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The Metabolic Syndrome and Mammographic Breast Density in a Racially Diverse and Predominantly Immigrant Sample of Women

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Abstract

Purpose—The metabolic syndrome (MetS, clustering of elevated blood pressure, triglycerides and glucose, reduced high-density lipoprotein cholesterol (HDL-C), abdominal obesity) has been associated with increased breast cancer risk, but less is known about its association with mammographic breast density, a strong risk factor for breast cancer.

Methods—We collected data on risk factors, body size and blood pressure via in-person interviews and examinations, and measured glucose, triglycerides, and HDL-C from dried blood spots from women recruited through a mammography screening clinic (n=373; 68% Hispanic, 17% African American; 63% foreign born). We performed linear regression models to examine the associations of each MetS component and the MetS cluster (≥ 3 components) with percent density and dense breast area, measured using a computer-assisted technique and Cumulus software.

Results—About 45% of women had the MetS, with the prevalence of the individual components ranging from 68% for abdominal obesity to 33% for elevated triglycerides. The prevalence of the MetS increased with higher body mass index (BMI) and postmenopausal status, but did not vary substantially by ethnicity, immigrant generational status, parity, age at menarche or alcohol consumption. Low HDL-C (< 50 mg/dL), but not the MetS cluster or the other MetS components, was associated with larger dense breast area after adjusting for age, BMI, fasting time, and

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Competing Interests

Authors declare they have no competing interests.

educational attainment (β=8.77, 95% CI=2.39, 15.14). The MetS and its individual components were not associated with BMI-adjusted percent density.

Conclusions—HDL-C alone may have an influence on dense breast tissue that is independent of BMI, and may be in the same direction as its association with breast cancer risk.

Keywords

mammographic breast density; breast cancer; metabolic syndrome; HDL-Cholesterol; waist circumference; hypertension; triglycerides; glucose; Hispanic; immigrants

Introduction

The metabolic syndrome (MetS) refers to the presence of multiple biochemical abnormalities and related clinical conditions, including elevated blood pressure, triglyceride and glucose levels, low high-density lipoprotein cholesterol (HDL-C) levels, and excess body weight or abdominal obesity [1, 2]. An established risk factor for type II diabetes and cardiovascular disease, the MetS has more recently been associated with the risk of many common cancer sites, with some associations being stronger in women and for female-specific cancers [3]. A meta-analysis of nine studies reported an overall 52% increased risk of postmenopausal breast cancer in women with MetS, which exceeded the range of 8% to 39% increased risk associated with any individual component of the MetS [4]. Additionally, the MetS and/or its individual components may be more prevalent in breast tumors with more aggressive and poorer prognostic characteristics (e.g., later stage, larger tumors, triple negative tumors), and may lower survival following breast cancer diagnosis [5–9].

Mammographic breast density reflects the amount of epithelial and stromal (dense) breast tissue, and may represent one intermediate marker for breast cancer risk [10]. In addition to strong associations with future breast cancer risk [11–13], the associations of mammographic density with risk factors that reflect estrogen-related exposures (e.g., hormone replacement use, parity) are in the same direction as their associations with breast cancer risk [14]. However, the evidence on the associations between mammographic density and other risk factors relevant to metabolic abnormalities are more mixed with physical activity showing mostly null associations [15], diabetes showing null to inverse associations [16, 17], and larger body size showing consistently strong and inverse associations [18–21]. The few studies that have examined the MetS or its components in relation to mammographic density have produced mixed results of null to modest positive as well as inverse associations [22–28]. These associations have been similar for both absolute and relative measures of mammographic density, which respectively capture the amount of dense breast tissue only and incorporate the amounts of both dense and fat breast tissues [22–24, 26–28].

Given that mammographic density can be monitored over time through routine screening mammography, quantifying its associations with potentially modifiable and easily assessed risk factors such as the MetS components may help in breast cancer risk reduction and prevention efforts. Research in this area can also benefit from studying diverse populations as the risk of the MetS components, breast cancer and mammographic density patterns show

variation by race/ethnicity and immigration [29–36]. Here, we examined the associations between the MetS as a cluster and its individual components with mammographic density in a socially diverse urban midlife sample of women.

Methods

Study Population

Between November 2012 and May 2014, we recruited 400 women as they presented for routine screening mammography appointments at Columbia University Medical Center (age range 40–64 years; mean±standard deviation [SD]: 50.5±5.8). The study sample represents the catchment community served by Columbia University Medical Center in terms of race/ethnicity and immigrant background, but the study sample has higher educational profile than the community [37]. The rate of recent mammography among women aged 40 and older in this community is about 80%, and thus, the study population also represents the majority of community women in this age group [37, 38]. Trained research personnel interviewed women in English (56%) or Spanish (44%) on sociodemographic and risk factors data, obtained anthropometric and blood pressure measurements, and collected blood samples. We collected copies of digital mammograms, performed on the same day as the enrollment and data collection, for 395 participants. We excluded participants with breast implants (n=9), and missing data on blood biomarkers of the MetS (n=13), leaving a final sample of 373 (93% of total sample) for the current analysis.

Measures

Body Size and Metabolic Syndrome—We measured women's height using a stadiometer, weight using a digital scale and waist circumference using a measuring tape; all measurements were done in light clothing and without shoes. After at least 5 minutes of rest time in sitting position, we obtained three consecutive blood pressure measures using an automated blood pressure machine, and used the average of the last two measures in data analysis.

We measured non-fasting glucose, triglycerides and HDL-C in dried blood spots (DBS), and converted the levels for each biomarker to plasma-equivalent levels as described below. We collected capillary whole blood samples from women's middle or ring finger, which were placed on DBS filter paper (903 protein saver card, Whatman, Piscataway, NJ), dried at room temperature and subsequently frozen in plastic bags with desiccant packs before being shipped to the University of Washington, Department of Laboratory Medicine (UWLM) where the samples were stored with desiccant at −80°c. For each assay, a single 3.2 mm diameter disc was punched from a DBS sample (BSD700 Semi-Automated Dried Sample Puncher; BSD Robotics, Brisbane, QLD, Australia) into a microtiter plate assay well (Greiner Bio-One, Monroe, NC) alongside UWLM assay calibrators and quality control DBS samples. UWLM biomarker-specific elution buffer was added to each microtiter plate well and the microplate was shaken for 1 hour at room temperature. An aliquot from each well was transferred to a microtiter assay plate (Greiner Bio-One), to which UWLM biomarker-specific reagents including a fluorophore were added. The plate was then shaken for 30 seconds, and incubated at 37°c for 30 minutes. The fluorescence intensity (RFU) of

each well was read at 530/25 nm excitation and 590/35 nm emission (Synergy HT Microtiter Plate Reader, BioTek, Winooski, VT). A linear regression calibration curve, constructed by plotting the concentrations of the calibrators (UniCel DxC 800 Synchron Clinical System, Beckman Coulter, Miami, FL) against their measured fluorescence values, was used to convert the blank-subtracted RFU value of each DBS sample into a biomarker concentration (Gen5, BioTek). Each DBS biomarker concentration was transformed into a plasma-equivalent biomarker concentration (i.e ., the biomarker concentration that would be expected to be obtained had the DBS sample been a conventional plasma sample) via a linear regression equation derived from analyses of DBS vs. DBS-matched plasma samples from venous blood (UniCel DxC 800 Synchron Clinical System). Assay performance characteristics for the biomarkers of HDL-C, triglycerides and glucose from DBS samples and venous blood plasma samples respectively had Pearson correlation coefficients of 0.86, 0.98, and 0.96 (n=86–132); intra-assay CVs of 5.2%, 3.7% and 5.1%; and inter-assay CVs of 8.0%, 4.4% and 6.5%.

As per modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines, we defined the MetS by the presence of at least three of the following components: measured systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or taking anti-hypertensive medication, abdominal obesity or waist circumference of > 88 cm, triglycerides ≥ 150 mg/dL, glucose ≥ 100 mg/dL, HDL-C < 50 mg/dL [39].

Mammographic density—We calculated the total dense area (in squared centimeters) and percent density (dense area/total breast area in percentage) using a computer assisted method, in which a trained reader, blinded to all study data, used a computer thresholding software (Cumulus) to outline the areas corresponding to the total breast and dense breast tissue on digital mammograms [40]. Additionally, we calculated the non-dense area by taking the difference between total breast area and dense area. We evaluated the cranio-caudal images of the left breast for all participants in randomly sorted batches of approximately 50 mammograms, and duplicated the assessment for 10% of mammograms. The intraclass correlation coefficient was 0.95 for percent density, 0.78 for dense area and 0.94 for nondense area. The Pearson correlation coefficients for repeated measures were 0.94 for percent density, 0.92 for dense area, and 0.99 for nondense area.

Covariates—Breast cancer risk factors considered included menopausal status (premenopausal or perimenopausal status defined as menstruating in the last 12 months with no bilateral oophorectomy or hysterectomy and no current hormone replacement therapy (HRT) use, post-menopausal status defined as no menstruation in the last 12 months or history of bilateral oophorectomy or hysterectomy within 18 months of last menstrual period and no HRT use), parity (nulliparous, 1–2, ≥3 births), age at first live birth (< 25, 25–29, ≥30 years), age at menarche (in years), family history of breast cancer in first degree relatives, alcohol consumption status (never, former, current defined as drinking in the past 12 months), smoking status (never, former, current), fasting time to blood sample taken (< 3, 3–6, ≥ 6 hours), BMI (in kg/m^2; continuous and categorized into <25, 25–29, ≥30), self-reported type II diabetes, immigrant generational status (first generation or foreign-born, second generation or U.S.-born to at least one foreign-born parent, third or higher generation

or U.S.-born with U.S.-born parents), educational attainment (less than high-school, high school graduate, some college, bachelor's or higher degree), and race/ethnicity (Hispanic, Non-Hispanic White, Non-Hispanic African American, Non-Hispanic Asian).

Statistical Analysis

We examined descriptive statistics for breast cancer risk factors and sociodemographic variables by the MetS status. We selected age, BMI, and fasting time as a priori covariates in multivariable analysis, and further identified possible confounders as variables that changed the age-adjusted estimates of the association between the MetS and any individual MetS component and either measures of mammographic density by more than 10%. We used linear regression models to examine the associations of the MetS and its components with continuous measures of percent density and dense area. We repeated the final multivariable models without adjustment for BMI given the possible causal relationship of BMI with the MetS. We further tested the interaction of the MetS and its components with: 1) BMI, 2) menopausal status, 3) race/ethnicity and 4) generational status, by introducing cross-product terms between these variables in the linear regression models of percent density and dense area. We repeated our multivariable analysis excluding the participants with type II diabetes and obtained similar results. Finally, we examined the associations between the MetS and its components with non-dense area as the outcome. All tests were 2-sided and performed using SAS 9.3 (SAS Institute, Gary, NC).

Results

About 45% of participants met the definition of the MetS. As compared with participants without the MetS, those with MetS were on average 3.2 years older, had lower educational attainment (e.g., 30% vs. 14% with less than high school education), were more likely to have BMI ≥30 kg/m^2 (63% vs. 28%), be postmenopausal (61% vs. 39%), and have Type II diabetes (18% vs. 3%) (Table 1). Participants with MetS were also slightly more likely to have fasting time of less than 3 hours (48% vs. 39%), but the average fasting time was not significantly different by MetS status, with the average fasting time of 4.7 and 4.5 hours respectively in those with and without the MetS ($p<0.67$). There were no significant differences in the MetS status by race/ethnicity, generational status, age at menarche, parity, age at first live birth, and alcohol consumption and smoking status (Table 1).

BMI was not correlated with HDL-C, but was strongly positively correlated with waist circumference (Pearson correlation coefficient [r] =0.84), and modestly positively correlated with other MetS components (range from r=0.12 for triglycerides to r=0.30 for diastolic blood pressure). BMI was also inversely linearly correlated with percent density (r=−0.36), but had minimal correlation with dense area (r=0.10).

The majority of participants with any individual MetS component had two or more other risk factors, and were therefore classified as having the MetS (Figure 1). Abdominal obesity, the most common individual MetS component, was present in 68% of all participants; about 60% of those with abdominal obesity met the MetS definition. The presence of elevated triglycerides was the least prevalent MetS component in the overall sample at 33%, but 77% of those with elevated triglycerides met the MetS definition (Figure 1). Abdominal obesity

was the most prevalent MetS component among all ethnic groups with the exception of the 13 participants of Asian ethnicity, for whom elevated blood pressure or taking hypertensive medications was the most common component (Figure 2, Panel A). About half of

Hispanic and white participants had elevated glucose while 57% of African Americans had elevated blood pressure or were taking antihypertensive medications. The relative distribution of MetS components varied slightly across generational status, with abdominal obesity as the most prevalent and elevated triglycerides as the least common MetS component in all immigrant generation levels (Figure 2, Panel B). The largest differences were observed for elevated blood pressure, which had lower prevalence in first-generation (45%) and second-generation women (33%) than in third-generation women (56%); however, this higher prevalence in third generation may have been due to the larger proportion of African Americans in this group (~64% of third-generation women with elevated blood pressure were African Americans, as compared to 8% Hispanics and 28% whites).

Beyond the selected *a priori* covariates of age, BMI and fasting time, all measured at the time of the mammographic screening, the only factor that altered the associations of the MetS and any individual MetS component with percent density or dense area was educational attainment; this variable was added to the final multivariable models. The MetS was inversely associated with percent density in the multivariable model that adjusted for age, fasting time and educational attainment (, but this association was largely accounted for after further adjustment for BMI (β=−1.05, 95% CI: −4.47, 2.37 in the fully adjusted model) (Table 2, Panel 1). Similarly, the inverse association between abdominal obesity and percent density was reduced and no longer statistically significant with adjustment for BMI. No other associations were observed between any of the MetS components and percent density.

With the exception of elevated triglycerides, the presence of the MetS and the remaining MetS components showed positive associations with dense area in age adjusted models, although only the associations for low HDL-C (β=9.55 95% CI: 3.20, 15.90) and abdominal obesity (β=9.36 95% CI: 2.58, 16.14) reached statistical significance (Table 2, Panel 2). The association between low HDL-C and larger dense area persisted after adjustment for BMI, fasting time, and educational attainment (β=8.77, 95% CI: 2.39, 15.14).

We did not find support for additive statistical interactions between the MetS or its components and BMI, menopausal status, race/ethnicity and immigrant generational status (all p-values for interaction terms > 0.05). We further explored variations in the observed associations through stratified analysis by obesity (obese or BMI≥30 and nonobese or BMI<30) and menopausal status (pre/peri- and postmenopausal) (data not shown). There were some indication of differences in the strength of the association between low HDL-C and larger dense area by menopausal status, with the association being stronger and statistically significant in premenopausal (β=12.48, 95% CI: 3.71, 21.26) as compared with postmenopausal women (β=4.52, 95% CI: −4.54, 13.58). Abdominal obesity also had a stronger association with lower percent density (β=−5.37, 95% CI:−10.10, −0.64) in non-obese womenthan in obese women (β=−0.38, 95% CI:−15.02, 14.26).

The MetS cluster, abdominal obesity, elevated glucose and high blood pressure were positively associated with non-dense area in age adjusted model, but there were no associations between any of these factors and nondensea area after adjustment for BMI (e.g., β=8.54, 95% CI: −4.22, 21.30 for MetS vs. no MetS) (Data not shown).

Given that we measured biomarkers from nonfasting blood, we repeated the multivariable models in the sample restricted to those who had fasted ≥3 hours and again to those who had fasted ≥ 6 hours. The results similarly showed only a positive association between low HDL-C and larger dense area (e.g., low HDL-C measured in blood with ≥ 3 hours and with ≥ 6 hours of fasting was associated respectively with 11.82 cm^2 (95% CI: 4.14, 19.50) and 7.19 cm^2 larger dense area (95% CI: −2.85, 17.22).

Discussion

In a predominantly racial/ethnic minority and immigrant study population of women in their midlife, we did not observe an association between the MetS as defined by the presence of three or more metabolic risk components and the absolute amount of fibroglandular breast tissues on mammograms as measured by dense breast area. However, we observed an association between low HDL-C and larger dense area, which persisted even after accounting for factors with strong influences on HDL-C and mammographic density including BMI. There were no associations between the MetS cluster or any of its individual components with percent density, capturing the amount of dense area relative to total breast area, after accounting for differences in BMI.

Two prior studies have used similar methodology for assessing the metabolic syndrome and mammographic density [22, 23]. One study, conducted in a cohort of predominantly Caucasian and Asian pre- and early perimenopausal women with a low prevalence of the MetS (15%), reported no associations between the MetS and mammographic density in cross-sectional analysis as well as in analysis involving longitudinal changes in mammographic density [22]. The second study included pre- and postmenopausal women in the Mexican Teacher's Cohort (ESMaestras) from two states in Mexico with a higher prevalence of the MetS (21–40% in premenopausal women and 39–51% in postmenopausal women) that was similar to the prevalence in our study (32% in premenopausal and 51% in postmenopausal women). The ESMaestras study reported a positive association between the MetS and percent density and dense area (differences of ~5% and 6.3 cm^2, respectively) that was limited to premenopausal women in one of the two states. Abdominal obesity was the most common MetS component in our and these two studies, but there were substantial differences in the prevalence and co-occurrence of other components across studies, suggesting different biological profiles of the MetS across these populations. The lack of strong support in these few studies using similar methodology in different study populations suggest that the MetS may not increase breast cancer risk through influencing mammographic density. However, it is also possible that a one-time assessment of the MetS may not sufficiently capture the mechanism linking the MetS to breast cancer risk via mammographic density.

More studies have assessed the associations of individual components of the MetS and mammographic density. Abdominal obesity as measured by waist circumference has been consistently associated with lower percent density and larger dense area, but these associations, as observed in our study, are largely reduced after adjustment for general obesity as measured by BMI [22, 23]. Compatible with our findings, there has been little to no support for associations between elevated glucose [41, 42, 22, 23], triglycerides [23, 22] and blood pressure [23, 22] with either percent density or dense area after accounting for BMI. The results are more mixed for HDL-C. In our study, we observed reduced HDL-C (< 50 mg/dL) to be associated with larger dense area after adjusting for BMI and other covariates, with the association being stronger in premenopausal women. Low HDL-C at the level used in our study was also associated with larger dense area and higher percent density among premenopausal women from one state in the ESTMaestra study [23]. The magnitude of the association between dense area and high HDL-C categories observed in our study is similar to that reported in the ESTMaestra study. HDL-C and percent density were also inversely associated in a small sample of postmenopausal women [26]. In contrast, other studies have reported positive associations between HDL-C levels and mammographic density in premenopausal women [25, 43, 44], as well as null associations in premenopausal [22] and postmenopausal women [24, 27]. Most, but not all [45, 46, 38], studies of HDL-C and breast cancer risk support a protective effect for high HDL-C although results across BMI categories and menopausal status have been inconsistent [47–51, 3]. Taken together, HDL-C may have an influence on breast cancer risk and this may be mediated through mammographic density, but the direction of the association remains unclear and is likely to depend on modification by other factors. The biological mechanisms underlying HDL-C and breast cancer may involve complex processes influencing exposures to proinflammatory factors and endogenous estrogen that stimulate breast tissue proliferation. Additional investigations are clearly needed to better understand these relationships, and are of substantial public health and clinical interest. As HDL-C may be modified through behavioral and pharmaceutical interventions [60], and if related to mammographic density, which is easily monitored through routine mammography, it may offer opportunities for combined efforts to reduce the risks for CVD and breast cancer.

Our results add to the limited empirical literature on the relationship between metabolic risk factors and mammographic density in a diverse study population with sufficient variations in metabolic risk factors and mammographic density. We did not find significant variations in the associations between metabolic risk factors and mammographic density across racial/ethnic groups and between foreign- and U.S.-born women, and only observed differences in the strengths of the association between HDL-C and dense area by menopausal status. However, caution should be exercised when interpreting these results as the small subgroup sizes may have limited the statistical power to detect significant differences. Study participants were not instructed to fast at the time of mammography and enrollment into the study, but we accounted for fasting time in our statistical analysis. Similar to other studies in this area, we used a single measure of metabolic biomarkers collected concurrently with mammographic density data; however, a single measure may not sufficiently capture the long-term risk of metabolic disorders and their associations with mammographic density. We used DBS samples for assessment of blood-based metabolic biomarkers, which while

not used in prior investigations of metabolic risk factors with breast cancer risk or mammographic density, have been validated against venous blood samples in prior studies [61–65], and are being increasingly used in large ongoing community surveys including the National Longitudinal Study of Adolescent Health and the National Social Life, Health, and Aging Project [66]. Our prior experience in collecting venous blood from women recruited in community-based mammography clinics similar to the setting in the present study had presented considerable logistical barriers and an overall low response rate for undergoing venipuncture. The DBS collection offers a highly feasible alternative as it is minimally invasive and easily collected by non-phlebotomists, and requires no centrifugation or immediate freezing [66]. However, the laboratory methodologies for DBS samples are less standardized. Given that the laboratory was blinded to mammographic density measures, any measurement error in biomarkers would be nondifferential, and may have contributed to an underestimation of the true association and hence the observed null associations of the MetS and most components with mammographic density in our study. Our study benefited from using digital mammograms that were all obtained at a single institution on the same day as blood sample collection and evaluated by the same reader, and from analyzing all blood samples at a single laboratory, thereby reducing potential errors associated with variations in these factors. Our measures of mammographic density were highly reproducible as determined by a subset of duplicated reads, and any error should be nondifferential with respect to metabolic risk factors as the reader was blinded to this data.

In summary, our results do not support an association between the MetS as a cluster of three or more metabolic risk factors and mammographic density as measured by percent and dense breast area. We found that HDL-C alone may have an influence on dense breast area that is independent of BMI, and may be in the same direction as its association with breast cancer risk. If confirmed in other studies, these results suggest that chronic disease prevention efforts to increase HDL-C levels may potentially have a favorable impact on breast density.

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List of abbreviations

MetS	metabolic syndrome
HDL-C	High density lipoprotein cholesterol

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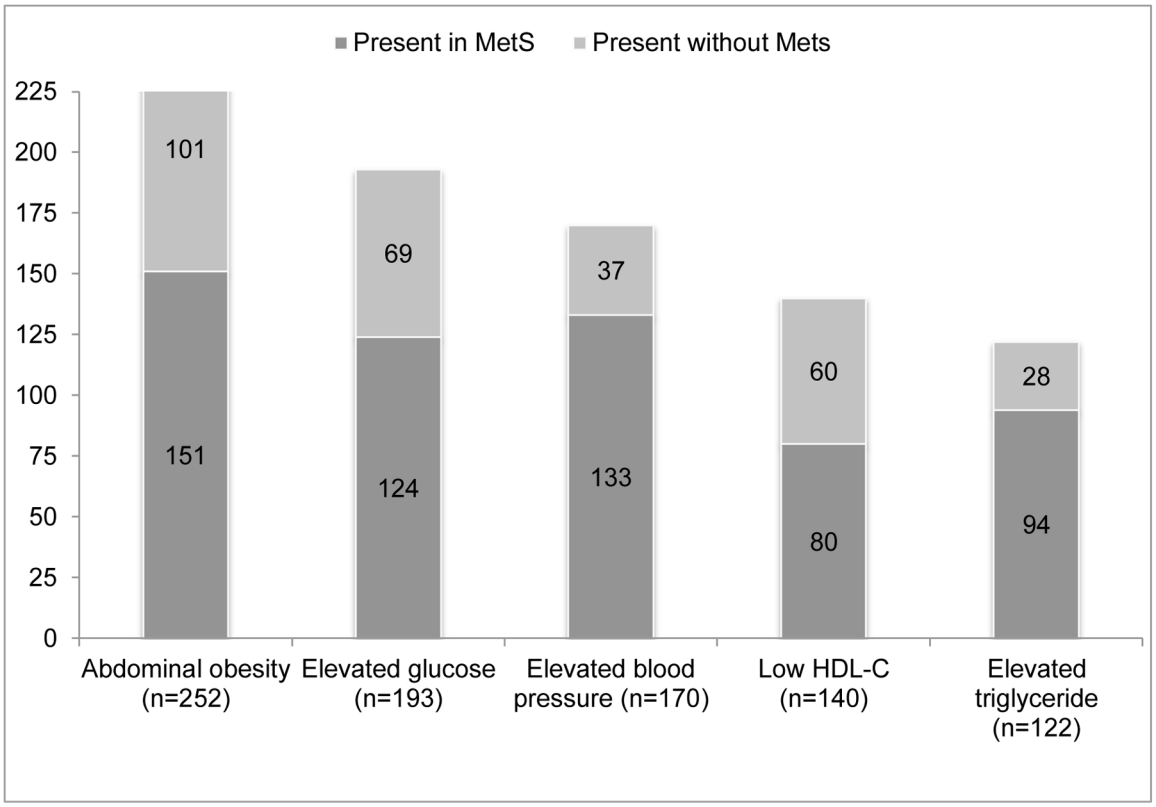

Figure 1.
Number of participants with each metabolic risk factors by metabolic syndrome status

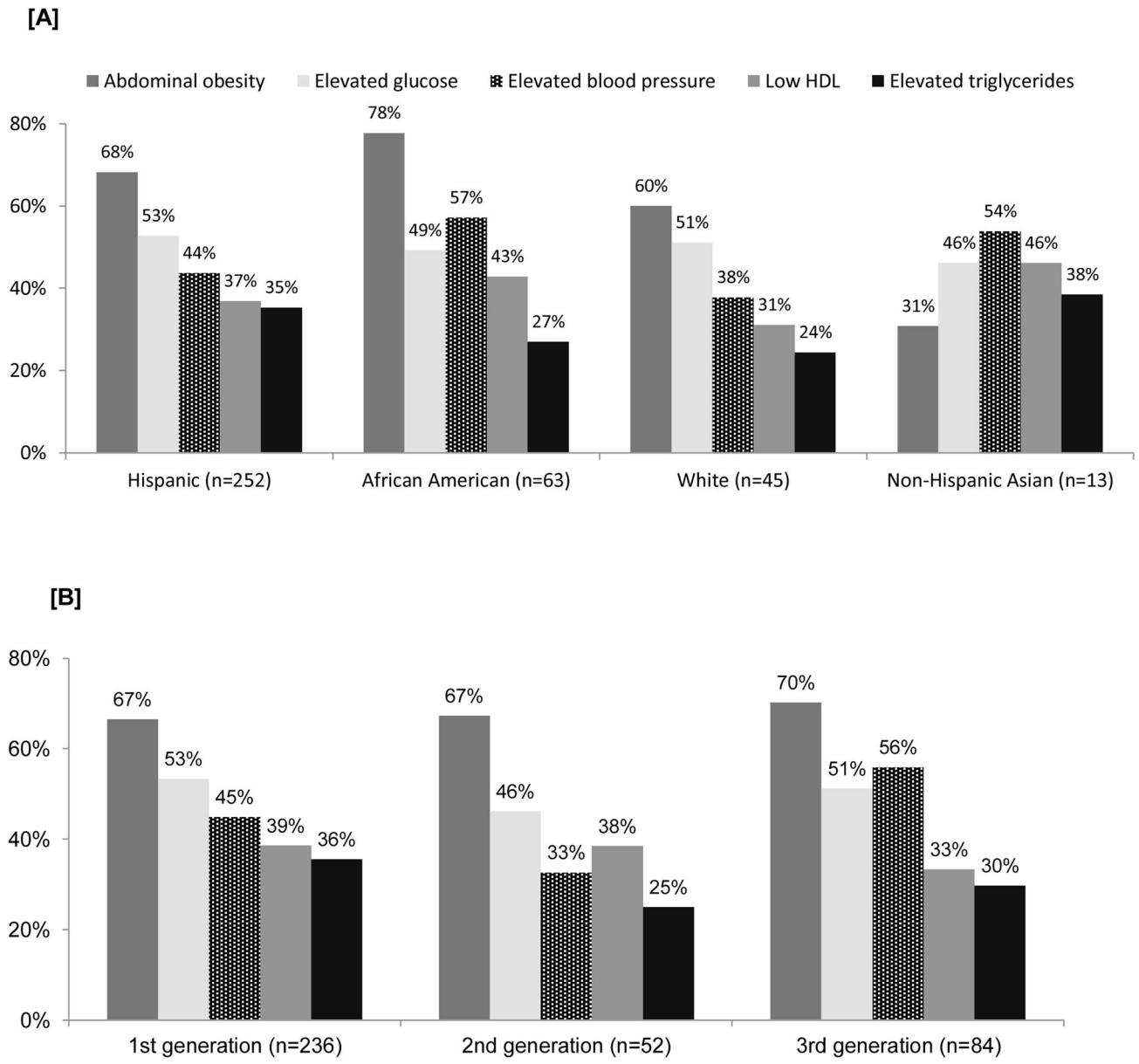

Figure 2.

Percentage of participants with each metabolic risk factor by race/ethnicity [A] and immigrant generational status [B]

Table 1

Sample characteristics by the metabolic syndrome status (n=373)

Characteristics	Total Cohort	With MetS (n=166)	Without MetS (n=207)
Age in years, Mean (SD)	50.5 (5.9)	52.3 (5.6)	49.1 (5.7)
Race/Ethnicity, n (%)			
Hispanic	252	116 (69.9)	136 (65.7)
Non-Hispanic White	45	16 (9.6)	29 (14.0)
Non-Hispanic Black	63	30 (18.1)	33 (15.9)
Non-Hispanic Asian	13	4 (2.4)	9 (4.4)
Education, n (%)			
Less Than High School	79	50 (30.1)	29 (14.0)
High School Graduate	85	40 (24.1)	45 (21.7)
Some College	86	36 (21.7)	50 (24.2)
Bachelor's or higher degree	123	40 (24.1)	83 (40.1)
Immigrant generational status, n (%)			
1st generation	236	110 (66.3)	126 (60.9)
2nd generation	52	18 (10.8)	34 (16.4)
3rd generation	84	38 (22.9)	46 (22.2)
Body Mass Index, n (%)			
<25.0 kg/m^2	70	5 (3.0)	65 (31.4)
25.0–29.9 kg/m^2	141	56 (33.7)	85 (41.1)
≥30 kg/m^2	162	105 (63.3)	57 (27.5)
Positive Family history of breast cancer	45	22 (13.3)	23 (11.1)
Menarche, mean (SD)	12.7 (1.9)	12.7 (1.9)	12.7 (1.9)
Number of Live Births, n (%)			
0	46	17 (10.2)	29 (14.0)
1–2	205	87 (52.4)	118 (57.0)
≥3	122	62 (37.4)	60 (29.0)
Age at First Birth, n (%)			
<25 Years Old	176	84 (50.9)	92 (44.9)
25–29 Years Old	69	30 (18.2)	39 (19.0)
30+ Years Old	79	34 (20.6)	45 (22.0)
No Live Births	46	17 (10.3)	29 (14.2)
Menopausal Status, n (%)			
Pre/Peri-menopausal	187	63 (38.9)	124 (60.8)
Post-menopausal	179	99 (61.1)	80 (39.2)
Alcohol consumption status, n (%)			
Never	170	79 (47.9)	91 (44.0)
Former	35	19 (11.5)	16 (7.7)
Current	167	67 (40.6)	100 (48.3)
Smoking status, n (%)			
Never	253	102 (62.2)	151 (73.0)

Characteristics	Total Cohort	With MetS (n=166)	Without MetS (n=207)
Former	76	40 (24.4)	36 (17.4)
Current	42	22 (13.4)	20 (9.7)
Fasting Time, n (%)			
< 3 Hours	159	79 (47.9)	80 (38.8)
3 ≤ Hours <6	131	48 (29.1)	83 (40.3)
≥ 6 Hours	81	38 (23.0)	43 (20.9)
Positive type II diabetes status	36	29 (17.5)	7 (3.4)

Table 2

Linear regression coefficients (β) and 95% confidence intervals (CI) for the associations between metabolic risk factors and mammographic density

	Adjusted for age		Adjusted for age and BMI		Adjusted for age, fasting time, education		Adjusted for age, fasting time, education, BMI	
	β	(95% CI)	β	(95% CI)	β	(95% CI)	β	(95% CI)
Percent Density								
Metabolic syndrome (≥3 metabolic components)	−4.71	(−8.06, −1.35)	−1.05	(−4.47, 2.37)	−4.47	(−7.84, −1.10)	−0.70	(−4.15, 2.74)
Individual components Abdominal Adiposity (WC ≥88cm vs. < 88cm)	−8.19	(−11.69, −4.69)	−2.16	(−6.42, 2.10)	−7.89	(−11.40, −4.39)	−1.86	(−6.09, 2.36)
Elevated Glucose (>100 mg/dL vs. ≤100 mg/dL)	−1.52	(−4.79, 1.74)	−0.22	(−3.34, 2.89)	−1.67	(−4.91, 1.58)	−0.28	(−3.38, 2.82)
Elevated Blood Pressure (SBP ≥130 or DBP≥85 or hypertensive med vs. SBP<130 & DBP<85 and no hypertensive medication)	−2.41	(−5.77, 0.96)	0.86	(−2.48, 4.20)	−1.99	(−5.35, 1.37)	1.44	(−1.91, 4.79)
Low HDL (<50 mg/dL vs. ≥50 mg/dL)	2.26	(−1.08, 5.60)	2.65	(−0.50, 5.81)	1.97	(−1.38, 5.33)	2.28	(−0.90, 5.45)
Elevated Triglycerides (≥150 mg/dL vs. <150 mg/dL)	−1.40	(−4.87, 2.07)	−0.44	(−3.73, 2.86)	−0.96	(−4.46, 2.53)	0.16	(−3.17, 3.48)
Dense Area								
Metabolic syndrome (≥3 metabolic components)	5.65	(−0.84, 12.13)	3.10	(−3.78, 9.98)	6.23	(−0.29, 12.75)	3.87	(−3.08, 10.82)
Individual components Abdominal Adiposity (WC ≥88cm vs. < 88cm)	9.36	(2.58, 16.14)	5.90	(−2.57, 14.36)	9.30	(2.51, 16.09)	6.39	(−2.01, 14.80)
Elevated Glucose (>100 mg/dL vs. ≤100 mg/dL)	3.20	(−3.06, 9.47)	2.23	(−4.04, 8.50)	3.06	(−3.19, 9.31)	2.08	(−4.18, 8.35)
Elevated Blood Pressure (SBP ≥130 or DBP≥85 or hypertensive medication vs. SBP<130 & DBP<85 and no hypertensive medication)	5.46	(−1.00, 11.92)	3.28	(−3.44, 10.00)	6.43	(−0.03, 12.89)	4.43	(−2.33, 11.19)
Low HDL (<50 mg/dL vs. ≥50 mg/dL)	9.55	(3.20, 15.90)	9.26	(2.95, 15.57)	8.91	(2.50, 15.33)	8.77	(2.39, 15.14)
Elevated Triglycerides (≥150 mg/dL vs. <150 mg/dL)	−4.67	(−11.32, 1.98)	−5.46	(−12.07, 1.15)	−3.73	(−10.46, 2.99)	−4.56	(−11.26, 2.15)