

# Perioperative Use of SGLT2 Inhibitors and Induced Euglycemic Diabetic Ketoacidosis in Type 2 Diabetic Patients Post Cardiac Surgery (THEORY)



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**Background**

- Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are a class of antihyperglycemic agents with indications in diabetes and heart failure<sup>1</sup>
- SGLT2i carry a risk of euglycemic diabetic ketoacidosis (euDKA) that is heightened in the cardiac surgery population due to risk factors of fasting state, intercurrent illness, and fluctuating insulin and hormone levels<sup>2</sup>
- EuDKA is defined as: plasma glucose <14 mmol/L, serum β-hydroxybutyrate ≥3.8 mmol/L and ≥1 of plasma pH <7.3, anion gap >10mmol/L<sup>2</sup>
- American Association of Clinical Endocrinologists (AACE) / American College of Endocrinology (ACE) recommends holding SGLT2i ≥24 hours prior to planned surgery to reduce euDKA risk<sup>2</sup>
- Royal Columbian Hospital (RCH) is the cardiac surgery centre for Fraser Health, servicing 1.8 million people, but exact practice regarding perioperative holding of SGLT2i is unknown

**Objectives**

**Primary:**

- To determine adherence to AACE/ACE recommendations to hold SGLT2i ≥24 hours pre-operatively in patients undergoing cardiac surgery at RCH

**Secondary:**

- Identify most common time frames that SGLT2i are held preoperatively
- Incidence of confirmed euDKA associated with SGLT2i
- Complications of euDKA:
  - Prolonged hospitalization
  - Prolonged length of stay in cardiac surgery intensive care unit (CSICU)
  - Acute kidney injury (AKI)

**Methods**

**Design:** Retrospective chart review

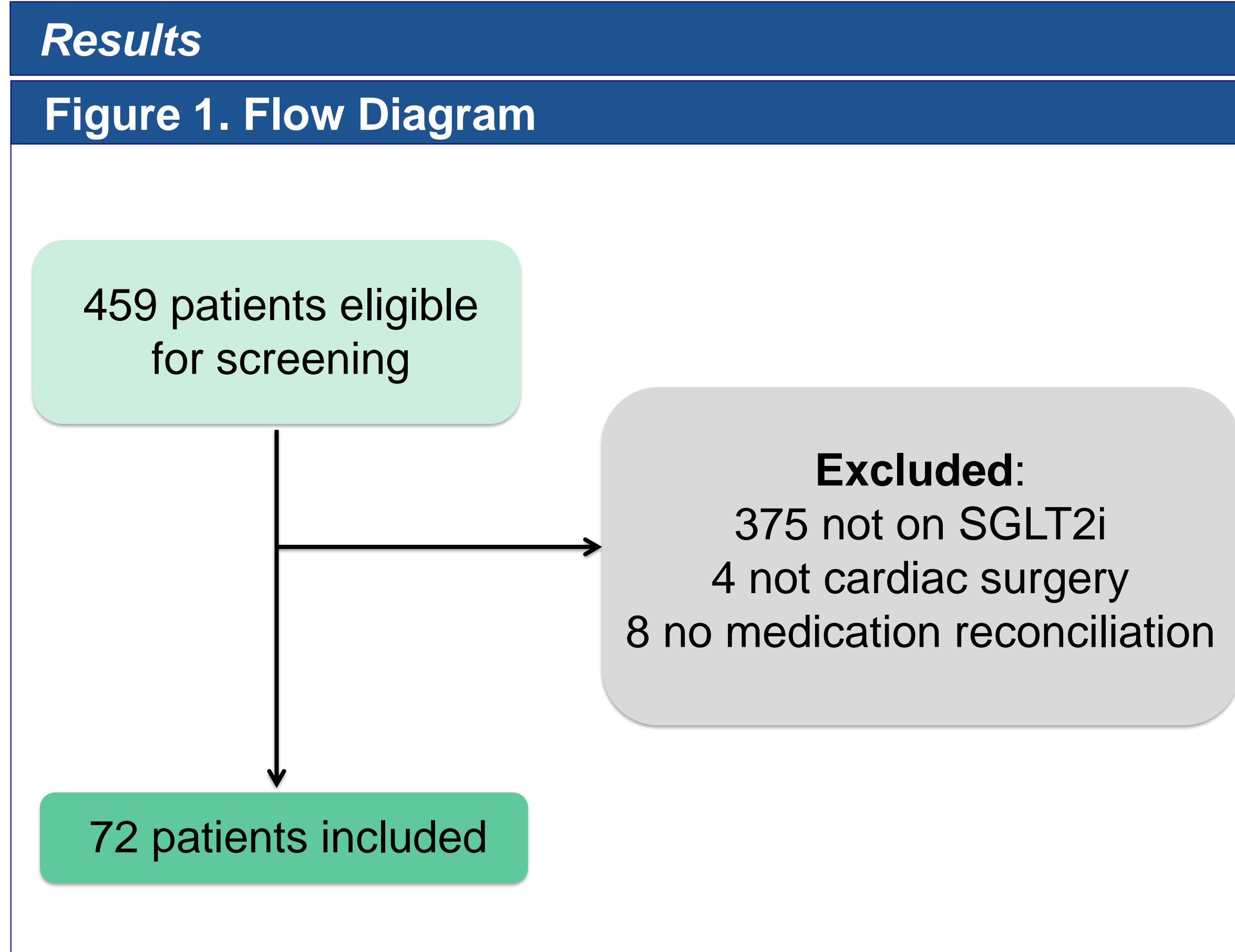
**Sample:** Patients with type 2 diabetes mellitus (T2DM) who have undergone cardiac surgery at RCH

**Timeline:** August 1, 2019 – July 31, 2020

**Inclusion Criteria:**

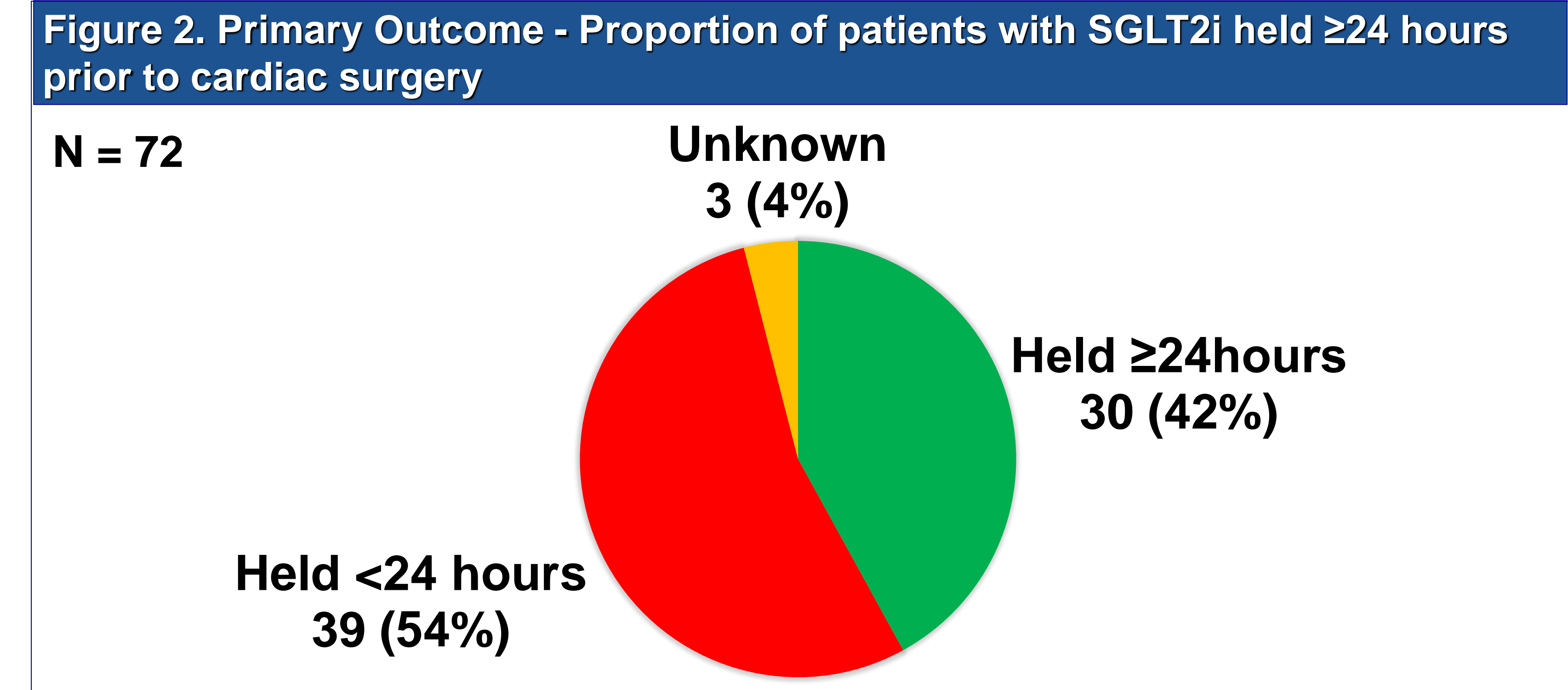
- >18 years old
- T2DM
- On SGLT2i: canagliflozin, dapagliflozin, empagliflozin
- Cardiac surgery patients: isolated on-pump coronary artery bypass graft (CABG), cardiac valve replacement, valve repair, or combination surgery

**Data Analysis:** Descriptive statistics



**Table 1. Patient Baseline Characteristics**

	N = 72
Age – Mean – years	63
Male – n (%)	64 (89)
Average BMI (SD) – kg/m <sup>2</sup>	29.6 (± 6.3)
A1c – Mean (SD) - %	7.8 (± 1.3)
<b>SGLT2i – n (%)</b>	
Canagliflozin	10 (14)
Dapagliflozin	10 (14)
Empagliflozin	52 (72)
<b>Cardiac Surgery – n (%)</b>	
CABG	60 (83)
Valve Repair	1 (1)
Valve Replacement	3 (4)
Combination Surgery	8 (11)
<b>Hypertension – n (%)</b>	58 (81)
<b>Heart Failure – n (%)</b>	
No	64 (89)
HFrEF	8 (11)
<b>CKD – n (%)</b>	
No	62 (86)
eGFR 45 – 59 ml/min/ 1.73 m <sup>2</sup>	9 (13)
eGFR 30 – 44 ml/min/ 1.73 m <sup>2</sup>	1 (1)



**Table 2. Secondary Outcomes**

	Timeframes that SGLT2i were held pre-operatively (hours)					Unknown
	< 24	24 – 47.9	48 – 71.9	72 – 95.9	≥ 96	
<b>No. of patients n (%) (N = 72)</b>	39 (54)	10 (14)	5 (7)	3 (4)	12 (17)	3 (4)
<b>Patients with euDKA n (%) (N = 5)</b>	4 (80)	1 (20)	0	0	0	0
	<b>EuDKA (n = 5)</b>					<b>No EuDKA (n = 67)</b>
<b>Average Duration of Hospital Stay (days)</b>	6.5 ± 0.7					9.4 ± 6.2
<b>Average Duration of CSICU Stay (days)</b>	2.0 ± 0.6					1.3 ± 0.9
<b>AKI – n (%)</b>	1 (20)					6 (9)

**Limitations**

- Study design: retrospective chart review, small sample size, single centre
- COVID-19 pandemic in study period resulted in cancelled elective cardiac surgeries
- Assumptions surrounding administration time of last pre-operative dose
- Missed euDKA diagnosis as serum β-hydroxybutyrate required

**Conclusions**

- SGLT2i were held ≥24 hours pre-operatively in 42% of cardiac surgery patients
- A total of 5 patients developed euDKA, with 80% of those cases occurring in patients whose SGLT2i was held <24 hours pre-operatively
- Further education may increase appropriate pre-operative holding of SGLT2i and reduce euDKA incidence

**References**

- Zannad, F., Ferreira, J.P, et al. 2020. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. *The Lancet* 396, 819–829.
- Handelsman Y, Henry RR, Bloomgarden ZT, et al. American association of clinical endocrinologists and American college of endocrinology position statement on the association of SGLT-2 inhibitors and diabetic ketoacidosis. *Endocr Pract.* 2016;22(6):753-762.

