

Fertility-Sparing Surgery of Borderline Ovarian Tumors



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Characteristics of Borderline Ovarian Tumors (BOT) Compared To Ovarian Cancers

- Age of patients: **30% of patients are <40 y**

- **Prognosis**

FIGO stage	N	5-year relative survival (%)	10-year relative survival (%)
I	2310	99	97
II	158	98	90
III	228	96	88
IV	87	77	69

NCI DATABASE Trimble et al. 2002

**Conservative management of BOT
increases the risk of recurrent
disease compared to radical
surgery**

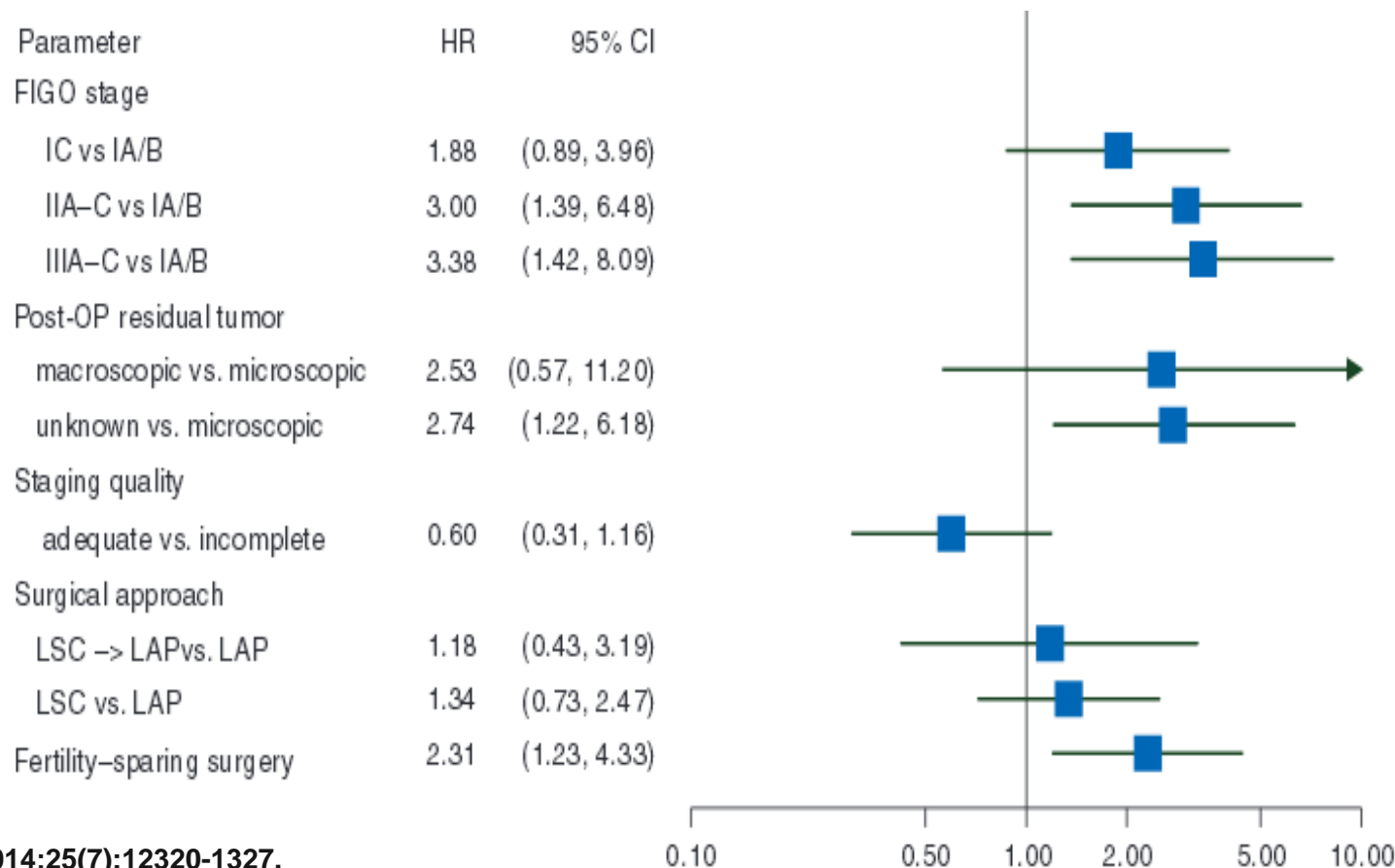
Recurrences

Radical : 0%-5%

Conservative: 10%-30%

Age-dependent differences in borderline ovarian tumours (BOT) regarding clinical characteristics and outcome: results from a sub-analysis of the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) ROBOT study

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Ann Oncol. 2014;25(7):12320-1327.

Figure 1. Multivariate analysis of prognostic factors regarding progression-free survival (PFS). Forest plots illustrating analysis of possible prognostic factors

Survival According to the Type of the Surgical Treatment

	n, recurrence	10-year DFS	Deaths
Radical	9 /175	92%	5/175
Conservative	9 /184	95%	1/184

Park JY, et al. *Gynecol Oncol*. 2009;113(1):75-82.

	DFS
Radical	100%
Conservative	99.3% (for stage I)

Zanetta G, et al. 2001.

Type of surgery doesn't influence the survival (Zanetta 2001, Morice 2001, Park 2009). This is explained by the fact that most recurrences were borderline disease and not invasive carcinoma. Rate of recurrence under the form of invasive carcinoma <1% (in stage I disease)

Fertility and borderline ovarian tumor: a systematic review of conservative management, risk of recurrence and alternative options

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Emile Daraï^{1,2,3,*}, Raffaèle Fauvet^{4,5}, Catherine Uzan^{6,7},
Sébastien Gouy⁶, Pierre Duvillard⁸, and Philippe Morice^{6,7,9}

Table 1 Oncological and fertility results of conservative treatment of early-stage borderline ovarian tumor (only series including >50 cases of conservative treatment are reported).

Authors	Conser- vative (n)	Mucinous (n)	Serous (n)	Salping-oopho- rectomy (n)	Cyst-ectomy (n)	Median time months	Oncological results					Fertility results		
							Recurrence (%)	Recurrence oopho- rectomy (n)	Recurrence cystectomy (n)	Invasive recurrence (n)	Death (n)	Patients wishing a pregnancy (n)	Patients pregnant (n)	Pregnancy rate (%)
Zanetta <i>et al.</i> (2001)	164	—	—	—	—	70	15	—	—	5	1	—	—	—
Camatte <i>et al.</i> (2002)	68 ^a	16	46	47	21	71	16 ^b	11%	21%	0 ^b	0	29	19	60
Maneo <i>et al.</i> (2004)	62	18	42	28	34	61 and 77 ^c	27 ^d	3 ^a	8 ^a	3	—	—	—	—
Boran <i>et al.</i> (2005)	62	27	33	40	22	44	7	1	3	0	0	25	10	40
Longacre <i>et al.</i> (2005)	53	—	—	—	—	> 5 years	17	—	—	2	0	—	—	—
Fauvet <i>et al.</i> (2005)	162	—	—	—	—	—	17	—	—	0	0	62	31	32
Suh-Burgmann (2006)	193 ^a	109	81	143	46	6.4 years	12	—	—	2	1	—	—	—
Romagnolo <i>et al.</i> (2006)	53 ^a	—	—	32	21	44 ^f	23	7	6	—	1	12	7	58
Yinon <i>et al.</i> (2007)	62 ^a	38	24	40	22	82	26	11	5	1	0	—	25	40
Wong <i>et al.</i> (2007)	116 ^a	—	—	78	38	21	3	2	2	2	1	—	—	—
De Iaco <i>et al.</i> (2009)	85 ^a	22	54	50	35	—	26	10	12	0?	0	—	—	—
Park <i>et al.</i> (2009)	184 ^a	139	43	128	56	65	5	3	6	1	1	31	27	73
Kokawa <i>et al.</i> (2009)	86	—	—	52	34	39 ^f	—	—	—	—	2	—	—	—
Kanat-Pektas <i>et al.</i> (2011)	55 ^a	24	29	36	19	61	5	1	2	0?	0	44	23	52
Koskas <i>et al.</i> (2011)	74	74	0	47	27	59	15	3	8	6	3	31	12	38
Song <i>et al.</i> (2011)	155 ^a	106	37	117	38	56	8	7	5	1	0	51	45	88
Khunamornpong <i>et al.</i> (2011)	60	60	0	59	1	—	7	—	—	4	2	—	—	—
Pooled estimate for proportion (%) (with 95% CI)							13 (10–16)					0.5 (0–1)		

Fertility and borderline ovarian tumor: a systematic review of conservative management, risk of recurrence and alternative options

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Maneo et al. (2004)	62	18	42	28	34	61 and 77 ^c	27 ^d	3*	8*	3	—	—	—	—
Uzomaka et al. (2004)	62	2	60	60	2	—	7	—	—	—	—	25	20	80
Longacre et al. (2005)	53	—	—	—	—	> 5 years	17	—	—	2	0	—	—	—
Fauvet et al. (2005)	162	—	—	—	—	—	17	—	—	0	0	62	31	32
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Pooled estimate for proportion (%) (with 95% CI)							13 (10–16)			0.5 (0–1)			54 (38–70)	

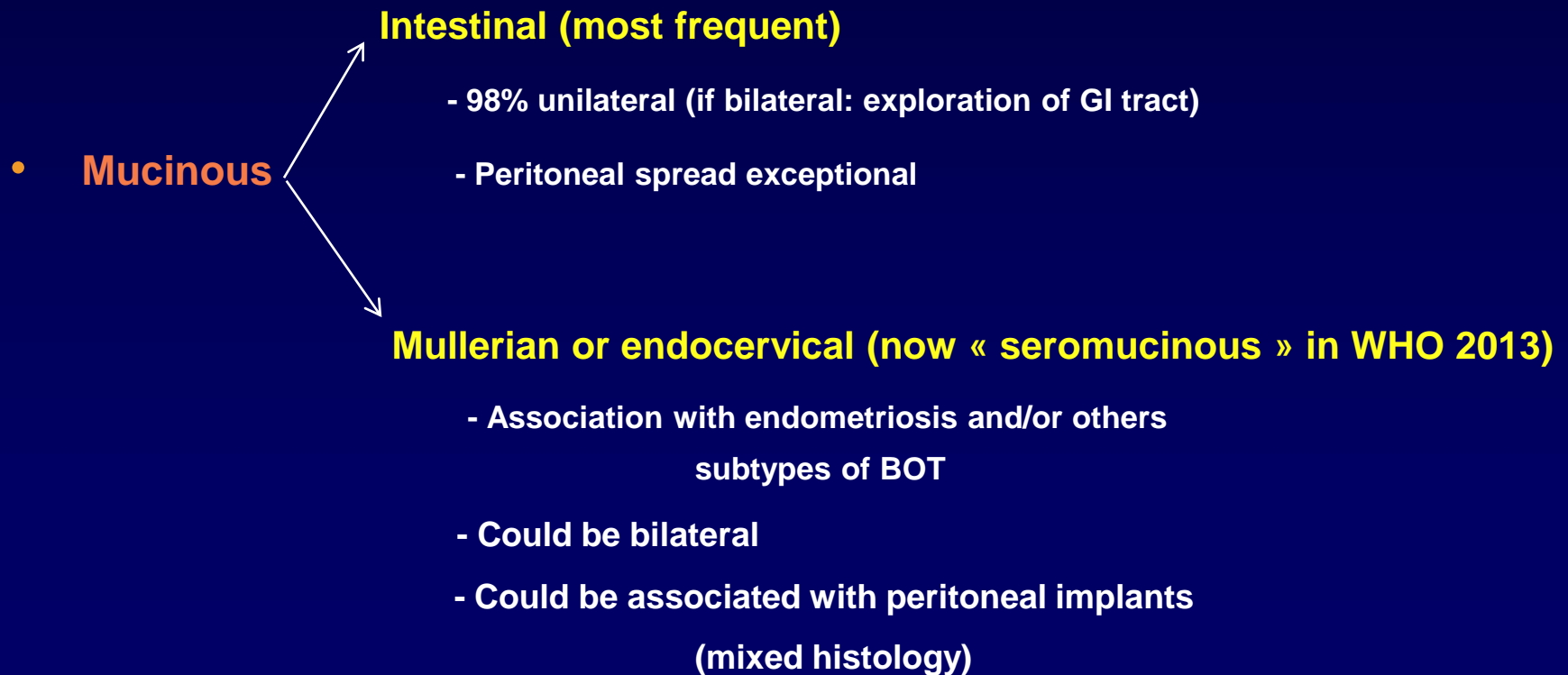
Pooled estimate for proportion (CI95%) **Recurrence 13 % (10-16)** **Death 0.5% (0-1)**

Serous BOT (Most Frequent)

- **Serous** → implants
(10%-40%)
 - noninvasive = 88 %
 - epithelial
 - desmoplastic
 - invasive = 12 %
- **Bilaterality: 25%-35%**
- **Micropapillary pattern** (described since 1996):
 - (infraclinic) implants (invasive or noninvasive) more frequent than in serous BOT without nonmicropapillary patterns
 - Bilaterality of the ovarian tumor more frequent
 - Involvement of the ovarian surface (excrecence) more frequent

Mucinous BOT

- Complex group of tumors. Evolution of the histologic classification
- Bulky tumors >15 cm ++++. Question of the histologic sampling
- Late recurrence under the form of invasive carcinoma recently reported 8%
- Uzan et al (2013). Single prognostic factor of recurrence: cystectomy +++



Unilateral Tumor Cystectomy Or Oophorectomy?

- Rate of recurrence « conventionally » increased in many papers after cystectomy (compared to salpingo-oophorectomy)
- But recent series don't report this increased rate (Yinon 2007; Park 2009)
- In cases of unilateral tumor: salpingo-oophorectomy is the standard management
 - Required in mucinous BOT (but macroscopic aspect is different from SBOT)
 - « Preferred » in case of micropapillary SBOT (this pattern could be diagnosed « only » at the time of permanent histologic examination)

Ultra-conservative fertility-sparing strategy for bilateral borderline ovarian tumours: an 11-year follow-up

Stefano Palomba ^{1,*}, Angela Falbo ¹, Serena Del Negro ¹, Morena Rocca ¹, Tiziana Russo ², Francesco Cariatì ¹, Gianluca Annunziata ¹, Achille Tolino ³, Pierosandro Tagliaferri ⁴, and Fulvio Zullo ²

Table III Oncological outcomes in patients with bilateral BOTs treated with bilateral cystectomy (experimental group) or with unilateral oophorectomy plus contralateral cystectomy (control group).

	Experimental group (<i>n</i> = 15)	Control group (<i>n</i> = 17)	<i>P</i>
Patients with recurrence (<i>n</i> , %)*	10 (66.7)	10 (58.8)	0.73
Multiple recurrence rate (<i>n</i> , %) [†]	3 (23.1)	0 (0.0)	0.09
Time to first recurrence (months) [‡]	16.2 (12, IQR; 3–36, range)	48 (7, IQR; 18–72, range)	<0.01
Age at first recurrence (years) [‡]	27 (7, IQR; 23–34, range)	32 (6, IQR; 23–34, range)	0.62
Age of patients who received radical surgery (years) [‡]	28.1 (4.5 IQR; 25–37 range)	37 (3 IQR; 28–38 range)	0.11
Radical treatment of recurrences (<i>n</i> , %)*	9 (60.0)	3 (17.6)	0.01

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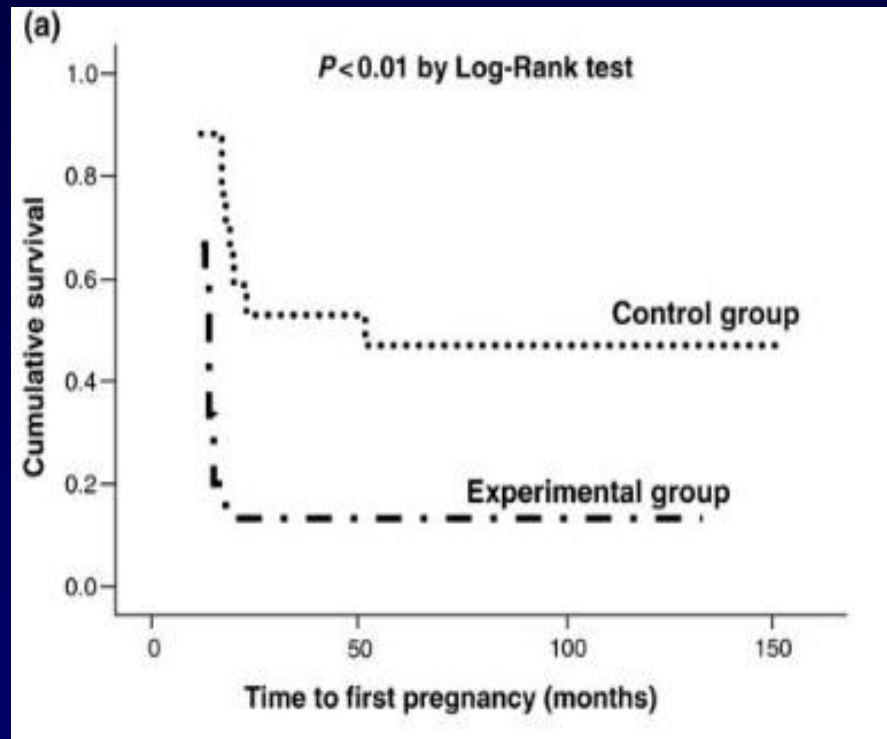
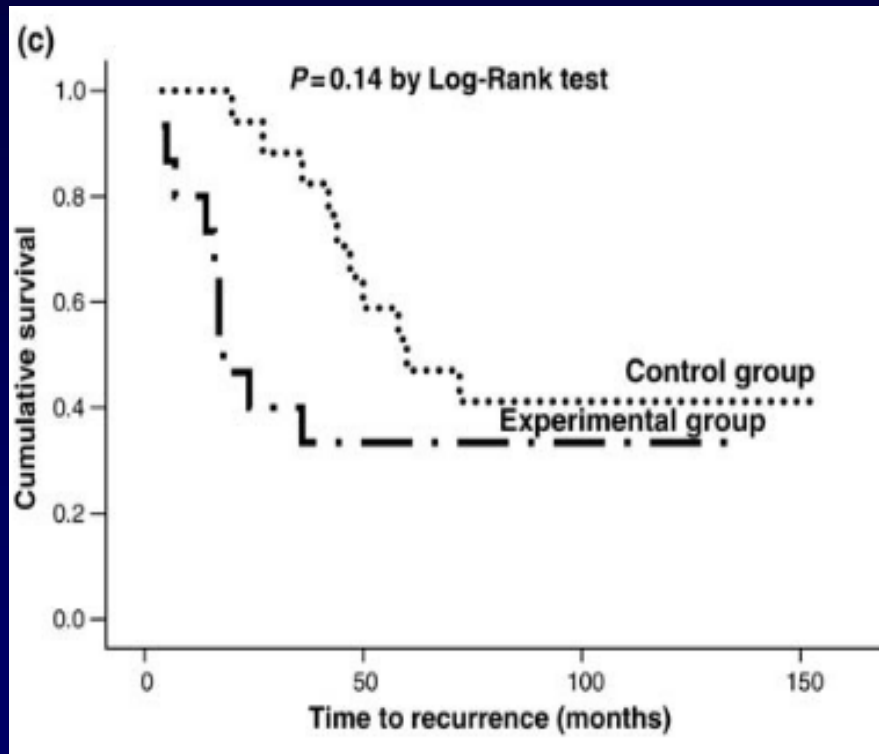
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Table II Reproductive outcomes in patients with bilateral BOTs treated with bilateral cystectomy (experimental group) or with unilateral oophorectomy plus contralateral cystectomy (control group).

	Experimental group (n = 15)	Control group (n = 17)	P
Total number of pregnancies (n)	21	21	
Patients with pregnancy (n, %)*	14 (93.3)	10 (58.8)	0.04
Distribution of pregnancy (n, %)*			
One pregnancy	5 (33.3)	2 (11.8)	0.13
Two pregnancies	5 (33.3)	5 (29.4)	
Three pregnancies	4 (26.7)	3 (17.6)	
Multiple births (n, %) ^o	2 (13.3)	3 (17.6)	0.77
Age at first conception (years) [†]	25 (6 IQR; 21–34 range)	27.5 (7 IQR; 22–31 range)	0.48
Time to conceive (months) [†]	5 (3 IQR; 3–21 range)	8.5 (5 IQR; 3–43 range)	0.01
Patients with a baby-in-arm (n, %) [‡]	13 (86.7)	9 (52.9)	0.06
Time to have a baby-in-arm (months) [†]	14 (3 IQR; 12–18 range)	18 (7 IQR; 12–52 range)	0.02

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- **Bilateral cystectomy preferred (if technically feasible)**

Specific Management of SBOT With Peritoneal Implants

Histologic Subtype Of Implants (Serous Tumors) Series With >50 Patients

	n	Died, noninvasive implants	Died, invasive implants
Bell 1988	56	3/50	5/6
Seidman 1996	65	1/52	6/13
Gershenson 1998	112	6/73	6/39
I.G.R. 2008	168	3/138	2/21
Longacre 2005	113	2/85	5/14
TOTAL	514	15/398 (3.7%)	24/83 (29%)

Conservative Treatment In Stage II/III Serous Bot

	n, recurrence	n, death
Zanetta et al 2001 n = 25	10 (on ovary/perit or nodes)	0
Uzan & Morice n = 41	22 (11 on ovary/11 peritoneum)	1 (noninv impl)
Prat & De Nictolis n = 10	3 (2 on ovary/1 peritoneum)	1 (inv impl)
Longacre et al 2005 n = 21	5 (on ovary)	0
Park et al 2009 n = 3	1 (on ovary)	0

- High rate of recurrence
- Location of the recurrence: peritoneum
- No (or little?) impact on the survival

Fertility Results and Management Of Infertility

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Fertility results

Patients wishing a pregnancy (n) Patients pregnant (n) Pregnancy rate (%)

54 (38–70)

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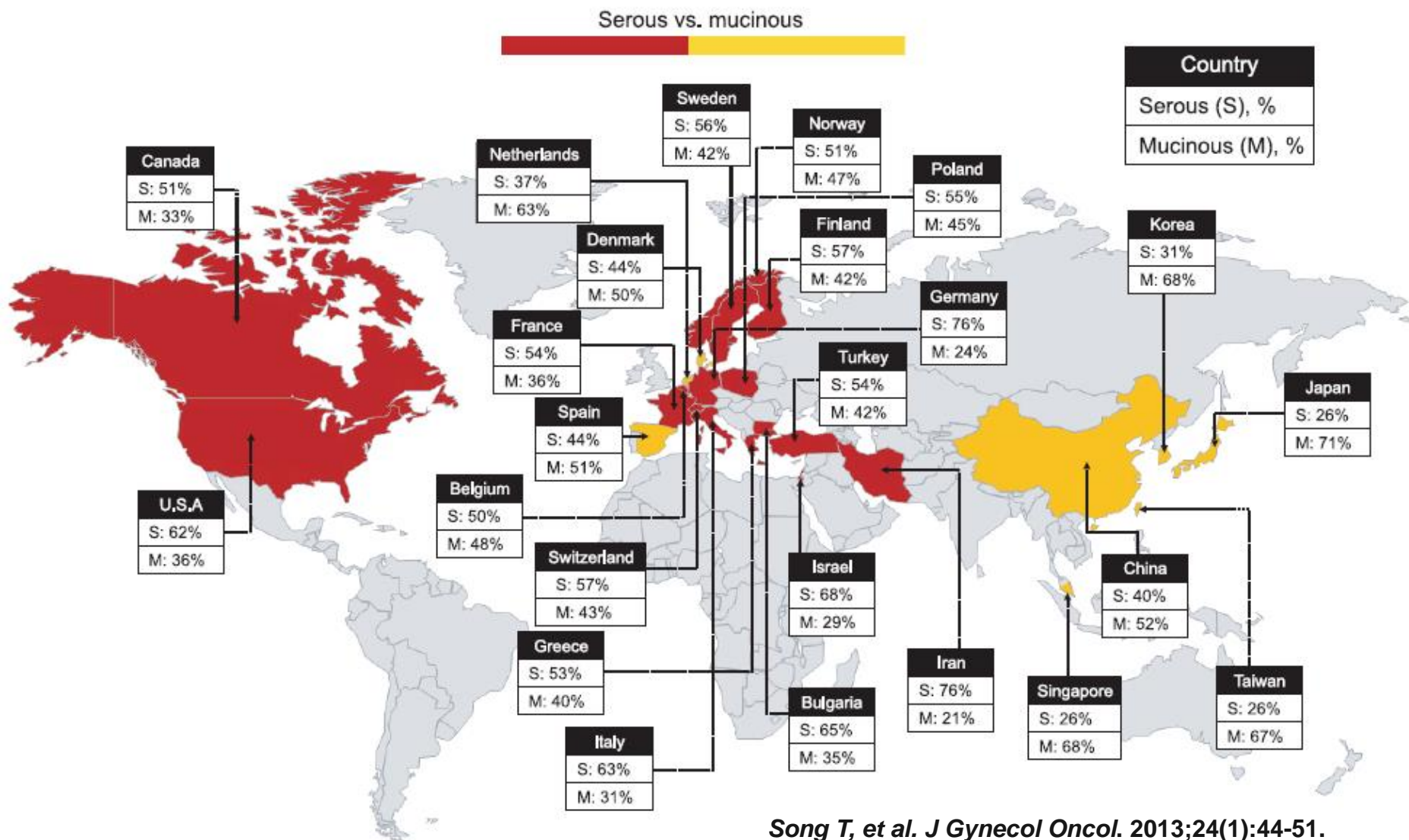
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Pooled estimate for proportion (%) (with 95% CI)								
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Romagnolo <i>et al.</i> (2006)	53*	—	—	—	1	12	7	58
Yinon <i>et al.</i> (2007)	62*	38	24	—	0	—	25	40
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Pooled estimate for proportion (%) (with 95% CI)								
					13 (10–16)			54 (38–70)
					0.5 (0–1)			54 (38–70)

Histologic distribution of borderline ovarian tumors worldwide: a systematic review

Taejong Song¹, Yoo-Young Lee², Chel Hun Choi², Tae-Joong Kim², Jeong-Won Lee², Duk-Soo Bae², Byoung-Gie Kim²

¹Department of Obstetrics and Gynecology, CHA Gangnam Medical Center, CHA University, Seoul; ²Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea



Epidemiologic Characteristics: BOTs vs Serous Ovarian Tumors

	TFO séreuses <i>n</i> = 224	TFO mucineuses <i>n</i> = 164	<i>p</i>
Âge (ans ± DS)	46,9 (± 16,7)	44,6 (± 17,6)	NS
IMC (kg/m ² ± DS)	26,7 (± 6,1)	24,9 (± 5,2)	NS
Gestité (± DS)	1,7 (± 1,7)	2 (± 2)	NS
Nulliparité	36 %	39 %	NS
Parité (± DS)	1,2 (± 1,4)	1,5 (± 1,8)	NS
Antécédent d'infertilité	17,2 %	3,9 %	< 0,0001
Ménopause	37,7 %	33,5 %	NS
Antécédent d'appendicectomie	32,3 %	21,8 %	0,04
Antécédent de chirurgie ovarienne	11,2 %	13,5 %	NS
Antécédent personnel de cancer	7,7 %	5,5 %	NS
Antécédent familial de cancer	19 %	15,8 %	NS
TFO symptomatiques au diagnostic	47,7 %	66,5 %	< 0,001
Taille tumorale (cm ± DS)	9,1 (± 5,1)	14,5 (± 7,7)	0,0001
Unilatéralité	73,6 %	95,7 %	0,0001
Bilatéralité	26,4 %	4,3 %	
Stade FIGO final			<0,0001
Stade I	81,3 %	95,1 %	
> Stade I	18,8 %	4,9 %	
Période d'étude			NS
1990-1999	58,3 % (127/218)	41,7 % (91/218)	
2000-2009	57,1 % (97/170)	42,9 % (73/170)	

Fertility outcome after conservative surgery for borderline ovarian tumors: a single center experience

Mine Kanat-Pektas • Mustafa Ozat •

Tayfun Gungor • Türkan Dikici • Bulent Yilmaz •

Leyla Mollamahmutoglu

	Able to conceive (<i>n</i> = 23)	Unable to conceive (<i>n</i> = 21)	<i>p</i>
Age (years)	36.8 ± 6.0	45.8 ± 2.2	0.001*
Marital duration (years)	12.6 ± 7.1	20.0 ± 4.6	0.001*
Nulliparity	5 (21.7%)	4 (19.1%)	0.466
Previous history of infertility	1 (4.3%)	3 (14.3%)	0.039*
Serum CA-125 level (mIU/ml)	63.79 ± 15.21	57.66 ± 15.81	0.179
Tumor size (cm)	8.3 ± 3.4	7.7 ± 3.2	0.559
Tumor histology			
Serous	3 (13.0%)	16 (76.2%)	0.001*
Non-serous	20 (87.0%)	5 (13.8%)	0.001*
Tumor stage			
Unstaged	9 (39.1%)	8 (38.1%)	0.944
Staged	14 (60.9%)	13 (61.9%)	0.944
Conservative surgery			
Unilateral cystectomy	12 (52.2%)	0 (0.0%)	0.001*
Other types	11 (47.8%)	21 (100.0%)	0.001*
Overall survival (months)	60.8 ± 26.0	58.2 ± 19.9	0.770
Disease-free survival (months)	61.1 ± 26.2	58.9 ± 19.7	0.748

Fertility a system manag and al

Emile Dar
Sébastien

Zanetta *et al.* (2001)

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Camatte *et al.* (2002)

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Maneo *et al.* (2004)

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Boran *et al.* (2005)

40

Longacre *et al.* (2005)

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32

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Romagnolo *et al.*

58

(2006)

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—

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—

Park *et al.* (2009)

73

Kokawa *et al.* (2009)

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Kanat-Pektas *et al.*

52

(2011)

Koskas *et al.* (2011)

38

Song *et al.* (2011)

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Khunamornpong *et al.*

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(2011)

38 56

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line ovarian tumor: of conservative of recurrence ions

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line ovarian tumor (only series including >50 cases of conservative

Results				Fertility results		
Recurrence oopho- rectomy (n)	Recurrence cystectomy (n)	Invasive recurrence (n)	Death (n)	Patients wishing a pregnancy (n)	Patients pregnant (n)	Pregnancy rate (%)
—	—	5	1	—	—	—
11%	21%	0*	0	29	19	60
3*	8*	3	—	—	—	—
1	3	0	0	25	10	40
—	—	2	0	—	—	—
—	—	0	0	62	31	32
—	—	2	1	—	—	—
7	6	—	1	12	7	58
11	5	1	0	—	25	40
2	2	2	1	—	—	—
10	12	0?	0	—	—	—
3	6	1	1	31	27	73
—	—	—	2	—	—	—
1	2	0?	0	44	23	52
3	8	6	3	31	12	38
7	5	1	0	51	45	88
—	—	4	2	—	—	—

0.5 (0–1)

54 (38–70)

Infertility Treatment in Patients With Previous History of BOT

	N, pts	N, IO/IVF	Pregnancy	Recurrence
Hoffman 1999	1 stage II/III	1 IVF	1	0
Nijman 1992	1 stage II/III	1 IVF	1	0
Mantzavinos 1994	2 stage II/III	2 IVF	1	0
Hershkovitz 1998	2 stage II/III	1/1	2 (1 spontan. after IVF)	0
Beiner 2001	7 (2 stage II/III)	0/7	5	2
Fasouliotis 2004	5 (stage I)	0/5	3	2
Fauvet 2005	11 (1 stage II)	6/5	3	?
Madelenat 2007	30 (8 stage II/III)	3/27	13	4
Park 2007	5 (1 stage I)	5 IVF	4/8 cycles	0

French Multicenter Study

30 Patients

- **3 simple ovarian stimulation and 27 IVF**
- **Mean number of cycles: 2.6 (1-10)**
- **Mean time of FU: 93 months (after the TT of the BOT) & 42 months after the ovarian stimulation**
- **20 stage I, 4 stage II, 4 stage III (noninvasive implants) & 2 stage ?**
- **5 patients having IVF « in emergency » with tumor « in place » (recurrent disease on a single ovary - previous history of oophorectomy)**

Ultrasound, Physical Examination, and CA 125 Measurement for the Detection of Recurrence after Conservative Surgery for Early Borderline Ovarian Tumors

Gerardo Zanetta, M.D.,¹ Sonia Rota, M.D., Andrea Lissoni, M.D., Alessandro Meni, M.D., Gaetano (Tano) Brancatelli, M.D., and Alessandro Buda, M.D.

- **164 stage I treated conservatively**
- **Clinical exams + US (transvaginal if feasible) every 3 mths/2 years, and every 6 mths thereafter**
- **Blood markers: CA 125/6 mths for serous BOT**
- **Median time of follow-up 71 months**
- **28 (17%) recurred**
 - **Data on follow-up characteristics in 24**
 - **5 invasive recurrence**
 - **19 borderline recurrence**

How to follow up advanced-stage borderline tumours?

Mode of diagnosis of recurrence in a large series stage II–III serous borderline tumours of the ovary

C. Uzan¹, A. Kane¹, A. Rey², S. Gouy¹, P. Pautier³, C. Lhomme³, P. Duvillard⁴ & P. Morice^{1,5*}

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Table 1. Mode of diagnosis of recurrences

	n (%)
Imaging	19 (42.2)
Systematic ultrasound examination	12 (26.7)
First trimester ultrasound	2 (4.4)
Computed tomography scan	5 (11.1)
Clinical symptoms	8 (17.8)
CA 125 elevation	7 (15.6)
Secondary surgery	5 (11.1)
Unknown	6 (13.3)
Total	45 (100)

CA, cancer antigen.

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Table 2. Mode of diagnosis according to the type of recurrence (this information was available for 39 patients of the 45 with a recurrence)

	Imaging	Clinical examination	Blood test	Other
Invasive recurrence	2	4	6	1
Noninvasive recurrence	16	2	1	4
Unknown	1	2	0	0

Follow-Up in Stage II/III (S)BOT

- Clinical examination
- CA 125
- Imaging:
 - **Abdominopelvic US** (in pts treated conservatively)
 - US or abdominopelvic CT scan and/or MRI in pts treated radically?
 - Depending on the spread of the disease
- At least 3/year during the 3 first years, 2/year between 3 & 5 years, and yearly thereafter
- Length?

Conclusions (BOT)

- Large indication of conservative surgery in stage I
- No completion surgery after childbearing (but long follow-up +++)
- Fertility rates between 30% and 80%
- In advanced stage disease removal of all peritoneal implants is the first goal
- Conservative surgery could be discussed in selected cases of patients with non-invasive peritoneal implants

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