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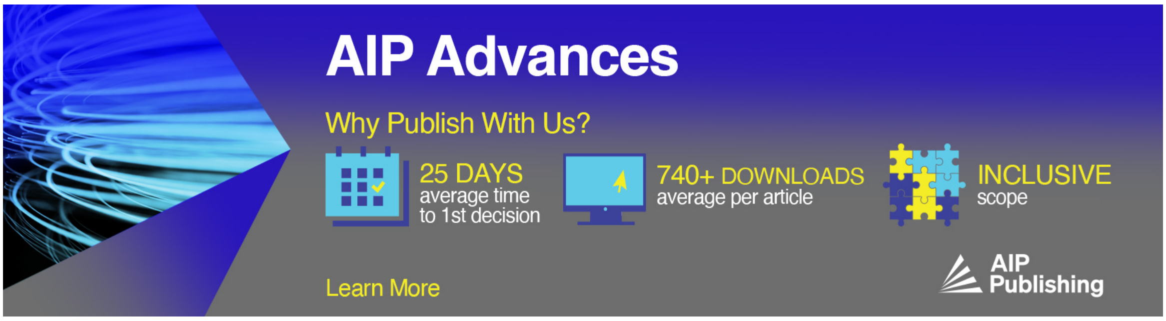

The Importance of Artificial Intelligence in Postprandial Blood Glucose Prediction for Insulin Bolus Calculation

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Abstract. Many works are using artificial intelligence to forecast postprandial blood glucose. However, the following questions arise: is it necessary to develop artificial intelligence techniques to predict blood glucose? How important is artificial intelligence for this purpose? This work gives some insights seeking the answer to these questions in the context of using postprandial blood glucose predictions to optimize the prandial insulin bolus. Considering the bolus optimization model proposed in this work, the error in the postprandial glycemia due to an inaccurate postprandial blood glucose prediction is in the same amount as the error made in the prediction. Therefore, more accurate postprandial blood glucose predictions lead to postprandial blood glucose values closer to the predefined blood glucose target defined for that patient. In this way, it is possible to conclude that artificial intelligence could have a relevant role in helping patients control their blood glucose levels. In particular, regarding non-controlled patients with high glucose variability.

INTRODUCTION

Patients with diabetes on an intensive insulin regimen need, in addition to basal insulin, a bolus of prandial insulin to compensate for the carbohydrates (CHO) ingested at meals. However, estimating the amount of CHO in a meal is a complex and error-prone task, becoming a significant cause of uncertainty in the optimal bolus calculation [1]. In addition to the difficulty of estimating the carbohydrates consumed, other individual lifestyle factors can affect blood glucose levels, such as physical activity and stress. Consequently, an inadequate prandial insulin bolus may lead blood glucose (BG) levels out of the safe range, triggering hypoglycemia or hyperglycemia events.

Aiming to minimize the impact of these errors, the bolus optimization model described in the next section uses the predicted postprandial BG to compute a correction factor. Thus, accurately predicting the postprandial BG becomes crucial for successful diabetes therapeutics and preventing complications. Recognizing this need, several authors have worked on predicting postprandial BG as accurately as possible, applying different methodologies based on intelligent algorithms. Stand out in the literature studies that use machine learning methods [2, 3, 4, 5], such as k-nearest neighbors, support vector machine, decision tree, random forest, and other Artificial Intelligence (AI) techniques, like neuronal networks [6, 7, 8, 9, 10] and case-based reasoning [11].

This paper aims to verify if AI is crucial to forecast postprandial blood glucose, analyzing in what proportion the errors made in this prediction affect insulin bolus calculation and, consequently, patients' glycemic outcomes.

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OPTIMAL INSULIN BOLUS

In accordance with the works [12] and [13], type 1 diabetes mellitus (T1DM) patients on intensive insulin regimens using carbohydrate counting and self-monitoring of blood glucose calculate their prandial insulin dosing according to Equation 1:

$$B(K) = \left(\frac{CHO}{ICR} + \frac{BG_{\text{preprandial}} - BGT}{ISF}\right) K - IOB, \tag{1}$$

where $B(K)$ is the required bolus in U (Units of Insulin) that depends of a correction factor K used to optimize the bolus, CHO is the amount of carbohydrates to be consumed in g, ICR is the insulin-to-carb ratio in g/U, $BG_{\text{preprandial}}$ is the preprandial blood glucose in mg/dL, BGT is the blood glucose target in mg/dL, ISF is the insulin sensitivity factor in mg/dL/U, and IOB (Insulin-on-Board) is an estimate of the insulin still active in the body from previous bolus in U [14]. Without any correction (i.e., $K = 1$), the error of the bolus will act as an unplanned correction bolus with a negative impact on the patients' glycemic control causing an undesired variation on the postprandial blood glucose, $BG_{\text{postprandial}}$, given by:

$$\delta_{BG_{\text{postprandial}}} = BG_{\text{postprandial}} - BGT = \delta_B \cdot ISF, \tag{2}$$

where $\delta_B = B_{\text{optimal}} - B(1)$ and B_{optimal} is the optimal insulin bolus that the patient should take to bring his BG to BGT. However, Equation 1 has a slight inconvenience when $CHO/ICR + (BG_{\text{preprandial}} - BGT)/ISF$ is equal to zero. In this way, no correction K can be used to obtain the optimal insulin bolus. To overcome this, it will be considered Equation 3 in place of Equation 1:

$$B(K) = \frac{CHO}{ICR} + \frac{BG_{\text{preprandial}} - BGT}{ISF} + K - IOB. \tag{3}$$

This way, if $CHO/ICR + (BG_{\text{preprandial}} - BGT)/ISF = 0$, it is possible to find the correction K to get the optimal insulin bolus, $B_{\text{optimal}} = K - IOB$. For this insulin bolus calculator (i.e., Equation 3), when $K = 0$ the bolus does not have any correction. To obtain the optimal insulin bolus, it is necessary to find the right K of correction. For that, Equation 2 is used as follows:

$$\begin{aligned}
&\delta_{BG_{\text{postprandial}}} = \delta_B \cdot ISF = (B(K) - B(0)) \cdot ISF \\
\Longleftrightarrow\ &\delta_{BG_{\text{postprandial}}} = \left[\frac{CHO}{ICR} + \frac{BG_{\text{preprandial}} - BGT}{ISF} + K - IOB - \left(\frac{CHO}{ICR} + \frac{BG_{\text{preprandial}} - BGT}{ISF} - IOB\right)\right] \cdot ISF \\
\Longleftrightarrow\ &\delta_{BG_{\text{postprandial}}} = K \cdot ISF \\
\Longleftrightarrow\ &K = \frac{\delta_{BG_{\text{postprandial}}}}{ISF}.
\end{aligned}$$

Therefore, the optimal insulin bolus is given by:

$$B_{\text{optimal}} = \frac{CHO}{ICR} + \frac{BG_{\text{preprandial}} - BGT + \delta_{BG_{\text{postprandial}}}}{ISF} - IOB. \tag{4}$$

Equation 4 allows computing the optimal prandial bolus maximizing the patient time in range and, in the worst scenarios, avoiding the adverse effects of hypo or hyperglycemic events. However, this relies on proper postprandial BG predictions. Therefore, it is necessary to know how imprecise postprandial BG predictions will affect the real postprandial BG of each patient.

IMPACT OF IMPRECISE POSTPRANDIAL BLOOD GLUCOSE PREDICTIONS

Now, the purpose is to quantify the deviation of the real postprandial blood glucose from the target, $\delta_{BG_{\text{postprandial}}}$, caused by the error in its prediction, $\delta_{BG^{\text{predicted}}_{\text{postprandial}}} = BG_{\text{postprandial}} - BG^{\text{predicted}}_{\text{postprandial}}$. For that, it is used:

$$\delta_{BG_{\text{postprandial}}} = \left(B_{\text{optimal}} - B_{\text{predicted}}\right) \cdot ISF, \tag{5}$$

where

$$B_{\text{predicted}} = B\left(\frac{BG^{\text{predicted}}_{\text{postprandial}} - BGT}{ISF}\right) = \frac{CHO}{ICR} + \frac{BG_{\text{preprandial}} + BG^{\text{predicted}}_{\text{postprandial}} - 2BGT}{ISF} - IOB.$$

It can easily be proved that Equation 5 is equivalent to

$$\delta_{BG_{\text{postprandial}}} = \delta_{BG^{\text{predicted}}_{\text{postprandial}}}. \tag{6}$$

Thus, the error obtained in the postprandial glycemia in relation to the target glycemia is in the same amount as the error made in the prediction of this postprandial glycemia, i.e., if the error is large in the predicted postprandial *BG*, then the variation in the real postprandial *BG* will also be large and thus have a negative impact on glycemic control. This demonstrates the need for accurate postprandial blood glucose predictions and, therefore, the use of proper tools. Artificial intelligence proved to be a good solution in previous works.

DISCUSSION

There is evidence in the literature that Glycemic Variability (GV), which refers to BG fluctuations, either postprandial hyperglycemia or hypoglycemic periods, is associated with microvascular and macrovascular complications [15, 16]. Moreover, patients with T1DM are more susceptible to these variations due to the difficulty of correctly dosing prandial insulin [17]. The results from the previous section (i.e., Equation 6) establish a direct relationship between the accuracy of the postprandial BG prediction and the proximity of the real postprandial BG to target glycemia. The more the postprandial BG deviates from the target, the more deteriorated the glycemic control will become, increasing the patient's GV. Thus, accurate postprandial BG estimates are crucial, particularly for those patients with high GV profiles. In such cases, AI could have a relevant role in developing proper prediction techniques.

CONCLUSION

This study aimed to answer the following questions: is it necessary to develop artificial intelligence techniques to predict blood glucose? How important is artificial intelligence for this purpose? We conclude that, for the presented insulin bolus controller, the deviation of the postprandial blood glucose from the blood glucose target value is identical to the error obtained in the postprandial blood glucose prediction. Therefore, the greater the error in the postprandial blood glucose estimates, the greater the deviation of the real postprandial blood glucose from the target value. From the discussion, it is possible to conclude that our study highlights the need for accurate postprandial blood glucose predictions, particularly for patients with high glycemic variability. Indeed, artificial intelligence is at the forefront of developing proper prediction techniques due to its ability to learn and adapt to the behaviour of non-controlled patients with high glycemic variability, helping to avoid undesirable effects.

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