Chirurgie du cancer de l'ovaire : quand ré-intervenir et comment prévenir le risque adhérentiel

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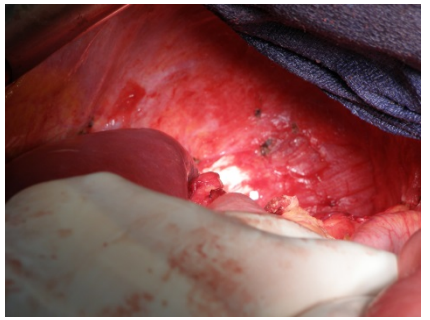
Définition

- Récidive : évolution après une période de rémission complète



- ~~II look~~
- Chirurgie d'intervalle
- Progression
- Urgence / occlusion

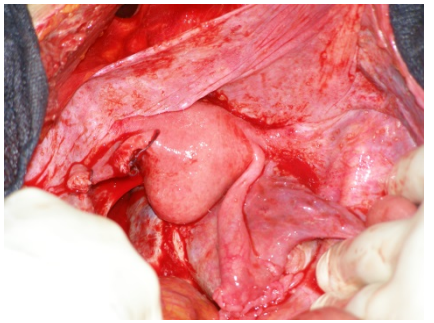


TABLE 2. Intraoperative findings

Peritoneal carcinomatosis, n (%)	
None	62 (48)
Only scattered/localized on peritoneal surface	26 (20)
Diffuse on parietal peritoneum	16 (12)
Diffuse involving visceral peritoneum	24 (19)
Tumor locations—intraoperative findings,* n (%)	
Pelvis	93 (72)
Intra-abdominal above pelvis	81 (63)
Retroperitoneal	44 (34)
Parenchymal organs	35 (27)
Liver	18 (14)
Spleen	16 (12)
Pancreas	3 (2)
Others	2 (2)
Others	3 (2)
No. tumor lesions—intraoperative findings, n (%)	
0	1 (1)
1–3	61 (47)
4–5	14 (11)
>5	53 (41)
Diameter of largest tumor, n (%), cm	
No tumor	1 (1)
<5	75 (58)
5–10	43 (33)
>10	10 (8)

*Multiple options possible.

TABLE 3. Characteristics of surgery

Surgical details, median (range)	
Duration of surgery, min	240 (37–810)
Blood loss, mL	350 (0–8000)
Surgical procedures, n (%)	
Hysterectomy	5 (4)
Ovariectomy	8 (6)
Omentectomy	28 (22)
Lymphadenectomy	
Pelvic	35 (27)
Para-aortic	40 (31)
Other	10 (8)
Peritonectomy	
Pelvis	52 (40)
Paracolic gutters	26 (20)
Diaphragm	28 (22)
Gastrointestinal resection	
Small bowel	19 (15)
Large bowel	39 (30)
Stomach	3 (2)
Anus praeter	
Temporary stoma	10 (8)
Permanent stoma	2 (2)
No. anastomosis	
1	27 (21)
2	14 (11)
4	2 (2)
Splenectomy	16 (12)
(Partial) hepatectomy	11 (9)
(Partial) pancreatectomy	3 (2)
Nephrectomy	1 (1)
(Partial) bladder resection	3 (2)
(Partial) ureter resection	10 (8)
Pleurectomy	2 (2)
Hepatoduodenal ligament/omentum minus	7 (5)
Cholecystectomy	5 (4)
Surgical results, n (%)	
Residual tumor after surgery for recurrence, mm	
0	98 (76)
1–10	13 (10)
>10	18 (14)
Residual lesions	
1–3	7 (5)
4–5	3 (2)
>5	15 (12)
Peritoneal carcinomatosis	21 (16)

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Harter P et al. 2006

TABLE 4. Postoperative characteristics and morbidity

	No. Patients	%
Postoperative at intensive care unit	67	52
Days in the intensive care unit, median (range)	2 (1–20)	
Patients administered packed blood cells	55	44
Patients with at least 1 complication	42	33
Infections requiring antibiotic treatment	31	24
Urinary tract	14	11
Peritonitis	10	8
Pneumonia	4	3
Others	7	5
Second laparotomy	14	11
Bowel leakage/perforation	6	5
Abscess/infection	3	2
Bleeding	3	2
Fistula	2	2
Thrombosis	3	2
Embolism	4	3
Other severe complications*	10	8
Mortality within 60 d	1	0.8

*Secondary wound healing (n = 3), fistula (n = 3), prolonged subileus (n = 2), atrial fibrillation (n = 1), and pneumothorax (n = 1).

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Prédicteurs de survie

Table 3. Prognostic factors for survival after cytoreductive surgery for recurrent ovarian cancer

Prognostic factor	Eisenkop [24]	Gronlund [26]	Harter [28]	Jaenicke [29]	Leitao [31]	Onda [35]	Scarabelli [37]	Tay [38]	Zang [40]	Zang [41]
Patients	106	38	267	30	26	44	149	46	60	117
Patient characteristics										
Age	NS	NS	NS	–	NS	NS	NS	–	–	NS
Performance status	NS	NS	NS	–	–	NS	–	–		0.004
Tumour characteristics										
Initial FIGO-stage	–	NS	NS	–	–	NS	NS	NS	NS	NS
Histologic subtype	–	NS	–	–	–	NS	NS	–	NS	NS
Treatment history/course										
Residual after first surgery	–	NS	NS	–	NS	NS	NS	–	NS	NS
TFI/DFI	0.005	NS (0.05)*	NS	NS	0.047	0.03	<0.01	0.01	0.01	NS
No prior salvage chemotherapy	0.001	–	–	–	–	NS	<0.01	–	NS	–
Characteristics of recurrence										
Disease localisation	NS	–	NS	–	–	NS	–	–	–	–
No. of disease sites	–	(0.03)*	–	–	NS	<0.001	–	–	–	0.002
Diameter of tumour lesion	0.04	NS	–	–	–	<0.001	–	–	NS	–
Ascites	–	–	0.004	–	–	NS	–	–	0.02	–
Characteristics of treatment										
Surgical outcome	0.007	0.02 (NS)*	<0.001	0.007	0.01	–	<0.01	0.01	0.004	0.03
Platinum containing chemotherapy after surgery	–	–	0.015	–	–	–	–	–	–	–
No. of chemotherapy cycles after surgery	–	–	–	NS	–	–	–	–	NS	0.0001

P value as reported in the published material; TFI, treatment-free-interval; DFI, disease-free-interval; NS, not significant; * in brackets, when no. of disease sites was included in multivariate analysis, which correlates with residual disease.

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Du Bois A et al. 2006

Prédicteurs de survie

Table 2 Independent prognostic factors for survival after cytoreductive surgery for recurrent ovarian cancer

Factor	Author (no. of pts)	Eisenkop 2000 (106)	Scarabelli 2001 (149)	Zang 2004 (117)	Harter 2006 (267)	Chi 2006 (157)	Oksefjell 2009 (217)	Tian 2010 (123)	Sehouli 2010 (240)
Age		-	-	-	-	-	+		-
Performance status		-		+					
Initial FIGO-stage			-	-	-	-	-	-	-*
Histo subtype			-	-		-	-	-	
Residuals 1st surgery/SLO			-	-	-	-	-	-	
TFI/PFI		+	-	-	-	+	+	-	-
No prior salvage chx		+	+						
Localization		-			-	-			-
No. of disease sites				-		+	(+)	-	
Diameter		+				-		-	
Ascites					+	-		-	+
Surgical outcome		+	+	+	+	+	+	+	+

*Only FIGO IV vs. II $p<0.05$. *SLO* Second-look-Operation, *TFI* Treatment-free-interval, *PFI* Progression-free-interval, *Chx* Chemotherapy

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Harter P et al. 2012

Prédicteurs de survie

- Analyse multivariée :

- Intervalle libre sans platine
- Récidive unique *vs.* multiple
- Reliquat post-opératoire

Chi D et al. 2006

Prédicteurs de survie

Table 2
Simple linear regression analyses of predictor variables versus median cohort survival time

Predictor variable	Weighted mean	Range	Increment	Change in median survival	95% confidence interval	*p*-value	Missing data[a] (%)
Year of publication	NA	1983 to 2007	(+) 1 year	1.12	0.43 to 1.82	0.002	0.0
Accrual interval	111.7 months	32 to 228 months	(+) 1 month	0.03	(−)0.05 to 0.10	0.51	3.7
Median age	55.6 years	46 to 64 years	(+) 1 year	0.19	(−)0.85 to 1.24	0.71	0.0
Median disease-free interval	20.2 months	6 to 48.2 months	(+) 1 year	0.35	(−)0.33 to 1.03	0.31	40.1
Localized disease	35.1%	0 to 100%	(+) 10%	0.57	(−)1.63 to 2.78	0.609	31.5
Ascites	15.6%	0 to 50%	(+) 10%	(−)4.33	(−)9.13 to 0.47	0.089	34.9
Serous histology	58.2%	39.5 to 100%	(+) 10%	3.02	(−)0.52 to 6.58	0.09	38.1
Grade 3 tumor	61.3%	0 to 100%	(+) 10%	1.54	(−)1.51 to 4.59	0.32	36.7
Surgery before chemotherapy	71.5%	0 to 100%	(+) 10%	(−)0.38	(−)23.67 to 22.91	0.974	37.9
Bowel resection	40.5%	0 to 80%	(+) 10%	(−)1.77	(−)2.90 to 0.51	0.129	17.4
Optimal cytoreduction	70.3%	22.2 to 100%	(+) 10%	2.69	0.90 to 4.49	0.004	0.0
Complete cytoreduction	52.2%	9.4 to 100%	(+) 10%	2.84	1.29 to 4.38	0.0008	15.8

[a] Proportion of total subjects.

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Bristow R et al. 2009

Impact de la maladie résiduelle sur la survie

Table 2. Surgical end point in relation to survival

Study [reference]	Surgical end point (cm)	Patients (%)	Median survival (months)	*P* value
Cormio [23]	0	15 (71)	32	0.02
	>0	6 (29)	9	
Eisenkop [24]	0	87 (82)	44.4	0.007
	>0	19 (18)	19.3	
Gadducci [25]	0	17 (57)	37	0.04
	>0	13 (43)	19	
Gronlund [26]	0	16 (42)	41.8	0.02
	>0	22 (58)	19.9	
Güngör [27]	0	34 (77)	19	0.007
	>0	10 (23)	9	
Harter [28]	0	133 (50)	45.3	0.0001
	>0	134 (50)	19	
Jaenicke [29]	0	14 (47)	29	0.004
	>0	16 (53)	9	
Leitao [31]	≤0.5	19 (73)	36.3	<0.0001
	>0.5	7 (27)	10.6	
Loehr [32]	0	30 (58)	NYR	0.0004
	>0	22 (42)	17	
Morris [33]	≤2	17 (57)	18	0.2
	>2	13 (43)	13.3	
Munkarah [34]	≤2	18 (72)	56.9	0.08
	>2	7 (28)	25.1	
Onda [35]	0	26 (59)	52	0.0019
	>0	18 (41)	22	
Scarabelli [37]	0	53 (36)	NA	<0.01
	≤1	51 (34)		
	>1	45 (30)		
Tay [38]	0	19 (41)	38	0.002
	>0	27 (59)	11	
Vaccarello [39]	≤0.5	14 (37)	75% (after 41 months)	NA
	>0.5	24 (63)	23	
Zang [40]	≤1	23 (38)	18	0.021
	>1	37 (62)	13	
Zang [41]	0	11 (9)	NYR	<0.0001
	≤1	61 (52)	26	
	>1	45 (38)	14.5	

NA, data not available; NYR, not yet reached.

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Résidu tumoral

Table 1
Study characteristics

Author	Reference	Year publication	Accrual interval (months)	*N* (total)	Age (median)	Median overall survival (months)	Disease-free interval (months)	Optimal criteria (cm)	Optimal cytoreduction (%)	Complete cytoreduction (%)
Berek et al. [a]	[8]	1983	60	32	54.5	10	6	<1.5	37.5	NA
Morris et al. [a]	[12]	1989	96	30	50	16.3	36	<2.0	56.7	30.0
Janicke et al. [a]	[13]	1992	NA	30	53	18	16	<2.0	86.7	46.7
Segna et al. [a]	[14]	1993	144	100	55	16.6	NA	<2.0	61.0	NA
Eisenkop et al. [b]	[15]	1995	54	36	60.6	43	22	≤1.0	91.7	83.3
Vaccarello et al. [a]	[16]	1995	120	57	57	18	20	<0.5	36.8	17.5
Lichtenegger et al. [a]	[17]	1998	73	81	58	23	NA	No gross	22.2	22.2
Landoni et al. [a]	[18]	1998	156	38	51 [c] (mean)	29	22	No gross	100.0	100.0
Cormio et al. [a]	[19]	1999	84	21	58	29	25	<2.0	90.5	71.4
Gadducci et al. [a]	[20]	2000	112	30	58.5	21	17.5	<2.0	83.3	56.7
Zang et al. [a]	[21]	2000	144	60	50	11	12	≤1.0	38.3	NA
Chen et al. [a]	[22]	2000	142	22	56.5	41	26	<1.0	86.4	63.6
Eisenkop et al. [b]	[23]	2000	108	106	60.5	35.9	16.8	No gross	82.1	82.1
Tay et al. [a]	[24]	2002	99	46	50.3	22.5	26	≤1.0	71.7	41.3
Bristow et al. [a]	[25]	2002	96	21	46	56.2	15.7	≤1.0	71.4	61.9**
Yoon et al. [b]	[26]	2003	163	24	47.5	62	36.5	≤1.0	100.0	87.5
Zang et al. [a]	[27]	2003	144	60	52	17	NA	≤1.0	38.3	NA
Meredith et al. [a]	[28]	2003	288	26	62	26.3	23.4	≤1.0	80.8	69.2
Look et al. [a]	[29]	2003	161	24	54	45.8	NA	<2.5	87.5	20.8
Loizzi et al. [d]	[30]	2003	105	31	57	38	34	<2.0	90.3	NA
Leitao et al. [a]	[31]	2004	156	26	55.5	33.4	13.4	≤0.5	73.1	53.8
Zang et al. [b]	[32]	2004	48	117	53	22	15.4	≤1.0	61.5	9.4
Zanon et al. [b]	[33]	2004	69	30	60	28.1	NA	≤0.25	76.7	NA
Uzan et al. [a]	[34]	2004	221	12	51	50	21	No gross	100.0	100.0
Gronlund et al. [b]	[35]	2005	73	38	59 [c]	27.4 [e]	16.3	No gross	42.1	42.1
Gungor et al. [a]	[36]	2005	120	44	54.3	16	27.1	<1.0	77.3	NA
Yap et al. [a]	[37]	2005	106	22	57.4	26	48.2	<0.5	100.0	NA
Onda et al. [b]	[38]	2005	165	44	52	32	18.5	<1.0	84.1	59.1
Ayhan et al. [a]	[39]	2006	144	64	50.6	18.6	15.5	≤1.0	82.8	43.8
Matsumoto et al. [a]	[40]	2006	192	23	55.7	41.7	22.5	<2.0	43.4	30.4
Manci et al. [a]	[41]	2006	120	24	54	56	26	≤0.5	100.0	66.7
Chi et al. [a]	[42]	2006	180	153	56.5	41.7	NA	≤0.5	51.6	40.5
Harter et al. [b]	[43]	2006	48	267	60	29.2	NA	≤1.0	75.7	49.8
Rufian et al. [b]	[44]	2006	96	14	55	57	NA	≤1.0	85.0	52.0
Helm et al. [a]	[45]	2007	32	18	64	31	24.6	≤0.5	94.4	61.1
Salani et al. [a]	[46]	2007	91	55	57.7	48	26	≤1.0	89.1	74.5
Santillan et al. [a]	[47]	2007	92	25	59	37	16	≤1.0	100.0	96.0
Benedetti Panici et al. [b]	[48]	2007	126	40	51	60 [c]	14	No gross	72.5	72.5
Benedetti Panici et al. [b]	[49]	2007	60	47	52	49	15	≤1.0	87.2	78.7
Cotte et al. [b]	[50]	2007	180	81	54.3	28.4	NA	≤0.5	80.2	55.6

NA = data not available.
[a] Retrospective review.
[b] Prospective, non-randomized.
[c] Median not yet reached.
[d] Retrospective case-control.
[e] Personal communication.

70% 50%
22-100 9-100

Bristow R et al. 2009

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Prédicteurs de résection complète

- Eisenkop S.
  - Absence de chimiothérapie pré-op, PS 0, taille de récidive <10cm.
- Gronlund B.
  - Récidive Unique *vs.* multiple.
- Zang R.
  - Maladie résiduelle initiale, absence d'ascite.
- DESKTOP I.
  - Maladie résiduelle initiale, PS 0, ascite < 500cc.

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Eisenkop S et al. 2000, Gronlung B et al. 2005
Zang R et al. 2004, Harter P et al. 2006

DESKTOP – OVAR 1. qui bénéficie de la chirurgie secondaire ?

TABLE 3. *Multivariate analysis of prognostic factors for survival*

Parameter	Estimate	Standard error	OR	95% CI	*P* value
Eastern Cooperative Oncology Group (ECOG)	.13	.25	1.15	.70–1.88	.588
Residual disease after primary surgery	.03	.27	.97	.57–1.67	.915
✓ Ascites	.83	.29	2.30	1.31–4.04	.004
Localization of recurrence in preoperative diagnostics in pelvis	.54	.32	1.72	.92–3.20	.090
✓ Residual disease after surgery for recurrence	1.08	.29	2.94	1.68–5.17	< .001
✓ Platinum-based chemotherapy after surgery for recurrence	.61	.25	1.84	1.13–3.01	.015
Treatment-free interval < 6 months vs. 6–12 months	.04	.34	.96	.49–1.86	.897
Treatment-free interval < 6 months vs. > 12 months	.07	.35	.93	.47–1.86	.837

OR odds ratio, *CI* confidence interval.

Harter P & al 2006

DESKTOP – OVAR 1. prédicteurs de résection complète

TABLE 5. *Multivariate analysis of factors for achieving complete resection*

Parameter	Estimate		OR	95% CI	*P* value
Eastern Cooperative Oncology Group (ECOG)	.98	.27	2.65	1.56–4.52	< .001
Residual disease after primary surgery (mm)*	.90	.27	2.46	1.45–4.20	< .001
Ascites	1.63	.48	5.08	1.97–13.16	< .001
Localization of recurrence in preoperative diagnostics	.44	.31	1.55	.85–2.82	.155

OR odds ratio, *CI* confidence interval.

* Alternatively International Federation of Gynecology and Obstetrics (FIGO) stage if residual disease after primary surgery is unknown [hazard ratio (HR) 1.87 (95% CI 1.04–3.37); $P = .036$].

Harter P & al. 2006

DESKTOP – OVAR 1. impact du résidu tumoral

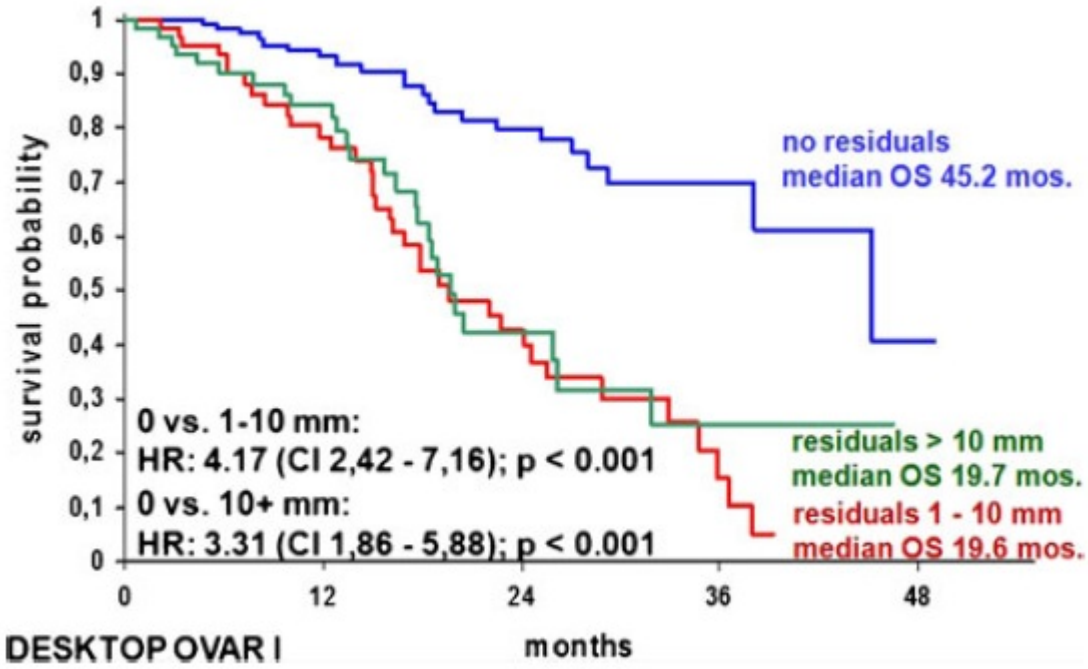


TABLE 3 Derivation of the scoring system for secondary cytoreductive surgery

Factors	β	β/0.34	Scores	Standard error	P value[a]
Stage					
I/II					Reference
III/IV	0.278	0.819	0.8	0.158	.079
Residual disease after primary surgery					
0					Reference
>0 cm	0.527	1.549	1.5	0.149	<.001
PFI					
≥16 months					Reference
<16 months	0.818	2.407	2.4	0.144	<.001
ECOG performance status					
0–1					Reference
2–3	0.803	2.362	2.4	0.220	<.001
CA125 at recurrence (U/ml)					
≤105					Reference
>105	0.616	1.813	1.8	0.141	<.001
Ascites at recurrence					
Absent					Reference
Present	1.025	3.016	3.0	0.200	<.001

By the logistic regression analysis. All variables entered

[a] Determined using six variables

Low risk group (0-4.7)(60.7% patients): 53.4% complete resection
High risk group (4.8-11.9)(39.3%): 20.1% complete resection

Tian W & al. 2012

Table 2 Scoring system for survival in patients with recurrent ovarian cancer undergoing secondary cytoreductive surgery

	Scoring[a]			
Impact factors	**0**	**1**	**2**	**4**
PFI	>23.1		⩽23.1	
Ascites	Absent	Present		
Extent of recurrent disease	Localised	Multiple		
Residual disease after SCR[b]	R0		R1	R2

Abbreviations: PFI = progression-free interval; SCR = secondary cytoreductive surgery. [a]Low-risk: 0–2; high-risk: 3–8. [b]R0 = complete resection of all visible disease; R1 = remaining small volume disease of 0.1–1 cm; R2 = remaining disease >1 cm.

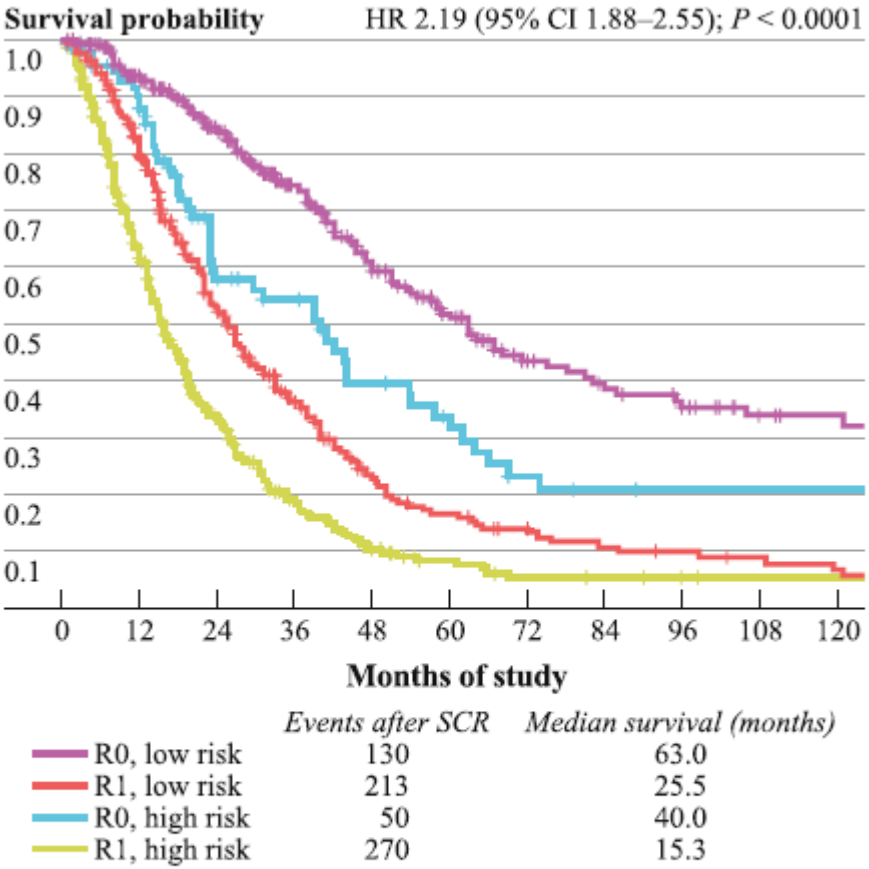
Table 3 Performance of survival risk model in the validation cohorts

Scores	No. (%)	Death (%)	Median survival after SCR (months)[a]	HR (95% CI)[b]	*P*-value[b]
0~2	418 (38.0)	162 (38.8)	63.0	Reference	
3~8	682 (62.0)	523 (76.7)	19.1	3.65 (3.05–4.36)	<0.001
Total	1100	685 (62.3)	28.0		–

Abbreviations: CI = confidence interval; HR = hazard ratio; SCR = secondary cytoreductive surgery. [a]The median survival after SCR was computed using Kaplan–Meier method. [b]The results were computed using Cox Regression analysis.

Low risk group (0-4.7)(60.7% patients): 53.4% complete resection
High risk group (4.8-11.9)(39.3%): 20.1% complete resection

Zang R &al. 2011

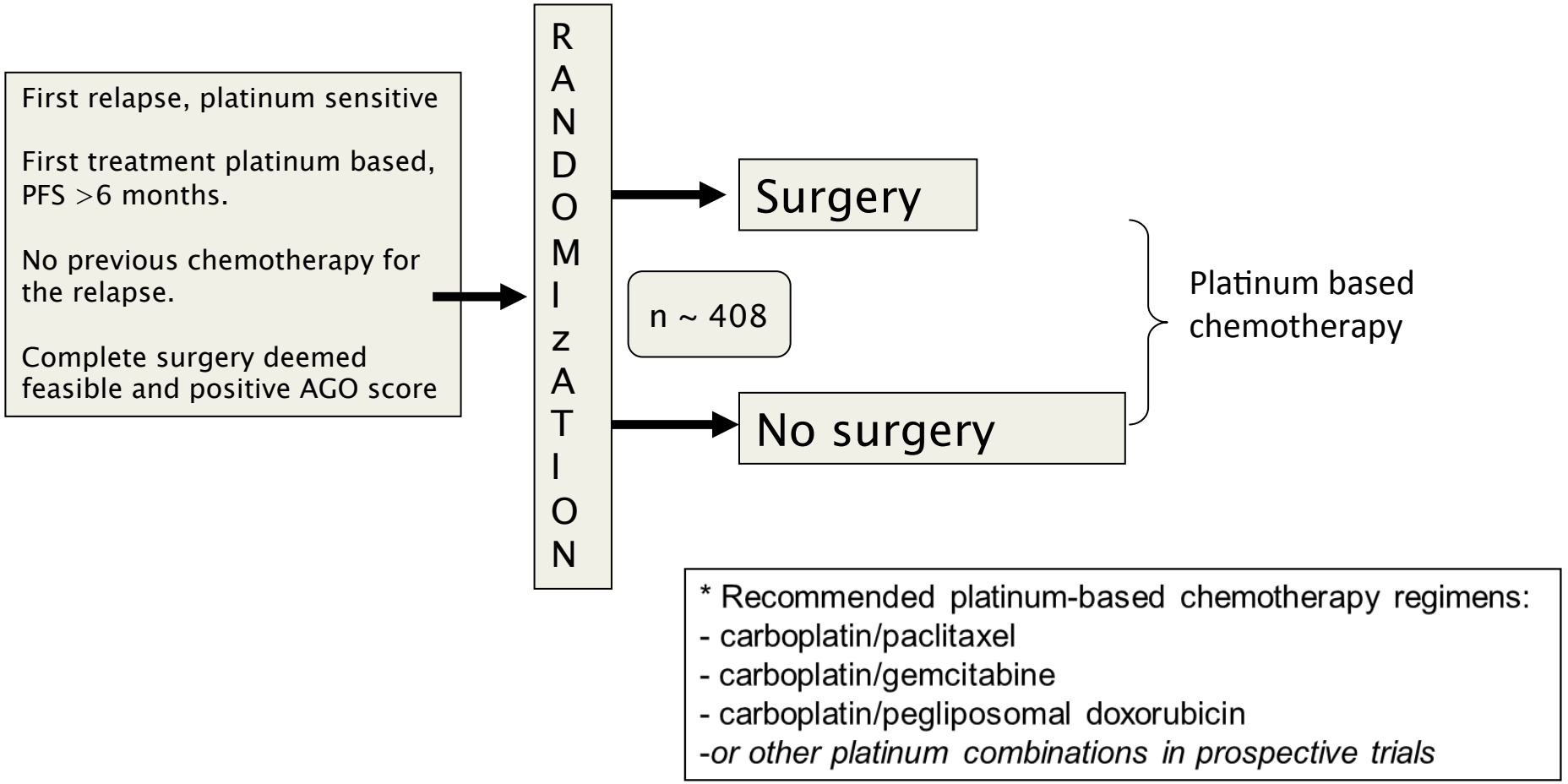


The cutoff point of the risk model is 4.75 with the sensitivity, 1 − specificity, and Youden index (Sen. + Spe. − 1) of 80.4%, 47.4%, and 0.33, respectively. **d** the survival of patients at low-risk and high-risk groups

Tian W & al. 2012

DESKTOP III

Randomized trial assessing the impact of surgery in patients with a first relapse of platinum sensitive ovarian cancer.



Anticiper

- Réduire le risque d'adhérences :
  - Réduire le traumatisme
  - Irrigation
  - Hémostase
  - Produits anti-adhérences

- Qualité de vie
- Morbidité péri-opératoire secondaire

- Complications liées aux adhérences

(adk ovaire) :

  - Douleurs
  - Lymphocèles
  - Occlusion du grêle (15% OIA après KO)
  - Difficultés opératoires lors des reprises/récidives
  - Mauvaise circulation des fluides (chimio IP, CHIP)

- Prospectif, unicentrique, 1 an, 14 patientes.
- “Ovariectomie radicale” pour cancer de l’ovaire. Anastomose digestive mécanique.
- Application de plaques sur le pelvis (tuiles), pas sur la cicatrice médiane (témoin), ni autour de l’anastomose.
- 1 drain pelvien

- Mesure des adhérences lors du II-look dans le pelvis (4 quadrants) vs laparotomie (4/4)

Table 1
Adhesion scoring system

Adhesion grade	Point score	Definition
Grade 0	0	No adhesions
Grade 1	1	Avascular: easily lysed and failing to bleed
Grade 2	3	Vascular: easily lysed, but bleeding at time of lysis
Grade 3	5	Thick: requiring extensive sharp surgical dissection

The adhesion score per quadrant was calculated by estimating the percentage of each quadrant involve in adhesions and multiplying by the grade (e.g. 20% involved by grade 1 adhesions [0.2] plus 40% involved by grade 3 adhesions [2.0] equals a total adhesion score of 2.2).

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- Aucun relicat macroscopique pelvien et 100% de chir optimale (1cm) abdominale.
- Chimio (platine) x6 ou 8.

- Adhérences LM : 92.9%
- Adhérences : 64% des quadrants pelviens
- Pas de complication spécifique
- Pas de fistule / abcès
- Taux de péritoine + RAS

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Table 3
Analysis of mean adhesion scores and the number of quadrants involved with adhesions

	Mean adhesion score	SD	Significance
Seprafilm® pelvis	0.91	1.04	
Abdominal wall (internal control)	5.56	4.55	0.002[a]
Untreated pelvis (historical control[b])	8.70	5.70	0.004[a]

	Quadrants with adhesions	Significance
Seprafilm® pelvis	15/56 (26.8%)	
Abdominal wall (internal control)	36/56 (64.3%)	<0.001[c]
Untreated pelvis (historical control[b])	24/28 (85.7%)	<0.001[c]

SD: standard deviation.
[a] Versus Seprafilm® by Student's *t* test.
[b] Ref. [3].
[c] Versus Seprafilm® by Fisher's Exact Test.

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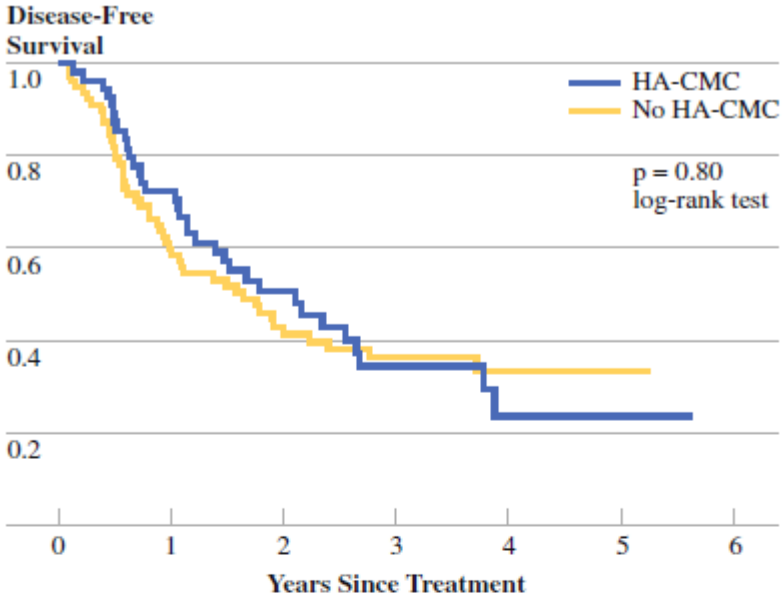

FIG. 1 Disease-free survival in patients with gynecologic malignancies, comparing those receiving ($n = 80$) vs. not receiving ($n = 122$) a sodium hyaluronate–carboxymethylcellulose (HA-CMC) barrier, $P = .80$, log rank test

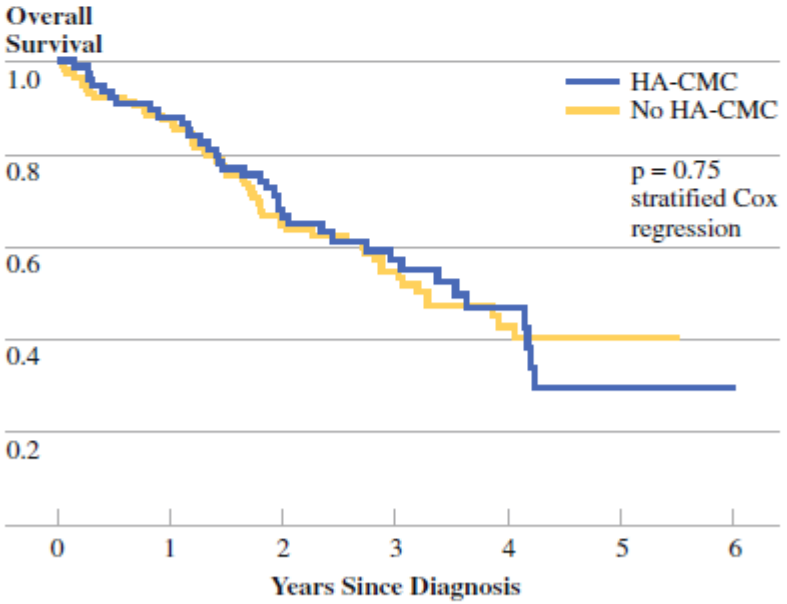

FIG. 2 Overall survival, comparing those receiving ($n = 80$) vs. not receiving ($n = 122$) a sodium hyaluronate–carboxymethylcellulose (HA-CMC) barrier, $P = .75$, stratified Cox regression

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