



RESPONSE TO COMMENT ON HAMBLIN ET AL.

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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We thank Dr. Thiruvengadarajan et al. (1) for their interest in our article (2). In developing the reference interval for blood ketone concentrations, we used the widely cited approved recommendation from the International Federation of Clinical Chemistry (IFCC) Expert Panel for dealing with nonparametric data by using the central 95% of the data set (3). We have strong concerns that referencing an opinion piece published in the *WikiJournal of Medicine* should form the basis for departing from this internationally accepted methodology for establishing reference intervals.

The cutoff for β -hydroxybutyrate concentrations of >1.0 mmol/L is not evidence-based. This was the very reason we undertook our study. Many colonoscopies are carried out in day procedure centers where there is no access to on-site blood gas analyzers or expertise for dextrose-insulin infusions.

If the ketone concentration cutoff of >1.0 mmol/L is used, a significant proportion of people would have their procedure canceled, given that 9% of normoglycemic individuals and 24% of sodium–glucose cotransporter 2 inhibitor (SGLT2i)-treated participants in our study had ketone levels >1.0 mmol/L. The very small risk of diabetic ketoacidosis (DKA) in SGLT2i-treated people undergoing colonoscopy must be balanced by potential delays in detecting and treating colorectal cancer. This is a real concern, given that a recent population-based study showed prediagnostic colonoscopies are associated with 17% lower risk of death from colorectal cancer (4).

Regarding the authors' previous publication (5), we note that ketone concentrations ranged from 2.9 to 5.2 mmol/L in all three of their reported SGLT2i-treated colonoscopy cases in

which the biochemistry completely supported the diagnostic criteria of DKA (pH ≤ 7.30 and bicarbonate ≤ 18 mEq/L) (6), well above the upper limit of 1.7 mmol/L for the normal reference range defined in our article.

We agree that people treated with SGLT2i need to be carefully evaluated for the small risk of DKA. However, it is also important to be aware that it is normal to have ketone concentrations up to 1.7 mmol/L in the context of colonoscopy preparation. We recommend blood gas analysis of all SGLT2i-treated patients with ketone levels above 1.7 mmol/L at the time of colonoscopy. While it may be confusing to have different ketone cutoff levels for colonoscopy versus surgical procedures, this is the first evidence-based study to define what is normal at the time of colonoscopy. We agree that further studies are required to establish ketone cutoff

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levels for noncolonoscopy procedures, which are currently based only on expert opinion. Taken together, we advocate ketone cutoff levels for colonoscopy be determined by the evidence we presented in our multicenter prospective study instead of expert opinion for the sake of consistency.

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