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REVIEW

# Preservation of fertility in surgery of benign and borderline malignant ovarian tumors

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## KEYWORDS

Benign ovarian tumor;  
Borderline ovarian tumor;  
Fertility;  
Fertility preservation

**Summary** Benign ovarian tumors occur in 7% of women during their procreative years and involve both organic and functional tumors. The average age of onset for borderline ovarian tumors is ten years younger than that for ovarian cancers. Women with benign and borderline malignant ovarian tumors are therefore more likely to be affected by fertility issues. The causal link between infertility and benign ovarian tumor stems more from the therapeutic strategies adopted than from the histological nature of the benign ovarian tumor. The question of fertility preservation must therefore be addressed in the management of these patients through respect for “correct” surgical indications, through gestures centered around ovarian preservation, and finally, if necessary, by recourse to fertility preservation techniques.

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## Introduction

The preservation of fertility in patients with benign and borderline malignant ovarian tumors must be considered because these tumors occur at a younger age than ovarian cancers. This is even more important in the current societal context where the desire for maternity is increasingly deferred to a later age. It is therefore the surgeons' duty to know how to approach this question with their patients in order to propose a therapeutic strategy aimed at protecting fertility. This approach comprises two levels: a direct strategy including the limitation of indications and more conservative surgical procedures, and an indirect level corresponding to the use of complementary techniques to preserve the ovarian reserve when deemed necessary. We

will successively address the case of benign ovarian tumors and then borderline malignant ovarian tumors.

The histologic classification of ovarian tumors includes:

- epithelial tumors, the most common type, which may be benign, borderline or malignant;
- stromal tumors;
- germ cell tumors (30%), which may be benign (dermoid tumors/teratomas) or malignant.

## Presumably benign ovarian tumor

### Definition and natural history

Most of the presumably benign ovarian tumors (PBOT) are cysts although not all cysts are PBOT. By definition, they are larger than 25–30 mm. PBOTs may be functional (follicle or corpus luteum cysts) or organic. The natural history of these cysts is a gradual increase in size or spontaneous resolution

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in the case of functional PBOTs. Three main complications may develop: adnexal torsion, cyst rupture and intracystic hemorrhage. Some large tumors may also result in a compressive syndrome.

## Epidemiology

Very few studies have examined the impact of PBOTs. Two studies have looked at PBOTs in a population group of asymptomatic patients. Borgfeldt [1], in 1999, found a 6.6% incidence of benign ovarian tumors in a population of 335 asymptomatic women aged 25–40 years, 83% of which spontaneously resolved over a three-month period. A German study by Heinemann in 2003 [2] evaluated the incidence in the general population of benign ovarian tumor to be 18.6 per 100,000 patient-years in a prospective cohort of 396,000 patient-years, involving asymptomatic women aged 18–65. The median age at diagnosis was 28.5 years.

## Diagnostic strategy

The diagnostic strategies for PBOTs depend on the clinical context, patient age and circumstances of discovery. Trans-vaginal pelvic ultrasound is the first-line imaging examination with 90% sensitivity and 80% specificity to define the characteristics and measure the size of the PBOT according to the International Ovarian Tumor Analysis (IOTA) classification [3]. The tumors are then categorized according to two criteria: unilocular vs. multilocular and liquid vs. solid (Fig. 1) [4]. Determinate masses are those for which the ultrasound makes it possible to propose a diagnosis: corpus luteum, hemorrhagic cyst, endometrioma or dermoid cyst. However, 6 to 16% of ovarian masses are indeterminate and will require magnetic resonance imaging (MRI) or surgical exploration for definitive diagnosis. MRI is recommended as the second-line study to characterize unilocular masses greater than 7 cm in size and complex and/or indeterminate ovarian masses [5,6]. Haggerty [7], in 2010, found a 95%-sensitivity for MRI with 94.1% specificity; the concordance rate between MRI and histopathology was 0.85 (95% CI; 0.716–0.976). Measurement of serum CA-125 level is not recommended for first-line diagnostic use in premenopausal women with PBOT. If an ovarian mass is accidentally discovered during laparoscopy, it is not possible to define a strategy precisely because the macroscopic appearance of such tumors is very non-specific.

## Therapeutic strategy

The 2013 clinical practice guidelines of the French National College of Gynecology and Obstetrics (CNGOF) define three therapeutic strategies for PBOTs based on the expected nature of this PBOT: dermoid, endometrioma, single unilocular cyst [8]. The therapeutic attitude must then be adapted to each patient's symptomatology, to the need to preserve endocrine function, and to the patient's wish to preserve her fertility. PBOT is clearly linked to infertility but this relationship seems to reside in the sequelae of surgical management and its impact on the ovarian reserve rather than to the histological nature of the tumor itself [9]. The impact of the adnexal surgical procedures relates to the resection of ovarian tissue and resultant decrease of follicular reserve as well as to the potential for ovarian devascularization. This impact will be all the more important if the patient's follicular reserve is already altered qualitatively or quantitatively, especially with advanced maternal age. The preservation of

fertility in these patients therefore involves restraint in surgical strategies including both the limitation of operative indications, the limitation of resection, and the development of techniques aimed at preserving ovarian function [10]:

- use of laparoscopy;
- conservative treatments whenever possible (cystectomy, unilateral adnexectomy);
- surgical techniques to conserve ovarian reserve (antimesial incision, avoidance of electrocoagulation of the ovarian cortex) [11].

Comprehensive management aimed at preserving fertility should therefore be systematically proposed and discussed with patients of reproductive age in whom a PBOT is found.

The principle of conservative treatment is operative at several levels:

- need to perform a minimal surgical procedure while preserving the uterus (no indication for hysterectomy for PBOT in patients of childbearing age);
- evaluation of the possibilities of leaving the maximum of healthy ovarian tissue.

Each of these elements should be evaluated successively and independently.

## Place and techniques for preserving fertility

When the patient's fertility is particularly at risk, *i.e.*, in cases of bilateral ovarian cysts, recurrent cysts, cysts with high potential for recurrence, and in the case of already depleted ovarian reserve (age > 35, risk of premature ovarian failure), ovarian preservation techniques may be offered to the patient. These techniques include:

- ovarian stimulation followed by oocyte or embryonic vitrification;
- aspiration harvesting of immature oocytes for *in vitro* maturation;
- surgical preservation of ovarian tissue (SPOT);
- harvesting of immature oocytes and *in vitro* maturation concomitantly with SPOT.

The technique of SPOT should be reserved in cases where follicular stimulation is impossible or contraindicated. Indeed, to date in France, the re-use of preserved tissues is subject to study protocols and its availability to patients is therefore limited.

## Specific attitude depending on the histological type

Attitude toward endometriotic cysts is discussed in the chapter on endometriosis.

### *Dermoid tumor*

Surgical management of dermoid cysts remains controversial. The main risk is adnexal torsion in 3.5–11% of cases [12–14], and malignant transformation, which remains rare (1–2%) and mainly concerns menopausal patients with cysts greater than 10 cm [15]. However, in series where an expectant attitude is advocated, the rate of secondary surgery for onset of symptomatology or at the patient's request is high [16,17]. The two management criteria are symptomatology and cyst size. For small volume cysts (<4–6 cm) expectant monitoring is an option after full discussion with the patient. For larger volume cysts, surgical management may be a reasonable option, but no formal argument imposes it [8]. For patients of childbearing

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