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Research Article

Normal-Weight Obesity and Normal-Central Weight Obesity in Older Adult and Geriatric Patients with Acute Coronary Syndrome

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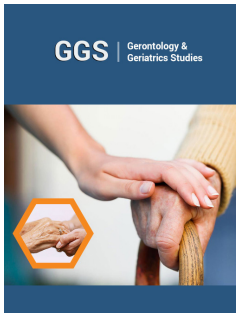

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Abstract

Background: The most recent evidence shows some nutritional phenotypes that may confer risk of unfavorable outcomes, but few investigations are undertaken to demonstrate risk profiles. Our study aimed to conduct a comparative analysis of the cardiometabolic risk between Normal-Weight Obesity (NWO) and Normal-Weight Central Obesity (NWCO) in patients hospitalized with Acute Coronary Syndrome (ACS).

Method: In our cross-sectional study, we included individuals aged over 50 years who were admitted to a cardiology hospital and diagnosed with ACS.

Result: Our study included a sample of 147 participants, with an average age of 65.9±8.2 years. The prevalence of NWO was 10.4%, and NWCO was 5.6%. NWO was found to be more frequent among men ($p=0.031$) in individuals with hypertension ($p=0.047$) and those who presented a sedentary lifestyle ($p=0.024$). The frequency of NWCO was higher among women ($p<0.001$). Our analysis revealed that mortality was more frequent among individuals with NWO ($p=0.038$). There was a greater need for surgical interventions in cases where excessive weight and excessive body fat coexisted ($p=0.033$). Notably, the occurrence of metabolic syndrome was more prominent in individuals with NWCO and in cases where both central obesity and excessive weight were present ($p<0.05$). Individuals with NWCO had higher levels of total blood cholesterol and troponin ($p<0.05$).

Conclusion: A higher prevalence of individuals with the NWO phenotype was observed, while the NWCO phenotype was present to a lesser extent. The NWO phenotype was indicative of the worst-case scenario, as it exhibited an association with higher mortality rates. The NWCO phenotype demonstrated a more pronounced association with metabolic syndrome and elevated serum levels of total cholesterol and troponin. Accurate diagnosis of both obesity phenotypes is of paramount importance, given their significant implications for clinical cardiovascular risk and overall survival.

Keywords: Obesity; Abdominal obesity; Cardiovascular diseases; Acute coronary syndrome

Introduction

According to the 2022 World Health Statistics Report by the World Health Organization (WHO), cardiovascular diseases and other conditions like cancer, diabetes and respiratory diseases led to around 33.2 million global deaths in 2019, marking a 28% increase from 2000. The report highlights that Ischemic Heart Disease (IHD) accounts for over 50% of premature female mortality in more than half of the world's countries and over 75% of premature male mortality in a similar proportion of countries. Excessive adipose tissue has been identified as a significant risk factor for coronary artery disease, as it is directly linked to causative factors of cardiovascular diseases. Well-established mechanisms, such as increased insulin resistance, heightened sympathetic nervous system activity, elevated free fatty acid turnover, and higher leptin levels, contribute to obesity triggering other clinical conditions like diabetes, hypertension, dyslipidemia, and obstructive sleep apnea, thus compounding the overall cardiometabolic risk [1].

The Body Mass Index (BMI) is commonly used in clinical practice and epidemiological studies as a diagnostic method for obesity. However, the obesity definition considered the gold standard by the WHO corresponds to excessive body fat, which is not fully addressed by BMI. The BMI does not adequately account for body fat and lean body mass, both of which are determinant components for analyzing the relationship with cardiovascular disease outcomes [1]. The limitations of the BMI become further pronounced when attempting to capture the body composition distribution in older individuals. This is due to the aging process, which triggers a redistribution of adipose tissue, leading to heightened fat deposition in the central region and a decline in lean body mass. Moreover, the constraints of the BMI are compounded by factors such as reduced skeletal mass and the accompanying loss of height that come with aging [2].

Certainly, particularly in older individuals, a normal BMI range (18.5-24.9kg/m^2) might not accurately indicate an appropriate body fat percentage and could obscure the presence of excessive fat. This specific scenario, where a normal BMI falls within the designated range but is coupled with a high body fat percentage, is known as Normal-Weight Obesity (NWO). This condition is linked to an increased risk of developing non-communicable chronic diseases [3]. Furthermore, when BMI falls within the normal range but there's an accumulation of abdominal fat, it presents another risk phenotype known as Normal-Weight Central Obesity (NWCO). Consequently, some individuals might possess a normal total body fat level but still be centrally obese. This underscores that despite having a within-range total body fat, they exhibit central obesity [1]. Within this context, research that investigates the risk linked to diverse profiles of body fat composition and distribution can substantially enhance comprehension of more high-risk nutritional phenotypes. This enhanced understanding, in turn provides guidance for directing preventive and therapeutic measures. Thus, our study aimed to conduct a comparative analysis of the cardiometabolic risk associated with NWO and NWCO in patients hospitalized due to Acute Coronary Syndrome (ACS).

Methods

Study design and participants

This is a cross-sectional study with an added prospective component (assessment of in-hospital complications and length of stay). The study involves individuals aged ≥50 years, diagnosed with ACS, and having a BMI>18.5kg/m^2. The participants were admitted for hospitalization between May and October 2022 at a renowned university hospital specializing in Cardiology in Northeast Brazil. Participants with clinical conditions that hindered accurate anthropometric measurements (such as limb amputation, edema, bedridden status, and bed confinement) were excluded from our study. Furthermore, individuals with concomitant wasting diseases or conditions that directly influenced body composition and fat redistribution were also excluded. This encompassed individuals with New York Heart Association functional class III or IV congestive heart failure, patients undergoing dialysis for kidney disease, individuals with chronic obstructive pulmonary disease, those afflicted by HIV infection, cancer patients and those in the postoperative phase after major surgeries. The sample size calculation was performed using Epi Info software, version 6.04, specifically within the STATCALC module. This calculation took into consideration the previous year's data on the number of ACS-related hospitalizations within the same study period (total hospitalizations in 6 months=250). With a presumed prevalence of 25% for normal weight obesity [4] a confidence level of 95%, and a standard error of 5%, the minimum required sample size was determined to be 134 patients. To account for potential losses, this sample size was increased by 10%, resulting in a total sample size of 148 participants.

Ethical aspects

Data collection occurred within a 72-hour window following patient admission to the ward. The initiation of data collection was contingent upon obtaining approval for the research protocol from the Human Research Ethics Committee (Protocol 5.371.274/2022). Comprehensive informed consent was obtained from all patients through the signing of the appropriate documentation.

Normal-weight obesity and normal-weight central obesity assessment

NWO was defined by the simultaneous presence of a BMI falling within the normal range (18.5-24.9kg/m^2) (WHO, 2000) and an elevated body fat percentage (%BF) (>30% in men and >40% in women) [5]. The identification of NWCO was based on the coexistence of a normal BMI (18.5-24.9kg/m^2) (WHO, 2000) and an abdominal circumference ≥102cm for men and ≥88cm for women (NCEP ATP III, 2002). The BMI was calculated as the quotient of weight divided by the square of height (Weight/Height^2) (WHO, 2000).

The %BF was obtained through tetrapolar Bioelectrical Impedance Analysis (BIA) [Byodinamics® model 310]. The following preparation protocol was observed: fasting for a minimum of 4 hours prior to the test; urination 30 minutes before the test; abstaining from caffeine-containing foods (such as coffee, cola-based sodas, chocolates, cocoa beverages, and teas) for 24 hours before the test [6-8]. For %BF classification in both genders, the cutoff points suggested by Donini et al. [5] were employed, wherein a %BF of ≥30% for men and ≥40% for women served as thresholds.

Cardiometabolic risk

For the assessment of cardiometabolic risk, the following factors were considered: fasting glucose and lipid profile alterations (total cholesterol, fractions, and triglycerides), elevated C-Reactive Protein (CRP), Metabolic Syndrome (MS), along with troponin levels, the need for coronary angioplasty or myocardial revascularization surgery during hospitalization, complications during hospitalization (requirement for Intensive Care Unit referral), outcomes and length of hospital stay (in days). Metabolic Syndrome (MS) was defined according to the criteria proposed by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III, 2002) [9] which diagnoses its presence when three or more of the following criteria are met: central obesity

(waist circumference ≥102cm for men and ≥88cm for women); elevated triglycerides (greater than 150mg/dL); low levels of HDL-C (less than 40mg/dL for men and less than 50mg/dL for women); elevated Blood Pressure (BP) (values equal to or greater than 135/85mmHg or the use of medication to lower BP); and elevated fasting glucose (values equal to or greater than 100mg/dL) or diabetes mellitus. In the analysis of blood samples, reference thresholds were employed: total cholesterol (TC) <190mg/dL, HDL-C >40mg/dL, triglycerides (TG) <150mg/dL, and LDL-C<70mg/dL, adhering to the guidelines delineated in the Brazilian Dyslipidemia and Atherosclerosis Prevention Guideline [10]. Elevated C-Reactive Protein (CRP) concentrations were regarded as significant for values exceeding 4.9mg/dL and troponin levels surpassing 0.014ng/mL were deemed noteworthy, consistent with the parameters endorsed by the institution's laboratory standards.

Demographic, clinical and behavioral data

In terms of sociodemographic variables, the dataset included information on gender, age, education (measured in years of schooling) and race. Race was self-reported by patients and categorized as white, black, or mixed race in accordance with the classification provided by the Brazilian Institute of Geography and Statistics [11]. Within the realm of clinical variables, consideration was given to the presence of comorbidities, encompassing conditions such as Diabetes Mellitus (DM), Systemic Arterial Hypertension (SAH) and Chronic Kidney Disease (CKD). Turning to behavioral variables, we assessed reported smoking status, categorized as smoker (regular consumption), non-smoker (individuals who never smoked or ceased smoking over 10 years ago) [12] and ex-smoker (those who quit smoking within the last 10 years). Physical activity was also assessed with classifications of sedentary (individuals abstaining from physical exercise for more than six months) and active (individuals engaging in regular sports activities at least three times a week) based on the American College of Sports Medicine (ACSM) [13].

Data analysis

The data underwent statistical analysis utilizing the Statistical Package for the Social Sciences (SPSS) version 13.0 (SPSS Inc., Chicago, IL, USA). Continuous quantitative variables were subjected to normality testing using the Kolmogorov-Smirnov test. Variables exhibiting a normal distribution were summarized with mean and standard deviation, while those with non-normal distribution were summarized with median and interquartile range. Categorical variables were depicted through frequency distribution, and the Pearson Chi-Square test was applied to assess potential associations between exposure and outcome variables. Mean comparisons across multiple groups were executed using the one-way ANOVA test (for more than two means), while the Kruskal-Walli's test (for more than two medians) was employed in the case of skewed data distributions. Statistical significance was acknowledged for values of $p < 0.05$.

Result

Within the study timeframe, 174 eligible patients were enrolled. However, 30 patients were subsequently excluded due to factors such as refusal to participate, data inconsistencies, or missing records, resulting in a final sample size of 144 patients. The mean age of the participants was 65.9±8.4 years, with a predominant male representation (59.0%) and a significant proportion falling within the geriatric category (79.9%). Among clinical diagnoses, the most prevalent was ST-Elevation Myocardial Infarction (STEMI) (45.2%) and 45.1% of the patients had a concurrent diagnosis of diabetes. Notably, a substantial portion of the cohort exhibited limited educational attainment (68.9%) and identified as sedentary (74.4%) (Table 1). Excessive weight was identified in 65.0% of the sample, while excess body fat and central obesity were evident in 54.9% and 59.7%, respectively. The prevalence of Normal-Weight Obesity (NWO) was 10.4% and the prevalence of Normal-Weight Central Obesity (NWCO) was 5.6%. Increased weight with normal body fat was observed in 38.9% of the patients (Table 2). When considering only patients with normal weight, NWO was present in 27.8% of the sample (data not shown in tables).

Table 1: Sociodemographic, clinical and lifestyle characteristics of hospitalized patients with Acute Coronary Syndrome (N=144). Recife, PE, 2022.

Variables	N	%
Sex		
Men	85	59
Women	59	41
Age		
Adults (>50y)	29	20.1
Geriatrics (>60y)	115	79.9
Race		
White	24	17.3
Mixed race	100	71.9
Black	15	10.8
Education Level (Years of schooling)		
≤9y	91	68.9
>9y	41	31.1
Cardiological diagnosis		
UA	33	22.9
NSTEMI	46	31.9
STEMI	65	45.2
SAH	125	86.8
T2DM	65	45.1
Metabolic Syndrome	70	63.6
Need for PCI	81	56.3
Surgical intervention	30	21
Transfer to ICU	7	4.9
Smoking		
Smoker	25	17.4
Non-smoker	48	54.2
Ex-smoker	41	28.5
Level of physical activity		
Sedentarism	93	74.4
Activeness	32	25.6

Table 2: Normal-Weight Obesity (NWO) and Normal-Weight Central Obesity (NWCO) in hospitalized patients with Acute Coronary Syndrome (N=144). Recife-PE, 2022.

Abbreviations: BMI: Body Mass Index; BIA: Bioelectrical Impedance Analysis; WC: Waist Circumference; NWO: Normal Weight Obesity; NWCO: Normal-Weight Central Obesity

Variables	N	%
BMI		
Eutrophy (BMI 18.5-25kg/m^2)	49	34
Excessive weight (BMI ≥25kg/m^2)	95	65
Body fat BIA-derived		
Normal	65	45.1
Elevated	79	54.9
WC		
Normal	58	40.3
Elevated	86	59.7
BMI + Body fat BIA-derived		
Normal weight and normal body fat	39	27.1
NWO	15	10.4
Excessive weight and normal body fat	56	38.9
Excessive weight and elevated body fat	34	23.6
BMI + WC		
Eutrophy without central obesity	41	28.5
NWCO	8	5.6
Excessive weight without central obesity	16	11.1
Excessive weight and central obesity	79	54.9
Variables	**N**	**%**
BMI		
Eutrophy (BMI 18.5-25kg/m^2)	49	34
Excessive weight (BMI ≥25kg/m^2)	95	65
Body fat BIA-derived		
Normal	65	45.1
Elevated	79	54.9
WC		
Normal	58	40.3
Elevated	86	59.7
BMI + Body fat BIA-derived		
Normal weight and normal body fat	39	27.1
NWO	15	10.4
Excessive weight and normal body fat	56	38.9
Excessive weight and elevated body fat	34	23.6
BMI + WC		
Eutrophy without central obesity	41	28.5
NWCO	8	5.6
Excessive weight without central obesity	16	11.1
Excessive weight and central obesity	79	54.9

NWO was more frequent in men (2.74 times higher; p=0.031), in hypertensive individuals (6.5 times higher; p=0.047) and sedentary individuals (p=0.024) (Table 3). The frequency of NWCO was greater among women (3 times higher; p<0.001), with a tendency to be higher among ex-smoker patients (probability value near the threshold of statistical significance (p=0.055) (Table 4). In comparison with other groups (normal weight and body fat, excessive weight and normal body fat, and excessive weight with increased body fat), mortality was more frequent in individuals with NWO (p=0.038). However, the need for surgical intervention was higher in the group where excessive weight and body fat coexisted (p=0.033). MS and serum levels of TC and TG were higher in the group of individuals with excessive weight and normal body fat (p<0.05) (Table 5). MS was more frequent in individuals with NWCO phenotype and in individuals whom central obesity coexisted with excessive weight (p<0.05). Levels of TC and troponin were higher in individuals with NWCO (p<0.05). Individuals with excessive weight and central obesity had higher serum levels of TG (Table 6).

Table 3: Sociodemographic, clinical and lifestyle factors associated with Normal-Weight Obesity (NWO) in hospitalized patients with Acute Coronary Syndrome (N=144). Recife-PE, 2022.

Abbreviations: Qui Quadrado; UA: Unstable Angina; STEMI: ST-Elevation Myocardial Infarction; NSTEMI: Non-ST-Elevation Myocardial Infarction; SAH: Systemic Arterial Hypertension; T2DM: Type 2 Diabetes Mellitus; PCI: Percutaneous Coronary Intervention; ICU: Intensive Care Unit. NWO: Normal-Weight Obesity

Variables	Both Normal Weight and Body Fat		NWO		Excessive Weight and Normal Body Fat		Excessive Weight and Elevated Body Fat		p*
	n	%	n	%	n	%	n	%	
Sex									
Men	18	46.2	11	73.3	30	53.6	26	76.5	0.031
Women	21	53.8	4	26.7	26	46.4	8	23.5	
Age									
50-59y	11	28.2	1	6.7	12	21.4	5	14.7	0.267
≥60y	28	71.8	14	93.3	44	78.6	29	85.3	
Race									
White	4	10.8	6	40	8	15.1	6	17.6	0.31
Mixed race	29	78.4	8	53.3	38	71.7	25	73.5	
Black	4	10.8	1	6.7	7	13.2	3	8.8	

Education level (Years of schooling)									
≤9y	18	54.5	10	66.7	39	75	24	75	0.198
>9y	15	45.5	5	33.3	13	25	8	25	
Cardiological diagnosis									
UA	9	23.1	0	0	17	30.9	7	20	0.545
NSTEMI	12	30.8	6	40	17	30.9	11	31.4	
STEMI	18	46.2	9	60	21	38.2	17	48.6	
SAH									
Yes	31	79.5	13	86.7	54	96.4	27	79.4	0.047
No	8	20.5	2	13.3	2	3.6	7	20.6	
T2DM									
Yes	21	53.8	3	20	27	48.2	21	53.8	0.142
No	18	46.2	12	80	29	51.8	18	46.2	
Smoking									
Yes	7	17.9	2	13.3	7	12.5	9	26.5	0.18
No	18	46.2	6	40	37	66.1	17	50	
Ex-smoker	14	35.9	7	46.7	12	21.4	8	23.5	
Level of physical activity									
Sedentarism	26	74.3	11	100	39	79.6	17	56.7	0.024
Activenes	9	25.7	0	0	10	20.4	13	43.3	

Table 4: Sociodemographic, clinical, and lifestyle factors associated with Normal-Weight Central Obesity (NWCO) in hospitalized patients with Acute Coronary Syndrome (N=144). Recife-PE, 2022.

Abbreviations: Qui Quadrado; UA: Unstable Angina; STEMI: ST-Elevation Myocardial Infarction; NSTEMI: Non-ST-Elevation Myocardial Infarction; SAH: Systemic Arterial Hypertension; T2DM: Type 2 Diabetes Mellitus; PCI: Percutaneous Coronary Intervention; ICU: Intensive Care Unit. NWCO: Normal-weight central obesity.

Variables	Normal Weight Without Abdominal Obesity		NWCO		Excessive Weight Without Abdominal Obesity		Excessive Weight With Abdominal Obesity		p *
	n	%	n	%	n	%	n	%	
Sex									
Men	35	85.4	2	25	32	40.5	16	100	<0.001
Women	6	14.6	6	75	47	59.5	0	0	
Age									
50-59y	5	12.2	1	12.5	4	25	19	24.1	0.41
≥ 60y	36	87.8	7	87.5	12	75	60	75.9	
Race									
White	11	26.8	1	12.5	1	6.7	11	14.7	0.484
Mixed race	26	63.4	7	87.5	12	80	55	73.3	
Black	4	9.8	0	0	2	13.3	9	12	
Education level (Years of schooling)									
≤9y	27	69.2	7	87.5	46	65.7	11	73.3	0.623
>9y	12	30.8	1	12.5	24	34.3	4	26.7	
Cardiological diagnosis									
UA	7	17.1	0	0	3	15	23	31.1	0.219
NSTEMI	15	36.6	2	22.2	6	30	23	31.1	
STEMI	19	46.3	7	77.8	11	55	28	37.8	
SAH									
Yes	33	80.5	7	87.5	13	81.3	72	91.1	0.368
No	8	19.5	1	12.5	3	18.8	7	8.9	

T2DM									
Yes	14	34.1	3	37.5	6	37.5	42	53.2	0.202
No	27	65.9	5	62.5	10	62.5	37	46.8	
Smoking									
Yes	11	26.8	0	0	2	12.5	12	15.2	0.055
No	21	51.2	2	25	9	56.3	46	58.2	
Ex-smoker	9	22	6	75	5	31.3	21	26.6	
Level of physical activity									
Sedentarism	22	64.7	6	85.7	12	80	53	76.8	0.456
Activeness	12	35.3	1	14.3	3	20	16	23.2	

Table 5: Cardiometabolic factors associated with Normal-Weight Obesity (NWO) in hospitalized patients with Acute Coronary Syndrome (N=144). Recife-PE, 2022.

Abbreviations: Qui Quadrado; aKruskall Wallis Test bOne-way ANOVA Test; SD: Standard deviation; QI: Quartile Interval; NWO: Normal-weight obesity; CRP: C-reactive Protein; PCI: Percutaneous Coronary Intervention (Angioplasty); CABG: Coronary Artery Bypass Grafting (Coronary Artery Bypass Surgery); ICU: Intensive Care Unit; LOS: Length of Stay; TIMI: Thrombolysis in Myocardial Infarction; LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol

Variables	Both Normal Weight and Body Fat		NWO		Excessive Weight and Normal Body Fat		Excessive Weight and Elevated Body Fat		P*
	n	%	n	%	n	%	n	%	
CRP									
Normal	2	6.5	1	7.1	6	13.6	1	4.2	0.537
Elevated	29	93.6	13	92.9	38	86.4	23	95.8	
Metabolic Syndrome									
Yes	22	71	4	36.4	37	82.2	7	30.4	<0.001
No	9	29	7	63.6	8	17.8	16	69.6	
Need for PCI									
Yes	19	48.7	7	46.7	34	60.7	21	61.8	0.506
No	20	51.3	8	53.3	22	39.3	13	38.2	
Need for CABG									
Yes	10	25.6	4	26.7	5	8.9	11	33.3	0.033
No	29	74.7	11	73.3	51	91.1	22	66.7	
Transfer to ICU									
Yes	0	0	2	13.3	4	7.1	1	2.9	0.156
No	39	100	13	86.7	52	92.9	33	97.1	
Mortality									
Yes	0	0	2	13.3	2	3.6	3	0	0.038
No	39	100	13	86.7	54	96.4	34	100.0	

Biochemical Parameters, LOS and TIMI Score	Mean±SD or Mean (QI)	Mean±SD or Mean (QI)	Mean±SD or Mean (QI)	Mean±SD or Mean (QI)	p
Fasting glucose	115.5(93.7-227.2)	104.0(90.5-126.7)	117.5(97.7-150.5)	139.0 (107.2-229.2)	0.122[a]
Cholesterol	157.8±47.0	89.6±52.3	175.6±46.9	145.3±37.8	0.039[b]
LDL-c	95.8±35.4	145.4±60.7	106.9±35.9	88.2±32.8	0.191[b]
HDL-c	29.0(25.0-36.5)	31.0(26.0-34.0)	33.0(28.0-40.7)	36.0(30.0-44.0)	0.216[a]
Triglycerides	134.0)110.0-162.0)	114.0 (77.8-136.7)	151.5(108.7-204.2)	105.5(80.2121.7)	<0.001[a]
Troponin	2049.0(35.8-26282.5)	8445.5 (3542.2-22502.5)	503.3(12.1-9291.7)	3380.0(231.2-26007.5)	0.084[a]
LOS	10.0(7.0-15.0)	10.0 (7.0-23.0)	9.0(7.0-14.7)	11.0(6.5-16.0)	0.589[a]
TIMI score	3.0(2.0-4.0)	5.0 (2.5-6.0)	3.0(2.0-4.0)	3.0(3.0-4.0)	0.098[a]

Table 6: Cardiometabolic Factors Associated with Normal-Weight Central Obesity (NWCO) in Hospitalized Patients with Acute Coronary Syndrome (N=144). Recife-PE, 2022.

Qui Quadrado; [a]Kruskall Wallis Test [b]One-way ANOVA Test; SD: Standard deviation; QI: Quartile Interval; NWCO: Normal-weight central obesity; WC: Waist circumference; CRP: C-reactive Protein; PCI: Percutaneous Coronary Intervention (Angioplasty); CABG: Coronary Artery Bypass Grafting (Coronary Artery Bypass Surgery); ICU: Intensive Care Unit; LOS: Length of Stay; TIMI: Thrombolysis in Myocardial Infarction; LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol

Variables	Both Normal Weight and WC		NWCO		Excessive Weight and Normal WC		Excessive Weight and Abdominal Obesity		P*
	n	%	n	%	n	%	n	%	
CRP									
Normal	1	53.3	1	12.5	2	13.3	6	10	0.629
Elevated	29	96.7	7	87.5	13	86.7	54	90	
Metabolic Syndrome									
Yes	5	18.5	6	85.7	5	35.7	54	87.1	<0.001
No	22	81.5	1	14.3	9	64.3	8	12.9	
Need for PCI									
Yes	25	61	3	37.5	10	62.5	43	54.4	0.599
No	16	39	5	62.5	6	37.5	36	45.6	
Need for CABG									
Yes	13	32.5	2	25.0	3	18.8	12	15.2	0.177
No	27	67.5	6	75.0	13	81.3	67	84.8	
Transfer to ICU									
Yes	3	7.3	0	0	1	6.3	3	3.8	0.752
No	38	92.7	8	100.0	15	93.8	76	96.2	
Mortality									
Yes	2	4.9	0	0	0	0	2	2.5	0.712
No	39	95.1	8	100.0	16	100.0	77	97.5	

Biochemical Parameters. LOS and TIMI Score	Mean±SD or Mean (QI)	Mean±SD or Mean (QI)	Mean±SD or Mean (QI)	Mean±SD or Mean (QI)	p
Fasting glucose	125.0(98.5-170.2)	138.5(103.7-194.0)	97.0(93.0-138.0)	118.0(98.5-175.0)	0.485[a]
Cholesterol	139.9±43.0	171.0±53.5	141.6±41.1	165.5±47.1	0.004
LDL-c	86.4±39.6	95.0±39.9	86.3±31.1	106.2±36.2	0.076
HDL-c	31.0(27.0-41.0)	40.0(36.0-49.0)	27.5(23.7-32.2)	33.0(28.0-41.7)	0.006[a]
Triglycerides	108.0(76.5-121.0)	118.0(87.0-166.0)	119.0(94.7-174.7)	146.0(111.0-190.0)	<0.001[a]
Troponin	5019.0(160.0-12967.5)	21880.0(1858.2-51770.0)	5564.0(117.9-25670.0)	537.1(11.9-9786.0)	0.035[a]
LOS	10.5(7.0-21.7)	13.5(8.7-14.7)	10.0(7.2-14.8)	9.0(7.0-15.0)	0.693[a]
TIMI score	4.0(3.0-5.0)	3.0(2.0-6.0)	3.0(2.2-4.0)	3.0(2.0-4.0)	0.206[a]

Discussion

The outcomes of our study revealed a significant prevalence of NWO in individuals with ACS. Approximately 1 in 10ACS patients exhibit this NOW phenotype. Notably, when narrowing our focus to patients falling within the normal weight range, this obesity phenotype was detected in almost 30% of them. These findings underscore the notion that relying solely on a normal BMI may not adequately exclude patients from the scrutiny of healthcare practitioners concerning potential associated risks. To the best of our knowledge, this is the first study that has specifically assessed NWO in patients with ACS. Investigations conducted in other population groups, which evaluated NWO and utilized BIA as a method for assessing body fat percentage, have reported lower prevalence. For instance, Coelho et al. [14] examined Brazilian adults aged 23 to 39 years and reported a prevalence of 6%. Another study conducted by Jia et al. [15] found a prevalence of 7.46% for NWO in Chinese adults aged over 20 years, with a mean age of 44.88±13.49 years. Berg et al. [16] demonstrated that 9% of Swedish adults aged 25 to 74 years were classified with NWO. Mannisto et al. also studied individuals aged 25 to 74 years and found similar results in their male population (10%), but a higher prevalence in females (19%).

Divergent findings with higher prevalence rates have also been documented in other studies. Kapoor et al., Correa-Rodriguez and He et al. [17-19] reported prevalence rates of 31.7%, 29.1%, and

17.0% for NWO, respectively. These investigations encompassed individuals aged between 30 and 60 years, 18 and 30 years, and 20 and 80 years, respectively. It's noteworthy that the age ranges of the participants in these studies are considerably wider leading to a notable diversity in the age distribution of patients. Furthermore, inconsistencies in defining the NWO phenotype, particularly regarding the specific body fat percentage cutoffs and their variation across sexes, along with the variability of ethnicities included in different studies, are factors that contribute to the variations in prevalence rates observed in the existing literature.

Regarding NWCO, the prevalence described in the literature exhibits considerable variability, making direct comparisons challenging, primarily due to the lack of standardized criteria for defining abdominal circumference cutoff points. In our study of ACS patients, we identified a lower prevalence of NWCO (5.6%) compared to NWO. A prior study by Mohamed et al. [20] reported a much higher prevalence of 21.2% for individuals aged 40 to 60. However, it's important to consider that this study employed a different waist circumference cutoff (waist circumference > 94cm for men and > 80cm for women) to define central obesity. Conversely, Kalvari et al. using the same waist circumference cutoff points as our study, found an NWCO prevalence of 10% in. Excessive abdominal fat, encompassing both visceral and subcutaneous adipose tissue, constitutes a predisposing factor for an elevated mortality risk, even in individuals with a normal BMI. Visceral fat behaves differently from subcutaneous fat, largely due to its metabolically active nature. Those with OCPN exhibit a limited capacity to store lipids subcutaneously in comparison to overweight and obese individuals. This circumstance could potentially place them at a disadvantage in terms of mortality risk, particularly among those with higher levels of visceral adipose tissue [21].

The higher prevalence of NWO in men contrasts with some previous findings that indicated a higher occurrence of this nutritional phenotype in females. Marques-Vidal et al. [22] reported a prevalence of 2.8% in men and 5.4% in women, while Correa-Rodriguez et al. [18] similarly noted a greater prevalence in females (2.0% in men and 46% in women). Conversely, Jia et al. [15] reported higher prevalence among men (6.71% to 10.16% in men and 1.73% to 6.64% in women), aligning with our observations. Nonetheless, like the overall NWO prevalence, these disparities can be attributed to variations in the cutoff points for percentage of body fat, ethnicities and age groups. Additionally, our study encompassed a distinct patient profile from the studies, focusing solely on ACS patients. On the other hand, NWCO was more prevalent in women, as has been demonstrated by other authors [20]. Kouvari et al. [23] indicated a fourfold higher number of NWCO cases in females. Shirasawa et al. [24], using the waist-to-hip ratio as a criterion for central obesity, also reported a higher prevalence in women (30.2% vs. 15.6%). Two significant factors related to fat distribution in females might explain these findings. Firstly, women with normal weight, despite having smaller adipocytes than men, have a greater number of adipocytes per unit of mass in the abdominal subcutaneous adipose tissue, suggesting hyperplastic expansion of subcutaneous abdominal adipose tissue [25]. Moreover, during menopause, a phase that corresponds to the age range of our patient profile, there is a substantial reduction in estrogen levels accompanied by an increase in adipose tissue mass. This transition is also associated with a change in fat distribution, shifting from a predominant gluteal-femoral subcutaneous adipose tissue to abdominal subcutaneous adipose tissue, resulting in a more central fat distribution pattern [26-28].

The higher prevalence of systemic arterial hypertension in individuals with NWO aligns with the findings presented by Correa-Rodrigues et al. [18], Jia et al. [15] and Romero-Corral et al. [29] when analyzing cardiometabolic risks in individuals aged >20 years. Kapoor et al. [17] investigating individuals between 20 and 60 years with diabetes risk, also found significantly elevated blood pressure levels in those with NWO when compared to individuals with normal BMI and percent body fat, as well as to individuals with obesity. Well-established mechanisms such as increased sodium reabsorption by the Henle loop, insulin resistance, heightened sympathetic nervous system activity, activation of the renin-angiotensin-aldosterone system and altered vascular function explain the relationship between elevated blood pressure and obesity. It is postulated that individuals with NWO have sufficient adipose tissue to trigger these mechanisms, elucidating the similar or even higher blood pressure levels observed in these individuals compared to the obese and overweight counterparts [30,15]. Furthermore, certain insights attained suggest that the cardiovascular risk in individuals with NWO can be attributed to compromised systolic and diastolic function of the left ventricle, which has been found in these patients. This impairment is secondary to abdominal fat deposition, pro-fibrotic and pro-inflammatory states, as well as increased insulin resistance. This pre-clinical myocardial dysfunction can even progress gradually to manifest cardiomyopathy [31] The higher number of sedentary individuals within the NWO group compared to all other analyzed phenotypes underscores that physical inactivity contributes to an inadequate nutritional profile. Even if an individual maintains their weight within the normal range, an unfavorable body composition with excess fat can still prevail. Prior studies have demonstrated that an active lifestyle imparts a more favorable body composition profile [32] while sedentary behavior favors the NWO phenotype [33].

The increased mortality observed in individuals with NWO aligns with findings presented by Romero-Corral et al. [29] who also demonstrated an independent association between cardiovascular mortality and NWO in women. These findings can be elucidated based on the various cardiovascular alterations present in individuals with NWO, including increased subclinical vascular inflammation, subclinical atherosclerosis with vulnerable plaques, greater vascular stiffness, and asymptomatic impairment of left ventricular systolic and diastolic function [31,34,35]. Furthermore, we also noted that patients with NWO exhibited a higher need for coronary artery bypass graft surgery. However, given the absence of previous studies reporting NWO in ACS patients, data regarding adverse outcomes secondary to ACS are still lacking in the literature. The higher frequency of MS in patients with NWCO, but not in individuals with NWO, can be attributed to the fact that waist circumference is included in the diagnostic criteria

for metabolic syndrome [9]. Notably, excessive abdominal fat, especially visceral adipose tissue, has been associated with insulin resistance, dyslipidemia and inflammation, which are predisposing factors for MS [36]. Another important aspect to consider regarding the metabolic risk associated with NWCO is the limited muscle mass in these patients. Like NWO, individuals with this phenotype of obesity may have sarcopenic obesity, as having a normal weight with a high percentage of body fat makes them strong candidates for having limited amounts of muscle mass, particularly among the older individuals who constitute a significant portion of our studied patient profile [37].

The observed higher troponin levels in patients with NWCO can be attributed to the fact that troponin serves as a marker for myocardial injury. The accumulation of abdominal fat, in and of itself, possesses the potential to induce detrimental effects on myocardial function through a cascade of mechanisms involving inflammatory cytokines, activation of the renin-angiotensin-aldosterone system, insulin resistance, hyperinsulinemia and the process of lipotoxicity due to lipid buildup in cardiac tissue. These interconnected factors collectively contribute to the impairment of myocardial energy utilization, apoptosis of myocardial cells and an increase in fibrotic processes [38,39].

Several limitations should be acknowledged in this study. First, the cross-sectional design inherently prevents us from establishing causality between variables. Second, our study was conducted within a single hospital center, which may limit the generalizability of our findings due to the non-representative sample of ACS patients. Third, the use of BIA for assessing body fat may have limitations, particularly concerning hydration issues often observed in older individuals, potentially leading to an underestimation of body fat and an overestimation of fat-free mass. Furthermore, the chosen cutoff points for %GC in this investigation correspond to elevated levels of body fat, exceeding those employed in prior studies. Nevertheless, it is important to note that the adopted cutoff was suggested by prominent scientific institutions (ESPEN and EASO) [5]. Another aspect to be considered is that important risk markers that could be added to the study of the topic were not evaluated, such as sirtuina, a promising marker in the study of obesity profiles and metabolic changes [40]. Despite these limitations, the key strength of our study lies in being, to the best of our knowledge, the first to explore the discussed obesity phenotypes within a cohort of ACS patients. This underscores the significance of employing alternative nutritional assessment measures beyond BMI for diagnosing and evaluating potential cardiometabolic risks [41-56].

Conclusion

Individuals with ACS exhibited a high prevalence of overweight, excessive body fat and central obesity. Furthermore, a substantial proportion of individuals displayed the NWO phenotype and, to a lesser extent, the NWCO phenotype. The NWO phenotype was more prevalent in men, individuals with hypertension, and those leading sedentary lifestyles, while the NWCO phenotype was more common among women. NWO was linked to increased mortality, and NWCO was associated with MS and higher levels of serum TC and troponin. The connection between NWO and NWCO with adverse outcomes and metabolic risk underscores the importance of characterizing distinct nutritional phenotypes. The combination of parameters used for their identification could serve as a screening tool for poor prognosis among ACS patients.

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