The Link Between Metabolic Syndrome, Type 2 Diabetes--and the Use of Precision Medicine to Treat the Whole Patient

Metabolic syndrome and type 2 diabetes mellitus (T2DM), or the "diabetes syndrome," are closely related, serious health conditions that share common risk factors and mechanisms. While they are each distinct conditions, there is a significant association between them--with metabolic syndrome often being considered a precursor to the development of T2DM.

Metabolic syndrome is a cluster of metabolic abnormalities that includes a combination of factors such as abdominal obesity, high blood pressure, elevated blood sugar levels, high triglyceride levels, and low levels of HDL cholesterol. These risk factors increase the likelihood of developing cardiovascular diseases, such as heart disease and stroke. The exact cause of metabolic syndrome is not fully understood, but insulin resistance and obesity are considered major contributors.

T2DM, on the other hand, is a chronic condition characterized by high blood sugar levels due to either inadequate insulin production or insulin resistance. It has been estimated that here will be staggering 3.1 billion people living with T2DM by 2050, according to a recent article in the Lancet. This is a devastating number that will be a heavy burden.

There are 4 common pathophysiologic causes of all T2DM, which damage the  $\beta$ -cells (ie, genetic and epigenetic changes, inflammation, an abnormal environment, and insulin resistance), along with 11 mechanisms of hyperglycemia, "the egregious eleven". The complications in T2DM are from a collection of conditions, with common, interrelated pathophysiological mechanisms, hence diabetes syndrome.

Metabolic syndrome and diabetes syndrome share several risk factors, including obesity, sedentary lifestyle, poor diet, and genetic predisposition. Obesity, particularly abdominal obesity, is a common feature of both conditions and is strongly associated with insulin resistance. When metabolic syndrome and insulin resistance are present, the pancreas may compensate by producing more insulin to maintain normal blood sugar levels. However, over time, the pancreas may become exhausted (ie,  $\beta$ -cell failure), leading to impaired insulin production—and the subsequent development of T2DM; therefore, the presence of metabolic syndrome are at a higher risk of developing diabetes compared to those without metabolic syndrome. The risk is even higher in individuals with more components of metabolic syndrome present.

The association between metabolic syndrome and diabetes highlights the importance of early intervention and lifestyle changes to reduce the risk of developing these conditions and their associated complications.

Precision medicine is an approach to health care that considers an individual's specific characteristics, such as genetic makeup, lifestyle, and environmental factors, to tailor medical treatments and interventions. In the context of T2DM, precision medicine's goal is to provide targeted therapies and interventions based on an individual's unique profile, with the goal of improving treatment outcomes and minimizing side effects. A benefit of precision medicine is the diabetes specialist is given the opportunity to treat the "whole patient" via defining the presence or absence of various markers. Additionally, many of the medications for treating T2DM can offer other side benefits for the patient (cardiovascular, renal) as the whole construct allows one to better understand the benefits of many common medications for treating T2DM (eg, GLP-1 RA, DPP-4 inhibitors , SGLT-2 inhibitors, metformin, cycloset).

The link between metabolic syndrome and T2DM is important to consider when applying precision medicine approaches for the management of T2DM. Here are some examples of how precision medicine is being applied in the management of T2DM:

Genetic testing: Genetic testing can help identify specific genetic variants or mutations that may influence an individual's risk of developing T2DM or their response to certain medications. By understanding a person's genetic predisposition, clinicians can make more informed decisions about treatment options and develop personalized strategies for their patients.

Pharmacogenomics: Certain genetic variations can impact how a person metabolizes and responds to specific diabetes medications. By analyzing an individual's genetic profile, medications that are more likely to be effective and have fewer adverse effects for that patient may be opted for.

Continuous glucose monitoring (CGM): CGM devices provide real-time information about an individual's blood glucose levels, allowing for more precise management of diabetes. By continuously monitoring glucose levels, patterns can be identified, allowing for adjustments to medication dosages, dietary recommendations, and lifestyle modifications on an individualized basis. Lifestyle interventions: Precision medicine also recognizes that lifestyle factors play a crucial role in the development and management of T2DM. Lifestyle interventions, such as diet and exercise plans, based on an individual's preferences, metabolic profile, and response to different interventions can be personalized (ie, some individuals may benefit more from a low-carbohydrate diet, while others may respond better to a Mediterranean-style diet).

Predictive modeling and risk stratification: Precision medicine leverages data analytics and predictive modeling to assess an individual's risk of developing complications associated with T2DM. By analyzing various factors such as medical history, genetics, lifestyle, and biomarkers, individuals who are at a higher risk of developing complications can be identified, and their treatment plans can be tailored accordingly. Precision medicine enables early identification of individuals who are at a higher risk of developing type 2 diabetes based on their metabolic syndrome status.

In summary, precision medicine for T2DM considers the link between metabolic syndrome and diabetes syndrome to develop personalized approaches for prevention, early intervention, and treatment. By understanding an individual's metabolic and genetic profile, targeted strategies to optimize management and improve outcomes for patients with metabolic syndrome and those at risk of developing diabetes can be implemented.

It's important to note that while precision medicine holds promise in improving diabetes management, it is still an evolving field, and its widespread implementation is not yet fully realized. Collaboration between clinicians, researchers, and technological advancements will continue to drive the progress of precision medicine in T2DM management