≥ 45ml/min/1.73m^2	38 (92.7%)	68 (98.6%)	106 (96.4%)

HbA1c glycosylated haemoglobin, TIA transient ischaemic attack, PAD peripheral arterial disease, AAA abdominal aortic aneurysm, MI myocardial infarction, PCI percutaneous intervention, CCF congestive cardiac failure, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, eGFR estimated glomerular filtration rate.

Table 2: Rationale for not initiating SGLT2 inhibitor.

Documented rationale *n*(%)	ACS (*n* = 73)	CABG surgery (*n* = 54)
HbA1c ≤ 7%	31 (42.5%)	28 (51.9%)
eGFR ≤ 45mL/min/1.73m^2	26 (35.6%)	10 (18.5%)
HbA1c marginally elevated	2 (2.7%)	3 (5.6%)
HbA1c not available in time	1 (1.4%)	0 (0%)
Newly commenced on first line therapy (e.g. metformin)	5 (6.8%)	0 (0%)
Documented adverse reaction	0 (0%)	2 (3.7%)
Insulin therapy and rapid glycaemic control prioritised	1 (1.4%)	2 (3.7%)
Concomitant GLP-1 receptor agonist use	3 (4.1%)	2 (3.7%)
Clinical or hemodynamic instability	0 (0%)	2 (3.7%)
Planned surgery	1 (1.4%)	0 (0%)
Active infection	1 (1.4%)	0 (0%)
Post-partum	0 (0%)	1 (1.9%)
Patient declined therapy	0 (0%)	1 (1.9%)
Unclear	2 (2.7%)	4 (7.4%)

HbA1c glycosylated haemoglobin, eGFR estimated glomerular filtration rate, GLP-1 glucagon-like peptide-1

Discussion

This observational study helps fill gaps in current knowledge of using SGLT2i early following a cardiac event.

SGLT2i initiation near to, or at, hospital discharge was not associated with 30-day diabetic ketoacidosis readmissions in our study. Clear guidance is required on the safe and timely initiation following ACS or CABG surgery.

SGLT2i should not be commenced until patients are well, eating at drinking. Our patient with hypoglycaemia and fasting ketosis had not recommenced adequate oral intake at the time of commencement. Education is required to raise the awareness of SGLT2i associated adverse effects, so ketones can be monitored.

PBS subsidy criteria remained the main barrier to prescription, despite evidence of cardiovascular/renal benefits in moderate renal dysfunction (eGFR ≥20-30mL/min/1.73m^2) and independent of diabetes status.