

Obesity does not increase the risk of side effects and complications of egg retrieval: delaying oocyte retrieval in obese patients is not a good strategy

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Abstract. – OBJECTIVE: Obesity is one of the main concerns for public health and is becoming an increasingly widespread problem worldwide. Women are more likely to require a cesarean section and have a longer hospital stay after delivery. Excess body weight can interfere with ovulation and make it more difficult for embryos to implant in the uterus. A high body mass index (BMI) has controversial effects on the outcomes of medically assisted reproduction treatments (IVF) and, if careful counseling is not performed, medical-legal risks may be incurred. While some researchers argue that obesity does not particularly affect ART outcomes, other studies claim that a high BMI does not interfere with embryonic development. Both the American Society for Reproductive Medicine (ASRM) and the European Society of Human Reproduction and Embryology (ESHRE) has stated that there is no clear evidence supporting a BMI limit for IVF treatment and that each patient should be evaluated on an individual basis. The purpose of our study was to evaluate whether performing in vitro fertilization on these patients increases the risk of medical, surgical, and anesthetic complications of oocyte retrieval.

PATIENTS AND METHODS: From January 2011 to December 2022, all patients with BMI higher than 25 were enrolled in the study (n=766). Complications and risks related to oocyte retrieval were evaluated, and patients were divided according to BMI groups.

RESULTS: With the one-way ANOVA test, all groups were compared with the control group, and none showed statistically significant differences, only the number of produced embryos in the BMI group between 30-34.9 was lower and statistically significant.

CONCLUSIONS: Only one study has analyzed these aspects, mainly focusing on the need for anesthesia drugs and any related complications, and the same author reported greater difficulty in performing oocyte retrieval. The same study recorded an increase in incomplete oocyte retrievals. Our work does not confirm any of these impressions.

Key Words:

Egg retrieval, Obesity, Side effect of egg retrieval.

Introduction

Obesity is one of the main concerns for public health and is becoming an increasingly widespread problem worldwide. According to the World Health Organization (WHO)¹, in 2022, more than 1.9 billion adults were overweight and of these, over 650 million were obese². Obesity is a risk factor for pregnancy because it increases the likelihood of certain complications, such as gestational diabetes³, hypertension⁴, and pre-eclampsia⁵. These conditions can lead to serious health problems for both the mother and the baby, such as birth defects^{6,7}, intrauterine fetal death⁸, and difficulties during delivery⁹. Additionally, obese women are more likely to require a cesarean section and have a longer hospital stay after delivery⁹. On the other hand, excess body weight can interfere with ovulation¹⁰ and make it more difficult for embryos to implant in the uterus¹¹.

A high body mass index (BMI) has controversial effects on the outcomes of medically assisted reproduction treatments (IVF) and, if careful counseling is not performed, medical-legal risks may be incurred¹². Several studies¹³ in literature have shown that women with a BMI ≥ 30 have a lower chance of success with *in vitro* fertilization (IVF) compared to women with a lower BMI. Some of these studies¹⁴ state that obesity can affect the quality of oocytes retrieved during an IVF cycle and can increase the prevalence of meiotic spindle abnormalities, resulting in misaligned chromosomes and failed fertilization of oocytes¹⁵. Additionally, high levels of inflammation, which are often associated with individuals with high BMI, can hurt embryonic development and survival through the alteration of epigenetic mechanisms¹⁶, reducing the likelihood of implantation and compromising the uterine environment¹⁷. Finally, obesity has been linked to an increased risk of developing polycystic ovary syndrome (PCOS)¹⁸, which can further interfere with ovulation and lead to the formation of lower-quality oocytes¹⁹. While some researchers²⁰ argue that obesity does not particularly affect ART outcomes, other studies²¹ claim that a high BMI does not interfere with embryonic development.

Both the American Society for Reproductive Medicine (ASRM)²² and the European Society of Human Reproduction and Embryology (ESHRE)²³ have stated that there is no clear evidence supporting a BMI limit for IVF treatment and that each patient should be evaluated on an individual basis²². Indeed, some authors²³ have highlighted how the pregnancy rate of obese patients after embryo transfer is comparable to that of normal-weight women; however, their rate of spontaneous abortion is increased. Based on these evaluations, the Australian public health organization²⁶ proposed in 2017 to deny treatment to patients with a BMI over 35. In other countries, while there is no absolute prohibition on treating patients with a BMI over 25, they are often not recruited and are advised to lose weight before treatment.

These patients, despite the latest weight loss treatments such as liraglutide or low-calorie or ketogenic diets, find it difficult to lose the required weight²⁴ and have a high dropout rate, therefore rarely accessing IVF treatments. Our study aimed to evaluate whether performing *in vitro* fertilization on these patients increases the risk of medical, surgical, and anesthetic complications of oocyte retrieval. Indeed, for treatment refusal, the dangers associated with oocyte retrieval should be evaluated, as it is the most gruesome part of the treatment^{25,26}.

Only one study has analyzed these aspects²⁷, mainly focusing on the need for anesthesia drugs and any related complications, and the same author reported greater difficulty in performing oocyte retrieval. The same study recorded an increase in incomplete oocyte retrievals. Our work does not confirm any of these impressions.

Patients and Methods

From January 2011 to December 2022, approximately 5,713 assisted reproductive technology (ART) cycles were performed at the ART MO-MO's Fertilife center, of which 3,104 were fresh cycles and 2,069 were thaw cycles.

A retrospective investigation was conducted on a sample of 3,104 fresh cycles, which encompassed all cycles conducted with an antagonist protocol. In order to decrease the risk of incomplete oocyte retrieval linked to the inexperience of the collecting doctor, all oocyte retrieval in patients with BMI > 25 was performed by 3 physicians. These physicians were chosen among those who showed a complete withdrawal rate of over 95% in the previous year.

Couples in which the male partner had severe oligoasthenospermia (<5,000,000 spz/ml), and female partners who had undergone ovarian surgery or suffered from endometriosis were excluded from the study. Cycles with unknown treatment outcomes and those with unknown pregnancy progression up to the 12th week were also excluded from the study.

Inclusion Criteria

1. Antagonist stimulation protocol.
2. Egg retrievals are always performed by the same physicians.

Exclusion Criteria

1. Severe oligoasthenospermia.
2. Patients with endometriosis.
3. Patients who had ovarian surgery.
4. Patients with progesterone >1.4 ng/ml on trigger day²⁸.
5. Patients whose treatment outcome is unknown.
6. Patients whose pregnancy outcome is unknown until 12 weeks.

All eligible participants (n=2,225) were included in the study and categorized into two groups: a control group of 1,489 patients with a BMI < 25 Kg/m² and a group of 766 patients with a BMI > 25 Kg/m².

The group consisting of patients with a BMI > 25 Kg/m² was subsequently divided into three subgroups. One with a BMI between 25.1 and 29.9 (n=529); one group with a BMI between 30 and 34.9 (n=156), and one with a BMI greater than 35 (n=81).

Before undergoing IVF treatment, all patients with BMI > 25 Kg/m² enrolled (766) were encouraged to lose weight through various options, including a hypocaloric and hypoglycemic diet, a ketogenic diet, and the use of liraglutide. Due to the cost of liraglutide treatment and its recent commercialization of the drug in Italy, only 8 patients accepted this approach. Of the total sample with a BMI > 25, only 20% (230 patients) agreed to undergo a diet. Unfortunately, at the 3-month follow-up, over 70% (161 patients) had dropped out of the diet, and only 15% had lost weight, but none within the control group with a BMI < 25. Besides, before starting the treatment, all patients underwent hysteroscopy to evaluate the presence of chronic endometritis²⁹.

Stimulation Protocol

The patients underwent ovarian stimulation using an antagonist protocol with follitropin alpha. In some cases, a deficient response was observed in the oocyte recovery compared to that expected from the data provided by Anti-Müllerian Hormone (AMH) and Antral Follicle Count (AFC)³⁰. The final maturation of the oocytes was induced with Gonasi (IBSA Pharmaceutical, Lugano, Swiss).

Oocyte Retrieval

To avoid biases related to the inexperience of new operators, only cases where the pick-up was performed by the same 3 experienced physicians were selected. The experience of the doctor who performed the oocyte retrieval was considered as the complete aspiration capacity of all follicles up to a diameter of 11 mm, at least in 97% of the pick-ups. The follicles of the ovaries were aspirated using our method³⁰, which involved attempting to enter the ovary with the needle only once and moving it inside the ovary without further pierces. During the procedure, sporadically, we had to use accessory maneuvers to complete the oocyte retrieval³¹.

The first maneuver consisted of applying simultaneous manual abdominal pressure and vaginal probe pressure to approach the ovaries located deep inside. The second involved placing the patient in an anti-Trendelenburg position. The third maneuver involved pulling the uterine cervix using a clamp. As a last resort, transabdominal or trans myometrial retrieval was performed³².

Contrary to what was described in the work of Liang et al²⁷, in no case the oocyte retrieval was suspended or aborted. After the procedure, vaginal bleeding was observed in some cases, which was resolved by hemostatic pinching of the bleeding area for approximately 5 minutes³¹. In only one case where peritoneal bleeding was observed, it was monitored but did not require hospitalization.

Also, we did not perform routine antibiotic prophylaxis. This was given only in cases of surgical complications. After the procedure, all patients were observed for 2 hours before being discharged in good health. Some patients who experienced pain were treated with painkillers and discharged after 4 hours.

Anesthesia

For oocyte retrieval, anesthesia was always administered parenterally, with a single dose of approximately 1.4 µg/kg of fentanyl (Piramal Critical Car S.P.A., Verona, Italy) given 10 to 30 minutes before the procedure, and 0.2 mg/kg of propofol (Aspen Pharma Tradin Limited, Dublin, Ireland), always in the presence of an anesthesiologist. No patient was treated without sedation. Throughout the procedure, patients were monitored with a pulse oximeter for continuous determination of blood pressure and electrocardiogram (ECG). Mild anesthesia-related complications were considered those that resulted in brief episodes of desaturation below 80% oxygen, hyper or hypotension for a few minutes, or those that quickly returned to normal. Before discharge, all patients were advised to immediately go to the hospital in case of episodes of pain or syncope. Severe complications were those that required hospitalization.

Oocyte and Embryo Treatment

Metaphase II oocytes were inseminated using the intracytoplasmic sperm injection (ICSI) technique, following sperm selection mediated by a technique published in our previous studies^{35,36}. Our technique consists of incubation at 37°C for 30–60 minutes, the motile sperm in the sample move horizontally across the dish, guided by the culture medium present. This allows for the separation of motile sperm from other components such as immotile sperm, debris, or seminal fluid. The motile sperm gradually concentrate in a specific area of the dish, forming a concentrated population that can be easily collected for further assisted reproductive procedures. All patients underwent vaginal progesterone supplementation until the day of transfer³⁴.

Statistical Analysis

After selection, the sample was divided into 4 patient groups:

1. A control group with BMI<25 (1,489 patients).
2. A studied group with BMI>25 Kg/m² (766 patients).
 - a) A subgroup with BMI between 25.1 and 29.9 Kg/m² (529 patients).
 - b) A subgroup with BMI between 30 and 34.9 Kg/m² (156 patients).
 - c) A subgroup with BMI>35 Kg/m² (81 patients).

These groups were compared to determine if their demographic characteristics were homogeneous using the Student's *t*-test (Table I). The data were analyzed using Prism 8 version 8.4.3 software (GraphPad Software, Boston, MA, USA). Statistical evaluation regarding the characteristics of the number of retrieved oocytes, metaphase II oocytes, inseminated oocytes, number of transferred embryos, and day of transfer was performed with a one-way multifactorial ANOVA test and reported according to Dunnett's multiple comparison test. The significance *p*-value was set at <0.05.

Results

During the study period, 3,104 fresh cycles were performed, and all cycles that did not meet the inclusion criteria or belonged to the exclusion criteria were excluded. Eventually, the number of cycles enrolled in the study was 2,255, divided into a control group (1,489) with BMI<25 kg/m², a group with BMI 25-29.9 (529), a group with BMI 30-34.9 (156), and a group with BMI>35 (81). To assess whether the groups were congruous in their demographic characteristics, a series of parameters were evaluated and compared using the Student's *t*-test. All parameters evaluated, from mean age to infertility diagnosis, did not show significance with the test, as shown in Table I.

Oocyte retrievals were mostly easy. Only in 5% of cases with BMI<25, 5.2% with BMI between 25-29.9, 4.9% with BMI between 30-34.9, and 5.2% with BMI >35 were necessary to perform accessory maneuvers for egg retrievals (30), which are listed in Table II.

Finally, only in 15 cases in the control group and 2 cases in the BMI 30-34.9 group, transab-

Table I. Demographic characteristics of the groups.

	BMI <25 (1,489)	BMI >25-29.9 (529)	BMI >30-34.9 (156)	BMI >35 (81)	<i>p</i> <0.05
Age	33.9±4.2	34.7±4.3	34.3±4.1	34.4±4	0.09
Causes of infertility					
Tubal factor	301 (20.3%)	110 (20.8%)	34 (21.6%)	15 (18.5%)	0.912
Male factor	485 (32.5%)	169 (32%)	48 (30.5%)	28 (34.5%)	0.84
PCOS (Polycystic Ovarian Syndrome)	98 (6.6%)	39 (7.3%)	12 (7.6%)	5 (6.1%)	0.14
DOR (Diminished Ovarian Reserve)	388 (26.1%)	140 (26.4%)	39 (24.8%)	21 (26%)	0.42
Unexplained	89 (5.9%)	30 (5.6%)	11 (7%)	5 (6.1%)	0.18
Other	128 (8.6%)	41 (7.7%)	13 (8.2%)	7 (8.6%)	0.35

Table II. Accessory maneuvers.

	1 st Maneuver Bimanual abdominal pressure and vaginal probe pressure	2 nd Maneuver Anti Trendelenburg position	3 rd Maneuver Cervical clamp traction	4 th Maneuver Transabdominal oocyte retrieval	5 th Maneuver Trans-myometrial oocyte retrieval
BMI<25 (1,489)	40	29	5	15	0
BMI>25-29.9 (529)	14	8	4	0	0
BMI>30-34.9 (156)	3	5	0	2	0
BMI>35 (81)	1	2	1	0	0

BMI: Body Mass Index.

dominal retrieval had to be used, without any complications. In no case was trans myometrial access used. Contrary to what was stated in the study by Liang et al²⁷, all retrievals allowed recovering the expected number of oocytes. Anesthesia drug consumption was proportional to BMI (1.4 µg/kg of fentanyl, Piramal Critical Care Italia S.P.A., Verona, Italia - 0.2 mg/kg of propofol, Aspen Pharma Tradin Limited, Dublin, Ireland). Complications such as hyperstimulation, anesthesia-related complications, and surgical complications did not show any statistically significant differences among the various groups, as indicated in Table III.

The patients who had experienced vaginal bleeding were treated³⁰ by placing the speculum, identifying the area where the bleeding was present, clamping it with hemostatic forceps for about 5 minutes, and subsequently removing it; no bleeding required the administration of sutures.

Subsequently, differences were evaluated among the four groups regarding the number of retrieved oocytes³⁵, the number of mature oocytes in Metaphase II (MII), and the number of fertilized oocytes in MII. The number of obtained embryos was also examined, taking into consideration the day of transfer. With the one-way ANOVA test, all groups were compared with the control group, and none showed statistically significant differences (Table IV), only the number of produced embryos in the BMI group between 30-34.9 was lower and statistically significant.

In Figure 1, a graphical representation of the medians of the examined groups is shown for the number of retrieved oocytes (A), oocytes in meta-

phase II (B), metaphase II oocytes fertilized (C), number of obtained embryos (D), and the day of embryo transfer (E).

Table V shows the data related to pregnancy outcomes correlated with the study groups. The human chorionic gonadotropin (βHcg) test in the various groups appears overlapping, the only different negative data is related to the group with BMI>35, and this value is statistically significant ($p=0.043$). A similar result was also obtained for the percentage of abortions in the continuation of pregnancy, always in the group with BMI >35.

Discussion

Obesity is currently a serious problem for public health. Even the treatment of infertility is not exempt from encountering difficulties in treating this type of patient. Some countries²⁶ have proposed denial of IVF treatments in patients with BMI>35. In other states, by the guidelines of scientific societies^{22,23}, it has been suggested to evaluate on a case-by-case basis whether or not to perform ART interventions on overweight patients.

The scientific basis for determining this choice is based on clinical data^{39,40} that show that pregnancy rates are lower in these patients compared to the normal population. Even worse are the data regarding the risk of miscarriage and those related to complications in pregnancy and childbirth³⁶. The reasons that discourage IVF treatment in these patients are all related to the risks associated with pregnancy³⁷.

Table III. Use of accessory maneuvers for retrieval and associated risks.

	BMI <25	BMI 25.1-29.9	BMI 30-34.9	BMI >35	$p<0.05$
Other maneuvers for egg retrieval	74 (5%)	28 (5.2%)	8 (4.9%)	4 (5.2%)	n.s.
Transabdominal access	15 (1%)	0	2 (1%)	0 (0%)	n.s.
Ovarian stimulation complications					
Hyperstimulation	21 (1.4%)	6 (1.2%)	1 (0.7%)	1 (1.2%)	n.s.
Surgical complications					
Vaginal bleeding	3 (0.2%)	1 (0.1%)	0 (0%)	0 (0%)	n.s.
Hemoperitoneum	1 (0.07%)	0 (0%)	0 (0%)	0 (0%)	n.s.
Hospitalization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	n.s.
Anesthetic complications					
Mild	1 (0.06%)	1 (0.02%)	0 (0%)	0 (0%)	n.s.
Hospitalization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	n.s.

n.s.: not significant.

Table IV. Comparison among the four groups for retrieved oocytes, MII oocytes, fertilized oocytes, number of embryos, and day of transfer.

Test ANOVA multiple comparisons					
No. of oocytes retrieved - A					
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant	Summary	Adjusted <i>p</i> -value
BMI<25 vs. BMI 25.1-29.9	0.3145	-0.2753 to 0.9044	No	n.s.	0.4919
BMI<25 vs. BMI 30-34.9	0.8609	-0.4253 to 2.147	No	n.s.	0.294
BMI<25 vs. BMI>35	0.6958	-1.289 to 2.680	No	n.s.	0.7853
No. of oocytes in M II - B					
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant	Summary	Adjusted <i>p</i> -value
BMI<25 vs. BMI 25.1-29.9	0.2485	-0.1937 to 0.6908	No	n.s.	0.4463
BMI<25 vs. BMI 30-34.9	0.6269	-0.3374 to 1.591	No	n.s.	0.3188
BMI<25 vs. BMI>35	0.64	-0.8479 to 2.128	No	n.s.	0.6617
No. fertilized M II oocytes - C					
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant	Summary	Adjusted <i>p</i> -value
BMI<25 vs. BMI 25.1-29.9	0.201	-0.1504 to 0.5525	No	n.s.	0.4309
BMI<25 vs. BMI 30-34.9	0.6389	-0.1274 to 1.405	No	n.s.	0.1328
BMI<25 vs. BMI>35	0.6813	-0.5012 to 1.864	No	n.s.	0.4245
No. embryos obtained - D					
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant	Summary	Adjusted <i>p</i> -value
BMI<25 vs. BMI 25.1-29.9	0.04097	-0.07882 to 0.1608	No	n.s.	0.7974
BMI<25 vs. BMI 30-34.9	-0.309	-0.5679 to -0.05003	Yes	*	0.0132
BMI<25 vs. BMI>35	-0.3378	-0.7369 to 0.06119	No	n.s.	0.1239
Transfer day - E					
Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant	Summary	Adjusted <i>p</i> -value
BMI<25 vs. BMI 25.1-29.9	-0.02264	-0.1754 to 0.1301	No	n.s.	0.9786
BMI<25 vs. BMI 30-34.9	0.1081	-0.1900 to 0.4061	No	n.s.	0.7673
BMI<25 vs. BMI >35	0.3274	-0.1376 to 0.7923	No	n.s.	0.2519

**p*-value<0.05 is significant. BMI: Body Mass Index.

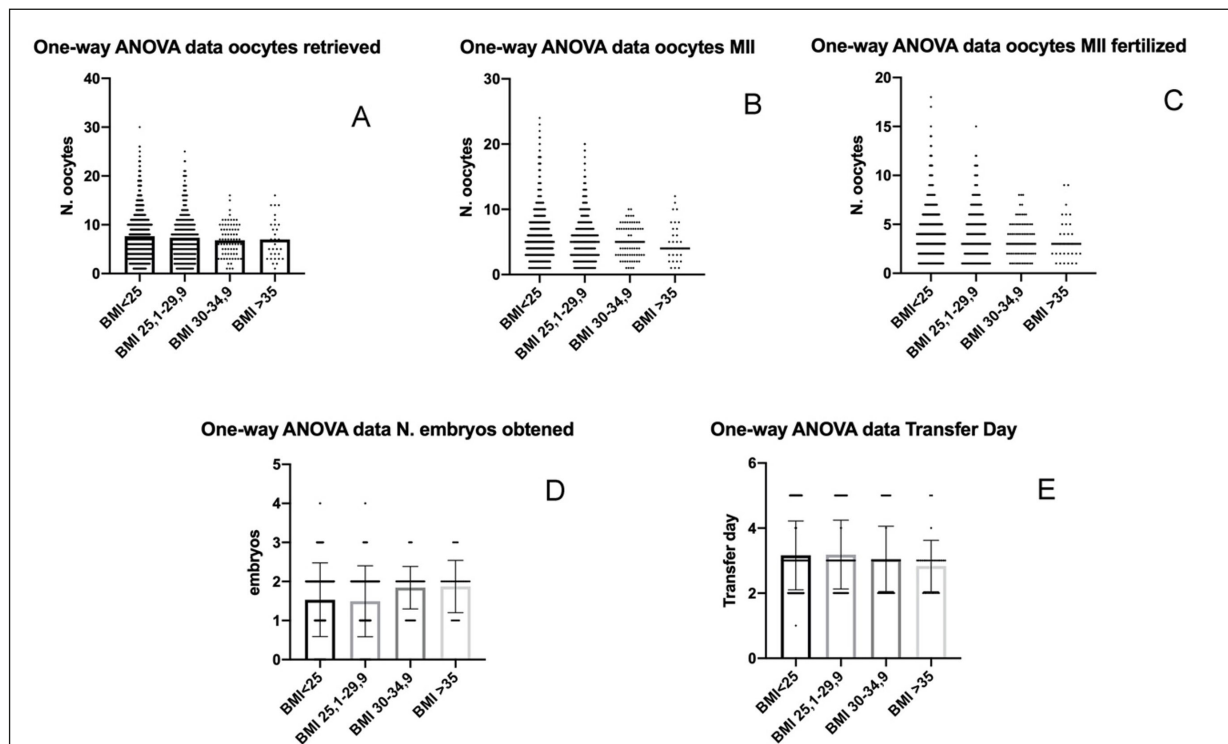


Figure 1. Comparison of median values among the four groups. A graphical representation of the medians of the examined groups is shown for the number of retrieved oocytes (A), oocytes in metaphase II (B), metaphase II oocytes fertilized (C), number of obtained embryos (D), and the day of embryo transfer (E).

Table V. Pregnancy outcomes up to 12 weeks among the four study groups.

	BMI <25	BMI 25.1-29.9	BMI 30-34.9	BMI >35	p<0.05
Enrolled patients	1,489	529	156	81	
beta HCG (+)	512 (34.38%)	158 (29.9%)	47 (30.26%)	18 (22%)	0.043
Biochemical pregnancy	67 (13%)	21 (13%)	7 (14%)	2 (10%)	n.s.
Ongoing pregnancy (12 weeks)	445 (86.91%)	138 (87.34%)	41 (87.22%)	13 (73.3%)	n.s.
Miscarriage	80 (18%)	25 (18%)	7 (18%)	5 (27.7%)	0.032

BMI: Body Mass Index.

Within IVF treatments, the moments with the most frequent risk of complications are stimulation and oocyte retrieval; while subsequent complications are related to the progression of pregnancy. On the other hand, if obese patients had become pregnant spontaneously, they would have developed the same risks that occur in obese infertile patients. Only one scientific study²⁷ has examined the risks associated with oocyte retrieval. We have re-evaluated these risks and come to different conclusions from those of Liang et al²⁷. Our results show that obese patients, compared to those with normal BMI, do not require an overdose of anesthetics, contrary to what is described in other works³⁰; the higher consumption is related to increased body mass. Many drugs are administered about body weight, and this does not mean that an overdose is necessary. Our study has also shown that the technique of oocyte retrieval is substantially identical to that of the control group, and contrary to what is claimed by Liang et al²⁷, it was always carried out successfully. In cases where egg retrieval seemed more difficult, the accessory maneuvers described above were performed, and all pick-ups were completed with the recovery of oocytes.

The statistical study of the number of retrieved oocytes, the number of metaphase II mature oocytes, as well as those fertilized in metaphase II, showed that the results are comparable without statistically significant differences in all groups. Even the evaluation of the day on which the transfer was performed showed no difference. Only in the group with a BMI between 30-34.9 the number of embryos produced did show a statistically significant lower value. According to our interpretation, this value is related to the small number of cases examined. This may have skewed the results, so larger samples will be needed to validate this data.

In line with international literature¹³, the comparison data between the group of patients with BMI>35 and the control group of β hCG and abortion rate show that they are statistically significant. These studies³⁹ suggest that the mechanisms that cause spontaneous abortion of these embryos, even when they are euploid following genetic investigations, are related to non-chromosomal components. Probably due to excess body weight, these patients develop endometrial disorders and hostile uterine environments for embryo implantation and growth⁴⁰.

Limitations

The most important limitation of our study is linked to the number of patients enrolled, especially in the group with BMI between 30 and 34.9 and the group with BMI over 35. It would be advisable to conduct further studies with a greater number of patients from these two groups to confirm our theses. In fact, the relevant statistical data on the production of embryos in the group with a BMI between 30 and 34.9, in our opinion, is linked to the low number of patients enrolled.

Conclusions

Our work clearly shows that oocyte retrieval in obese patients does not increase the risk of acute complications. Oocyte retrieval was always completed, even using accessory maneuvers when ovaries were difficult to access. This approach was not limited to patients with high BMI but was also used in the control group. Furthermore, as previously reported in other studies⁴⁰, this technique does not seem to increase the risk of complications. Anesthetic dosages were also proportional, based on pharmacokinetics, as patients with a higher weight require a higher dose. In terms of oocyte recovery and embryo yield,

data were compared among the groups, and even in patients with increased BMI, data overlapped with the control group.

The prohibition or postponement of ART procedures in obese patients is not scientifically validated except in the context of a decrease in live birth rates and pregnancy complications. Considering the high dropout rate from weight loss programs and their poor long-term success, waiting is unjustified. Especially given the fact that with time and advancing age, results will inevitably worsen.

On the other hand, once the patient is properly informed of the risks, especially those related to pregnancy, and considering our study's results and others in the literature, the contraindication to perform ART procedures appears senseless.

Given the high dropout rate of obese patients from IVF treatments and the chronic difficulty in achieving optimal weight, it would be appropriate for this type of patient to undergo embryo cryopreservation and transfer them after weight loss. By doing so, patients would also be protected in terms of producing embryos at a younger age, which is better for the outcome.

Conflict of Interest

The Authors declare no conflict of interest.

Funding

This research received no external funding.

Informed Consent

Written informed consent was obtained, at the first clinical evaluation, from all patients enrolled voluntarily in the study after being well-informed about the hypothetical risks of the procedure.

Ethics Approval

This study was regularly approved by the Local Ethical Board of MOMO' FertiLIFE (approval number 12/2016) according to the Declaration of Helsinki's ethical principles.

Authors' Contributions

Conceptualization: G.M.B. and D.B.; methodology, D.B.; software: G.T.; validation: G.M.B. and D.B.; formal analysis: D.L. and M.D.; investigation: A.M. and S.H.; resources: A.M.; data curation: E.C. and G.C.; writing original draft preparation: G.M.B. and D.B.; writing-review and editing: E.C., G.C., M.D., S.H., and D.L.; supervision: D.L.; project administration: G.T., G.M.B., and D.B.; funding acquisition: G.M.B. and D.B. All authors have read and agreed to the published version of the manuscript.

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