婦人科がんの手術療法

Cancer Institute Hospital
Hiroyuki Kanao

本日のAgenda

1: 子宮頸がんに対する手術療法

1-a: 早期子宮頸がんに対するMIS (LACC trial)

1-b: 最近のtopics

2: 子宮体がんに対する手術療法

2-a: 早期子宮体がんに対するMIS

2-b: 子宮体がんに対するリンパ節郭清術

3: 卵巣がんに対する手術療法

3-a: 卵巣がんに対するMIS

3-b: PDSとNAC-IDS, SDS卵巣がんに対するリンパ節郭清術

3-c:卵巣がんに対するリンパ節郭清術

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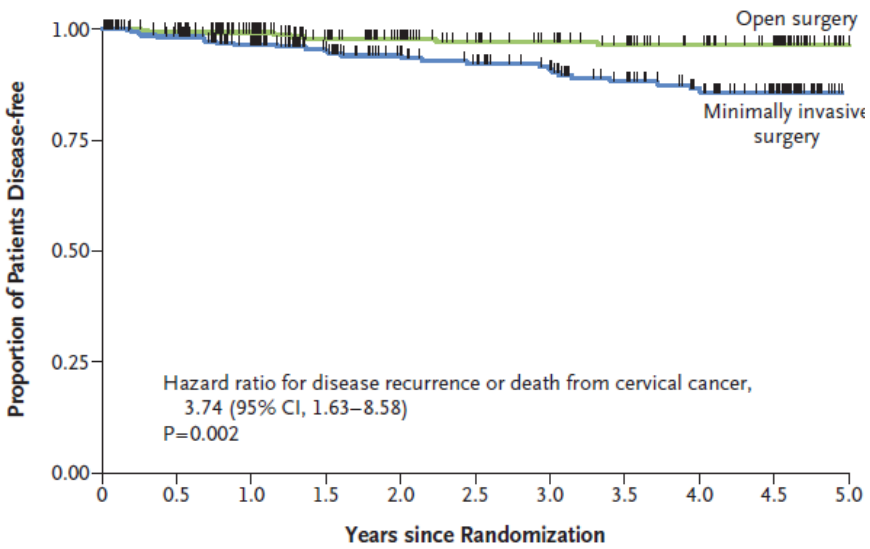
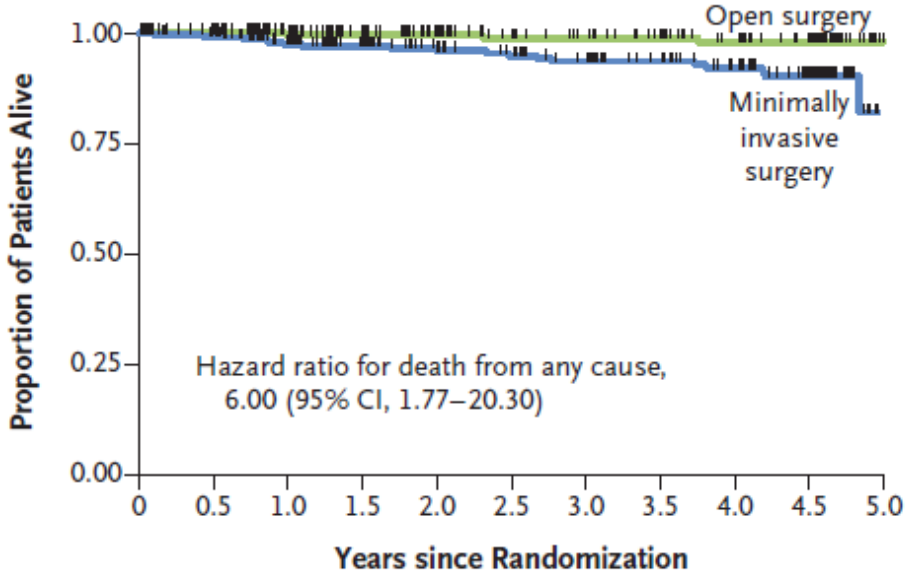
ORIGINAL ARTICLE

Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer





CONCLUSIONS

In this trial, minimally invasive radical hysterectomy was associated with lower rates of disease-free survival and overall survival than open abdominal radical hysterectomy among women with early-stage cervical cancer. (Funded by the University of Texas M.D. Anderson Cancer Center and Medtronic; LACC ClinicalTrials.gov number, NCT00614211.)

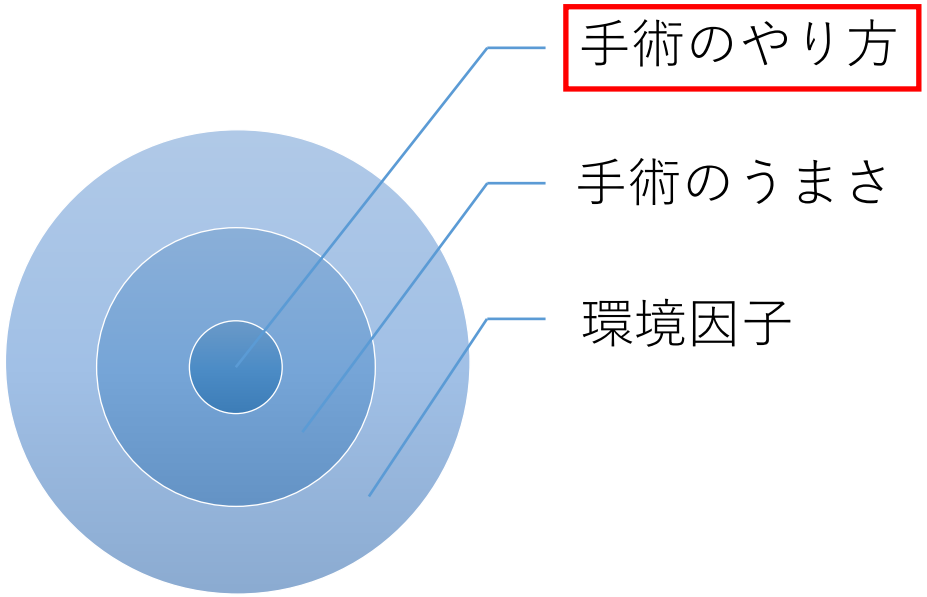
Is “RCT” an absolute truth??

The challenges faced in the design, conduct and analysis of surgical randomized controlled trials

-Cook JA. Trials 2009;10:9

Surgical trials are difficult to successfully undertake and pose particular practical and methodological challenges.

Main constituent elements of a surgical intervention

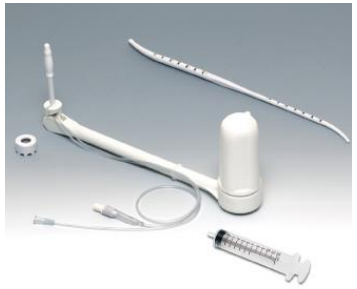


Uterine Manipulator

- The use of uterine manipulator in robotic-assisted radical hysterectomy, did not yield any clinico-pathological differences in depth of invasion, LVSI, or parametrial involvement compared those seen in cases of open surgery.

Rakowski JA, Tran TA, Ahmad S, James JA, Brudie LA, Pernicone PJ, Radi MJ, Holloway RW. Does a uterine manipulator affect cervical cancer pathology or identification of lymphovascular space involvement? Gynecol Oncol. 2012 Oct;127(1):98-101.

- Artifactual displacement of cervical epithelium showing CIN III to fallopian tubes during laparoscopic hysterectomy performed with the use of an intrauterine balloon manipulator has been reported, which means that use of a uterine manipulator poses a theoretical possibility of peritoneal dissemination of cervical cancer.



McFarland M, Craig E, Lioe TF, Dobbs SP, McCluggage WG. Artefactual displacement of cervical epithelium showing CIN III to fallopian tubes during laparoscopic hysterectomy with intrauterine balloon manipulator. Histopathology. 2014 Jul;65(1):139-41.

Recurrence rates in cervical cancer patients treated with abdominal versus minimally invasive radical hysterectomy: A multi-institutional analysis of 700 cases

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Associate Professor, Gynecologic Oncology

University Of Michigan

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

Maybe !

	NED N=476	Recurred N=43	p-value
No Manipulator	28 (100.0%)	0 (0.0%)	0.08
Intrauterine (V-care/ Zumi/ Rumi)	251 (93.0%)	19 (7.0%)	
Vaginal only (EAA sizer/ Colpoprobe)	187 (89.0%)	23 (11.0%)	
Missing	10 (90.9%)	1 (9.1%)	

6.2 INTERVENTION: TLRH or TRRH + LAPAROSCOPIC PELVIC / AORTIC LYMPH NODE DISSECTION (LACC trial protocolより抜粋)

…A tube or a similar device for uterine mobilization is inserted transvaginally, the bladder peritoneum is reflected and the bladder pillars are lateralized over the edge of the tube;…

Colpotomic approach

- On the basis of results of an experimental animal study, Volz et al. suggested that intraperitoneal tumor spread may be connected to inadvertent presentation of cancerous tumor cells to the circulating pneumoperitoneum CO_2 gas and disturbance of the superficial mesothelial layer caused by the high CO_2 pressure; this may provoke cancer cell implantation.

Volz J, Köster S, Spacek Z, Paweletz N. The influence of pneumoperitoneum used in laparoscopic surgery on an intraabdominal tumor growth. Cancer. 1999 Sep 1;86(5):770-4.

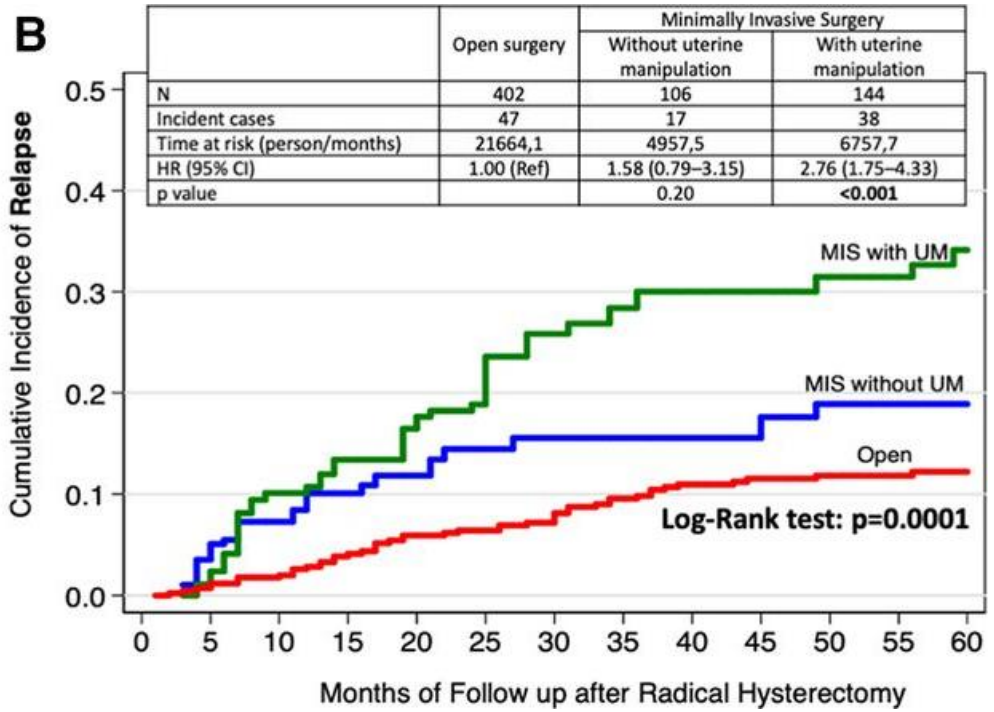
- Kong et al. investigated the pattern of recurrence after open versus laparoscopic/robotic radical hysterectomy in patients with early cervical cancer, and multivariate analysis of factors in the MIS group showed laparoscopic intracorponeal colpotomy under CO_2 pneumoperitoneum to be a strong prognostic factor related to disease recurrence. They concluded that total laparoscopic/robotic intracorponeal colpotomy under CO_2 pneumoperitoneum may pose a risk of a positive vaginal cuff margin and of intraperitoneal tumor spread in patients with early-stage cervical cancer treated by means of laparoscopic/robotic radical hysterectomy.

Kong TW, Chang SJ, Piao X, Paek J, Lee Y, Lee EJ, Chun M, Ryu HS. Patterns of recurrence and survival after abdominal versus laparoscopic/robotic radical hysterectomy in patients with early cervical cancer. J Obstet Gynaecol Res. 2016 Jan;42(1):77-86.

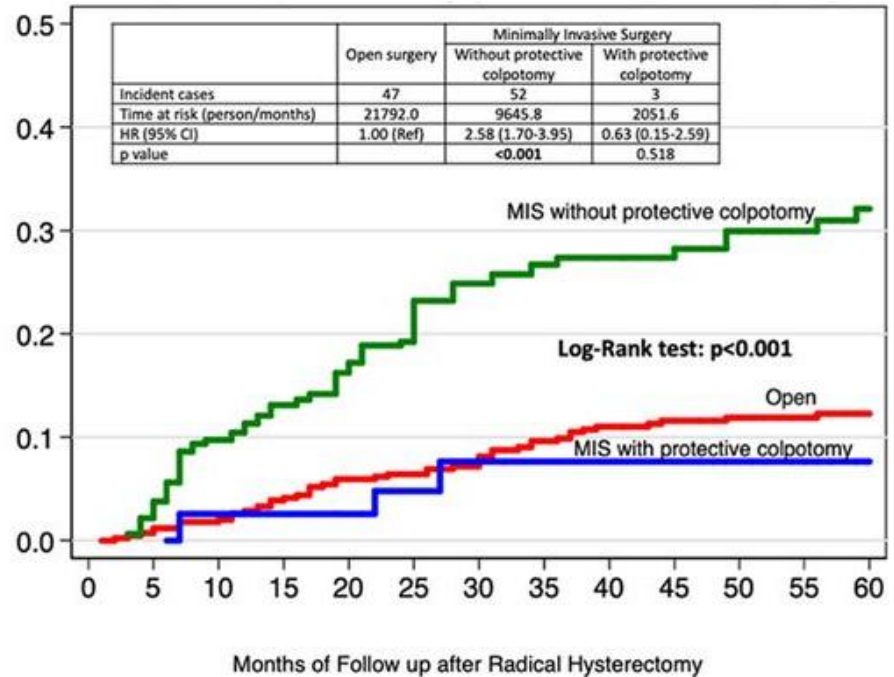
SUCCOR study: an international European cohort observational study comparing minimally invasive surgery versus open abdominal radical hysterectomy in patients with stage IB1 cervical cancer

B

	Open surgery	Minimally Invasive Surgery	
		Without uterine manipulation	With uterine manipulation
N	402	106	144
Incident cases	47	17	38
Time at risk (person/months)	21664,1	4957,5	6757,7
HR (95% CI)	1.00 (Ref)	1.58 (0.79–3.15)	2.76 (1.75–4.33)
p value		0.20	**<0.001**

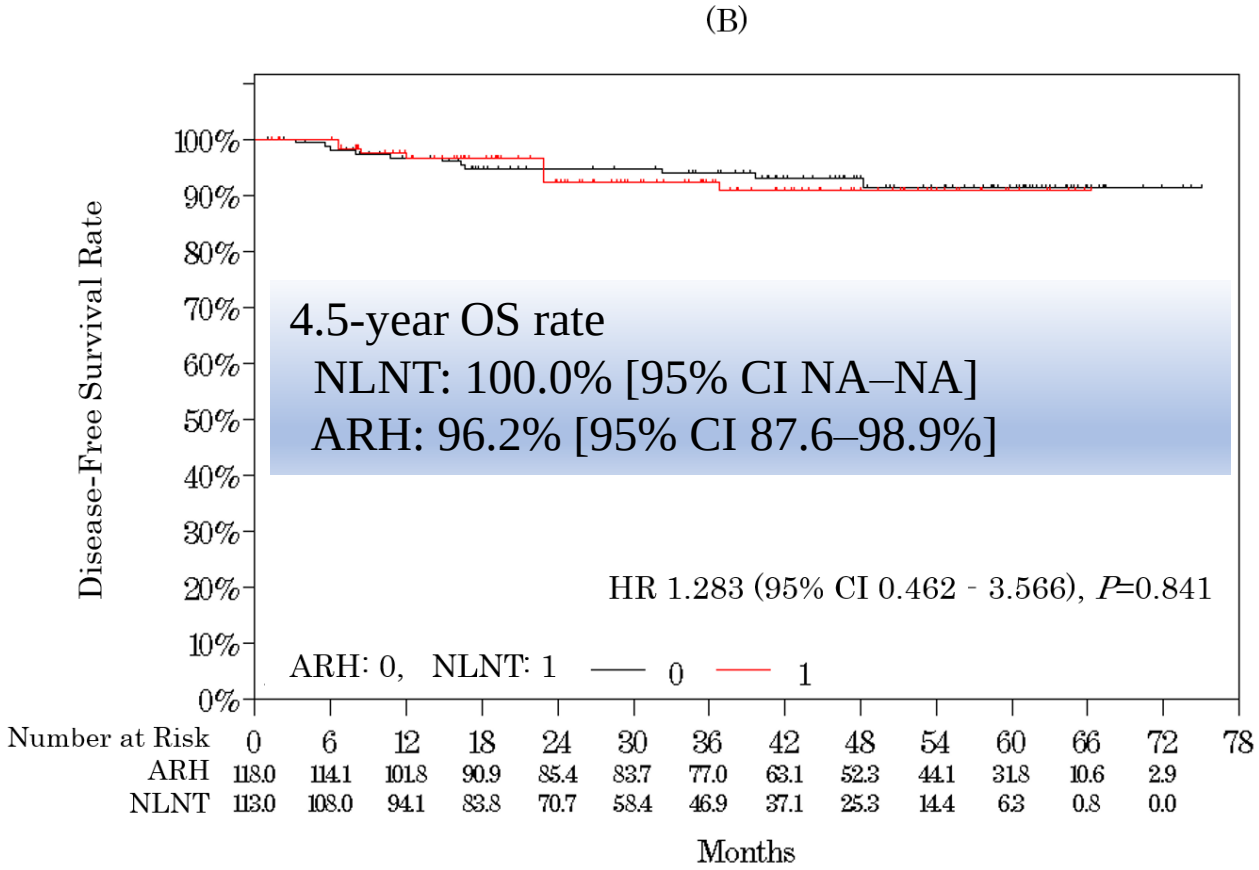


	Open surgery	Minimally Invasive Surgery	
		Without protective colpotomy	With protective colpotomy
Incident cases	47	52	3
Time at risk (person/months)	21792.0	9645.8	2051.6
HR (95% CI)	1.00 (Ref)	2.58 (1.70-3.95)	0.63 (0.15-2.59)
p value		**<0.001**	0.518



当科におけるTLRH (no-look, no-touch technique)

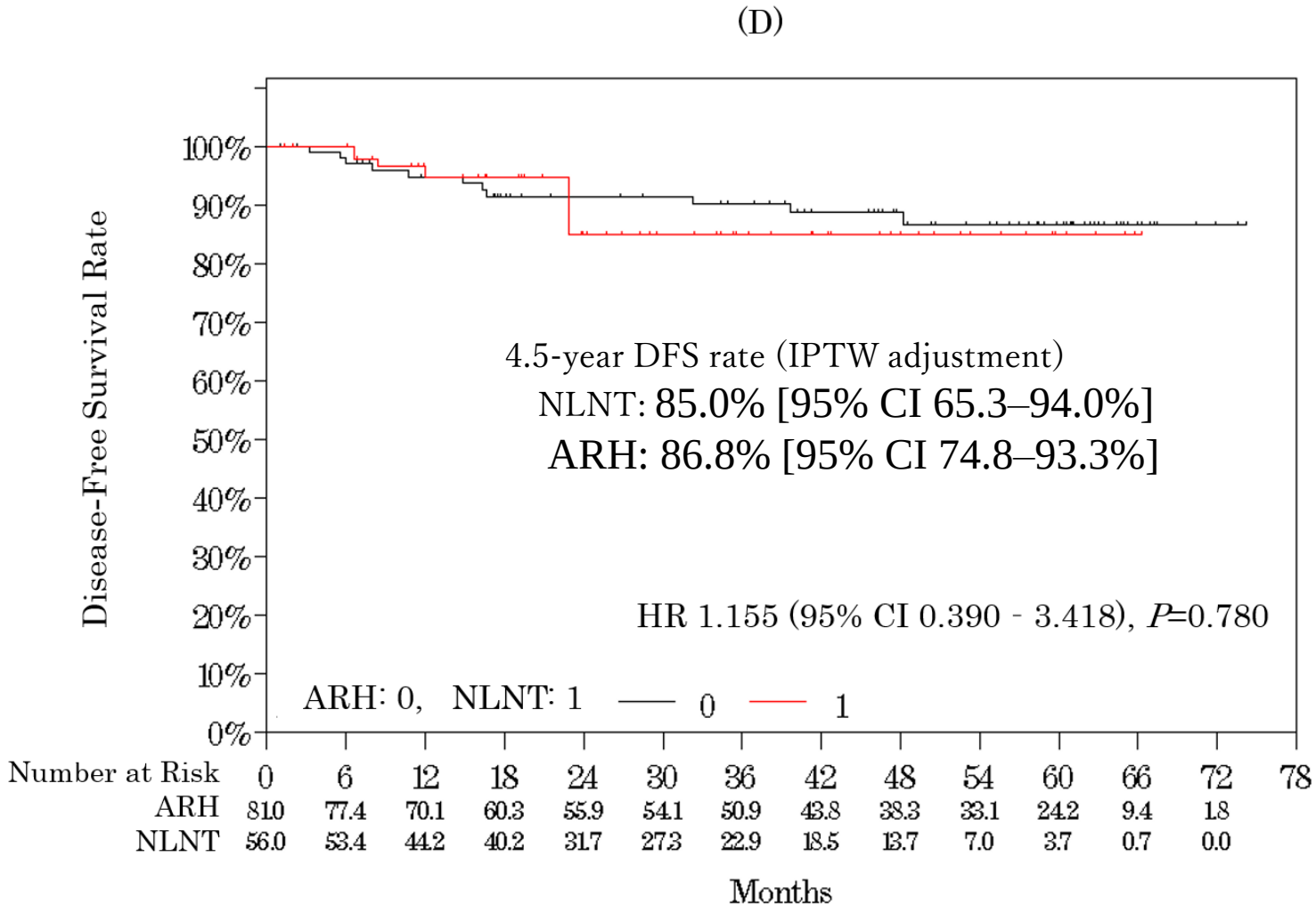
- The **IPTW (**Inverse probability of propensity-score weighting) method to reduce the effect of confounding
- Adjusted by preoperative factors including …
  - ① Age ② BMI ③ Diameter ④ Histology ⑤ preoperative conization and ⑤ Clinical FIGO stage -



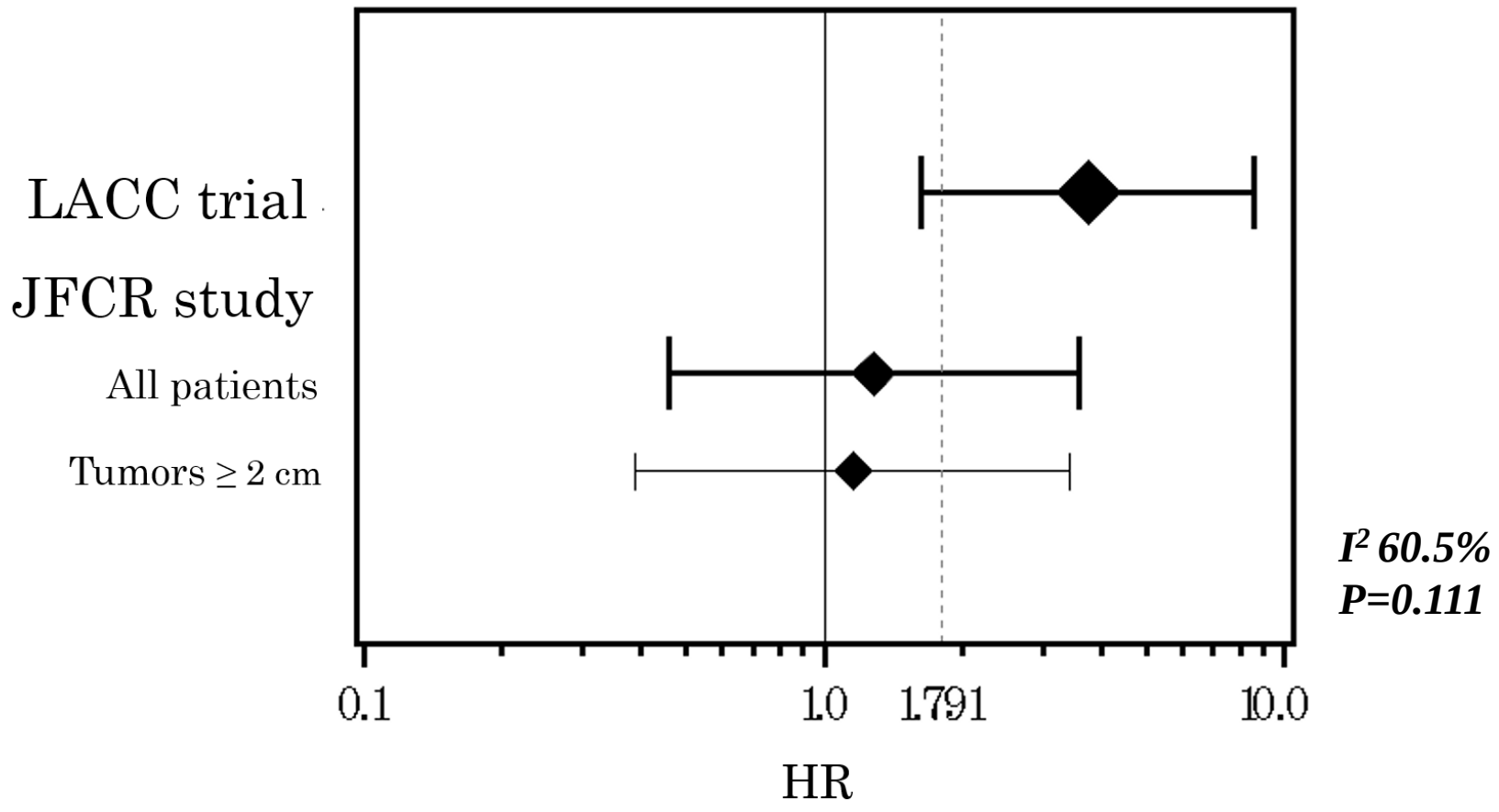
LACC trial

54ヶ月RFS
TLRH 86.0% (95%CI: 79.7-90.4%)
ARH 96.5% (95%CI: 92.7-98.4%)

Uterine cervical cancer ≧2cm (stage 1b1) with no-look no-touch technique



LACC trialとの異質性（heterogeneity）の検討



日本産科婦人科学会の見解

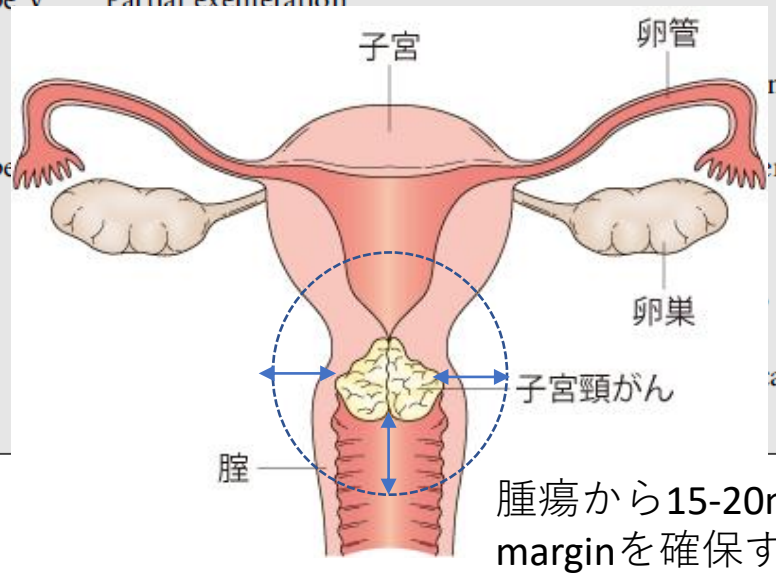
低侵襲手術群の予後が開腹手術群と比較して不良であった理由は明らかになっていませんが、LACC試験における手術手技や研究デザイン上の課題が指摘されていることから、本学会としては、LACC試験の結果をもって、全ての子宮頸癌に対する低侵襲手術群の有効性が完全に否定されたと結論づけることはできない

現在Japanese-TLRHの予後を検証する前向き試験をJGOGで計画中。

Classification of radical hysterectomy

Table 2. Classification of radical hysterectomy adopted by the EORTC-GCG [14]

Type I	Simple hysterectomy
Type II	Modified radical hysterectomy
	Ureters dissected to the point of their entry to the bladder
	Proximal uterosacral ligaments resected
	Medial half of the cardinal ligaments removed
	1–2 cm of upper vagina removed
Type III	Radical hysterectomy
	Removal of as much of the uterosacral ligaments as possible
	Entire width of the parametria is resected
	Upper third of the vagina is removed
Type IV	Extended radical hysterectomy
	As type III but three-quarters of the vagina and paravaginal tissue is removed
Type V	Partial exenteration

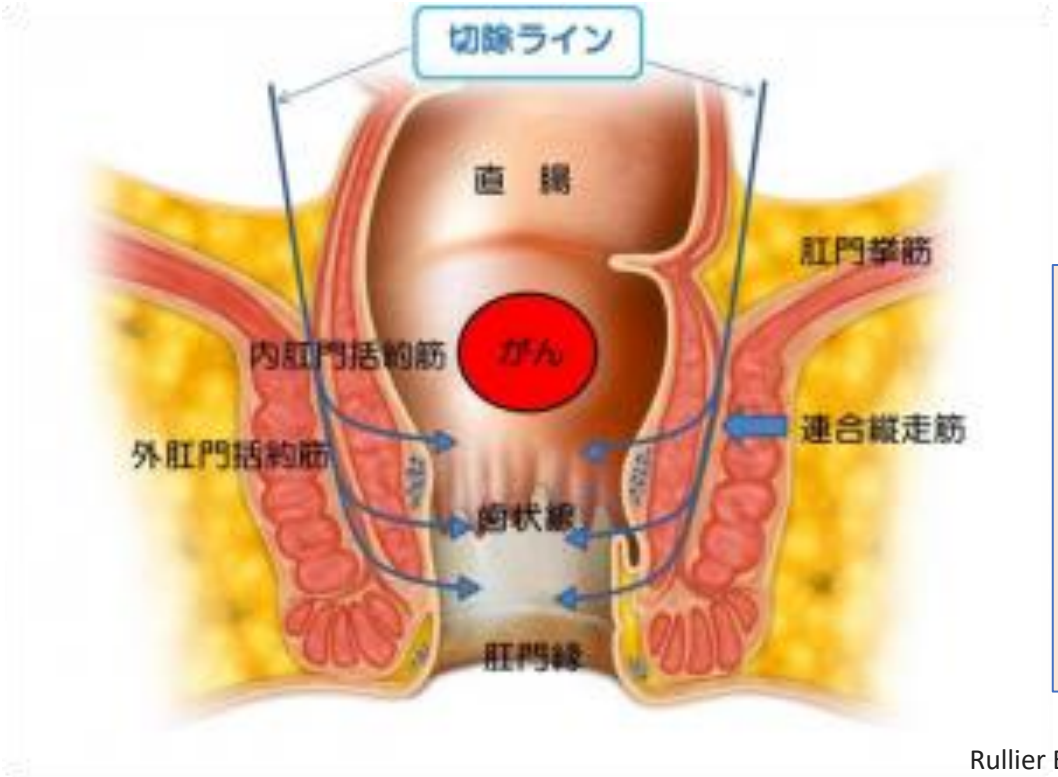


腫瘍から15-20mmのmarginを確保する

Table 3. Classification of radical hysterectomy according to Querleu and Morrow [15]

Type A	Extrafascial hysterectomy
	Visualization and/or palpation of the ureters without dissection of the ureteral bed
	Uterine artery, uterosacral ligament and cardinal ligament are not transected at a distance from the uterus
	Minimal vaginal cuff removed (<10 mm)
Type B	Ureters are unroofed and rolled laterally
	Partial removal of uterosacral and vesicouterine ligaments
	Transection of the paracervix at the level of the ureteral tunnel
	At least 10 mm of the vagina from the cervix or tumor is resected
	Type B1: without removal of lateral paracervical lymph nodes
	Type B2: with additional removal of lateral paracervical lymph nodes
Type C	Ureters are completely mobilized
	Transection of the uterosacral ligament at the rectum
	Transection of the vesicouterine ligament at the bladder
	Complete transection of the paracervix
	15–20 mm of the vagina from the cervix or tumor and the corresponding paracolpos is resected routinely
	Type C1: with preservation of autonomic nerves
	Type C2: without preservation of autonomic nerves
Type D	Type D1: resection of the entire paracervix at the pelvic side wall together with the hypogastric vessels, exposing the roots of the sciatic nerve
	Type D2: type D1 plus resection of the entire paracervix with the hypogastric vessels and adjacent fascial or muscular structures

ISR(Inter-sphincteric resection)



従来APRを行っていた症例に対しなぜこの術式で予後が担保されるのであろうか？

内肛門括約筋は直腸と同一のcompartmentであるが、外肛門括約筋は仙骨由来の別のcompartmentに含まれる。
そのためある程度進行しない限り直腸がんは外肛門括約筋には浸潤せず、ISRで予後が担保される。

Rullier E, Laurent C, Bretagnol F, Rullier A, Vendrely V, Zerbib F. Sphincter-saving resection for all rectal carcinomas: the end of the 2-cm distal rule. *Ann Surg*. 2005;241(3):465-469. doi:10.1097/01.sla.0000154551.06768.e1

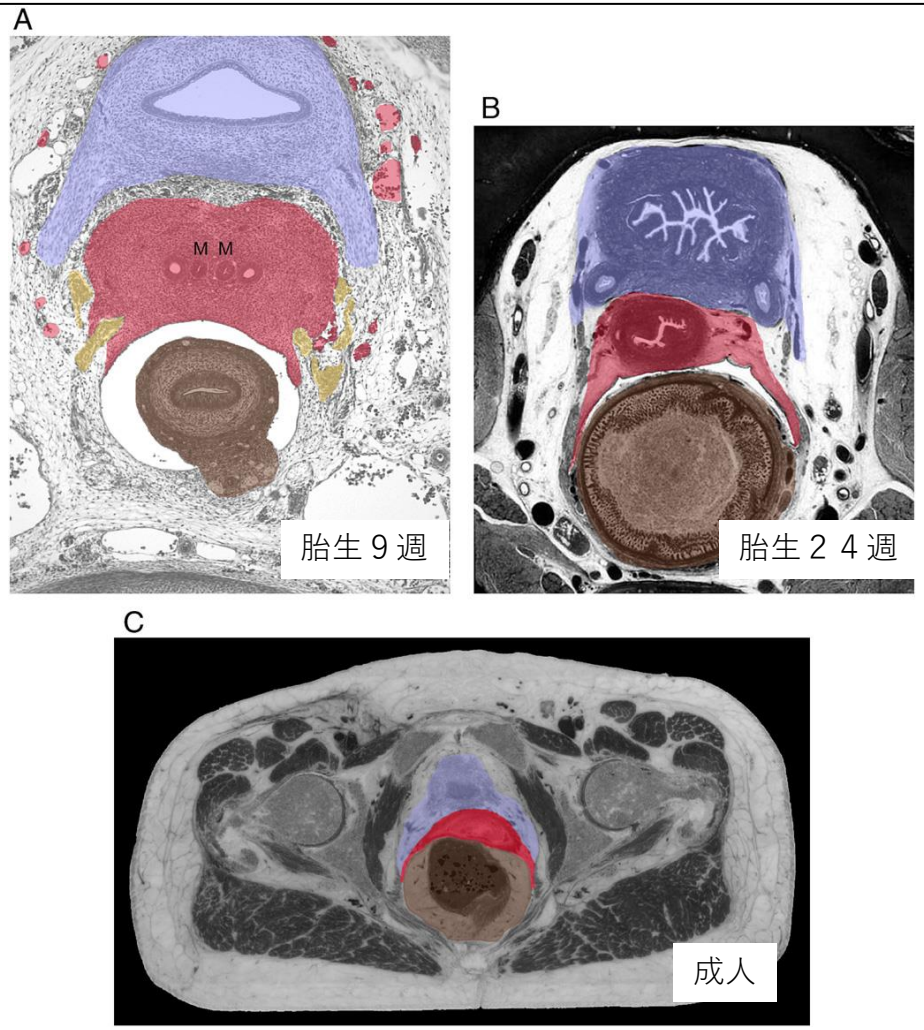
乳がんやすい臓がんでもcompartment theoryは適応できる

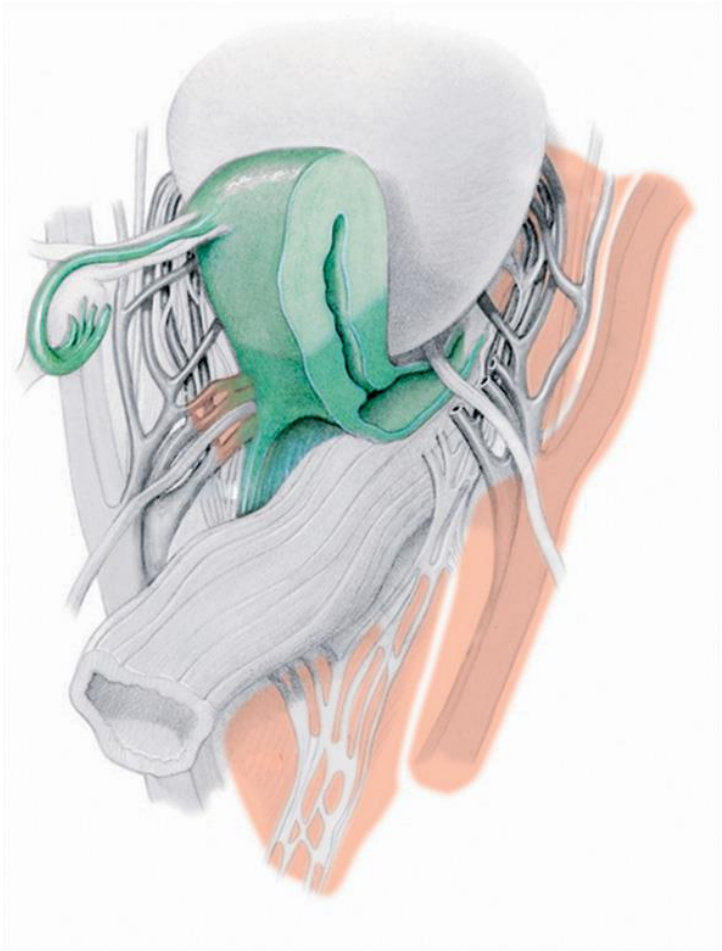
Mannino M, Yarnold J. Effect of breast-duct anatomy and wound-healing responses on local tumour recurrence after primary surgery for early breast cancer. *Lancet Oncol*. 2009;10(4):425-429. doi:10.1016/S1470-2045(09)70040-3

Makino I, Kitagawa H, Ohta T, et al. Nerve plexus invasion in pancreatic cancer: spread patterns on histopathologic and embryological analyses. *Pancreas*. 2008;37(4):358-365. doi:10.1097/mpa.0b013e31818166e6

Resection of the embryologically defi ned uterovaginal (Mullerian) compartment and pelvic control in patients with cervical cancer: a prospective analysis

Michael Hockel, Lars-Christian Horn, Norma Manthey, Ulf-Dietrich Braumann, Ulrich Wolf, Gero Teichmann, Katrin Frauenschlager, Lancet Oncology 2009





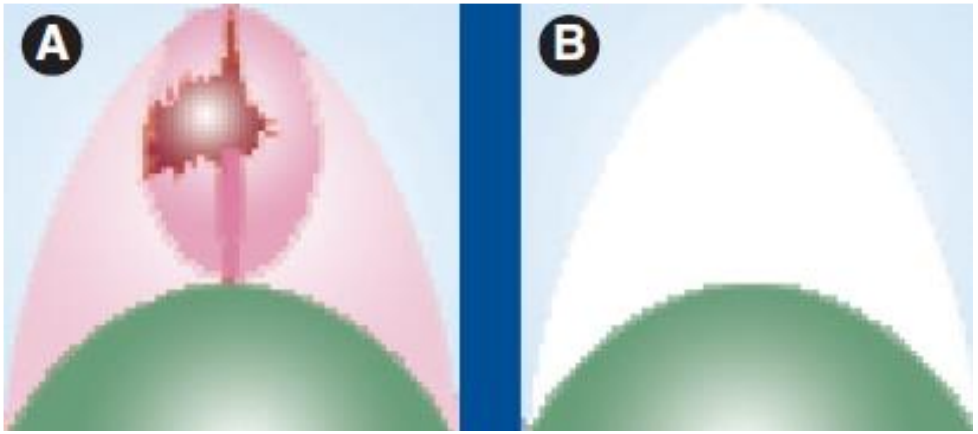
Suppression of tumor growth at the compartment border (cervical cancer)

- Compartment切除（TMMR）された場合は、surgical margin<1mmで追加補助療法（adjuvant RT）がなくても局所再発率は5%以下。

Höckel M, Horn LC, Manthey N, et al. Resection of the embryologically defined uterovaginal (Müllerian) compartment and pelvic control in patients with cervical cancer: a prospective analysis. *Lancet Oncol*. 2009;10(7):683-692. doi:10.1016/S1470-2045(09)70100-7

- 同じ大きさのbulky tumorで隣接臓器浸潤した腫瘍（IVA期）はcompartment内にとどまっている腫瘍に比較し、明らかに細胞内酸素分圧が高い（better energy balance）。

Höckel M, Kahn T, Einenkel J, et al. Local spread of cervical cancer revisited: a clinical and pathological pattern analysis. *Gynecol Oncol*. 2010;117(3):401-408. doi:10.1016/j.ygyno.2010.02.014



がんの発生母地となったコンパートメントを
完全に切除する（≒TMMR）

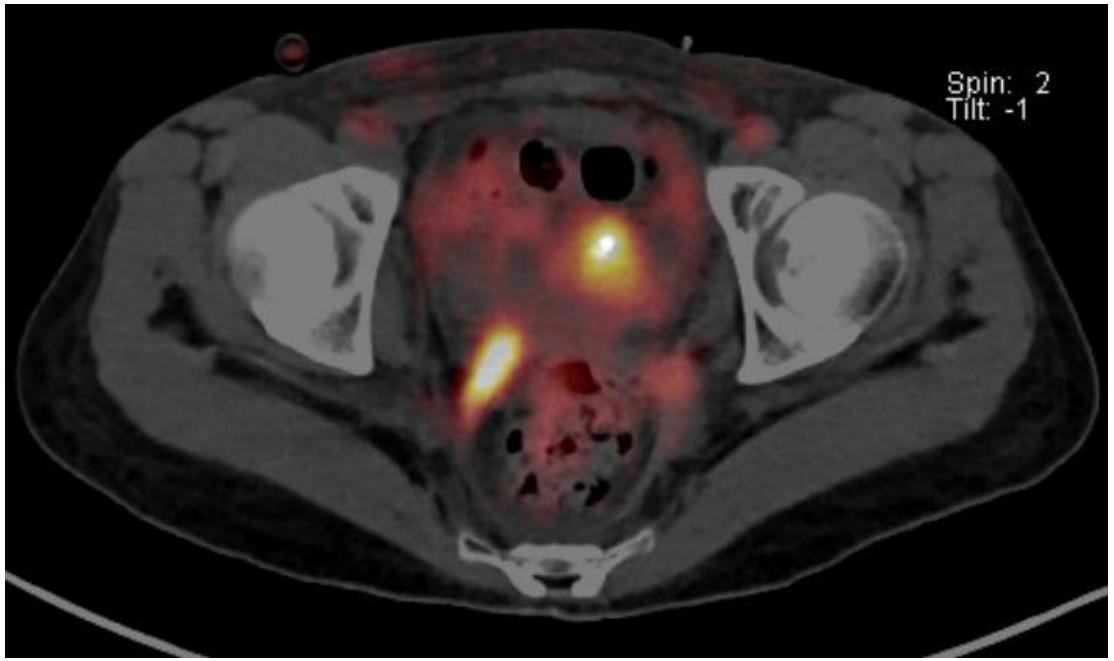
Methods

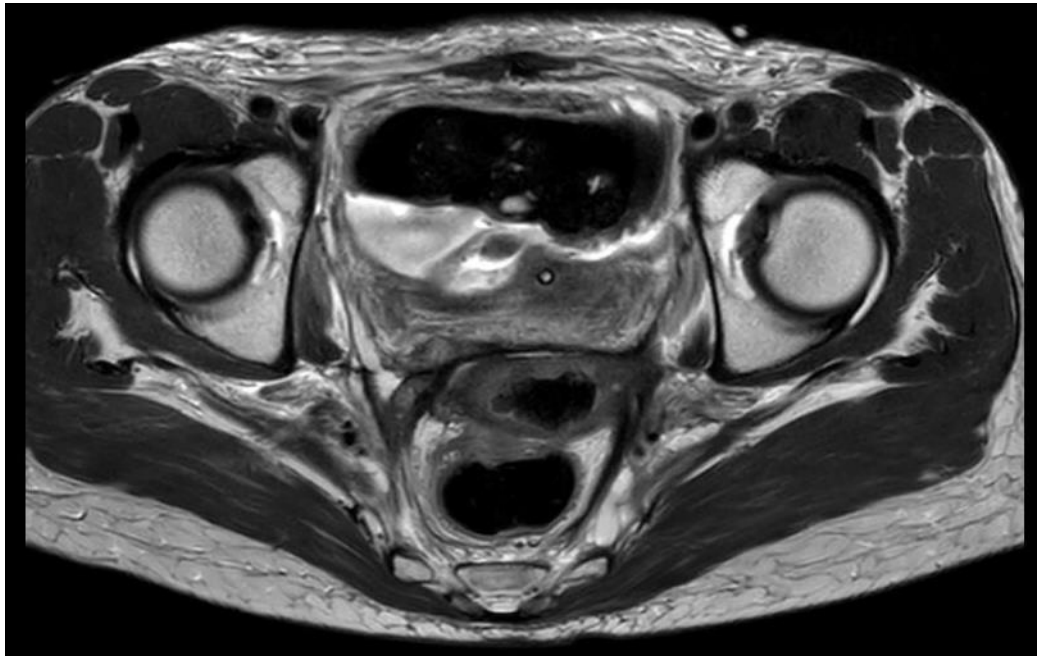
We did a prospective trial to assess the effectiveness of TMMR without adjuvant radiation in patients with International Federation of Gynecology and Obstetrics (FIGO) stage IB, IIA, and selected IIB cervical cancer. We also generated MRI-based pelvic relapse landscapes from patients who had experienced pelvic failure after conventional radical hysterectomy.

Findings

212 consecutive patients underwent TMMR without adjuvant radiation. 134 patients (63%) had high-risk histopathological factors. At a median follow-up of 41 months (5–110), three patients developed pelvic recurrences, two patients developed pelvic and distant recurrences, and five patients developed distant recurrences. Recurrence-free and overall 5-year survival probabilities were 94% (95% CI 91–98) and 96% (93–99), respectively. Treatment-related grade 2 morbidity was detected in 20 (9%) patients, the most common being vascular complications. Resection of the Müllerian compartment resulted in local tumour control irrespective of the metric extension of the resection margins. The pelvic topography of the peak relapse probability after conventional radical hysterectomy indicates an incomplete resection of the posterior subperitoneal and retroperitoneal extension of the Müllerian compartment.

“仙骨子宮靭帯/直腸膣靭帯の取り残し”
が再発の原因と考えられた症例

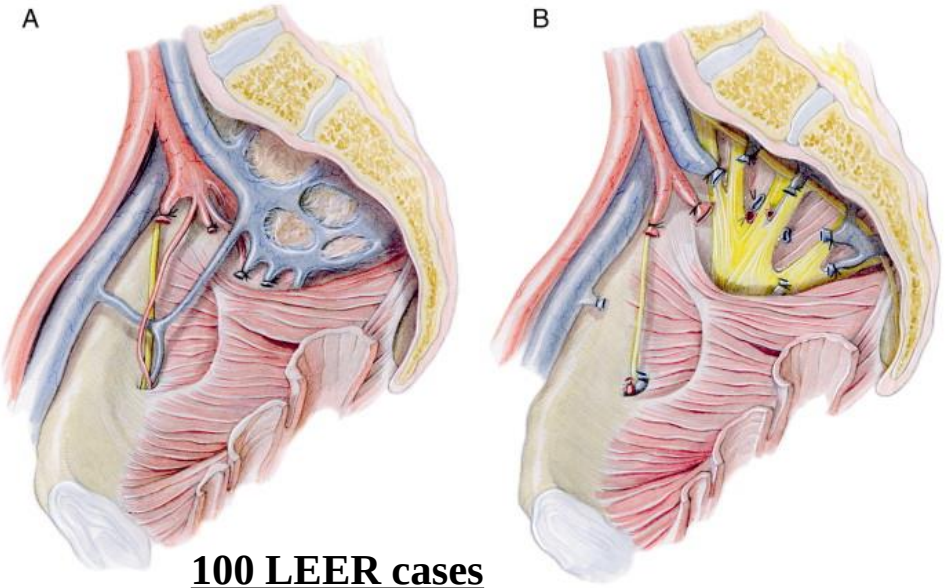


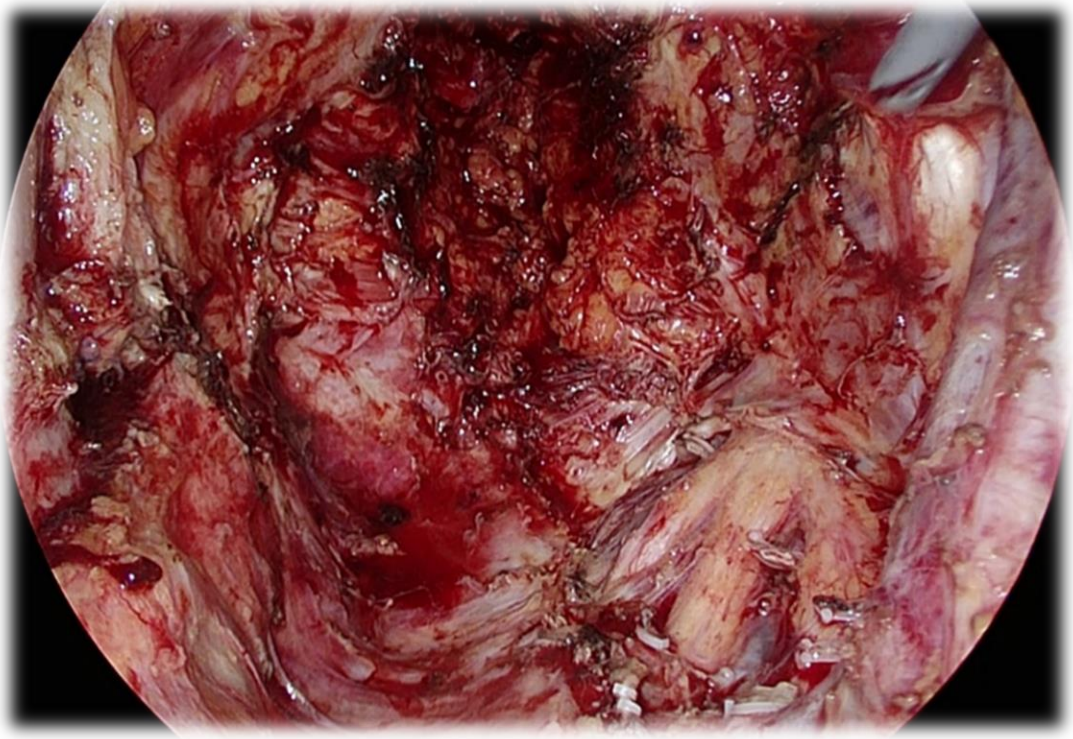


Laterally Extended Endopelvic Excision; LEER

Höckel M, Horn LC, Einenkel J.
(Laterally) extended endopelvic resection: surgical treatment of locally advanced and recurrent cancer of the uterine cervix and vagina based on ontogenetic anatomy.
Gynecol Oncol. 2012 Nov;127(2):297-302

LEER includes lateral extension of the surgical excision, moving toward the medial aspect of the lumbosacral plexus, piriform muscle, internal obturator muscle, and acetabulum





100 LEER cases
Achievements of R0: 100%
Median follow up: 30 months (1-136 months)
5y OS: 55%
Morbidity rate: 70%
Mortality rate: 2%

CQ 27

照射野内再発に対して推奨される治療は？

推奨

① Best supportive care (BSC) を考慮する（グレード C1）。
②症状緩和を目的とした化学療法も考慮される（グレード C1）。
③腟断端，子宮頸部の中央再発に対しては，骨盤除臓術や子宮全摘出術も考慮される（グレード C1）。
④再照射は推奨されない（グレード C2）。

側方再発：骨盤除臓術の適応とならず予後不良とされてきたが、最近内腸骨血管系、内閉鎖筋、尾骨筋、腸骨尾骨筋及び恥骨尾骨筋を含めより広範囲に切除するLEERにより、あるいはそれに組織内照射を併用したcombined operative and radiotherapeutic treatment (CORT)により、5年生存率がそれぞれ44%,46%と報告されている。しかしその適応に関しては骨盤除臓術以上に厳格な基準、評価が要求されまだ一般的には受け入れられておらず、側方再発には化学療法が考慮される。

Laparoscopic pelvic exenteration and laterally extended endopelvic resection for postradiation recurrent cervical carcinoma: Technical feasibility and short-term oncologic outcome

Hiroyuki Kanao [a,*], Yoichi Aoki [a], Makiko Omi [a], Hidetaka Nomura [a], Terumi Tanigawa [a], Sanshiro Okamoto [a], Erica J. Chang [b], Tomoko Kurita [a], Sachiho Netsu [a], Maki Matoda [a], Kohei Omatsu [a], Koji Matsuo [b,c]

- *From 2015/2 to 2019/12, we performed 17 cases (APE 10 cases, TPE 7cases) of laparoscopic pelvic exenterations and 11 cases of laparoscopic LEER for recurrent cervical carcinomas after (CC)RT (including 5 cases of heavy-particle beam therapy).*

	PE (*n* =17)	LEER (*n* =11)
Age, median (range)	54(46-57)	51(41-58)
BMI, median (range), kg/m2	23.1(19.4-26.5)	19.5(18.3-21.3)
Stage of the primary tumor, n		
IB/IIA/IIB/IIIB/IVA/IVB	4/2/4/5/1/1	2/1/7/0/1/0
Histologic type, n		
SCC/non-SCC	10/7	7/4
Treatment for the primary tumor, n		
(CC)RT alone	6	4
(CC)RT,Chemo	3	1
Ope,(CC)RT	6	2
Ope,(CC)RT,Chemo	2	4
Total radiation dose, median (range) Gy	57.8(50.0-74.0)	56.9(50.4-59.4)
Recurrence-free interval, median (range), month	21(8-26)	16(7-60)
Recurrent tumor diameter, median (range), mm	25.8(18.0-42.0)	35.9(30.5-43.0)

Details of LEER

	Number of cases
Resected part of pelvic sidewall	
vessels	
internal iliac vessels	11
external iliac vessels	2
muscles	
internal obturator muscle	9
coccygeal muscle(sacrospinous ligament)	11
piriform muscle	11
levator ani muscles	4
nerve	
obturator nerve	8
sciatic nerve	2
Visceral resection	
bladder	7
rectum	6
ureter	9
kidney	3
coccygeal bone	1
ileocecum	1
Reconstruction	
ileal conduit	4
ureterostomy	1
ureterocystostomy	1
colostomy	6
FEEA	1
FAB	1

Operation outcomes　（既存の報告との比較）

	PE (*n* =17)	LEER (*n* =11)
Operation time, median (range), min	454 (385-527)	562 (446-664)
Blood loss, median (range), ml	285 (110-460)	325 (165-450)
Intraoperative complication, n (%)	0 (0%)	1 (9%)
Postoperative complication, n (%)	7/17 (41%)	5/11 (45%)
Surgical retared death, n (%)	0 (0%)	0 (0%)
Hospital stay, median (range), day	34 (21-41)	41 (26-49)
Pathological complete resection, n (%)	17 (100%)	8 (73%)

PE

Operation time:10h, Blood loss:1089ml, Complication:44%, Surgical related death:0%, Hospital stay:34days, R0 rate:85%

Yoo, H. J., Lim, M. C., Seo, S. S., Kang, S., Yoo, C. W., Kim, J. Y., & Park, S. Y. (2012). Pelvic exenteration for recurrent cervical cancer: Ten-year experience at national cancer center in Korea. *Journal of Gynecologic Oncology*, *23*(4), 242–250.

LEER

Operation time:14.4h, Blood loss:3700ml, Complication:39%, Surgical related death:3%, Hospital stay:28days, R0 rate:94%

M. Höckel, Laterally extended endopelvic resection: Novel surgical treatment of locally recurrent cervical carcinoma involving the pelvic side wall, Gynecol. Oncol. 91 (2003) 369–377

腹腔鏡を用いることで出血量は減少するも合併症率は変わらず。高いR0 resection rateの達成可能。

Oncologic outcome （既存の報告との比較）

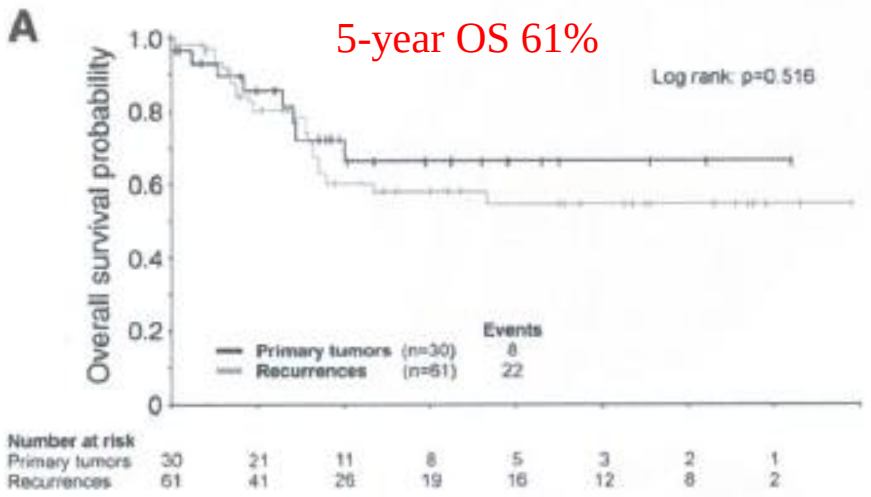
PE

61 recurrent cervical cancer patients underwent PE.

The five-year OS was 56%. (median follow-up periods:22 months)

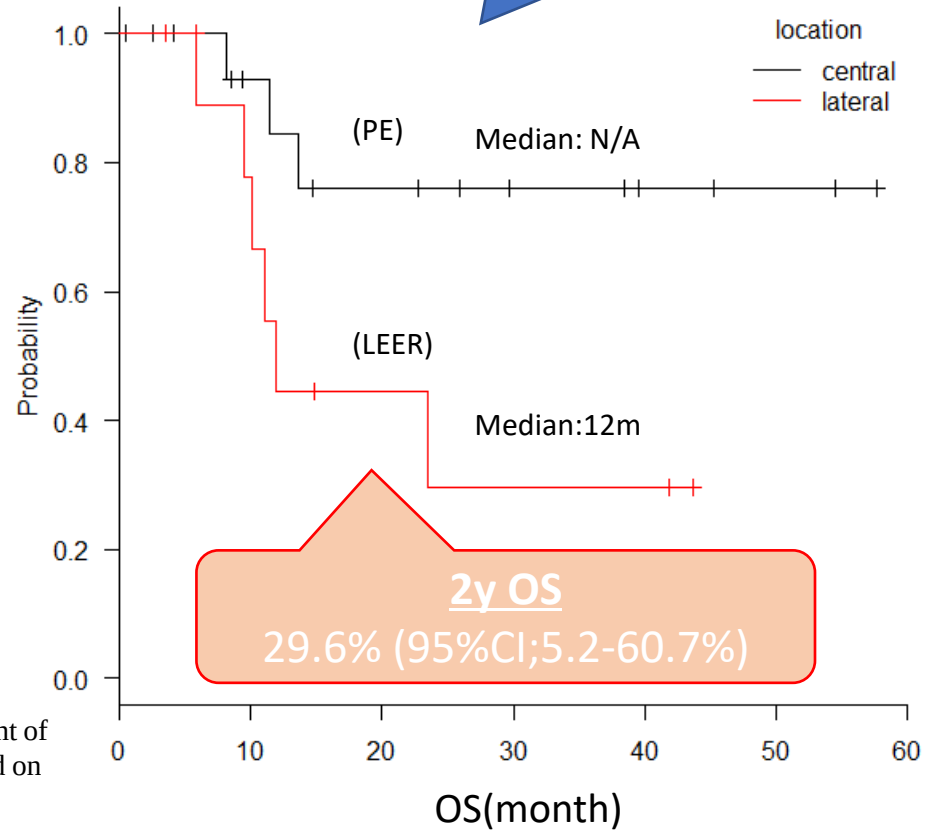
Yoo, H. J., Lim, M. C., Seo, S. S., Kang, S., Yoo, C. W., Kim, J. Y., & Park, S. Y. (2012). Pelvic exenteration for recurrent cervical cancer: Ten-year experience at national cancer center in Korea. *Journal of Gynecologic Oncology*, *23*(4), 242–250.

LEER



Höckel M, et al. (Laterally) extended endopelvic resection: surgical treatment of locally advanced and recurrent cancer of the uterine cervix and vagina based on ontogenetic anatomy. Gynecol Oncol. 2012 Nov;127(2):297-302

2y OS
76% (95%CI;42.2-91.6%)



2y OS
29.6% (95%CI;5.2-60.7%)

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- 1-b: 最近のtopics

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- 2-a: 早期子宮体がんに対するMIS
- 2-b: 子宮体がんに対するリンパ節郭清術

3: 卵巣がんに対する手術療法

- 3-a: 卵巣がんに対するMIS
- 3-b: PDSとNAC-IDS, SDS卵巣がんに対するリンパ節郭清術
- 3-c:卵巣がんに対するリンパ節郭清術

CQ 12

腹腔鏡下手術の適応は？

推奨

①子宮内膜異型増殖症や推定Ⅰ期子宮体癌のうち再発低リスク群に対して奨める（グレードB）。

②推定Ⅰ・Ⅱ期症例のうち再発中・高リスク群が疑われる場合にも考慮する（グレードC1）。

③進行例に対しては奨めない（グレードC2）。

2018年度版　子宮体癌治療ガイドライン

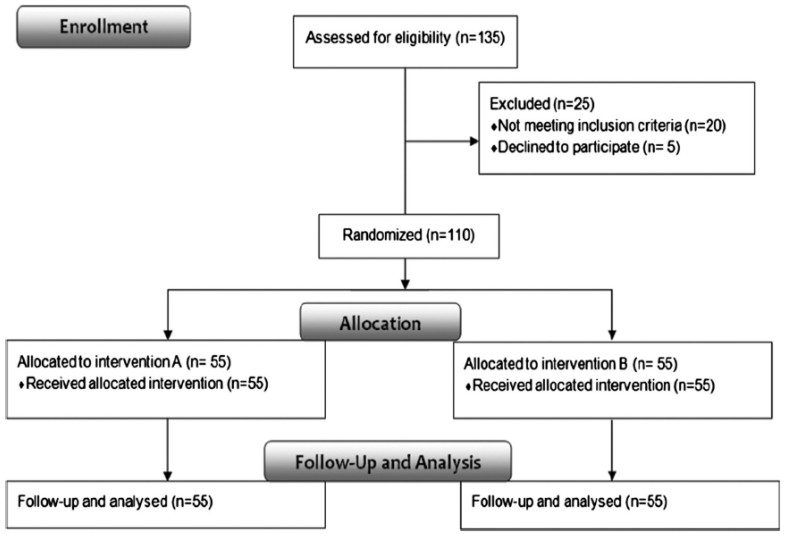
早期子宮体がんに対する開腹手術v.s.腹腔鏡手術の9つのRCT

- 手術時間：開腹＜腹腔鏡　（開腹favor）
- 出血量：開腹＞腹腔鏡　（腹腔鏡favor）
- 入院期間：開腹＞腹腔鏡　（腹腔鏡favor）
- 術中合併症：開腹＜腹腔鏡　（開腹favor）
- 術後合併症：開腹＞腹腔鏡　（腹腔鏡favor）
- 根治性（長期予後）：開腹≒腹腔鏡

早期子宮体がんに対する子宮マニピュレーターの使用は再発を惹起するのか？

Effects of Uterine Manipulation on Surgical Outcomes in Laparoscopic Management of Endometrial Cancer

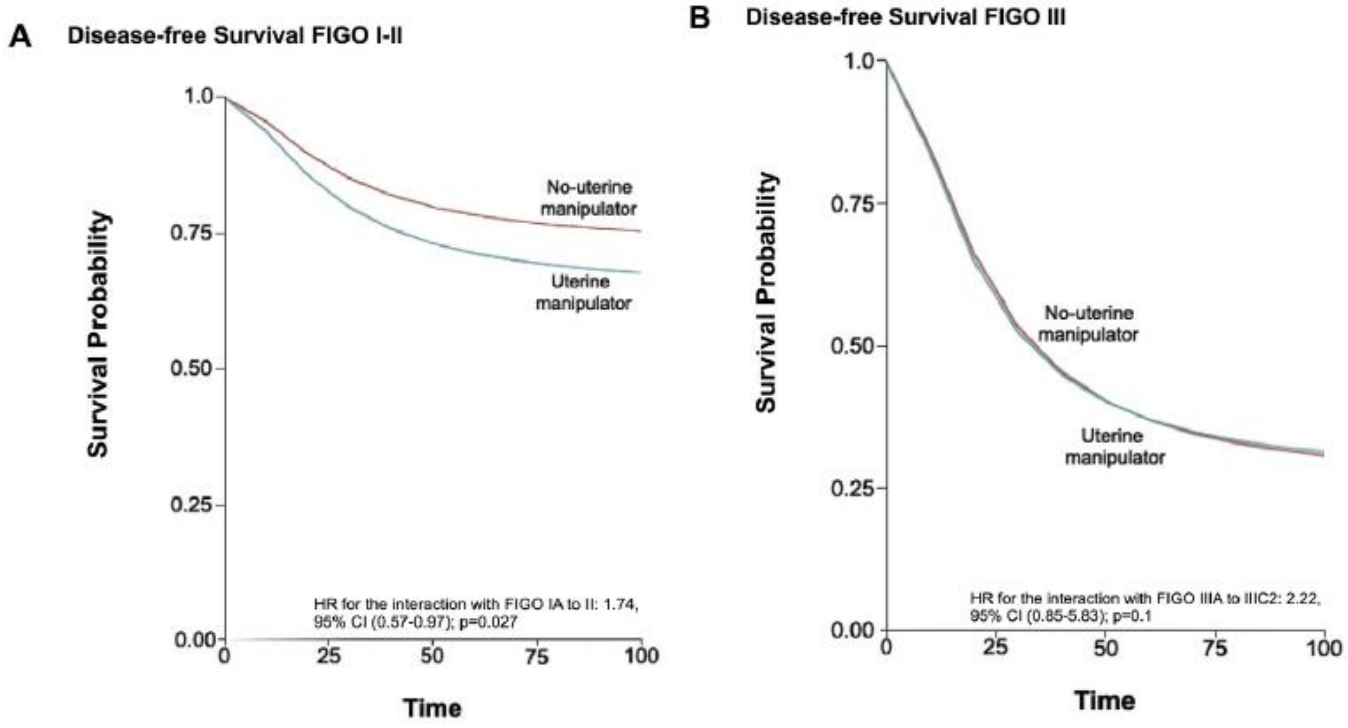
A Prospective Randomized Clinical Trial



子宮マニピュレーターの使用の有無での予後に差はなし。
RCTといえども55例ずつでの検討。

GYNECOLOGY

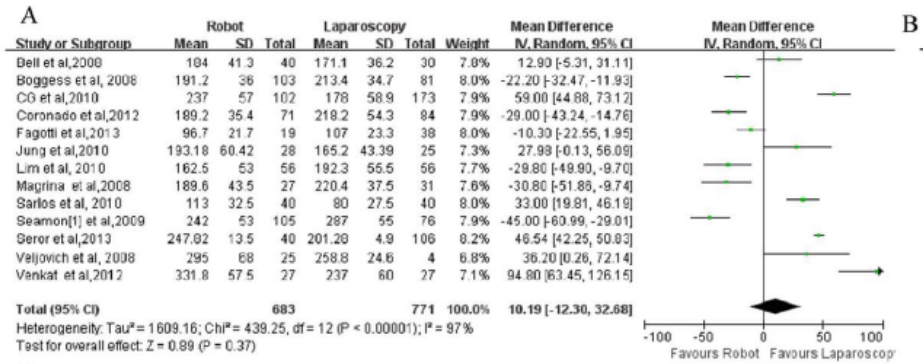
Impact of uterine manipulator on oncological outcome in endometrial cancer surgery



Retrospective studyではあるものの、マニピュレーター使用群1756例、非使用群905例での検討

Favor Robot　　Favor Lap

A.手術時間　B.合併症　C.入院期間　D.出血量　E.輸血　F.摘出リンパ節個数　G.開腹移行



OPEN ACCESS Freely available online

PLOS ONE

Comparison of Robotic Surgery with Laparoscopy and Laparotomy for Treatment of Endometrial Cancer: A Meta-Analysis

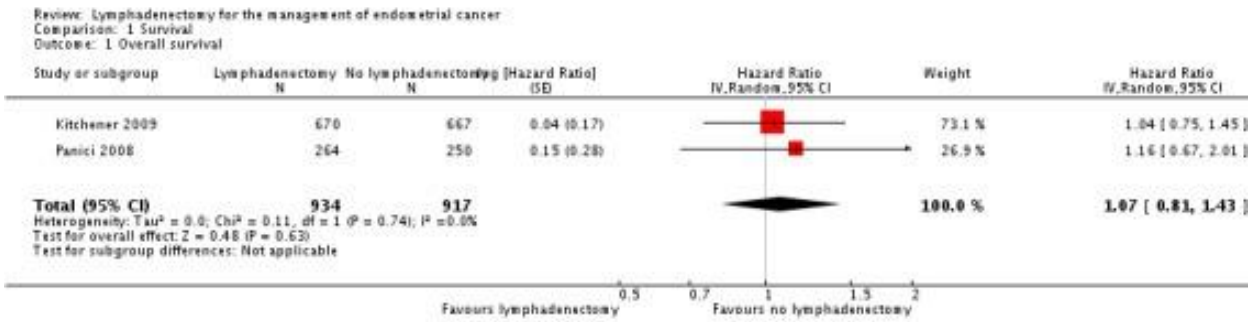
骨盤内リンパ節郭清術の治療的意義は？ (2つのRCT)

Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study

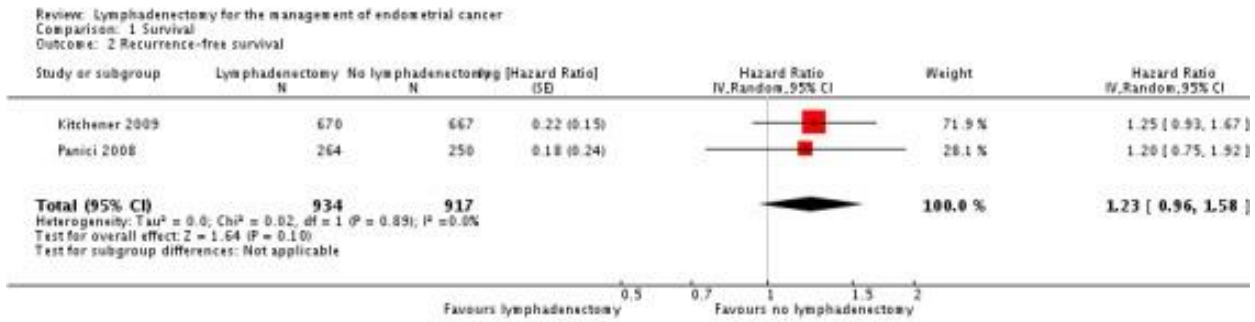
RCT, low-high risk, adjuvant RT
Efficacy of PLA: no
Efficacy of PALA: N/A

- PALA: not performed
- Average no. of PLA is 12. (Low quality of operation?)
- Majority (40%) is low-risk group.

Overall survival



Recurrence free survival



傍大動脈リンパ節郭清術の治療的意義は？ (RCTなし)

Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis

Retrospective, low-high, adjuvant RT or CT
Efficacy of PLA: N/A
Efficacy of PALA: low: no, intermediate-high: yes

- Retrospective study
- Adjuvant: not uniformed

Phase III trial to confirm the superiority of pelvic and para-aortic lymphadenectomy to pelvic lymphadenectomy alone for endometrial cancer: JCOG1412（IB-IIIC1）

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Laparoscopic cytoreduction After Neoadjuvant ChEmotherapy (LANCE)

Roni Nitecki [1], Jose Alejandro Rauh-Hain [2], Alexander Melamed [3], Giovanni Scambia [4 5], Rene Pareja [6], Robert L Coleman [7], Pedro T Ramirez [1], Anna Fagotti [4 5]

Affiliations + expand

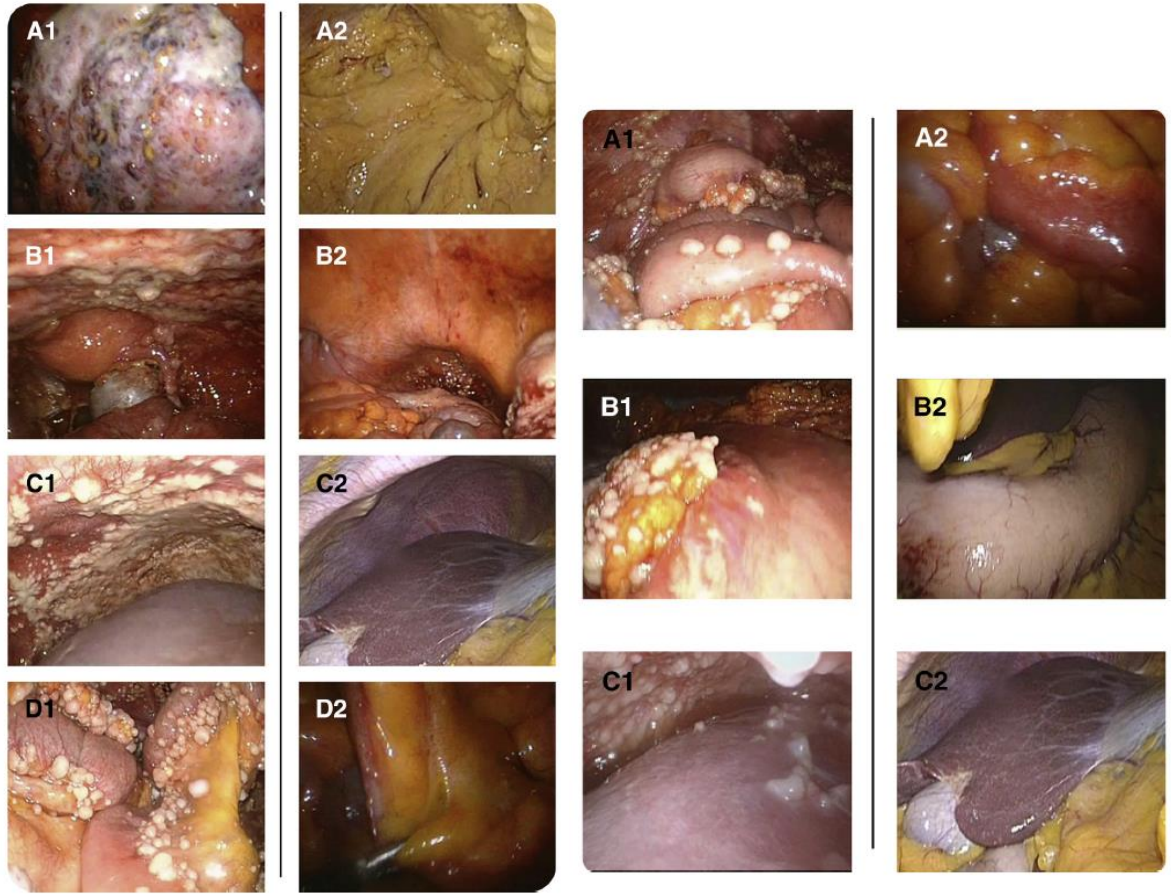
PMID: 32690591 DOI: 10.1136/ijgc-2020-001584

Minimally invasive interval debulking surgery in ovarian neoplasm (MISSION trial-NCT02324595): a feasibility study

Salvatore Gueli Alletti [1], Carolina Bottoni [2], Francesco Fanfani [3], Valerio Gallotta [2], Vito Chiantera [4], Barbara Costantini [2], Francesco Cosentino [2], Alfredo Ercoli [5], Giovanni Scambia [2], Anna Fagotti [6]

残存する播種病変の見落とし（死角の存在）、腫瘍細胞の散布（高い腹水細胞診陽性率）などから卵巣がん治療における腹腔鏡手術の問題点は多そう…

卵巣がんに対する腹腔鏡手術の意義
１：診断的（生検）目的
２：PDS可能かどうかの判断

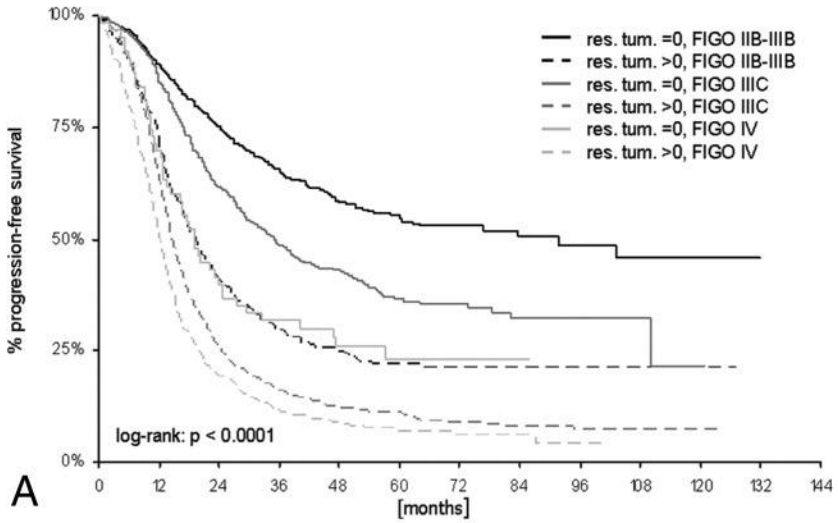


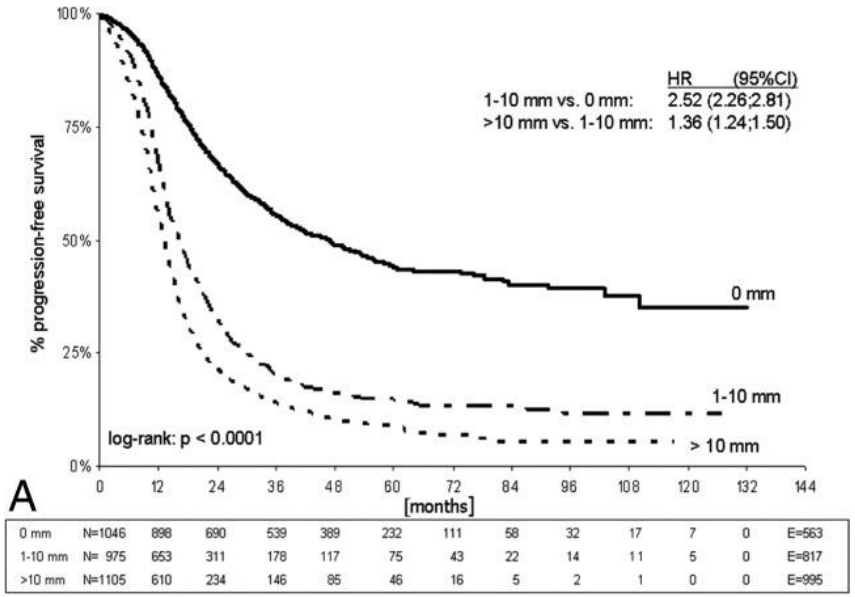
PI score
0-6:PDS容易
8-12:PDS困難
14:PDS不可能
＊SCORPION試験ではPI score 8-12が対象

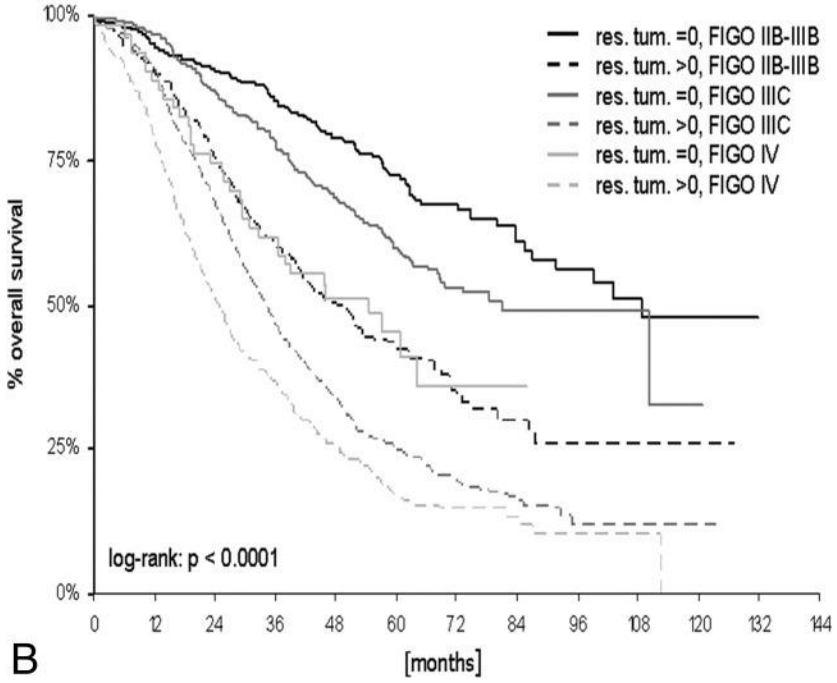
Predictive index parameter（PI score）	Score 0	Score 2
Omental cake	胃大湾に至る腫瘤形成がない	胃大湾に至る腫瘤形成がある
Peritoneal carcinomatosis	腹膜摘出術により外科的に切除可能	粟粒状に広がり切除不能
Diaphragmatic carcinosis	横隔膜表面の大部分を覆う広範囲の浸潤を伴う腫瘤形成はない	横隔膜表面の大部分を覆う広範囲の浸潤を伴う腫瘤形成がある
Mesenteric retraction	腸間膜根に消化管の動きを制限する腫瘍の浸潤がない	腸間膜根に消化管の動きを制限する腫瘍の浸潤がある
Bowel infiltration	消化管の切除を要せず、粟粒状の腫瘤形成を認めない	消化管の切除を要するまたは、粟粒状の腫瘤形成を認める
Stomach infiltration	胃壁に腫瘤形成を認めない	胃壁に腫瘤形成を認める
Liver metastasis	肝臓表面に腫瘤がない	肝臓表面に腫瘤がある

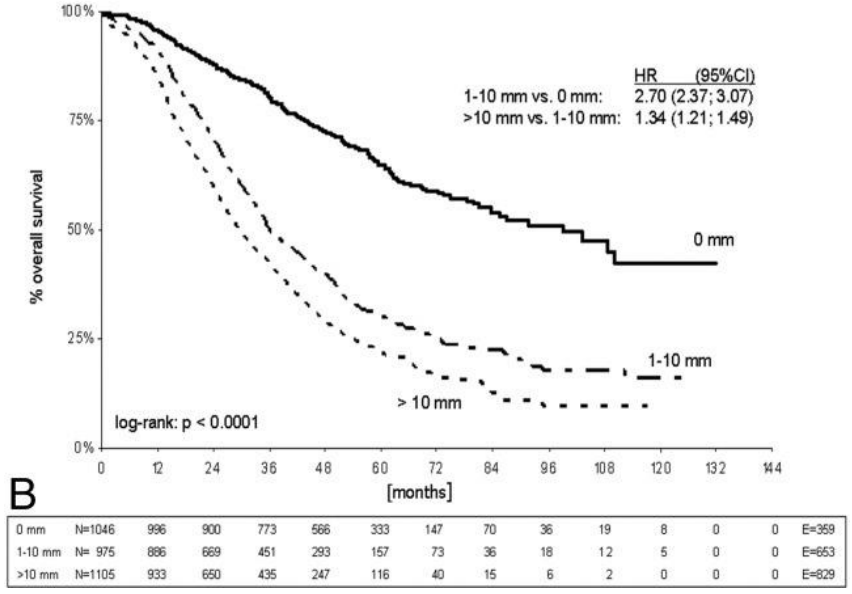
Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: A combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials

Cancer, Volume: 115, Issue: 6, Pages: 1234-1244, First published: 03 March 2009, DOI: (10.1002/cncr.24149)



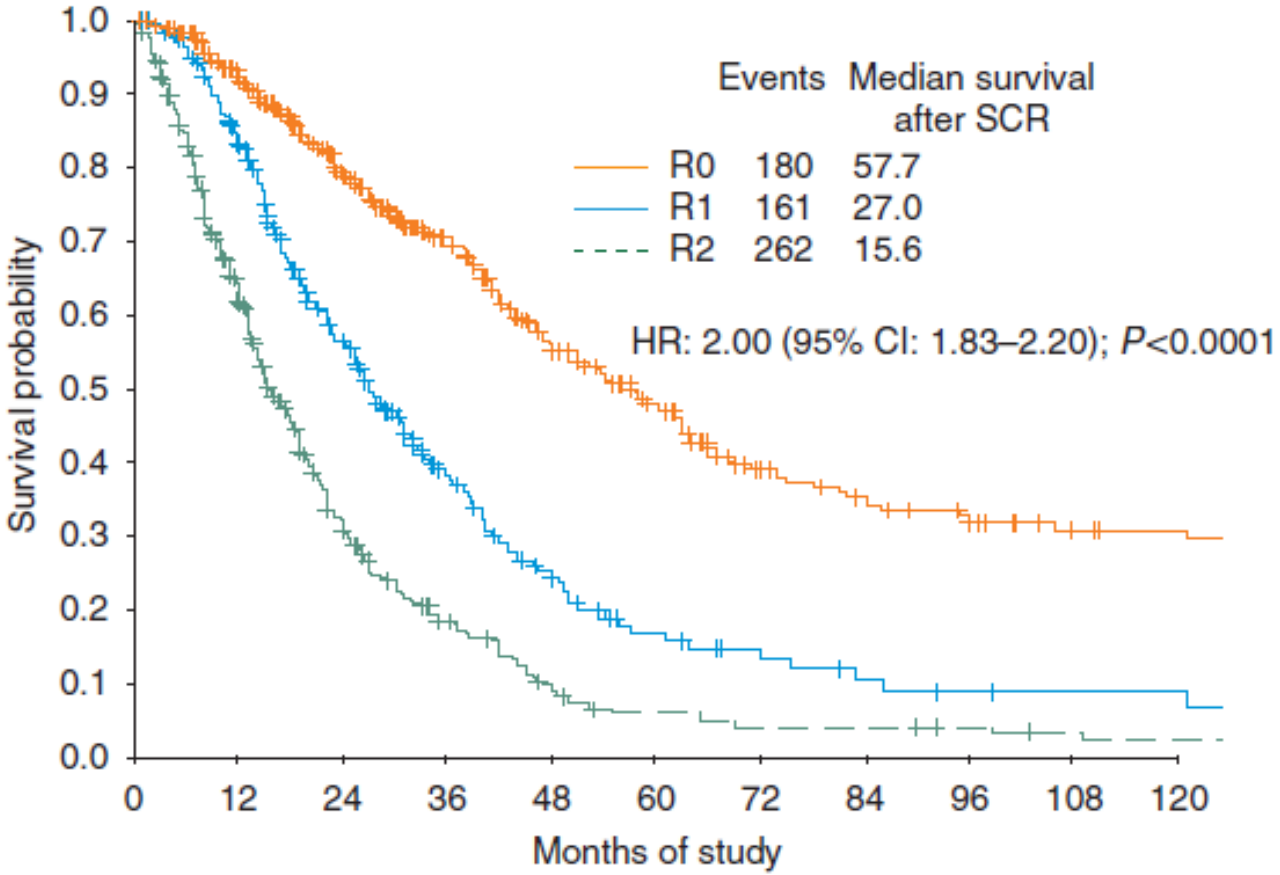






Predictors of survival in patients with recurrent ovarian cancer undergoing secondary cytoreductive surgery based on the pooled analysis of an international collaborative cohort

British Journal of Cancer (2011) 105, 890–896



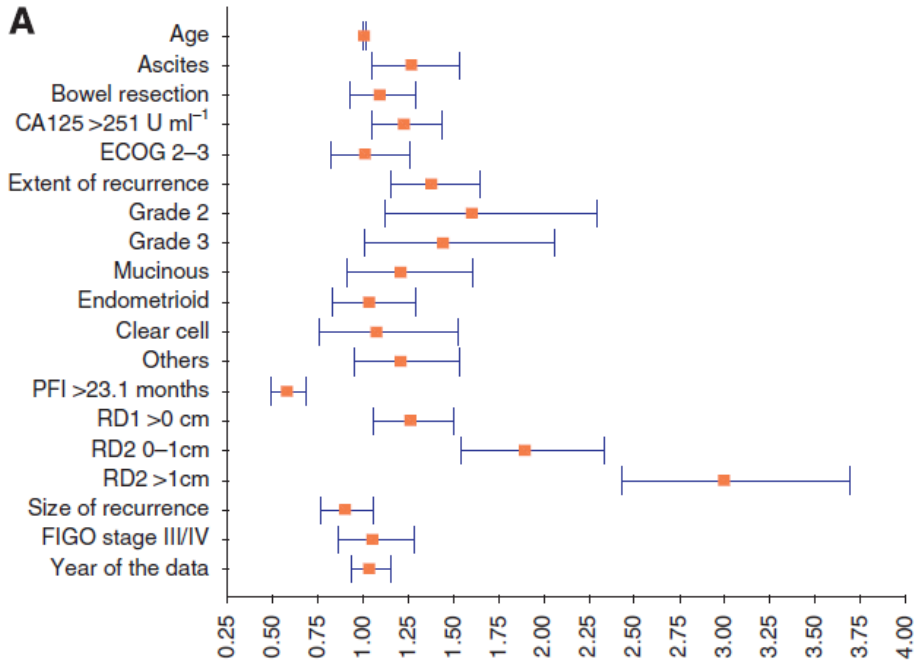


Table 2 Scoring system for survival in patients with recurrent ovarian cancer undergoing secondary cytoreductive surgery

	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.

JP-36033

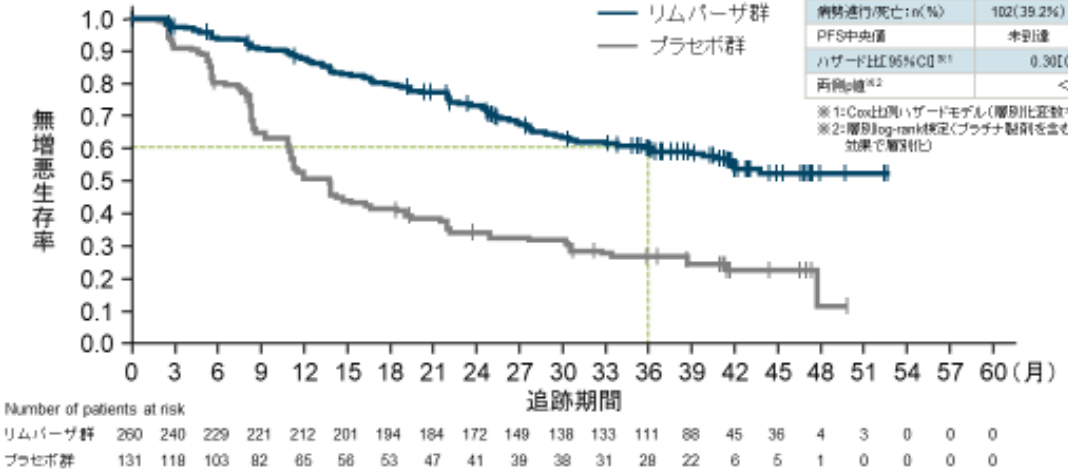
SOLO1試験（国際共同第Ⅲ相試験/日本を含む国際共同試験）

主要評価項目

無増悪生存期間 - PFS

- リムパーザ群はプラセボ群に比べてPFSを有意に延長し、優越性が検証された。PFS中央値はリムパーザ群が未到達、プラセボ群が13.8ヵ月であった。
- 36ヵ月時点における無増悪生存割合は、リムパーザ群では60.4%、プラセボ群では26.9%であった。

PFSのKaplan-Meier曲線（最大解析対象集団）



	リムパーザ群（n=260）	プラセボ群（n=131）
病勢進行/死亡：n(%)	102(39.2%)	96(73.3%)
PFS中央値	未到達	13.8ヵ月
ハザード比[95%CI]※1	0.30[0.23~0	
両側p値※2	<0.0001	

※1：Cox比例ハザードモデル（層別比較を共変
※2：層別log-rank検定（プラチナ製剤を含む初回化
効果で層別化）

承認時評価資料・社内資料（BRCA変異を有する進行卵巣癌患者を対象としたオラパリブの国際共同第Ⅲ相試験

JP-36033

PAOLA-1試験（日本を含む国際共同第Ⅲ相試験）

主要評価項目

無増悪生存期間 - PFS

国際共同第Ⅲ相試験（PAOLA-1試験）により国内で承認された効能又は効果と異なる成績が含まれるが、本資料は承認時に評価された試験成績のため紹介する。

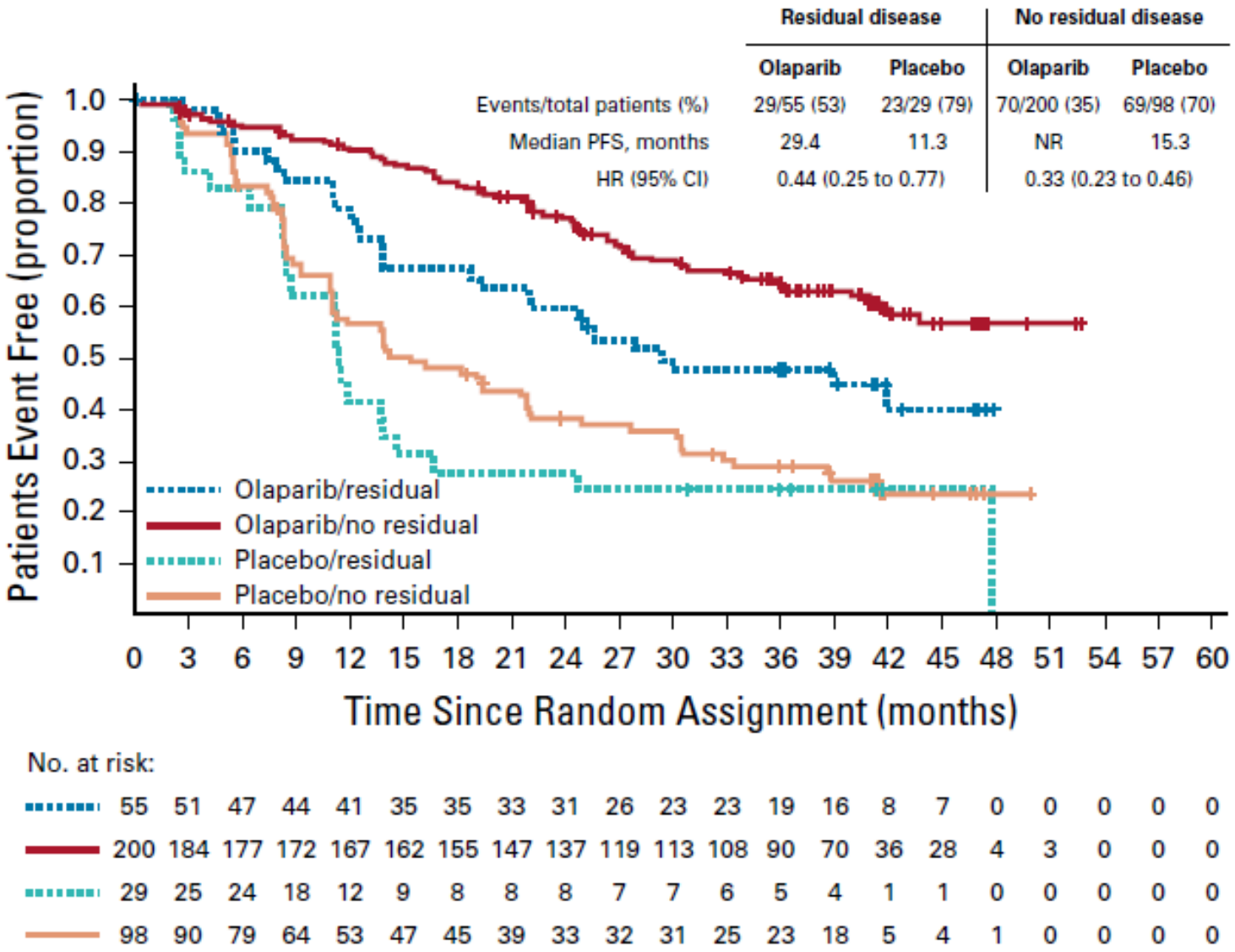
- リムパーザ＋ベバシズマブ群は、プラセボ＋ベバシズマブ群に比べてPFSを有意に延長し、優越性が検証された。
- PFS中央値はリムパーザ＋ベバシズマブ群が22.1ヵ月、プラセボ＋ベバシズマブ群が16.6ヵ月と、5.5ヵ月の延長を示した。ハザード比は0.59であった。

	リムパーザ＋ベバシズマブ群（n=537）	プラセボ＋ベバシズマブ群（n=269）
病勢進行/死亡：n(%)	280(52.1%)	194(72.1%)
PFS中央値	22.1ヵ月	16.6ヵ月
ハザード比[95%CI]	0.59[0.49~0.72]	
両側p値※2	<0.0001	

※1：Cox比例ハザードモデル（層別比較を共変量とする）
※2：層別log-rank検定（初回治療で得られた奏効およびBRCA変異状態で層別化）

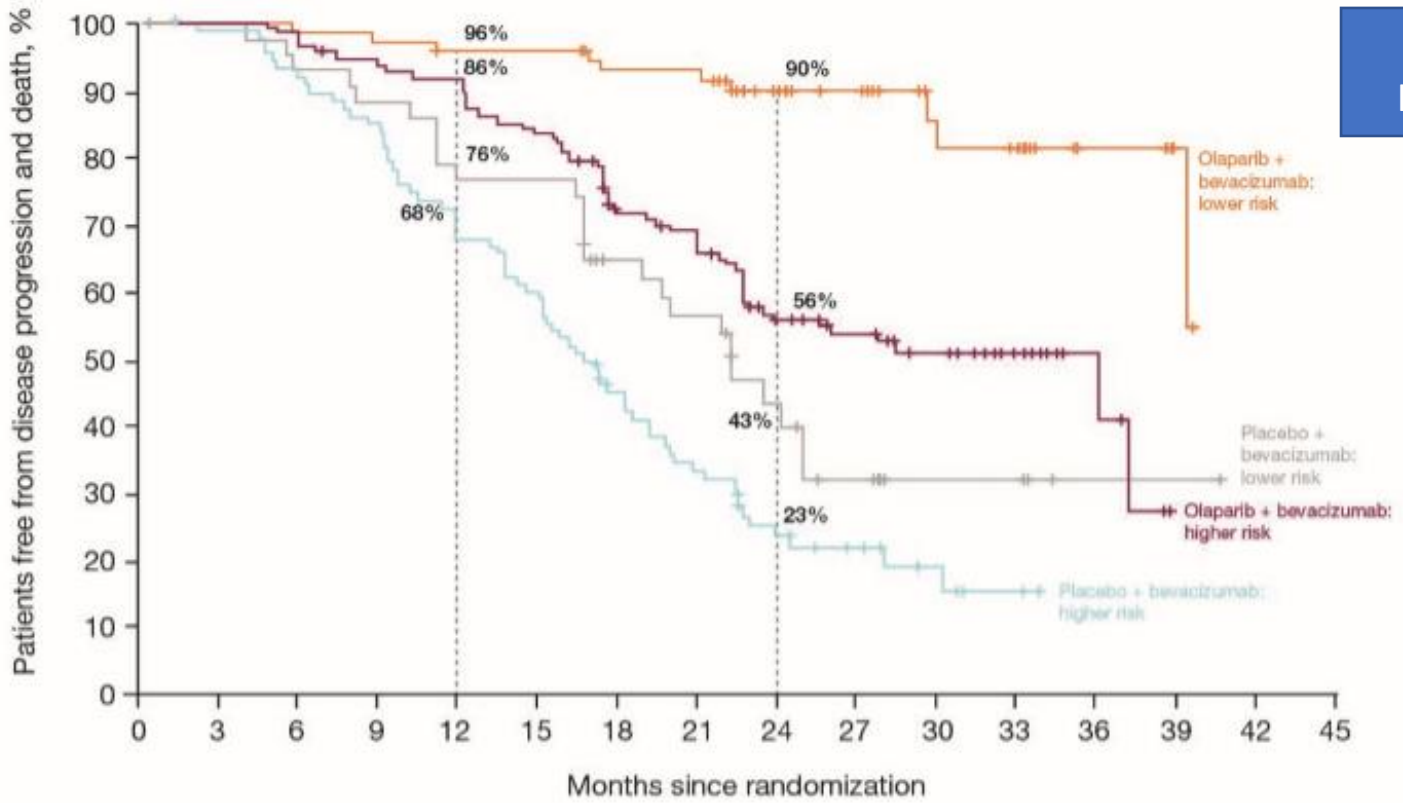
承認時評価資料・社内資料（進行卵巣癌患者を対象としたオラパリブの国際共同第Ⅲ相試験，2019）

Efficacy of Maintenance Olaparib for Patients With Newly Diagnosed Advanced Ovarian Cancer With a BRCA Mutation: Subgroup Analysis Findings From the SOLO1 Trial



PAOLA-1 subanalysis

Figure 1. Kaplan–Meier estimates of investigator-assessed PFS in higher-risk and lower-risk HRD-positive patients*



Number of patients at risk:

Olaparib + bevacizumab: higher risk	177	175	166	161	150	140	109	95	63	50	27	15	5	0	0
Placebo + bevacizumab: higher risk	89	86	78	66	59	47	31	24	16	11	5	2	0	0	0
Olaparib + bevacizumab: lower risk	78	77	76	75	73	73	60	60	40	35	19	14	6	3	0
Placebo + bevacizumab: lower risk	43	42	39	37	32	32	23	20	12	7	3	3	1	1	0

*HRD-positive defined as a tumour BRCAm and/or genomic instability score of ≥42. BRCAm, BRCA mutation; HRD, homologous recombination deficiency; PFS, progression-free survival

Lower risk=PDS R0
Higher risk=それ以外

Improved progression-free and overall survival in advanced ovarian cancer as a result of a change in surgical paradigm ☆

Dennis S. Chi [a,*], Eric L. Eisenhauer [a], Oliver Zivanovic [a], Yukio Sonoda [a], Nadeem R. Abu-Rustum [a], Douglas A. Levine [a], Matthew W. Guile [b], Robert E. Bristow [b], Carol Aghajanian [c], Richard R. Barakat [a]

Cytoreductive procedures performed.

Procedures performed	Group 1 ($n=168$)	Group 2 ($n=210$)
Standard		
Hysterectomy	129 (77%)	183 (87%)
USO/BSO	153 (91%)	184 (88%)
Omentectomy	135 (80%)	182 (87%)
Small bowel resection	6 (4%)	8 (4%)
Large bowel resection	10 (6%)	73 (35%)
Appendectomy	17 (10%)	37 (18%)
Pelvic lymph node dissection	11 (7%)	59 (28%)
Para-aortic lymph node dissection	11 (7%)	47 (22%)
Extensive upper abdominal		
Diaphragm peritonectomy/resection	0 (0%)	73 (35%)
Splenectomy	0 (0%)	26 (12%)
Distal pancreatectomy	0 (0%)	9 (4%)
Liver resection	0 (0%)	13 (6%)
Resection porta hepatis tumor	0 (0%)	11 (5%)
Cholecystectomy	0 (0%)	10 (5%)

USO, unilateral salpingo-oophorectomy; BSO, bilateral salpingo-oophorectomy.

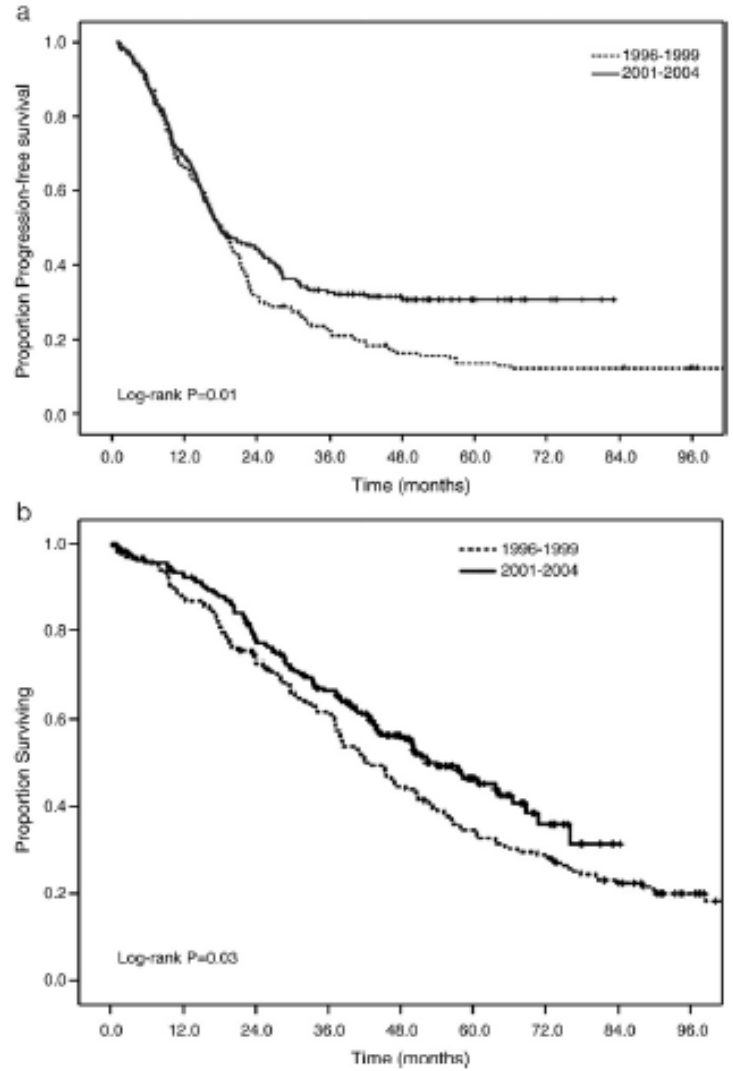
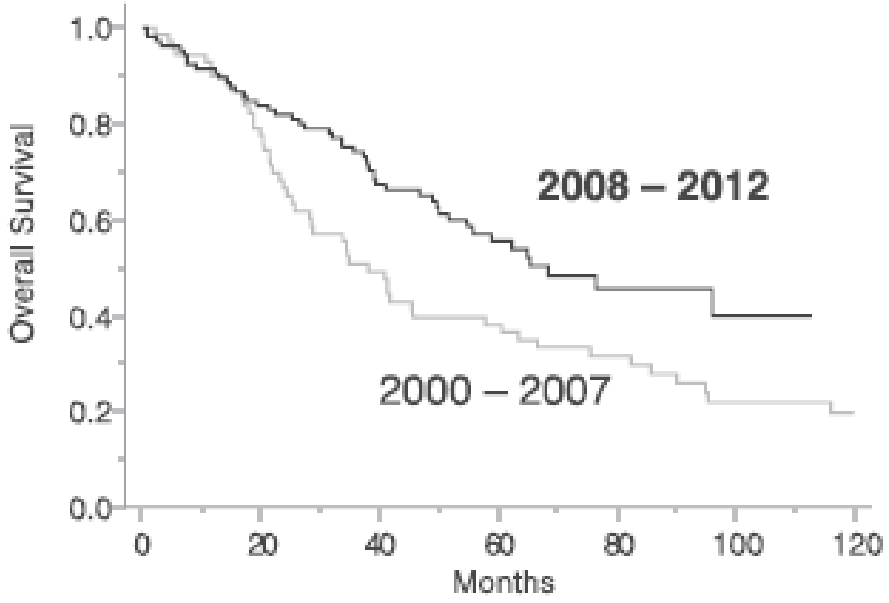


Fig. 1. (A) Progression-free survival, 1996–1999 vs 2001–2004. (B) Overall survival, 1996–1999 vs 2001–2004.

Survival and safety associated with aggressive surgery for stage III/IV epithelial ovarian cancer: A single institution observation study

Shinichi Tate [a], Kazuyoshi Kato [b], Kyoko Nishikimi [a], Ayumu Matsuoka [a], Makio Shozu [a,*]

[a] Department of Gynecology, Chiba University Hospital, 1-8-1 Inohana, Chuo-ku, Ciba 260-8670, Japan
[b] Department of Gynecology, Cancer Institute Hospital, 3-8-31 Ariake, Koutou-ku, Tokyo 135-8550, Japan



	2000-2007	**2008-2012**
5y Survival	38.0%	55.5%
Median OS	38.1M	68.5M
Complete rate	43%	78%
Median SCS*	2	8

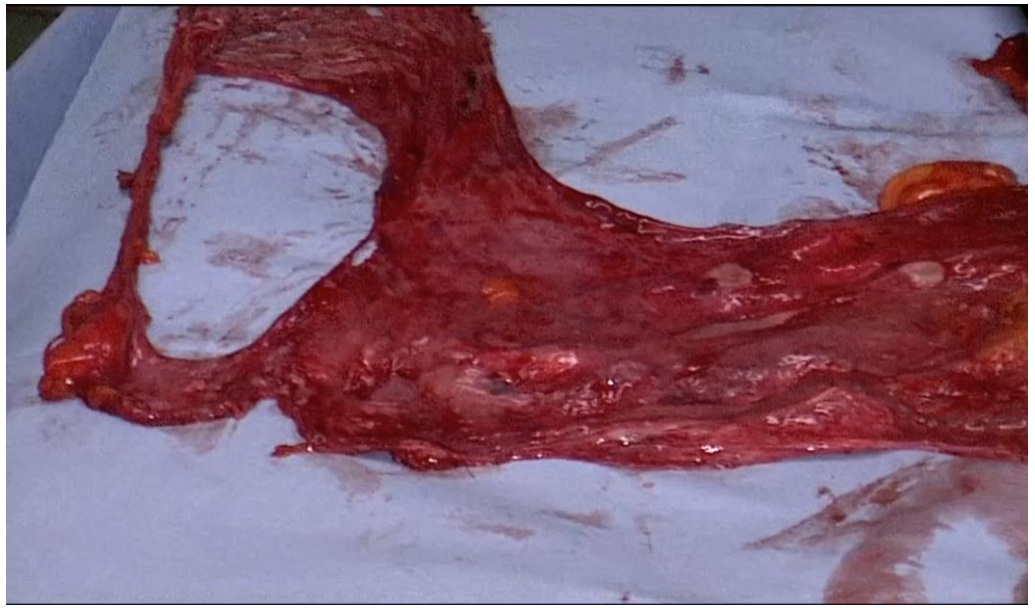
*: Surgical complexity score

Surgical Complexity Score	
Median (range)	8 (0-16)
Low (0—3)	15 (14%)
Moderate (4- 7)	30 (28%)
High (8-18)	61 (58%)

Surgical Complexity Score (Aletti score)

Surgical complexity scoring system based upon complexity and number of surgical procedures performed

	Points
Procedure	
TH-BSO	1
Omentectomy	1
Pelvic lymphadenectomy	1
Para-aortic lymphadenectomy	1
Pelvic peritoneum stripping	1
Abdominal peritoneum stripping	1
Recto-sigmoidectomy _ T–T anastomosis	3
Large bowel resection	2
Diaphragm stripping/resection	2
Splenectomy	2
Liver resection/s	2
Small bowel resection/s	1
Complexity score groups	
1 (low)	≤3
2 (intermediate)	4–7
3 (high)	≥8



TAH-BSO:1
Omentectomy:1
Pelvic peritoneum stripping:1
Abdominal peritoneum stripping:1
Recto-sigmoidectomy:3
Diaphragm stripping:2 **SCS:9**

Quality of care in advanced ovarian cancer: The importance of provider specialty

Cheryl Mercado [a], David Zingmond [a], Beth Y. Karlan [b], Evan Sekaris [a], Jenny Gross [b], Melinda Maggard-Gibbons [a,c], James S. Tomlinson [a,d], Clifford Y. Ko [a,d,*]

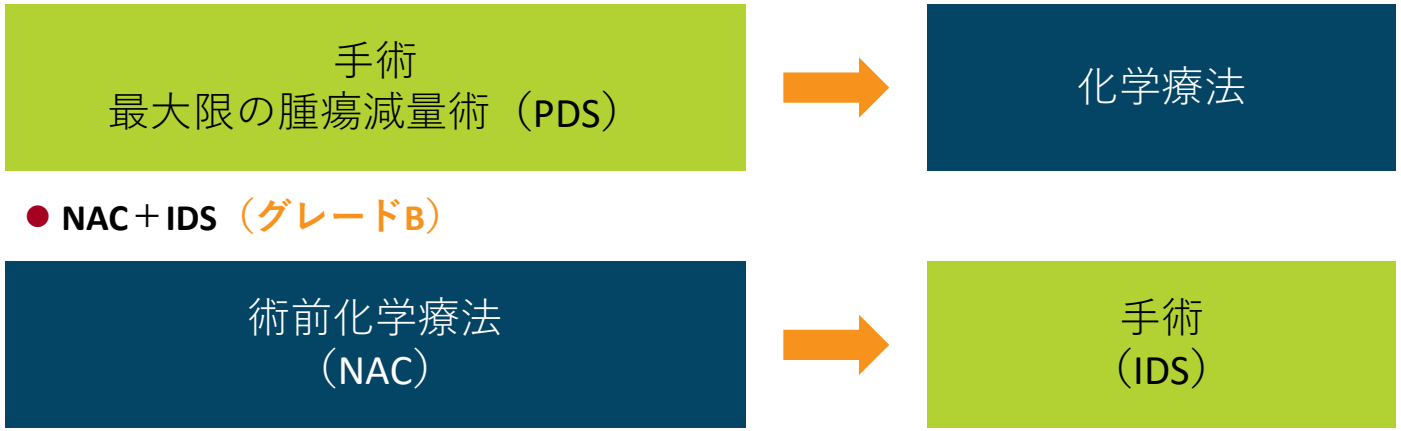
Table 4

Cox regression predicting mortality for Stage IIIC/IV ovarian cancer patients.[a]

Variable	Unadjusted hazard ratio	95% CI	*P*-value
Race			
Non-Hispanic Black[b]	1.15	1.08–1.22	<0.0001
Poverty			
25–34% of census area below poverty line[c]	1.05	1.00–1.09	0.019
≥35% of census area below poverty line[c]	1.10	1.06–1.15	<0.0001
Hospital volume			
High hospital volume[d]	0.89	0.86–0.93	<0.0001
Very high hospital volume[d]	0.79	0.76–0.83	<0.0001
Treating physician			
General surgeon[e]	1.63	1.56–1.71	<0.0001
Other MD[e]	1.56	1.52–1.61	<0.0001

術前化学療法（NAC）

進行卵巣癌に対する標準治療



● **NAC＋IDS（グレードB）**

PDS：primary debulking surgery
NAC：neoadjuvant chemotherapy
IDS：interval debulking surgery

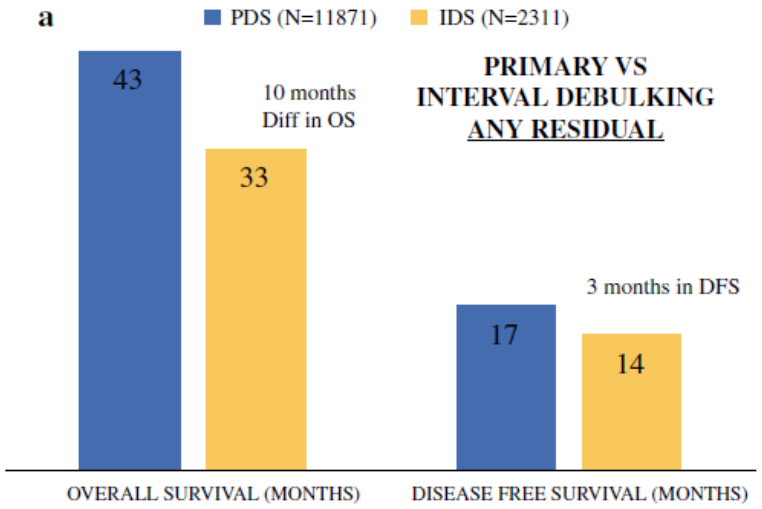
NAC＋IDSが適応される症例：
- 初回手術でoptimal surgery が困難と思われる症例
- 高齢者、全身状態が不良で初回手術が十分行えない症例
- 原発巣が摘出困難な症例
- 試験開腹

●NAC＋IDSとPDSを比較した臨床試験

試験名	報告
EORTC55971/NCIC OV13試験（対象670例）	Vergote I 2010
CHORUS試験（対象552例）	Kehoe S 2013
JCOG0602	Onda T 2008

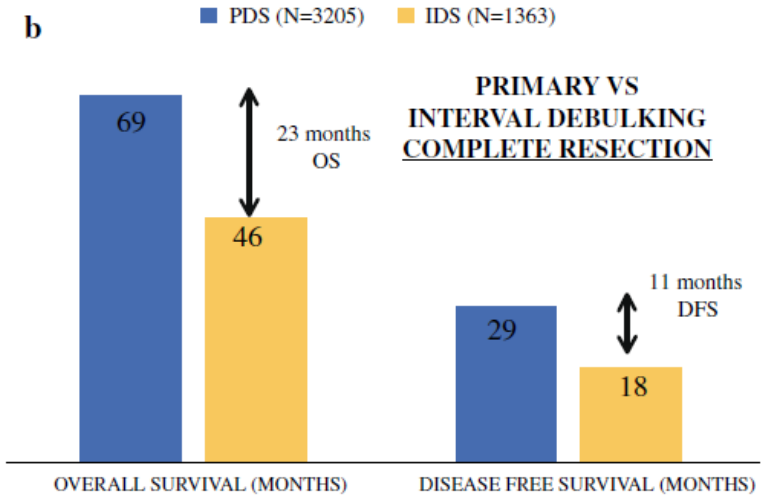
What Should We Expect After a Complete Cytoreduction at the Time of Interval or Primary Debulking Surgery in Advanced Ovarian Cancer? (FIGO stage III-IV)

Systematic Review



後方視的検討ではあるものの…
完全切除できた場合は、PDSはIDSに対して
DFS約1年、OS約2年の延長あり。

IDSでcomplete surgeryを達成しても、73%の症例にoptimal, suboptimalとなったPDS群とほぼ同等の予後。

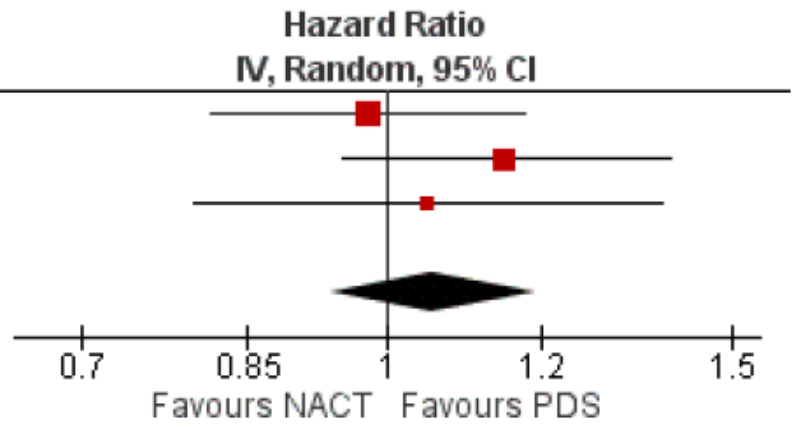


"Neoadjuvant chemotherapy is nothing but a dead-end street regarding further improvement of ovarian cancer surgery." – Du Bois

Overall Survival

Study or Subgroup	log[Hazard Ratio]	SE	Favours NACT Total	PDS Total	Weight	Hazard Ratio IV, Random, 95% CI
Vergote 2010 (1)	-0.0202	0.0937	334	336	42.3%	0.98 [0.82, 1.18]
Kehoe 2015	0.14	0.098	274	276	38.7%	1.15 [0.95, 1.39]
Onda 2016	0.05	0.14	152	149	19.0%	1.05 [0.80, 1.38]
Total (95% CI)			**760**	**761**	**100.0%**	**1.06 [0.94, 1.19]**

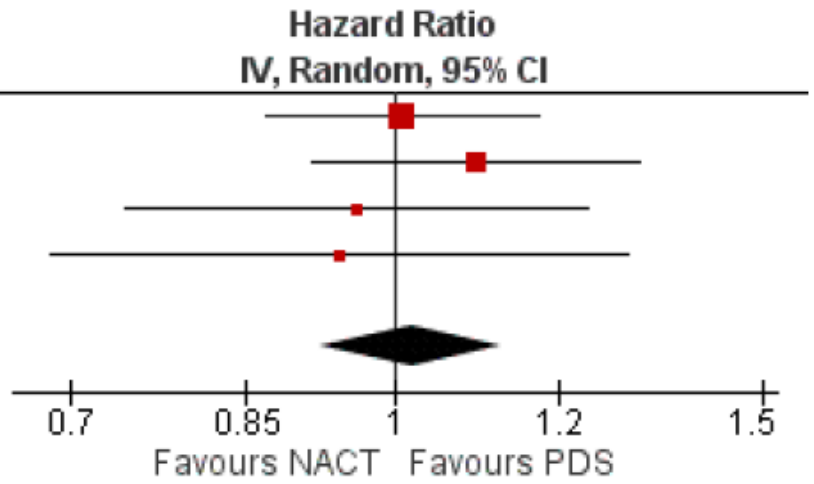
Heterogeneity: Tau² = 0.00; Chi² = 1.40, df = 2 (P = 0.50); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)



Progression Free survival

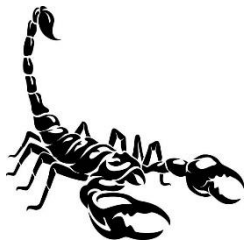
Study or Subgroup	log[Hazard Ratio]	SE	NACT Total	PDS Total	Weight	Hazard Ratio IV, Random, 95% CI	Year
Vergote 2010 (1)	0.01	0.0769	334	336	44.0%	1.01 [0.87, 1.17]	2010
Kehoe 2015 (2)	0.09	0.092	274	276	30.8%	1.09 [0.91, 1.31]	2015
Onda 2016	-0.04	0.13	152	149	15.4%	0.96 [0.74, 1.24]	2016
Fagotti 2016	-0.06	0.163	55	55	9.8%	0.94 [0.68, 1.30]	2016
Total (95% CI)			**815**	**816**	**100.0%**	**1.02 [0.92, 1.13]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 3 (P = 0.79); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.69)



PDS v.s. NAC-IDS

	EORTC	CHORUS	JCOG0602
HR (PFS)	1.01	0.91	0.99
HR (OS)	0.98	0.87	1.05
PDS complete率	19%	17%	12%
PDS optimal率	41%	41%	38%



SCORPION試験

PI score 8-12点が対象

PDS(n=84) versus NAC/IDS(n=74)

PDS群のOptimal surgery 93% (Complete surgery 48%)

PDSとNAC/IDSは同等(PFS HR:1.06, OS HR:1.12)

（ただしPDSの手術合併症率が高く（死亡率8%）、PI score 8点以上の症例にはNAC/IDSが適当。）

Does postoperative morbidity worsen the oncological outcome after radical surgery for gastrointestinal cancers? A systematic review of the literature

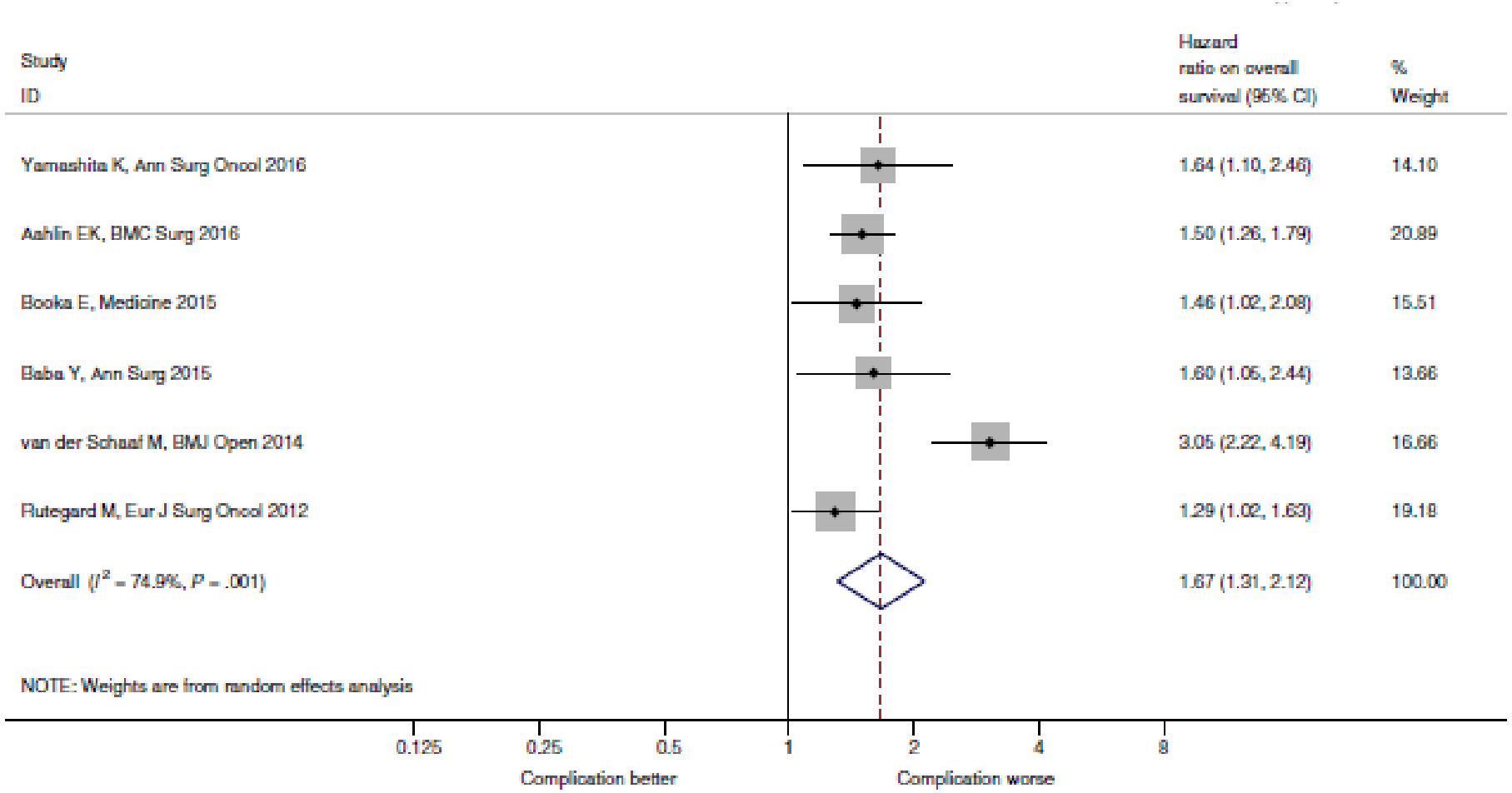


FIGURE 1 Postoperative morbidity and long-term survival after radical surgery for esophageal cancer. BMI, body mass index.

Review > Ann Thorac Cardiovasc Surg. 2005 Feb;11(1):4-6.

Surgical oncotaxis--excessive surgical stress and postoperative complications contribute to enhancing tumor metastasis, resulting in a poor prognosis for cancer patients

Toshihiro Hirai [1], Hideo Matsumoto, Kazuki Yamashita, Atsushi Urakami, Katsumichi Iki, Masahiro Yamamura, Tsukasa Tsunoda

Affiliations + expand

PMID: 15788961

Abstract

We investigated the relationship between surgical stress and tumor metastasis. The excessive surgical stress of a thoracolaparotomy enhanced tumor metastasis remarkably in an experimental model. We would like to propose that this phenomenon be termed "surgical oncotaxis". This effect has previously been attributed to some mechanisms of immunosuppression, excessive secretion of corticoids, and active oxygen production of granulocytes. An increase in lipid peroxide (LPO) in the liver was observed after a thoracolaparotomy, but a strong radical scavenger of a DL-alpha-tocopherol-L-ascorbic acid 2-0-phosphate diester (EPC-K1) restrained LPO levels in the liver and the effect of tumor metastasis in parallel. As clinical strategies for restraining the surgical oncotaxis, the control of any cytokine storm after surgery and/or the scavenging of active oxygen appears to be possible and hopeful, since it might be intermediated by cytokine. When pre-administration findings for EPC-K1 and methylpredonisolone were compared, EPC-K1 was found to be more suitable for restraining surgical oncotaxis, because serum LPO was only controlled with EPC-K1. The cytokine storm which occurs after surgery is augmented by a second stimulation, such as the administration of lipopolysaccharide, and no drug could control this well experimentally. Postoperative complications are a clinical model of a second stimulation (a so-called second attack). Our data showed the prognosis of a group with complications to be worse than that of a group without them even though no difference existed in the background of the esophageal cancer patients studied. Based on these results, safe surgery and the choice of minimally invasive surgery are the best ways to control surgical oncotaxis. Following a major surgical procedure, such as a thoracolaparotomy, the use of corticoids and/or radical scavengers can contribute to restraining surgical oncotaxis.

PDS v.s. NAC-IDS

	EORTC	CHORUS	JCOG0602
HR (PFS)	1.01	0.91	0.99
HR (OS)	0.98	0.87	1.05
PDS complete率	19%	17%	12%
PDS optimal率	41%	41%	38%

G3以上の手術合併症
- PDS群 60%
- NAC+IDS群 11%

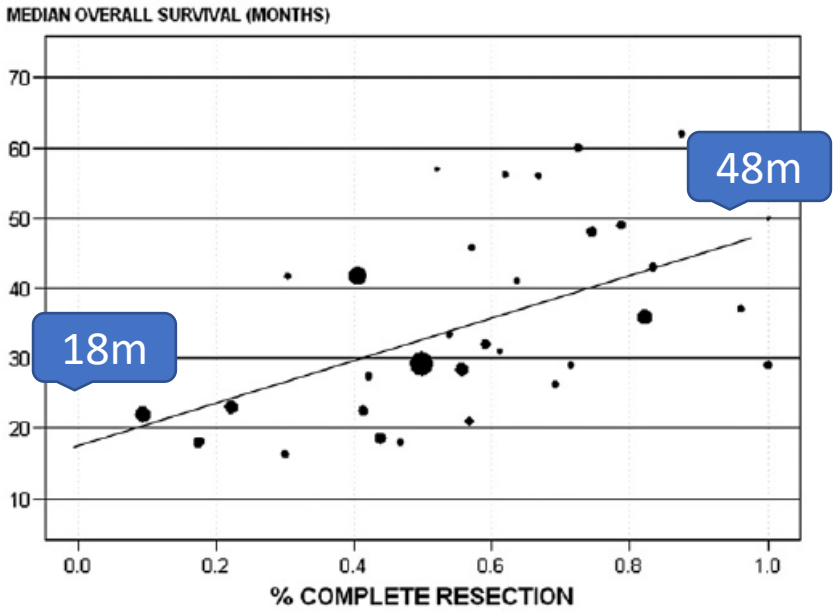
SCORPION試験
PI score 8-12点が対象
PDS(n=84) versus NAC/IDS(n=74)
PDS群のOptimal surgery 93% (Complete surgery 48%)
PDSとNAC/IDSは同等(PFS HR:1.06, OS HR:1.12)
（ただしPDSの手術合併症率が高く（死亡率8%）、PI score 8点以上の症例にはNAC/IDSが適当。）

Cytoreductive surgery for recurrent ovarian cancer: A meta-analysis

Robert E. Bristow [a,*], Isha Puri [a], Dennis S. Chi [b]

Gynecologic Oncology

www.elsevier.com/locate/ygyno



Multiple linear regression analysis of selected predictor variables versus median cohort survival time using imputed data set

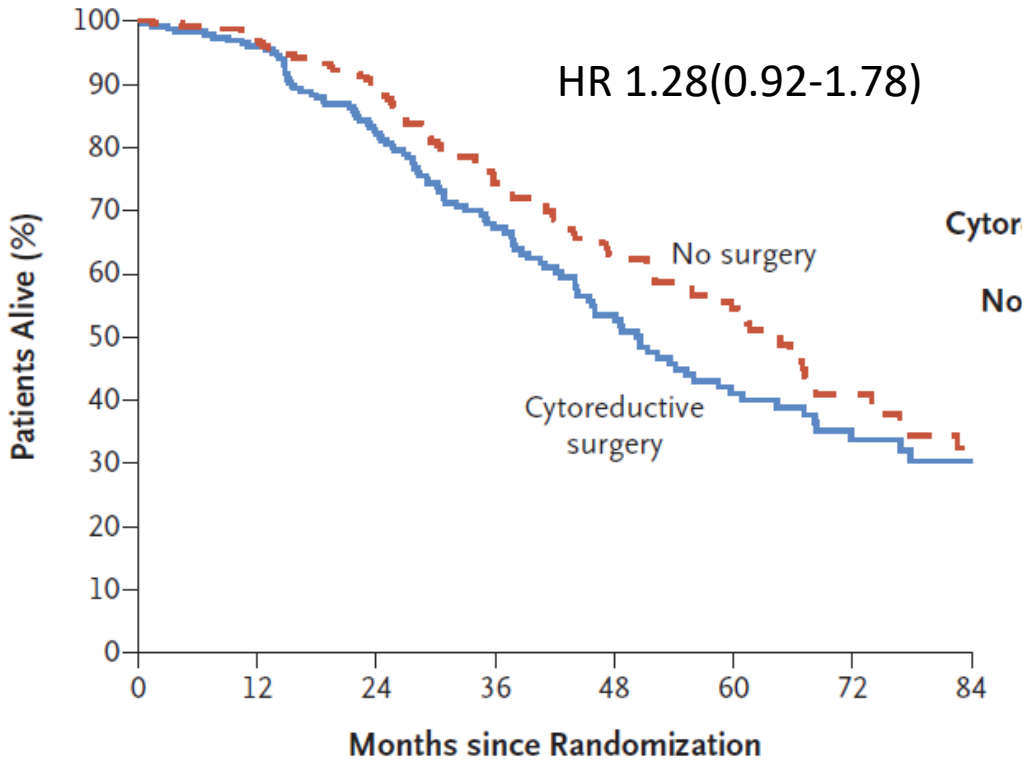
Predictor variable (incremental increase)	Change in median survival time (months)	95% confidence interval	*p*-value
Proportion complete cytoreduction (+10%)	(+) 3.00	0.50 to 5.53	0.02
Year of publication (+1 year)	(+) 1.00	0.26 to 1.77	0.01
Study accrual interval (+1 month)	(+) 0.0007	(−) 0.09 to 0.087	0.98
Median cohort age (+1 year)	(−) 0.55	(−) 1.84 to 0.725	0.39
Proportion surgery before chemotherapy (+10%)	(+) 0.43	(−) 1.64 to 2.51	0.66
Proportion serous histology (+10%)	(+) 1.09	(−) 4.29 to 6.47	0.68
Proportion grade 3 tumor (+10%)	(+) 0.43	(−) 2.92 to 3.79	0.79
Proportion localized disease (+10%)	(−) 1.16	(−) 3.33 to 1.003	0.28
Proportion bowel resection (+10%)	(+) 0.83	(−) 1.97 to 3.64	0.56

Three large, multicenter, randomized, phase 3 trials
—the DESKTOP III (NCT01166737), GOG-0213 (NCT00565851) and the SOC-1 trial (NCT01611766)—
were designed to evaluate SCS followed by platinum-based chemotherapy in patients with platinum sensitive recurrent ovarian cancer.

Secondary Surgical Cytoreduction for Recurrent Ovarian Cancer

GOG213

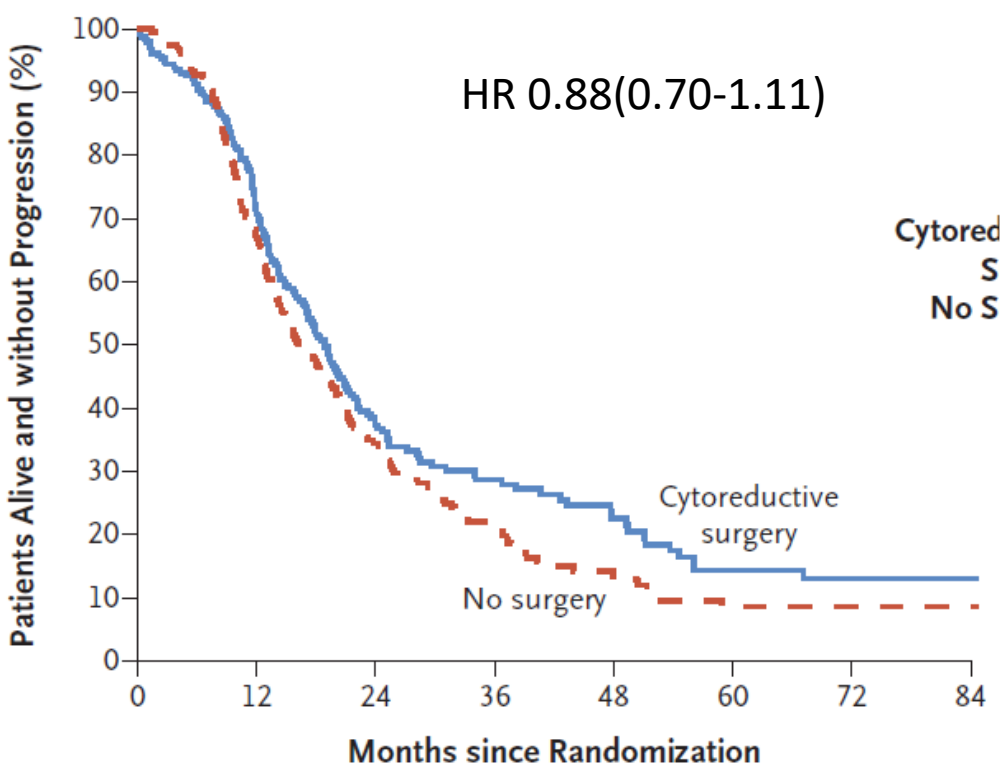
A Overall Survival



HR 1.28(0.92-1.78)

No. at Risk								
Cytoreductive surgery	240	205	157	98	67	41	23	14
No surgery	245	217	172	124	75	50	28	16

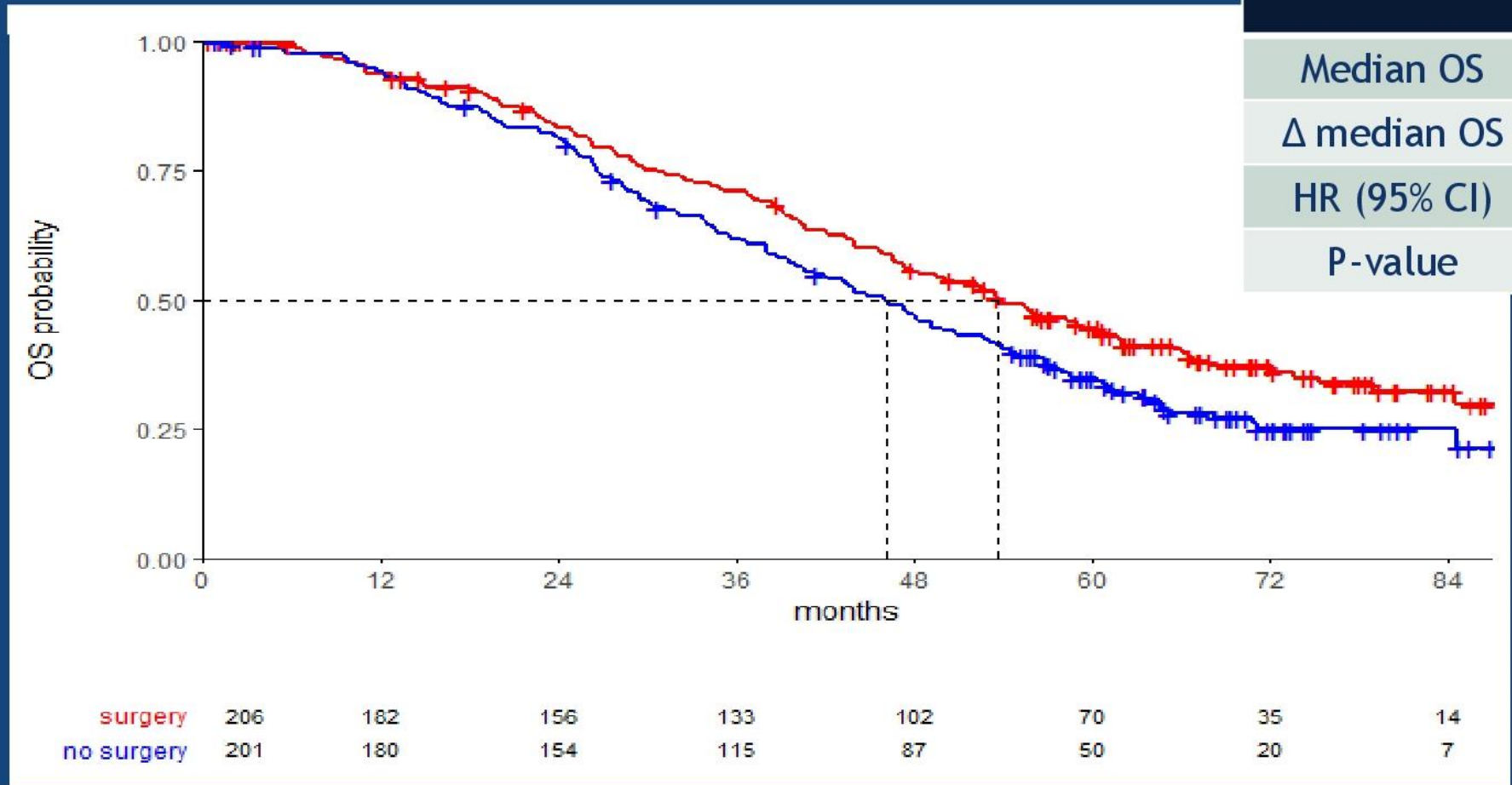
B Progression-free Survival



HR 0.88(0.70-1.11)

No. at Risk								
Cytoreductive surgery	240	152	68	38	22	13	10	6
No surgery	245	153	68	36	19	8	6	5

AGO DESKTOP III: Outcome 1 (OS, ITT population)
(AGO–OVAR OP.4; ENGOT-ov20; NCT01166737)

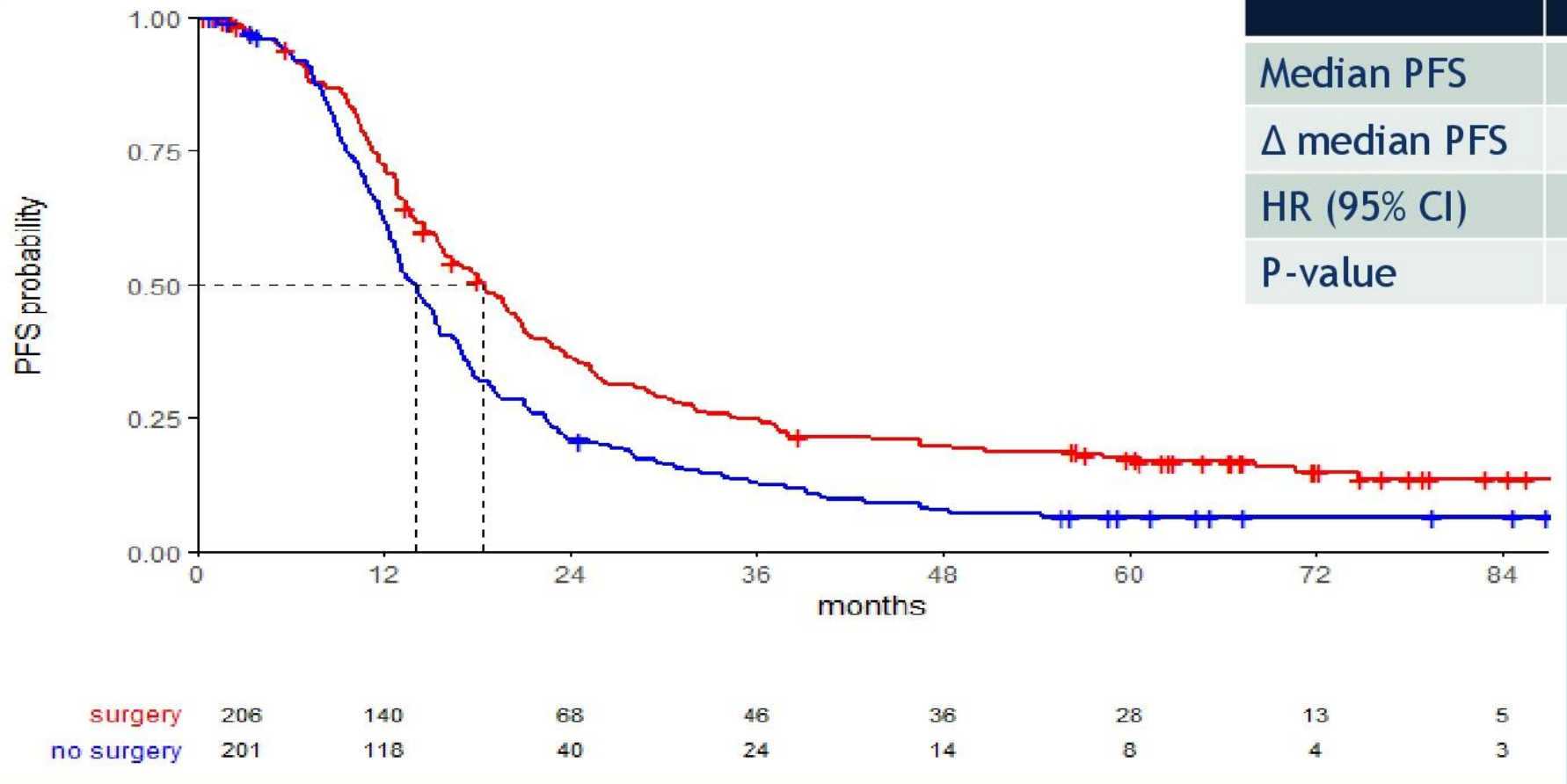


	surgery	no surgery
Median OS	53.7 mos	46.0 mos
Δ median OS	**7.7 mos**	
HR (95% CI)	**0.75** (0.58 - 0.96)	
P-value	**0.02**	

PRESENTED BY: Andreas du Bois
AGO & KEM Essen, Germany

AGO DESKTOP III: Outcome 2 (PFS, ITT population, after DB closure Jan 17th 2020)

(AGO–OVAR OP.4; ENGOT-ov20; NCT01166737)



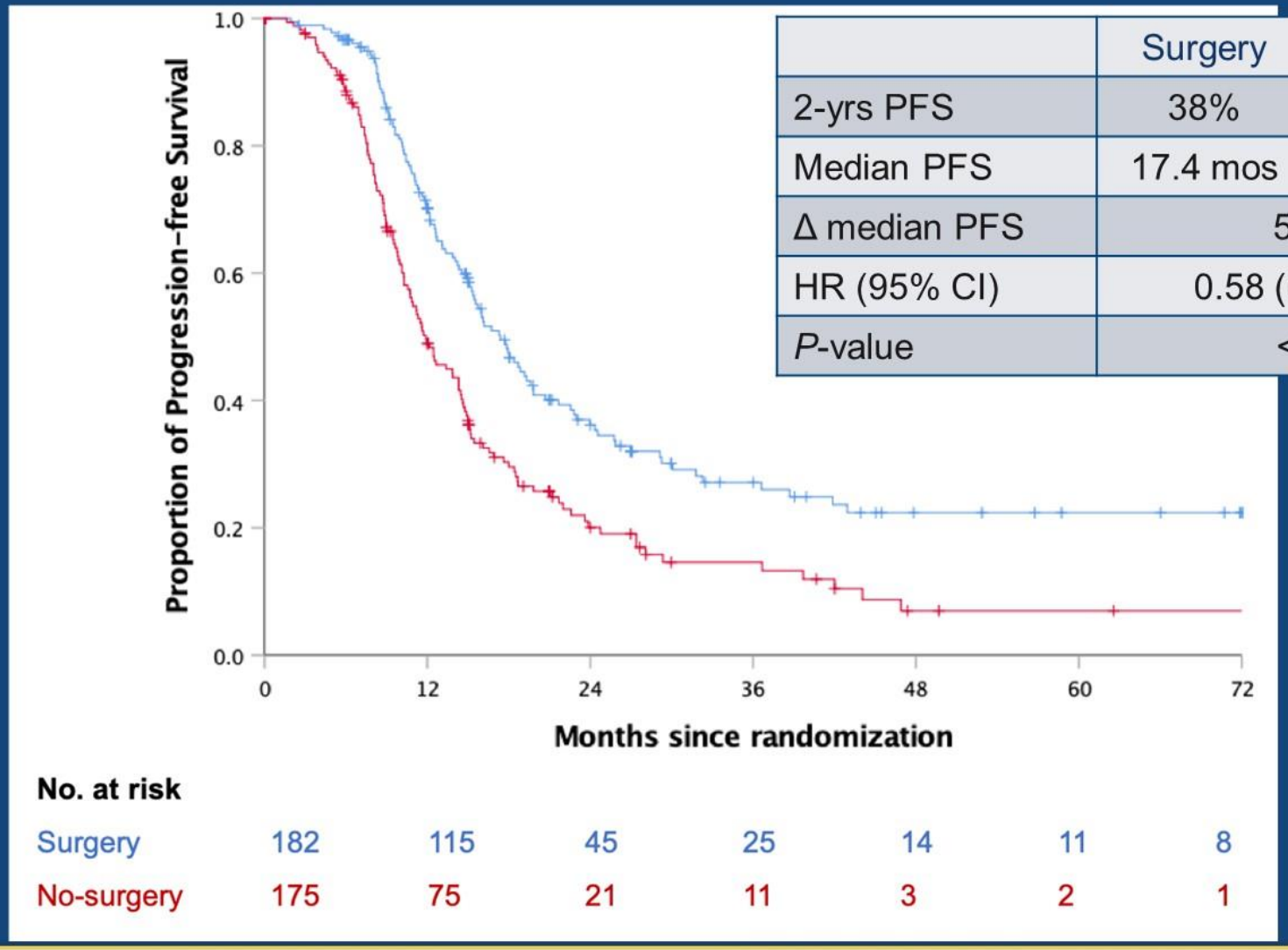
	surgery	no surgery
Median PFS	18.4 mos	14.0 mos
Δ median PFS	4.4 mos	
HR (95% CI)	0.66 (0.54 - 0.82)	
P-value	< 0.001	

PRESENTED BY: Andreas du Bois
AGO & KEM Essen, Germany

Secondary cytoreduction followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1): a multicentre, open-label, randomised, phase 3 trial

Tingyan Shi, Jianqing Zhu*, Yanling Feng, Dongsheng Tu, Yuqin Zhang, Ping Zhang, Huixun Jia, Xiao Huang, Yunlang Cai, Sheng Yin, Rong Jiang, Wenjuan Tian, Wen Gao, Jihong Liu, Huijuan Yang, Xi Cheng, Rongyu Zang*

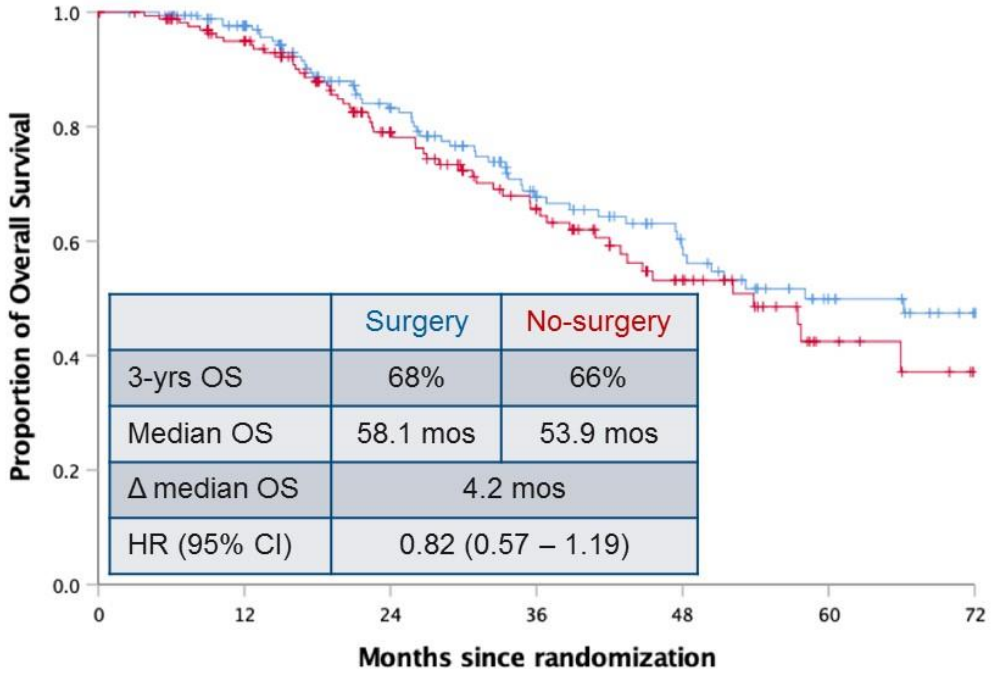
SGOG SOC-1 : Co-Primary Endpoint -PFS



	Surgery	No-surgery
2-yrs PFS	38%	22%
Median PFS	17.4 mos	11.9 mos
Δ median PFS	5.5 mos	
HR (95% CI)	0.58 (0.45 – 0.74)	
P-value	< 0.001	

SOC-1: Interim Analyses of OS and TFSa

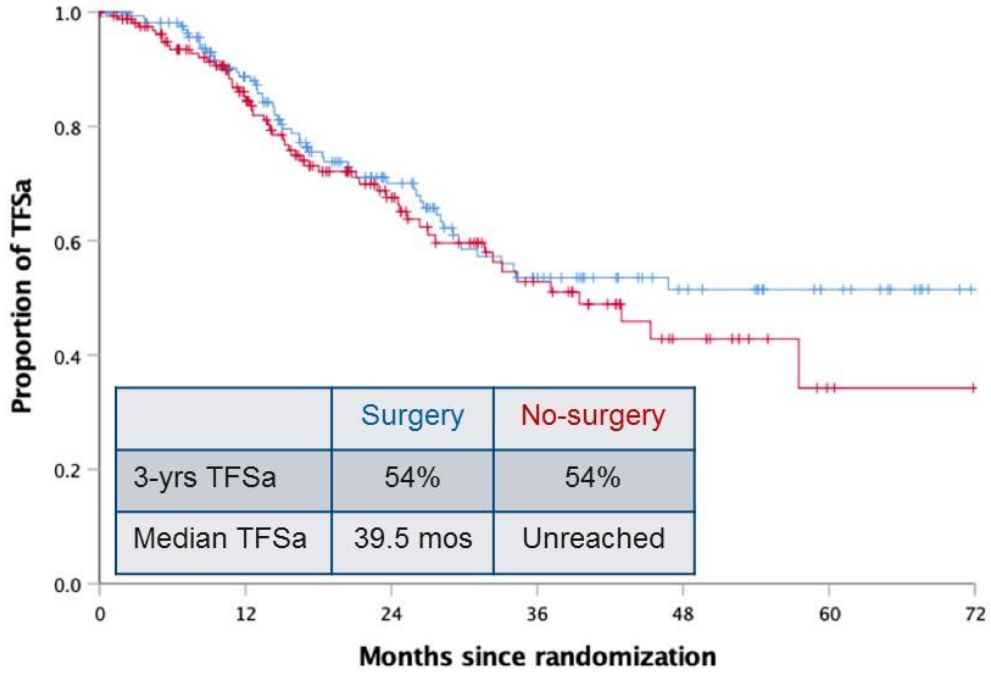
Co-Primary Endpoint -OS



	Surgery	No-surgery
3-yrs OS	68%	66%
Median OS	58.1 mos	53.9 mos
Δ median OS	4.2 mos	
HR (95% CI)	0.82 (0.57 – 1.19)	

No. at risk							
Surgery	182	157	105	64	42	24	13
No-surgery	175	145	89	56	31	10	3

TFSa



	Surgery	No-surgery
3-yrs TFSa	54%	54%
Median TFSa	39.5 mos	Unreached

No. at risk							
Surgery	179	120	68	40	24	15	4
No-surgery	167	107	56	29	11	2	0

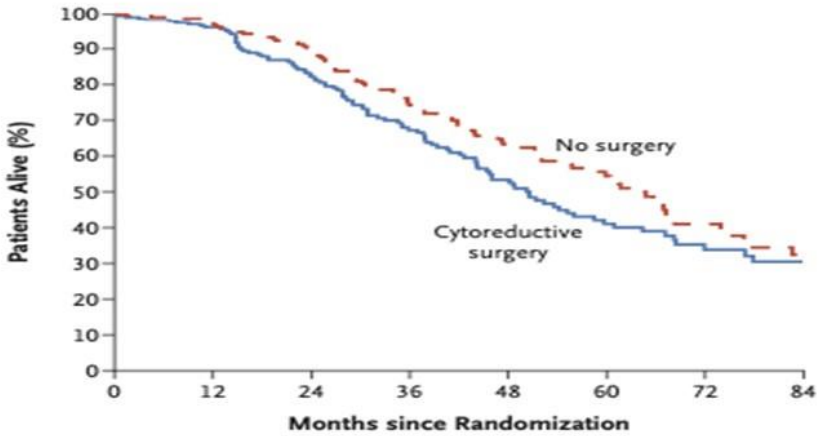
PRESENTED BY: Rongyu Zang MD, PhD
SGOG/Fudan University Zhongshan Hospital

TFSa: accumulating treatment free survival

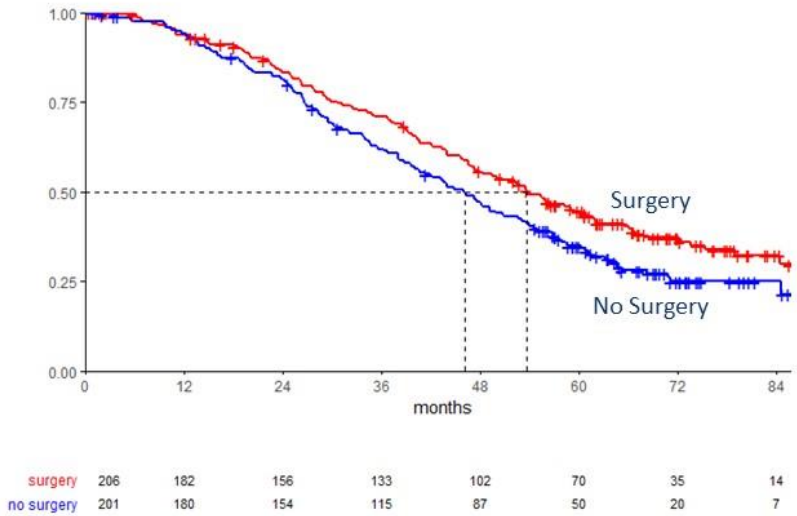
GOG-213, DESKTOP III and SOC-1 Comparison: OS

	GOG-213	AGO Desktop III	SGOG SOC-1
OS – Surgery (median)	53.6 mos	53.7 mos	58.1 mos
OS - No Surgery (median)	**65.7 mos**	46.0 mos	53.9 mos
HR, 95% CI	1.28 (0.92-1.78) **P = NS**	0.75 (0.58-0.96) **P = 0.04**	0.82 (0.57-1.19) **P = NS**

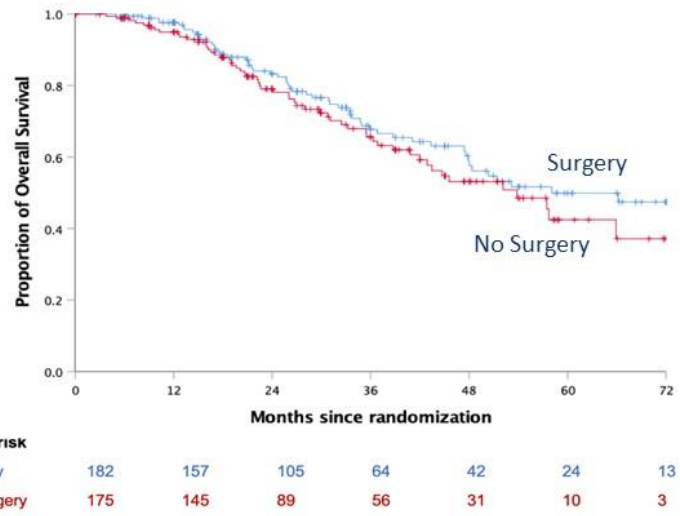
GOG-213



DESKTOP III

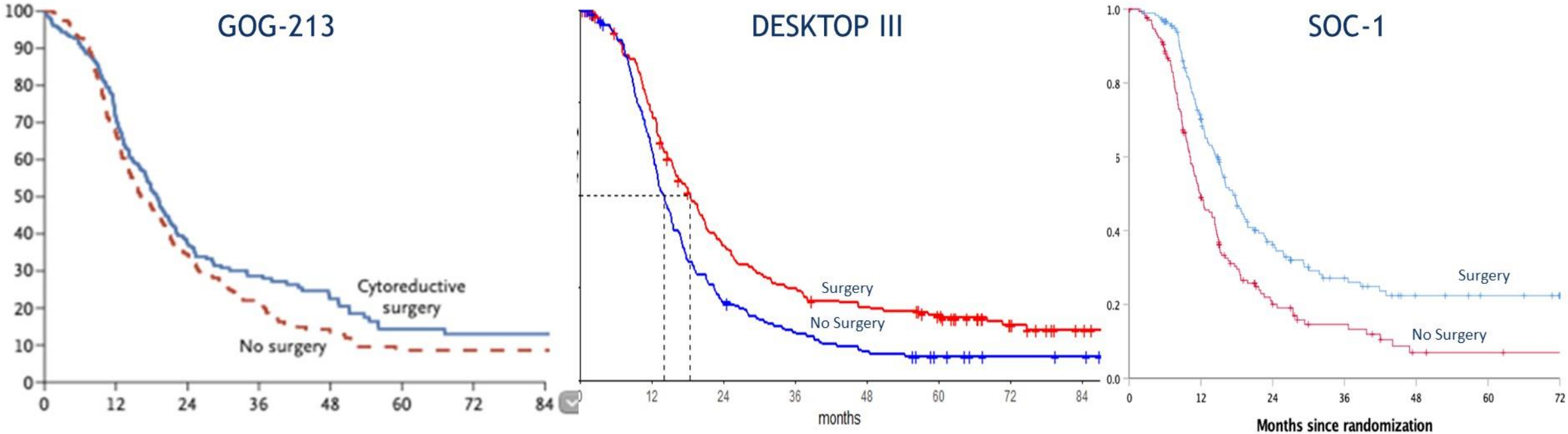


SOC-1



GOG-213, DESKTOP III and SOC-1 Comparison: PFS

	GOG-213	AGO Desktop III	SGOG SOC-1
PFS - Surgery (median)	18.2 mos	18.4 mos	17.4 mos
PFS - No Surgery (median)	**16.5 mos**	14.0 mos	11.9 mos
HR, 95% CI	0.88 (0.70-1.11)	0.66 (0.54-0.82)	0.58 (0.45-0.74) **P < 0.001**



GOG-213, DESKTOP III and SOC-1 Comparison

	GOG-213	AGO Desktop III	SGOG SOC-1
Complete Response to primary Platinum-based chemotherapy	Yes	Yes	Yes
Platinum-free Interval	> 6 months (67%)	> 6 months (75%)	> 6 months (76.7%)
Prior lines of Therapy allowed	**1**	**1**	**1**
Surgical Candidacy	Investigator	AGO Criteria	iMODEL < 4.7
Goal of surgery	CGR	CGR	CGR
Adjuvant Therapy	Platinum Combination	Platinum Combination	Platinum Combination
Maintenance	Allowed	Allowed	Allowed
Mortality	30-day: 0.4%	90-day: 0.5%	60-day: 0%
Subsequent Surgery in Control Arm after Relapse	NA	11.0%	36.9%
Platinum-based Combination Therapy	100%	89%	? (100%)
The 2nd line bevacizumab	**84%**	23%	1%
The 2nd line PARPi maintenance	NA	<5%	10%

Guidelines and Selection Criteria for Secondary Cytoreductive Surgery in Patients with Recurrent, Platinum-Sensitive Epithelial Ovarian Carcinoma

MSK criteria

Recommendation for Secondary Cytoreduction Based on Disease-free Interval, the Number of Recurrence Sites, and Evidence of Carcinomatosis

DFI	Single Site	Multiple Sites: No Carcinomatosis	Carcinomatosis
6–12 Mo	Offer SC	Consider SC	No SC
12–30 Mo	Offer SC	Offer SC	Consider SC
>30 Mo	Offer SC	Offer SC	Offer SC

DFI: disease-free interval; Mo: months; SC: secondary cytoreduction.

A Risk Model for Secondary Cytoreductive Surgery in Recurrent Ovarian Cancer: An Evidence-Based Proposal for Patient Selection

iMODEL

TABLE 4 Risk model for secondary cytoreductive surgery in patients with recurrent ovarian cancer based on the international collaborative cohort

Impact factors	Scoring[a]					
	0	0.8	1.5	1.8	2.4	3.0
FIGO stage	I/II	III/IV				
RD after primary surgery[b]	0		>0			
PFI (months)	≥16				<16	
ECOG performance status[b]	0–1				2–3	
CA125 at recurrence (U/ml)	≤105			>105		
Ascites at recurrence[b]	Absent					Present

FIGO International Federation of Gynecology and Obstetrics, *RD* residual disease, *PFI* Progression-free interval, *ECOG* Eastern Cooperative Oncology Group

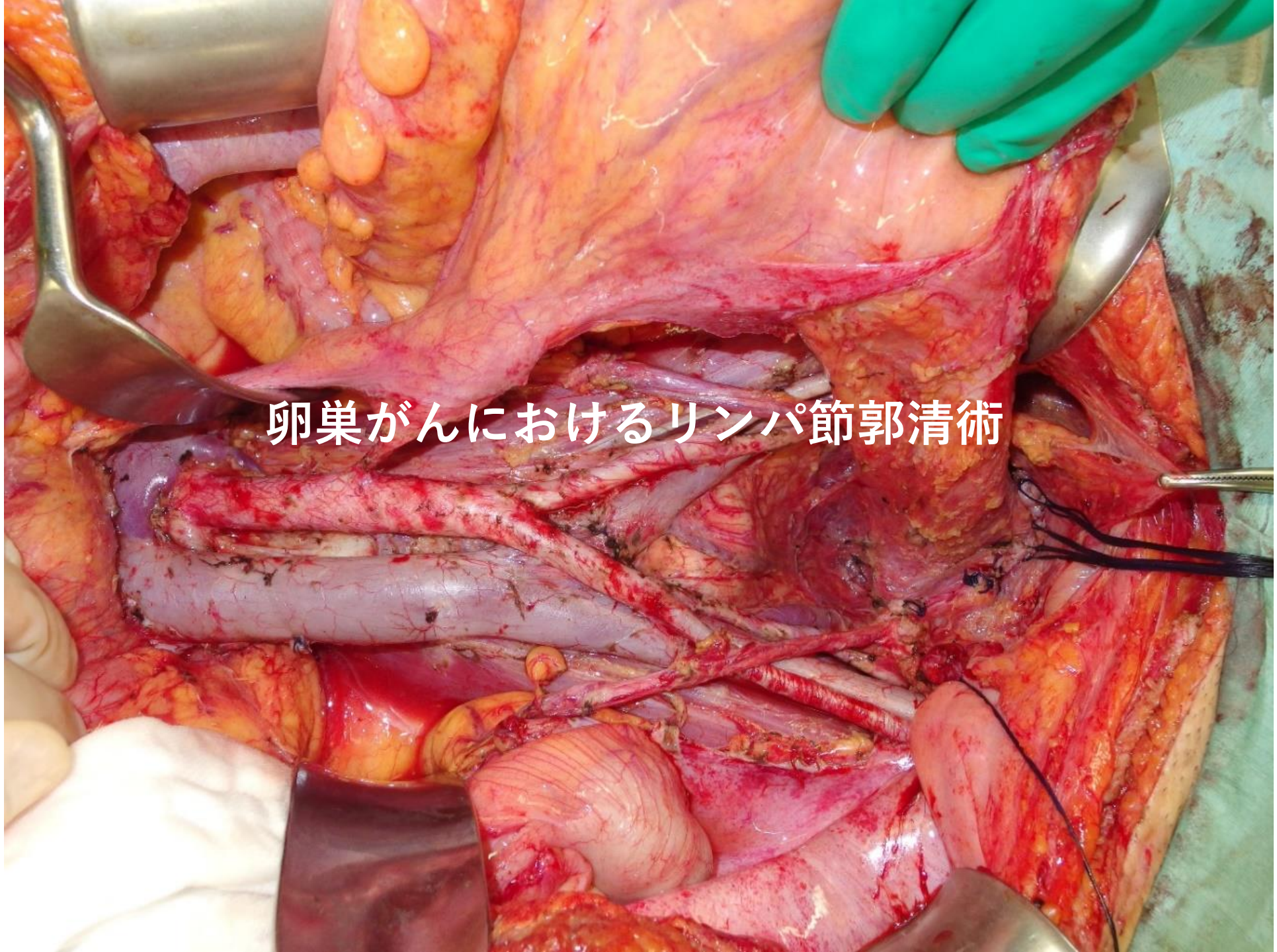
[a] Low-risk: ≤4.7; high-risk: >4.7

[b] The Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) score system

AGOscore

i) good performance status
ii) ascites less than 500 mL
iii) CGR at primary debulking surgery

The accuracy in prediction was 49% for the AGO score, 86% for MSK criteria, and 88% for the iMODEL


卵巣がんにおけるリンパ節郭清術

Design: LION

Pre-operative In/exclusion criteria

Registration at least one day prior to surgery

Intra-operative randomisation if:

- Epithelial ovarian cancer
- FIGO IIB-IV
- Macroscopic complete resection
- No contra-indication to LNE
- Absence of „bulky“ nodes

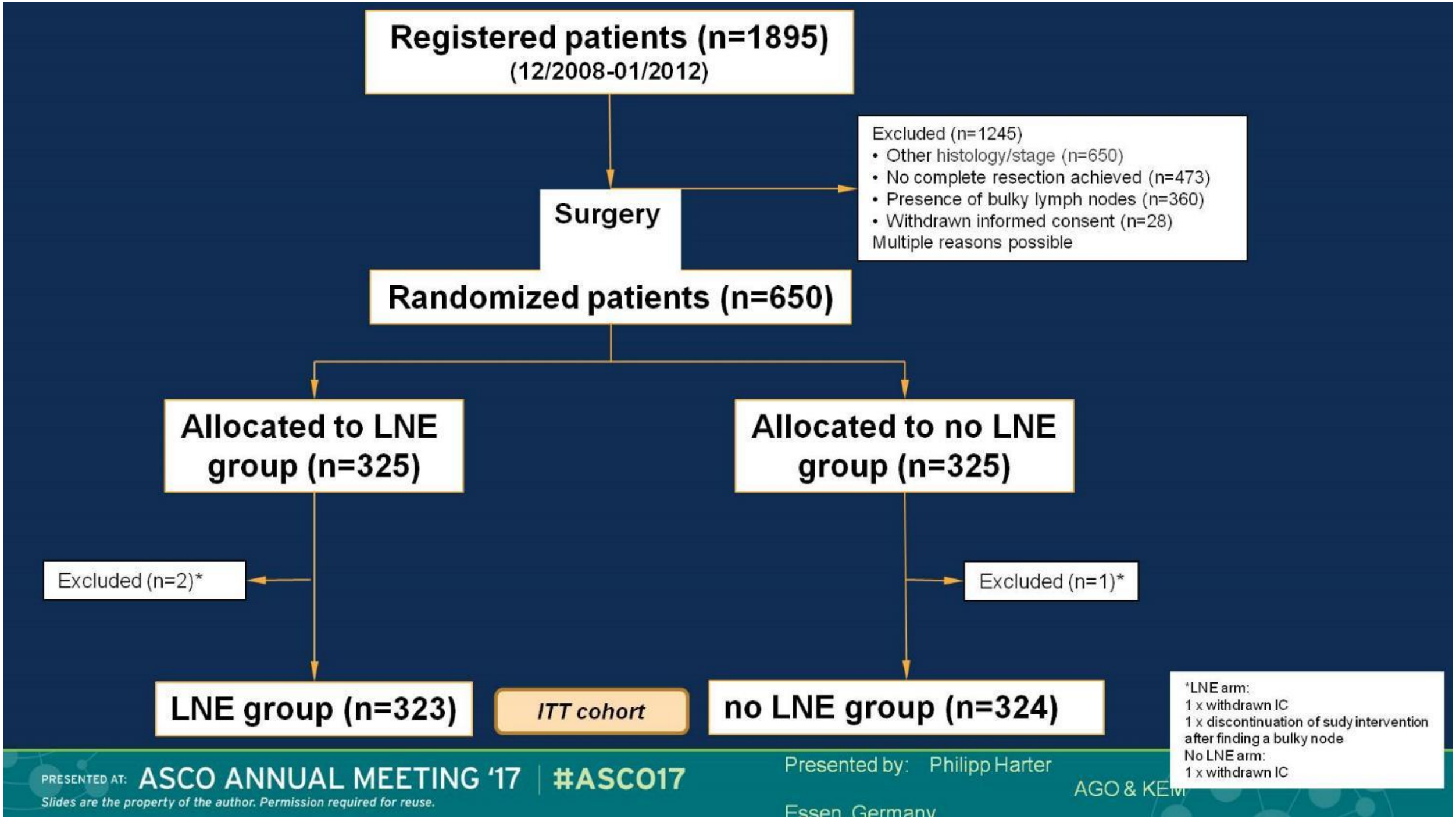
Randomization (n=640)

Systematic pelvic and para-aortic lymphadenectomy

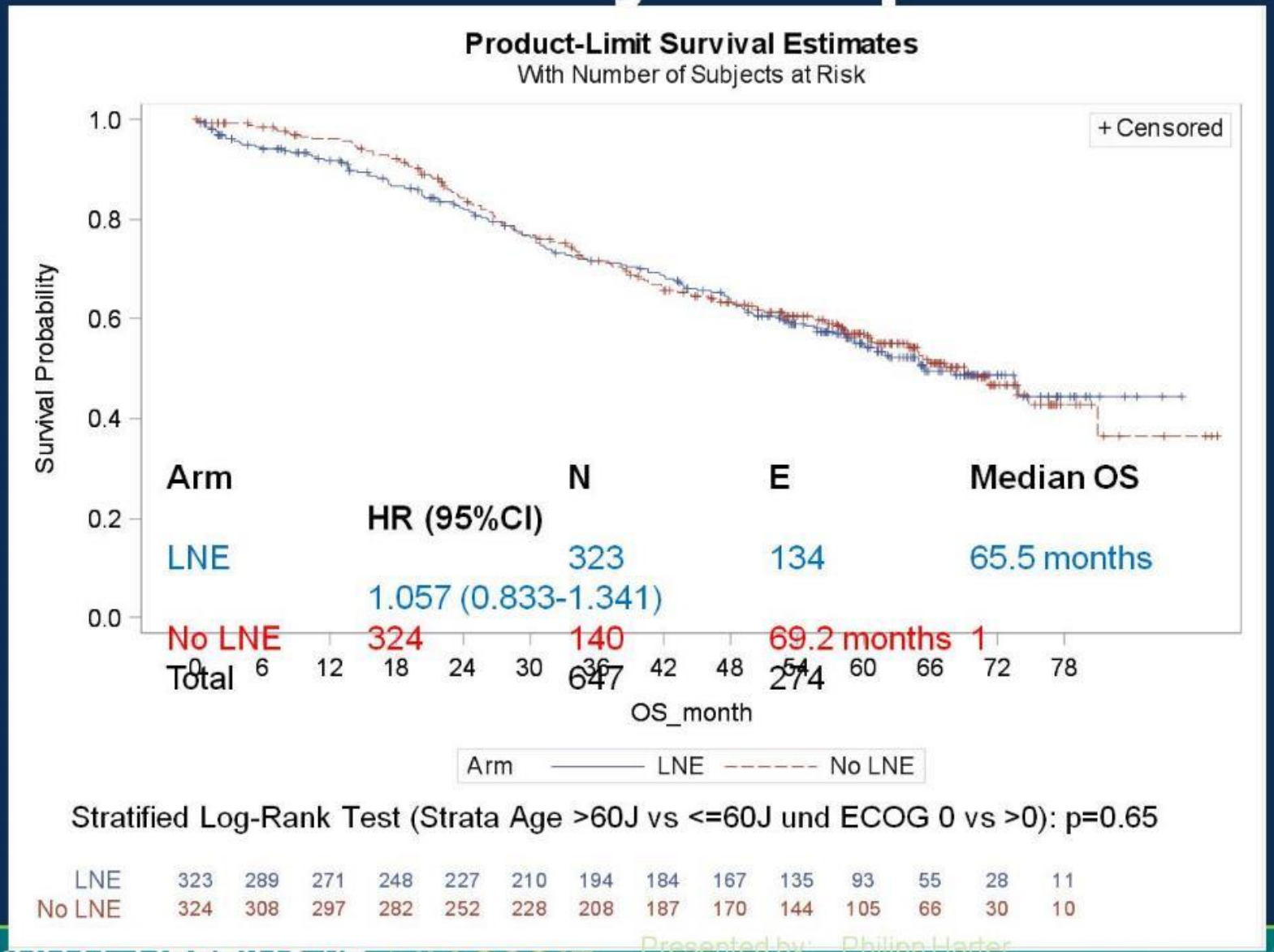
No lymphadenectomy

Strata:
- Center
- Age
- PS ECOG

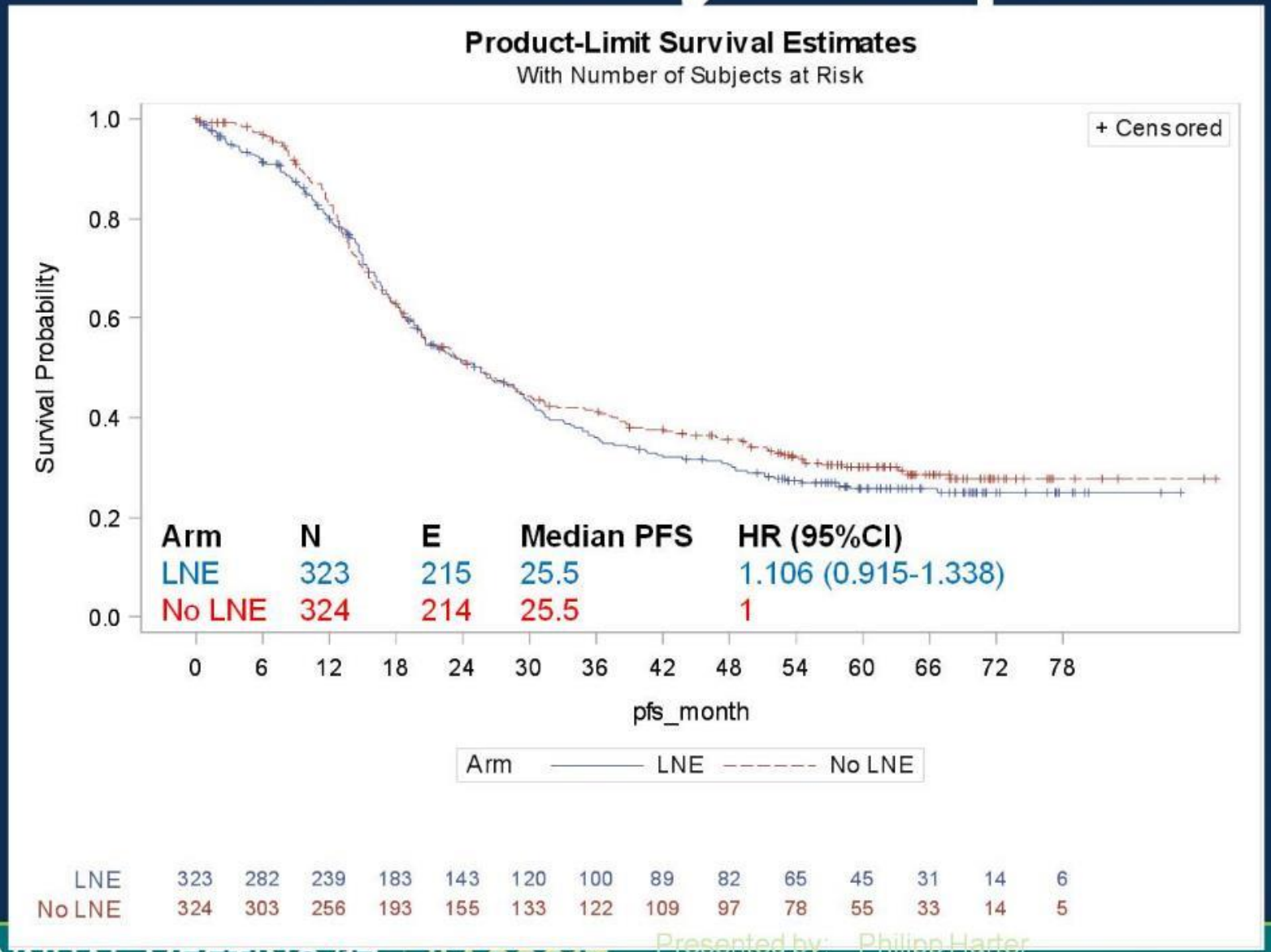
Presented by: Philipp Harter
Essen, Germany
AGO & KEM



LION: Primary endpoint OS



LION: Secondary endpoint PFS



LION: Conclusions

- Patients with complete resection during upfront surgery and treated in quality assured centres have an excellent prognosis (median OS ~ 67.2 months; median PFS ~ 25.5 months)
- Systematic pelvic and para-aortic LNE in patients with advanced ovarian cancer with both intra-abdominal complete resection and clinically negative LN neither improve overall nor progression-free survival

  ….despite detecting (and removing) sub-clinical retroperitoneal lymph node metastases in 56% of patients.
- Our data indicate that systematic LNE of clinical negative LN in patients with advanced ovarian cancer and complete resection should be omitted.

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