Obesity and age affect male fertility potential

A case–cohort study of 2,157 patients, aged 17–67 years was performed to assess the impact of body mass index and age on male fertility. Using a multiple regression analysis across the total cohort, only age correlated significantly with all spermiogram parameters and serum hormones, but in patients aged 20–30 years (n = 617) the total sperm count was significantly negatively correlated with body mass index. (Fertil Steril® 2010;94:2898–901. ©2010 by American Society for Reproductive Medicine.)

Key Words: Body mass index, age, sperm counts, testosterone, FSH, inhibin-B, LH

Age (1) and a high body mass index (BMI) are expected to negatively influence semen quality (2–6). Age-related testicular alterations are associated with decreased T levels (7). Obese males frequently show T deficiencies, possibly contributing to decreases in semen quality (8), as measured by reduced total sperm counts (TSC) (2), a higher frequency of oligozoospermia (3), and a significantly negative relationship between BMI and total number of normal, motile sperm (5). In contrast, only a slightly lower adjusted TSC was measured in overweight males (9). This study examines this relationship between BMI, age, semen quality, and fertility-related hormones in a large group of infertility patients.

Data from 2,157 patients aged 17–67 years (mean ± SD, 30 ± 8.5 years) were collected prospectively into our data warehouse, Winsperm (10, 11). To examine the factors affecting semen quality, only the first ejaculate of males attending the clinic from 1999 to 2005 were included. Patients with azoospermia, varicocele, maldescensus testis, malignoma, hypogonadism, genital inflammation, or with chronic diseases were excluded. Body mass index was calculated as kilograms per meter squared (k/m^2), with the classifications as per criteria established by the US Centers for Disease Control and Prevention National Task Force (12): underweight = <20 kg/m^2, normal = 20–25 kg/m^2, overweight = 25–30 kg/m^2, and obese = ≥30 kg/m^2.

Semen samples were collected after a period of 3–5 days of sexual abstinence, and subjects provided written, informed consent. This study was approved by the institutional review board of the University of Leipzig, Germany, and conducted in accordance with ethical standard guidelines of the University. Semen sample parameters were determined according to World Health Organization guidelines (13). Sperm morphology was estimated by the Tygerberg strict criteria (13–15). Computer-aided sperm motion analysis (CASA) was performed using Mika cell motion analysis (Mika Medical, Montreux, Switzerland). Aliquots (5 μL) of semen samples were placed into 10-μm-deep disposable counting chambers (Mika Medical) on a 36°C microscope stage warmer. For each specimen, a minimum of 100 spermatozoa were analyzed (16). Our study measured the following semen parameters: TSC; total count of normomorph sperm (TCN); and percentage of motile spermatozoa. In addition, serum concentrations of T, inhibin-B, LH, and FSH were measured. Luteinizing-hormone, FSH, and T were measured by the Elecsys platform (Roche, Mannheim, Germany). Inhibin-B was determined by immunoradiometric assays (Beckmann-Coulter, Sinsheim, Germany).

Data retrieval from Winsperm and statistical analysis were performed using Statistica 7.0 (StatSoft, Tulsa, OK). Results are expressed as mean ± SEM, as well as median plus the 10th and 90th percentiles. The Shapiro-Wilk's W test using the Royston (1982) version for normality of large samples excluded a normal distribution for TSC, TCN, FSH concentrations in serum, and the inhibin-B/FSH ratio. These parameters were transformed into log-normal distributions. An unpaired Mann-Whitney U test was performed to calculate the differences between the BMI groups. Spearman's rank correlation coefficients were used to determine the linear associations between different parameters. All tests were two-tailed, and significance was indicated by $P<.05$. Moreover, the results were analyzed using a stepwise multiple linear regression with BMI and age as the main dependent variable as well as the interaction term BMI × age.

Of 2,157 male patients 4.6% (n = 99) were underweight, 46.5% (n = 1,003) were of normal weight, 37.6% (n = 810) were overweight, and 11.3% (n = 245) were obese (Table 1). The patient ages in the four BMI groups differed significantly ($P<.005$) from each other. The TSC was maximized in the group with

Uwe Paasch, M.D., Ph.D.[a]
Sonja Grunewald, M.D., Ph.D.[a]
Juergen Kratzsch, M.D., Ph.D.[b]
Hans-Juergen Glander, M.D., Ph.D.[a]
[a] *Department of Dermatology, Training Center of the European Academy of Andrology, University of Leipzig, Leipzig, Germany*
[b] *Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Leipzig, Germany*

Received February 16, 2010; revised June 8, 2010; accepted June 16, 2010; published online July 29, 2010.
U.P. has nothing to disclose. S.G. has nothing to disclose. J.K. has nothing to disclose. H-J.G. has nothing to disclose.
H-J.G. received a funding grant from the German Research Council (GL 199/4-4). U.P. and J.K. received funding from the German Research Council (PA 834.7-1 KFO152.8A 152/8).
Reprint requests: Uwe Paasch, M.D., Ph.D., Department of Dermatology, Training Center of the European Academy of Andrology, University of Leipzig, Philipp-Rosenthal-Strasse 23, D 04103 Leipzig, Germany (FAX: 49-341-9718749; E-mail: uwe.paasch@medizin.uni-leipzig.de).

0015-0282/$36.00
doi:10.1016/j.fertnstert.2010.06.047

TABLE 1

Age, semen sample parameters, and serum hormone concentrations.

Parameter	Total (n = 2,157)	Underweight (n = 99)	Normal (n = 1,003)	Overweight (n = 810)	Obese (n = 245)
Age (y)	30.1 ± 0.18	21.9 ± 0.64	27.8 ± 0.26	32.6 ± 0.25	34.3 ± 0.56
	31.0 (18–40)	19.0 (17–32)[a,b,c]	28.0 (18–38)[a,d]	33.0 (23–41)[b,d,e]	33.0 (25–46)[b,c,e]
BMI (kg/m^2)	25.0 ± 0.08	18.6 ± 0.08	22.5 ± 0.04	26.6 ± 0.05	32.7 ± 0.19
	24.0 (21–30)	19.0 (17.2–19.2)	23.0 (20.6–24.0)	26.1 (25.0–29.0)	31.0 (30.0–36.0)
Age × BMI	761.6 ± 6.06	405.2 ± 12.18	624 .9 ± 6.27	865.0 ± 7.06	1,123.7 ± 20.56
	756.0 (397.5–1,089)	342.0 (323–608)[a]	630.0 (380–874)[a,b]	864.0 (600–1,102)[b,d]	1054.0 (775–1,568)[d]
Total sperm count (×10^6)	151.3 ± 3.80	154.8 ± 16.81	159.2 ± 5.51	143.7 ± 6.26	143.0 ± 11.68
	90.0 (7–381)	99.0 (16.5–345)[f]	102.5 (8.0–384.0)[e]	79.6 (7.0–391.8)[e]	66.0 (5.0–371.0)[f]
Total sperm count with normal morphology (×10^6)	14.3 ± 0.53	18.64 ± 2.83	16.24 ± 0.79	12.49 ± 0.88	10.62 ± 1.19
	5.0 (0.04–40.7)	7.68 (0.56–51.48)[b]	6.48 (0.07–44.40)[a,d]	4.20 (0.01–36.0)[a]	3.30 (0.00–34.20)[b,d]
Motile sperm (%)	40.2 ± 0.66	45.8 ± 3.70	40.9 ± 1.01	39.7 ± 0.99	38.1 ± 2.06
	37.6 (12.9–70.7)	43.0 (26.0–67.6)	38.2 (13.7–71.4)	37.6 (12.7–69.3)	35.3 (11.9–67.2)
VSL ($\mu m \cdot s^{-1}$)	28.4 ± 0.39	28.8 ± 2.47	28.5 ± 0.59	28.3 ± 0.59	28.0 ± 1.28
	26.0 (14.7–45.1)	25.7 (12.8–45.9)	26.2 (14.7–45.9)	26.3 (15.1–44.3)	24.2 (14.1–44.8)
VAP ($\mu m \cdot s^{-1}$)	39.7 ± 0.47	38.2 ± 2.99	40.1 ± 0.71	39.3 ± 0.71	39.5 ± 1.56
	36.8 (22.8–61.0)	36.2 (25.0–59.8)	37.9 (22.9–61.0)	36.3 (22.6–60.8)	36.1 (23.1–61.3)
FSH ($mU \cdot mL^{-1}$)	7.2 ± 0.18	7.5 ± 1.28	7.4 ± 0.32	7.1 ± 0.25	6.8 ± 0.45
	4.7 (2.0–16.1)	4.2 (2.0–19.5)	5.0 (2.2–16.5)	4.6 (2.0–15.7)	4,6 (1.8–15.0)
LH ($mU \cdot mL^{-1}$)	4.5 ± 0.13	5.6 ± 0.88	4.7 ± 0.24	4.4 ± 0.19	4.4 ± 0.33
	3.9 (1.7–8.2)	4.5 (3.1–10.6)	4.2 (1.8–8.3)	3.7 (1.6–8.1)	3.7 (1.8–7.8)
T ($nmol \cdot L^{-1}$)	16.2 ± 0.17	17.2 ± 1.23	16.5 ± 0.26	16.1 ± 0.26	15.7 ± 0.44
	15.4 (9.3–23.7)	15.3 (10.0–28.2)	16.2 (9.5–23.7)[f]	15.2 (9.4–23.5)	14.6 (8.6–23.2)[f]
Inhibin-B ($ng \cdot mL^{-1}$)	107.8 ± 1.9	115.5 ± 13.7	113.0 ± 3.1	107.1 ± 2,74	95.5 ± 4.4
	95.2 (15.0–207.0)	94.5 (15.0–250.0)	101.0 (15.5–214)[d]	93.2 (15.0–207.0)[f]	81.8 (15.0–173.5)[c,f]
T/LH	14.7 ± 2.0	3.6 ± 0.5	13.0 ± 3.8	16.3 ± 2.9	13.8 ± 4.8
	4.0 (1.8–9.0)	4.1 (1.8–5.1)	3.8 (1.8–9.0)	4.1 (1.8–9.0)	3.9 (1.4–9.0)
Inhibin-B/FSH	36.8 ± 1.5	42.6 ± 9.9	35.9 ± 2.3	37.6 ± 2.2	35.4 ± 3.6
	21.6 (1.6–79.1)	21.9 (0.9–108.7)	22.3 (1.4–75.0)	21.5 (1.9–80.8)	19.6 (1.2–73.8)

Note: Values are mean ± SEM, median (10th–90th percentile); Mann Whitney *U* test. VSL = straight line velocity; VAP = average path velocity.
[a–f] Values with an identical character in each line are significantly different.

Paasch. Correspondence. Fertil Steril 2010.

normal BMI. Sperm counts decreased in the underweight and overweight BMI groups ($P<.05$). The TSC with normal morphology (TCN) showed a similar inverse, U-shaped distribution. An increase in normomorph sperm was observed in men who were under- to normal weight and decreased in men in the normal to obese weight groups. The CASA failed to detect significant differences between BMI groups. Hormone analyses indicated a significantly ($P<.05$) lower serum concentration of T and inhibin-B in obese males than in males with normal BMIs.

In all participating patients, BMI was significantly correlated with TSC ($r = -0.07$, $P=.0005$), with a higher level of significance to TCN ($r = -0.13$, $P=.0000001$). However, patient age was also correlated with TSC and TCN. In fact, TSC ($r = -0.09$, $P=.00003$) and TCN ($r = -0.23$, $P=.0000001$) correlated at higher levels of significance with age than BMI. Motility was not significantly influenced by the age or BMI of patients, with the exception of the percentage of motile sperm ($r = -0.09$, $P=.004$), which significantly decreased with age. Hormone levels were also somewhat influenced by BMI and age. Specifically, BMI was significantly negatively correlated with inhibin-B ($r = -0.07$, $P=.003$) and LH ($r = -0.08$, $P=.04$). Age was positively correlated with FSH ($r = 0.05$, $P=.03$) but negatively correlated with T ($r = -0.15$, $P=.0000001$) and inhibin-B ($r = -0.06$, $P=.009$). The ratio inhibin-B/FSH, as a marker of the Sertoli-cell sensitivity to FSH, was negatively correlated with age ($r = -0.08$, $P=.002$) but not with BMI ($P>.05$). The T/LH ratio, as an indicator of Leydig-cell function, did not significantly correlate with either BMI or age ($P>.05$).

According to multiple regression analysis, BMI was influenced mostly by patient age. Thus, age correlated significantly with the following parameters: TSC, TCN, percentage of motile sperm, serum concentrations of T and inhibin-B, and the inhibin-B/FSH ratio. The BMIs of the total patient group did not significantly correlate with the examined parameters ($P>.05$). However, in a limited range of men aged 20–30 years (n = 617), a significant negative correlation was measured between TSC and BMI ($r = -0.102$, $P<.05$) with no correlation to age ($r = -0.067$, not significant). The other parameters examined did not show an analogous relationship.

This study revealed that semen quality was in general more closely associated with age than with BMI. However, we demonstrated that a normal BMI is important for male fertility, especially in the reproductive age of 20–30 years.

Studies of the relationships between male BMI and fertility-related parameters have shown conflicting results. The negative relationship between sperm concentration or TSC and BMI has been described (2, 5, 17, 18) but not confirmed (9, 19). Furthermore, the