



# Capillary Ketone Concentrations at the Time of Colonoscopy: A Cross-Sectional Study With Implications for SGLT2 Inhibitor–Treated Type 2 Diabetes

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A recent case series of diabetic ketoacidosis (DKA) associated with colonoscopy in sodium–glucose cotransporter 2 inhibitor (SGLT2i)-treated diabetes (1) prompted a clinical alert update to include colonoscopy (2). That update advised colonoscopy cancellation when capillary ketone concentrations are >1.0 mmol/L (if blood gas analysis is unavailable) when SGLT2i have not been withheld for 72 h. However, those guidelines were formulated in the absence of data regarding the normal range for capillary ketone concentrations at the time of colonoscopy. Unnecessary colonoscopy cancellation carries risks, including delays in possible cancer detection, and psychological consequences, whereas a ketone cutoff that is too high increases the risk of DKA.

To define a ketone concentration that may serve as an empirical determinant

of the need for further investigation, we now report a nondiabetic reference interval for capillary ketone concentrations at the time of colonoscopy from a multicenter observational study conducted between June and December 2020 at four tertiary health services (Alfred, Austin, Eastern, and Western Health) in Melbourne, Australia. Multisite approval was granted by the Alfred Human Research Ethics Committee.

Inclusion criteria for the reference population were community-dwelling, normoglycemic adults undergoing colonoscopy. Exclusion criteria were a history of diabetes, pancreatitis, pancreatic cancer, pancreatic surgery, hemochromatosis, cystic fibrosis, starvation ketosis (defined as fasting >72 h), pregnancy, or the discovery during recruitment of a fasting capillary glucose >5.5 mmol/L (100 mg/dL).

Participants with type 2 diabetes were also recruited to compare capillary ketone concentrations with the reference interval population. Except for physician-adjudicated type 2 diabetes, exclusion criteria were the same as those for the reference interval population. These participants were assigned to two prespecified subgroups: those treated with and without SGLT2i.

One hundred fifty-one normoglycemic participants formed the reference interval population (3). Of the 142 participants with type 2 diabetes, 105 were assigned to the non-SGLT2i-treated subgroup (102 not usually treated with SGLT2i and three who had taken their last SGLT2i doses 99–168 h before colonoscopy). Thirty-seven in the SGLT2i-treated subgroup had taken their last SGLT2i dose  $59 \pm 17$  h (mean  $\pm$  SD) before the colonoscopy (range 14–77 h).

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Participants were predominantly Caucasian, with ethnicity being similar across the three groups. Those with diabetes were older (non-SGLT2i-treated, 67.1 ± 11.0 years; SGLT2i-treated, 64.4 ± 0.6 years; reference population, 53.8 ± 14.0 years; *P* < 0.001 overall) and had higher BMI (31.0 ± 6.6, 33.4 ± 7.3, and 27.4 ± 5.7 kg/m<sup>2</sup>, respectively; *P* < 0.001 overall). The percentage of males was similar (53%, 70%, and 60%; *P* = 0.18,  $\chi^2$  test), as was fasting duration (21.3 ± 11.7, 18.2 ± 7.7, and 18.6 ± 8.8 h; *P* = 0.18, ANOVA). Use of standard versus extended bowel preparations was similar among the groups. Diabetes treatments (except for SGLT2i), duration, and HbA<sub>1c</sub> were also similar in both groups.

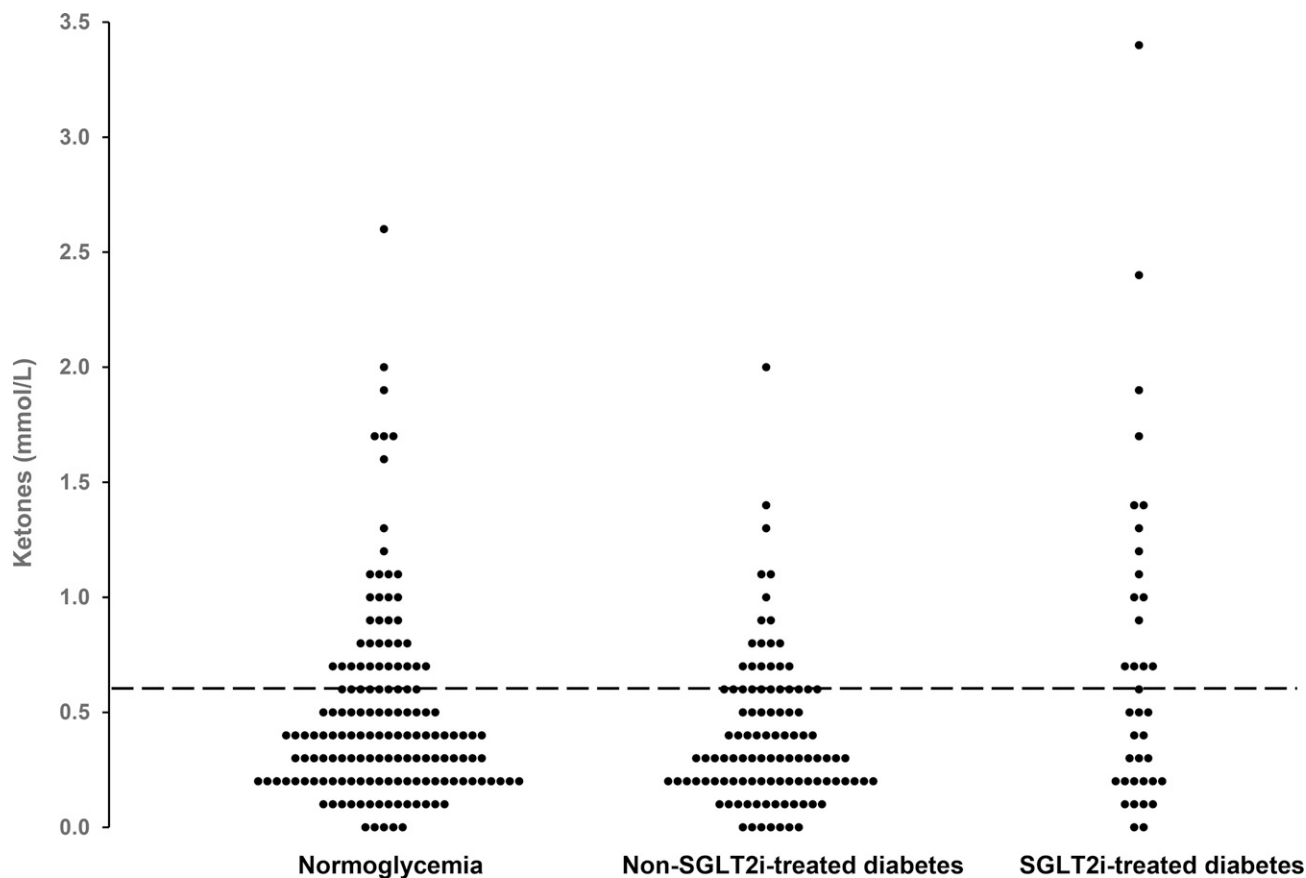
Point-of-care capillary glucose and ketone concentrations were measured in all participants <90 min before colonoscopy, using Nova Biomedical meters or

Abbott Freestyle Optium Neo meters (two study sites each). Nova Biomedical StatStrip and Abbott ketone test strips measure  $\beta$ -hydroxybutyrate; the measurement range for both is 0–8.0 mmol/L with a coefficient of variation <5.5% (4). Venous blood gases were also measured when ketones were >1.0 mmol/L.

The nondiabetic reference interval for capillary ketone concentrations was 0.0–1.7 mmol/L using the central 95% of the data set. Thirteen participants (9%) had ketone concentrations >1.0 mmol/L, and seven (5%) had >1.5 mmol/L. The median (interquartile range) capillary ketone concentration was 0.4 mmol/L (0.2, 0.7), with no sex difference. Figure 1 displays capillary ketone concentrations in the reference population without diabetes compared with the subgroups with diabetes (overall *P* = 0.051, Kruskal-

Wallis test). In the non-SGLT2i-treated diabetes subgroup, median capillary ketone concentration was 0.3 mmol/L (0.2, 0.6). Five participants (5%) had capillary ketone concentrations >1.0 mmol/L, and 1 (1%) had >1.5 mmol/L. These proportions were not significantly different from the normoglycemic reference group. In the SGLT2i-treated diabetes subgroup, median capillary ketone concentration was 0.5 mmol/L (0.2, 1.1). A greater proportion in this subgroup had capillary ketone concentrations >1.0 mmol/L: nine (24%) >1.0 mmol/L (*P* < 0.05 vs. reference population and non-SGLT2i,  $\chi^2$  test) and four (11%) >1.5 mmol/L (NS vs. reference group, *P* < 0.05 vs. non-SGLT2i).

Only one participant (in the normoglycemic reference population) had venous pH <7.30 (pH 7.27). She was clinically well, and the colonoscopy and



**Figure 1**—Capillary ketone concentrations at the time of colonoscopy in people with normoglycemia and with diabetes. The dashed line represents capillary ketone concentration 0.6 mmol/L, the generally quoted overnight fasting upper limit of normal. Normoglycemia, reference population of community-dwelling adults with capillary fasting glucose <5.5 mmol/L and no history of diabetes (*n* = 151); non-SGLT2i-treated diabetes, people with type 2 diabetes either not usually treated with SGLT2i or not receiving SGLT2i within 80 h of colonoscopy (*n* = 105); SGLT2i-treated diabetes, people with type 2 diabetes who have received SGLT2i within 80 h of colonoscopy (*n* = 37). Ketones refers to the measurement of  $\beta$ -hydroxybutyrate. *P* = 0.051 overall between the three groups, Kruskal-Wallis test.

recovery period were uneventful. No participant had a venous bicarbonate <18 mmol/L.

The key finding of this study is that the reference range for capillary ketone concentrations in normoglycemic people undergoing colonoscopy is 0.0–1.7 mmol/L. This 1.7-mmol/L cut-off is clearly relevant when assessing a person with SGLT2i-treated diabetes at the time of colonoscopy. Colonoscopy management guidelines for SGLT2i-treated patients should be revised to reflect the normal capillary ketone concentration upper limit of 1.7 mmol/L.

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**Author Contributions.** P.S.H. designed and coordinated the study, researched data, and wrote the manuscript. R.W. contributed to study design, coordinated a site, researched data, and wrote the manuscript. E.I.E. and A.M. contributed to study design and revised the manuscript. S.S.-M. and R.H. each coordinated a site, researched data, and revised the manuscript. S.B., A.F., T.P.H., S.N.K., M.N., and S.R. researched data and revised the manuscript. L.A.B. contributed to study design, performed statistical analyses, and revised the manuscript. P.S.H. is the guarantor of this study and, as such, had full access to all the

data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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