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Diabetes & Metabolism 42 (2016) 126–129

Research letters

Association between multiple skin tags and metabolic syndrome: A multicentre cross-sectional study in primary care

1. Introduction

Metabolic syndrome (MetS) affects a quarter of the world's adult population [1]. According to International Diabetes Federation (IDF) Criteria, MetS consists of central obesity plus two of the following: raised triglyceride (TG); reduced high-density lipoprotein (HDL) cholesterol; diabetes mellitus (DM); or hypertension (HT). People with MetS have a two-fold increased risk of cardiovascular events and a fivefold greater risk of type 2 diabetes [2]. As delays in the treatment of these conditions incurs a heavy economic burden to society [3], early identification to facilitate earlier treatment and prevention of severe cardiovascular events is needed to reduce any subsequent related healthcare costs.

An increasing number of studies have shown that skin tags (STs) are a potential cutaneous marker of increased metabolic risk. STs (synonyms: acrochorda, skin fibroma, fibroepithelial polyps) are the most common fibrous lesion of the skin and presents as a soft, skin-coloured to slightly hyperpigmented, pedunculated papule on the skin [4]. As early as 1976, Margolis and Margolis [5] reported that STs were frequently observed with DM. More recently, the association of STs with HT and lipid disorders have also been demonstrated [6]. Researchers from various countries, including Iran, India, Egypt, Turkey and Chile, have also observed positive associations of STs with obesity, leptin, C-reactive protein (CRP), fasting insulin and insulin resistance (IR) defined by homoeostasis model assessment (HOMA) [3,7–10]. Interestingly, Sudy et al. [10] identified multiple STs as a stronger predictor of DM than acanthosis nigricans, while Shaheen et al. [9] demonstrated that its association with HOMA as a proxy measure of IR persisted even after adjusting for body mass index (BMI).

The present study is the first to examine the association between STs and IDF-defined MetS in a Chinese primary-care population. All previous similar researches were conducted in Central Asia and Europe [7,8], and focused only on specific components of MetS. Furthermore, all studies were conducted in hospitalized patients. However, primary care is ideal for implementing screening and preventative interventions, thus making the present study particularly relevant for community-dwelling people with STs who may be at increased risk of MetS.

2. Materials and methods

2.1. Study subjects and settings

Patients attending four general outpatient clinics (GOPCs) in the New Territories East Cluster (NTEC) of Hong Kong were consecutively recruited from January to June 2013. Although the median household income, age and gender of residents in this district are largely comparable with the general population [11], GOPCs usually serve patients who are of low socioeconomic status or are elderly, or have chronic conditions. Patient recruitment was based on the presence of STs regardless of MetS status. Inclusion criteria for the study sample were: aged 18–80 years old; understanding Cantonese; and giving informed consent to participate. Patients with any of the following conditions were excluded even if reported to have STs [12,13]: endocrinopathy (history of Cushing's syndrome, acromegaly, phaeochromocytoma, glucagonoma, hyper- or hypothyroidism); history of cancer; history of gastrointestinal polyps; or pregnancy.

2.2. Measurements

MetS was defined according to the IDF definition, which includes previous diagnoses of conditions related to the syndrome (such as DM and HT), as well as abnormal blood levels of glucose, TG and HDL cholesterol. All blood samples were obtained after 8 h of fasting and analyzed by an accredited laboratory. The following data were also collected: patients' demographic data; smoking status; body weight (to the nearest 0.1 kg); body height (to the nearest 0.01 m); waist circumference (to the nearest 0.01 m); and information related to STs (number, location and duration). Medical histories of DM, hyperlipidaemia and HT were retrieved from the clinical management system (CMS), the electronic medical-record system used by GOPCs.

Abbreviations: BMI, body mass index; CI, confidence interval; COS, Chief of Service; CREC, Clinical Research Ethics Committee; CRP, C-reactive protein; DM, diabetes mellitus; FPG, fasting plasma glucose; GOPCs, general outpatient clinics; HbA_{1c}, haemoglobin A_{1c}; HDL, high-density lipoprotein; HOMA, homoeostasis model assessment; HT, hypertension; IDF, International Diabetes Federation; LDL, low-density lipoprotein; noST, no skin tags; NTEC, New Territories East Cluster; OR, odds ratio; PI, principal investigator; RR, relative risk; ST, skin tags; TC, total cholesterol; TG, triglyceride.

Table 1
Demographic and biochemical parameters in subjects with (ST) and without (NoST) multiple skin tags.

	NoST ($n = 129$)	ST ($n = 120$)	Total ($n = 249$)	P^*
Age (years)	56.99 ± 12.67	59.76 ± 10.97	58.33 ± 11.94	0.068
Male (%)	53 (41.1)	63 (52.5)	116 (46.6)	0.094
Smoker (%)	11 (8.6)	20 (16.7)	31 (12.5)	0.084
Height (m)	1.61 ± 0.09	1.61 ± 0.09	1.61 ± 0.09	0.817
Body weight (kg)	62.96 ± 12.85	68.35 ± 12.31	65.56 ± 12.86	0.001
Body mass index (kg/m)	24.27 ± 3.95	26.49 ± 4.09	25.34 ± 4.16	0.000
Metabolic syndrome (%)	36 (27.9)	74 (61.7)	110 (44.2)	<0.001
Central obesity (%)	66 (51.2)	94 (78.3)	160 (64.3)	<0.001
Raised TG (%)	52 (40.3)	78 (65.0)	130 (52.2)	<0.001
Reduced HDL cholesterol (%)	51 (39.5)	75 (62.5)	126 (50.6)	<0.001
Hypertension (%)	48 (37.2)	75 (62.5)	123 (49.4)	<0.001
Raised FPG or DM (%)	22 (17.1)	59 (49.2)	81 (32.5)	<0.001

* By *t* test for continuous variables and Chi-squared test for categorical variables; TG: triglyceride; HDL: high-density lipoprotein; FPG: fasting plasma glucose; DM: diabetes mellitus.

2.3. Participants with skin tags

Subjects with three or more STs were recruited by research assistants, who excluded cases of uncertain clinical diagnosis. An ST was defined clinically as a soft, skin-colored or brown, round or oval, pedunculated skin protrusion measuring from 1–10 mm to its base. Multiple STs were defined as three or more in number, as this is a commonly used cutoff number [3,7,9]. The presence of STs was confirmed by family-medicine specialists who had undergone formal dermatological training.

2.4. Participants with no skin tags (NoSTs)

This group of participants was recruited consecutively during the same period and with the same criteria. These participants had no STs on their bodies. For both ST and NoST recruitment, research assistants were unaware of the patients' MetS status.

2.5. Statistical analysis

MetS and the five components of the IDF-defined criteria were coded as binary outcomes, and logistic regression was performed to estimate the corresponding relative risk associated with STs [odds ratio (OR) of ST *vs* NoST], with adjustments for potential confounding factors including gender, age, height, BMI and smoking status. To explore ST potential as a putative marker of MetS, patients with no previous diagnosis of (or treatment for) DM, HT or abnormal lipid levels were also selected for further subgroup comparisons.

In all analyses, Akaike's Information Criterion (AIC) was use to examine model fitness. Statistical significance was considered a P value < 0.05.

2.6. Sample size

This number was determined on the basis that 120 subjects were needed in each group to achieve 85% power with a type 1 error rate of 0.05. Sample size calculation for cases of diagnosed DM with at least three STs was based on another study with an OR of 3.3 [3].

2.7. Ethical considerations

The present study was approved by the Joint Chinese University of Hong Kong–NTEC Clinical Research Ethics Committee (CREC; Ref number: CREC-2012.372).

3. Results

From January to June 2013, 249 patients were recruited, including 120 with three or more STs and 129 who were NoSTs. The most common site for STs was the neck (mean = 9.12), followed by the axilla (mean = 3.49), trunk (mean = 0.74) and groin (mean = 0.31).

As shown in Table 1, 46.6% of patients were male with an average age of 58.33 years; 12.5% were smokers. Participants tended to be overweight, as indicated by an average BMI of 25.3 kg/m^2. Almost half (44.2%) of the participants had MetS. Those with three or more STs tended to be older and male with higher BMI scores, smokers and with MetS compared with subjects in the NoST group.

Fig. 1 shows the association of MetS with the five IDF components of MetS and the presence of STs. The adjusted OR of having MetS associated with multiple STs was 3.92 (95% CI: 2.00–7.71), while the risk of those with STs to have central obesity was 2.98 times that for the NoSTs (95% CI: 1.32–6.77). As for raised TG, reduced HDL cholesterol and high blood pressure, people with STs had around twice the risk compared with the NoSTs. Lastly, the risk of having raised fasting plasma glucose (FPG) in patients with STs was 3.37 (95% CI: 1.38–6.37) times higher than in NoSTs.

Further stratified analyses revealed a positive association between various MetS components and the presence of STs in those with no clinical history of DM, HT or lipid disorders. Although not reaching statistical significance, all point estimates of unadjusted ORs were > 1 and ranged from 1.08 to 3.10. Magnitudes of the estimated ORs were greater among patients with a history of DM, HT or abnormal lipid levels, and ranged from 1.41 to 3.49. In addition, the unadjusted OR for MetS itself was markedly higher in those diagnosed or treated for DM, HT or lipid disorders at 3.13 *vs* 1.08.