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ORIGINAL ARTICLE

Sperm Quality

The impact of male overweight on semen quality and outcome of assisted reproduction

Lise Thomsen[1], Peter Humaidan[1,2], Leif Bungum[3], Mona Bungum[4]

It is well-documented that male overweight and obesity causes endocrine disorders that might diminish the male reproductive capacity; however, reports have been conflicting regarding the influence of male body mass index (BMI) on semen quality and the outcome of assisted reproductive technology (ART). The aim of this study was to investigate whether increased male BMI affects sperm quality and the outcome of assisted reproduction in couples with an overweight or obese man and a non-obese partner. Data was prospectively collected from 612 infertile couples undergoing ART at a Danish fertility center. Self-reported information on paternal height and weight were recorded and BMI was calculated. The men were divided into four BMI categories: underweight BMI < 20 kg m^{-2}, normal BMI 20–24.9 kg m^{-2}, overweight BMI 25–29.9 kg m^{-2} and obese BMI > 30 kg m^{-2}. Conventional semen analysis was performed according to the World Health Organization guideline and sperm DNA integrity was analyzed by the Sperm Chromatin Structure Assay (SCSA). No statistically significant effect of male BMI was seen on conventional semen parameters (sperm concentration, total sperm count, seminal volume and motility) or on SCSA-results. Furthermore, the outcome of ART regarding fertilization rate, number of good quality embryos (GQE), implantation and pregnancy outcome was not influenced by the increasing male BMI.

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Keywords: assisted reproductive technology; body mass index; male obesity; sperm chromatin structure assay; sperm quality

INTRODUCTION

The average body mass index (BMI) in Denmark for both men and women is rising in accordance with the trend seen in other Western countries.[1–3] In 2003, 26% of 18-year-old Danish conscripts were overweight (BMI > 25 kg m^{-2}), of whom 25% were obese (BMI > 30 kg m^{-2}).[4] During the last decade this figure has increased by 20%, thus, at present every third Danish 18-year-old man is overweight.[4] In parallel with the global increase in obesity, a possible decrease in sperm count and fecundity was reported.[5,6]

It is well-known that female weight disturbances has impact on the fertility potential and that obesity affects fertility negatively in terms of hormonal disturbances,[7,8] increased risk of polycystic ovary syndrome,[7] anovulation[8] as well as poorer results after assisted reproductive technology (ART).[3,9,10] As a consequence, many European fertility clinics require female weight loss to a specific BMI threshold before initiating ART treatment.[11]

From the male perspective, however, it is still unclear to what extent overweight and obesity affects sperm quality and the chances of conceiving—spontaneously as well as after ART. The relatively limited data published are conflicting,[12–15] and therefore, it is still uncertain whether male weight loss will increase natural or assisted fertility. However, it has been shown that obesity may affect male fertility in several ways: either through an increased risk of erectile dysfunction,[9,16] increased temperature of the testes,[17] hormonal disturbances,[18–20] impaired sperm quality[21,22] or impaired sperm DNA integrity.[23–25] Two recently published meta-analyses[19,20] reported no clear correlation between increasing male BMI and the conventional sperm parameters. However, there could be other factors in the overweight male which diminish the reproductive capacity, for example, an increased sperm DNA fragmentation rate[23,24] or a reduced oocyte-sperm binding capacity.[26] These changes, if present, will not be reflected in the conventional semen analysis, but could affect the outcome of ART.

In clinical life we are often presented with overweight male patients and there is a need for more studies to clarify whether male overweight represents a problem for the outcome of ART as this topic until now has only been discussed in a few studies.[12–14,27]

Therefore, the primary aim of this study was to investigate whether increased male BMI affects the outcome of ART in terms of fertilization rate, number of good quality embryos (GQE), implantation rate (IR), clinical pregnancy rate and delivery rate. A second aim was to explore whether increased BMI has any impact on sperm DNA integrity as measured by Sperm Chromatin Structure Assay (SCSA) as well as the conventional semen parameters (sperm concentration, toal sperm count, semen volume and sperm motility) in men undergoing ART. Thirdly, we wanted to examine whether the mode of fertilization has any impact on the outcome of ART in different BMI categories.

MATERIALS AND METHODS

Patients and study design

The study was based on a cohort of 1250 infertile couples undergoing ART at The Fertility Clinic, Skive, Viborg Hospital, Denmark during

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the period April 2002 to December 2003. Couples were included consecutively in the study. Data regarding the predictive value of SCSA have already been reported,[28–30] however, in these publications data were not analyzed in relation to male BMI. In 612 of the 1250 cycles, self-reported information about paternal height and weight were available and BMI could thus be calculated. The population included 167 intrauterine inseminations (IUIs), 233 *in vitro* fertilization (IVF) cycles, 126 intracytoplasmic sperm injection (ICSI) cycles and 86 split cycles (50%IVF/50%ICSI). Maternal height and weight were measured by trained staff. For each individual, the BMI was calculated as kg m^{-2}. Male patients were initially grouped according to BMI as follows: underweight < 20 kg m^{-2}, normal weight 20–24.9 kg m^{-2}, overweight 25–29.9 kg m^{-2} and obese > 30 kg m^{-2}. These BMI categories were used in previous studies with similar aims as the present study.[12,23] When analyzing data regarding pregnancy and delivery, the underweight (<20 kg m^{-2}) group was omitted, due to its small sample size (n = 11).

Using the World Health Organization class I, II and III on the obese group, the 74 males were distributed as follows: class I: 64, class II: 6 and class III: 4. Due to the limited number of patients in groups II and III, all statistical analysis on the obese male patients were made on the total obese group (n = 74).

Data in this study was collected as part of a larger study designed to investigate the predictive role of sperm DNA fragmentation in assisted reproduction. In order to minimize a potential influence of female infertility problems, women with BMI > 30 kg m^{-2} and follicle stimulating hormone >10 IU were excluded.

In order to obtain sufficient numbers of sperm for SCSA analysis, only men having a sperm concentration of at least one million per ml in neat semen were included in the study.

All female partners were self-reported nonsmokers. Male smoking habits are given in **Table 1**.

Prior to the ART treatment all male participants were asked to complete a questionnaire to report the length of sexual abstinence prior to providing the semen sample. Moreover, information on medical and reproductive history and lifestyle factors, including alcohol consumption and smoking status was recorded.

The primary study on the role of sperm DNA fragmentation for the outcome of ART was approved by the Ethics Committee of Viborg County (No. VN2002/25). An Institutional Review Board approval was not required for the present study due to its retrospective nature and the fact that the study data completely excluded the identification of subjects. All patients had given written authorization at the time of treatment for the future use of their clinical data.

Table 1: Demographic data according to male BMI, total study population

	BMI				Total population (n=612)
	<20 (n=11)	20-24.9 (n=259)	25-29.9 (n=268)	>30 (n=74)	
Male BMI, kg m^{-2}	19.0±0.5	23.1±1.3	27.0±1.4	32.4±3.1	25.9±3.5
Male age, year	31.7±5.3	33.0±5.2	32.7±5.2	33.0±4.1	32.8±5.1
Abstinence time, day	4.3±3.1	4.6±3.4	4.5±3.3	4.7±4.1	4.6±3.4
Female age, year	29.6±4.5	31.9±4.4	31.0±4.2	33.2±4.5	31.6±4.4
Female BMI, kg m^{-2}	22.0±2.2	23.7±3.4	24.6±3.3	25.3±3.4	24.3±3.4
Female FSH, IU	6.4±1.7	6.5±2.0	6.4±2.1	7.1±2.1	6.5±2.0
Alcohol consumption, units/week	3.8±4.3	5.6±5.1	5.7±4.9	7.4±5.9	5,9±5,1
Smoking	0.4±0.05	0.3±0.05	0.3±0.05	0.4±0.05	0.4±0.05
No. of previous ART treatments	1.8±0.8	1.89±1.1	1.9±1.1	1.9±1.1	1.9±1.1

All data in the table are presented as mean±s.d. BMI: body mass index; FSH: follicle stimulating hormone; ART: assisted reproductive technology

ART procedures

In IUI-patients, all hormone stimulation and insemination procedures were performed as previously described.[28] In IVF/ICSI patients hormonal treatment, ovum pick up, gamete handling and culture and embryo transfer (ET) were performed as previously described.[28,29] A maximum of two embryos were transferred on day 2 or 3 following ovum pick up.

Conventional semen analysis

Semen was collected onsite by masturbation in sterile containers on the day of ovum pick up or IUI. A period of 3–5 days of sexual abstinence prior to the sample collection was recommended. Semen analysis was performed within 1 h after ejaculation. One hundred microliters of the raw semen sample was frozen at −80 °C for later SCSA analysis. Semen analysis was performed according to the World Health Organization guidelines[31] in regard to semen volume, sperm concentration, total sperm count and sperm motility. Sperm morphology was not assessed.

Sperm chromatin structure assay

Sperm DNA integrity was analyzed by the SCSA at the Reproductive Medicine Centre, Skanes University Hospital, Malmö, Sweden. Details of this analysis have previously been described elsewhere.[28]

In brief, SCSA is a flow cytometric technique which identifies spermatozoa with abnormal chromatin packaging defined as susceptibility to acid-induced DNA denaturation *in situ*.[32,33] The analysis is based on the fact that damaged sperm chromatin denatures when exposed to an acid-detergent, whereas normal double-stranded chromatin remains stable and intact. After a low pH challenge acridine orange staining is used to distinguish between denaturated single stranded DNA and native double stranded DNA regions as acridine orange under these experimental conditions emits red fluorescence when intercalated with single-stranded damaged DNA and green fluorescence when associated with stable native double stranded DNA. The level of DNA breaks is expressed by the DNA fragmentation index (DFI) which is the ratio of red to total (red plus green) fluorescence intensities in the flow cytometric analysis, i.e. the level of denatured DNA over the total DNA. In addition to DFI the SCSA-parameter high DNA stainability (HDS) was also assessed. HDS was calculated as the percentage of sperm with high levels of green fluorescence, which are thought to represent immature spermatozoa with incomplete chromatin condensation.[33]

Cells were analyzed using an FACScan flow cytometer (Becton Dickinson, San Jose, CA, USA), equipped with an air-cooled argon ion laser. A total of 10 000 events were accumulated for each measurement at a flow rate 200–300 cells per second. A reference sample was run for every fifth sample. The intralaboratory coefficient of variation was found to be 4.5% for DFI and 10% for HDS, respectively.

Reproductive outcome parameters

Normal fertilization was defined as two visible pronuclei (PN) 16–18 h after ICSI or IVF insemination. Fertilization rate was calculated as numbers of 2PN per metaphase II oocytes available. GQE represents the number of embryos for ET plus the number of embryos cryopreserved.

A positive pregnancy was determined as a serum beta-human chorionic gonadotropin (hCG) level > 10 IU on day 12 after ET. IR was calculated as the ratio of gestational sacs determined by ultrasound after 7 weeks in relation to the total number of embryos transferred (a maximum of two).

A clinical pregnancy was determined as the presence of a fetal heartbeat on ultrasound examination 4–6 weeks after ET (pregnancy week 7 or 8).

Statistical analysis

For the analysis of potential associations between BMI and sperm quality in terms of sperm concentration, total sperm count, motility, volume, DFI and HDS the total study group regardless of ART treatment type (IUI, IVF, ICSI and split) was included.

In the analysis of reproductive outcome for *in vitro* fertilization only IVF and ICSI cycles were included. Split cycles were excluded as some of these patients had a mix of IVF and ICSI embryos transferred.

The reproductive outcome regarding IUI is presented separately.

As the distribution of semen parameters was skewed, we calculated the median and range in each BMI category. Where appropriate, for background data and reproductive outcome parameters mean and standard deviation (s.d.) was calculated.

Mean values for all parameters except reproductive outcome were tested in a linear regression analysis model with the respective parameters as dependent factors and the four BMI categories as independent factors. For the reproductive outcome parameters (implantation, positive hCG, clinical pregnancy rate and deliveries); however, odds ratios (OR) with 95% confidence intervals (CI) were estimated for the three highest BMI categories, using binary logistic regression analysis. The normal weighted men (20–24.9 kg m^{-2}) were used as reference for this analysis. After inclusion of male smoking habits, female age, female BMI and number of previous ART-treatments in the statistical model, the ORs for reproductive outcome were unchanged.

The underweight group (<20 kg m^{-2}) was omitted from this part of the statistical analysis, due to its small sample size.

Statistical analysis was performed using statistical software (Statistical Package for Social Sciences 17.0 for Windows; SPSS Inc, Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

RESULTS

Demographic data

The mean (s.d.) age of the men in the total study population of 612 ART cycles was 32.8 (5.1) years and the corresponding age for the women was 31.6 (4.4) years. For both men and women, no statistical difference in age was seen between the four BMI categories (**Table 1**).

The mean BMI of the total study population was 25.9 (3.5). Of 612 male patients 1.8% (n = 11) were underweight, 42.3% (n = 259) were of normal weight, 43.8% (n = 268) were overweight and 12.1% (n = 74) were obese. Of the obese male patients 64 were Class I (BMI 30–34.9 kg m^{-2}), six were Class II (BMI 35–39.9 kg m^{-2}) and four were Class 3 (BMI > 40 kg m^{-2}). There was no statistically significant difference in the cause of infertility (anovulation/tubal disease/endometriosis/male factor/unexplained) between the groups (data not shown); nor in the number of previous ART treatments performed, female follicle stimulating hormone and female BMI (**Table 1**). Neither alcohol consumption nor smoking habits differed between the male BMI categories. The incidence of diabetes mellitus, recent infections or use of medicine with potential negative effect on sperm quality did not differ between male BMI categories (data not shown).

When sorting data according to mode of fertilization (IVF or ICSI), an identical analysis was performed. Women from the IVF group with overweight partners (BMI 25–29.9 kg m^{-2}) had a slightly higher number of oocytes retrieved compared to those with an obese partner with a BMI > 30 kg m^{-2}, a mean (s.d.) of 9.0 (4.7) *vs* 7.1 (7.0) oocytes ($P = 0.04$) (**Table 2**). After adjusting for female BMI the P values remained unchanged.

Sperm quality

No significant effect of male BMI was seen on sperm concentration, total sperm count, semen volume or motility. Levels of DFI and HDS as measured with SCSA did not differ significantly across the BMI groups (**Table 3**).

Reproductive outcome

IVF and ICSI

In IVF and ICSI patients neither rates of positive hCG, clinical pregnancy and deliveries differed significantly between BMI categories (**Table 4**). Setting the normal BMI group (BMI 20–24.9 kg m^{-2}) as a reference, for IVF patients the ORs and 95% CI for positive hCG for the overweight and obese groups were 0.6 (0.3–1.5) and 0.5 (0.1–1.8), respectively. The corresponding values for positive hCG in the ICSI group were 1.2 (0.6–2.2) and 1.0 (0.4–2.3). Regarding delivery the ORs and 95% CI for the overweight IVF group were 1.1 (0.6–2.1) and 0.8 (0.3–2.6) in the obese group. For ISCI patients ORs for delivery were 0.5 (0.2–1.1) in the overweight group and 0.4 (0.1–1.6) in the obese group (**Table 4**).

No statistically significant differences were seen in fertilization rate, number of GQE or IR between the three BMI groups—neither when data was treated as one group (IVF + ICSI) nor when treated separately (IVF *vs* ICSI) (**Table 2**). As previously reported,[29] fertilization and embryo development were not related to DFI or HDS levels.

IUI

A comparison of the three BMI groups revealed no statistically significant differences regarding positive hCG, clinical pregnancy rate or deliveries. Setting the normal BMI group as reference, the OR and 95% CI for both positive hCG and clinical pregnancy were 0.8 (0.4–2.0) for BMI group 25.0–29.9 kg m^{-2} and 0.8 (0.2–3.2) for the group with BMI > 30 kg m^{-2} (**Table 5**). Odds ratio for delivery in the overweight group (BMI 25.0–29.9 kg m^{-2}) was 0.9 (0.3–2.6) and 1.7 (0.4–7.0) for the obese group (BMI > 30 kg m^{-2}).

DISCUSSION

The present study indicates that male overweight and obesity does not seem to have any negative impact on the outcome of ART (IUI, IVF and ICSI) in males patients in the reproductive age partnered with non-obese females. Moreover, the present data show that in men undergoing ART, sperm quality in terms of sperm DNA integrity and conventional sperm parameters are not negatively affected by a higher male BMI.

During the last decade several reports on the effects of increased male BMI on fertility have been published.[19,21,12–15] It is well-documented that male overweight causes endocrine disorders in terms of decreased sex hormone binding globulin and decreased total testosterone levels.[19] As spermatogenesis is driven mainly by the action of free testosterone and follicle stimulating hormone which seem to be only slightly influenced by male overweight and obesity;[19,20] it seems biologically plausible that semen parameters are not affected in this group of patients in spite of an altered endocrine profile.

While some studies reported that male overweight leads to a decreased sperm count,[12,15,21,34,35] others did not find this association.[18,19,36,37] Most studies reported that neither sperm motility[18,21,24,38,39] nor morphology[12,21,24,38] and semen volume[21,34,36,38,39] were impaired as a result of increased male BMI.

Due to the poor predictive role of conventional sperm parameters,[40,41] an increasing focus on the role of sperm DNA integrity in fertility has been noted.[42] While the negative role of a high DFI as measured by

Table 2: Fertilisation, number of good quality embryos and implantation in IVF and ICSI groups according to male BMI

	IVF (BMI)			*ICSI (BMI)*			*Total IVF/ICSI (BMI)*		
	20-24.9	*25-29.9*	*>30*	*20-24.9*	*25-29.9*	*>30*	*20-24.9*	*25-29.9*	*>30*
Ovum pick-up (OPU), *n*	96	99	33	52	61	11	148	160	44
Ocytes, *n*, mean±s.d.	8.8±4.9	9.0±4.7*	7.1±4.0*	8.4±4.6	8.3±4.8	6.2±3.7	8.5±4.8	8.6±4.6	7.0±3.9
Fertilisation (2PN), %, mean±s.d.	60.1±29.5	60.1±28.7	52.9±31.1	57.0±27.7	57.4±29.2	59.9±27.1	59.9±28.3	62.0±26.5	53.5±26.5
GQE, mean±s.d.	2.2±2.0	2.0±1.5	1.8±1.3	2.5±2.2	1.8±1.4	1.8±0.8	2.2±2.0	2.0±1.5	1.8±1.3
Implantation, %	25	40	31	29	30	31	34	29	32

No statistically significant differences were found between groups except the number of oocytes retrieved, *P=0.04. BMI: body mass index, kg m^{-2}; GQE: good quality embryos (number of embryos for embryo transfer plus the number of embryos cryopreserved),IVF: *in-vitro* fertilization; ICSI: intracytoplasmic sperm injection

Table 3: Conventional semen analysis and SCSA-results according to male BMI, total study population

	BMI				*Total population (n=612)*
	<20 (n=11)	*20-24.9 (n=259)*	*25-29.9 (n=268)*	*>30 (n=74)*	
Sperm concentration, million ml^{-1}, median (range)	116.0 (2.9-170.0)	48.5 (1.2-530.0)	45.0 (1.2-250.0)	52.0 (1.3-345.0)	47.0 (1.2-530.0)
Total sperm count, million, median (range)	334.5 (7.3-468.0)	134.0 (1.2-1020.0)	131.0 (1.0-876.0)	139.0 (2.6-564.0)	134.0 (1.0-1020.0)
Motile sperm, %, median (range)	75 (36-90)	65 (6-114)	65 (3-98)	65 (22-98)	65 (3-114)
Total progressive motile sperm (million), median (range)	279.8 (2.6-355.2)	82.2 (0.1-717.8)	82.3 (0-692.0)	90.0 (1.61-309.7)	83.3 (0.1-717.8)
DFI, %, median (range)	20.4 (8.2-32.5)	18.9 (0.4-74.7)	19.7 (3.7-95)	17.1 (3.3-52.9)	19.0 (0.4-95.0)
HDS, %, median (range)	9.7 (4.3-16.9)	9.0 (3.3-32.2)	9.3 (4.1-48.3)	8.4 (4.1-33.7)	9.1 (3.3-48.3)

No statistically significant differences were found between groups, BMI: body mass index, kg m^{-2}; DFI: DNA fragmentation index; HDS: high DNA stainability; SCSA: sperm chromatin structure assay

Table 4: Reproductive outcome of IVF and ICSI according to male BMI

	IVF					*ICSI*				
	BMI 20-24.9	*BMI 25-29.9*	*OR (95% CI)*	*BMI>30*	*OR (95% CI)*	*BMI 20-24.9*	*BMI 25-29.9*	*OR (95% CI)*	*BMI>30*	*OR (95% CI)*
Ovum pick-up (OPU), *n*	96	99		33	-	52	61		11	
Embryo transfer (ET), *n*	78	83	-	29	-	45	51	-	11	-
Positive hCG/ET, %	43	47	0.6 (0.3-1.5)	45	0.5 (0.1-1.8)	61	55	1.2 (0.6-2.2)	45	1.0 (0.4-2.3)
Clinical pregnancy/ET, %	39	41	2.0 (0.9-4.6)	40	2.4 (0.6-9.6)	56	43	1.0 (0.5-1.8)	40	1.0 (0.4-2.5)
Delivery/ET, %	35	36	1.1 (0.6-2.1)	28	0.8 (0.3-2.6)	51	33	0.5 (0.2-1.1)	27	0.4 (0.1-1.6)

Reproductive outcomes are adjusted for female BMI, female age, male smoking and number of previous ART treatments. No statistically significant differences were found between groups. BMI: body mass index, kg m^{-2}; OR: odds ratio; IVF: *in-vitro* fertilization; ICSI: Intracytoplasmic sperm injection; hCG: human chorionic gonadotropin

Table 5: Reproductive outcome of intrauterine insemination according to male BMI

	BMI 20-24.9	*BMI 25-29.9*	*OR (95% CI)*	*BMI>30*	*OR (95% CI)*
Intrauterine inseminations, *n*	73	73	-	19	-
Positive hCG, %	18	15	0.8 (0.4-2.0)	16	0.8 (0.2-3.2)
Clinical pregnancy rate, %	18	15	0.8 (0.4-2.0)	16	0.8 (0.2-3.2)
Deliveries, %	10	10	0.9 (0.3-2.6)	16	1.7 (0.4-7.0)

No statistically significant differences were found between groups. BMI: body mass index, kg m^{-2}; hCG: human chorionic gonadotropin; OR: odds ratio

SCSA is very clear in *in vivo* fertility, natural conception[43–45] and IUI;[28,29] the role of a high DFI in IVF and ICSI is more unclear. The risk of having a high number of DNA damaged sperm has been linked to several causes and mechanisms,[42] among others increased BMI.[23,24] Recently, Dupont *et al.*,[46] Chavarro *et al.*[24] and Kort *et al.*[23] reported an increased sperm DNA fragmentation rate in overweight[23] and obese[23,24,46] men compared to normal weight men; however, these findings have been contrasted by others.[15,47,48]

So far, only a few previous reports have studied the effects of an increased BMI on the outcome of ART.[12–14,27,35] Thus, Bakos and colleagues[12] found no relationship between paternal BMI and early embryo development in a retrospective study including 305 men undergoing IVF or ICSI; however, a reduced blastocyst development, impaired IR, reduced clinical pregnancy rate and live birth rate were observed with increasing male BMI. The authors hypothesized that the decrease in blastocyst development might be caused by increased DNA damage in the overweight and obese group as demonstrated by Kort *et al.*[23] and Charvarro *et al.*[24]

Recently, Keltz and colleagues[13] also reported the clinical pregnancy rate to be declining with increasing male BMI, reporting a 79% reduction in the chance of conceiving if IVF rather than ICSI was chosen in obese men; thus, underlining a possible negative influence on oocyte-spermatozoa interaction. This was contrasted by Kupka *et al.*[14] who retrospectively analyzed data covering 12 years from the national German IVF Registry, including 650 452 cycles from 120 centers. In their large retrospective analysis, the highest clinical pregnancy rates for both IVF and ICSI were seen in a normal-weight female with an obese male partner (P = 0.0028). A recent Danish study by Petersen *et al.*[27] analyzed 25.191 IVF/ICSI cycles from the IVF registry and showed that IVF-treated couples with both partners having BMI > 25 kg m^{-2} had the lowest odds of live birth compared with couples with both partners having BMI < 25 kg m^{-2}. They found higher odds of live birth after ICSI treatment compared with IVF among overweight and obese men supporting the hypothesis that ICSI may overcome a possible obesity-related impairment of the sperm-egg interaction.[27]

On the other hand, another recent study by Braga *et al.*[35] found no effect of male overweight on the fertilization rate, IR and pregnancy rate after ICSI. However, as none of the studies mentioned were randomized controlled trials several potential confounders and selection biases might have influenced the findings.

Taken together, in most of the studies performed until now the number of men with BMI > 35 kg m^{-2} has been low which might disguise the possible true negative effect of morbid obesity on male reproductive potential. Although a good epidemiological study is often better than a small prospective trial, the study by Håkonsen and colleagues[15] calls for attention, showing a significant impact of weight loss on sperm quality in morbidly obese men. As this study included 43 patients, only, there is clearly a need for a larger follow-up study.

The present study was based on the hypothesis that sperm quality could be impaired in overweight and obese men, which might affect the results of ART; however, no effect of a high BMI was seen on the results of IUI, IVF and ICSI. Our findings obviously contrast those of Bakos *et al.*[12] who reported a linear correlation between increasing male BMI and the ART outcome, when assessing blastocyst development, IR, pregnancy rate, clinical pregnancy rate and live birth rate. The mode of fertilization (IVF or ICSI) could potentially play a role for the outcome parameters, in particular if our hypothesis of an increased DFI in the obese men was correct. Previously we published evidence for a threefold better clinical pregnancy rate if ICSI was chosen prior to IVF in couples where the male partner had a DFI above 30%.[29]

In concordance with the findings of Håkonsen and co-workers,[15] the present study found DFI to be similar in all BMI groups. Thus, a potential decreased sperm-egg interaction in overweight male patients seems not to be caused by increased DNA damage in spermatozoa. While Håkonsen *et al.*[15] included 43 obese men, only, with a BMI > 33, our study was based on as many as 612 men with BMI of wider ranges.

A recent study by Sermondade *et al.*[49] evaluated for the first time in humans the association between male BMI and sperm-zona pellucida binding ability by the zona binding test and found no statistically significant effect of BMI on the ability of sperm to bind to the zona pellucida.

Limitations of the present study are the reduced number of patients with severe obesity (World Health Organization Class II and III) and the fact that male BMI were only available as self-reported data which in general tends to overestimate height and underestimate weight[50] although this seems to be more modest in male patients.[51] A recent Danish study concerning body size and time-to-pregnancy showed an excellent agreement between self-reported BMI and measures provided by the Danish Medical Birth Registry on the same women indicating that Danish participants respond honestly when asked about weight and height.[52]

From a clinical point of view, data is still scarce concerning the question whether male weight loss prior to ART is likely to improve sperm quality and the reproductive outcome and can only be answered through well-designed prospective randomized controlled intervention studies. At present, only two smaller studies with this design have been published[15,53] due to the limited sample size of these study populations; however, no firm conclusions could be reached.

In conclusion, the results of the present study indicate that in men with a non-obese partner a high male BMI does not have a negative impact on neither the ART outcome nor the semen quality. However, in order to draw firm conclusions, relevant for daily clinical practice, the findings should be replicated in a larger ART-cohort including a wider range of BMI levels.

AUTHOR CONTRIBUTIONS

LT, PH, LB and MB have all given substantial contributions to conception and design of the present study. All authors have contributed to acquisition of data, analysis as well as interpretation of data. MB has conducted the statistical analysis. LT has drafted the manuscript and PH, LB and MB have revised the content critically. All co-authors approved the final draft prior to submission.

COMPETING INTERESTS

All authors declare no competing interests.

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