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Prevalence and Comorbidity Network Analysis of Obesity and Related Complications: A Real-World Study Based on 233,004 Individuals

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Purpose: To determine the prevalence of overweight/obesity and their major complications, and to map comorbidity relationships by means of large-scale, real-world data.

Patients and Methods: This cross-sectional study included individuals undergoing routine health examinations from January 2021 to April 2024. Clinical and demographic data were systematically collected. Obesity-related complications were diagnosed using standardized criteria. Descriptive statistics assessed prevalence; correlation and network analyses characterized comorbidity relationships.

Results: A total of 233,004 participants (57.5% male; mean age 43.51 ± 13.28 years) were enrolled. Among these, 41.1% were overweight and 6.1% had obesity. The most prevalent complications were dyslipidemia (30.9%), fatty liver disease (26.4%), and hyperuricemia (20.0%). Over 60% of participants had at least one obesity-related comorbidity. Network analysis indicated a central disease cluster comprising overweight/obesity, fatty liver disease, hypertension, diabetes, and carotid plaque, with diabetes playing a key role linking metabolic abnormalities to cardiovascular risks.

Conclusion: Overweight prevalence was high in this large-scale examined population and frequently coexisted with multiple metabolic and cardiovascular conditions. Network analysis highlighted diabetes as a central condition, supporting early targeted interventions for overweight individuals to reduce obesity-related chronic disease burden.

Keywords: obesity, overweight, obesity-related complications, comorbidity network, epidemiology

Introduction

Obesity has emerged as a significant global public health issue, characterized by substantial increases in prevalence and related health burdens.[1] According to the World Health Organization (WHO), the number of overweight and obese individuals has reached approximately 2.5 billion globally, significantly straining healthcare systems and negatively impacting socio-economic development.[2] In China, rapid urbanization, dietary transitions, and sedentary lifestyles have accelerated the obesity epidemic. Recent nationwide surveys indicate that the prevalence of overweight and obesity has risen dramatically, currently at 34.3% and 16.4%, respectively, with the onset occurring increasingly at younger ages.[3] Such trends highlight obesity as a pressing issue warranting urgent scientific attention and public health interventions.

Obesity is now increasingly recognized not merely as a result of energy imbalance, but as a chronic disease characterized by systemic low-grade inflammation and metabolic disturbances.[4,5] Excess adipose tissue secretes

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numerous pro-inflammatory cytokines and adipokines, promoting chronic inflammation and subsequently driving insulin resistance, endothelial dysfunction, hepatic lipid accumulation, and metabolic dysregulation.[5] These pathophysiological mechanisms substantially elevate the risk for a range of chronic cardiometabolic conditions, including dyslipidemia, type 2 diabetes mellitus, non-alcoholic fatty liver disease, and hypertension.[6] These obesity-related complications rarely occur independently but tend to coexist, forming complex patterns of comorbidity that exacerbate overall clinical outcomes and complicate disease management strategies.[7,8]

Although accumulating evidence consistently underscores obesity's pivotal role in the development of metabolic comorbidities, previous studies have predominantly focused on investigating relationships between obesity and individual disease conditions.[7,8] Thus, a comprehensive understanding of the interconnected comorbidity patterns associated with obesity remains limited.[7,8] Network analysis offers a novel epidemiological approach that leverages large-scale real-world datasets to systematically explore and identify key disease interactions, cluster patterns, and mechanistic pathways linking obesity with a broader spectrum of cardiometabolic disorders.[9,10] Compared to conventional statistical approaches that typically assess associations between obesity and individual complications in isolation, network analysis can simultaneously capture the complex, multidimensional relationships among multiple comorbidities. This enables the identification of central diseases or clusters in the comorbidity network that may play a pivotal role in disease progression or serve as targets for intervention, thus providing additional insights into the dynamics and structure of disease co-occurrence in real-world populations.[9,10]

In this study, we conducted a large-scale cross-sectional analysis based on health examination data from Shanghai, China. This research aimed to determine the prevalence of overweight, obesity, and their related complications, and to systematically examine the comorbidity networks among these obesity-related disorders. The findings are anticipated to provide robust evidence to inform public health strategies for obesity prevention, optimize clinical management, and facilitate personalized interventions for high-risk populations.

Materials and Methods

Study Design and Setting

This was a cross-sectional study conducted at the Health Management Center of Zhongshan Hospital, Fudan University, Shanghai, from January 2021 to April 2024. Ethical approval was obtained from the hospital's Institutional Review Board (Approval No. B2021-642). All study procedures were conducted strictly in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from each participant prior to enrollment in the study.

Study Population

Eligible participants were adults aged 18 years or older who underwent routine health examinations and had complete anthropometric and biochemical measurement data, including height, weight, blood pressure, fasting blood glucose, and lipid profiles. In addition, participants were required to have undergone relevant ultrasound examinations (such as abdominal and carotid artery ultrasound) to assess gallbladder disease, fatty liver, and carotid atherosclerosis. Exclusion criteria included: (1) diagnosis of conditions associated with substantial body-weight fluctuations (eg, tuberculosis, hyperthyroidism, malignancies); (2) presence of acute or severe medical conditions (eg, severe infections, diabetic ketoacidosis, respiratory failure, end-stage liver or renal disease); and (3) pregnancy or breastfeeding status.

Data Collection and Variable Definitions

Baseline variables, including demographic information (age, sex), anthropometric measurements (height, weight), medical histories, blood pressure, blood counts, hepatic and renal function tests, lipid profiles, and imaging findings (ultrasound, CT), were obtained through the hospital's big data platform. BMI was classified according to the guideline of the National Health Commission of China: underweight (<18.5 kg/m²), normal weight (18.5–23.9 kg/m²), overweight (24.0–27.9 kg/m²), and obesity (≥28.0 kg/m²).[11] This standard reflects evidence from large Chinese cohorts and is widely used in domestic clinical practice.[12] For international comparison, we also calculated the BMI distribution and

comorbidity prevalence using the categories proposed by Hsu et al (Diabetes Care 2014); results are shown in Supplementary Tables S2-S4.[13] Given the absence of universally standardized criteria for obesity-related complications, we referred to the American Association of Clinical Endocrinology (AACE, 2016) recommendations, which are commonly used in clinical and research settings.[14] Considering the clinical context and population characteristics specific to this study, we defined obesity-related complications as diabetes mellitus, prediabetes, hypertension, gallbladder disease, fatty liver disease, carotid plaque, hyperuricemia, and dyslipidemia. The detailed definitions and diagnostic criteria for all analyzed obesity-related complications are provided in Supplementary Table S1.

Statistical Analysis

Descriptive analyses were performed to characterize the study population. Continuous variables were reported as mean ± standard deviation for normally distributed data and as median (Q1, Q3) for skewed data, with group comparisons via independent sample *t* test or Mann–Whitney *U*-test, respectively. Categorical variables were expressed as frequencies (%), compared using chi-square or Fisher's exact tests. Restricted cubic spline models evaluated non-linear relationships between BMI and the incidence of obesity-related complications.

Participants with missing values for all key variables (such as height, weight, blood pressure, fasting blood glucose, or lipid profile) were excluded from the analysis (complete case exclusion). For variables with partial missing data, where the missing rate was less than 20%, multiple imputation by chained equations (MICE) was used. Five imputed datasets were generated, and results were pooled using Rubin's rules.

Comorbidity Network Analysis

Comorbidity network analysis was conducted to determine whether any two diseases co-occurred more frequently than would be expected by chance. Overweight/obesity (BMI ≥24.0 kg/m²) was designated as a node in the network, alongside other diseases (eg, diabetes, hypertension, dyslipidemia, etc). For each disease pair (i and j), the observed-to-expected ratio (OER) was calculated as:

$$OER = \frac{a}{b \times c}$$

where a is the proportion of participants simultaneously diagnosed with diseases i and j, b is the prevalence of disease i, and c is the prevalence of disease j. An OER>1.0 with $P<0.05$ was considered statistically significant, indicating that the two diseases co-occurred more often than expected by independent distribution. Statistical significance was tested using continuity-corrected methods. We employed Python 3.13 (NetworkX and Matplotlib libraries) for network visualization, in which nodes represent diseases and edge weights reflect the magnitude of comorbidity. Four centrality measures were used to evaluate node prominence: Strength (sum of connection weights), Degree (number of directly connected nodes), Closeness (inverse of average distance to other nodes), and Betweenness (extent to which a node is positioned on the shortest paths among other nodes). A higher centrality score suggests a stronger or more influential role in the network. A two-sided $P<0.05$ denoted statistical significance.

Results

Baseline Characteristics

Between January 2021 and April 2024, a total of 281,712 individuals underwent routine health examinations at the Health Management Center of Zhongshan Hospital, Fudan University. Participants were excluded from analysis due to tuberculosis (n=97), hyperthyroidism (n=211), malignancies (n=672), pregnancy (n=80), and incomplete data (n=47,648), resulting in 233,004 eligible participants included in the final analysis. Table 1 summarizes the baseline characteristics of the study population. Overall, 134,003 (57.5%) participants were male, and the mean age was 43.51 ± 13.28 years. Males exhibited significantly greater mean height (172.20 ± 3.54 cm vs 160.68 ± 3.42 cm) and weight (74.27 ± 7.69 kg vs 57.19 ± 6.50 kg) compared with females (both $P<0.001$). The mean BMI was also significantly higher in males compared to females (25.03 ± 2.36 kg/m² vs 22.17 ± 2.58 kg/m²; $P<0.001$). According to BMI classification, 1.0% of participants were underweight, 51.7% normal weight, 41.1% overweight, and 6.2% obese. The prevalence of

Table 1 Baseline Characteristics of the Study Population

Indicator	Total (n=233,004)	Male (n=134,003)	Female (n=99,001)	*P*-value
Age (years, mean ± SD)	43.51 ± 13.28	43.81 ± 13.30	43.11 ± 13.24	<0.001
Age Group [n (%)]				
18–29	28,841 (12.4%)	16,422 (12.3%)	12,419 (12.5%)	<0.001
30–34	30,934 (13.3%)	17,601 (13.1%)	13,333 (13.5%)	
35–39	35,650 (15.3%)	19,668 (14.7%)	15,982 (16.1%)	
40–44	34,511 (14.8%)	18,970 (14.2%)	15,541 (15.7%)	
45–49	26,418 (11.3%)	14,834 (11.1%)	11,584 (11.7%)	
50–54	23,852 (10.2%)	14,169 (10.6%)	9683 (9.8%)	
55–59	19,546 (8.4%)	12,924 (9.6%)	6622 (6.7%)	
60–64	12,436 (5.3%)	7999 (6.0%)	4437 (4.5%)	
65–69	9443 (4.1%)	5113 (3.8%)	4330 (4.4%)	
70–74	5763 (2.5%)	3091 (2.3%)	2672 (2.7%)	
75–79	3125 (1.3%)	1720 (1.3%)	1405 (1.4%)	
80+	2485 (1.1%)	1492 (1.1%)	993 (1.0%)	
Weight (kg, mean ± SD)	67.01 ± 11.10	74.27 ± 7.69	57.19 ± 6.50	<0.001
Height (cm, mean ± SD)	167.30 ± 6.68	172.20 ± 3.54	160.68 ± 3.42	<0.001
BMI (kg/m², mean ± SD)	23.82 ± 2.83	25.03 ± 2.36	22.17 ± 2.58	<0.001
Weight Classification [n (%)]				
Obesity	14,499 (6.2%)	12,412 (9.3%)	2087 (2.1%)	<0.001
Overweight	95,786 (41.1%)	74,517 (55.6%)	21,269 (21.5%)	
Normal Weight	120,347 (51.7%)	46,730 (34.9%)	73,617 (74.4%)	
Underweight	2372 (1.0%)	344 (0.3%)	2028 (2.0%)	
Laboratory Indicators				
Hemoglobin (g/L, mean ± SD)	143.26 ± 12.98	153.41 ± 5.97	129.53 ± 4.49	<0.001
White Blood Cell Count (×10^9/L, mean ± SD)	5.60 ± 0.60	5.92 ± 0.49	5.17 ± 0.44	<0.001
Neutrophil Percentage (%)	54.53 ± 2.99	55.26 ± 2.65	53.54 ± 3.12	<0.001
Lymphocyte Percentage (%)	35.39 ± 3.16	34.30 ± 2.67	36.87 ± 3.16	<0.001
Monocyte Percentage (%)	7.06 ± 0.62	7.37 ± 0.52	6.65 ± 0.48	<0.001
Eosinophil Percentage (%)	2.71 ± 0.76	3.03 ± 0.76	2.28 ± 0.50	<0.001
Basophil Percentage (%)	0.57 ± 0.09	0.57 ± 0.09	0.56 ± 0.09	<0.001
AST [U/L, Median (Q1, Q3)]	25.07 (17.14, 31.46)	29.13 (24.93, 34.28)	16.21 (13.37, 21.41)	<0.001
ALT [U/L, Median (Q1, Q3)]	23.09 (19.83, 26.44)	24.70 (22.59, 27.93)	19.67 (17.58, 22.93)	<0.001
Creatinine [μmol/L, Median (Q1, Q3)]	82.88 (63.36, 87.58)	86.84 (84.29, 89.72)	62.53 (60.00, 65.26)	<0.001

(*Continued*)

Table 1 (Continued).

Indicator	Total (n=233,004)	Male (n=134,003)	Female (n=99,001)	*P*-value
Uric Acid [μmol/L, mean ± SD]	345.37 ± 89.66	390.43 ± 79.23	284.38 ± 62.88	<0.001
Cholesterol (mmol/L, mean ± SD)	5.00 ± 0.96	4.98 ± 0.95	5.03 ± 0.98	<0.001
Triglycerides (mmol/L, mean ± SD)	1.57 ± 1.29	1.81 ± 1.45	1.24 ± 0.93	<0.001
LDL-C (mmol/L, mean ± SD)	2.90 ± 0.83	2.94 ± 0.83	2.85 ± 0.84	<0.001
HDL-C (mmol/L, mean ± SD)	1.40 ± 0.38	1.24 ± 0.29	1.60 ± 0.38	<0.001
HbA1c (% mean ± SD)	5.54 ± 0.69	5.61 ± 0.77	5.45 ± 0.53	<0.001
Glucose (mmol/L, mean ± SD)	5.15 ± 1.12	5.26 ± 1.28	5.01 ± 0.86	<0.001

Abbreviations: BMI, Body Mass Index; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; LDL-C, Low-Density Lipoprotein Cholesterol; HDL-C, High-Density Lipoprotein Cholesterol; HbA1c, Glycated Hemoglobin.

overweight and obesity was significantly higher among males than females (both $P<0.001$). Significant sex-related differences were likewise observed across laboratory parameters including hemoglobin levels, white blood cell counts, liver enzyme levels, uric acid concentrations, and lipid profiles (all $P<0.001$).

Overweight and Obesity Prevalence and Distribution

The overall prevalence of overweight in the study population was 41.1% and increased with advancing age, reaching 74.1% among individuals aged 80 years or older. Obesity prevalence was 6.2%, exhibiting less distinct variation with age. Among males, 55.6% were classified as overweight, with prevalence steadily rising across increasing age groups. Male obesity prevalence was 8.2%, peaking at 10.6% in the 45–49-year age group. In females, the rates of overweight and obesity were lower (21.5% and 2.1%, respectively) and markedly increased after age 50. Detailed prevalence patterns by age and sex are presented in Figure 1. The prevalence of overweight and obesity based on the BMI classification by Hsu et al (Diabetes Care 2014) are presented in Supplementary Tables S2–S4.

Prevalence of Obesity-Related Complications

Dyslipidemia was the most prevalent obesity-related complication in the study population (30.9%), followed by fatty liver (26.4%) and hyperuricemia (20.0%). Figure 2 presents the prevalence of these conditions across different BMI categories. Participants classified as overweight or obese showed significantly higher prevalence rates of obesity-related complications compared with those classified as normal-weight or underweight. Among participants classified as obese, the prevalence was notably high for fatty liver (94.3%), dyslipidemia (63.7%), hyperuricemia (52.9%), and hypertension (42.5%), substantially exceeding the corresponding rates observed in the overall study population. Those classified as overweight also demonstrated higher prevalence rates of gallbladder disease (12.0%), carotid plaque (4.8%), and prediabetes (18.3%), compared with the normal-weight and underweight groups.

Age- and sex-specific prevalence trends are illustrated in Figure 3. Males generally exhibited higher prevalence rates for obesity-related metabolic disorders than females, especially fatty liver, dyslipidemia, hyperuricemia, and hypertension. Specifically, the prevalence of fatty liver exceeded 60% among males aged 45–64 years and remained higher than females up to approximately 70 years of age. Dyslipidemia prevalence peaked among males aged 40–54 years (exceeding 45%), subsequently converging with female rates after 65 years of age. The prevalence of hyperuricemia among males declined progressively from a peak of 39.8% in the 18–29-year age group to lower levels with advancing age. The prevalence of prediabetes and diabetes rose steadily with increasing age in both sexes, but remained generally higher among males. Similarly, hypertension prevalence consistently increased with age and was higher in males than females across all age groups. Gallbladder disease prevalence increased steadily until about 55 years of age and then plateaued.

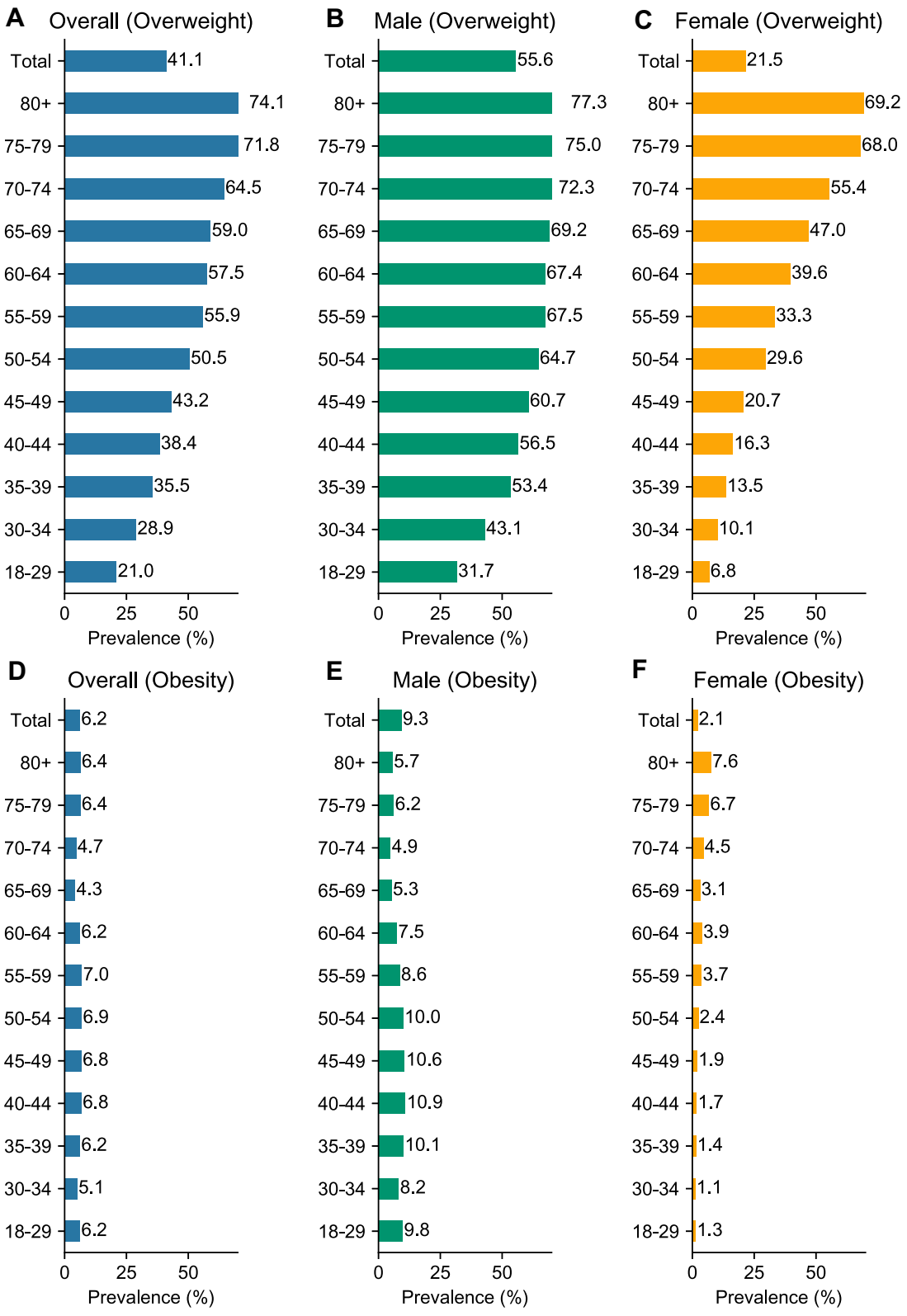

Figure 1 Overweight and Obesity Prevalence by Age Group and Sex. (**A**) Overall prevalence of overweight in the study population stratified by age group; (**B**) Prevalence of overweight among male participants by age group; (**C**) Prevalence of overweight among female participants by age group; (**D**) Overall prevalence of obesity in the study population stratified by age group; (**E**) Prevalence of obesity among male participants by age group; (**F**) Prevalence of obesity among female participants by age group.

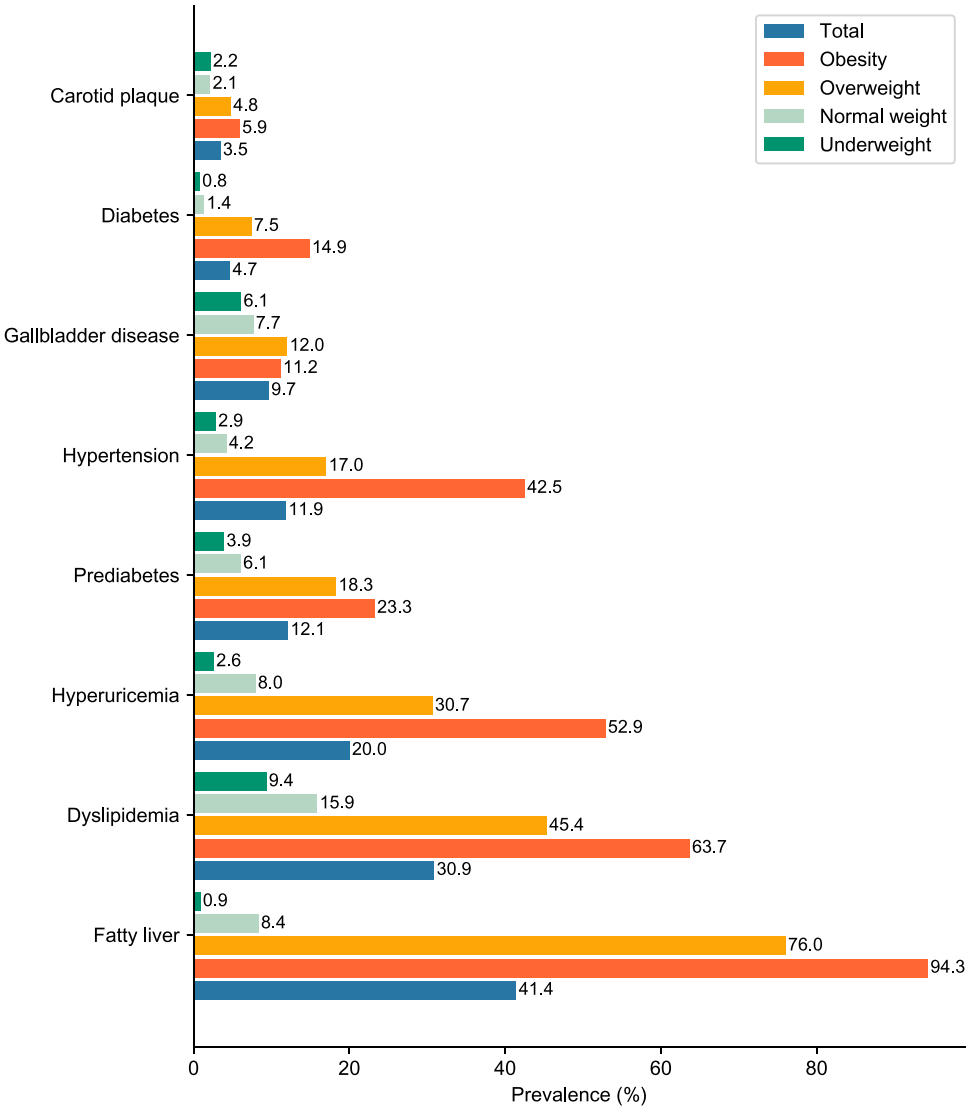

Figure 2 Prevalence of Major Obesity-Related Diseases Across Different Weight Categories.

The prevalence of carotid plaque was minimal (<1%) among individuals younger than 40 years but increased significantly thereafter, reaching 19.2% in males and 20.8% in females aged 80 years or older.

Comorbidities by BMI Classification

Figure 4 presents the distribution of comorbidities according to BMI classification (underweight, normal-weight, overweight, and obese). Overall, more than 60% of participants had at least one comorbidity, including 25.8% with one comorbidity, 17.2% with two, 11.0% with three, 4.7% with four, and 1.4% with five or more comorbidities. Among overweight participants, 29.9% had one comorbidity and 28.2% reported two, whereas 67.3% of obese participants had three or more comorbidities. In comparison, multiple comorbidities (≥2) were present in only 22.0% of underweight and 35.5% of normal-weight participants. The overall number of comorbidities generally increased in parallel with BMI, being most pronounced in obese individuals.

When stratified by age and sex, younger female participants generally exhibited fewer comorbidities compared with males (Figure 5). Among participants aged 18–29 years, 81.5% of females had no comorbidities versus only 39.8% of males; additionally, the prevalence of ≥3 comorbidities was higher in young males (9.2%) than in females (0.6%). With increasing age, the proportion of individuals without comorbidities markedly declined in both sexes, particularly among

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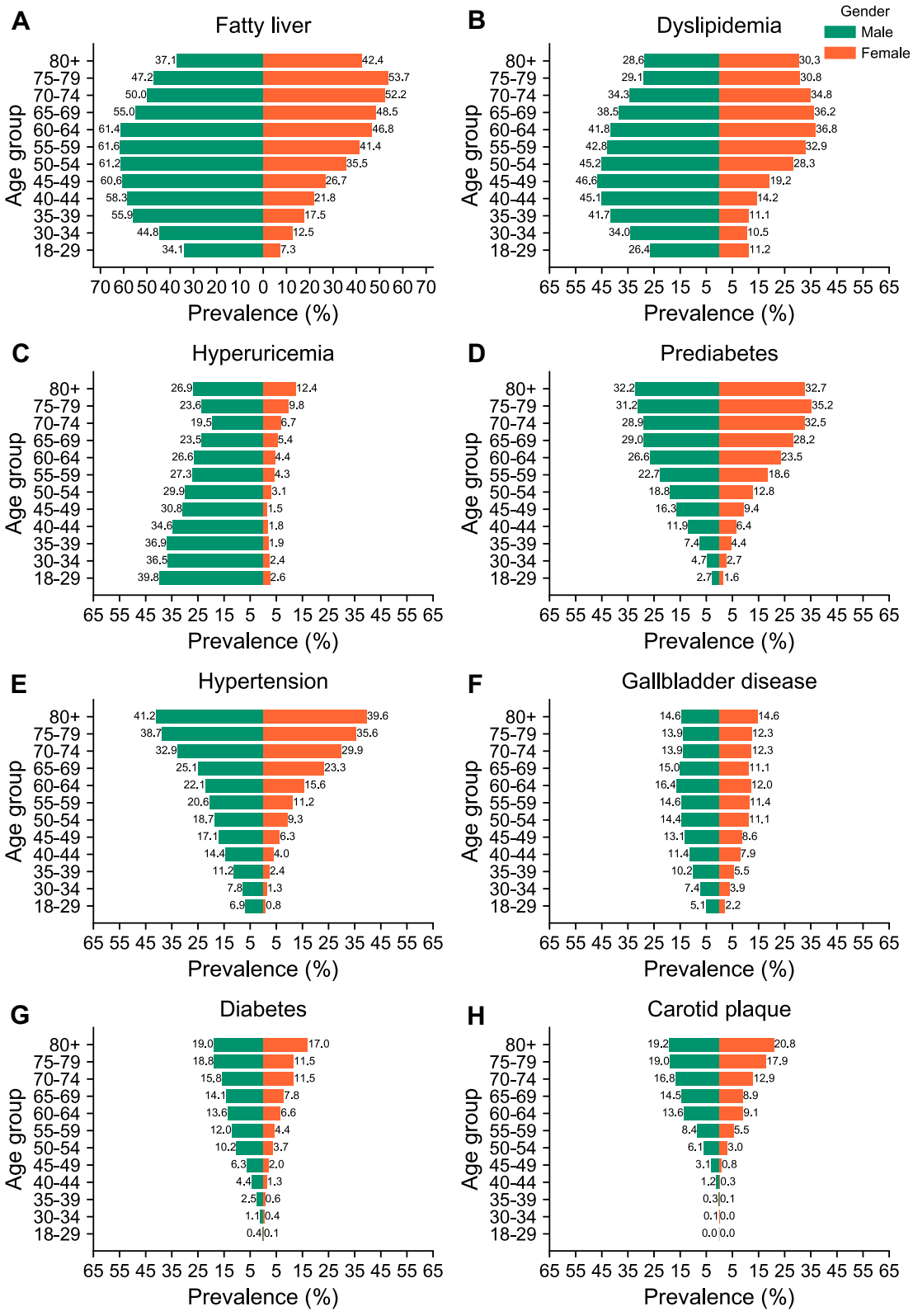

Figure 3 Prevalence of Obesity-Related Complications by Age Group and Sex. Age- and sex-specific prevalence (%) of eight major obesity-related complications: (**A**) Fatty liver, (**B**) Dyslipidemia, (**C**) Hyperuricemia, (**D**) Prediabetes, (**E**) Hypertension, (**F**) Gallbladder disease, (**G**) Diabetes, and (**H**) Carotid plaque.

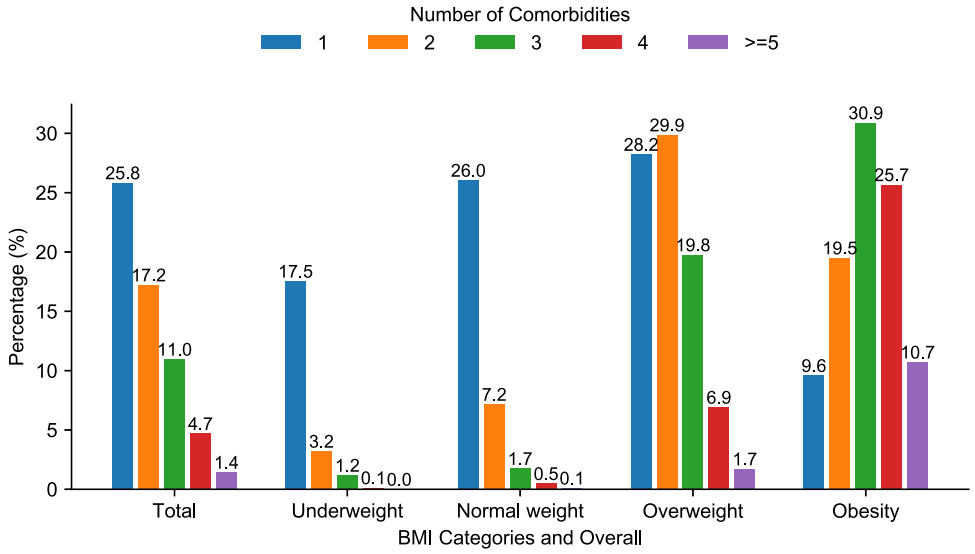

Figure 4 Distribution of the Number of Comorbidities Across Different BMI Classifications.

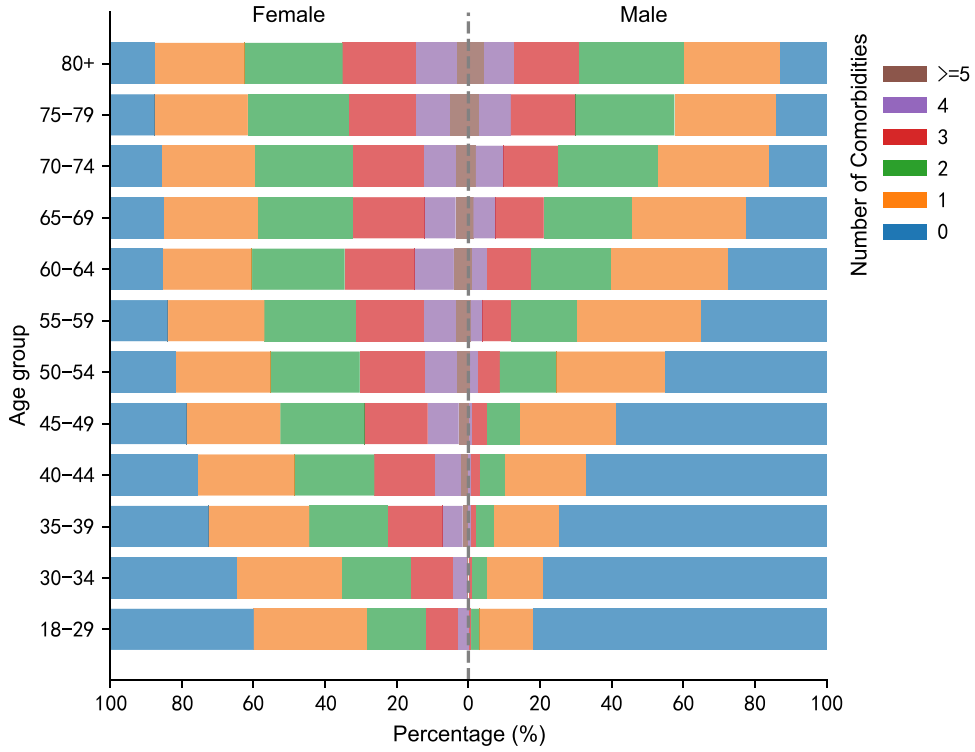

Figure 5 Percentage Distribution of the Number of Comorbidities by Age Group and Sex.

males. For example, within the 50–54-year age group, only 17.8% of males had no comorbidities compared with 42.5% of females; conversely, three or more comorbidities were reported by 30.6% of males versus 9.3% of females. Among older adults (≥70 years), fewer than 15% of participants had no comorbidities, while more than half exhibited two or more. In individuals aged ≥80 years, approximately 30% of males had three or more comorbidities, notably higher compared with females of the same age.

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Nonlinear Associations Between BMI and Obesity-Related Complications

Restricted cubic spline regression analyses illustrated distinct nonlinear associations between BMI and several obesity-related complications (Figure 6). Specifically, the risk of fatty liver and hypertension rose sharply once BMI exceeded the normal range (≥24 kg/m²), suggesting a pronounced positive association with overweight and obesity. In contrast, hyperuricemia risk exhibited a curvilinear pattern, peaking in the normal-to-mildly overweight categories and declining thereafter at higher BMIs. Gallbladder disease demonstrated a similar trend, characterized by peak risk at low-overweight levels followed by a plateau or slight reduction at higher categories. Prediabetes risk increased within the overweight category; however, the association was characterized by wide confidence intervals and considerable inter-individual variability. Notably, the odds ratios for diabetes and carotid plaque remained close to 1 with minimal fluctuation across BMI values, indicating only modest associations between BMI and these outcomes.

Comorbidity Network

As illustrated in Figure 7, the most prominent disease cluster in the overall cohort consisted of overweight/obesity, fatty liver, hypertension, diabetes, and carotid plaque. Within this cluster, diabetes exhibited multiple high-strength connections (Strength=5.00, Degree=3) and notable centrality (Closeness=0.8, Betweenness=0.67). By contrast, overweight/obesity primarily co-occurred with fatty liver (Strength=1.12, Degree=1). Among male participants, the dominant pattern—hypertension, diabetes, and carotid plaque—again positioned diabetes at the core (Degree=2, Closeness=1, Betweenness=1). In contrast, female participants demonstrated a broader "web-like" network, centered on fatty liver (Strength=12.41, Degree=6) and diabetes (Strength=21.49, Degree=6), each exhibiting high connectivity (Closeness ≥0.86). Detailed metrics from the comorbidity analysis are provided in Table 2.

When stratified by age, younger male participants (≤39 years) displayed a network primarily centered on diabetes (Strength=11.05, Degree=4, Betweenness=0.9), which frequently co-occurred with hypertension and carotid plaque. Among younger female participants (≤39 years), hypertension (Strength=40.22, Degree=7) represented the primary node, closely linked to fatty liver, diabetes, overweight/obesity, and hyperuricemia. In middle-aged female participants (40–59 years), the comorbidity network remained highly interconnected; diabetes (Degree=6, Closeness=1, Betweenness=0.27) formed robust links with fatty liver, hypertension, and overweight/obesity. Hyperuricemia also demonstrated elevated strength and connectivity in this group, indicating a need for further clinical attention.

Discussion

In this large-scale cross-sectional study of adults undergoing health examinations in Shanghai, we systematically characterized the patterns and comorbidity networks associated with overweight- and obesity-related complications. Our findings indicate that overweight prevalence substantially exceeds that of obesity and that comorbidities may already be evident in individuals classified as overweight. Moreover, overweight and obese individuals demonstrated significantly higher risks for metabolic disorders—including fatty liver, dyslipidemia, hyperuricemia, and hypertension—underscoring the early disease burden linked to elevated body mass. Notably, the disease cluster comprising "overweight/obesity, fatty liver, hypertension, diabetes, and carotid plaque" emerged as the principal network node, suggesting complex interconnections between overweight/obesity and multiple metabolic-cardiovascular conditions in this population.

Overweight: A Critical Stage for Early Intervention

Our findings indicate that the prevalence of overweight (41.1%) in this study population exceeds the national average of 34.3% and increases with age, whereas the obesity rate of 8.2% is below the reported national figure of 16.5%. Notably, many individuals classified as overweight already exhibited one or two metabolic abnormalities, such as dyslipidemia, hypertension, or hyperuricemia, underscoring the necessity for heightened vigilance and proactive intervention during the overweight stage.

Various factors—including regional characteristics and higher health literacy—likely contribute to these discrepancies.[15] In Shanghai, a well-developed healthcare infrastructure and strong public awareness facilitate better

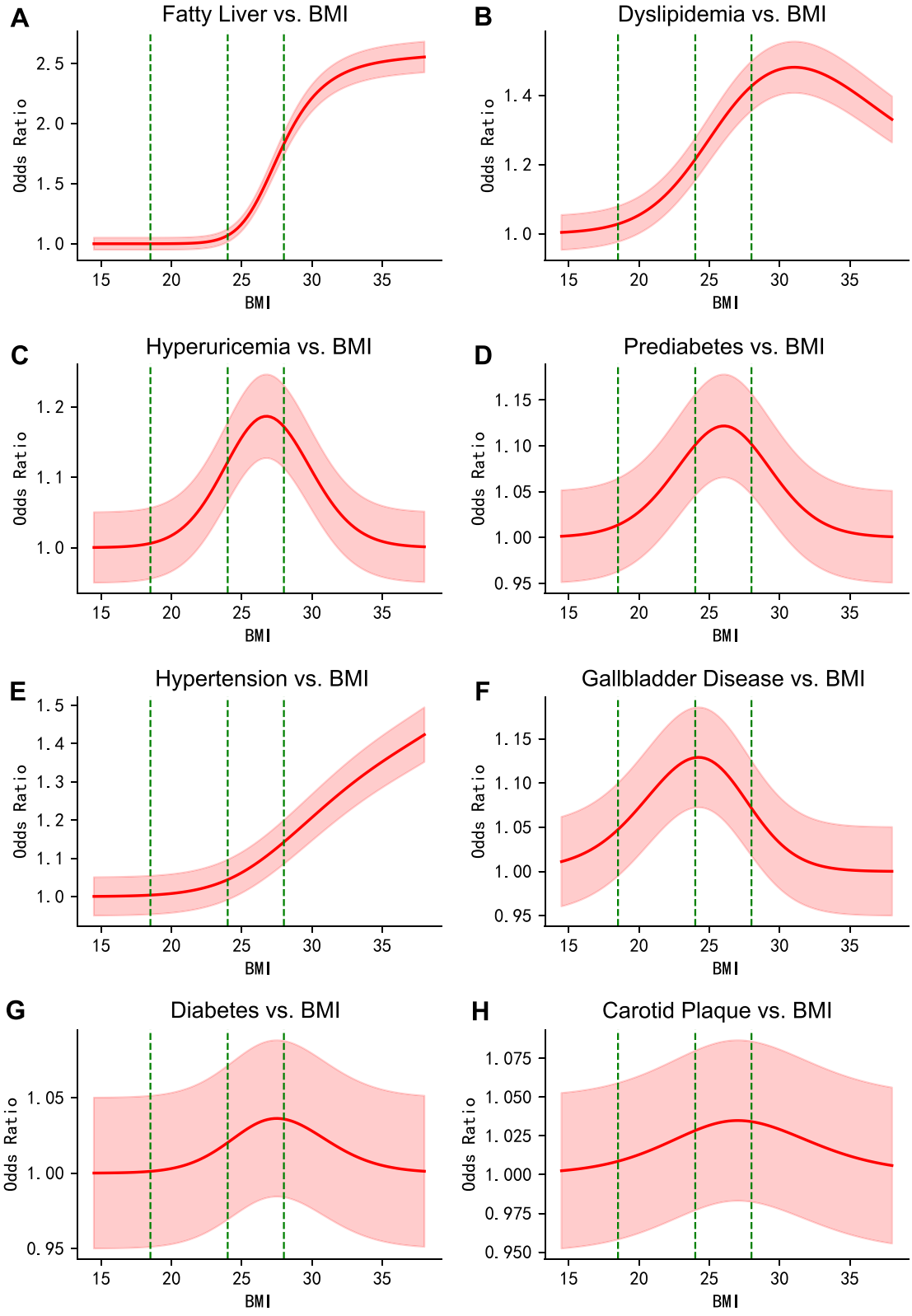

Figure 6 Nonlinear Associations Between BMI and the Risk of Obesity-Related Complications. Restricted cubic spline regression curves illustrating the relationships between BMI and the odds ratios of developing major obesity-related complications: (**A**) Fatty liver, (**B**) Dyslipidemia, (**C**) Hyperuricemia, (**D**) Prediabetes, (**E**) Hypertension, (**F**) Gallbladder disease, (**G**) Diabetes, and (**H**) Carotid plaque.
Abbreviation: BMI, Body Mass Index.

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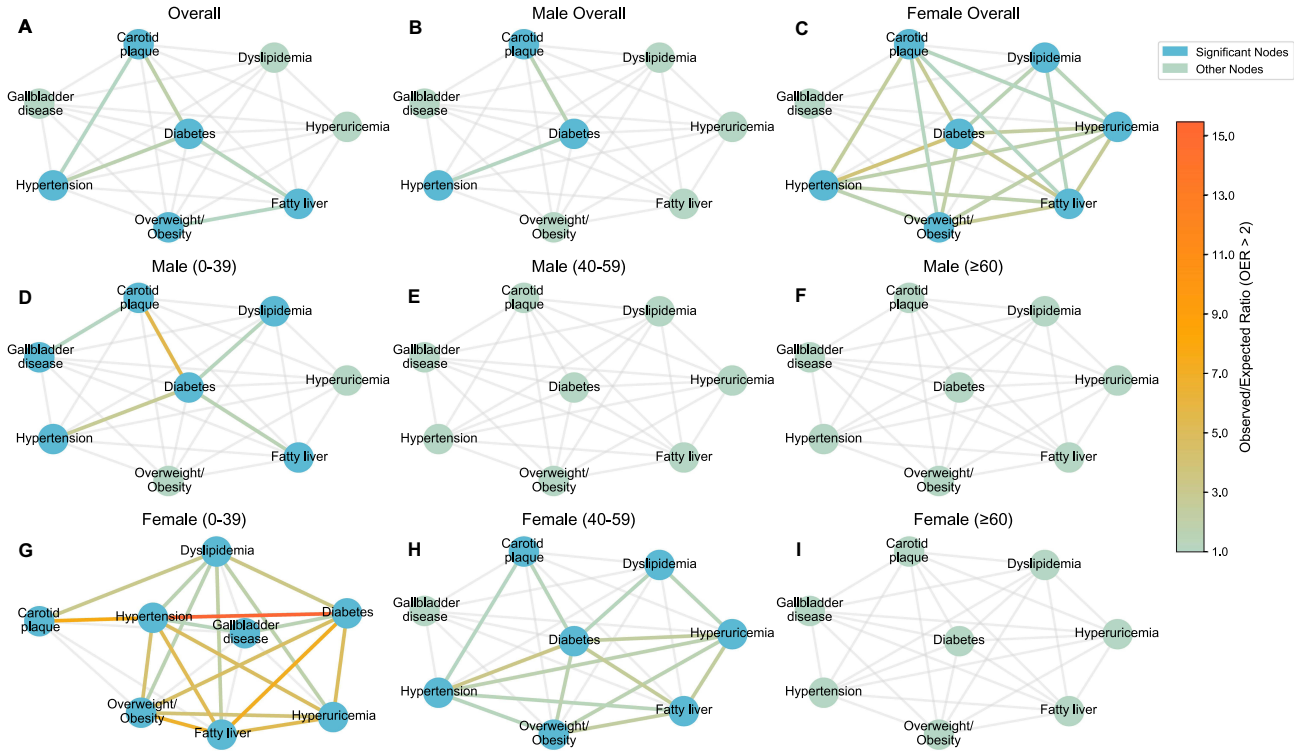

Figure 7 Comorbidity Network of Obesity-Related Complications by Sex and Age Group. Network graphs illustrating significant comorbidity relationships among obesity-related complications in: (**A**) the overall population, (**B**) males overall, (**C**) females overall, (**D**) males aged 0–39 years, (**E**) males aged 40–59 years, (**F**) males aged ≥60 years, (**G**) females aged 0–39 years, (**H**) females aged 40–59 years, and (**I**) females aged ≥60 years.

weight management.[16] For example, data from the Shanghai Health Promotion Center (2024) indicate that 42.09% of residents attain high health literacy, and 61.30% are aware of how to calculate their BMI, often undergoing routine check-ups and adopting professional recommendations to control weight.[17] Additionally, local dietary habits—which are generally lower in calories—may enable some individuals to stay in the overweight range without progressing to full-fledged obesity.[18] In broader regional or national contexts, disparities between urban and rural regions and diverse lifestyle factors inevitably influence BMI distribution patterns.[19]

Table 2 Node Centrality Indicators in the Comorbidity Network of Obesity-Related Complications

Comorbidity Network	Disease	Strength	Degree	Closeness	Betweenness
Total Population	Hypertension	4.78	2	0.57	0.00
	Diabetes	8.00	3	0.80	0.67
	Carotid Plaque	5.02	2	0.57	0.00
	Fatty Liver	4.25	2	0.67	0.50
	Overweight/Obesity	2.00	1	0.44	0.00
Total Male	Hypertension	2.09	1	0.67	0.00
	Diabetes	4.63	2	1.00	1.00
	Carotid Plaque	2.54	1	0.67	0.00

(*Continued*)

Table 2 (Continued).

Comorbidity Network	Disease	Strength	Degree	Closeness	Betweenness
Total Female	Dyslipidemia	7.04	3	0.67	0.00
	Hyperuricemia	17.43	6	1.00	0.07
	Diabetes	21.49	6	1.00	0.07
	Fatty Liver	18.41	6	1.00	0.07
	Hypertension	16.72	5	0.86	0.00
	Carotid Plaque	13.54	5	0.86	0.00
	Overweight/Obesity	14.69	5	0.86	0.00
Male (0–39 years)	Dyslipidemia	2.22	1	0.50	0.00
	Diabetes	15.05	4	0.83	0.90
	Hypertension	3.76	1	0.50	0.00
	Gallbladder Disease	2.08	1	0.42	0.00
	Carotid Plaque	8.59	2	0.63	0.40
	Fatty Liver	2.56	1	0.50	0.00
Female (0–39 years)	Dyslipidemia	19.45	6	0.88	0.10
	Hyperuricemia	25.64	5	0.78	0.00
	Hypertension	47.22	7	1.00	0.24
	Diabetes	42.81	6	0.88	0.10
	Carotid Plaque	12.68	2	0.58	0.00
	Fatty Liver	31.69	5	0.78	0.00
	Overweight/Obesity	26.08	5	0.78	0.00
	Gallbladder Disease	4.86	2	0.58	0.00
Female (40–59 years)	Dyslipidemia	4.62	2	0.60	0.00
	Hyperuricemia	14.32	5	0.86	0.10
	Diabetes	18.38	6	1.00	0.27
	Hypertension	13.62	5	0.86	0.10
	Fatty Liver	12.51	4	0.75	0.00
	Overweight/Obesity	10.76	4	0.75	0.00
	Carotid Plaque	4.43	2	0.60	0.00

Notes: Strength indicates the connection intensity between nodes, with a higher sum indicating more evident comorbidity; Degree is the number of directly connected nodes, suggesting tighter coexistence relationships; Closeness measures the average distance of one node to all others, indicating its influence on other diseases; Betweenness reflects the extent of a node acting as an intermediary, with higher values showing stronger influence among different diseases.

These observations also underscore the limitations of employing only a BMI cutoff of ≥28 kg/m² to define obesity, as it may overlook overweight individuals who already exhibit one or two metabolic complications. Our study identified a substantial proportion of "overweight" individuals experiencing early metabolic disturbances, such as dyslipidemia,

hypertension, or hyperuricemia, categorizing them as "Metabolically Unhealthy Overweight (MUO)".[20] Compared to Metabolically Healthy Overweight (MHO), MUO status confers an elevated risk of cardiovascular disease, type 2 diabetes, and other metabolic disorders.[21] Once BMI surpasses 28 kg/m², metabolic dysfunction often intensifies and becomes more challenging to reverse, decreasing intervention effectiveness and increasing healthcare costs.[21,22] Moreover, relying solely on BMI can fail to distinguish between individuals who have a healthy muscle-to-fat ratio and those with excess adiposity at genuine risk, potentially complicating cardiovascular risk assessment.[23,24] Accumulating evidence suggests that central (visceral) obesity, rather than overall weight, is more strongly associated with adverse metabolic and cardiovascular outcomes.[5,23] Therefore, a more comprehensive assessment strategy—including waist circumference, waist-to-hip ratio, and body composition analyses such as bioelectrical impedance or dual-energy X-ray absorptiometry—offers greater accuracy for identifying individuals at elevated cardiometabolic risk, especially in populations with higher variations in fat distribution.[5,23] The integration of these measures into routine screening may facilitate earlier identification and more targeted intervention, thereby improving the prevention and management of obesity-related complications.

Sex and Age Impacts on Obesity and Related Complications

Study results indicate that male participants exhibit higher rates of metabolic conditions (eg, fatty liver, dyslipidemia, hyperuricemia, hypertension, prediabetes, and diabetes) than female participants, with differences becoming apparent from early to mid-adulthood. Factors such as lifestyle habits, hormonal variation, and social roles lead males to develop metabolic disorders earlier, making ages 40 to 64 a critical period for the clustering of chronic diseases.[25] Work-related stress, high-calorie diets, reduced physical activity, and inadequate health screenings all contribute to weight gain and disturbances in blood lipids, blood pressure, and blood glucose profiles.[26] By approximately age 50, the proportion of males without comorbidities declines sharply, while the proportion with three or more comorbidities increases significantly, underscoring a need for proactive interventions by age 40, including regular monitoring of blood pressure, lipid profiles, and cardiac and renal function. In contrast, female participants benefit from estrogenic protection initially but face a substantial drop in estrogen levels during perimenopause, leading to more pronounced metabolic dysregulation.[27,28] Around age 50, the risks of diabetes, hypertension, and fatty liver increase notably in females, often matching or exceeding levels observed in males. Consequently, enhanced weight management, metabolic surveillance, and hormone assessments before menopause may help avert abrupt transitions to high multimorbidity. Meanwhile, hyperuricemia has also risen among younger adults, particularly in males aged 18 to 29, driven by Westernized diets, irregular routines, and insufficient preventive care, highlighting the importance of early interventions (eg, dietary modifications, physical activity, and periodic assessment of serum uric acid).[29,30]

Gallbladder disease and carotid plaque also demonstrate strong associations with age. Gallbladder disease prevalence increases continuously until approximately age 55, then plateaus, emphasizing the significance of early-to-midlife management of weight and metabolic factors.[31] If obesity, dyslipidemia, or hyperglycemia manifests before middle age, cholesterol accumulation accelerates disease progression, reinforcing the need for timely treatment.[32] Although carotid plaque is uncommon before age 40, it rises sharply after age 60 and presents a major cardiovascular risk in older adulthood. In the presence of endothelial dysfunction and arterial calcification, which are exacerbated by dyslipidemia, hypertension, and diabetes, routine carotid ultrasound after age 40 may mitigate vascular aging and reduce the incidence of stroke and other major cardiovascular events.[33,34]

BMI and Obesity-Related Complications

This study identified dyslipidemia, fatty liver, and hyperuricemia as the most common obesity-related complications, often co-occurring with metabolic risks such as hypertension and prediabetes in individuals with elevated BMI. However, our restricted cubic spline regression analysis revealed that the association between BMI and these comorbidities is nonlinear and disease-specific. The risk of fatty liver and hypertension rises sharply once BMI exceeds 24 kg/m², aligning with previous reports.[35] In contrast, the risk curves for hyperuricemia and gallbladder disease exhibit multiple peaks, suggesting that risk levels may escalate within certain BMI intervals but do not invariably increase with further BMI

gains.[36,37] Notably, the risk for diabetes and carotid plaque appears relatively less dependent on BMI, implying that genetic predisposition, dietary patterns, activity levels, and environmental exposures may play more decisive roles.[38]

In our analysis, the risk for diabetes did not show a clear increase across higher BMI categories, remaining relatively stable. This finding contrasts with the consistent positive association between BMI and diabetes observed in previous large-scale epidemiological studies.[39] Several factors may explain this discrepancy. First, our cohort consisted of Shanghai health check-up participants, who may be more health-conscious and proactive in diabetes prevention, potentially underestimating their true risk.[17] Second, BMI may not accurately reflect visceral adiposity or metabolic risk, especially in Asian populations where diabetes can develop even at lower or normal BMI.[23,24] Additionally, residual confounding and the cross-sectional nature of this study may have further attenuated any observable relationship. These results underscore the limitations of using BMI alone to assess diabetes risk, and further prospective research is warranted to validate our findings.

Clinically, a uniform approach that equates higher weight with uniformly higher risk across all metabolic phenotypes is ill-advised. Instead, interventions should be tailored according to disease-specific features and individual patient characteristics. For some complications—such as hypertension and fatty liver—risk rises rapidly past the overweight threshold, whereas for conditions like diabetes, a broader assessment including waist circumference, body composition, and genetic background may be necessary. By defining critical BMI cutoffs for each obesity-related condition and considering genetic, behavioral, and socioeconomic determinants, high-risk populations can be identified promptly, enabling more targeted management strategies to alleviate the burden of these complications.

Comorbidity Network of Obesity-Related Complications

Network analysis revealed that the cluster of "overweight/obesity, fatty liver, hypertension, diabetes, and carotid plaque" dominated the comorbidity landscape, with diabetes displaying prominent centrality among both male and female participants. In male participants, strong associations were frequently observed between hypertension, diabetes, and carotid plaque; in females, a more "web-like" structure emerged, centered around fatty liver and diabetes. Different age groups also exhibited distinct patterns: younger male participants were primarily affected by diabetes, whereas younger females were more strongly linked to hypertension; among middle-aged females, diabetes, hypertension, and fatty liver showed intense interconnections. These findings suggest that obesity drives multisystem metabolic disorders, intertwining metabolic, cardiovascular, and inflammatory pathways. By contrast, no single node prevailed in males aged 40–59 years, probably because several metabolic disorders reach comparable prevalence while medical management begins to attenuate their relative weights. In adults ≥60 years, multimorbidity approaches a ceiling and the pair-wise network becomes saturated, making additional dominant modes less detectable. Recognizing these stage-specific configurations is critical for tailoring prevention strategies across the life-course. These findings suggest that obesity drives multisystem metabolic disorders, intertwining metabolic, cardiovascular, and inflammatory pathways.

Current evidence indicates that fatty liver mediates most of the effect BMI exerts on hypertension, with nonalcoholic fatty liver disease (NAFLD) accounting for around 92% of BMI's influence on hypertension risk in young adults, consistent with our results.[40] This trend suggests that obesity-induced NAFLD may be a pivotal pathway contributing to blood pressure elevation, potentially through chronic inflammation and insulin resistance.[40] Furthermore, diabetes consistently emerged in our network analysis as the node with the highest centrality and most extensive interconnections—underscoring robust interactions with hypertension, fatty liver, and carotid plaque. Insulin resistance, persistent inflammation, and endocrine dysregulation provide a physiological basis by which diabetes and other metabolic-cardiovascular diseases mutually exacerbate one another.[41] In patients with diabetes, coexisting conditions such as hypertension, hyperlipidemia, and central obesity converge with atherosclerosis, end-organ damage, and inflammatory pathways, suggesting that diabetes functions as a prime "ignition point" or amplifier within an integrated comorbidity network.[41,42]

Targeting obesity-related chronic diseases effectively requires prioritizing diabetes prevention and management as a central strategy to decelerate individual disease progression and mitigate population-level healthcare burdens. Furthermore, directing management efforts toward key nodes—hypertension, diabetes, and fatty liver—may regulate the expansion of multimorbidity at a wider community scale, ultimately easing the large healthcare burdens shouldered by patients and society. Understanding obesity's multifaceted impact can enhance insights into its pathophysiological

basis and support the design of comprehensive prevention strategies encompassing metabolic, cardiovascular, and inflammatory mechanisms, thus paving the way for holistic management of obesity-related chronic conditions.

Limitations

This cross-sectional, real-world study underscores the high prevalence of overweight and obesity, as well as the complex multimorbidity observed in a Shanghai health examination population. Comorbidity network analysis highlighted the pivotal roles of diabetes, hypertension, and fatty liver in obesity-related chronic conditions, offering valuable insights for targeted prevention and intervention. Nonetheless, several limitations warrant consideration. First, the cross-sectional design precludes establishing causality or confirming the temporal sequence between obesity and subsequent complications. Future prospective cohort studies or randomized controlled trials are necessary to elucidate the dynamic processes of weight change and metabolic disease evolution. Second, the network was built on pair-wise OER; when prevalences are uniformly high or similar the ratios approach 1, edge weights flatten, and important links can be missed. Because this pair-wise approach ignores conditional or higher-order relations, future studies should apply conditional, multilayer, or longitudinal network models for finer resolution in dense multimorbidity settings. Third, these data were obtained from a single-center health checkup cohort, potentially introducing selection bias and limiting external validity to other geographical or sociocultural settings. Finally, although BMI is a widely accepted measure of obesity, it does not account for crucial factors such as visceral adiposity and muscle mass. Future research should incorporate additional parameters (eg, waist circumference, waist-to-hip ratio, body composition) to enhance the accuracy of obesity assessment and risk stratification.

Conclusion

This study reveals that overweight is highly prevalent in the population assessed and is frequently associated with multiple metabolic and cardiovascular risks. These findings underscore that being overweight is not merely a transitional phase toward obesity but represents a significant independent threat to health. Network analysis identified "obesity, fatty liver, hypertension, diabetes, and carotid plaque" as the most prevalent and closely interconnected disease cluster, with diabetes occupying a pivotal position. Earlier and more targeted interventions for individuals classified as overweight could significantly reduce the burden of obesity-related chronic diseases.

Abbreviations

AACE, American Association of Clinical Endocrinology; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; BMI, Body Mass Index; CI, Confidence interval; CT, Computed Tomography; HbA1C, Glycated Hemoglobin; HDL-C, High-density Lipoprotein Cholesterol; LDL-C, Low-density Lipoprotein Cholesterol; MUO, Metabolically Unhealthy Overweight; NAFLD, Non-alcoholic Fatty Liver Disease; OER, Observed-to-Expected Ratio; OR, Odds Ratio; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SD, Standard Deviation; SEM, Standard Error of Mean; SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; WHO, World Health Organization.

Data Sharing Statement

The datasets generated and/or analyzed during the present study are not publicly available owing to institutional data-sharing regulations. They are, however, available from the corresponding author, Dr Sunfang Jiang (zsjkglzx@163.com), upon reasonable request.

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Disclosure

The authors report no conflicts of interest in this work.

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