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Exploration of the Association between Obesity and Semen Quality in a 7630 Male Population

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Abstract

This study aimed to explore the association between body mass index (BMI), other anthropometric indexes and semen quality in a general male population in Taiwan. In this cross-sectional cohort study, the study cohort consisted of 7941 healthy male individuals aged 18 years or older who participated in a standard medical screening program run by a private firm from January 2008 to May 2013. Semen parameters including sperm concentration (SC), total sperm motility (TSM), progressive motility (PRM), and normal sperm morphology (NSM) were recorded. Anthropometric indexes including BMI, waist circumference (WC), hip circumference (HC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR) and body fat percentage were measured. A total of 7630 men were enrolled for the final analysis, of whom 68.5% had a normal weight distribution and 31.4% were overweight or obese. Total sperm motility, progressive motility, normal sperm morphology and sperm concentration showed a statistically linear decline with increasing age ($p < 0.001$, $p < 0.001$, $p < 0.001$ and $p = 0.004$). Sperm concentration showed a significantly negatively linear association with BMI ($p = 0.005$), and normal sperm morphology showed an inverse association with BMI and waist-to-height ratio ($p < 0.001$ and $p = 0.004$). The prevalence of abnormal total sperm motility, progressive motility, normal sperm morphology and sperm concentration increased with increasing age ($p = 0.011$, $p < 0.001$, $p < 0.001$ and $p = 0.002$). Lower normal sperm morphology and sperm concentration were associated with increasing body adiposity ($p<0.05$). No relationship between obesity and sperm motility was identified.

Introduction

It is well-known that overweight and obese women are more likely to experience ovulatory and menstrual disorders, which consequently lead to delayed fertility [1]. A cross-sectional study of 47835 Danish couples reported that overweight and obese women are at an increased risk of subfertility, with a statistically significant trend of a prolonged time to pregnancy of more than 12 months [2]. However, an association between high adiposity and subfertility has not been clearly demonstrated in men. Several studies have reported inverse correlations of sperm concentration and total sperm count with obesity when assessed by body mass index (BMI) [3], central adiposity according to waist circumference (WC) [4] and hip circumference (HC) [5]. Meanwhile, a systemic review by meta-analysis found no association between a high BMI and male semen parameters [6]. In addition, another study explored the relative risks for semen parameters being below World Health Organization reference limits in overweight and obese men, and found no significant associations between BMI and semen parameters with the exception of normal sperm morphology [7]. Furthermore, a recent meta-analysis of 21 studies with 13,077 subjects reported a J-shaped association between BMI and abnormal total sperm count, and also that overweight and obesity were associated with an increased prevalence of azoospermia or oligospermia [8]. Palmer et al. ever concluded from a literature review that the relationship between obesity and semen quality was conflicting [9]. Colaci group [10] reported that fertilization rate was higher among obese men than among normal weight in conventional IVF cycle. No statistically significant associations were identified between male BMI and proportion of poor-quality embryos. Moreover the largest subjects of single institute including 10,665 males declared that increasing BMI being associated with decreased semen quality, affecting volume, concentration and motility recently [11].

In order to identify factors affecting semen quality, this study aimed to assess the relationship between obesity and sperm parameters in a large study cohort in Taiwan, and to investigate the separate anthropometric indexes and age effects on male fertility.

Materials and Methods

This cross-sectional study consisted of 7941 healthy Taiwanese male individuals aged 18 years or older who participated in a standard medical screening program run by a private firm (MJ Health Management Institution, Taipei, Taiwan) between January 2008 and May 2013. The firm attracted paying participants from all over Taiwan because of its known quality services, operational efficiency, and key facilities that were easily accessible. Membership to the program was required, with discounts in examination fees offered for people with a large-size family or related individuals and for regular members who came back for repeated examinations in subsequent years, and these incentives succeeded in attracting and sustaining a large number of customers. Each participant signed a consent form authorizing MJ Health Management Institution to process the data generated from medical screening. Ethical reviews and assessments were processed and approved by MJ Institutional Review Boards in Taiwan. Data related to individual identification were removed, ensuring the anonymity of each individual during the entire study process.

After excluding those with incomplete records, a total of 7630 subjects were enrolled into the study. Semen sample was collected via masturbation following 3 days of abstinence using home collection kits, and the sample was sent to the laboratory for analysis within one hour. Four dependent semen parameters including sperm concentration (SC), total sperm motility (TSM), progressive motility (PRM) and normal sperm morphology (NSM) were recorded. Sperm concentration was evaluated by hemocytometer (Improved Neubauer; Hauser Scientific, Inc., Horsham, PA, USA). Samples were diluted in a solution of 0.6 M NaHCO3 and 0.4%

(v/v) formaldehyde in distilled water. Sperm motility was classified as progressive motility (WHO class A+B) and total sperm motility (WHO class A+B+C) [12]. Briefly, a 10 ml of well-mixed semen was placed on a clean glass slide that had been kept at 37°C and covered with a 22 × 22 mm coverslip. The preparation was placed on the heating stage of a microscope at 37°C and immediately examined at ×400 magnification. Morphology was assessed using strict criteria [13].

In addition, we recorded anthropometric indexes [BMI, waist circumference, hip circumference, waist-to-hip ratio (WHR), waist-to-height ratio (WHtR) and body fat percentage] and biochemistry data to analyze the relationships between obesity or derivative markers and semen quality. BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was obtained from the mid-point between the iliac crest and the costal margin, and hip circumference was measured at the widest point around the greater trochanter. Waist-to-hip ratio was calculated as waist circumference divided by hip circumference, and waist-to-height ratio was calculated as waist circumference divided by height. Measurements of percentage body fat were performed by the bioelectrical impedance analysis (BIA) technique by using a body-composition analyzer. A venous blood sample was taken after at least an 8-h fast for the measurement of plasma triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol. These assays were performed on a HITACHI 7150.

As Asian populations have different criteria of obesity as compared with Western populations [14–16], we used quartiles to evaluate the relationships between the anthropometric indexes and semen quality. Differences in the sperm parameters by varying degrees of obesity as assessed by the different anthropometric indexes were compared by one-way analysis of variance (ANOVA). The *p* values of statistics after adjusting confounding factors were calculated by the linear regression models.

Abnormal sperm parameters were defined as sperm concentration < 15 M/ml, total sperm motility $< 40\%$, progressive motility $< 32\%$ and normal sperm morphology $< 30\%$. The frequencies of abnormal sperm parameters in each quartile were compared by the chi-square test. We assessed the relationships between adiposity and age with semen parameters by first conducting logistic trend analysis, and then estimating the odds ratios (ORs). Moreover, the topics of smoking have been hot and popular in the public health, thus we applied a questionnaire to assess the relationship associated with male infertility. According to the questionnaire, the smoking duration was assessed as "0": no smoking, "1": smoking $<$ 1 year, "2": 1 year to $<$ 3 years, "3": 3 years to $<$ 5 years, "4": 5 years to $<$ 10 years, "5": 10 years to $<$ 20 years, "6": 20 years or more. We then explored the association between smoking and semen quality by the quartile method (dividing ["0"], ["1"+"2"], ["3"+"4"], ["5"+"6"]). To avoid the risk of false positive result from multiple testing between potential correlated factors and 4 groups of age, BMI, anthropometric measurements (waist and hip circumference, waist-to-hip and waist-to-height ratio, and body fat) and smoking duration by quartiles (in Table 1 and 2). The one-way ANOVA with Bonferroni post hoc procedures was considered. First, we identified the total number of different statistical tests were equal to 6. Subsequently, we calculated the Bonferroni corrected p-value threshold in this present study from 0.05 to 0.008 (P corrected = 0.05/6 = 0.008) and values of $p<0.008$ were considered statistically significant. All analyses were conducted using SPSS statistical software (version 13.0, SPSS Inc, Chicago, IL).

Results

The mean age of the participants in this cross-sectional study was 31.75 years (range, 18 to 75 years), with a mean height of 172.21 cm and a mean body weight of 70.65 kg. The mean BMI,

Table 1. Characteristics of the general male population (n = 7630).

Characteristics	BMI < 21.60 (n = 1907) Mean (95% CI for mean)	BMI: 21.60–23.48 (n = 1908) Mean (95% CI for mean)	BMI: 23.49–25.61 (n = 1908) Mean (95% CI for mean)	BMI ≥ 25.62 (n = 1907) Mean (95% CI for mean)	Total (n = 7630) Mean (95% CI for mean)	$p^{a,c}$
Age (years)	30.83 (30.64, 31.02)	31.78 (31.58, 31.98)	32.16 (31.95, 32.38)	32.21 (31.99, 32.43)	31.75 (31.64, 31.85)	< 0.001
Triglyceride	87.55 (85.27, 89.83)	106.81 (103.98, 109.64)	127.90 (124.23, 131.56)	153.93 (148.83, 159.04)	119.06 (117.16, 120.95)	< 0.001
Cholesterol	179.18 (177.73, 180.62)	188.62 (187.17, 190.07)	192.64 (191.13, 194.16)	198.11 (196.55, 199.68)	189.64 (188.87, 190.40)	< 0.001
HDL	55.22 (54.63, 55.81)	51.13 (50.61, 51.65)	48.04 (47.54, 48.53)	46.17 (45.71, 46.64)	50.18 (49.91, 50.46)	<0.001
LDL	106.65 (105.33, 107.97)	116.63 (115.26, 117.99)	119.97 (118.57, 121.37)	122.93 (121.51, 124.35)	116.47 (115.77, 117.17)	< 0.001
Cholesterol ratio	3.38 (3.34, 3.42)	3.84 (3.80, 3.89)	4.16 (4.11, 4.21)	4.44 (4.38, 4.49)	3.95 (3.92, 3.97)	< 0.001
CRP	0.16 (0.15, 0.18)	0.19 (0.17, 0.21)	0.21 (0.19, 0.23)	0.30 (0.26, 0.33)	0.22 (0.20, 0.23)	< 0.001
Prolactin	13.21(12.76, 13.67)	12.62 (12.26, 12.97)	12.19 (11.85, 12.53)	12.62 (12.24, 13.00)	12.66 (12.47, 12.85)	0.011
SC[b] (M/ml)	55.72 (53.74, 57.69)	52.85 (51.15, 54.55)	54.39 (52.62, 56.16)	50.25 (48.50, 51.99)	53.30 (52.40, 54.20)	< 0.001
TSM[b] (%)	65.29 (64.66, 65.92)	65.23 (64.57, 65.88)	64.98 (64.31, 65.66)	64.86 (64.20, 65.51)	65.09 (64.76, 65.41)	0.299
PRM[b] (%)	46.00 (45.31, 46.70)	46.21 (45.50, 46.93)	46.44 (45.71, 47.17)	46.04 (45.32, 46.77)	46.18 (45.82, 46.53)	0.832
NSM[b] (%)	68.40 (67.74, 69.06)	67.19 (66.53, 67.85)	67.03 (66.35, 67.70)	66.25 (65.58, 66.92)	67.22 (66.88, 67.55)	< 0.001

BMI: Body Mass Index, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, Cholesterol Ratio: Cholesterol/HDL, CRP: C-Reactive Protein, SC: Sperm Concentration, TSM: Total Sperm Motility, PRM: Progressive Motility, NSM: Normal Sperm Morphology.

[a] by one-way analysis of variance (ANOVA).

[b] the p value of SC, TSM, PRM, NSM are 0.005, 0.442, 0.452, <0.001, respectively after adjustment for age, triglyceride, cholesterol, CRP, prolactin and smoking duration (years) by linear regression models.

[c] the Bonferroni corrected values of $p < 0.008$ were considered statistically significant.

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waist circumference, hip circumference, waist-to-hip ratio, waist-to-height ratio and body fat percentage were 23.79 ± 3.30 kg/m^2, 81.06 ± 8.52 cm, 96.24 ± 6.44 cm, 0.84 ± 0.14, 0.47 ± 0.05 and 23.47% ± 5.49%, the means of sperm concentration, total sperm motility, progressive motility and normal sperm morphology were 53.3 M/ml, 65.09%, 46.18% and 67.22% (Table 1), and the prevalence of abnormal semen quality showed 9.6%, 4.8%, 19.8% and 0.8%, respectively.

Total sperm motility, progressive motility, normal sperm morphology and sperm concentration were all statistically inversely correlated with increasing age (Table 2, simple linear regression; $p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.004$). The sperm concentration of each upper quartile anthropometric index was lower than that of the lower quartile index. The mean sperm concentration value of BMI had significantly negative correlations (simple linear regression; $p = 0.005$) with each quartile of obesity and smoking duration had nominally significantly reverse association with the mean sperm concentration (simple linear regression; $p = 0.036$). Normal sperm morphology had a statistically inverse correlation with BMI and waist-to-height ratio (simple linear regression; $p < 0.001$, $p = 0.004$). Although other semen parameters including total sperm motility, progressive motility and normal sperm morphology had a reverse

Table 2. Age and anthropometric indexes by semen parameters.

Characteristics	Quartile	Concentration (M/ml) median (n = 7630) Mean (95% CI for mean)	% Total Motility median (n = 7613) Mean (95% CI for mean)	% Progressive Motility median (n = 7601) Mean (95% CI for mean)	% Normal Morphology median (n = 7624) Mean (95% CI for mean)
Age[a] (years)	Q1: <29	55.34 (53.39, 57.30)	67.56 (66.94, 68.17)	48.23 (47.50, 48.96)	69.45 (68.76, 70.14)
	Q2: 29–30	53.84 (52.01, 55.66)	66.84 (66.16, 67.52)	47.59 (46.82, 48.35)	68.70 (68.00, 69.40)
	Q3: 31–33	51.89 (50.17, 53.61)	65.18 (64.58, 65.78)	46.33 (45.66, 47.01)	66.87 (66.25, 67.49)
	Q4: ≥34	52.60 (50.89, 54.31)	61.719 (61.05, 62.39)	43.33 (42.64, 44.01)	64.64 (64.00, 65.29)
	p^b, *adjusted p*	0.015, 0.004	<0.001, <0.001	<0.001, <0.001	<0.001, <0.001
BMI[a] (kg/m^2)	Q1: <21.60	55.72 (53.74, 57.69)	65.29 (64.66, 65.92)	46.00 (45.31, 46.70)	68.40 (67.74, 69.06)
	Q2: 21.60–23.48	52.85 (51.15, 54.55)	65.23 (64.57, 65.88)	46.21 (45.50, 46.93)	67.19 (66.53, 67.85)
	Q3: 23.49–25.61	54.39 (52.62, 56.16)	64.89 (64.31, 65.66)	46.44 (45.71, 47.17)	67.03 (66.35, 67.70)
	Q4: ≥25.62	50.25 (48.50, 51.99)	64.86 (64.20, 65.51)	46.04 (45.32, 46.77)	66.25 (65.58, 66.92)
	p^b, *adjusted p*	<0.001, 0.005	0.299, 0.403	0.832, 0.488	<0.001, <0.001
Waist circumference (cm)	Q1: <75.00	55.05 (53.04, 57.06)	65.66 (64.97, 66.34)	45.80 (45.06, 46.55)	68.29 (67.57, 69.01)
	Q2: 75.00–79.00	54.39 (52.50, 56.28)	64.92 (64.24, 65.60)	46.24 (45.48, 46.99)	67.01 (66.30, 67.73)
	Q3: 80.00–85.00	54.03 (52.30, 55.75)	65.21 (64.59, 65.84)	46.41 (45.74, 47.09)	67.38 (66.75, 68.01)
	Q4: ≥86	50.29 (48.65, 51.94)	64.73 (64.10, 65.36)	46.246 (45.56, 46.94)	66.41 (65.79, 67.04)
	p^b, *adjusted p*	<0.001, 0.685	0.108, 0.939	0.394, 0.129	0.001, 0.219
Hip circumference (cm)	Q1: <92.00	56.11 (53.96, 58.27)	65.67 (64.98, 66.36)	45.85 (45.08, 46.61)	68.22 (67.51, 68.92)
	Q2: 92.00–95.99	52.93 (51.27, 54.59)	64.90 (64.25, 65.55)	46.10 (45.39, 46.81)	66.95 (66.29, 67.61)
	Q3: 96–99.99	54.67 (52.86, 56.47)	65.06 (64.41, 65.71)	46.37 (45.66, 47.08)	67.65 (66.99, 68.32)
	Q4: ≥100	50.19 (48.54, 51.84)	64.91 (64.28, 65.53)	46.39 (45.71, 47.08)	66.30 (65.66, 66.94)
	p^b, *adjusted p*	<0.001, 0.457	0.185, 0.543	0.258, 0.218	0.001, 0.712
Waist-to-hip ratio (%)	Q1: <80	53.89 (51.91, 55.87)	65.25 (64.50, 66.01)	46.41 (45.57, 47.24)	68.238 (67.435, 69.041)
	Q2: 80–83	54.56 (52.75, 56.37)	65.34 (64.72, 65.95)	46.09 (45.42, 46.76)	67.172 (66.537, 67.808)
	Q3: 84–87	53.27 (51.64, 54.91)	65.20 (64.60, 65.80)	46.29 (45.63, 46.96)	67.318 (66.703, 67.934)
	Q4: ≥88	51.50 (49.68, 53.31)	64.64 (63.97, 65.30)	46.05 (45.32, 46.78)	66.416 (65.757, 67.074)
	p^b, *adjusted p*	0.035, 0.991	0.178, 0.383	0.660, 0.853	0.002, 0.579
Waist-to-height ratio (%)	Q1: <44	54.62 (52.74, 56.51)	65.46 (64.82, 66.10)	45.93 (45.23, 46.63)	68.00 (67.33, 68.67)
	Q2: 44–46	53.72 (51.99, 55.46)	65.28 (64.63, 65.93)	46.74 (46.02, 47.46)	67.21 (66.54, 67.89)
	Q3: 47–49	53.71 (51.94, 55.48)	65.25 (64.59, 65.92)	45.92 (45.21, 46.64)	66.97 (66.29, 67.65)
	Q4: ≥50	51.21 (49.39, 53.03)	64.48 (63.79, 65.11)	46.20 (45.48, 46.93)	66.72 (66.06, 67.37)
	p^b, *adjusted p*	0.012, 0.052	0.038, 0.735	0.997, 0.529	0.007, 0.004

(*Continued*)

Table 2. (*Continued*)

Characteristics	Quartile	Concentration (M/ml) median (*n* = 7630) Mean (95% CI for mean)	% Total Motility median (*n* = 7613) Mean (95% CI for mean)	% Progressive Motility median (*n* = 7601) Mean (95% CI for mean)	% Normal Morphology median (*n* = 7624) Mean (95% CI for mean)
Body fat (%)	Q1: <19.80	54.36 (52.42, 56.31)	64.62 (63.96, 65.28)	45.59 (44.86, 46.31)	67.63 (66.95, 68.31)
	Q2: 19.80–23.29	53.26 (51.55, 54.97)	64.88 (64.23, 65.53)	45.80 (45.09, 46.50)	67.13 (66.47, 67.79)
	Q3: 23.30–26.79	54.32 (52.50, 56.14)	65.54 (64.89, 66.20)	46.79 (46.07, 47.51)	67.10 (66.43, 67.77)
	Q4: ≥26.80	51.30 (49.55, 53.04)	65.33 (64.69, 65.97)	46.55 (45.84, 47.26)	67.03 (66.37, 67.69)
	p^b, *adjusted p*	0.048, 0.846	0.062, 0.209	0.018, 0.403	0.232, 0.057
Smoking duration[a] (years)	Q1: 0	57.47 (54.08, 62.85)	65.08 (63.22, 66.95)	45.79 (45.33, 46.25)	67.70 (65.49, 69.91)
	Q2: <3	53.94 (52.32, 56.32)	64.58 (64.16, 65.01)	44.18 (42.02, 46.34)	67.04 (66.61, 67.47)
	Q3: 3–20	53.46 (51.56, 54.61)	66.12 (65.29, 66.95)	47.07 (46.13, 48.02)	67.44 (66.55, 68.34)
	Q4: ≥20	52.01 (50.04, 53.99)	65.84 (65.15, 66.52)	46.88 (46.11, 47.66)	67.49 (66.79, 68.19)
	p^b, *adjusted p*	0.132, 0.036	0.001, 0.275	0.002, 0.667	0.328, 0.556

the *p* values are calculated by one-way analysis of variance (ANOVA).

the adjusted *p* values are adjustment for age, BMI, triglyceride, cholesterol, CRP, prolactin and smoking duration (years) by linear regression models.

[a] the adjusted *p* values are adjustment for age, BMI, triglyceride, cholesterol, CRP, prolactin and smoking duration (years) but excluded itself by linear regression models.

[b] the Bonferroni corrected values of $p < 0.008$ were considered statistically significant.

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trend with each quartile of smoking duration, this was without statistical significance (Table 2, simple linear regression; $p = 0.275$, $p = 0.667$, $p = 0.556$).

To examine the relationships between age, obesity, smoking and semen quality, the semen quality as assessed by the prevalence of abnormal sperm parameters was examined by quartiles of the anthropometric indexes (BMI, waist circumference, hip circumference, waist-to-hip ratio and waist-to-height ratio). A linear association was found between a higher age and an increased incidence of low sperm concentration (Table 3, < 15 M/ml, $p = 0.011$), low total sperm motility (< 40%, $p < 0.001$), low progressive motility (< 32%, $p < 0.001$) and abnormal sperm morphology (< 30%, $p = 0.002$). A higher BMI was associated with a higher incidence of low sperm concentration and abnormal sperm morphology ($p = 0.020$ and $p = 0.049$, respectively). A higher waist circumference was correlated with a higher incidence of low sperm concentration ($p = 0.038$). No correlation was identified between smoking duration and increased incidence of abnormal semen quality (Table 3).

The obese men with the highest BMI quartile had a 1.305-fold higher odds ratio of a low sperm concentration (Table 4, 95% confidence interval (CI): 1.056–1.613) as compared with the lowest BMI quartile. In addition, waist circumference had a 1.397-fold higher odds ratio (95% CI: 1.114–1.751), hip circumference a 1.350-fold higher odds ratio (95% CI: 1.081–1.686), and waist-to-height ratio a 1.241-fold higher odds ratio (95% CI: 1.000–1.539) of oligospermia. Men with the highest BMI quartile had a 2.463-fold higher odds ratio (95% CI: 1.131–5.362) and hip circumference had a 2.185-fold higher odds ratio (95% CI: 1.017–4.695) of abnormal sperm morphology as compared with each of the lowest anthropometric index quartiles.

Table 3. The associations of abnormal semen quality with age and anthropometric indexes.

Characteristics	Quartile	Concentration < 15 M/ml, *n* (%)	Total Motility < 40%, *n* (%)	Progressive Motility < 32%, *n* (%)	Normal Morphology < 30%, *n* (%)
Age (years)	Q1: <29	142 (8.0)	49 (2.8)	295 (16.7)	9 (0.5)
	Q2: 29–30	145 (9.1)	56 (3.7)	266 (16.7)	8 (0.5)
	Q3: 31–33	207 (10.0)	76 (3.7)	391 (19.0)	11 (0.5)
	Q4: ≥34	242 (11.0)	183(8.4)	558 (25.6)	30 (1.4)
	p^a	0.011	<0.001	<0.001	0.002
BMI (kg/m^2)	Q1: <21.60	170 (8.9)	85 (4.5)	362 (19.0)	9 (0.5)
	Q2: 21.60–23.48	186 (9.7)	92 (4.8)	376 (19.8)	10 (0.5)
	Q3: 23.49–25.61	164 (8.6)	96 (5.0)	375 (19.7)	17 (0.9)
	Q4: ≥25.62	216 (11.3)	91 (4.8)	397 (20.9)	22 (1.2)
	p^a	0.020	0.869	0.537	0.049
Waist circumference (cm)	Q1: <75.00	130 (8.0)	65 (4.0)	311 (19.2)	9 (0.6)
	Q2: 75.00–79.00	172 (9.6)	97 (5.4)	373 (20.9)	15 (0.8)
	Q3: 80.00–85.00	206 (9.8)	100 (4.8)	390 (18.6)	16 (0.8)
	Q4: ≥86.00	227 (10.9)	100 (4.8)	428 (20.6)	18 (0.9)
	p^a	0.038	0.282	0.201	0.721
Hip circumference (cm)	Q1: <92.00	137 (8.4)	72 (4.4)	315 (19.3)	9 (0.6)
	Q2: 92.00–95.99	181 (9.4)	93 (4.8)	390 (20.2)	10 (0.5)
	Q3: 96–99.99	187 (9.6)	99 (5.1)	379 (19.6)	14 (0.7)
	Q4: ≥100	230 (11.0)	98 (4.7)	418 (20.1)	25 (1.2)
	p^a	0.057	0.796	0.899	0.052
Waist-to-hip ratio (%)	Q1: <80	135 (9.5)	72 (5.1)	278 (19.6)	11 (0.8)
	Q2: 80–83	200 (9.3)	95 (4.4)	435 (20.4)	17 (0.8)
	Q3: 84–87	204 (9.6)	92 (4.3)	417 (19.6)	14 (0.7)
	Q4: ≥88	196 (10.3)	103 (5.4)	372 (19.6)	16 (0.8)
	p^a	0.774	0.325	0.893	0.920
Waist-to-height ratio (%)	Q1: <44	165 (8.7)	87 (4.6)	368 (19.4)	12 (0.6)
	Q2: 44–46	186 (9.9)	84 (4.5)	367 (19.5)	13 (0.7)
	Q3: 47–49	180 (9.5)	91 (4.8)	381 (20.2)	17 (0.9)
	Q4: ≥50	204 (10.5)	100 (5.2)	386 (20.1)	16 (0.8)
	p^a	0.266	0.735	0.905	0.764
Body fat (%)	Q1: <19.80	181 (9.7)	98 (5.3)	386 (20.8)	14 (0.8)
	Q2: 19.80–23.29	181 (9.4)	99 (5.1)	400 (20.8)	11 (0.6)
	Q3: 23.30–26.79	183 (9.6)	83 (4.4)	353 (18.6)	16 (0.8)
	Q4: ≥26.80	191 (9.9)	83 (4.3)	367 (19.2)	16 (0.8)
	P^a	0.943	0.375	0.213	0.745
Smoking duration (years)	Q1: 0	13 (6.9)	6 (3.2)	40 (21.2)	1 (0.5)
	Q2: <3	441 (9.5)	246 (5.3)	946 (20.4)	33 (0.7)
	Q3: 3–20	101 (9.6)	33 (3.1)	185 (17.7)	8 (0.8)
	Q4: ≥20	181 (10.5)	79 (4.6)	337 (19.6)	16 (0.9)
	P^a	0.078	0.097	0.122	0.197

[a] by the Chi-square test.

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Discussion

Our study was the first to report the largest cross-sectional study in a single institute that enrolled subjects from a general population and used standardized protocols of a regular medical

screening program including measurements of body size and biochemical data to assess anthropometric characteristics and semen quality. The findings demonstrated that age and obesity were correlated with semen quality.

Age was statistically inversely correlated with all of the measured sperm parameters (total sperm motility, progressive motility, normal sperm morphology and sperm concentration; $p < 0.001$, $p < 0.001$, $p < 0.001$ *and* $p = 0.004$), and abnormal incidences ($p = 0.011$, $p < 0.001$, $p < 0.001$ *and* $p = 0.002$), indicating that an increasing age was associated with poorer semen quality and higher incidences of abnormal sperm parameters. Two recent review articles concluded that semen quality, including volume, sperm motility and morphology, deteriorated with increased age; however, the results concerning sperm concentration were inconsistent [17, 18]. However, most previous studies have included a smaller number of cases and a narrower age range as compared with the present study.

Two recent meta-analyses [6, 8] explored the relationship between obesity and semen production; however, the conclusions of these studies were inconsistent. One of the studies reviewed 31 studies with 5 included in the pooled meta-analysis, a total of 6,793 men, and found no significant association between BMI and sperm parameters [6]. Another study of Sermondade reported that the overweight men had significantly higher levels of oligozoospermia or azoospermia as compared with the men with a normal BMI [8]. Neither of these meta-analyses showed a linear relationship between BMI and sperm concentration or total sperm count, but had contrasting conclusions with regards to obesity and the incidence of an abnormal sperm concentration. A possible explanation is that most of the enrolled subjects had subfertility or infertility and BMI was self-reported. In addition, both of these meta-analyses were limited in only assessing general obesity with BMI, and so whether or not central obesity was correlated with semen quality could not be clarified. Moreover, some studies of other anthropometric measures have reported that abdominal fat may be a risk factor for several diseases independent of BMI [19].

Several studies have discussed the association between central obesity or other measures of fat distribution and sperm parameters [4, 5, 20]. Higher wait circumference and hip circumference have been shown to be associated with a lower total sperm count, total motile sperm count and progressive motile sperm count [5]. There is evidence that sperm concentration and total motile sperm count are detrimentally affected by a high BMI and waist circumference [4]. Study using data from the Longitudinal Investigation of Fertility and Environment has demonstrated that ejaculate volume and total sperm count have inverse linear associations with waist circumference [20]. The results of our current study showed that obesity was inversely correlated with sperm concentration and normal sperm morphology both in terms of general obesity assessed with BMI (both $p < 0.001$) and central obesity assessed with waist circumference ($p < 0.001$; $p = 0.001$) and hip circumference ($p < 0.001$; $p = 0.001$) before the co-factors being adjusted. However only BMI illustrated significantly statistical relationship ($p = 0.005$; $p < 0.001$) after adjusting related factors. Meanwhile the general obesity as assessed by BMI displayed significantly positive correlations with incidence of oligospermia and abnormal sperm morphology ($p = 0.020$; $p = 0.049$), but also the other anthropometric indexes of waist circumference ($p = 0.038$) and hip circumference ($p = 0.057$; $p = 0.052$) declared the similar trend.

Several studies have proposed waist-to-height ratio as another proxy for central obesity, correcting the waist circumference for the height of the individuals. A systematic review suggested that waist-to-height ratio is a more useful global clinical screening tool than waist circumference [21], and a meta-analysis supported the use of waist-to-height ratio in identifying adults at increased cardiometabolic risk and concluded that waist-to-height ratio appeared to be more useful in Asian than in non-Asian populations [22]. In addition, population-based cross-sectional studies reported that waist-to-height ratio is the best screening tool for detecting

Table 4. The odds ratio (OR) and 95% confidence interval (CI) of abnormal semen quality with age and anthropometric indexes.

Characteristics	Quartile	Concentration < 15 M/ml, OR (95% CI)	Total Motility < 40%, OR (95% CI)	Progressive Motility < 32%, OR (95% CI)	Normal Morphology < 30%, OR (95% CI)
Age (years)	Q1: <29	Reference	Reference	Reference	Reference
	Q2: 29–30	1.15 (0.90, 1.46)	1.28 (0.87, 1.89)	1.00 (0.84, 1.20)	0.99 (0.38, 2.57)
	Q3: 31–33	**1.28 (1.02, 1.60)**	1.35 (0.94, 1.94)	1.17 (0.99, 1.38)	1.05 (0.44, 2.54)
	Q4: ≥34	**1.42 (1.15, 1.77)**	**3.22 (2.33, 4.44)**	**1.72 (1.47, 2.01)**	**2.72 (1.29, 5.75)**
BMI (kg/m^2)	Q1: <21.60	Reference	Reference	Reference	Reference
	Q2: 21.60–23.48	1.10 (0.89, 1.37)	1.09 (0.80, 1.47)	1.05 (0.89, 1.23)	1.11 (0.45, 2.74)
	Q3: 23.49–25.61	0.96 (0.77, 1.20)	1.14 (0.84, 1.53)	1.05 (0.89, 1.23)	1.90 (0.84, 4.26)
	Q4: ≥25.62	**1.31 (1.06, 1.61)**	1.08 (0.79, 1.46)	1.13 (0.96, 1.32)	**2.46 (1.13, 5.36)**
Waist circumference (cm)	Q1: <75.00	Reference	Reference	Reference	Reference
	Q2: 75.00–79.00	1.22 (0.96, 1.55)	1.38 (0.99, 1.908)	1.11 (0.94, 1.32)	1.52 (0.66, 3.48)
	Q3: 80.00–85.00	1.241 (0.99,1.56)	1.19 (0.87, 1.64)	0.96 (0.81, 1.13)	1.37 (0.60, 3.11)
	Q4: ≥86.00	**1.40 (1.11, 1.75)**	1.21 (0.88, 1.66)	1.09 (0.93, 1.28)	1.56 (0.70, 3.47)
Hip circumference (cm)	Q1: <92.00	Reference	Reference	Reference	Reference
	Q2: 92.00–95.99	1.13 (0.90, 1.43)	1.10 (0.80, 1.50)	1.06 (0.90, 1.25)	0.94 (0.38, 2.32)
	Q3: 96.00–99.99	1.17 (0.93, 1.47)	1.17 (0.86, 1.60)	1.02 (0.86, 1.20)	1.32 (0.57, 3.05)
	Q4: ≥100	**1.35 (1.08, 1.69)**	1.07 (0.78, 1.46)	1.05 (0.89, 1.23)	**2.19 (1.02, 4.70)**
Waist-to-hip ratio (%)	Q1: <80	Reference	Reference	Reference	Reference
	Q2: 80–83	0.98 (0.78, 1.24)	0.87 (0.64, 1.19)	1.00 (0.84, 1.19)	1.03 (0.48, 2.20)
	Q3: 84–87	1.01 (0.80, 1.27)	0.85 (0.62, 1.16)	1.05 (0.90, 1.23)	0.85 (0.38, 1.87)
	Q4: ≥88	1.09 (0.87, 1.37)	1.07 (0.79, 1.46)	1.00 (0.86, 1.17)	1.08 (0.50, 2.34)
Waist-to-height ratio (%)	Q1: <44	Reference	Reference	Reference	Reference
	Q2: 44–46	1.15 (0.92, 1.43)	0.97 (0.72, 1.32)	1.01 (0.86, 1.18)	1.09 (0.50, 2.40)
	Q3: 47–49	1.11 (0.90, 1.39)	1.06 (0.78, 1.43)	1.05 (0.90, 1.23)	1.43 (0.68, 3.01)
	Q4: ≥50	**1.24 (1.00, 1.54)**	1.14 (0.85, 1.53)	1.04 (0.90, 1.22)	1.31 (0.62, 2.78)
Body fat (%)	Q1: <19.80	Reference	Reference	Reference	Reference
	Q2: 19.80–23.29	0.96 (0.77, 1.19)	0.97 (0.73, 1.29)	0.99 (0.85, 1.17)	0.76 (0.34, 1.67)
	Q3: 23.30–26.79	0.98 (0.79, 1.22)	0.82 (0.61, 1.11)	0.87 (0.74, 1.02)	1.12 (0.54, 2.29)
	Q4: ≥26.80	1.02 (0.83, 1.27)	0.81 (0.60, 1.10)	0.90 (0.77, 1.06)	1.11 (0.54, 2.28)
Smoking duration (years)	Q1: 0	Reference	Reference	Reference	Reference
	Q2: <3	1.42 (0.80, 2.51)	1.71 (0.75, 3.89)	0.96 (0.67, 1.36)	1.35 (0.18, 9.88)
	Q3: 3–20	1.44 (0.79, 2.62)	0.99 (0.41, 2.40)	0.80 (0.54, 1.17)	1.44 (0.18, 11.60)
	Q4: ≥20	1.58 (0.88, 2.83)	1.46 (0.63, 3.40)	0.91 (0.63, 1.31)	1.75 (0.23, 13.31)

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cardiometabolic risk factors in Chinese populations [23, 24]. However, in the current study, the waist-to-height ratio of anthropometric index showed a negative trend with sperm concentration with only borderline significance ($p = 0.052$) and a statistically inverse association with normal sperm morphology ($p = 0.004$). Therefore, it was not as powerful as BMI, waist circumference and hip circumference in the prediction of sperm parameters.

The etiology of the relationship between adiposity and sperm production is complex and unclear. Overweight and obesity, and particularly central obesity, have been shown to affect the GnRH-FSH/LH pulse, which may impair Leydig and Sertoli cell functions and thus interfere with the release of sex hormones and production of mature of sperm [25, 26]. The inverse association between a high BMI and sperm parameters found in this study support the findings of the aforementioned studies. However, as the majority of previous studies have focused only on BMI as the predominant measure of adiposity and not on other anthropometric indexes, our

current study is the second to show associations between hip circumference, waist-to-height ratio and sperm parameters [5], and is the first to focus on the relationship between waist-to-height ratio and semen quality in a large number of cases within the general population at a single institute.

In this study, we found inverse associations between obesity and sperm parameters including sperm concentration and normal sperm morphology. This is in accordance with the results of previous studies [3, 27, 28], all of which concluded that a high BMI (> 25 kg/m^2) was significantly associated with reduced sperm concentration and a lower percentage of normal spermatozoa without significance. The meta-analysis by Sermondade, Faure [8] demonstrated that the underweight (BMI < 18.5 kg/m^2) and obese (BMI > 30 kg/m^2) groups had higher risks of oligozoospermia or azoospermia. However, the results of the current study did not show a similar relationship, but rather a positive linear association. It is possible that the number of underweight subjects (2.21% of 13077 subjects) was too low in Sermondade *et al.*'s study to illustrate the real correlation between obesity and a lower total sperm count. Our report showed that only sperm concentration was nominally inversely correlated with increased smoking duration, which was similar with Collodel's study [29]. Although sperm concentration, motility and/or morphology are often reduced as compared with the results observed in nonsmokers, they often remained within the normal range. However the 2012 ASRM (American Society for Reproduction Medicine) Practice Committee concluded that semen parameters and results of sperm function tests are 22% poorer in smokers than in nonsmokers with a dose-dependent effect, but smoking has not yet been conclusively shown to reduce male fertility [30]. The result of our current study was promising but requiring further confirmation/replication in an independent study, and the questionnaire of the smoking intensity would be considered to explore the real association between smoking and semen quality in future.

There were some limitations to this study. We lacked data on semen volume and total sperm count due to the protocol of the physical health examination. It was regretful that we did not have detailed records of endocrine levels to assist in achieving a greater understanding of the mechanisms behind the association between semen quality and obesity. Some parameters of our study were relatively gross measures of fertility, and we did not attempt to examine functional parameters such as the DNA fragmentation index and seminal oxidative stress. Studies using the DNA fragmentation index as a measure of genetic quality have reported statistically significantly positive correlations between BMI and DFI [31, 32], indicating that obesity may still reduce the semen quality even if the sperm count and other sperm parameters remain unchanged. A higher BMI has been shown to have a statistically significant association with increased seminal reactive oxidative stress, and that elevated semen inflammation detected increased seminal plasma polymorphonuclear leukocytes (PMNs) elastase and neopterin concentrations in 81 men [33]. A positive correlation between BMI and sperm DNA fragmentation has been found in two mouse models of obesity [34], suggesting that sperm chromatin integrity is positively associated with BMI. Another longitudinal cross sectional study of Håkosen [35] ever concluded that obesity was associated with poor semen quality and altered reproductive hormonal profile. Meanwhile the group with the largest weight loss had a statistically significant increase in total sperm count and normal sperm morphology. However they observed no significant difference in DFI from baseline to follow-up.

Further studies including those with the abovementioned sperm molecular markers should be designed to explore the mechanism between obesity and semen quality. Meanwhile, the enrolled subjects were centralized in the relatively young populations, although the age distribution of the study varied from 18 to 75 years. We could hypothesize the associated trend between age and semen quality in a larger size population with the limitation of the majority subjects being in the relatively young age distribution. In addition, the participants had to pay a fee ($\sim$US$100) to

participate in the medical screening program, which, although acceptable for the middle classes of the general population in Taiwan, may exclude poorer populations. As the participants had only been asked to have more than 3 days of abstinence, but longer abstinence duration has not been recorded in the data of MJ Health Management Institution, and therefore the effect of abstinence time could not be performed. Furthermore, as this was a large sample size study, it was difficult to perform on-site collection of semen samples. Therefore, semen samples were collected using home-collection kits. As the semen samples were requested to be sent to the laboratory within one hour, the quality may not be equal to that resulting from on-site collection. Ultimately the effect of environmental chemicals like PFCs and lipophilics food should be took into consideration for comprehensive association between obesity and semen quality owing to the expectedly increased intake of above chemicals combined with food in the obese subjects, however the above data and records were unavailable on account of the original study design.

Conclusions

The results of this study showed that increased age was statistically inversely associated with semen quality, and that increased adiposity was significantly negatively correlated with sperm concentration and normal sperm morphology in a large population of healthy Taiwanese men.

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Author Contributions

Conceived and designed the experiments: CWT CYH. Performed the experiments: CWT CYL TLC SCC. Analyzed the data: YCC. Contributed reagents/materials/analysis tools: CWT CYL YCC CYH. Wrote the paper: CWT. Applied the data: CWT CYL.

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