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New evidences about the strict relationship between the epicardial fat and the aerobic exercise

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ABSTRACT

Background/aims: In this study, we report some experimental results about the strong correlation between the physical activity and the cardiovascular prevention that has been confirmed by many epidemiological studies. In particular, we examined the epicardial fat (EF) behavior in order to investigate its direct role in coronary disease through vasocrine and paracrine cytokines secretions. The purpose of this study was the determine the effects of aerobic exercise on epicardial fat volume in patients with metabolic syndrome.
Methods: We have studied, in primary prevention, 54 non-diabetic patients, 23 female and 31 male, mean age of 60 ± 15 years, affected by metabolic syndrome. Patients performed a multi detector computed tomography (MDCT) scan, a non-invasive approach for epicardial fat (EF) quantification
Results: Our findings show that sedentary patients exhibit an EF volume very high compared to subjects with moderate/intensive exercise training. These results, obtained in patients affected by metabolic syndrome, demonstrate sedentary patients to have an epicardial fat volume statistically higher compared to non-sedentary patients.
Conclusion: This study confirms that lifestyle, and in particular aerobic exercise, plays a fundamental role in the cardiovascular risk prevention.

1. Introduction

Epicardial fat is considered as an important emerging cardiovascular risk factor. In fact, epicardial fat or EF shows significant independent associations with cardiovascular risk predictors, such as hypertension, low HDL cholesterol, high LDL cholesterol, high triglycerides, and insulin resistance. Our attention has been paid to the EF recognized as marker of cardiac risk and of the development of an unfavorable metabolic risk profile [1].

In a recent study, EF is indicated as the best predictor for angiographic disease severity, even better than waist circumference or visceral abdominal fat volume [2].

EF is responsible of the production of inflammatory cytokines and other vasoactive substances that work systemically or locally to alter vascular endothelial function by promoting the growing of coronary atherosclerosis [3–6]. An increased epicardial fat volume has been associated with insulin resistance in non-diabetic obese patients and with the presence of diabetes mellitus type 2 [7].

In addition, the activation of lipid-induced protein kinase might be involved in premature adipocyte apoptosis and heart failure. Finally, accumulation of lipids increases diacylglycerol and ceramide levels, resulting in a reduction in mitochondrial fatty acid oxidation occurs with a consequent alteration of cardiac function [7,8]. The fact that a sedentary lifestyle causes a significant increase in total and cardiovascular morbidity and mortality has now been amply demonstrated [9]. In addition, it is estimated that eliminating this risk factor may reduce cardiovascular disease (CVDs by 15–39%, stroke by 33%, colon cancer by 22–33% and bone fractures secondary to osteoporosis by 18%). A sedentary lifestyle is therefore emerging as the main risk factor in the third millennium [10,11]. Regular exercise attenuates the age-associated increase in oxidative stress and stimulates the chronic anti-inflammatory effects [12,13]. For these reasons, and for the important role of the epicardial fat in the mechanism of atherosclerosis progression, several new studies have pointed out that aerobic exercise training, even without diet restriction, may be an effective strategy for decreasing epicardial fat (EF) volume and, thus, the development of atherosclerosis plaque [14].

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2. Methods

Our study involved 54 patients, 23 females and 31 males, mean age of 60 ± 15 years, affected by metabolic syndrome [15] who underwent cardiac MDCT for the epicardial fat evaluation. Patients were recruited at the Prevention of Cardiovascular Diseases ambulatory of Fatebenefratelli Hospital, Isola Tiberina. All subjects were divided into two groups on the basis of positive or negative aerobic exercise history at the moment of MDCT (27 sedentary and 27 non-sedentary). The MDCT has been performed for the group of patients not sedentary, after 6 months of regular physical activity, and in the group of sedentary patients, CT was performed in combination with with the other group. Participants belong to the non-sedentary group performed a 30-min warm-up session in the fitness studio, followed by aerobic exercise around the Villa Pamphili Park in Rome. All exercise training sessions were supervised by an exercise physiologist. Participants in the group with a history of physical activity completed a 12-week supervised exercise training program (60–70% of the maximal heart rate; 60 min/day, 3 days/wk for 6 months). To estimate energy expenditure of exercise, heart rate was monitored continuously during each training session by using a telemetric heart rate monitor (RS 400; Polar Electro Accurex Plus).

To evaluate a homogeneous sample, patients with a positive history for diabetes were not included in the study. Because of the retrospective nature of the study, informed patient consents were not required.

2.1. CT imaging

Patients performed MDCT scan, according to protocol normally used for Calcium Score. This method is a non-invasive approach for research and quantification of EF (Fig. 1).

The imaging parameters for cardiac MDCT were as follows: prospective sequential ECG gating; 64 channel detectors along the *z*-axis, scan FOV 15–21 cm (depend on the patient size), matrix 512 × 512, by means of axial scans detector collimation 3 mm; reconstruction 2.5 mm, gantry rotation time 0.25 ms, tube 9 current range 50–100 mA (depending on the patient size and with automated modulation), 100 kV or 120 kV (according to BMI). CT images were reconstructed with a slice thickness of 2.5 mm and with a slice distance of 0.5 mm with an overlap of 0.5 mm, both in CAS and CTA images. EF volume was defined as the adipose tissue between the surface of the heart and the visceral layer of the pericardium. For the quantification of the EF, DICOM images were transferred to a research workstation. Epicardial surface was computed by using an interactive procedure previously developed at the CNR Institute of Clinical Physiology. The procedure required the radiologist to trace the pericardial contours both in axial contiguous slices. Furthermore, the procedure allowed the radiologist to split the cardiac region into left and right zones by tracing an interventricular plane in two axial slices. The summation of the individual silhouette images determines the total volume of epicardial fat that is expressed in cc.

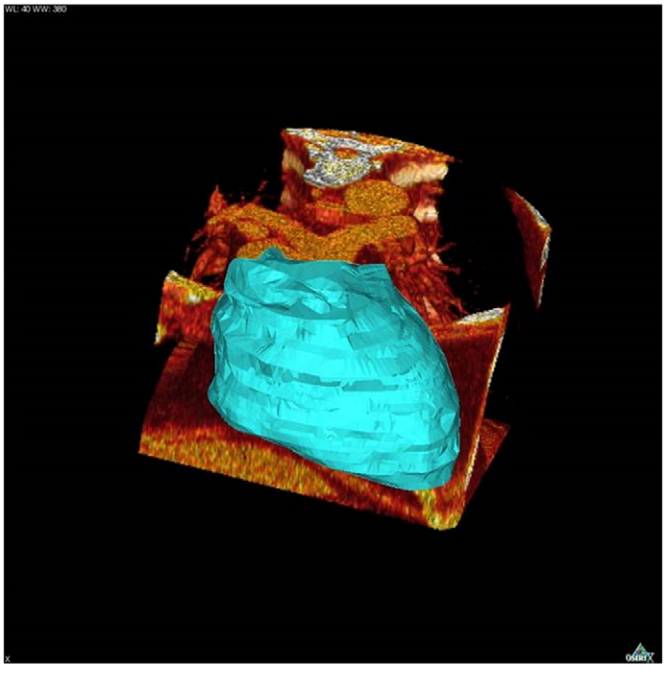

Fig. 1. Epicardial fat volume represented in three dimensions (3D) as result of the semiautomatic computation.

Every single cardiac silhouette and the subsequent volume were analyzed in a blinded fashion by two radiologists with respectively four and ten years of experience on thorax CT imaging. in order to evaluate the correlation between individuals [16].

We decided to calculate the EF quantity as a volumetric measurement, to obtain higher reproducibility and inter-observer agreement compared to a distance measurement [17].

2.2. Anthropometric measurements

Body height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Body weight was measured to the nearest 0.01 kg using calibrated electronic digital scales in barefoot subjects. Body mass index (BMI) was calculated by dividing the weight (expressed in kg) by the square of the height (expressed in m^2). Waist circumference was measured at the level of the umbilicus in standing position. The calculation of body surface area (BSA) has been done using the well-known formula of Mosteller BSA = ([height (cm) × weight (kg)] / 3600)$^{(1/2)}$ [18].

2.3. Blood pressure

Blood pressure (systolic and diastolic) was measured after a 20-min rest period using a mercury manometer. During measurements, patients lay bare-armed in a bed. We calculated the average value originated from two different measurements temporally separated by at least a 3-min interval for each subject.

2.4. Biochemical analysis

Blood exams were put into 8-ml tubes containing thrombin-neutralizing agents. The tubes were immediately centrifuged at 3,000 rpm for 10 min at 4 °C. The blood was used for analyses of plasma concentrations of free fatty acids, insulin, and lipids. Plasma TG concentrations were determined by means of the enzymatic method by using a TG kit, and plasma free fatty acids were measured by the colorimetric method. Low-density lipoprotein (LDL)-cholesterol was calculated according to Friedewald's formula [19].

2.5. Statistical analysis

Bland–Altman method was used to determine the relationships between the variables [20]. In order to determine the variables that are independently associated with changes in the epicardial fat levels, a stepwise multiple regression analysis was performed. The normality of distribution of the variables was assessed using the Shapiro–Wilks test. Data are shown as mean ± SEM or median (25th percentile; 75th percentile). p values <0.05 were regarded as statistically significant. Statistical analysis was carried out using the NCSS software (Kaysville, UT, USA)

Table 1
Principal characteristics of the study population.

	Aerobic exercise	No aerobic exercise	*p*
Age (years)	57 (54; 60)	58 (54;64)	0.52
BMI (kg/m^2)	26.5 (24;32)	28.5 (24;38)	0.26
BSA (m^2)	1.89 (1.78;2)	2 (1.78;2.42)	0.12
Waist circumference (cm)	104 (101;108)	107 (100;113)	0.60
BPs (mmHg)	150 (130;155)	145 (140;145)	0.23
BPd (mmHg)	80 (76;90)	86 (84;92)	0.17
Triglycerides (mmol/L)	1.2 (1.1;1.7)	2.0 (1.5;2.3)	0.42
Glucose (mmol/L)	5.1 (4.7;5.8)	5.0 (4.8;5.7)	0.83
HDL (mmol/L)	1.03 (0.96;1.26)	1.03 (0.97;1.29)	0.81
Epicardial fat (ml)	68.3 (50; 87)	121.3 (96;145)	0.0035
HbA1c (mmol/mol)	42 (31;44)	40 (35;59)	0.87
Insulin (pmol/L)	68.7 ± 8.8	88.3 ± 15.2	0.32
Uric acid (μmol/L)	47 ± 3.9	54 ± 5.2	0.10

Data are mean ± SEM or median (25th percentile; 75th percentile). BPs: systolic blood pressure; BPd: diastolic blood pressure; HDL: high density lipoproteins.

3. Results

The characteristics of the study population are showed in Table 1.The population observed in the study shows the following distribution: 26% (8 patients in the sedentary group and 6 patients in the group owned by sedentary) of our population met three risk factors for metabolic syndrome diagnosis, while the other 75 % (19 patients in the sedentary group and 21 patients in the non-sedentary group) satisfies more than three criteria (balanced distribution between the 2 groups).

The average values of EF were 115.1 cc in the study population. We found a significant correlation ($p = 0.03$ using non-parametric Kruskal–Wallis test) between EF and aerobic exercise without gender differences. In sedentary patients, an average epicardial fat of 121 cc was found, while in non-sedentary patients, the average epicardial fat thickness was 68.3 cc ($p = 0.0035$) (Fig. 2).

4. Discussion

In the present study, we investigated the effects of exercise training on the epicardial fat volume in patients with metabolic syndrome and tested the hypothesis that a regular aerobic physical activity reduces the volume of epicardial fat. In fact, we considered two balanced distribution populations with the exception of physical activity and our results demonstrate sedentary patients to have an epicardial fat volume statistically higher compared to non-sedentary patients. Several studies have reported a correlation of epicardial fat with insulin resistance, rise of triglycerides, blood pressure, and metabolic syndrome. Moreover, epicardial fat, through the release of bioactive molecules (IL-6, IL1B, and MCP-1), as well as the down-regulation of adiponectin, play a direct role in causing coronary atherosclerosis through increased coronary artery calcium, coronary plaque burden, and major adverse cardiac event (s) [21]. Although the intimate mechanisms correlating the EF with physical activity have been not yet well identified, clinical evidences show that the aerobic exercise (without diet restriction) caused a reduction of epicardial fat and a reduction of visceral adipose tissue. Exercise causes a loss of epicardial fat respect to reduce BMI, waist circumference, and causes losses in abdominal and visceral fat, even in the absence of any loss of body weight [22–24].

Regular exercise reduces the risk of cardiorespiratory diseases. The effects of regular exercise may be mediated via both a reduction in visceral fat mass, in particolar EF, with a subsequent decreased release of adipokines and through the induction of an anti-inflammatory environment with each bout of exercise.

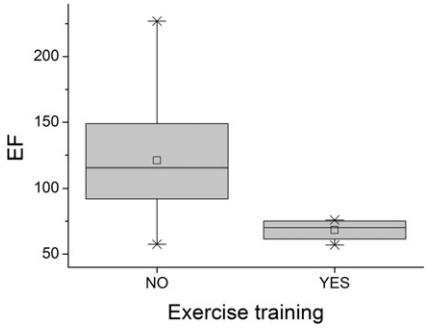

Fig. 2. Box-whisker plot: results demonstrate sedentary patients to have an epicardial fat volume statistically higher compared to non-sedentary patients.

5. Conclusions

These results indicate that aerobic exercise influences the quantity of epicardial fat, through a statistically significant difference between two balanced distribution groups of people with metabolic syndrome. However, further studies are required to understand better how the physical activity can reduce the epicardial fat and, ultimately, the cardiovascular risk.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Authors contribution

Manuel Monti is the main author and he has conceived the paper and drafted its first version.

Giovanni Maria Vincentelli has contributed to the study conception and has participated to its drafting providing a critical revision of the paper in many important intellectual aspects.

Maria Rosaria Pirro has contributed to the data analysis and to the interpretation of results.

Paolo Di Renzi has contributed to the acquisition of data and to the execution of radiological studies.

Francesco Borgognoni, as emergency department director, has made the overall revision of the paper and he is the guarantor of integrity of the entire study.

All the authors have read and approved the manuscript.

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