In Reply: We thank Dr. Emmett for his interest in our article[1] and his thoughtful comments regarding the exclusion of the anion gap as a diagnostic, severity, and resolution criterion for diabetic ketoacidosis.[2]

We would like to clarify that, in our view, the anion gap remains a fundamental tool in the evaluation of any patient with metabolic acidosis, including its correction for serum albumin and the calculation of the delta anion gap/delta bicarbonate ratio. Its exclusion from the diagnostic criteria for diabetic ketoacidosis should not in any way be interpreted as discouragement of its use in acid–base assessment.

Although the rationale behind this decision is not clear to us from the text of the consensus report,[2] we believe it may be related to the observation that indirect or potential bicarbonate losses may eventually become the dominant mechanism of acidosis in diabetic ketoacidosis,[3] potentially reducing the anion gap's diagnostic accuracy. Moreover, because the anion gap is most useful when a baseline value is available, its negative predictive value may be limited in the absence of this value.

Nevertheless, Dr. Emmett rightly highlights an important subgroup of patients who present with hyperglycemia, severe ketonemia, metabolic acidosis, and a commonly coexisting metabolic alkalosis (due to volume contraction, vomiting, or both). In these cases, overt acidemia may be absent, and some patients may even exhibit alkalemia, a scenario described as "diabetic ketoalkalosis."[4] As a result, they may not meet the A (acidosis) criterion of diabetic ketoacidosis (pH < 7.3, bicarbonate < 18 mmol/L, or both),[2] and an elevated anion gap may be the only diagnostic clue. In a retrospective study, of 157 patients presenting to the emergency department with hyperglycemia, elevated anion gap, and beta-hydroxybutyrate of 3 mmol/L or greater, 30.2% did not meet the pH or bicarbonate thresholds for the A criterion, underscoring the frequency of this presentation.[5]

In summary, we concur with Dr. Emmett that excluding the anion gap from the diagnostic criteria for diabetic ketoacidosis may pose challenges, and we believe it could have been retained as an alternative component within the A criterion for diagnosis. However, we can appreciate the rationale behind its removal from the severity and resolution criteria in favor of including beta-hydroxybutyrate levels. Ketonemia is the hallmark of diabetic ketoacidosis, and beta-hydroxybutyrate is its principal and most specific biochemical marker.

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■ REFERENCES

1. Rodriguez Alvarez P, San Martin VT, Morey-Vargas OL. Hyperglycemic crises in adults: a look at the 2024 consensus report. Cleve Clin J Med 2025; 92(3):152–158. doi:10.3949/ccjm.92a.24089
2. Umpierrez GE, Davis GM, ElSayed NA, et al. Hyperglycemic crises in adults with diabetes: a consensus report. Diabetes Care 2024; 47(8):1257–1275. doi:10.2337/dci24-0032
3. Kamel KS, Halperin ML. Acid–base problems in diabetic ketoacidosis. N Engl J Med 2015; 372(6):546–554. doi:10.1056/NEJMRA1207788
4. Wuttiputhanun T, Townamchai N, Eiam-Ong S, Takkavatakarn K. Metabolic alkalosis masked presentation of diabetic ketoacidosis: a case report. Clin Case Rep 2023; 11(12):e8250. doi:10.1002/ccr3.8250
5. Cao S, Cao S. Diabetic ketoalkalosis: a common yet easily overlooked alkalemic variant of diabetic ketoacidosis associated with mixed acid-base disorders. J Emerg Med 2023; 64(3):282–288. doi:10.1016/j.jemermed.2022.12.023

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