ORIGINAL ARTICLE: ENVIRONMENT AND EPIDEMIOLOGY

Men's body mass index in relation to embryo quality and clinical outcomes in couples undergoing in vitro fertilization

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Objective: To evaluate the association between men's body mass index (BMI), early embryo quality, and clinical outcomes in couples undergoing in vitro fertilization (IVF).
Design: Prospective cohort study.
Setting: Fertility clinic in an academic medical center.
Patient(s): 114 couples who underwent 172 assisted reproduction cycles.
Intervention(s): None.
Main Outcome Measure(s): Fertilization rate, embryo quality, implantation rate, clinical pregnancy rate, and live birth rate.
Result(s): The fertilization rate was higher among obese men than among normal weight men in conventional IVF cycles. No statistically significant associations were found between men's BMI and the proportion of poor-quality embryos on day 3, slow embryo cleavage rate, or accelerated embryo cleavage rate. Men's BMI was unrelated to positive β-human chorionic gonadotropin rate, clinical pregnancy rate, or live-birth rate per embryo transfer. Among couples undergoing intracytoplasmic sperm injection, the odds of live birth in couples with obese male partners was 84% lower than the odds in couples with men with normal BMI.
Conclusion(s): Our data suggest a possible deleterious effect of male obesity on the odds of having a live birth among couples undergoing intracytoplasmic sperm injection. (Fertil Steril® 2012;■:■–■. ©2012 by American Society for Reproductive Medicine.)
Key Words: Body mass index, men's obesity, IVF, ICSI

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The effects of obesity and overweight status on reproductive health have been studied in both women and men. There has been increasing evidence that female obesity has a negative effect on assisted reproductive technology (ART) outcomes (1–4). Excessive weight in women undergoing ART has been associated with lower pregnancy rates, lower live-birth rates, fewer normally fertilized eggs, and a need for higher doses of gonadotropins (1, 2, 5, 6). Furthermore, couples in whom both members are obese are at an increased risk of subfertility (7).

Obesity has also been related to impairments in men's reproductive function. Studies have shown that men's body mass index (BMI) is inversely related to androgen levels and positively related to estrogen levels, resulting in a hormone profile consistent with hypogonadotropic hyperestrogenic hypoandrogenemia (8–10). The higher estrogen levels have a deleterious effect on endogenous gonadotropin

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secretion because they interfere with gonadotropin-releasing hormone (GnRH) pulsatility (8, 11). In addition, overweight condition and obesity in men have been associated with poorer semen quality (12, 13), higher sperm DNA damage (10, 14, 15), and infertility (16). Nevertheless, the relationship between men's BMI and ART outcomes has not been examined extensively. We evaluated the association of men's BMI with fertilization rate, early embryo quality, and clinical outcomes in couples undergoing in vitro fertilization (IVF).

MATERIALS AND METHODS

Study Sample

Women and men presenting for evaluation at the Massachusetts General Hospital (MGH) Fertility Center were invited to participate in the EARTH Study, an ongoing study on environmental factors and fertility (17). Enrollment as a couple is not required for participation. Male partners from couples undergoing ART (both techniques: IVF with conventional insemination and intracytoplasmic sperm injection [ICSI]), aged 18 to 55 years, and without a history of vasectomy were eligible to be enrolled in the study. Men were included in the analysis if they were enrolled with their female partner, were using their own gametes for ART, had complete information on age and BMI, and had a partner who had completed at least one ART cycle by March 31, 2011. Of the 291 men recruited between December 2004 and March 2011, 114 men fulfilled the eligibility criteria. The study was approved by the human subject committees of the Harvard School of Public Health and the MGH, and informed consent was obtained from all participants.

Height and weight were measured at study enrollment by trained research nurses. A lifestyle and medical questionnaire was administered by a trained research nurse to all men who agreed to participate in the study. In addition, men were asked to complete a detailed self-report questionnaire focused on lifestyle factors and medical history.

Female partners of eligible men underwent one of three stimulation protocols: [1] luteal phase GnRH-agonist protocol, [2] GnRH-antagonist protocol, or [3] follicular phase GnRH-agonist/flare protocol. Briefly, on day 3 of induced menses, treatment with exogenous gonadotropins (FSH, Gonal-F, Follistim, Bravelle)] and/or human menopausal gonadotropin (hMG, Repronex, Menopur) was initiated, and the GnRH agonist or antagonist was continued or started after the usual ovarian stimulation protocols. Human chorionic gonadotropin (hCG) was administered 36 hours before oocyte retrieval to trigger ovulation. The oocyte retrieval was performed when transvaginal ultrasound showed $\geq$3 dominant follicles (16 mm or greater) and the estradiol level had reached at least 500 pg/mL. Blood samples were drawn to assess the baseline FSH level on the third day of any menstrual cycle before the treatment (Elecsys FSH reagent; Roche Diagnostics). Height and weight were also measured in all women enrolled in the study. In addition, they also completed a food and lifestyle questionnaire.

Embryologic Assessment

Couples underwent IVF with conventional insemination or with ICSI, as clinically indicated. As is the standard practice in ART procedures, the nuclear maturity of oocytes was determined before ICSI but not before conventional IVF. Embryologists classified oocytes as germinal vesicle, metaphase I, metaphase II (M2), or degenerated. Fertilized oocytes were classified as normally fertilized if they had two pronuclei; otherwise, they were classified as abnormally fertilized. On day 3, the embryos were assessed for quality and were graded from 1 (best) to 5 (worst) according to their morphologic characteristics. Embryos of grades 3, 4, and 5 were considered poor quality. In addition, the cleavage rate was assessed by counting the number of cells in the embryo on day 3. Embryos that had six to eight cells on day 3 were considered to have a normal cleavage rate. Embryos with fewer than six cells were considered to be cleaving at a slow rate, and embryos with more than eight cells were considered to be cleaving at an accelerated rate. Day-2 embryo transfers (n = 6 couples, n = 9 cycles) were excluded from the embryo quality analysis as no information was available for day-3 quality. Complete embryo quality was available in 149 cycles.

Clinical outcomes were assessed among all couples who initiated a cycle (n = 172) and among couples who underwent an embryo transfer (n = 158). Positive β-hCG rate was defined as an elevation in β-hCG levels above 6 IU/L after embryo transfer. Clinical pregnancy was defined as the presence of an intrauterine pregnancy confirmed by ultrasound. Finally, live birth was defined as the birth of a neonate on or after 24 weeks' gestation.

STATISTICAL ANALYSIS

The body mass index (BMI) of the men and women was calculated from the anthropometric assessment obtained at study entry. Men were divided into three categories according to the World Health Organization classification: 18.5–24.9 kg/m^2 (normal), 25–29.9 kg/m^2 (overweight), or $\geq$30 kg/m^2 (obese) (18).

We used generalized estimating equations (GEE) logistic regression models to take advantage of all the available information while accounting for correlations in outcomes across cycles within the same couple. Three sets of regression models were fit for each of the analyses. The first set of models was fit to assess the crude association between male BMI and the outcomes of interest. The second set of models included additional terms for men's age (centered to the mean: 36 years old), women's age (centered to the mean: 35 years old), women's day-3 FSH level (binary: $<$10 mIU/mL vs. $\geq$10 mIU/mL), infertility diagnosis (categorical: female, male, unexplained/other), day of embryo transfer (binary: day 2 or 3 vs. day 5), and stimulation protocol (binary: agonist vs. antagonist). Finally, the third set of models included all the covariates in the second set of models plus a term for women's BMI (centered to the mean: 23 kg/m^2). Per initiated cycle analyses were not adjusted for embryo transfer day to avoid inputting an arbitrary day to those cycles without embryo transfer. Covariates were chosen using prior knowledge based on clinical relevance and a statistical approach based on

change in point estimates. Given the sample size, we prioritized the inclusion of potential confounders and known predictors of the ART outcomes considered to be clinically relevant regardless of statistical significance. None of the variables evaluated as potential confounders (men's race, men's smoking status, abstinence time) were associated with both male BMI and ART outcomes and were therefore not included in the final multivariate models. Female age, day-3 FSH, infertility diagnosis, and stimulation protocol were included based on their clinical relevance.

We used a test for linear trend where a variable with the median value of each category of male BMI was modeled as a continuous variable. To present crude and adjusted rates for each category of male BMI, we used linear combinations of the regression parameters and centered men's and women's age and BMI at their mean values in all models. Men with normal BMI were considered the reference group. To evaluate whether the association between male BMI and clinical outcomes was modified by couples' characteristics, we added interaction terms between male BMI and female BMI and between male BMI and infertility diagnosis. Similarly, to formally test whether the associations of male BMI with clinical outcomes statistically significantly differed between IVF and ICSI cycles, we added cross-product terms between male BMI and an indicator of the cycle type. Whenever this test of heterogeneity was statistically significant, we presented separate results for IVF and ICSI cycles accordingly. Finally, we conducted a sensitivity analysis in which we excluded blastocyst transfer.

We considered that an association was present whenever we found evidence of a statistically significant linear trend at $P<.05$. The analyses were performed using Statistical Analysis Software (SAS) version 9.2 (SAS Institute Inc.).

RESULTS

Our study sample consisted of 114 couples who collectively underwent 172 ART cycles and for whom complete anthropometric and clinical information was available. Of the 114 couples, 104 had at least one M2 oocyte retrieved and at least one embryo transfer. The men's mean age (± standard deviation [SD]) was 36.5 (±5.0) years; the majority was Caucasian (88%) and had never smoked (64%). The men's mean BMI was 27.3 (±4.3) kg/m^2, and 20% were obese (BMI $>$ 30 kg/m^2). Of all the couples, 27% were diagnosed as having primarily male factor infertility, and 20% reported undergoing previous IVF/ICSI cycles. The median (25th to 75th centile) semen parameter values were sperm concentration 57 million/mL (29–104 million/mL), progressive sperm motility 41% (24% to 62%), and normal sperm morphology 5% (3% to 7%). The women's baseline characteristics and responses to ovarian stimulation were similar across all categories of male BMI with the exception of female BMI, which was positively related to their partner's BMI (P trend=.001) (Table 1). There were 158 cycles with an embryo transfer: 9 (5.7%) were day-2 embryo transfers, 110 (69.6%) were day 3, and 39 (24.68%) were day 5. Overall, there were 98 positive β-hCG tests, 85 clinical pregnancies, and 69 live births.

Among the 172 initiated cycles, 7 cycles had no M2 oocytes retrieved. The fertilization rate was assessed among the remaining 165 cycles from 108 couples. The overall fertilization rate was not associated with the men's BMI (Table 2). Although the fertilization rate in conventional IVF cycles was higher among obese men than among normal weight men (P trend=.04), male BMI was unrelated to the fertilization rate in ICSI cycles (P trend=.87). However, a test for heterogeneity in the relationship between male BMI and fertilization rate by fertilization technique indicated that this relationship did not differ statistically significantly by fertilization technique (P heterogeneity=.72).

Next, we evaluated the relation of men's BMI with in vitro embryo development and clinical outcomes. We did not find a statistically significant association between the men's BMI and the proportion of poor-quality embryos on day 3 (P trend=.67), slow embryo cleavage rate (P trend=.17), or accelerated embryo cleavage rate (P trend=.07) (Supplemental Table 1, available online).

The men's BMI was unrelated to the positive β-hCG rate (P trend=.37), clinical pregnancy rate (P trend=.91), or live-birth rate (P trend=.42) per embryo transfer (Table 3). Further adjustment for the women's BMI did not considerably change these estimates. The results were similar when the association was examined per initiated cycle. Furthermore, we evaluated whether the associations between male BMI and clinical outcomes were modified by female BMI or infertility diagnosis, and we found no evidence of effect modification by these variables (data not shown). The relation between male BMI and live birth differed statistically significantly between the IVF and ICSI cycles (P heterogeneity=.04). Among the couples undergoing ICSI, the odds of a live birth in couples with an obese male partner were 84% (95% CI, 10% to 97%) lower than the odds in couples with male partners of normal BMI (P trend=.04) (Table 4). This association persisted after adjustment for semen quality parameters (data not shown). Among couples undergoing conventional IVF, there was a suggestion of higher live-birth rates with increasing male BMI but it was not statistically significant.

Finally, we conducted a sensitivity analysis in which we excluded all blastocyst transfer cycles. In this analysis, the inverse association between men's BMI and the proportion of accelerated cleavage embryos was slightly more pronounced (P=.01) than that observed in the entire group (P=.07). We did not find any statistically significant associations between male BMI and the other outcomes.

DISCUSSION

We evaluated whether men's BMI was related to fertilization rate, in vitro embryo quality, or clinical outcomes in couples undergoing ART. We found that obese men had a higher fertilization rate than lean men in IVF cycles, and this relationship was unchanged after adjusting for semen quality. No statistically significant associations were found between men's BMI and day-3 embryo quality. The men's BMI was not associated with clinical outcomes among couples undergoing conventional IVF. However, in couples undergoing ICSI cycles, male obesity was related to lower odds of having a live birth.

TABLE 1

Study sample characteristics in relation to men's body mass index (n = 114 couples, 172 cycles).

Characteristic	Male BMI 18.5–24.9 kg/m^2	25–29.9 kg/m^2	≥30 kg/m^2	*P* value[a]
Men				
Number	38	53	23	
Age	35.9 (4.7)	36.6 (5.2)	37.4 (4.5)	.50
BMI	22.9 (1.4)	27.7 (1.2)	33.7 (3.1)	<.001
Smoking status (%)				.48
Never	71	62	57	
Former or current	29	38	43	
Race %				.05
White	81	90	92	
Black	0	4	4	
Asian	16	0	4	
Other	3	6	0	
Semen analysis (%)[b]				
Sperm concentration <15 million/mL	9 (24%)	18 (47%)	13 (34%)	.06
Sperm motility <32%	4 (8%)	15 (28%)	16 (30%)	.06
Sperm morphology <4%	2 (9%)	6 (26%)	4 (17%)	.18
Abstinence time (d)	3.0 (2.7)	3.0 (8.2)	2.0 (2.5)	.79
Prior pregnancies with this or other couple (%)	22	34	50	.17
Women				
Age	34.5 (2.7)	35.0 (4.0)	36.1 (4.3)	.25
BMI	23.2 (3.5)	23.2 (3.6)	26.8 (5.4)	<.001
Day 3 FSH	6.7 (2.1)	6.6 (2.2)	7.4 (2.3)	.34
Smoking status (%)				.50
Never	79	68	74	
Former or current	21	32	26	
Race %				.52
White	82	88	91	
Black	0	2	0	
Asian	13	4	9	
Other	5	6	0	
Ovarian stimulation protocol (%)				.08
GnRH agonist, long luteal phase	90	83	70	
GnRH antagonist	5	9	4	
GnRH agonist, follicular phase initiation (flare)	5	8	26	
Total oocyte yield[c]	11 (9–13)	11 (10–12)	10 (8–12)	.40
Total M2 yield[c]	9 (8–11)	9 (8–10)	8 (7–10)	.42
Couple				
Primary etiology of infertility (%)				.73
Female factor	42	43	52	
Male factor	34	25	22	
Unexplained/other	24	32	26	
Had any previous infertility evaluation (%)	84	85	83	.97
Previous IVF or ICSI cycle (%)	16	21	26	.62
Day of embryo transfer (%)				.34
2	6	4	10	
3	65	57	76	
5	29	39	14	

Note: Continuous variables are expressed in mean (95% CI). BMI = body mass index; CI = confidence interval; FSH = follicle-stimulating hormone; GnRH = gonadotropin-releasing hormone; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; M2 = metaphase II.

[a] From analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables.

[b] Normal values for semen parameters were assessed using the World Health Organization Manual, Laboratory manual for the examination and processing of human semen, 5th ed. (Geneva: WHO, 2010).

[c] Mean and (95% CI) for total and M2 oocytes.

Colaci. Men's BMI and IVF outcomes. Fertil Steril 2012.

To the best of our knowledge, this is the third study assessing the association between male BMI and IVF/ICSI outcomes, and it is the first prospective study in which these associations were adjusted for the most important female characteristics that are known to have critical effect on the overall outcomes (19–23). Our findings are in agreement with Bakos et al. (24), who reported no association of male BMI with overall fertilization rate or in vitro embryo quality on day 3. They did find, however, a statistically significant reduction of blastocyst development and lower pregnancy rate associated with increasing men's BMI. Due to our small sample size of day-5 embryo transfers, we were not able to perform an analysis on blastocyst transfer outcomes. Nevertheless, a recent animal study concluded that male obesity was related to reduced embryo cleavage, decreased development to the stage of blastocyst, lower implantation rate, and lower fetal development (25). Contrary to our findings, Keltz et al. (26) conducted a retrospective analysis and showed that couples

TABLE 2

Fertilization rate in relation to men's body mass index (n = 108 couples, 165 cycles).

	Male BMI			
Fertilization rate	**18.5–24.99 kg/m²**	**25–29.99 kg/m²**	**≥30 kg/m²**	***P* trend[c]**
Total % (95% CI)				
Number	52	78	35	
Crude	67 (58–75)	72 (67–76)	71 (62–79)	.44
Adjusted[a]	68 (58–76)	72 (66–77)	72 (62–80)	.48
Adjusted + Women BMI[b]	68 (59–76)	72 (66–77)	75 (66–82)	.28
IVF cycles % (95% CI)				
Number	23	31	20	
Crude	61 (46–73)	70 (64–76)	77 (68–76) [c]	.05
Adjusted[a]	59 (42–73)	70 (62–77)	76 (65–84) [c]	.04
Adjusted + Women BMI[b]	59 (44–73)	69 (60–77)	77 (66–86) [c]	.04
ICSI cycles % (95% CI)				
Number	29	47	15	
Crude	72 (63–79)	71 (65–77)	65 (49–78)	.50
Adjusted[a]	74 (65–80)	73 (66–79)	66 (50–79)	.37
Adjusted + Women BMI[b]	73 (64–80)	74 (67–80)	71 (56–82)	.87

Note: BMI = body mass index; CI = confidence interval; FSH = follicle-stimulating hormone; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization.
[a] Mean rates (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, and stimulation protocol.
[b] Mean rates (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, and women's BMI.
[c] $P < .05$ compared with the reference group (men's BMI 19–24.99 kg/m²).

Colaci. Men's BMI and IVF outcomes. Fertil Steril 2012.

with an overweight or obese man (BMI ≥ 25 kg/m²) who were undergoing traditional IVF had lower clinical pregnancy rates than couples with a lean man. However, they did not find this association for ICSI cycles. Due to the scarce literature available on this topic, it is difficult to assess correctly the origins of the difference between our findings and those of the Keltz study. Clearly, it is important to examine further the relationship between male obesity and ART outcomes.

We found that among couples undergoing ICSI those with an obese male partner had statistically significantly lower odds of having a live birth. Semen alterations are usually the main cause for choosing ICSI over traditional IVF, and

TABLE 3

Odds ratios (95% CI) for clinical outcomes per embryo transfer cycle in relation to men's body mass index (n = 172 initiated cycles, 158 cycles with embryo transfer).

	Male body mass index			
Clinical outcomes	**18.5–24.99 kg/m²**	**25–29.99 kg/m²**	**≥30 kg/m²**	***P* trend**
Per initiated cycle				
Number (cycle)	54	80	38	
Positive β-hCG rate				
Adjusted[a]	Ref	0.57 (0.25–1.32)	0.79 (0.28–2.24)	.51
Adjusted + Women BMI[b]	Ref	0.58 (0.25–1.36)	1.04 (0.31–3.44)	.78
Clinical pregnancy				
Adjusted[a]	Ref	0.88 (0.41–1.87)	1.08 (0.44–2.66)	.93
Adjusted + Women BMI[b]	Ref	0.90 (0.42–1.96)	1.53 (0.52–4.52)	.55
Live birth				
Adjusted[a]	Ref	0.83 (0.40–1.74)	0.72 (0.28–1.82)	.47
Adjusted + Women BMI[b]	Ref	0.85 (0.40–1.79)	0.91 (0.32–2.60)	.79
Per embryo transfer				
Number (cycles)	50	73	35	
Positive β-hCG rate				
Adjusted[c]	Ref	0.57 (0.23–1.42)	0.68 (0.24–1.98)	.37
Adjusted + Women BMI[d]	Ref	0.57 (0.23–1.44)	0.76 (0.23–2.55)	.47
Clinical pregnancy				
Adjusted[c]	Ref	0.99 (0.44–2.20)	1.07 (0.42–2.67)	.91
Adjusted + Women BMI[d]	Ref	1.03 (0.45–2.33)	1.31 (0.45–3.80)	.66
Live birth				
Adjusted[c]	Ref	0.83 (0.37–1.83)	0.69 (0.27–1.73)	.42
Adjusted + Women BMI[d]	Ref	0.84 (0.38–1.85)	0.79 (0.28–2.21)	.62

Note: BMI = body mass index; CI = confidence interval; FSH = follicle-stimulating hormone; hCG = human chorionic gonadotropin; Ref = reference value.
[a] Odds ratio (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, and stimulation protocol.
[b] Odds ratio (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, and women's BMI.
[c] Odds ratio (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, and embryo transfer day.
[d] Odds ratio (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, embryo transfer day, and women's BMI.

Colaci. Men's BMI and IVF outcomes. Fertil Steril 2012.

TABLE 4

Odds ratios (95% CI) for clinical outcomes in couples undergoing assisted reproduction according to fertilization method (conventional in vitro fertilization and intracytoplasmic sperm injection).

		Male BMI			
Clinical outcome	**No. of cycles**	**18.5–24.99 kg/m^2**	**25–29.99 kg/m^2**	**≥30 kg/m^2**	***P* trend**
IVF cycles					
Clinical pregnancy per initiated cycle[a,b]	74	Ref	0.83 (0.34–2.06)	1.69 (0.52–5.46)	.38
Live birth per initiated cycle[a,b]	74	Ref	1.80 (0.58–5.65)	1.84 (0.48–7.06)	.35
Clinical pregnancy per embryo transfer[c,b]	72	Ref	0.92 (0.38–2.22)	1.54 (0.47–5.06)	.51
Live birth per embryo transfer[c,b]	72	Ref	1.81 (0.59–1.71)	1.63 (0.43–6.16)	.44
ICSI cycles					
Clinical pregnancy per initiated cycle[b,d]	91	Ref	0.57 (0.20–1.63)	0.62 (0.14–2.67)	.35
Live birth per initiated cycle[b,d]	91	Ref	0.40 (0.14–1.17)	0.20 (0.04–1.00)	.03[f]
Clinical pregnancy per embryo transfer[b,e]	86	Ref	0.53 (0.16–1.68)	0.53 (0.11–2.55)	.29
Live birth per embryo transfer[b,e]	86	Ref	0.40 (0.12–1.37)	0.16 (0.03–0.90)[f]	.04[f]

Note: BMI = body mass index; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; Ref = reference value.
[a] 53 Couples initiate an IVF cycle and underwent 74 IVF cycles.
[b] Odds ratio (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, and women's BMI.
[c] 52 couples underwent 72 embryo transfers among IVF cycles.
[d] 55 couples initiated an ICSI cycle and underwent 91 ICSI cycles.
[e] 52 couples underwent 86 embryo transfers among ICSI cycles.
[f] $P<.05$ compared with the reference group (men's BMI 19–24.99 kg/m^2).

Colaci. Men's BMI and IVF outcomes. Fertil Steril 2012.

the relationship between men's BMI and semen quality impairment is well established. Therefore, one could speculate that the effect of obesity on clinical outcomes was mediated through semen quality. However, our analysis indicated that the relationship of male obesity with live-birth rates was independent of sperm parameters.

The literature does not suggest any plausible biologic explanation for the significantly higher fertilization rate and the apparently higher live-birth rates observed among couples with an obese male partner undergoing conventional IVF cycles. Men's BMI has been previously related to lower total sperm count (10, 27), sperm concentration (27, 28), sperm motility (12), higher DNA fragmentation (10, 14, 15, 29), and deleterious effects on reproductive hormone levels (30–32), including in our previous publication (10) which included some of the men in this report. Given that available data suggest either a deleterious or null effect of men's BMI on semen quality, we would have expected an inverse relation, if any, of male BMI with fertilization and live-birth rates. Relying on this evidence and the lack in our data of differences between fertilization rate in IVF and ICSI cycles when testing for heterogeneity, we believe that the higher fertilization and live rates observed could be either a chance finding or related to unmeasured confounding for which we were unable to adjust. Given the paucity of data in this area, it is important that future studies examine this association.

A potential limitation of our analysis is the limited sample size to evaluate the association between men's weight and blastocyst development. As is the most frequent practice in the United States, the majority of the couples included in our study underwent day-3 embryo transfers, so we were not able to fully examine the impact of male BMI on in vitro blastocyst development. Because the embryonic genome is activated after the four- to eight-cell stage, we may have missed an effect of male BMI on early genome activation (33). Another potential limitation is that, given our limited sample size, we used logistic regression to examine the relationship between male BMI and clinical ART outcomes (thereby modeling the odds of each outcome) instead of regression models for proportions such as log-binomial models. Because all the clinical ART outcomes are common, odds ratios from these models are always farther away from the null than risk ratios. Nevertheless, we were careful throughout the study to clearly note that the results were expressed as odds and odds ratios and not as probabilities or risk ratios precisely to avoid difficulties in the interpretation of the results.

The strengths of our analysis include accurate measurements of male and female BMI and complete prospective information on cycle outcomes for the whole study sample. In addition, as we had complete information on the female partners, we were able to adjust for female characteristics that are known to affect overall embryologic and clinical outcomes (3–6).

We did not find evidence of an association between men's BMI and early embryo development or clinical outcomes among couples undergoing conventional IVF. Our analysis suggested an inverse relation between men's BMI and live birth among couples undergoing ICSI. Because this study was conducted among couples seeking fertility treatment, it is not possible to generalize the results to the general population or derive conclusions on the effect of men's BMI on natural fertility. Given the paucity of data on the role of men's BMI on ART outcomes, compelling data suggesting a deleterious effect of male obesity on semen quality, data on the beneficial effects of weight loss on semen quality (32), and the extensive literature on nonreproductive adverse consequences of obesity (34), we feel general counseling on the benefits of weight reduction among overweight and obese men should remain the norm for men in couples seeking fertility treatment.

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SUPPLEMENTAL TABLE 1

Day-3 embryo development in relation to men's body mass index (n = 149 cycles).

	Male BMI			
Embryo development	**18.5–24.99 kg/m^2**	**25–29.99 kg/m^2**	**≥30 kg/m^2**	***P* trend**
Poor quality % (95% CI)				
Crude	24 (17–33)	22 (17–29)	21 (14–30)	.56
Adjusted[a]	23 (16–32)	21 (16–28)	19 (13–28)	.50
Adjusted + Women BMI[b]	23 (16–32)	22 (16–28)	20 (12–32)	.67
Accelerated cleavage % (95% CI)				
Crude	8 (5–14)	6 (4–8)	4 (2–8)	.12
Adjusted[a]	8 (4–15)	5 (3–9)	4 (2–8)	.12
Adjusted + Women BMI[b]	8 (4–15)	5 (3–9)	3 (1–7)	.07
Slow cleavage % (95% CI)				
Crude	32 (24–41)	33 (25–41)	36 (28–45)	.54
Adjusted[a]	34 (25–45)	33 (24–43)	36 (27–46)	.86
Adjusted + Women BMI[b]	33 (25–43)	33 (25–43)	46 (34–58)	.17

Note: Only cycles that had at least one embryo developed were considered for this analysis. Day-2 embryo transfers (n = 9) were excluded from this analysis. BMI = body mass index; CI = confidence interval.

[a] Mean rates (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, and stimulation protocol.

[b] Mean rates (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, and women's BMI.

Colaci. Men's BMI and IVF outcomes. Fertil Steril 2012.