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# Fertility preservation strategies and long-term reproductive outcomes in women treated for breast cancer

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**Research Article**

**Keywords:** Fertility preservation, Breast cancer, oocyte vitrification, in vitro maturation, and ovarian tissue cryopreservation, Live Birth

**Posted Date:** July 3rd, 2026

**DOI:** https://doi.org/10.21203/rs.3.rs-9001315/v1

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**Additional Declarations:** No competing interests reported.

## Abstract

# Purpose

What are the fertility preservation(FP) strategies and long-term reproductive outcomes in women with breast cancer?

# Methods

Cohort study including women aged 18–40 years referred for FP counseling between 2015 and 2019 at a tertiary care centre. FP strategies comprised controlled ovarian stimulation (COS) or in vitro maturation (IVM) with oocyte and/or embryo vitrification, and ovarian tissue cryopreservation (OTC), used alone or in combination. Long-term follow-up (≥ 5 years) assessed ovarian function, pregnancy intention, conception modalities, and reproductive outcomes.

# Results

A total of 165 patients were included (mean age 33.2 ± 3.9 years). Chemotherapy was administered as adjuvant setting in 47.3%(n = 78) and as neoadjuvant in 41.2%(n = 68) of patients, while 11.5% (n = 19) did not receive chemotherapy. A FP strategy was proposed to 151 patients (91.5%) and performed in 123(74.5%). COS was the most frequently used technique (40,6%), followed by IVM (33,3%) and OTC (5,4%). Forty-two patients (25.5%) did not undergo FP. Long-term follow-up was available for 94 patients (57.0%). Among them, 45(47.9%) reported an attempt to conceive. 60.0% (27/45) achieved a live birth (LB). 18(66.7%) conceived spontaneously, whereas 9(33.3%) achieved a LB using assisted reproductive technologies. Cryopreserved material was used by 9 women (9/45, 20.0%) resulting in 2 LB. Compared with women without a pregnancy intention, women who reported an attempt to conceive more frequently had hormone receptor negative disease, received less adjuvant chemotherapy, and more often reported regular cycles; embryo cryopreservation was also more frequent.

# Conclusion

FP is feasible in young women with breast cancer. Despite exposure to potentially gonadotoxic treatments, pregnancy and LB remain achievable, most often spontaneously.

## Introduction

Breast cancer (BC) is the most common malignancy in women of reproductive age [1–3]. Advances in treatment have significantly improved survival; however, these therapies, particularly chemotherapy, can impair ovarian reserve and compromise future fertility [4–6]. In addition, the prolonged duration of oncologic treatment and follow-up often delays childbearing, further reducing the likelihood of pregnancy

[7]. In this context, fertility preservation (FP) has become an essential component of care, and international guidelines recommend early and systematic referral to specialized consultations at the time of diagnosis [8, 9].

Nevertheless, selecting the most appropriate FP strategy in the setting of breast cancer remains challenging [9, 10]. Several FP options are currently available, including oocyte cryopreservation and/or embryo cryopreservation after controlled ovarian stimulation (COS), in vitro maturation (IVM) of oocytes, and ovarian tissue cryopreservation (OTC). Each technique presents specific advantages and limitations, and the choice of the most appropriate strategy depends on multiple factors such as the type of disease and oncological safety, the gonadotoxic nature of the therapies, the urgency of treatment, patient age and ovarian reserve. The often-limited time before treatment initiation restricts the feasibility of COS [11–13]. Moreover, COS raises concerns in hormone-sensitive cancers due to the transient increase in estradiol levels and the use of exogenous gonadotrophins [14–18]. IVM may be considered when COS is not feasible, although its reproductive outcomes remain less well established [19–21]. Finally, OTC is not routinely proposed in BC, as most contemporary chemotherapy regimens are associated with a low to moderate gonadotoxic risk, in case of advanced reproductive age, or in specific genetic contexts such as BRCA mutation carriers [9, 22, 23]. Overall, these considerations highlight the absence of a clear consensus regarding the optimal fertility preservation strategy in such contexts, given the balance between potential benefits and limitations of each approach, and the limited availability of long-term reproductive outcome data.

At the same time, spontaneous pregnancies after BC are regularly reported, indicating that fertility is not uniformly impaired [6, 24, 25]. However, fertility rates appears globally reduced compared with the general population [17, 26], and the actual benefit of FP strategies, particularly in terms of long-term reproductive outcomes and real-life utilization rate of cryopreserved material and long-term reproductive outcomes, remains insufficiently documented [5, 27, 28].

To address this gap, the primary objective of this study was to describe fertility preservation strategies in women referred for fertility preservation in the context of breast cancer. The secondary objective was to evaluate long-term reproductive outcomes beyond five years after diagnosis, including spontaneous and assisted pregnancies, live births, and the use of cryopreserved material.

## Materials and methods

# Study population

This retrospective cohort study included women aged 18–40 years diagnosed with breast cancer between March 2015 and December 2019, who attended a FP consultation at the department of gynecology and reproductive medicine at our tertiary care center. All patients seen for FP consultation were included, regardless of whether a cryopreservation procedure was ultimately performed (COS, IVM, or OCT).

## Fertility preservation consultation

At the initial consultation, standardized counseling was provided regarding the potential gonadotoxic effects of cancer treatments and the available FP options. Ovarian reserve assessment was systematically performed using serum anti-Müllerian hormone (AMH) levels and antral follicle count (AFC). The indication and choice of FP technique were discussed in a dedicated fertility multidisciplinary team setting, taking into account oncologic parameters, fertility status, and patient preferences [9].

## Fertility preservation techniques

Depending on the clinical context, different FP strategies were offered [9]:

Oocyte or embryo vitrification after COS: Eligible patients underwent COS using either a GnRH antagonist or agonist protocol to prevent premature ovulation. Stimulation was carried out with gonadotropins at an individualized starting dose, adjusted according to age, body mass index (BMI), and ovarian reserve, following our center's protocol [29]. Monitoring included pelvic ultrasound and serial hormonal assays. Final oocyte maturation was triggered with a GnRH (Gonadotropin-Releasing Hormone) agonist and/or r-hCG (recombinant human Chorionic Gonadotropin), depending on the protocol. Oocyte retrieval was scheduled 36 hours later under local or general anesthesia, depending on patient preference and technical considerations. Mature oocytes were either vitrified or fertilized by ICSI with partner sperm in case of a parental project, and resulting embryos at blastocyst stage were cryopreserved[30].

Oocyte vitrification after IVM: IVM was offered when COS was contraindicated or when urgent initiation of anticancer therapy precluded stimulation, in patients selected based on a satisfactory ovarian reserve [21]. Without prior stimulation, immature oocytes were retrieved transvaginally from follicles > 5 mm, then cultured in a gonadotropin-enriched medium (IVM, CooperSurgical, USA) for 24–48 hours. Maturation (metaphase II) was confirmed by the presence of the first polar body. Mature oocytes were vitrified or fertilized, depending on the parental project.

Ovarian tissue cryopreservation (OTC): In cases of contraindication to COS or urgent treatment initiation, OTC can be proposed alone or in combination with IVM [9]. Ovarian cortical tissue was retrieved laparoscopically, either by unilateral oophorectomy or partial cortical biopsy. Then, ovarian tissue was cut into thin slices and cryopreserved using slow-freezing, a method that preserves primordial follicle viability.

## Patient Follow-up

Long-term follow-up (≥ 5 years after the initial consultation) was conducted through telemedicine visits. Collected data included oncologic treatments, ovarian function (regularity of menstrual cycles, AMH, and AFC), and fertility outcomes, including desire for pregnancy, mode of conception (spontaneous or using ART), use of cryopreserved material, and pregnancy outcomes.

## Data Collection

Data were retrospectively collected from baseline medical records and subsequent follow-up consultations.The following variables were analyzed:

1. Sociodemographic and fertility characteristics at the time of FP consultation: age, BMI, gravidity, parity, AMH, and AFC.
2. Oncologic characteristics: Immunohistochemical profile of the tumor **(**hormone receptor status and HER2 expression), chemotherapy setting (adjuvant or neoadjuvant), endocrine therapy, administration of a GnRH agonist during chemotherapy and cancer recurrence.
3. FP techniques: oocyte/embryo vitrification after COS, IVM, OTC, and their technical details (e.g. protocol type, trigger, number of oocytes and/or embryos cryopreserved) [9].

Among patients with long-term follow-up, ovarian function was assessed based on menstruation resumption, regularity of menstrual cycles, and hormonal testing (AMH, AFC) when available. Fertility outcomes included pregnancy intent, occurrence of a clinical pregnancy (defined as sonographic visualization of an intrauterine sac with cardiac activity), live birth [31], mode of conception (spontaneous or with ART) and use of cryopreserved gametes or tissue.

# Statistical Analysis

A descriptive analysis was performed on the entire cohort, including sociodemographic characteristics, oncologic data, treatments received, FP modalities, and immediate outcomes of FP procedures (number and type of cryopreserved gametes/embryos).

Among patients with ≥ 5 years of follow-up, a specific analysis evaluated long-term fertility outcomes. Comparisons were made according to pregnancy intent, and among those with a parental project, according to whether a live birth was achieved. Quantitative variables were compared using the Mann–Whitney test, and qualitative variables using the Chi-square or Fisher's exact test when appropriate. A two-sided p-value < 0.05 was considered statistically significant. This study was approved by the Ethics Review Committee of the Cochin University Hospital (CLEP) (n° AAA-2026-10008). All of the data were fully anonymized before use.

## Results

# Patient characteristics

A total of 165 women attended a FP consultation in the context of breast cancer. The mean age was 33.2 ± 3.9 years. Most patients were partnered (n = 107; 64.8%) and nulliparous (n = 120 ; 72.7%). Baseline ovarian reserve assessment showed a mean AMH level of 2.8 ± 2.8 ng/mL and a mean AFC of 15.9 ± 9.3 (Table 1). Regarding oncologic features, 70.6% (n = 115) had hormone receptor (HR) positive tumors, 27.5% (n = 44) had triple-negative (HR- HER2-) breast cancer, and 21.3% (n = 34) were HER2-

positive BC. Nineteen patients (11.5%) did not receive chemotherapy, whereas 47.3% (n = 78) underwent adjuvant and 41.2% (n = 68) neoadjuvant chemotherapy. Endocrine therapy was given in 68.7% of cases (n = 112).

Table 1
Baseline characteristics of patients

| **Baseline characteristics** | **n = 165** |
|---|---|
| **Women characteristics** | |
| Age (years) | 33.2 ± 3.9 |
| ≤ 35 years | 119 (72.1) |
| Partnered | 107 (64.8) |
| Nulligravid | 92 (55.8) |
| Nulliparous | 120 (72.7) |
| BMI (kg/m²) | 22.7 ± 4.4 |
| **Ovarian reserve** | |
| AMH (ng/mL) | 2.8 ± 2.8 |
| AFC | 15.9 ± 9.3 |
| **Cancer characteristics** [a] | |
| HER2-HR- | 44/160 (27.5) |
| HER2- HR+ | 115/163 (70.6) |
| HER2 + HR+/- | 34/160 (21.3) |
| **Chemotherapy setting** | |
| None | 19 (11.5) |
| Adjuvant chemotherapy | 78 (47.3) |
| Neoadjuvant chemotherapy | 68 (41.2) |
| Endocrine therapy [a] | 112/163 (68.7) |

[a] *Data missing for these variables (< 5%).*

*Data are presented as mean ± SD or n (%), unless otherwise specified. BMI : body mass index ; AMH : anti mullerian hormone ; AFC : antral follicle count ;* HR : *hormone receptors ; HER2 : Human Epidermal Growth Factor Receptor 2*

# Fertility preservation strategies

A FP strategy was proposed to 151/165 patients (91.5%) and performed in 123 (74.5%). COS was the most frequently used technique (n = 67; 40.6%), followed by IVM (n = 55; 33.3%) and OTC (n = 9; 5.4%) (Fig. 1). Overall, 42 patients (25.5%) did not undergo FP, reasons included patient refusal, immediate chemotherapy, or medical contraindication. Some patients underwent combined procedures: Among the nine who had OTC, eight also underwent an associated IVM procedure (Fig. 1). IVM was mainly performed in women treated with neoadjuvant chemotherapy (48/55, 87.3%), whereas COS was predominantly performed in women receiving adjuvant chemotherapy (52/67, 77.6%). Patients who did not receive chemotherapy mostly underwent COS (14/19, 73.7%), while 5/19 (26.3%) did not undergo any FP procedure.

In total, 71 COS cycles were performed in 67 women. Details concerning COS characteristics are presented in the Table 2. No complications such as infection or ovarian hyperstimulation syndrome occurred. For women undergoing IVM, the mean number of immature oocytes retrieved was 5.8 ± 5.2, and the mean number of mature oocytes obtained after in vitro maturation was 3.3 ± 3.0. For women undergoing OTC, the mean number of ovarian tissue fragments cryopreserved per patient was 13.8 ± 2.8.

Table 2
Characteristics of controlled ovarian stimulations

| **Number of women who underwent COS** | **n = 67** |
|---|---|
| Number of COS cycles initiated [a] | 71/165 (43) |
| Duration (days) | 9.3 ± 1.9 |
| Daily gonadotropin dose (IU) | 287.0 ± 41.6 |
| Antagonist protocol | 70/71 (98.6) |
| Agonist protocol | 1/71(1.4) |
| Trigger with GnRH agonist only [b] | 58/70 (82.9) |
| Trigger with r-hCG only [b] | 9/70 (12.9) |
| Dual trigger [b] | 3/70 (4.3) |
| Estradiol level at trigger (pg/mL) | 1607.7 ± 855.5 |
| Progesterone level at trigger (ng/mL) | 1.7 ± 2.8 |
| Number of oocytes retrieved | 8.5 ± 7.6 |
| Number of oocytes cryopreserved | 5,9 ± 6,4 |
| Number of embryos cryopreserved | 3.8 ± 2.1 |
| COS with planned oocyte cryopreservation [c] | 64/71(90.1) |
| COS with planned embryo cryopreservation [c] | 9/71(12.6) |
| COS with no gamete vitrification | 4/71 (5.6%) |
| [a] *Four patients underwent a double stimulation cycle* | |

[b] *One patient had her COS cancelled before triggering.*

[c] *Patients could combine different strategies.*

*COS: controlled ovarian stimulation; IU: international unit; GnRH: Gonadotropin-Releasing Hormone; r-hCG : recombinant human Chorionic Gonadotropin*

*Data are expressed as mean ± SD or n (%), unless otherwise specified.*

*COS (n = 67; 40.6%); IVM (n = 55; 33.3%); ovarian tissue cryopreservation (n = 9; 5.4%); no fertility preservation (n = 42; 25.5%). Eight patients underwent a combination of IVM and ovarian tissue*

*cryopreservation.*

# Long-term follow-up

Long-term follow-up (≥ 5 years) was available for 94 patients (57.0%) (Table 3). Baseline characteristics of patients according to follow-up status (long-term follow-up versus lost to follow-up) are presented in Supplementary Table 1. Among these 94 women, 81 had received chemotherapy, and 62 of them were treated with a GnRH agonist during chemotherapy. Among those women, 66 patients (70.2%) reported regular cycles, 15 (16.0%) irregular cycles, and 13 (13.8%) persistent amenorrhea. Among the 13 patients with persistent amenorrhea, 12 had received chemotherapy, and 11 had been treated with a GnRH agonist. Among the 81 women who resumed menstruation, 69 had received chemotherapy (85.2%).

Between the initial consultation and the 5-year follow-up, forty-five patients (47.9%) reported attempting to conceive (Fig. 2). Among them 64.4% (29/45) achieved a clinical pregnancy and 60.0% (27/45) achieved a live birth. Of the 27 patients who had a live birth, 18/27 (66.7%) conceived spontaneously, whereas 9/27 (33.3%) achieved a live birth using ART. Among the 18 women who did not achieve a live birth, five used cryopreserved material without success, ten did not use their cryopreserved material, and three had no preserved material available. Among the 9 patients who achieved a live birth through ART, 2 (22.2%) conceived following IUI as part of a single-woman pathway, and 7 (77.8%) underwent in vitro fertilization / intracytoplasmic sperm injection (IVF/ICSI). Among those treated with IVF/ICSI, 2 (28.6%) obtained a live birth with the use of vitrified oocytes from FP (in both women, the oocytes had been vitrified following SOC), 3 (42.9%) used donor oocytes, and 2 (28.6%) conceived after a new IVF/ICSI attempt performed after cancer treatment. No live birth was obtained using mature oocytes derived from IVM, and cryopreserved ovarian tissue was not used for conception. Among patients who attempted to conceive, the utilization rate of vitrified oocytes was 9/45 (20.0%) (in six women, the oocytes were vitrified following COS, and in three following IVM).

Table 3
Evaluation of fertility at long-term follow-up

| **Menstrual cycle status** | **Total (n = 94)** |
|---|---|
| Regular cycles | 66 (70.2) |
| Irregular cycles (≤ 25 or > 35 days) | 15 (16.0) |
| Amenorrhea | 13 (13.8) |
| **Ovarian reserve evaluation** [a] | |
| AMH (ng/mL) | 0.5 ± 1.0 |
| AFC | 7.3 ± 6.6 |
| **Conception outcomes** | |
| Reported pregnancy attempt | 45 (47.9) |
| Clinical pregnancy rate | 29/45 (64.4) |
| Live birth rate | 27/45 (60.0) |
| Live birth after spontaneous pregnancy | 18/27 (66.7) |
| Live birth after assisted reproduction techniques | 9/27 (33.3) |
| Miscarriage rate | 8/45 (17.8) |
| Use of cryopreserved material [b] for conception | 9/45 (20.0) |
| Live birth using cryopreserved material | 2/45 (4.4) |

[a] *The data were available only for 16 and 11 patients for AMH and AFC, respectively.*

[b] *Only cryopreserved oocytes were used.*

**AMH : anti mullerian hormone ; AFC : antral follicle count**

# Comparisons based on pregnancy attempt

Patients who reported a pregnancy attempt more frequently had hormone receptor negative breast cancer (15/44, 34.1% vs 8/49, 16.3%; p = 0.047), were more likely to have received neoadjuvant treatment rather than adjuvant chemotherapy (17/45, 37.8% vs 29/49, 59.2%; p = 0.034), and had a lower tumor recurrence rate (3/45, 6.7% vs 14/49, 28.6%; p = 0.006) (Table 4). Regular menstrual cycles were reported more frequently in this group (37/45, 82.2% vs 29/49, 59.2%; p = 0.006). Regarding FP, embryo cryopreservation was more frequent in this group (7/42, 16.7% vs 0/31, 0%; p = 0.017). Characteristics of patients with and without a live birth are described in supplementary table 2. The only significant

difference between those with and without a live birth was a lower BMI in women with live birth (20.8 ± 3.3 vs 24.1 ± 5.2 kg/m²; p = 0.021).

Table 4
Characteristics of patients who did or did not attempt pregnancy

| Characteristics | With pregnancy attempt (n = 45) | Without pregnancy attempt (n = 49) | p-value |
|---|---|---|---|
| **Baseline characteristics** | | | |
| **Women characteristics** | | | |
| Age (years) | 33.1 ± 3.9 | 32.65 ± 4.2 | 0.632 |
| ≤ 35 years | 33 (73.3) | 38 (77.6) | 0.635 |
| Ovarian reserve evaluation | | | |
| AMH (ng/mL) | 2.9 ± 2.6 | 2.5 ± 1.8 | 0.835 |
| AFC | 16.3 ± 9.5 | 14.4 ± 8.7 | 0.441 |
| BMI (kg/m²) | 22.1 ± 4.4 | 23.0 ± 4.5 | 0.194 |
| Nulligravid | 28 (62.2) | 27 (55.1) | 0.484 |
| Nulliparous | 38 (84.4) | 33 (67.3) | 0.054 |
| Partnered | 31 (68.9) | 33 (67.3) | 0.862 |
| **Cancer characteristics** [a] | | | |
| HER2-HR- | 12/44 (27.3) | 8/47 (17) | 0.238 [k] |
| HER2-HR+ | 29/44 (65.9) | 41/49 (83.7) | 0.047 [k] |
| HER2 + HR+/- | 8/44 (18.2) | 15/47 (31.9) | 0.132 [k] |
| Chemotherapy setting | | | 0.034 [k] |
| None | 10 (22.2) | 3 (6.1) | |
| Adjuvant chemotherapy | 17 (37.8) | 29 (59.2) | |
| Neoadjuvant chemotherapy | 18 (40.0) | 17 (34.7) | |
| Endocrine therapy [a] | 28/44 (63.6) | 40 (81.6) | 0.05 [k] |
| **FP characteristics** | | | |
| FP techniques | | | 0.51 [k] |
| COS | 24/45 (53.3) | 21/49 (42.9) | |
| IVM | 18 (40.0) | 10 (20.4) | |
| Ovarian tissue cryopreservation | 5 (11.1) | 2 (4.1) | |

| Characteristics | With pregnancy attempt (n = 45) | Without pregnancy attempt (n = 49) | p-value |
|---|---|---|---|
| **Baseline characteristics** | | | |
| **Women characteristics** | | | |
| Planned oocyte cryopreservation [b] | 35 (83.3) | 31 (100) | 0.017 |
| Planned embryo cryopreservation [b] | 7 (16.7) | 0 (0) | 0.017 |
| GnRH agonist treatment during chemotherapy | 26/35 (74.3) | 36/46 (78.3) | 0.777 |
| **Follow-up characteristics** | | | |
| Cancer recurrence | 3 (6.7) | 14 (28.6) | 0.006 |
| Menstrual cycle status | | | 0.006 |
| Regular cycles | 37 (82.2) | 29 (59.2) | |
| Irregular cycles (≤ 25 d or> 35d) | 7 (15.6) | 8 (16.3) | |
| Amenorrhea | 1 (2.2) | 12 (24.5) | |
| Ovarian reserve evaluation [c] | | | |
| AMH (ng/mL) | 0.5 ± 1.0 | NA | |
| AFC | 7.3 ± 6.6 | NA | |

[a] *Data missing for these variables (< 5%).*

[b] *Patients could combine different strategies.*

[c] *The data were available only for 16 and 11 patients for AMH and AFC, respectively.*

*Data are expressed as mean ± SD or n (%), unless otherwise specified. AMH = Anti-Müllerian Hormone; AFC = Antral Follicle Count; BMI = Body Mass Index; HR + = Hormone Receptor positive ; HER2 + = Human Epidermal growth factor Receptor 2 positive; COS = Controlled Ovarian Stimulation; IVM = In Vitro Maturation; GnRH = Gonadotropin-Releasing Hormone; NA = Not Available ; ⁂ Mann–Whitney test; ⁑ Pearson's chi-square test; d = day*

# Discussion

In our cohort of women referred for FP in the context of breast cancer, a FP procedure was performed in nearly three-quarters of patients. FP was carried out both in women treated with adjuvant or neoadjuvant

chemotherapy and in those who did not receive chemotherapy. The most frequently used techniques were COS and IVM, whereas OTC remained marginal. Almost half of the patients followed for more than five years expressed a desire for parenthood. Among them, approximately two-thirds achieved a live birth, most often after spontaneous conception, highlighting that pregnancy remains possible after breast cancer despite potentially gonadotoxic treatments.

The strengths of this study include its conduct in a referral center with a structured oncofertility program and the prospective, comprehensive collection of data concerning FP. The database was well documented regarding FP techniques (COS, IVM, OTC), enhancing the reliability of the findings. The sample comprised a large number of young women with breast cancer, ensuring good representativeness for this population. The diversity of oncologic setting (e. g. no chemotherapy, adjuvant or neoadjuvant chemotherapy) also allowed evaluation of FP feasibility across therapeutic modalities. Finally, long-term follow-up was conducted through individual interviews, providing detailed information on gynecological outcomes and parenthood projects.

However, several limitations should be acknowledged. The main one is the high proportion of patients lost to follow-up (43%), reducing statistical power and introducing a potential attrition bias. The single-center design may also limit generalizability, especially in settings with different FP organization. Some oncologic data were incomplete, and follow-up information relied partly on patient self-report, which may introduce recall bias. In particular, detailed information on chemotherapy regimens (e.g. specific drugs, cumulative doses, and alkylating agent exposure) was not systematically available, which limited our ability to perform a more refined analysis of gonadotoxicity. Key parameters, such as adherence to oncologic treatments (particularly duration of endocrine therapy) or the interval between the end of treatment and initiation of a pregnancy attempt, were not always available. Furthermore, incomplete collection of long-term biological data (AMH, AFC) limited interpretation of ovarian reserve evolution. Although follow-up beyond five years is already meaningful, it does not capture all reproductive projects that may arise later. In addition, the absence of a control group, whether breast cancer patients who did not attend an FP consultation or women from the general population, restricts comparisons and precludes precise estimation of the excess infertility risk. Despite these limitations, our findings provide valuable insights for the management of young women with breast cancer. It not only to illustrate real-life FP pathways in a reference center but also document long-term reproductive outcomes, which remain seldom reported in the literature [5, 27].

In our study, most patients underwent COS. This is consistent with most studies in the literature [15, 27], where COS remains the reference technique for FP in this setting, particularly because of its superior efficacy in terms of subsequent pregnancy rates compared with IVM [8]. In some series, particularly those by Oktay et al., IVM was more widely offered in urgent oncologic contexts, when timing or treatment requirements precluded COS [20]. However, with the development of random-start stimulation protocols and earlier referral from oncologists, COS is now feasible in the vast majority of situations and remains the standard approach when not contraindicated [13, 32]. Moreover, when time allowed, a double stimulation protocols can also be performed to maximize oocyte yield [33].

In our study, nearly half of the patients followed more than five years after diagnosis expressed a pregnancy intent. Among them, about two-thirds achieved a live birth, most often spontaneously. These findings are reassuring, as FP may not always be feasible because of time constraints or contraindications to ovarian stimulation. Consistently, previous studies have shown that most pregnancies after breast cancer occur naturally, without recourse to cryopreserved material [25, 27, 28, 34]. In our cohort, the utilization rate of cryopreserved gametes remained limited, in line with the literature, in which this rate rarely exceeds 10–20% [27, 28, 35, 36]. We have reported that cryopreserved material was used by 9 out of 45 women who attempted to conceive (20%) and resulted in two live births. Moreover, 20% of women who attempted to conceive achieved a live birth through ART, highlighting the substantial contribution of ART to post-cancer fertility. Finally, the proportion of women reporting a pregnancy project in our cohort remained modest, which may reflect a degree of reluctance to consider pregnancy after cancer [6, 37].

The choice of FP technique in breast cancer remains complex and must account for oncologic characteristics, treatment urgency, and parental project. Compared to other cancers, breast cancer carries an intermediate gonadotoxic risk [10]: it entails a non-negligible risk of ovarian reserve impairment, depending mainly on age, but is also associated with a substantial proportion of spontaneous pregnancies in long-term survivors. The relatively older age at diagnosis and potential hormone sensitivity of the tumor further complicate decision-making. However, in the literature, as in our study, we observed no significant difference in cancer recurrence across fertility preservation techniques [17, 18].

In practice, COS remains the preferred option whenever feasible in BC context. IVM is a useful alternative when COS cannot be performed, but its effectiveness in terms of live birth rates remains limited [21]. OTC may be discussed in selected cases, particularly among highly motivated patients or when COS is contraindicated, but it carries surgical risks and may itself reduce ovarian reserve [8, 22]. Decisions must therefore be individualized and made within a multidisciplinary framework, oncologic management remaining the priority [38].

Breast cancer affects an increasing number of young women, often at a time when they are considering parenthood. FP has thus become a major issue in their management. Our study confirms the feasibility of the available techniques and supports the systematic integration of oncofertility consultation into the initial care pathway.

## Declarations

# Funding:

no funding was obtained for this study.

Competing interests: the authors declare no competing interests.

Ethics approval: this study was approved by the Ethics Review CLEP (n° AAA-2026-10008).

Consent to Participate: in accordance with French regulations for retrospective studies using anonymized data, formal written informed consent was not required. Patients were informed of the possible use of their anonymized data for research purposes, and no opposition was recorded.

Consent for publication: not applicable.

Data availability: the datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

# Author Contribution

MB and PS were the coordinators of the project. CW, MB, and PS designed the study and supervised the drafting and redrafting of the manuscript. MB, CW, VBL, FC, LM, CM, JG, KPC, CC and PS contributed to the data collection. All of the authors contributed substantially to the analyses and interpretation of the data. MB supervised and reviewed the statistical analysis. All of the authors approved the final version of the manuscript.

# Acknowledgement

The authors wish to thank the staff members from our department for their expert assistance with the data collection.

# Data Availability

the datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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# Figures

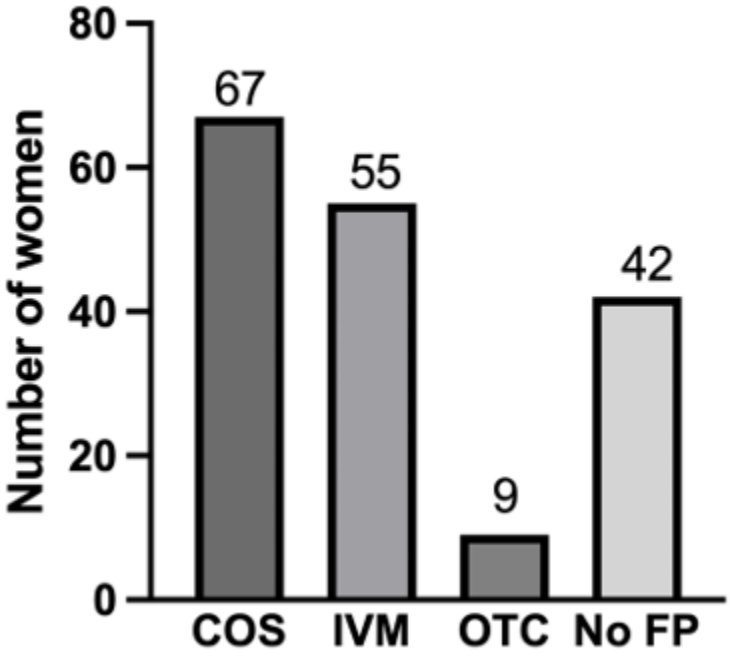



**Figure 1**

**Distribution of fertility preservation techniques.**

*COS (n=67;* 40.6 %*); IVM (n=55;* 33.3 %*); ovarian tissue cryopreservation (n=9;* 5.4 %*); no fertility preservation (n=42; 25.5 %). Eight patients underwent a combination of IVM and ovarian tissue cryopreservation.*

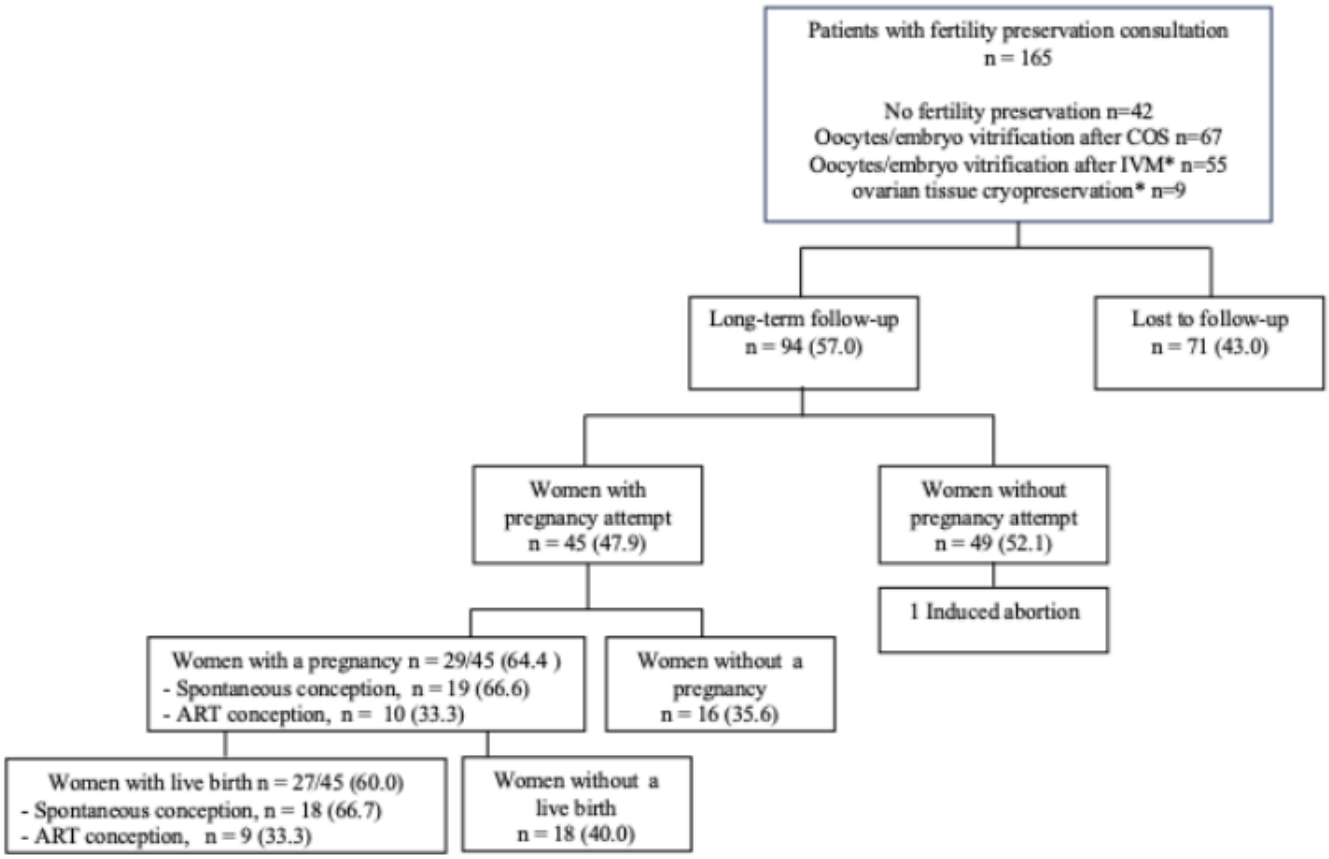



**Figure 2**

**Follow-up and reproductive outcomes after fertility preservation consultation in breast cancer patients**

*Data are expressed as n (%), ART : assisted reproductive technologies*.

**Eight patients underwent a combination of IVM and ovarian tissue cryopreservation*

# Supplementary Files

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