Is polycystic ovarian morphology related to a poor oocyte quality after controlled ovarian hyperstimulation for intracytoplasmic sperm injection? Results from a prospective, comparative study

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Objective: To evaluate the relationship between polycystic ovarian morphology (PCOM) and oocyte quality after controlled ovarian stimulation for intracytoplasmic sperm injection (ICSI).
Design: Prospective, comparative study with concurrently treated and age-matched controls.
Setting: Academic IVF unit of the Lille University Hospital.
Patient(s): A total of 194 women were prospectively included before their first IVF-ICSI attempt for exclusive male infertility. They were classified into PCOM (n = 97) or control groups (n = 97) according to their follicle number per ovary. The nuclear maturation and morphologic aspects of 1,013 oocytes from PCOM patients were assessed and compared with those of 774 oocytes from controls.
Intervention(s): None.
Main Outcome Measure(s): Rate of metaphase II (MII) and morphologically abnormal oocytes.
Result(s): The mean number of total and MII oocytes retrieved was significantly higher in the PCOM group. The rate of MII and morphologically abnormal oocytes was equivalent between the two groups. The mean number of embryos was significantly higher in the PCOM group. However, the percentage of top-quality embryos on day 3 was similar between the two groups. The implantation and clinical pregnancy rates were significantly higher in the PCOM group.
Conclusion(s): Polycystic ovarian morphology does not have a negative impact on the quality of oocytes and embryos or the outcome of IVF-ICSI. (Fertil Steril® 2015;103:112–8. ©2015 by American Society for Reproductive Medicine.)
Key Words: PCOS, PCOM, IVF, oocyte quality, oocyte morphology

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Polycystic ovarian morphology (PCOM) according to ultrasonographic criteria is a very common finding in an IVF center population. This includes symptomatic patients with polycystic ovary syndrome (PCOS), identified in 18%–25% of infertile couples (1), and so called "sonographic only" PCO, the prevalence of which has

been estimated as high as 33% in asymptomatic patients (2–4). Polycystic ovarian morphology is characterized by a significantly enlarged cohort of early-growing and recruitable follicles. This excessive follicle number is linked to disturbances in folliculogenesis, which are thought to be the consequence of intraovarian hyperandrogenism (5–7). The cohort of growing follicles during controlled ovarian hyperstimulation (COH) is frequently heterogeneous in size, with mature, intermediate, and small follicles. In addition, the number and quality of mature oocytes has been proposed as being poor (6, 8, 9); and recent data suggested that oocyte competence could be impaired in PCO patients owing to an inadequate dialogue between the cumulus cells and oocyte (10, 11).

Despite these assumptions, the paucity of studies focusing on oocyte quality in women with PCOM does not allow us to make this conclusion. Most studies are retrospective and compared PCO patients with a historical control group (12–17). Furthermore, the criteria used to diagnose PCOM were extremely heterogeneous because of a lack of consensus. The results provided by these studies are thus conflicting, finding either a better oocyte/embryo quality and pregnancy rate or vice versa (18). Moreover, in most of these studies, the oocyte quality evaluation was only based on the evaluation of the nuclear stage (i.e., the mean number of metaphase II [MII] oocytes) (12, 14, 16). It is now well recognized that some specific morphologic oocyte abnormalities, such as the presence of a wide perivitelline space (PVS) or a granular cytoplasm, must be given attention because it has been reported that they are associated with a significant decrease in the chance of fertilization (19–21). Likewise, after COH, it is interesting to note that more than half of oocytes retrieved present one or more morphologic abnormalities (19, 21). Only one retrospective study focused on the oocyte morphology in PCOM patients and found no difference with age-matched controls (13). Taking into account the lack of well-designed studies in this specific topic, we aimed to prospectively investigate the relationship between PCOM and oocyte quality after COH by performing a prospective, comparative study with concurrently treated and age-matched controls.

MATERIALS AND METHODS

Study Design

This was a prospective, comparative study performed in the Academic IVF Center of Lille University Hospital (France). It was approved by the local institutional review board of Lille University Hospital. Written, informed consent was obtained from all subjects before beginning COH.

A total of 194 patients, aged 21–37 years, undergoing their first intracytoplasmic sperm injection (ICSI) attempt for an exclusive male factor indication, were prospectively recruited from January 2008 to December 2011.

The study was designed with 80% power to detect a relative 30% difference between groups (with a significance level of 5%) for the MII/total oocytes ratio. With the assumption of a ratio at 70% in the control group, it was calculated that at least 82 patients had to be included in each group. We therefore recruited 97 patients with PCOM according to standardized criteria: we used the revisited threshold for follicle number per ovary (FNPO) proposed by Dewailly et al. (22), from our own experience with a new ultrasound machine (i.e., ≥ 19 follicles of 2–9 mm diameter in at least one ovary). This threshold corresponds to the former threshold of 12 with our previous ultrasound machine. Among these 97 PCOM patients, 51 (52.5%) had PCOS (i.e., ultrasonographic criteria of PCOM together with either oligoanovulation or hyperandrogenism or both) and 46 (47.5%) had "PCOM only" (i.e., ultrasonographic criteria of PCOM, ovulatory cycles, and no clinical or biological hyperandrogenism).

Concomitantly, we recruited 97 age-matched controls. These were "non-PCOM patients" who underwent their first ICSI for exclusively male infertility during the same time period, according to the following criteria: ovulatory cycles, no hyperandrogenism, FNPO between 8 and 18 follicles in each ovary, and FSH <10 IU/mL. This group was defined as the control group.

Because it has been suggested in several studies that obesity could adversely affect oocyte quality, we excluded patients with a body mass index (BMI) >32 kg/m^2, for both PCOM patients and controls.

Hormonal Assays

All patients had had day-3 baseline hormonal investigations on a blood sample before the ICSI attempt, at least 3 months after any hormonal treatment, including FSH, antimüllerian hormone, E_2, LH, Δ4-androstenedione, and T.

The FSH, LH, and E_2 were measured using chemiluminescent, two-site immunoassays on a multiparameter system (Axsym; Abbott Laboratories). Antimüllerian hormone was measured using a kit of second immuno-enzymatic generation antimüllerian hormone–EnzymeImmunoAssays (ref. A16507) provided by Beckman Coulter Immunotech. Delta4-androstenedione was measured in duplicate by radioimmunoassay using a kit provided by Beckman Coulter Immunotech. Testosterone was measured in duplicate by radioimmunoassay using the Coat-a-Count kit provided by Siemens DPC.

Ultrasound Examination

The baseline FNPO assessment was performed with a Voluson E8 Expert (General Electric Systems) with a 5–9 MHz transvaginal transducer by counting all the 2–9 mm diameter follicles. During COH, follicles were counted and classified into 3 different size categories: 10–12 mm, 13–15 mm, and >15 mm. All the ultrasonographic examinations were performed on the same machine by only two different operators.

COH Protocol

Patients received either an agonist or an antagonist protocol. In the agonist protocol daily injections of triptorelin (0.1 mg) were started in the mid-luteal phase of the preceding cycle (for women with regular menstruations) or on the first day of bleeding (for women with oligomenorrhea or amenorrhea). Desensitization was checked 12–15 days after initiation of GnRH agonists (desensitization day). Daily injections of