SUMMARY

Diabetes is a group of metabolic diseases the common denominator for which is chronic hyperglycemia resulting from defects in insulin secretion and/or action. Despite the increasingly intricate understanding of the pathogenic processes of the disease, diagnosing its specific types still poses challenges. Two main types are still identified: type 1 and type 2, as well as rarer monogenic types and diabetes that is secondary to other diseases. In 2021 type LADA diabetes has been classified as autoimmune diabetes, i.e. T1D.

It is not completely understood. who should qualify for routine testing of the levels of pancreatic islet-cell antibodies or of the C-peptide. Similarly, it is uncertain in whom and at what stage of the natural development of diabetes should the glucagon test be performed.

Therefore, the goal of my dissertation is to answer the following questions:

1. Should fasting C-peptide values be measured in adults with newly diagnosed diabetes?
2. Is the glucagon test necessary to differentiate between autoimmune and T2D?
3. Is it possible to determine a C-peptide cut-off in a glucagon test in the diagnosis of T1D with the differentiation of LADA and T2D?
4. In what way does the secretory reserve of pancreatic beta cells change after 7 years of T2D treatment on average?

The study was prospective and case-control in nature. 398 patients with newly diagnosed diabetes took part in the study conducted between 2010-2022. After excluding 5 patients due to being diagnosed with other types of diabetes, 104 patients with T1D remained in the study, including 23 patients with LADA and 289 patients with T2D. All of the patients with newly diagnosed diabetes were subjected to a glucagon test to determine the secretory reserve of pancreatic beta cells. After, on average, 7 years from the diagnosis, 30 patients with T1D (including 9 patients with LADA) and 59 with T2D participated in the second stage of the study. The glucagon test was not repeated in patients diagnosed with classic T1D.

The cut-off point that will best differentiate patients with newly diagnosed T1D and T2D was determined by performing an analysis of ROC (Receiver Operating Characteristic) curves for fasting and post-glucagon concentrations of the C-peptide. The cut-off point (below which T1D is recognized while T2D is above it) was determined by the closest distance criterion method, for the fasting C-peptide value = 1.65 ng/ml (0.55 mmol/l) for which the sensitivity and specificity are, respectively 85% and 79%. A similar determination was made for C-peptide concentration 6 minutes after glucagon = 2.49 ng/ml (0.83 mmol/l) for which the sensitivity and specificity are 83% and 84%, respectively. Both fasting and post-glucagon C-peptide

curves have a high predictive value as the area under the curve for fasting C-peptide is 89% and for 6-minute glucagon-C-peptide, it is 90%. A comparative analysis of both ROC curves was also carried out based on J. Hantley's algorithm that implements the U-statistic calculation method, showing no statistically significant difference between the two curves (p=0.37). After an average of 7 years of treatment patients with type 2 diabetes had significantly higher C-peptide concentrations at the sixth minute after glucagon (5.46 ng/dL vs 4.37 ng/dL, p=0.027) and a larger area under the glucagon test curve (25.2 vs 20.2, p=0.029) in comparison to the examination on diabetes diagnosis.

The following conclusions were drawn from the conducted research:

1. Testing for C-peptide levels should be a routine procedure for every patient with newly diagnosed diabetes because it allows for an initial differentiation between patients with T1D and T2D.
2. The glucagon test is not necessary for every patient with newly diagnosed diabetes, as it does not significantly affect the differentiation of individual types of diabetes.
3. Patients with T1D and T2D diabetes can be differentiated on the basis of a determined cut-off point of fasting C-peptide concentration of 1.65 ng/ml (0.55 mmol/l) with sensitivity and specificity of 85% and 79%, respectively.
4. On average, after 7 years of treatment, the secretory reserve of pancreatic beta cells improves in patients with T2D, possibly due to improved insulin sensitivity.

Finding markers that can facilitate early diagnosis of specific types of diabetes would enable the implementation of an optimal treatment approach to normalizing glycemia.