

Impact of class III obesity on outcomes and complications of transvaginal ultrasound-guided oocyte pickup

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Objective: To assess the impact of class III obesity on outcomes and complications of transvaginal ultrasound-guided oocyte pickup (OPU).

Design: Retrospective cohort study.

Setting: Hospital-based fertility clinic.

Patient(s): All women undergoing OPU procedures during autologous in vitro fertilization (IVF) and oocyte banking cycles, grouped by patient body mass index (BMI: <25, 25–29.9, 30–34.9, 35–39.9, ≥40 kg/m²).

Intervention(s): Transvaginal OPU under conscious sedation.

Main Outcome Measure(s): Sedation and procedure-related parameters and complications.

Result(s): A total of 2,141 OPU procedures in 1,579 patients were analyzed, including 121 OPU procedures in 94 patients with BMI ≥40 kg/m². There was a statistically significant increase in total fentanyl and midazolam doses and procedure duration as BMI increased. Compared with patients with BMI <25 kg/m², those with BMI ≥40 kg/m² were more likely to require additional sedation during the procedure (adjusted odds ratio [aOR] 1.99; 95% confidence interval [CI], 1.14–3.49). The rate of difficult access was 28.9% for procedures with BMI ≥40 kg/m² compared with 5.2% with BMI <25 kg/m² (aOR 7.57; 95% CI, 4.66–12.29). The OPU was incomplete due to inaccessible follicles through a transvaginal approach in 18.2% of procedures with BMI ≥40 kg/m² compared with 1.3% with BMI <25 kg/m² (aOR 16.94; 95% CI, 8.24–34.84). The rates of sedation and procedure-related complications were low, and none occurred in patients with BMI ≥40 kg/m².

Conclusion(s): There was no increased risk of complications for women with class III obesity undergoing OPU with conscious sedation. However, the operator was more likely to encounter difficult access and to incompletely aspirate follicles through a transvaginal approach. (*Fertil Steril Rep*® 2020;1:270–6. ©2020 by American Society for Reproductive Medicine.)

Key Words: BMI, obesity, oocyte pickup, oocyte retrieval

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The prevalence of obesity, defined as body mass index (BMI) ≥30 kg/m², has nearly tripled worldwide from 1975 to 2016 (1). Women are also disproportionately affected compared with men overall (2). The prevalence of obesity among women

of reproductive age in Canada and the United States is 22.7% (3) and 36.8% (4), respectively, and 10% are in the class III obesity category (BMI ≥40 kg/m²) in the United States (4).

Female obesity has adverse effects on reproductive health, including an

increased risk of menstrual dysfunction, oligo-ovulation, and infertility (5). An increasing number of obese women are presenting for fertility care, but provision of assisted reproductive technology (ART) for these women can be challenging due to concerns regarding procedural safety, feasibility, and poor outcomes. Due to these concerns, women with class III obesity are frequently denied access to ART treatment (6).

Transvaginal ultrasound-guided oocyte pickup (OPU) during ART normally carries a low risk of complications (7). However, the additional

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concerns regarding the procedure for obese women include anesthetic-related risks and technical difficulties such as inability to access the ovaries (8, 9). Because of the paucity of data on OPU-related outcomes in obese women compared with normal-weight women, it is difficult to determine when ART may be offered safely and to appropriately counsel obese women regarding their risks and expected outcomes. Our study assessed the impact of class III obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$) on outcomes and complications of transvaginal ultrasound-guided OPU.

MATERIALS AND METHODS

We conducted a retrospective cohort study of all OPU procedures during autologous in vitro fertilization (IVF) and oocyte banking cycles at the Fertility Clinic at London Health Sciences Centre, a university-affiliated, hospital-based fertility clinic in London, Ontario, Canada, from January 1, 2013, to November 30, 2019. Ethics approval was obtained from the Western University Health Sciences Research Ethics Board (115719). Cases of OPU with missing patient BMI information or missing procedure records were excluded. Patient BMI was calculated using weight measured at the start of each treatment cycle and height measured at initial patient consultation. We grouped OPUs by patient BMI based on the World Health Organization classification: normal and underweight ($\text{BMI} < 25 \text{ kg/m}^2$); overweight ($\text{BMI} 25\text{--}29.9 \text{ kg/m}^2$); class I obesity ($\text{BMI} 30\text{--}34.9 \text{ kg/m}^2$); class II obesity ($\text{BMI} 35\text{--}39.9 \text{ kg/m}^2$); and class III obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$). Demographic data for cycles were collected from the clinic's electronic ART database. The OPU outcomes and complications were collected from the patients' paper-based treatment charts which contained procedure records as well as records of any additional points of patient contact due to complications of treatment.

Before undergoing fertility treatment, obese women with comorbidities and all women with class III obesity were referred to a multidisciplinary specialized obesity and pregnancy clinic led by a maternal-fetal medicine specialist. Patients underwent assessment and screening for comorbidities including hypertension and diabetes, as well as preconception counseling, nutritional assessment, and follow up evaluation. All treatment cycles involved controlled ovarian stimulation with gonadotropin-releasing hormone (GnRH) antagonist, long GnRH agonist, or flare GnRH agonist protocols. Ultrasound monitoring was begun on day 4 or 5 of stimulation until the lead follicle(s) reached 17–18 mm in diameter. Final oocyte maturation was triggered with recombinant human chorionic gonadotropin (hCG) or GnRH agonist, and OPU was performed 36 to 37 hours later.

The OPU procedures were routinely performed under conscious sedation, defined as a “drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation and no interventions are required to maintain a patent airway when spontaneous ventilation is adequate” (10). This was administered using intravenous fentanyl and midazolam under the direction of the physician performing the OPU procedure. Additional fentanyl and/or

midazolam could be administered during the procedure as needed, based on patient response. Occasionally on patient request the OPU could be performed without sedation, defined as an awake state with normal response to verbal stimulation without any intravenous or parenteral medications. Additionally, under rare circumstances of patient preference, OPU could be performed under total intravenous anesthesia, defined as general anesthesia in an unconscious state using intravenous propofol administered by an anesthesiologist. Before 2015, paracervical blocks were also routinely performed in addition to sedation as per clinic protocol. This was revised in 2015, and subsequent patients only received sedation. Patients were monitored by continuous pulse oximetry and electrocardiogram along with intermittent noninvasive blood pressure recordings. As per clinic protocol, antibiotic prophylaxis was routinely administered for all patients before the procedure with intravenous ceftriaxone or clindamycin. If endometriomas or hemorrhagic cysts were punctured during OPU, patients were given an additional course of oral antibiotic prophylaxis after the procedure. The specific regimen was determined by the physician performing the OPU.

All OPUs were performed using a transvaginal approach under ultrasound guidance using a 17-gauge single-lumen oocyte-aspiration needle mounted on a transvaginal probe with needle guide. The OPU procedure was performed by a reproductive endocrinology and infertility consultant on a rotating schedule or by a clinical fellow under the direct supervision of a consultant. None of the physicians during the study period performed OPUs using a transabdominal approach.

Ovarian follicles were aspirated in the minimal possible number of ovarian cortex punctures. Difficult access was noted during instances where external abdominal pressure or suprapubic pressure were applied by an assistant to stabilize and access the ovary. If the ovary or a portion of the ovary remained inaccessible through a transvaginal approach despite multiple attempts, the procedure was discontinued, and incomplete retrieval of follicles was noted. A speculum examination was performed after the procedure, and any vaginal bleeding was treated with direct pressure. Vaginal bleeding that required repeated or prolonged pressure (≥ 15 minutes total) or requiring additional intervention was recorded. The duration of procedure was recorded from the time of fentanyl administration to the completion of the speculum examination.

After the procedure, patients were transferred to and monitored in a recovery room for approximately 2 hours. Patients were required to tolerate oral intake, ambulate, and void before discharge. Major sedation-related complications were defined as adverse events occurring as a result of intravenous sedation that required transfer of the patient or admission to a hospital. Transient episodes of desaturation $< 80\%$ and heart rate or blood pressure changes were recorded as minor sedation-related complications. Patients were advised to contact the clinic or physician on call or present to our hospital for any worsening abdominal pain, vaginal bleeding, or fevers after discharge from the clinic. Procedure-related complication was defined as an adverse event occurring as

TABLE 1

Demographic characteristics of oocyte pickup according to body mass index.

Characteristic	BMI category (kg/m ²)					P value
	< 25 (n = 1,010)	25–29.9 (n = 579)	30–34.9 (n = 274)	35–39.9 (n = 157)	≥40 (n = 121)	
Patient age at OPU (y)	33.7 ± 4.3	34.2 ± 4.2	34.2 ± 4.1	34.1 ± 4.0	34.1 ± 3.6	.082
Treatment indication ^a						
Endometriosis	155 (15.3)	87 (15.0)	43 (15.7)	21 (13.4)	16 (13.2)	.936
Tubal factor	226 (22.4)	154 (26.6)	64 (23.4)	39 (24.8)	34 (28.1)	.309
Male factor	420 (41.6)	248 (42.8)	101 (36.9)	56 (35.7)	61 (50.4)	.061
PCOS	96 (9.5)	63 (10.9)	48 (17.5)	48 (30.6)	28 (23.1)	< .001
DOR	197 (19.5)	117 (20.2)	30 (10.9)	19 (12.1)	16 (13.2)	.001
Unexplained	92 (9.1)	36 (6.2)	31 (11.3)	8 (5.1)	6 (5.0)	.022
Fertility preservation	35 (3.5)	6 (1.0)	3 (1.1)	6 (3.8)	1 (0.8)	.007
Other	142 (14.1)	68 (11.7)	46 (16.8)	19 (12.1)	21 (17.4)	.212
Type of anesthesia						
Conscious sedation	1,005 (99.5)	577 (99.7)	274 (100)	157 (100)	121 (100)	—
Total intravenous anesthesia	0	1 (0.2)	0	0	0	—
None	5 (0.5)	1 (0.2)	0	0	0	—

Note: Data presented as mean ± standard deviation for continuous variables or n (%) for dichotomous variables. BMI = body mass index; DOR = diminished ovarian reserve; OPU = oocyte pickup; PCOS = polycystic ovary syndrome.

^a Treatment indications are not mutually exclusive.

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a result of the retrieval aspect of OPU which required intervention outside of routine postprocedure care.

Data were analyzed using IBM SPSS Statistics, version 26 (IBM Corp.). Continuous variables were reported as mean and standard deviation (±SD), and categorical variables were expressed as percentages. Missing data were excluded from the analysis for the specific variable. The chi square test was used to test the association between two categorical variables. One-way analysis of variance (ANOVA) with Tukey's honestly significant difference post hoc test was used to compare differences in the mean between the BMI categories. Multiple linear regression models were used to determine the relationship between a continuous outcome variable and several predictor variables, and binary logistic regressions assessed the correlation between a dichotomous outcome and relevant independent variables. Regression models adjusted for potential confounders included total number of follicles, diagnosis of endometriosis, use of paracervical block, and first cycle for patient in study period. Multicollinearity was assessed using the variance inflation factor, tolerance statistic, and condition index. There were no high intercorrelations between any of the independent variables. $P < .05$ was considered statistically significant.

RESULTS

During the study period, 2,157 OPU procedures were performed during autologous IVF and oocyte banking cycles. After excluding two OPU procedures with missing patient BMI information and 14 OPU procedures with missing records, a total of 2141 OPU procedures in 1,579 patients were included for analysis. There were 1,010 OPUs in 736 patients with BMI <25 kg/m², 579 OPUs in 416 patients with BMI 25–29.9 kg/m², 274 OPUs in 210 patients with BMI 30–34.9 kg/m², 157 OPU procedures in 123 patients with BMI 35–39.9 kg/m²,

and 121 OPU procedures in 94 patients with BMI ≥40 kg/m². Of the OPUs in the class III obesity category (BMI ≥40 kg/m²), there were 20 OPU procedures in 16 patients with BMI ≥50 kg/m², of which the highest BMI was 64. Table 1 shows the demographic characteristics of the patients undergoing OPU procedures according to BMI categories.

Of all included OPU procedures, 2,134 (99.7%) were performed under conscious sedation. Six procedures in five patients were performed without sedation, and one procedure was performed under total intravenous anesthesia due to patient preference. The mean patient age at OPU was 34 years across all BMI categories. There was no statistically significant difference among the BMI categories in the proportion of OPU procedures with a treatment indication of endometriosis; there were more OPU procedures in the higher BMI categories with a treatment indication of polycystic ovary syndrome (PCOS).

Sedation-related outcomes of OPU are shown in Table 2. As BMI increased, there was a statistically significant increase in the total dose of fentanyl and midazolam required. The OPU procedures for patients with BMI ≥40 kg/m² required mean total fentanyl and midazolam doses of 111.2 μg and 2.6 mg, respectively, compared with 101.3 μg and 2.1 mg in OPU procedures for patients with BMI <25 kg/m². Obese patients were also more likely to require additional fentanyl and/or midazolam during the procedure (17.8% of OPU procedures for BMI ≥40 kg/m² compared with 10.3% of OPU procedures for BMI <25 kg/m²).

Procedure-related outcomes of OPU are shown in Table 3. As BMI increased above 30 kg/m² there was a statistically significant increase in the duration of procedure as well as the rate of difficult access to ovaries and rate of incomplete retrieval of follicles. The mean procedure duration was 15.7 minutes for BMI ≥40 kg/m² compared with 13.3 minutes for BMI <25 kg/m² ($P < .001$). The rate of difficult access

TABLE 2

Sedation-related outcomes of oocyte pickup according to body mass index.

Outcome	BMI category (kg/m ²)								
	< 25 (n = 1,005)	25–29.9 (n = 577)	P value	30–34.9 (n = 274)	P value	35–39.9 (n = 157)	P value	≥40 (n = 121)	P value
Total fentanyl dose (μg)	101.3 ± 25.4	104.9 ± 21.4	.004	108.0 ± 22.4	<.001	114.8 ± 25.8	<.001	111.2 ± 23.7	<.001
Regression coefficient B (95% CI)	Reference	3.4 (1.1, 5.6)		6.2 (3.2, 9.1)		12.3 (8.6, 16.0)		9.6 (5.5, 13.8)	
Total midazolam dose (mg)	2.1 ± 1.2	2.2 ± 1.2	.003	2.4 ± 1.2	<.001	2.5 ± 1.0	<.001	2.6 ± 1.2	<.001
Regression coefficient B (95% CI)	Reference	0.1 (0.04, 0.2)		0.4 (0.3, 0.5)		0.3 (0.2, 0.4)		0.4 (0.2, 0.5)	
Additional sedation required ^a	87 (10.3)	52 (10.6)	.665	44 (18.6)	.001	25 (17.9)	.010	19 (17.8)	.016
aOR (95% CI)	Reference	1.09 (0.75, 1.57)		1.95 (1.30, 2.93)		1.92 (1.17, 3.16)		1.99 (1.14, 3.49)	

Note: Data presented as mean ± standard deviation for continuous variables or n (%) for dichotomous variables. Regression models adjusted for number of follicles, diagnosis of endometriosis, use of paracervical block and first cycle for patient in study period. aOR = adjusted odds ratio; BMI = body mass index; CI = confidence interval.

^a Data unavailable for 318 oocyte pickups.

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TABLE 3

Procedure-related outcomes of oocyte pickup according to body mass index.

Outcome	BMI category (kg/m ²)								
	< 25 (n = 1,010)	25–29.9 (n = 579)	P value	30–34.9 (n = 274)	P value	35–39.9 (n = 157)	P value	≥40 (n = 121)	P value
Procedure duration (min) ^a	13.3 (5.3)	13.1 (5.6)	.813	14.6 (5.3)	.002	15.5 (6.0)	<.001	15.7 (6.3)	<.001
Regression coefficient B (95% CI)	Reference	−0.1 (−0.6, 0.5)		1.1 (0.4, 1.9)		2.1 (1.2, 3.0)		2.7 (1.7, 3.7)	
Difficult access	53 (5.2)	40 (6.9)	.167	39 (14.2)	<.001	24 (15.3)	<.001	35 (28.9)	<.001
aOR (95% CI)	Reference	1.35 (0.88, 2.06)		3.07 (1.98, 4.76)		3.41 (2.03, 5.72)		7.57 (4.66, 12.29)	
Incomplete retrieval	13 (1.3)	8 (1.4)	.854	18 (6.6)	<.001	9 (5.7)	.001	22 (18.2)	<.001
aOR (95% CI)	Reference	1.09 (0.45, 2.64)		5.34 (2.58, 11.06)		4.63 (1.94, 11.04)		16.94 (8.24, 34.84)	

Note: Data presented as mean ± standard deviation for continuous variables or n (%) for dichotomous variables. Regression models adjusted for number of follicles, diagnosis of endometriosis, use of paracervical block and first cycle for patient in study period. aOR = adjusted odds ratio; BMI = body mass index; CI = confidence interval.

^a Data unavailable for 205 oocyte pickups.

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TABLE 4

Complications of oocyte pickup according to body mass index.

Complication	BMI category (kg/m ²)				
	< 25 (n = 1,010)	25–29.9 (n = 579)	30–34.9 (n = 274)	35–39.9 (n = 157)	≥40 (n = 121)
Minor sedation-related complication					
Transient desaturation <80%	4 (0.4)	0	0	0	0
Transient bradycardia	2 (0.2)	0	0	0	0
Transient hypotension	0	0	1 (0.4)	0	0
Procedure-related complication					
Vaginal bleeding	2 (0.2)	0	0	4 (2.5)	0
Hemoperitoneum	3 (0.3)	0	0	0	0
Bladder injury	1 (0.1)	0	0	0	0

Note: Data presented as n (%). BMI = body mass index.

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was 28.9% for BMI ≥ 40 kg/m² compared to 5.2% for BMI < 25 kg/m² with adjusted odds ratio (aOR) of 7.57 (95% CI, 4.66–12.29), while the rate of incomplete retrieval was 18.2% compared with 1.3% with aOR of 16.94 (95% CI, 8.24–34.84). Of the OPU with incomplete retrievals, two procedures were discontinued in patients with BMIs of 40.3 and 42.5 before aspiration of any follicles as both ovaries were deemed inaccessible transvaginally.

All OPU complications were diagnosed during or shortly after the procedure before patient discharge. No OPU complications occurred in patients with BMI ≥ 40 kg/m² during the study period (Table 4). There were no major sedation-related complications, and there were seven minor sedation-related complications (0.3% overall) consisting of transient episodes of desaturation $< 80\%$, bradycardia, and hypotension. Of these, six complications occurred in patients with BMI < 25 kg/m² (0.6%), and one in patients with BMI 30–34.9 kg/m² (0.4%). These were all resolved with patient arousal and a short period of supplemental oxygen in the procedure room. None required further intervention in the recovery room.

There were a total of 10 procedure-related complications (0.5% overall) with six in patients with BMI < 25 kg/m² (0.6%) and four in patients with BMI 35–39.9 kg/m² (2.5%). All six cases of vaginal bleeding were resolved with direct pressure up to 30 minutes (n = 3) or vaginal sutures (n = 3). Two of three cases of hemoperitoneum were admitted to hospital for observation and were discharged within 48 hours without further intervention. None required a blood transfusion. One patient sustained a minor bladder injury identified by post-procedure hematuria, which resolved spontaneously and did not require intervention.

DISCUSSION

Data from our center showed that women with class III obesity required a small but statistically significant increase in total dose of sedation medications and longer duration of procedure compared with normal-weight and underweight women during OPU. Although the operators were more likely to

encounter difficult access and to incompletely retrieve ovarian follicles through a transvaginal approach for women with class III obesity, there was no increased risk of sedation or procedure-related complications for these women in our data set.

The literature on outcomes of conscious sedation among obese women is limited. Our observation of an increase in fentanyl and midazolam dose associated with increasing BMI is in keeping with two studies of other procedures using conscious sedation including bronchoscopy and first-trimester surgical abortion (11, 12). Similarly, an increase in propofol dose has been observed with increasing BMI in endoscopy under deep sedation (13), as well as OPU for IVF under total intravenous anesthesia (9). This may be a result of increased volume of distribution of drugs due to higher percentage of body fat.

Similar to the observation of longer time spent in the operating room for obese patients undergoing OPU procedures under total intravenous anesthesia (9), we also observed an increase in the duration of the procedure, although our finding does not take into account the time needed to position and transfer patients before and after the procedure. Nevertheless, our increase in procedure time is likely a reflection of additional time necessary to achieve optimal view on ultrasound and obtain safe access to the ovary in obese women.

We found a statistically significant increase in incidence of difficult access in women with obesity, necessitating abdominal or suprapubic pressure by an assistant. This association also accounts for the increased incidence of incomplete retrieval of follicles in women with obesity, including two women with class III obesity where no follicles were retrievable. At our center, every effort was made to retrieve the maximal number of follicles transvaginally, after which the procedure was discontinued despite the presence of remaining follicles because we do not perform transabdominal retrievals. The transabdominal approach for OPU has been used for patients with ovaries inaccessible by the transvaginal approach (14–16), and has been used more frequently in women with class III obesity (9).

Our data showed no major sedation-related complications and seven cases of minor sedation related complications consisting of transient episodes of desaturation, bradycardia, and hypotension, with all but one case occurring in the normal and underweight category. This is reassuring and supports the use of conscious sedation over deeper levels of sedation or general anesthesia in obese women. We also found that women with obesity were more likely to require additional sedation medications during the procedure, which suggests a comparative lighter level of sedation with the initial dosage of fentanyl and midazolam. This likely contributes to the low sedation related complication rate in these women. Given sedation is a continuum, and the variation in individual patient response which cannot always be predicted, the safest approach is to administer sedation in small incremental doses and titrate to a desired response (10, 17). Additionally, a contingency plan must be in place in cases where the level of sedation becomes deeper than initially intended (10). Hence, we agree with Romanski et al. (9) that the availability of appropriate resources, such as in our hospital-based clinic setting, is important for treating women with obesity.

The only procedure-related complications we observed in obese women were four cases (2.5%) of vaginal bleeding in women with class II obesity, which were all managed with pressure or suture. This rate is in keeping with previously reported rates of vaginal bleeding after OPU in all women, which varies widely from 0.01% to 3.0%, likely due to variations in the definition used for the outcome (18–21). Therefore, this is reassuring for the question of procedural safety in women with higher class obesity.

This is one of few studies examining the outcomes and safety of OPU in women with obesity undergoing ART. To our knowledge, it is the only study including women with class III obesity undergoing OPU procedures with conscious sedation, a method of analgesia widely used in IVF centers. It provides valuable information for counseling patients with obesity before ART.

Although we controlled for various confounders in the assessment of OPU outcomes in relation to BMI, our data did not contain experience level of the operator performing the OPU (fellow versus staff or consultant). This is a variable that has been previously shown to affect OPU outcomes (19). Because our center does not routinely perform OPU procedures through a transabdominal approach, patients who were identified as having inaccessible ovaries transvaginally before their treatment cycle were referred to other centers for transabdominal OPU procedures and were not included in our study.

Although the recording of difficult access was a routine aspect of the OPU record, we cannot be certain that every instance was recorded due to the retrospective nature of the study. The recording of difficult access and incomplete retrieval also did not routinely indicate a specific cause that may be unrelated to BMI such as uterine fibroids. Additionally, although patients were advised to contact our clinic or present to our hospital for concerns after discharge from the clinic, it is possible patients may have sought care in the community for complications without our knowledge. Therefore, there is the possibility of missing complications from our database.

CONCLUSION

We found no increased risk of sedation or procedure-related complications in OPU procedures performed under conscious sedation in women with class III obesity. However, the operator performing the OPU was more likely to encounter difficult access to the ovary and to incompletely aspirate follicles through a transvaginal approach in this patient population.

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