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Ectopic and Visceral Fat Deposition in Lean and Obese Patients With Type 2 Diabetes

Eylem Levelt, MBBS, DPhil,[a,b] Michael Pavlides, MBBS,[a,c] Rajarshi Banerjee, BMBCh, DPhil,[d] Masliza Mahmod, DPhil,[a] Catherine Kelly, PhD,[d] Joanna Sellwood, BSc,[a] Rina Ariga, MBBS, BSc,[a] Sheena Thomas, PgC, BsC, BA,[e] Jane Francis, DCR(R), DNM,[a] Christopher Rodgers, MChem, DPhil,[a] William Clarke, MChem,[a] Nikant Sabharwal, BSc, BM, BCh, DM,[f] Charalambos Antoniades, MD, PhD,[e] Jurgen Schneider, PhD,[a] Matthew Robson, PhD,[a] Kieran Clarke, PhD,[b] Theodoros Karamitsos, MD, PhD,[a] Oliver Rider, BMBCh, DPhil,[a] Stefan Neubauer, MD[a,d]

ABSTRACT

BACKGROUND Type 2 diabetes (T2D) and obesity are associated with nonalcoholic fatty liver disease, cardiomyopathy, and cardiovascular mortality. Both show stronger links between ectopic and visceral fat deposition, and an increased cardiometabolic risk compared with subcutaneous fat.

OBJECTIVES This study investigated whether lean patients (Ln) with T2D exhibit increased ectopic and visceral fat deposition and whether these are linked to cardiac and hepatic changes.

METHODS Twenty-seven obese patients (Ob) with T2D, 15 Ln-T2D, and 12 normal-weight control subjects were studied. Subjects underwent cardiac computed tomography, cardiac magnetic resonance imaging (MRI), proton and phosphorus MR spectroscopy, and multiparametric liver MR, including hepatic proton MRS, T_1- and T_2*-mapping yielding "iron-corrected T_1" [cT_1].

RESULTS Diabetes, with or without obesity, was associated with increased myocardial triglyceride content ($p = 0.01$), increased hepatic triglyceride content ($p = 0.04$), and impaired myocardial energetics ($p = 0.04$). Although cardiac structural changes, steatosis, and energetics were similar between the T2D groups, epicardial fat ($p = 0.04$), hepatic triglyceride ($p = 0.01$), and insulin resistance ($p = 0.03$) were higher in Ob-T2D. Epicardial fat, hepatic triglyceride, and insulin resistance correlated negatively with systolic strain and diastolic strain rates, which were only significantly impaired in Ob-T2D ($p < 0.001$ and $p = 0.006$, respectively). Fibroinflammatory liver disease (elevated cT_1) was only evident in Ob-T2D patients. cT_1 correlated with hepatic and epicardial fat ($p < 0.001$ and $p = 0.01$, respectively).

CONCLUSIONS Irrespective of body mass index, diabetes is related to significant abnormalities in cardiac structure, energetics, and cardiac and hepatic steatosis. Obese patients with T2D show a greater propensity for ectopic and visceral fat deposition. (J Am Coll Cardiol 2016;68:53-63) © 2016 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

From the [a]University of Oxford Centre for Clinical Magnetic Resonance Research, Radcliffe Department of Medicine, Division of Cardiovascular Medicine, Oxford, United Kingdom; [b]Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, United Kingdom; [c]Translational Gastroenterology Unit, University of Oxford, Oxford, United Kingdom; [d]Perspectum Diagnostics Ltd., Oxford, United Kingdom; [e]Division of Cardiovascular Medicine, University of Oxford, Oxford, United Kingdom; and the [f]Cardiology Department, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom. The study was supported by the Oxford Partnership Comprehensive Biomedical Research Centre, with funding from the Department of Health's National Institute for Health Research Biomedical Research Centers funding plan. Drs. Pavlides, Kelly, Robson, and Neubauer are shareholders in Perspectum Diagnostics and have patents in the field of MR for the assessment of liver disease. Dr. Banerjee is an employee of, company director for, and stockholder in Perspectum Diagnostics. Dr. Rodgers is supported by a Sir Henry Dale Fellowship jointly funded by the Welcome Trust and the Royal Society (grant number 098436/Z/12/Z). Dr. Antoniades has received an unrestricted grant from Sanofi. Drs. Rider and Neubauer have received support from the Oxford British Heart Foundation Centre of Research Excellence. Dr. Neubauer is a non-executive director of and consultant for Perspectum Diagnostics. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

^{1}H-MRS = proton magnetic resonance spectroscopy

^{31}P-MRS = phosphorus magnetic resonance spectroscopy

ATP = adenosine triphosphate

BMI = body mass index

BP = blood pressure

CT = computed tomography

cT_1 = iron-corrected T_1

HOMA-IR = homeostasis model assessment of insulin resistance

Ln-T2D = lean patients with type 2 diabetes

LV = left ventricular

MR = magnetic resonance

MRI = magnetic resonance imaging

NAFLD = nonalcoholic fatty liver disease

Ob-T2D = obese patients with type 2 diabetes

PCr = phosphocreatine

T2D = type 2 diabetes

Type 2 diabetes (T2D) and obesity are both associated with nonalcoholic fatty liver disease (NAFLD), cardiomyopathy (1,2), and increased cardiovascular mortality (3,4). The incidence of T2D continues to increase, driven predominantly by the obesity epidemic. Although obesity is likely to be a strong contributor to diabetic cardiomyopathy (5), many patients with diabetic cardiomyopathy have normal body mass index (BMI), suggesting that diabetes and obesity may have different mechanisms by which they mediate cardiovascular change and that diabetic cardiomyopathy may occur in patients with T2D without obesity. Furthermore, evidence suggests that distribution of excess fat is an important determinant of cardiovascular risk, and ectopic and visceral adiposity confer a much higher risk than subcutaneous adiposity (6,7).

Ectopic and visceral fat storage may be linked to insulin resistance, and it is widely known that insulin resistance is the strongest predictor of development of diabetes (8). Increasing evidence points to a strong association between insulin resistance and nonischemic heart failure (9), although there are differing opinions regarding whether this relationship is of a protective or pathological nature (10–12). Thus, the presence of ectopic and visceral fat deposition in patients with T2D even in the absence of a global increase in total body fat may potentially play a significant role in this association. Assessing body composition is, therefore, likely to be more important in patients with T2D than simple metrics of obesity. Liver fat is considered a key feature of ectopic fat associated with dysfunctional adipose tissue and visceral fat deposition (13), and there is also growing interest in the imaging of epicardial adipose tissue as a proxy measure of visceral fat.

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Epicardial adipose tissue, a form of visceral fat, may affect the underlying myocardium by secreting a wide range of adipokines (14). Furthermore, excess liver fat has been shown to be accompanied by cardiac structural and functional changes (15). Computed tomography (CT) allows quantification of epicardial fat volume, and proton magnetic resonance spectroscopy (^{1}H-MRS) allows quantification of lipid content in the liver and the heart. Multiparametric magnetic resonance (MR) of the liver, including ^{1}H-MRS for assessment of steatosis and T_1 and T_2* mapping (yielding iron corrected T_1 [cT_1]) (16), allows noninvasive quantification of liver fat and identification of the presence of hepatic fibroinflammatory disease with a high diagnostic accuracy (16).

Myocardial energetic compromise is an important feature of both the diabetic (17) and the nondiabetic obese heart (5). However, changes in cardiac energy metabolism in lean patients with diabetes have not been previously studied. Myocardial phosphocreatine to adenosine triphosphate concentration ratio (PCr/ATP) is a sensitive indicator of the myocardial energy status, and phosphorus magnetic resonance spectroscopy (^{31}P-MRS) allows noninvasive assessment of the PCr/ATP.

Our primary aim was to test the hypothesis that lean patients (Ln) with T2D exhibit increased ectopic and visceral fat deposition. Our secondary aim was to test whether or not ectopic and visceral adiposity in diabetes is associated with insulin resistance and cardiac and hepatic changes. We used cardiac CT, multiparametric liver magnetic resonance imaging (MRI), cardiac MRI, ^{1}H-MRS, and ^{31}P-MRS to assess and compare epicardial, hepatic, and myocardial fat deposition; hepatic fibroinflammatory changes; and cardiac structure, function, and energetics in lean and obese patients (Ob) with T2D and in control subjects without diabetes.

METHODS

The study was approved by the National Research Ethics Committee (Ref 13/SW/0257), and informed written consent was obtained from each participant. Patients were recruited from general practice surgeries in Oxfordshire, United Kingdom. A total of 27 Ob-T2D, 15 Ln-T2D, and 12 healthy normal weight control subjects were recruited to the study. We have previously reported changes in myocardial energetics, triglyceride content, and left ventricular (LV) structure and function in patients with diabetes compared with healthy volunteers (18,19). Using this database, and expanding the data with novel recruitment of 12 healthy volunteers to the study, here we report a comparison of the changes in these cardiac features in 2 subgroups of patients with diabetes (obese and lean) compared with healthy volunteers. Additionally, we report an analysis of epicardial fat volumes, liver triglyceride content, and liver fibroinflammatory changes.

EXCLUSION CRITERIA. Subjects were excluded if they had a previous diagnosis of cardiovascular or liver disease, hypertension (resting systolic blood pressure >140 mm Hg and diastolic blood pressure >90 mm Hg), contraindications to MRI, ischemic