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Decrease in Pancreatic Perfusion of Patients with Type 2 Diabetes Mellitus Detected by Perfusion Computed Tomography

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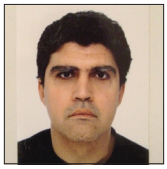

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ABSTRACT

Objectives: The objectives of the study was to compare pancreatic perfusion by computed tomography in type 2 diabetes and non-diabetic subjects.

Material and Methods: In this case–control study, 17 patients with type 2 diabetes and 22 non-diabetic controls were examined with a dynamic 192-slices perfusion computed tomography for estimating pancreatic perfusion parameters.

Results: Thirty-nine patients were included (22 with Type 2 diabetes mellitus [T2DM]), with a mean age of 64 years. There were significant differences in some pancreatic perfusion parameters in patients with and without type 2 diabetes. Blood volume (BV) was lower in pancreatic head (with T2DM: 14.0 ± 3.4 vs. without T2DM: 16.1 ± 2.4 mL/100 mL; $P = 0.033$), pancreatic tail (with: 14.4 ± 3.6 vs. without: 16.8 ± 2.5 mL/100 mL; $P = 0.023$), and in whole pancreas (with: 14.2 ± 3.2 vs. without: 16.2 ± 2.5 mL/100 mL; $P = 0.042$). Similar behavior was observed with mean transit time (MTT) in pancreatic head (with: 7.0 ± 1.0 vs. without: 7.9 ± 1.2 s; $P = 0.018$), pancreatic tail (with: 6.6 ± 1.3 vs. without: 7.7 ± 0.9 s; $P = 0.005$), and in whole pancreas (with: 6.8 ± 1.0 vs. without: 7.7 ± 0.9 s; $P = 0.016$). BV in head, tail, and whole pancreas had negative correlations with age (head r: –0.352, $P = 0.032$; tail r: –0.421, $P = 0.031$; whole pancreas r: –0.439, $P = 0.007$), and fasting plasma glucose (head r: –0.360, $P = 0.031$; tail r: –0.483, $P = 0.003$; whole pancreas r: –0.447, $P = 0.006$). In a multivariate linear regression model, HbA1c was independently associated with decrease in BV in whole pancreas (β: –0.884; CI95%: –1.750 to –0.017; $P = 0.046$).

Conclusion: Pancreatic BV and MTT were significantly lower in patients with type 2 diabetes. BV was decreased with older age and poorer glycemic control.

Keywords: Type 2 diabetes mellitus, Pancreas, Radiology, Tomography, Perfusion imaging

INTRODUCTION

Diabetes mellitus (DM) is characterized by chronic hyperglycemia resulting from increased peripheral insulin resistance and/or decreased insulin secretion.[1] Type 1 DM (T1DM) is caused by autoimmune destruction of pancreatic beta cells, while in type 2 DM (T2DM) the pathogenic mechanism is related to an increase in insulin resistance and a relative deficiency in insulin secretion.[2] There are other types of diabetes, including the monogenic maturity onset diabetes of the young, which may be associated with pancreatic morphological changes.[3,4] This observation

led to interest in defining if pancreatic volume,[5-8] shape, and blood flow would vary in the most common forms of diabetes.

Despite accounting for only 1–2% of pancreatic mass, islets of Langerhans receive around 10–23% of the total pancreatic blood flow.[9,10] In Computed tomography (CT), there is a linear relationship between concentration of iodinated contrast media and the recorded density in Hounsfield units, and it is considered the ideal technique for perfusion images acquisition.[11] Some studies have assessed normal values of pancreatic perfusion by CT.[12,13] Pancreatic perfusion impairments have been evaluated in pancreatic[12,14-18] and hepatic[19] diseases, and modifications of pancreatic perfusion after oncologic therapy have been reported.[20] Satisfactory intra-observer reproducibility of pancreatic perfusion parameters measured by CT, such as time to peak (TTP), blood flow (BF), and blood volume (BV) has already been shown,[21] although experience in performing the readings is essential. Therefore, the aim of this study is to compare quantitatively the pancreatic perfusion by CT in T2DM and non-diabetic subjects.

MATERIAL AND METHODS

We retrospectively investigated seventeen patients with T2DM and 22 non-diabetic subjects who were referred to abdominal CT scan for reasons not related to pancreatic symptoms or disease, from October 2015 to September 2016. The study was performed in accordance non the Helsinki Declaration and was approved by the Ethics Committee of our institution. Exclusion criteria were pregnancy, history of allergic reaction to iodinated contrast media, kidney failure, and history of pancreatic disease.

All patients were scanned in a Siemens Somatom® Force 192-slices scanner. The CT protocol is shown in Table 1. Images were analyzed by a radiologist with 25 years of experience in abdominal imaging blinded to the clinical information, who participated in a training program on abdominal perfusion CT. The following parameters were measured on a workstation Syngo.via® (Siemens) with commercial perfusion CT software (CT Body Perfusion, Siemens) based on the maximum slope model: BF, BV, mean transit time (MTT), and TTP. BF is defined as the volume of flowing blood moving through a given volume of tissue in a specific amount of time. BV is defined as the volume of flowing blood for a given volume of tissue. MTT is defined by the formula – MTT = BV/BF – corresponding to the average amount of time blood takes to transit through a given volume of tissue. TTP is defined as the time elapsed to reach the peak of enhancement in each tissue.

Reading sections were performed twice by the single reader (session 1 and 2). The reader placed three circular ROI in each part of the pancreas (head, body, and tail) to measure these parameters. The mean value of each parameter on each part of the pancreas was considered for analysis.

Table 1: CT acquisition protocol.

CT parameters	Precontrast	Perfusion	Venous
Voltage (kVp)	90	80	90
Delay after contrast injection (s)		test*	70
Collimation (mm)	192×0.6	48×1.2	128×0.6
Rotation time (s)	0.5	0.25 (full rotation) 1.5 (cycle time)	0.5
Pitch	0.6	0.6	0.8
Slice thickness reconstructed (mm)	3	5	3
Contrast agent dose (mL)		50	70
Contrast injection rate (mL/s)		4	4
Bolus NaCl (mL)		20	20

*Depends on test phase, CT: Computed tomography

Statistical analysis

Data are expressed as mean (±SD), median (interquartile range) or absolute and relative frequencies. Variables were compared by student t test and χ^2 between subjects with and without T2DM. Correlations between CT perfusion parameters and clinical and laboratory characteristics were performed by Pearson correlations coefficients. A model of multivariate regression was carried out for CT perfusion parameters and clinical and laboratory characteristics.

RESULTS

A total of 39 patients (M: F ratio = 1.16) were included in the study, with a mean age of 64-year-old and a body mass index of 27.9 kg/m^2. Seventeen patients had T2DM, while 22 did not. One patient from each group was excluded due to technical difficulties, which lead to impossibility in measuring pancreatic perfusion parameters (large ascites and improper contrast media injection); the final analysis included 37 patients.

Clinical and laboratory characteristics of patients, according to the DM status, are presented in Table 2. T2DM subjects were older and had higher fasting plasma glucose levels than those without diabetes, as expected. There were more men in T2DM group than in control group. Of note, low-density lipoprotein (LDL)-cholesterol was lower in T2DM group.

Pancreas volume was similar in patients with and without T2DM (with: 64.3 ± 28.1 vs. without: 63.6 ± 23.1; $P = 0.929$).

Considering the mean values of BF and TTP in both sessions, no significant differences between these pancreatic perfusion parameters in T2DM patients and controls were found. BV and MTT in pancreatic head, tail, and whole pancreas were lower in patients with T2DM than in controls [Table 3]. No differences between T2DM subjects and controls were observed for BF and TTP. An example of perfusion CT image is shown in Figure 1.

Table 2: Clinical and laboratory characteristics of patients.

	Diabetes		*P*-value
	No (*n*=21)	Yes (*n*=16)	
Age (years)	59±13	70±10	0.004
DM duration (years)		11±5	
Men – *n* (%)	7 (33)	12 (75)	0.012
BMI (kg/m^2)	27±5	28±4	0.434
Fasting plasma glucose	105±33	170±60	<0.001
HbA1c	5.7±0.3	7.6±2.4	0.065
C-peptide	1.6±1.4	1.8±0.4	0.902
Cholesterol	196±46	181±55	0.493
HDL	64±21	41±46	0.131
LDL	112±38	73±43	0.028
Triglycerides	96±28	175±147	0.093
DM treatment			
Diet		1	
Oral medications		12	
Insulin		3	

DM: Diabetes mellitus, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Table 3: Mean values of BF, BV, MTT, and TTP of the reader in both sessions.

	Diabetes		*P*-value
	No	Yes	
	(*n*=21)	(*n*=16)	
BF head	132.5±33.0	125.7±40.3	0.577
BF body	139.6±37.7	131.6±41.6	0.543
BF tail	144.3±32.9	133.9±38.8	0.385
BF whole pancreas	138.8±32.4	130.4±38.5	0.476
BV head	16.1±2.4	14.0±3.4	0.033
BV body	15.7±3.3	14.3±3.8	0.223
BV tail	16.8±2.5	14.4±3.6	0.023
BV whole pancreas	16.2±2.5	14.2±3.2	0.042
MTT head	7.9±1.2	7.0±1.0	0.018
MTT body	7.4±1.4	7.0±1.4	0.302
MTT tail	7.7±0.9	6.6±1.3	0.005
MTT whole pancreas	7.7±0.9	6.8±1.0	0.016
TTP head	21.2±2.8	22.3±2.0	0.193
TTP body	20.6±2.6	21.6±1.7	0.215
TTP tail	20.5±2.5	21.5±2.0	0.190
TTP whole pancreas	20.8±2.5	21.8±1.8	0.182

TTP: Time to peak, BF: Blood flow, BV: Blood volume, MTT: Mean transit time

BV in head, tail, and whole pancreas had an inverse correlation with age (head – r: –0.352, P = 0.032; tail – r: –0.421, P = 0.031; whole pancreas – r: –0.439, P = 0.007) and with fasting plasma glucose (head – r: –0.360, P = 0.031; tail – r: –0.483, P = 0.003; whole pancreas – r: –0.447, P = 0.006). BV in pancreatic head showed also negative correlation with HbA1c (r: –0.607, P = 0.021). MTT in pancreatic head had negative correlation with C-peptide (r: –0.682, P = 0.043), and MTT in tail and in whole pancreas had negative correlation with fasting plasma glucose (tail – r: –0.441, P = 0.007; whole pancreas – r: –0.417, P = 0.011).

In a multivariate linear regression model including T2DM patients and controls, the glycemic status based on HbA1c was independently associated with decrease in BV in whole pancreas (β: –0.884; CI95%: –1.750 to –0.017; P = 0.046).

DISCUSSION

In this sample of subjects undergoing pancreatic perfusion CT, BV and MTT were decreased in those with T2DM in comparison with controls, and no significant differences in pancreatic BF and TTP was observed between these two groups. In addition, we demonstrated that there is a negative correlation between pancreatic BV and MTT and some clinical aspects, such as age, fasting plasma glucose, HbA1c and C-peptide, and higher HbA1c values were independently associated with lower pancreatic perfusion, measured by BV.

Few studies have compared pancreatic perfusion parameters in patients with diabetes and health controls. Miles *et al*.,[12]

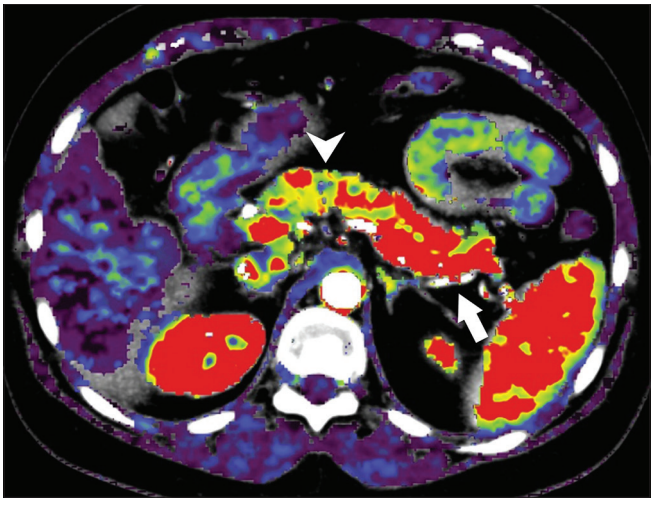

Figure 1: Blood volume color-coded map on computed tomography (CT). Axial CT image showing pancreatic perfusion processed on a workstation (Syngo.via®, Siemens) with commercial perfusion CT sofware (CT Body Perfusion, Siemens) based on the maximum slope model. Red colored areas show more perfused regions of the pancreas (white arrow on the pancreatic tail). Green/blue colored areas indicate less perfused regions (white arrowhead in the pancreatic body).

in 1995, reported reduced BF in one patient with diabetes; this patient, however, was the only one with diabetes from a total of 12 individuals evaluated. Our study advanced in the evaluation of pancreatic perfusion in patients with T2DM. By comparing a group of T2DM patients with a control group, we demonstrated that BV and MTT are lower in patients with T2DM.

We observed reduced BV in T2DM patients, which may be explained by ischemia in pancreatic microvascular network or by the absence of trophic effect of insulin in pancreatic microcirculatory system. As defined previously, MTT is directly related to BV and inversely to BF. As no differences in BF were detected in this sample, and BV was decreased in the T2DM group, lower MTT was expected in T2DM patients. Pancreatic BV is also reduced in other pancreatic diseases, such as pancreatic adenocarcinoma[14,15] and acute and chronic pancreatitis.[14]

Tal[22] hypothesized that pancreatic microvascular endothelial dysfunction and subsequent islet ischemia is the cause of initial dysfunction and subsequent apoptosis of beta cells seen in T2DM as disease progresses. This mechanism of lesion is like to the observed in other tissues classically associated with damage caused by hyperglycemia, such as the retina, kidney, and peripheral nerves. The same injury is likely to cause vascular endothelial dysfunction and affects blood vessels within the pancreas. In this sense, besides being the main cause of the disease, the pancreas could be also a target-organ for diabetes complications, perpetuating the beta cell damage observed as the disease progress.

The relationship between altered perfusion by CT and microvascular disease has been already demonstrated in other organs, such as the brain[23] and the heart.[23,24] We showed for the first-time differences in pancreatic perfusion CT in patients with T2DM in comparison to non-diabetic patients, probably related to microvascular changes in the pancreas.

Our study had some limitations. First, pancreatic perfusion parameters were obtained by only one reader, which limits reproducibility of our results. Second, this sample was powered to detect differences in BF and some of the negative results may be due to lack of power for other variables.

CONCLUSION

Pancreatic perfusion, assessed by BV and MTT, was significantly lower in T2DM patients in comparison to controls.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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