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Identifying Hypothyroidism as Complication of Type 1 Diabetes from Continuous Glucose Monitoring Data

Agnese Piersanti, *Member, IEEE,* Agnese Callegari, Libera L. Del Giudice, *Student Member, IEEE,*
Christian Göbl, Laura Burattini, *Member, IEEE,* Andrea Tura and Micaela Morettini, *Member, IEEE*

***Abstract*—Recent studies have shown that type 1 diabetes mellitus (T1DM) is an important risk factor for the development of hypothyroidism. In this regard, a timely intervention is fundamental to limit adverse effects. Providing real-time measurements of interstitial glucose, Continuous Glucose Monitoring (CGM) devices may represent a powerful source of data to feed machine-learning based algorithms for the discovery of hidden patterns related to the development of diabetes complications such as hypothyroidism. Aim of this study was to setup a machine-learning-based approach capable to identify subjects with hypothyroidism among those with T1DM, starting from CGM tracings. CGM data acquired during a period of 26 weeks and relating to 79 subjects with T1DM taken from the REPLACE-BG campaign database, of which 51 had hypothyroidism and 28 had T1DM with no other complication, were used. The CGM traces were pre-processed to handle the presence of missing data and 41 features were extracted with the use of AGATA software. The feature set was then reduced through Two-Step Decision Tree-Embedded Feature Selection (DT-EFS), leading to the inclusion of 8 final features. The best performing model was the decision tree, showing the following testing performances: area under receiver operating characteristics of 72.3%, accuracy of 71.4%, precision of 74.6%, F1 score of 70.1%, sensitivity of 71.4% and specificity of 69.5%. The 8 features identified herein describe the long-term variability of the subjects' glycemic trace which may suggests a possible connection with the presence of hypothyroidism in T1DM.**

***Clinical Relevance*—This establishes the possibility to automatically detect hypothyroidism in T1DM from clinically meaningful CGM glycemic patterns.**

I. INTRODUCTION

Thyroid diseases and diabetes mellitus represent the most widespread endocrine disorders in the world, and are often associated. Indeed, an altered thyroid function can influence glucose tolerance and worsen metabolic control in patients with diabetes. Hypothyroidism is a common chronic endocrine disease often relatively asymptomatic, whose symptoms are nonspecific and overlap with those typical of healthy individuals. It is also associated with cardiovascular morbidity and mortality and if left untreated can lead to severe adverse health outcomes and even death [1]. Type 1 Diabetes Mellitus (T1DM) is a form of diabetes which has an autoimmune nature since it originates from the destruction of the pancreatic β-cells. Of note, T1DM and hypothyroidism share an autoimmune predisposition, and a casual relationship among them has been observed [2]. Thyroid autoimmunity prevalence among subjects with T1DM reach 17-30%, with a higher prevalence in women [3]. The development of hypothyroidism in subjects with T1DM can worsen glycemic control, increasing the risk of hypoglycemic crisis and delays in development and growth in pediatric patients. Moreover, there is evidence that hypothyroidism in T1DM also associates with the development of microvascular complications, among which the vision threatening condition of diabetic retinopathy [4]. Thus, to ensure timely diagnosis and management, regularly performing thyroid function tests in patients with T1DM is highly recommended.

In recent years, the use of machine-learning (ML) is extensively boosting research on diabetes by taking advantage of the availability of a huge amount of heterogeneous data. The application of such techniques to diabetes field for the development of decision support systems has been aimed at different purposes, such as the early diabetes prediction and diagnosis, the assessment of risk factors related to future type 2 diabetes development in women who had gestational diabetes, the prediction of hypoglycemia events, also when induced by physical activity, the development of personalized treatment and management strategies and the identification of related complications [5-13]. In relation to hypothyroidism, automated detection from the components of the thyroid test performed for diagnosis has been investigated by using different ML models, such as decision tree, random forest and Naïve Bayes, achieving good results [14,15]. Identification of the presence of hypothyroidism was also explored in patients with type 2 diabetes starting from genetic and health information and by using random forest, K-nearest neighbors, and multilayer perceptron classification algorithms [16].

However, as far as we know, the application of such techniques to discover hidden patterns related to the development of hypothyroidism in patients with T1DM has still been scarcely explored. A very important opportunity for an early detection of hypothyroidism in such population can be found in the recent availability of data collected in real-time

A. Piersanti is with the Department of Information Engineering, Università Politecnica delle Marche, 60131 Ancona, Italy.

A. Callegari, was with the Department of Information Engineering, Università Politecnica delle Marche, 60131 Ancona, Italy.

L. L. Del Giudice is with the Department of Information Engineering, Università Politecnica delle Marche, 60131 Ancona, Italy.

C. Göbl is with the Division of Obstetrics and Feto-Maternal Medicine, Department of Obstetrics and Gynaecology, Medical University of Vienna, A-1090 Vienna, Austria.

L. Burattini is with the Department of Information Engineering, Università Politecnica delle Marche, 60131 Ancona, Italy.

A. Tura is with the CNR Institte of Neuroscience, 35127 Padova, Italy.

M. Morettini is with the Department of Information Engineering, Università Politecnica delle Marche, 60131 Ancona, Italy (e-mail: m.morettini@univpm.it).

from T1DM patients thanks to the use of continuous glucose monitoring (CGM) devices, which provide interstitial glucose measurements every 1-5 minutes. The exploitation of such kind of data has the additional advantages of ensuring early screening, being used by the vast majority of patients with T1DM for daily management, and, carrying both intra-day and inter-day information, it allow a deeper characterization of glycemic fluctuations. Thus, the main objective of this study is to use ML techniques to identify the presence of hypothyroidism in subjects with T1DM through the characterization of their long-term glycemic profiles. An interpretable feature-based approach is employed to discover potential risk factors related to hypothyroidism.

II. MATERIALS AND METHODS

A. Dataset

The cohort analyzed in the present study consisted of a subgroup that was selected from the freely available dataset pertaining to the REPLACE-BG study [17], involving subjects who received T1DM diagnosis from at least one year and were all under insulin pump therapy and with a good glycemic control as for the glycated hemoglobin (HbA1c) percentage (mean age of 44±14 years, mean diabetes duration of 24±12 years, and mean HbA1c of 7.0±0.7%). A total of 79 subjects were analyzed, of which 51 (13 males and 38 females) had hypothyroidism diagnosed before the study period (IPTD group) and 28 subjects (13 males and 10 females) had only T1DM with no other complications (CNT group). All subjects underwent CGM monitoring for 26 weeks, performed through a Dexcom G4 Platinum CGM device which measures glucose concentrations from the interstitial fluid in the range of 40-400 mg/dl and records its readings every 5 minutes.

B. Data Preprocessing and Feature Extraction

The recently developed MATLAB based software package AGATA (version 2.1.0) was used for both data preprocessing and feature extraction [18], after verifying its appropriateness against relevant criteria discussed in a review study by our group regarding the available software packages and tools for the analysis of CGM data [19]. Data quality assessment was performed through the *missingGlucosePercentage* function, which provides the percentage of missing values with respect to that expected by considering the total number of days of observation. Missing data imputation was performed through the *imputeGlucose* dedicated function using linear interpolation and time gaps were filled up to a maximum of 30 minutes. Moreover, each CGM recording was resampled with *retimeGlucose* function to ensure the exact time interval of 5 minutes between each value and formatted in a two column frame in the “timetable” format of MATLAB, to be given as input to the functions needed for CGM data analysis.

Feature extraction was performed through the function *AnalyzeOneArm*, which enables the computation of relevant CGM metrics for all the subjects of each group. To ensure standardization in metric computations the AGATA built-in functions were checked and those that implemented different settings (i.e., thresholds) were modified according to [19]. A total of 41 CGM metrics were extracted and their description is reported in Table I. Local Outlier Factor (LOF) with 20 neighbors and Euclidean distance was used to detect and exclude outliers from the dataset.

TABLE I. DESCRIPTION OF THE EXTRACTED CGM METRICS

CGM Metric	**Description**
mageIndex	Mean amplitude of glycemic excursions
stdGlucoseROC	Standard deviation of the rate of change of glucose
conga*	Continuous overall net glycemic action
modd	Mean of daily differences in glucose
aucGlucose	Area under the glycemic curve
CVGA	Control variablity grid analysis
cogi	Continuous glucose monitoring index
cvGlucose	Coefficient of variation of glucose trace
efIndex	Excursion frequency, corresponding to the sum of all excursions
gmi	Glucose management indicator
iqrGlucose	Interquartile range of glucose
jIndex	Measure of both the mean level and variability of glycemia
magePlusIndex	Mean amplitude of glycemic excursions, through to peak direction
mageMinusIndex	Mean amplitude of glycemic excursions, peak to through direction
meanGlucose	Mean glucose over all days
medianGlucose	Median glucose over all days
rangeGlucose	Difference between max and min glucose over all days
sddmIndex	Standard deviation of within-day means index
sdwIndex	Mean of within-day standard deviation index
stdGlucose	Standard deviation of glucose trace
adrr	Average daily risk range, assessment of total daily glucose variations within risk space
bgri	Blood glucose risk index of the glucose concentration
hbgi	High blood glucose index
lbgi	Low blood glucose index
gri	Glycemia risk index
timeInHyperglycemia	Percentage of time spent in hyperglycemia
timeInL1Hyperglycemia	Percentage of time spent in level 1 hyperglycemia
timeInL2Hyperglycemia	Percentage of time spent in level 2 hyperglycemia
timeInHypoglycemia	Percentage of time spent in hypoglycemia
timeInL1Hypoglycemia	Percentage of time spent in level 1 hypoglycemia
timeInL2Hypoglycemia	Percentage of time spent in level 2 hypoglycemia
timeInTarget	Percentage of time spent in the target range
timeInTightTarget	Percentage of time spent in the tight range
gradeScore	Glycemic risk assessment in diabetes equation
gradeEuScore	Glycemic risk assessment in diabetes equation, euglycemia component
gradeHyperScore	Glycemic risk assessment in diabetes equation, hyperglycemia component
gradeHypoScore	Glycemic risk assessment in diabetes equation, hypoglycemia component
hypoIndex	Hypoglycemia index
hyperIndex	Hyperglycemia index
igc*	Index of glycemic control, sum of hyper index and hypo index
mrIndex	Measure of variation of glucose values around a reference value, aka M_value

*CGM metrics computed with modified versions of functions provided by AGATA [19].

C. *Feature Selection and Classification Model*

Feature selection was carried out through Two-Step Decision Tree-Embedded Feature Selection (DT-EFS). In a first step feature multicollinearity was addressed by evaluating features with a correlation coefficient greater than or equal to 0.98. For each couple of highly correlated metrics, only the one with the highest correlation with the label variable (CNT or IPTD) was retained. The second step exploited an embedded feature selection based on the decision tree, which determines the most relevant predictive features by dividing the data into homogeneous partitions with respect to the class.

Decision Tree, Gradient Boosting and Logistic Regression classification algorithms were evaluated. Hyperparameters optimization was performed with 20-fold cross-validation and a grid search strategy, similarly to that used in other studies related to the diabetes field [20]; options and parameters were set as shown in Table II. A 70% training-30% test split was used to validate the algorithms. Features were z- score normalized.

D. *Statistical Analysis and Performance Evaluation*

The Lilliefors test was used to assess whether each variable followed a normal distribution with an unspecified mean and variance. Differences between the two groups were analyzed using an unpaired Student's t-test for equal means and unknown but equal variance or the Wilcoxon rank-sum test for equal medians. Statistical significance was set at $p < 0.05$.

Considering the IPTD class as positive and the CNT class as negative, cases correctly classified as IPTD and CNT by the algorithm were defined as true positives (TP) and true negatives (TN), respectively. IPTD cases misclassified as CNT were considered false negatives (FN), while CNT cases misclassified as IPTD were considered false positives (FP). The classification algorithms were evaluated using the following performance metrics: area under the receiver operating characteristic curve (AUC), classification accuracy, precision, sensitivity, specificity and the F1-score, computed as the weighted harmonic mean of precision and sensitivity.

TABLE II. MODEL PARAMETERS SETTINGS

Classification Model	**Parameter/Option**	**Value/Setting**
Decision Tree	Minimum number of instances in terminal node	2
	Minimum samples split	6
	Maximum tree depth	10
	Induce binary tree	yes
	Minimum percentage of classified samples before stopping	90%
Gradient Boosting	Number of estimators	100
	Learning rate	0.1
	Lambda	10
	Maximum tree depth	3
	Method	catboost
Logistic Regression	Regularization	Ridge (L2)
	1/lambda	0,001

Hyperparameter tuning performed during cross-validation.

E. *Feature Importance and Explainability Analysis*

The best-performing model was furtherly evaluated to allow interpretability of the results obtained. Permutation Feature Importance method, which provided the contribution of each feature toward the model prediction, by measuring the increase in the prediction error and the related decrease in AUC, was leveraged. Shapley additive explanations (SHAP) were used to approximate the individual contribution of each CGM metric for each individual data.

III. RESULTS

The percentage of missing values in the two groups resulted to be 13.7% and 15.6% for IPTD group and the CNT group respectively, thus confirming that more than 70% of CGM data were present in the analyzed dataset, as recommended in the consensus for time in range [21]. Of the 79 initial subjects, 7 were considered outliers, and of these 4 belonged to the IPTD group and the remaining 3 to the CNT group. The model was then trained on 51 and tested on 21 subjects. Averaged CGM profiles across 24 hours for the two groups were mostly overlapping, as shown in Figure 1. According to Student's t-test or Wilcoxon rank-sum test, a total of 17 out of 41 metrics showed statistically significant differences in feature values between the two groups. The application of the DT-EFS allowed to further narrow down the final number of features to 8 CGM metrics, namely sddmIndex, aucGlucose, cvGlucose, mageIndex, igc, cogi, conga and stdGlucoseROC. Decision tree classification algorithm showed the best performances, as shown in Figure 2. Related numerical results are reported in Table III.

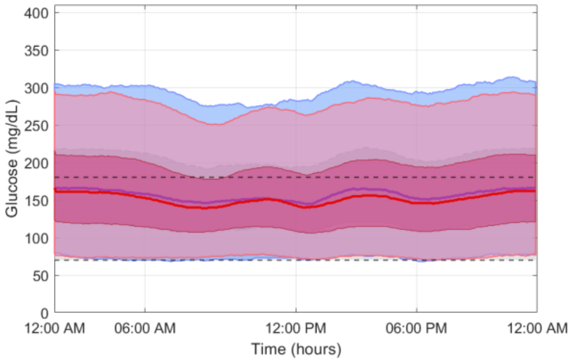

Figure 1. Averaged 24 hours CGM profiles for the two groups.

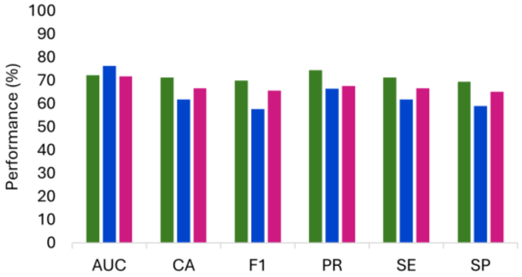

Figure 2. Bar-plot showing Decision Tree (green), Gradient Boosting (blue) and Logistic Regression (magenta) model performances. AUC: area under the receiver operating characteristic curve; CA: classification accuracy; F1: F1-score; PR: precision; SE: sensitivity; SP: specificity.

TABLE III. RESULTS FOR TESTING

Classification Model	**AUC (%)**	**CA (%)**	**F1 (%)**	**PR (%)**	**SE (%)**	**SP (%)**
Decision Tree	72.3	71.4	70.1	74.6	71.4	69.5
Gradient Boosting	75.5	61.9	57.8	66.5	61.9	59.0
Logistic Regression	71.8	66.7	65.7	67.7	66.7	65.2

AUC: area under the receiver operating characteristic curve; CA: classification accuracy; F1: F1-score; PR: precision; SE: sensitivity; SP: specificity.

Figure 3 represents the characterization through the selected features of a 24-hour CGM signal from an example patient of the IPTD group.

Among the finally selected features, 4 resulted different between the CNT and IPTD groups, while aucGlucose, mageIndex, igc and sddmIndex did not show statistically significant difference. Feature distributions and differences between groups are shown in Figure 3. Feature importance and SHAP explainability plots, depicted in Figure 5, provide insights into model behavior to aid interpretation.

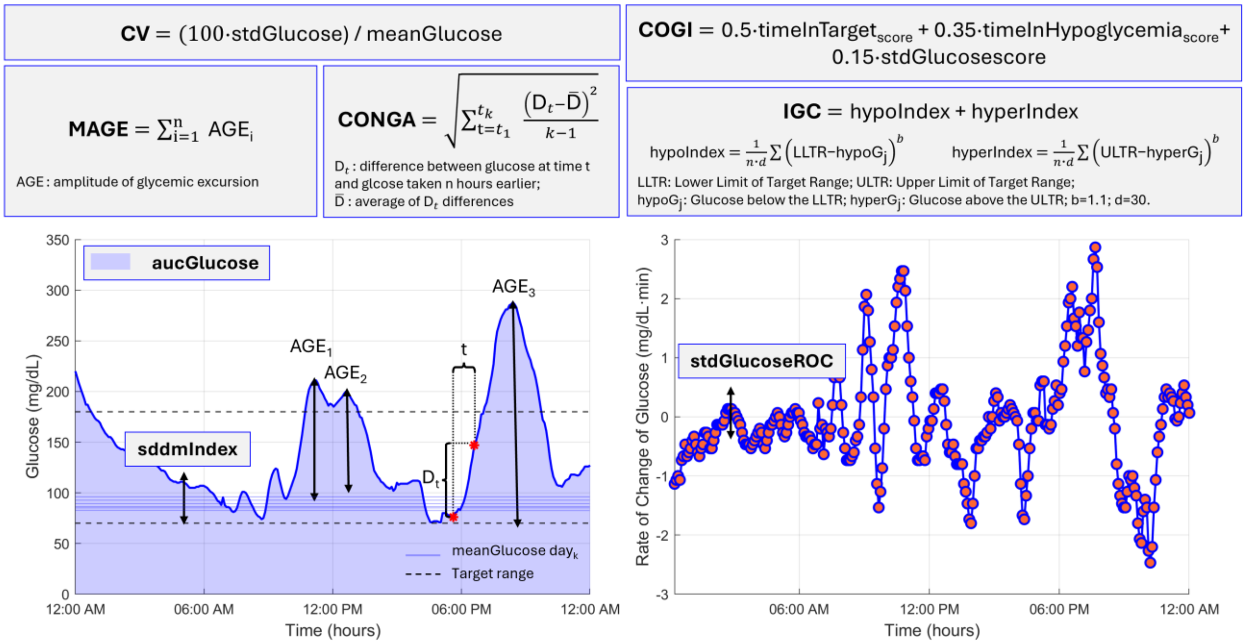

Figure 3. The 8 finally selected CGM metrics (aucGlucose, cvGlucose, cogi, igc, mageIndex, conga, sddmIndex, and stdGlucoseROC).

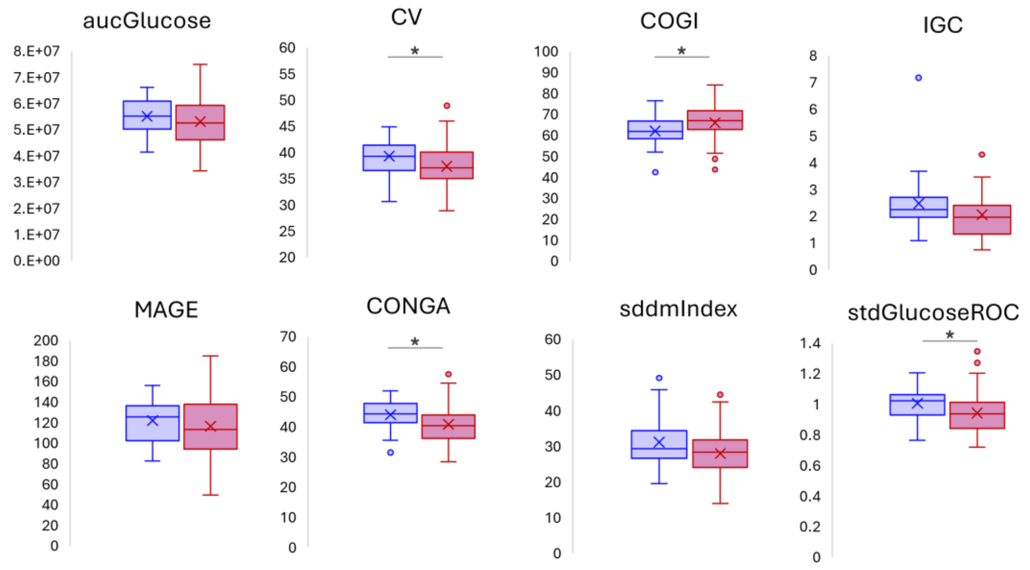

Figure 4. Box-plots of the 8 finally selected CGM metrics showing differences in the distributions between the control group (CNT) in blue and the hypothyroidism group (IPTD) in red. *Statistically significant differences ($p<0.05$).

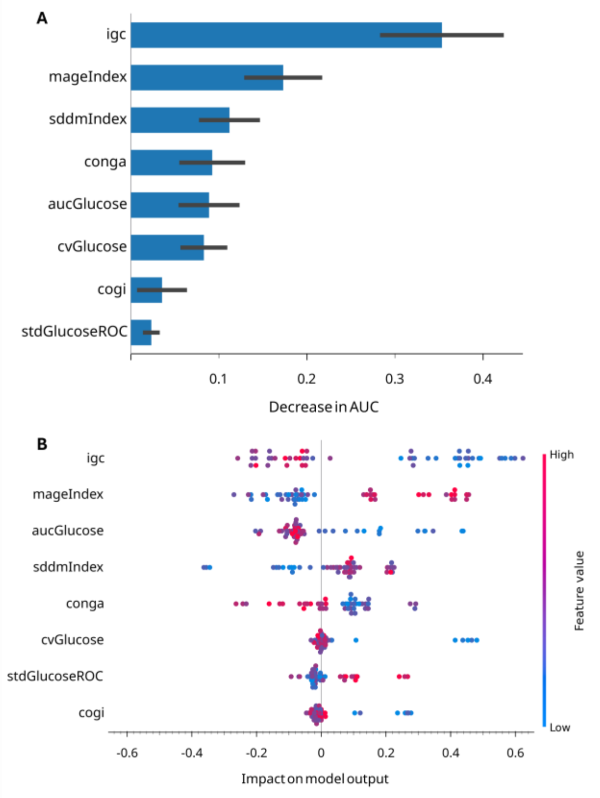

Figure 5. A) Feature importance in terms of decrease in Decision Tree AUC for each selected CGM metric. B) CGM metrics ranked based on their impact on the Decision Tree model output; positive SHAP values contributing to the calculation of higher risk scores for the hypothyroidism class (IPTD).

IV. DISCUSSION

This study investigated which CGM metrics extracted from data of patients with type 1 diabetes may be indicators of risk for having hypothyroidism. Being type 1 diabetes and hypothyroidism strongly connected by their autoimmune origin, the existence of a possible “glycemic pattern” linking the two diseases and expressed as a set of CGM metrics may help in improving the outcomes for both the diseases.

Our approach, instead of using deep learning-based algorithms directly on raw CGM data, applied a feature-based learning strategy, which has the advantage of being more easily interpretable and less complex, thus suitable for real-time applications. However, a direct comparison with other studies to support the choice of using feature-based approaches over fully “black-box” is not possible, being the present study the first to attempt automatically identifying hypothyroidism in type 1 diabetes starting from CGM as source of data. For comparison’s sake, we can rely only on similar studies related to the identification of diabetic retinopathy (a diabetes complication associated to hypothyroidism [22]) from CGM data; in that case, both feature-based and deep-learning approaches demonstrated promising results (F1-score of 72.7% and 73.0%, respectively) [13, 23].

Characterization of CGM signal through features extracted from it has been increasingly improved in recent years, despite this characterization remains less exploited compared to other physiological signals. Indeed, a plethora of metrics were proposed to account for glycemic variability, control, frequency content, entropy and complexity, but just a limited set of them was currently used in clinical settings. Moreover, the use of such metrics as input for machine learning-based approaches is still underexplored [24].

According to feature importance analysis and SHAP values (Figure 5), low values of igc and high values of mageIndex (which captures long-term glycemic variability) and of sddmIndex (which accounts for within-day glucose variability), had the highest impact on best-performing model output, highlighting the importance of glycemic control and multiscale variability patterns in glucose data [13]. Of note, such metrics did not show statistically significant difference between CNT and IPTD groups, thus underscoring the importance of machine learning approaches in capturing complex patterns that traditional statistical methods may overlook.

We compared Decision Tree, Gradient Boosting and Logistic Regression algorithms, with the latter serving as the baseline model. While Gradient Boosting achieved a competitive AUC (75.5%), it failed to obtain acceptable specificity and performed worse overall than the baseline model (Figure 2). Conversely, Decision Tree outperformed Logistic Regression, with 71.4% sensitivity, 69.5% specificity, F1-score of 70.1% and precision of 74.6%, compared to 66.7% sensitivity, 65.2% specificity, F-1 score of 65.7% and precision of 67.7% obtained by Logistic Regression.

Listed among the common limitations decision trees may suffer from, there is the risk of overfitting. In this study, to mitigate this issue and enhance the robustness of our model, we implemented pruning techniques (Table II), so as to balance the tradeoff between complexity and generalizability. In particular, “Minimum samples split” parameter equal to 6 may have played a role in reducing the likelihood of creating too small branches that risk to capture noise rather than patterns. Another possible limitation was the relatively small dataset, which was compensated by the fact that long CGM traces were available for each patient. However, CGM studies are characterized by a generally limited amount of data, especially when exploiting freely available datasets as recently reviewed by our group [25].

Future studies on larger datasets may confirm the proposed classification approach as a feasible tool for identifying individuals with type 1 diabetes at risk of hypothyroidism, prompting them to undergo timely thyroid function testing and thereby preventing adverse hypothyroidism-related outcomes associated with an undiagnosed condition.

V. CONCLUSION

In conclusion, this study demonstrated promising results in identifying the presence of hypothyroidism in individuals with type 1 diabetes from CGM patterns, with a view to providing adequate support systems capable of preventively alerting individuals at risk.

REFERENCES

[1] Y. S. Eom, J. R. Wilson, and V. J. Bernet, “Links between Thyroid Disorders and Glucose Homeostasis,” *Diabetes Metab. J.*, vol. 46, no. 2, pp. 239–256, Mar. 2022.

[2] Y. Zhao, S. Si, K. Zhang, J. Yuan, J. Li, and F. Xue, “Causal relationship between type 1 diabetes and hypothyroidism: A Mendelian randomization study,” *Clin. Endocrinol.*, vol. 97, no. 6, pp. 740–746, Dec. 2022.

[3] B. Biondi, G. J. Kahaly, and R. P. Robertson, “Thyroid Dysfunction and Diabetes Mellitus: Two Closely Associated Disorders,” *Endocr. Rev.*, vol. 40, no. 3, pp. 789–824, Jun. 2019.

[4] T. Fang, et al., “The effect of hypothyroidism on the risk of diabetes and its microvascular complications: a Mendelian randomization study,” *Front. Endocrinol.*, vol. 14, pp. 1288284, Dec. 2023.

[5] M. Bernardini, M. Morettini, L. Romeo, E. Frontoni, and L. Burattini, “Early temporal prediction of Type 2 Diabetes Risk Condition from a General Practitioner Electronic Health Record: A Multiple Instance Boosting Approach,” *Artif. Intell. Med.*, vol. 105, pp. 101847, May 2020.

[6] B. Lobo, L. Farhy, M. Shafiei, and B. Kovatchev, “A data-driven approach to classifying daily continuous glucose monitoring (CGM) time series,” *IEEE Trans. Biomed. Eng.*, vol. 69, no. 2, pp. 654–665, Feb. 2022.

[7] J. Xie and Q. Wang, “Benchmarking Machine Learning Algorithms on Blood Glucose Prediction for Type I Diabetes in Comparison With Classical Time-Series Models,” *IEEE Trans. Biomed. Eng.*, vol. 67, no. 11, pp. 3101–3124, Nov. 2020.

[8] L. Ilari, et al., “Unraveling the Factors Determining Development of Type 2 Diabetes in Women With a History of Gestational Diabetes Mellitus Through Machine-Learning Techniques,” *Front. Physiol.*, vol. 13, pp. 789219, Feb. 2022.

[9] C. Mosquera-Lopez, et al., “Predicting and preventing nocturnal hypoglycemia in type 1 diabetes using big data analytics and decision theoretic analysis,” *Diabetes Technol. Ther.*, vol. 22, no. 11, pp. 801–811, Nov. 2020.

[10] R. Reddy, N. Resalat, L. M. Wilson, J. R. Castle, J. El Youssef, P. G. Jacobs, et al., “Prediction of hypoglycemia during aerobic exercise in adults with type 1 diabetes,” *J. Diabetes Sci. Technol.*, vol. 13, no. 5, pp. 919–927, Sep. 2019.

[11] A. Piersanti, B. Salvatori, C. Göbl, L. Burattini, A. Tura and M. Morettini, “A Machine-Learning Framework based on Continuous Glucose Monitoring to Prevent the Occurrence of Exercise-Induced Hypoglycemia in Children with Type 1 Diabetes,” in *2023 IEEE 36th International Symposium on Computer-Based Medical Systems (CBMS)*, L'Aquila, Italy, 2023, pp. 281–286.

[12] G. Noaro, G. Cappon, M. Vettoretti, G. Sparacino, S. D. Favero and A. Facchinetti, “Machine-Learning Based Model to Improve Insulin Bolus Calculation in Type 1 Diabetes Therapy,” *IEEE Trans. Biomed. Eng.*, vol. 68, no. 1, pp. 247–255, Jan. 2021.

[13] R, Tao, et al., “DDLA: a double deep latent autoencoder for diabetic retinopathy diagnose based on continuous glucose sensors,” *Med. Biol. Eng. Comput.*, vol. 62, no. 10, pp. 3089–3106, May 2024.

[14] M. B. Hossain, et al., “An Explainable Artificial Intelligence Framework for the Predictive Analysis of Hypo and Hyper Thyroidism Using Machine Learning Algorithms,” *Hum-Cent. Intell. Syst.*, vol. 3, no. 3, pp. 211–231, Sep. 2023.

[15] K. Guleria, S. Sharma, S. Kumar, and S. Tiwari, “Early prediction of hypothyroidism and multiclass classification using predictive machine learning and deep learning,” *Measurement: Sensors*, vol. 24, pp. 100482, Dec. 2022.

[16] R. P. Adelson, et al., “Machine Learning Approach with Harmonized Multinational Datasets for Enhanced Prediction of Hypothyroidism in Patients with Type 2 Diabetes,” *Diagnostics*, vol. 14, no. 11, pp. 1152, May 2024.

[17] G. Aleppo, et al., “REPLACE-BG: A Randomized Trial Comparing Continuous Glucose Monitoring With and Without Routine Blood Glucose Monitoring in Adults With Well-Controlled Type 1 Diabetes,” *Diabetes care*, vol. 40, no. 4, pp. 538–545, Apr. 2017.

[18] G. Cappon, G. Sparacino, and A. Facchinetti, “AGATA: A Toolbox for Automated Glucose Data Analysis,” *J. Diabetes Sci. Technol.*, vol. 18, no. 5, pp. 1109–1121, Sep. 2024.

[19] A. Piersanti, F. Giurato, C. Göbl, L. Burattini, A. Tura, and M. Morettini, “Software Packages and Tools for the Analysis of Continuous Glucose Monitoring Data,” *Diabetes Technol. Ther.*, vol. 25, no. 1, pp. 69–85, Jan. 2023.

[20] A. Piersanti, et al., “Assessing hypoglycemia risk during hemodialysis using an explainable machine learning approach based on continuous glucose monitoring metrics,” *Biomed. Signal Process. Control*, vol. 102, pp. 107319, Apr. 2025.

[21] T. Battelino, et al., “Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range,” *Diabetes Care*, vol. 42, no. 8, pp. 1593–1603, Aug. 2019.

[22] C. Ellervik, et al., “Thyroid Function, Diabetes, and Common Age-Related Eye Diseases: A Mendelian Randomization Study,” *Thyroid*, vol. 34, no. 11, pp. 1414–1423, Nov. 2024.

[23] A. Piersanti, et al., “Diabetic Retinopathy Detection: A Machine-Learning Approach Based on Continuous Glucose Monitoring Metrics,” in *Advances in Digital Health and Medical Bioengineering*, vol 109, H. N. Costin, R. Magjarević, G.G. Petroiu, Ed., IFMBE Proceedings, Cham: Springer, 2023, pp. 763–773.

[24] P. G. Jacobs, et al., “Artificial Intelligence and Machine Learning for Improving Glycemic Control in Diabetes: Best Practices, Pitfalls, and Opportunities,” in *IEEE Rev. Biomed. Eng.*, vol. 17, pp. 19–41, Jan. 2024.

[25] L. L. Del Giudice, A. Piersanti, C. Göbl, L. Burattini, A. Tura, and M. Morettini, “Availability of Open Dynamic Glycemic Data in the Field of Diabetes Research: A Scoping Review,” *J. Diabetes Sci. Technol.*, Feb. 2025.