

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 failure¹
- 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 levels²
- 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/L²
- American Association of Clinical Endocrinologists (AACE) / American College of Endocrinology (ACE) recommends holding SGLT2i ≥ 24 hours prior to planned surgery to reduce euDKA risk² (i.e. last dose taken at least 48 hours prior to surgery)
- 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

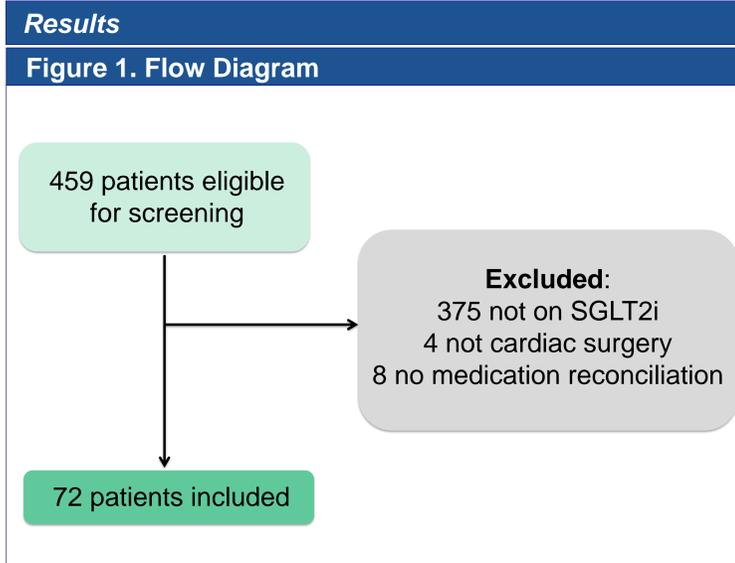


Table 1. Patient Baseline Characteristics

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

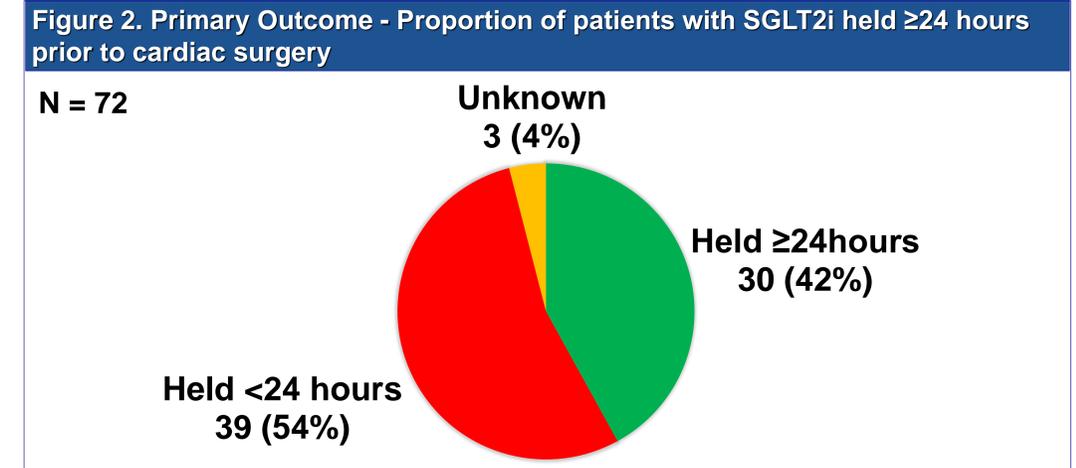


Table 2. Secondary Outcomes

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

