Impact of Obesity on Coronary Artery Disease in Obese Egyptians

Thesis Submitted for Partial Fulfillment of Master Degree in Cardiology

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ABSTRACT

Introduction: The prevalence of obesity is reaching epidemic proportions in many countries. Recently, Egypt is enlisted as one of the top10 fattest countries in the world. However, little is known about which parameter of obesity can be associated with severity of coronary artery disease (CAD).

Objectives: In this study, we examined the relationship between various parameters of obesity and extent of CAD in Egyptian patients.

Methods: The study population consisted of 450 patients in whom elective coronary angiography was performed. All patients had measurement of BMI, WC, WHR and WHtR. Obesity was defined as BMI ≥30 kg/m^2, WC ≥ 94cm for men and ≥ 80 cm for women, WHR≥ 0.85 in women and ≥0.90 in men or WHtR 0≥.5. Markers for significant CAD were >3 vessel disease (VD), >3 plaques causing ≥50% diameter stenosis (DS) or ≥ one proximal plaque (PP) causing ≥50% DS. CAD was considered severe if the patient had≥2 of these markers.

Results: According to BMI, markers of significant CAD were less in obese patients. one or more PP causing ≥50% DS was met in only 41.4 of obese patients vs. 52.8% of non obese, p= 0.018. Classifying patients according to WC failed to show any significant difference between obese and non obese patients as regards prevalence and severity of CAD. High WHtR showed higher prevalence of CAD in obese patients. Increased WHR was the only measure of obesity that showed increased prevalence of >3 VD (15.3 vs. 2.7, p= 0.045), one or more PP causing 50% DS (49.9 vs. 18.9, p< 0.000) and severe CAD (19.6 vs. 5.4, p= 0.043).

Conclusion: Compared with BMI, WC and WHtR, WHR showed the best association with severe CAD in Egyptian patients.

Key words: Obesity parameters, severity of coronary artery disease.

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ABBREVIATIONS

BMI	Body mass index
WHO	World health organization
WC	Waist circumference
WHR	Waist to hip ratio
WHtR	Waist to height ratio
PCI	Percutaneous coronary intervention
CAD	Coronary artery disease
OSA	Obstructive sleep apnea
OHS	Obesity hypoventilation syndrome
FFA	Free fatty acids
TNF-α	Tumor necrosis factor- α
IL-6	Interleukin 6
Ang II	Angiotensin II
GLUT4	Glucose transport type 4
Apo	Apolipoprotein
VLDL	Very low-density lipoprotein
IDL	Intermediate density lipoprotein
LDL	Low-density lipoprotein
HDL	High-density lipoproteins
NAFLD	Non-alcoholic fatty liver disease
NHANES III	Third National Health and Nutrition Examination Survey
RAAS	Renin-angiotensin-aldosterone system
mRNA	Messenger ribonucleic acid
HF	Heart failure
CNS	Central nervous system
CKD	Chronic kidney disease

HUC	Hyperuricemia
TGs	Triglycerides
GB	Gallbladder
P-P	Postprandial
AHA	American Heart Association
IDF	International Diabetes Federation
BIA	Bioelectrical impedance analysis
DXA	Dual energy x-ray absorptiometry
CT	Computed tomography
NHANES II	Second National Health and Nutrition Examination Survey
CVD	Cardiovascular disease
FMD	Flow-mediated dilation
hs-CRP	High-density C-reactive protein
HRCA	High risk coronary anatomy
DHS	Dallas Heart Study
CAC	Coronary artery calcium
CABG	Coronary artery bypass grafting
BP	Blood pressure
SCD	Sudden cardiac death
UA	Unstable angina
NSTEMI	Non ST elevation myocardial infarction
STEMI	ST elevation myocardial infarction
ECG	Electrocardiogram
CTA	Computed tomography coronary angiography
CVS	Cerebrovascular stroke
PVD	Peripheral vascular disease
MI	Myocardial infarction
CHF	Congestive heart failure

COPD	Chronic obstructive pulmonary disease
FPG	Fasting plasma glucose
TTE	Transthoracic echocardiogram
LVEF	Left ventricular ejection fraction
WMSI	Wall motion score index
DS	Diameter stenosis
SD	Standard deviation
ROC	Receiver operating characteristic
HTN	Hypertension
DM	Diabetes mellitus
OHD	Oral hypoglycemic drug
CA	Coronary angiography
LMA	Left main coronary artery
LAD	Left anterior descending
D1	First diagonal
D2	Second diagonal
LCX	Left circumflex
OM1	First obtuse marginal
OM2	Second obtuse marginal
RCA	Right coronary artery
PDA	Posterior descending artery
PL	Posterolatral artery
AUC	Area under the curve
BF	Body fat
ORs	Odds ratios
CACS	Coronary artery calcification score

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INTRODUCTION

Obesity is known to be associated with an increased risk of morbidity and reduced life expectancy (1). Obese patients have an increased prevalence of major co-morbidities including cardiovascular disease, respiratory dysfunction and diabetes. The risk that these problems will develop is rising with increasing body mass index (BMI) (2). It is also thought to be a risk factor for perioperative morbidity and mortality with cardiac surgery (3).

The prevalence of obesity is reaching epidemic proportions not only in western world but also in many developing countries. It has been called the disease of the twenty-first century (4). Egypt is shown to be one of the top ten fattest countries in the world, based on national health surveys compiled by world health organization (WHO) between year 2000 and 2008 (5). Various anthropometric indices of obesity have been suggested to predict cardiovascular risk. Although BMI is the most studied index being related to cardiovascular risk factors, there is increasing doubt about its role in predicting the outcome of patients undergoing coronary revascularization. Waist circumference (WC), waist to hip ratio (WHR) and waist to height ratio (WHtR) indicate abdominal fat deposition. A computed tomography study had demonstrated that WHtR showed the highest correlations with intrabdominal fat compared to BMI, WC or WHR (6).

According to the INTERHEART study (7), the population attributed risk from abdominal obesity was shown to be 33.7% after adjustment for age, sex and smoking in the region of the Middle East. In addition, the age of first presentation of acute myocardial infarction in the region of Middle East was 51 years which is the lowest age throughout the world.

Although current evidence may suggest that the impact of obesity on all-cause mortality is declining; (8) recent American Heart Association Statistics (9) and a meta-analysis (10) showed excess mortality associated with obesity. Recently, the "*obesity paradox*" leads to a suggestion that increasing BMI had shown an association with decreased risk of myocardial infarction, death, need for urgent revascularization and bleeding complications after percutaneous intervention (PCI) (11). It also suggested the negative impact of BMI on the severity of coronary artery disease (CAD) specially the left main involvement (12-14).

So far, it is not known whether the so-called *obesity paradox* is a genuine protective mechanism of obesity, or it is simply representing an apparent phenomenon molded by asymmetrical distribution of cardiovascular risk and co morbidities across different BMI categories in patients with CAD (15).

With the respect to this background and the recent term "*obesity paradox*", it becomes important to understand the impact of different aspects of obesity on Egyptian patients scheduled for coronary angiography (11, 16, 17).

AIM OF WORK

The aims of this study were to:

1- Examine the pattern and severity of coronary artery involvement in obese Egyptians scheduled for coronary angiography.

2- Test different indices of obesity e.g. BMI, WC, WHR and WHtR with other risk factors of cardiovascular disease, and with the pattern and severity of coronary artery involvement.

3- To delineate the best correlation of obesity indices with cardiovascular risk factors and severity of coronary artery disease.

Chapter 1

Problem of Obesity

During the last six or seven decades, we as humans have been developing machines that could help us save energy. The result is that nowadays our daily lives require minimal energy expenditure. From that point, the genetically determined energy storing capacity turns against us making us becoming obese, with type 2 diabetes, hypertensive, etc. This is how, what was initially a positive genetic trait, becomes a deleterious characteristic, leading to what the WHO has qualified as the 21st Century epidemic: obesity (18).

Over the past decade, obesity has become recognized as a national health threat and a major public health challenge (19). Due to its high worldwide prevalence, obesity is currently the most common metabolic disease in the world. The WHO estimates that more than one billion people are overweight and, of these, 300 million can be considered as obese, with a BMI above 30 kg/m^2 according to its own BMI based classification of obesity. Actually, there is a great concern because the global figures of obesity are progressively increasing from an estimate of 200 million people affected in 1995 to the current 300 million, which is a 50% increase in only seven years. It is estimated that if no action is taken against this, these figures could double in 20 years (20). In 2007–2008, based on measured weights and heights, approximately 72.5 million adults in the United States were obese (21). In Europe, the prevalence of obesity in men ranged from 4.0% to 28.3% and in women from 6.2% to 36.5%. The highest prevalences (i.e. greater than 25%) were found in regions of Italy and Spain in both sexes (22, 23), as well as in Portugal,

Poland, the Czech Republic, Romania, and Albania in women (24, 25). Eastern Europe and the Mediterranean countries showed higher prevalences of obesity than countries in Western and Northern Europe (26, 27).

In the past 20 years, the rates of obesity have tripled in developing Countries (28). Overweight and obesity are emerging in developing countries as a result of rapidly changing lifestyle patterns, such as those of diet and physical activity, leading to an accelerated increase in overweight, obesity, and related chronic diseases. A transition in diet and physical activity patterns, leading to an energy-dense diet and a sedentary lifestyle, is known as the *nutrition transition* (29). The nutrition transition as a global phenomenon has been documented to include the industrialized nations of Europe and North America as well as lower- and middle-income countries of Asia, Latin America, the Caribbean, Africa, and the Middle East (30). In low-income countries experiencing the nutrition transition, obesity is usually observed first in urban areas and in the high-income elite. Urban lifestyles are associated with diet and activity patterns associated with the nutrition transition, contributing further to obesity (31, 32). Although the urban elite are usually the first to experience it, the obesity epidemic is also shifting to the middle and lower classes (33, 34). The highest levels of obesity (grade II and above) were in the Middle East, Western Pacific, and Latin America. In contrast, countries in sub-Saharan Africa and Asia have some of the lowest prevalences for overweight and obesity (30). The Middle East, including the Arabian Peninsula, Eastern Mediterranean, Turkey and Iran, and North Africa, are no exception to the worldwide increase in obesity (35). The IDEA study found that obesity in Middle Eastern women ranged from 38 to 40%. A review of the Middle East as a whole found that