# Updates in Advanced Ovarian Cancer Care

Dr. Kais Razzouk, Pr. Rafii Arash, Dr Justine Cagnat

Institut du Sein
NICE SANTA MARIA

Weill Cornell
Medicine-Qatar

# **What** is Ovarian Cancer?

- The most common type of Ovarian Cancer that starts from <u>epithelial cells –gland forming cells</u>
  - **Adenocarcinoma ***

    * Other common adenocarcinomas are found in the breast, colon, lung, prostate, uterus, sometimes cervix

- Other types of Ovarian Cancer start in the:
  - "eggs"(germ cell tumors)
  - body of the Ovary (stromal tumors)

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

# **Who** develops Ovarian Adenocarcinoma?

- **15%  Genetic Susceptibility known genetic susceptibility**
  - BRCA 1 / 2,  HNPCC
  - Lifetime risk up to 50% of developing Ovarian Cancer

- **85% *spontaneous somatic mutation***
  - *Lifetime risk < 2% of developing Ovarian Cancer*

Institut du Sein
NICE SANTA MARIA

Weill Cornell
Medicine-Qatar

# How do we treat Ovarian Cancer?

- Current Approach -- **Surgery and Chemotherapy**
  - ***Primary Tumor Reductive Surgery (PDS)***
    - **Surgery** → Chemotherapy
  - ***Neoadjuvant Chemotherapy (NACT)***
    - **Chemotherapy** →Surgery →Chemotherapy

  - Goal of Surgery →remove all visible disease
  - Goal of Chemotherapy →kill all cancer cells

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

- The objectives of surgery in early stages are standardized and easy to meet

- In the recent years, survival of **advanced ovarian** cancer has substantially improved –

  - median overall survival **47 months**
  - combination of chemotherapy and COMPLETE surgery

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

# BACK TO BASICS


1- Why DEBULKING Surgery?

2- What is DEDULKING Surgery

3- Lymphadenectomy?

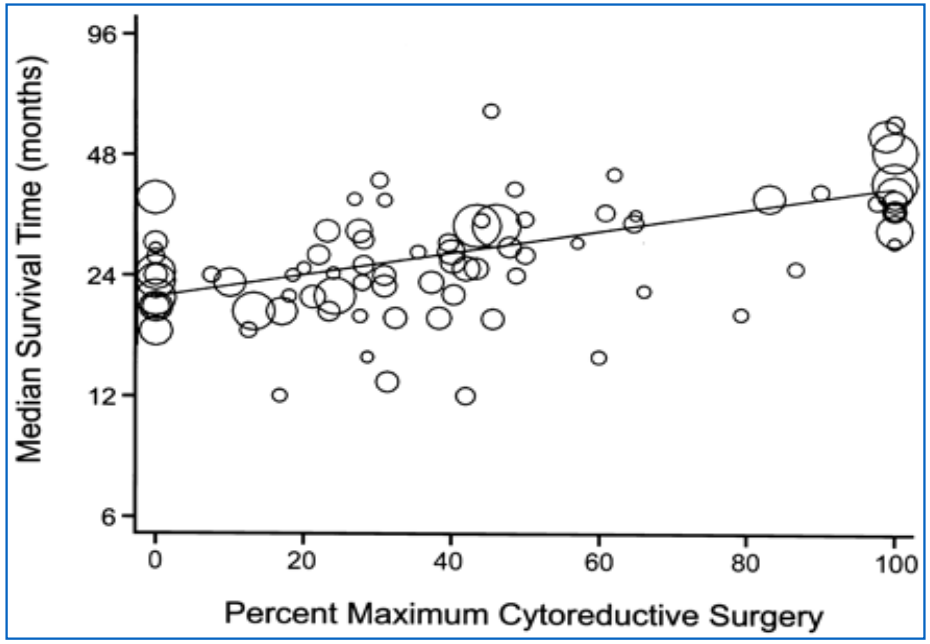
4- HIPEC?

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

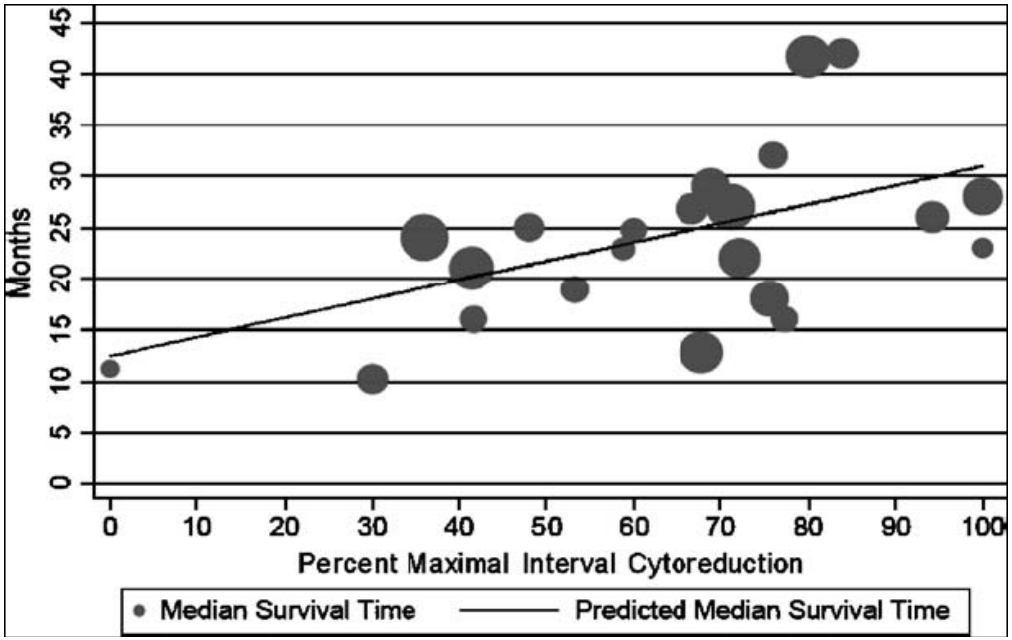
# 1. Complete surgery is a mainstay of therapy

**Every 10% increase of « optimal » surgery increases DFS by 2 months**




*81 studies, 6885 patients - JCO 2002*

**Bristow's Metanalyses**



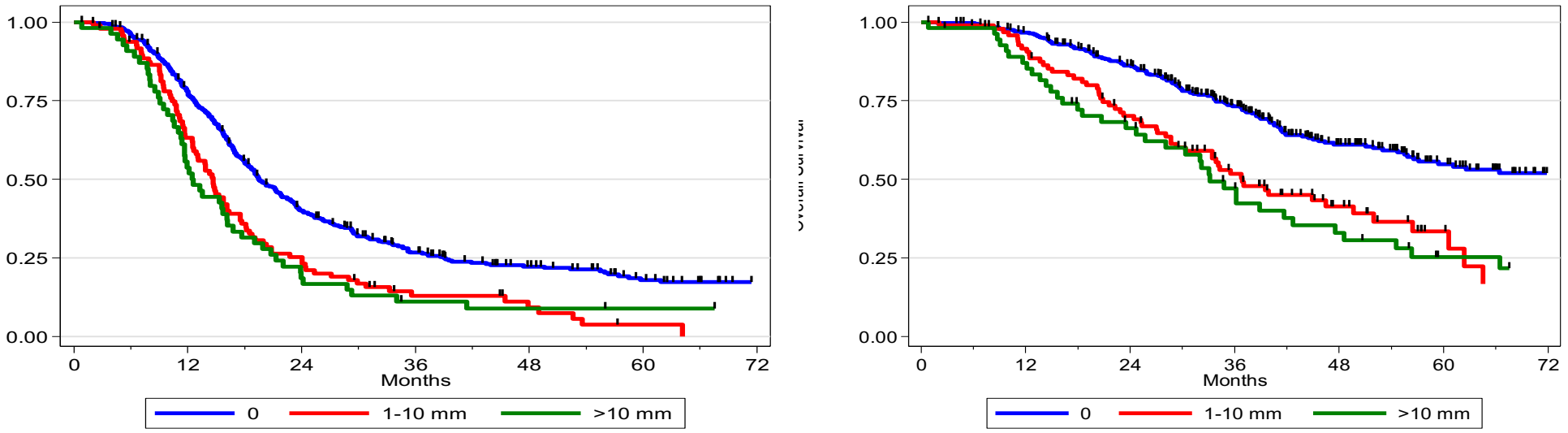

*22 studies, 835 patients - Gynecol Oncol 2006*

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

# 1. Complete surgery is a mainstay of therapy

*International Journal of Gynecological Cancer* • Volume 22, Number 8, October 2012




**527 French patients**
**Consistent with literature**

Institut du Sein
NICE SANTA MARIA

Weill Cornell
Medicine-Qatar

# 2.The issue of operative complications : the 2010 French survey

**Patients**

82% had neoadjuvant chemotherapy

Complete cytoreduction : 82%

Average duration of surgery : 270 minutes

Procedures :

- péritonectomy 81%
- **bowel resection 68%** including

55% sigmoidectomy

28% major upper abdominal surgery (splenectomy,pancreatectomy, full thickness diaphragm resection, glissonectomy)

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

# 2.The issue of operative complications : the 2010 French survey

**Results**

Transitory colostomy 12%

Blood loss over 1000 ml  25% (94-3000)

Average ICU stay 4 days
Average hospital stay 10 days - 14% were still admitted at 30 days

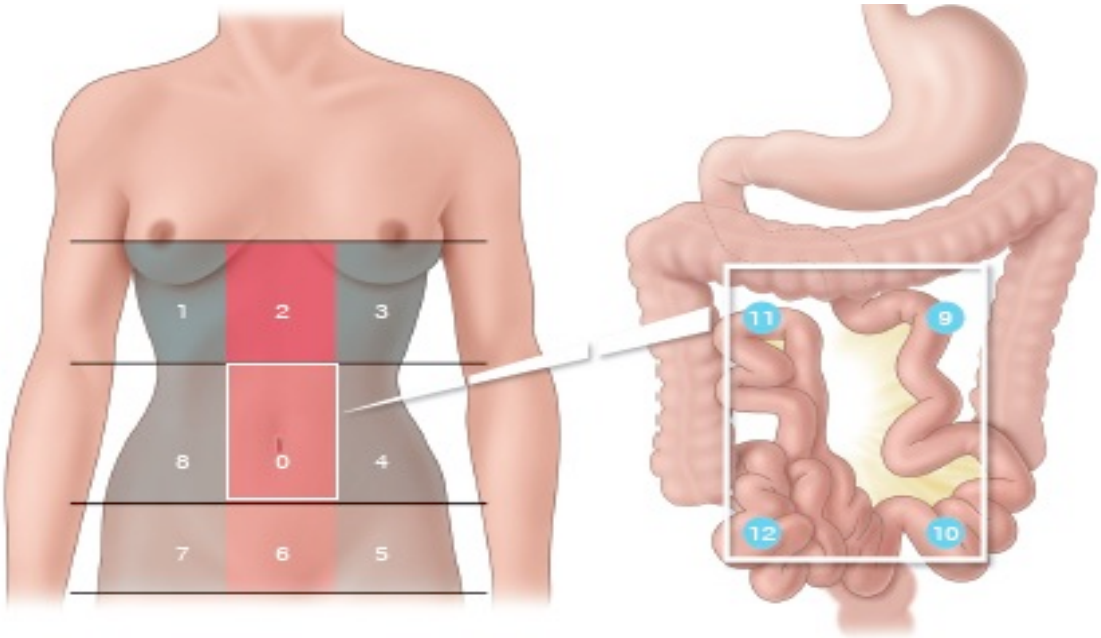
45% had no complication
40% had grade 1 or 2 complications.
**15% had grade  3 or more complications**, including 2 deaths (1,6%).

10 reoperations (4 for bleeding, 6 for bowel complication)
1 urinary fistula
4 pulmonary embolisms

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

# 3. What is complete resection?




**Stadification coelioscopique première**

Préparer la patiente

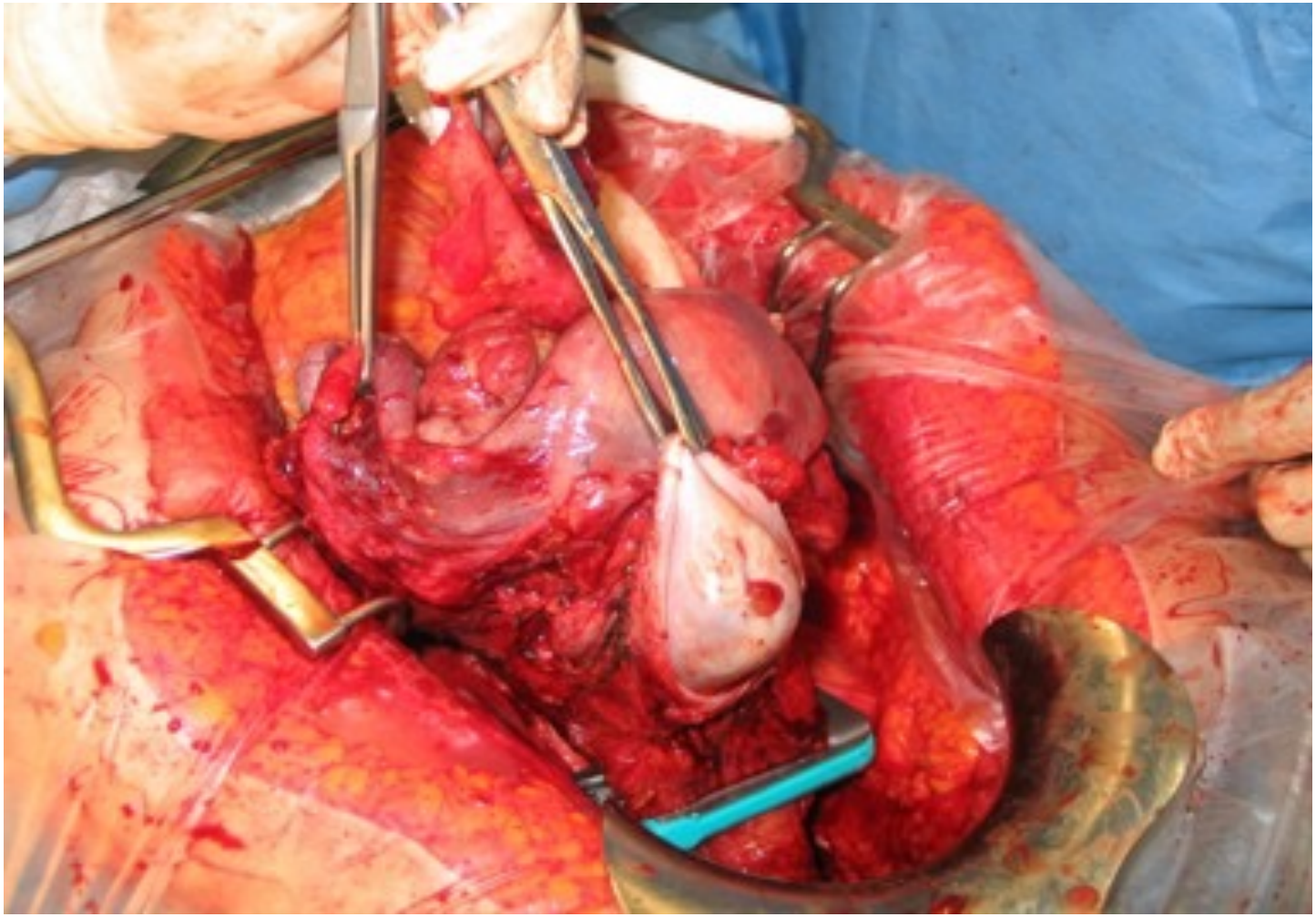
Préparer l'équipe

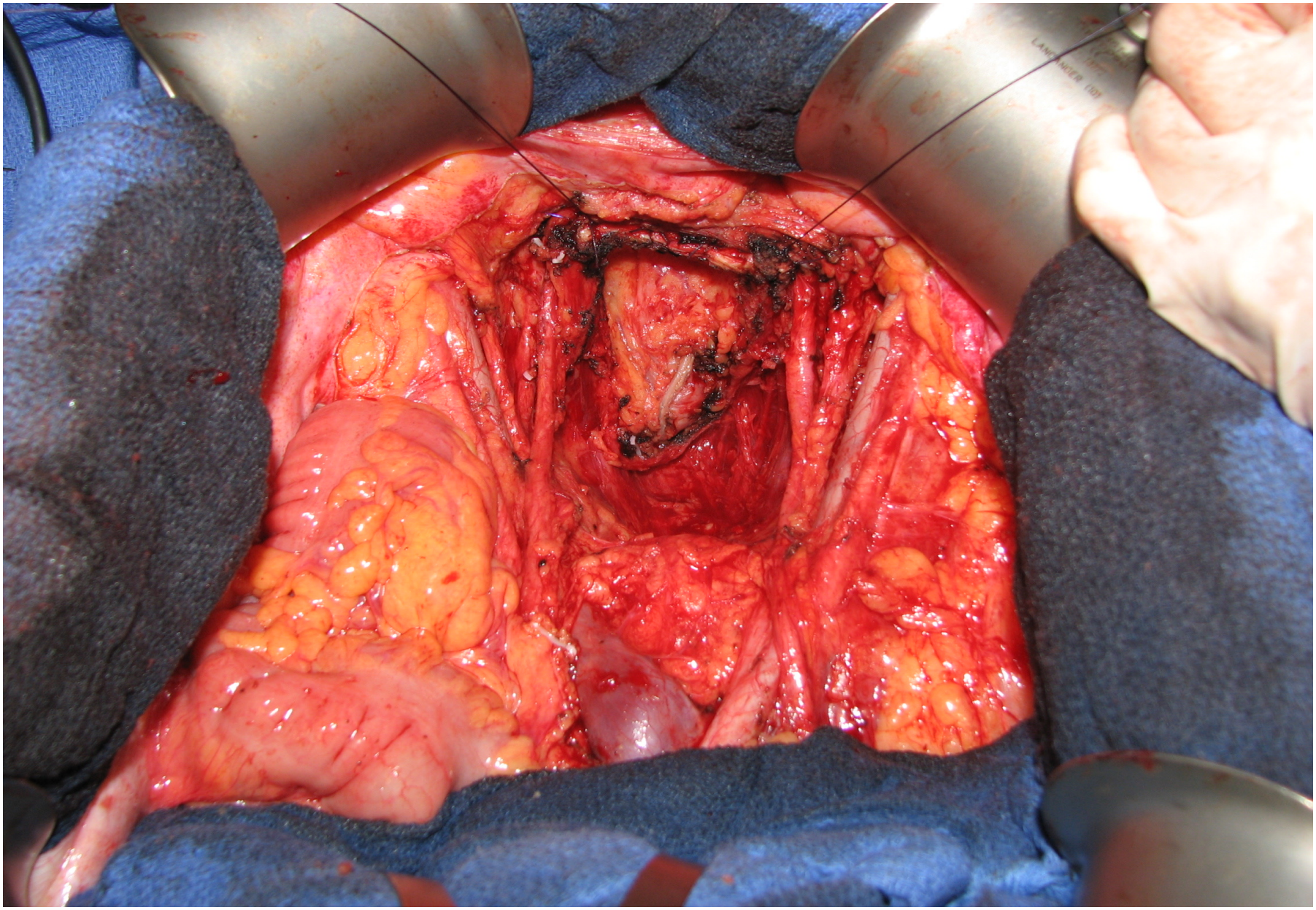
**PCI**

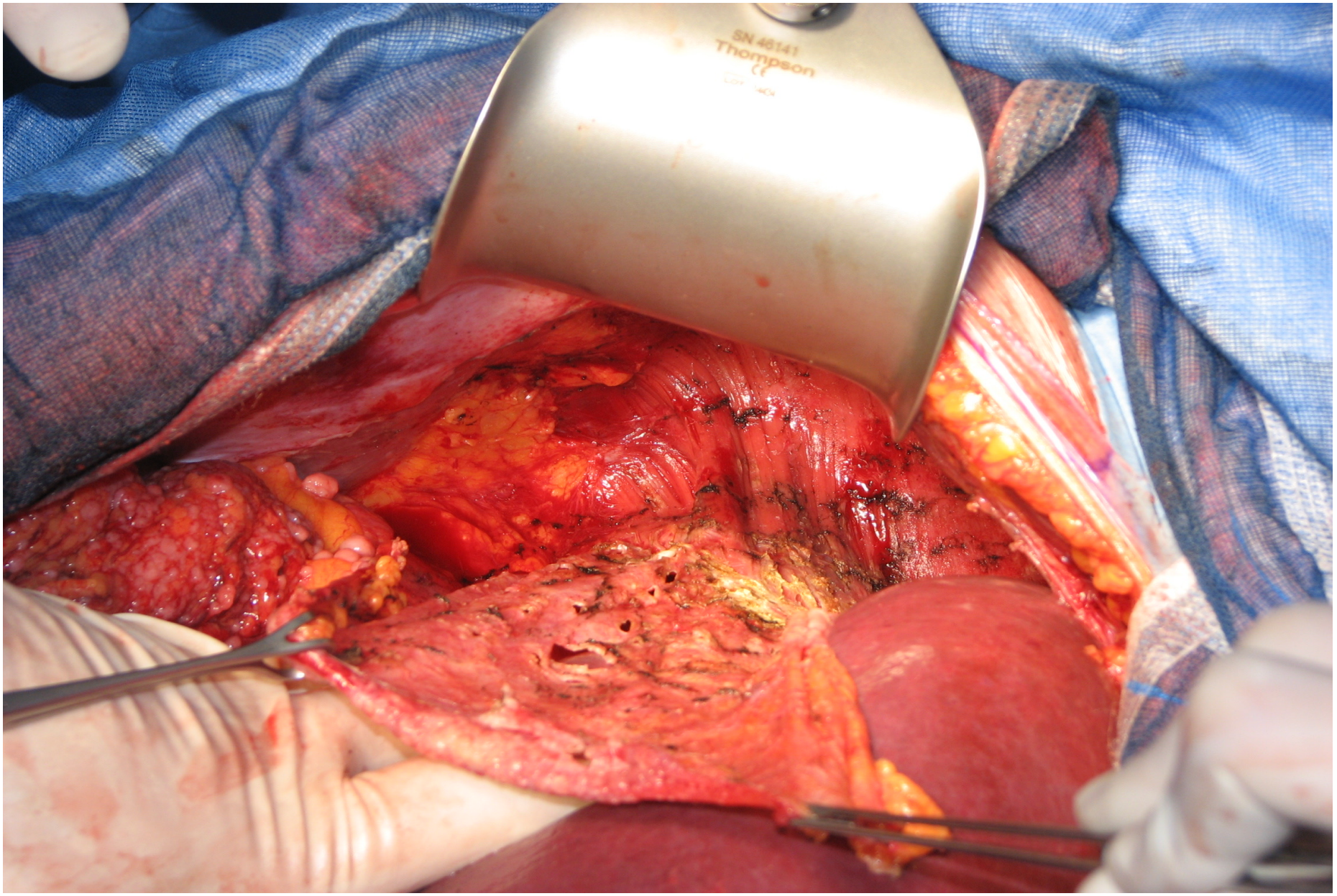
Institut du Sein
NICE SANTA MARIA

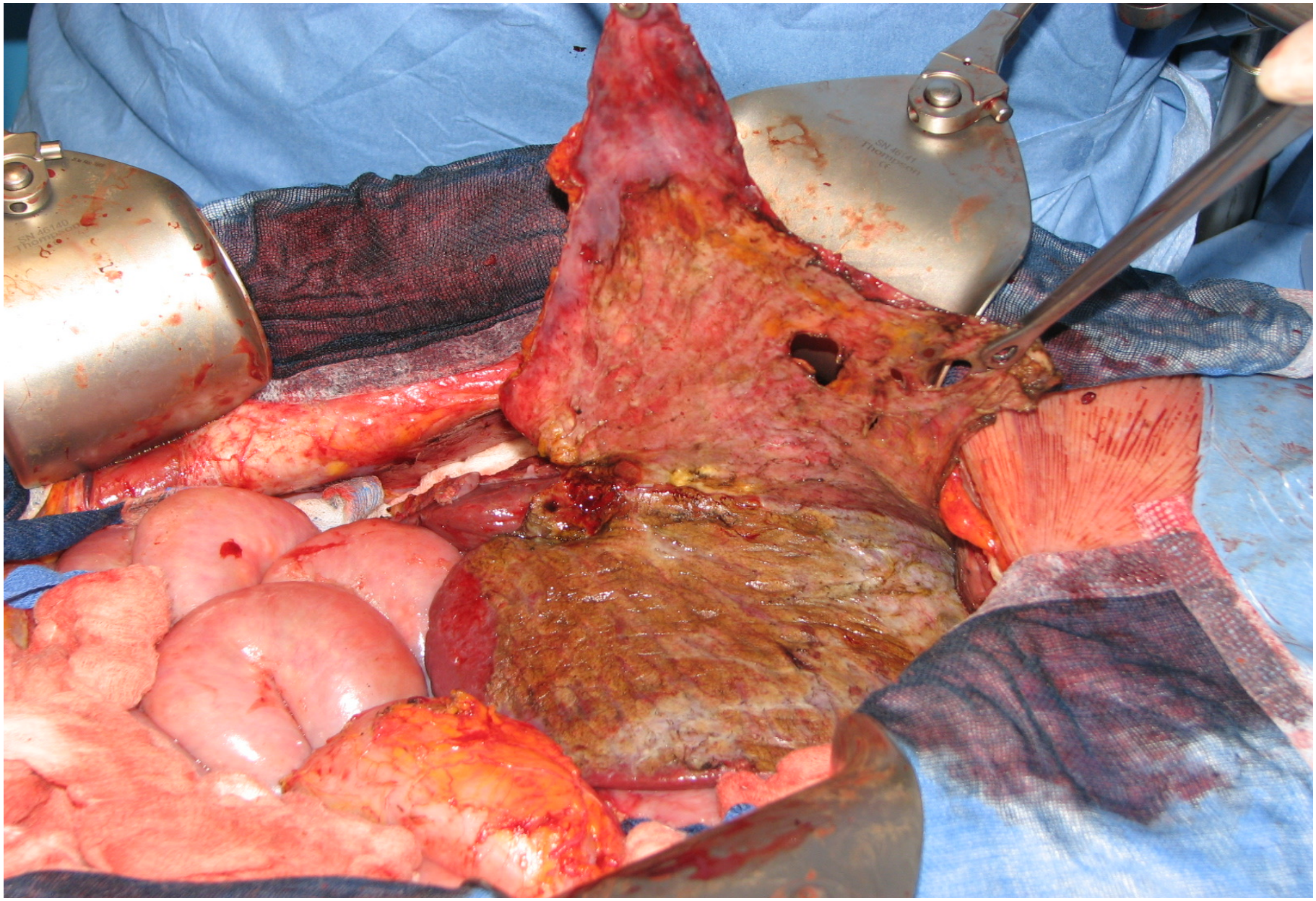
Weill Cornell Medicine-Qatar

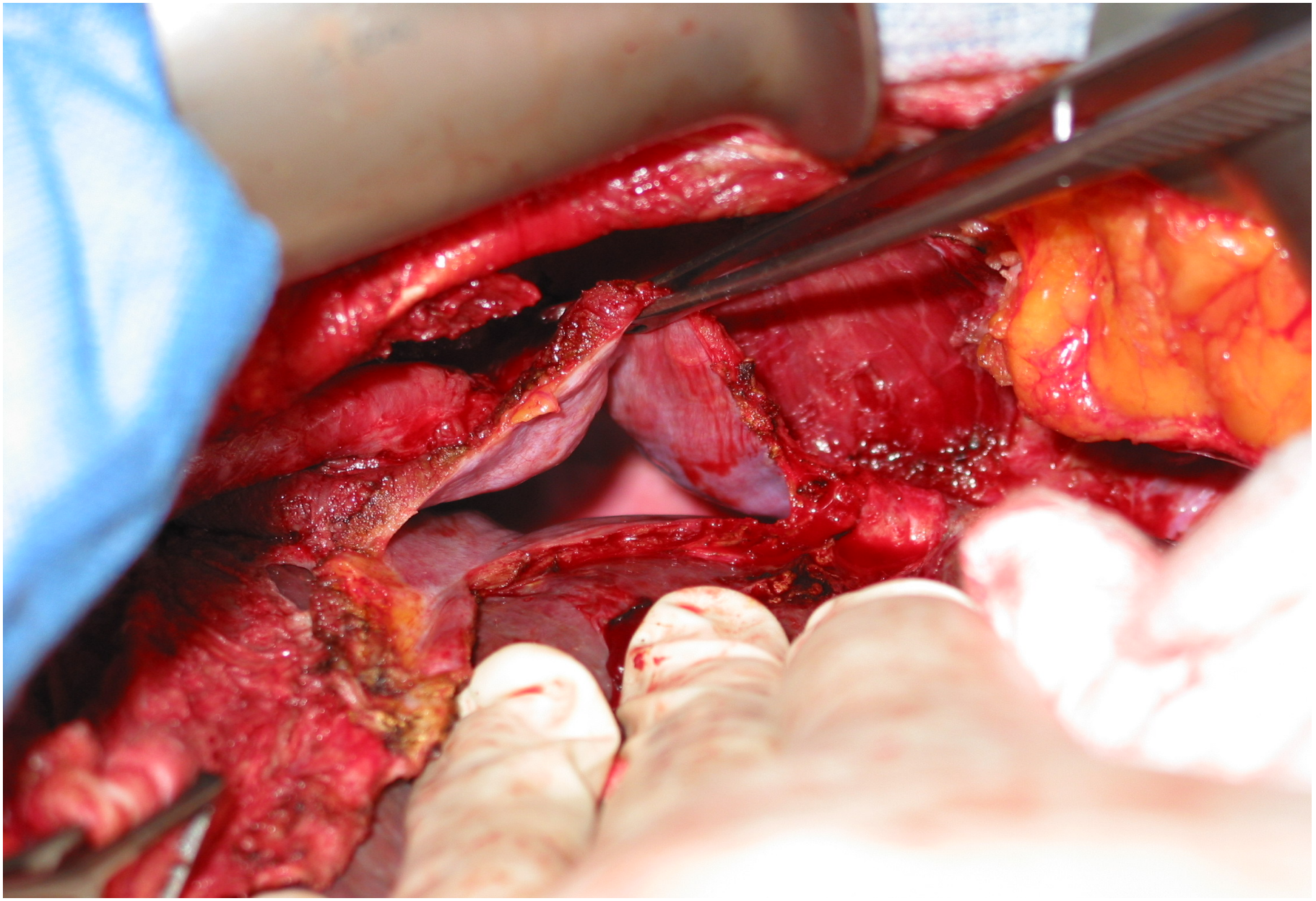
3. What is complete resection?

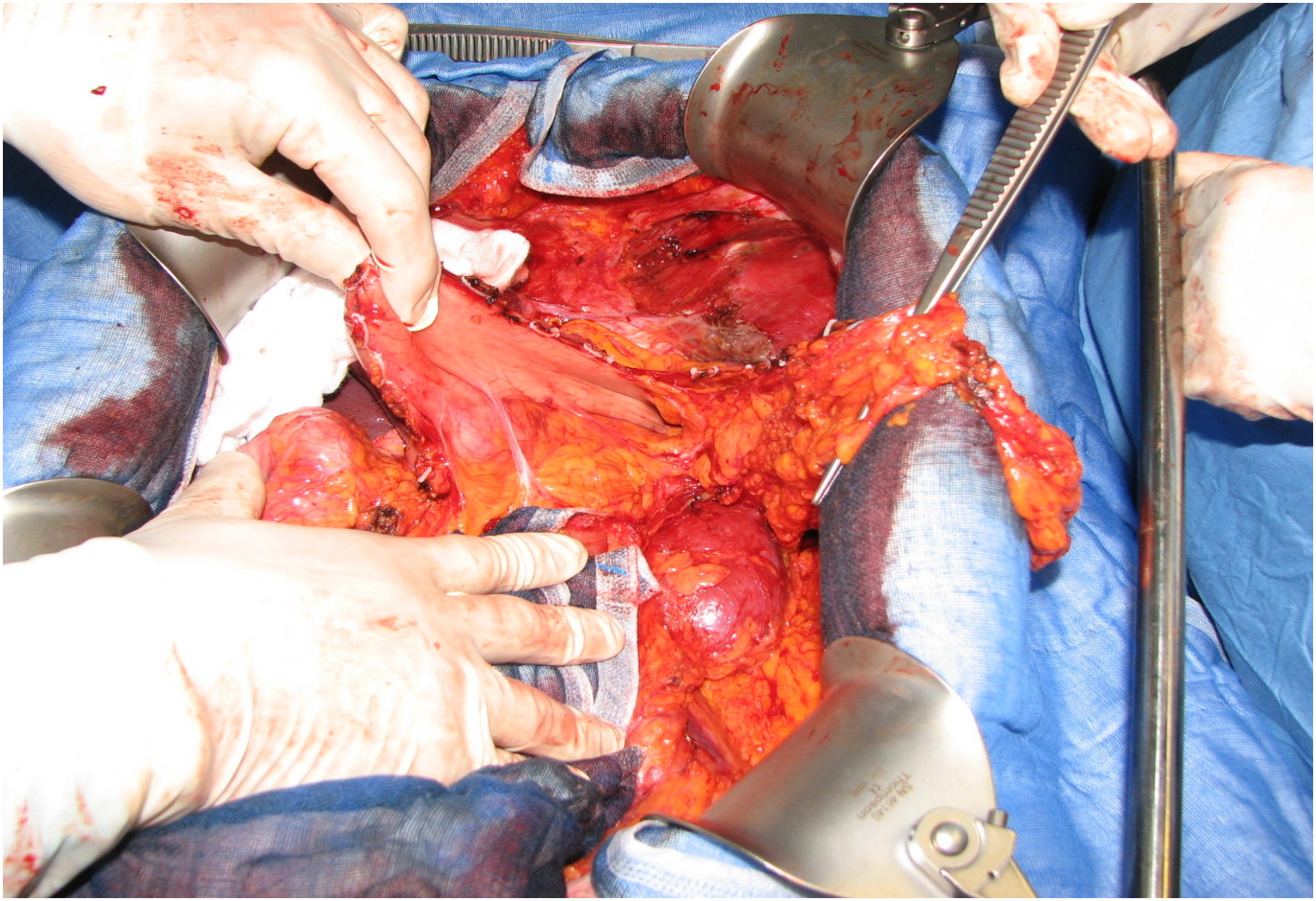


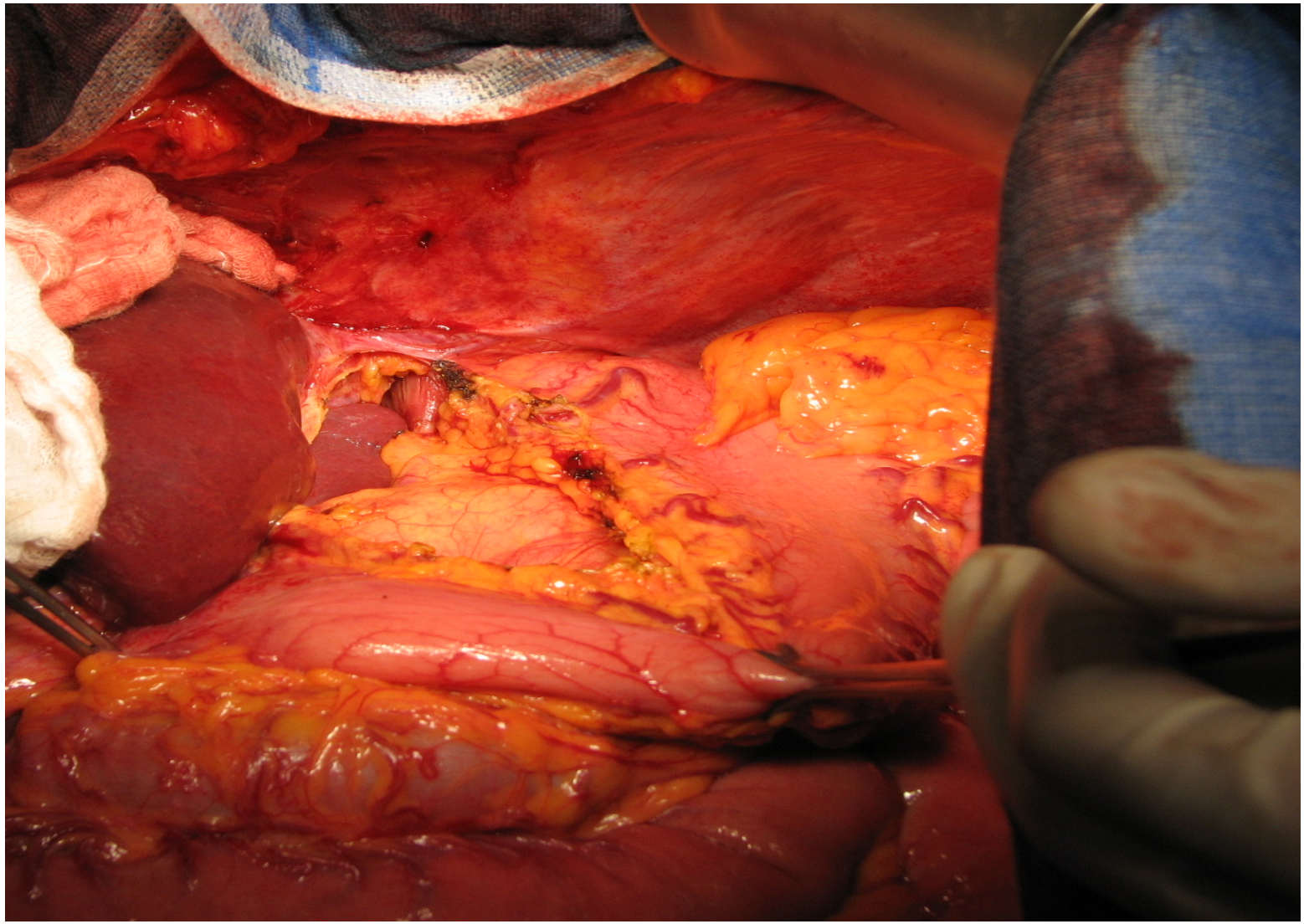


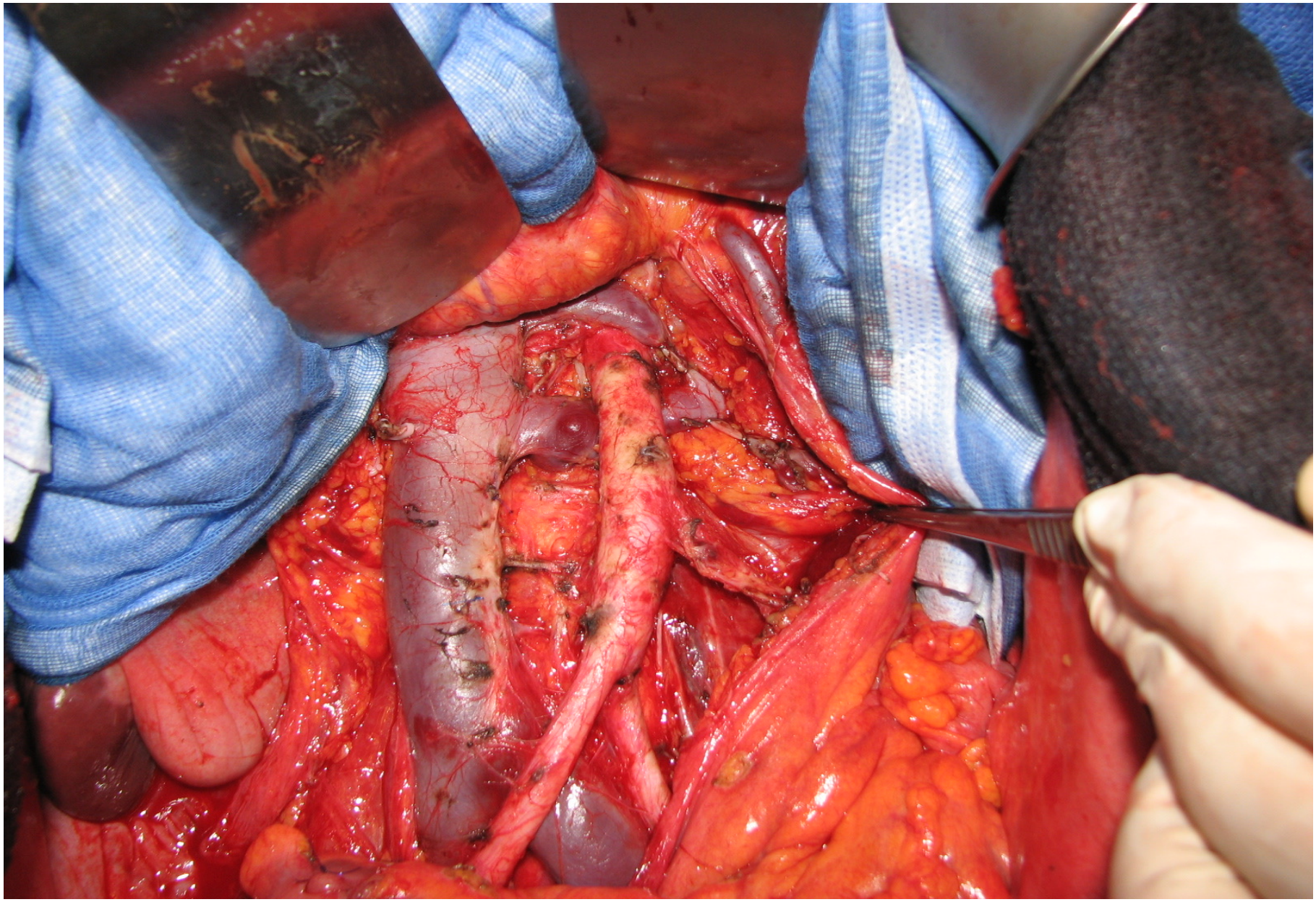

SN 46141
Thompson











4. Lymphadenectomy?

ORIGINAL ARTICLE

# A Randomized Trial of Lymphadenectomy in Patients with Advanced Ovarian Neoplasms

P. Harter, J. Sehouli, D. Lorusso, A. Reuss, I. Vergote, C. Marth, J.-W. Kim, F. Raspagliesi, B. Lampe, G. Aletti, W. Meier, D. Cibula, A. Mustea, S. Mahner, I.B. Runnebaum, B. Schmalfeldt, A. Burges, R. Kimmig, G. Scambia, S. Greggi, F. Hilpert, A. Hasenburg, P. Hillemanns, G. Giorda, I. von Leffern, C. Schade-Brittinger, U. Wagner, and A. du Bois

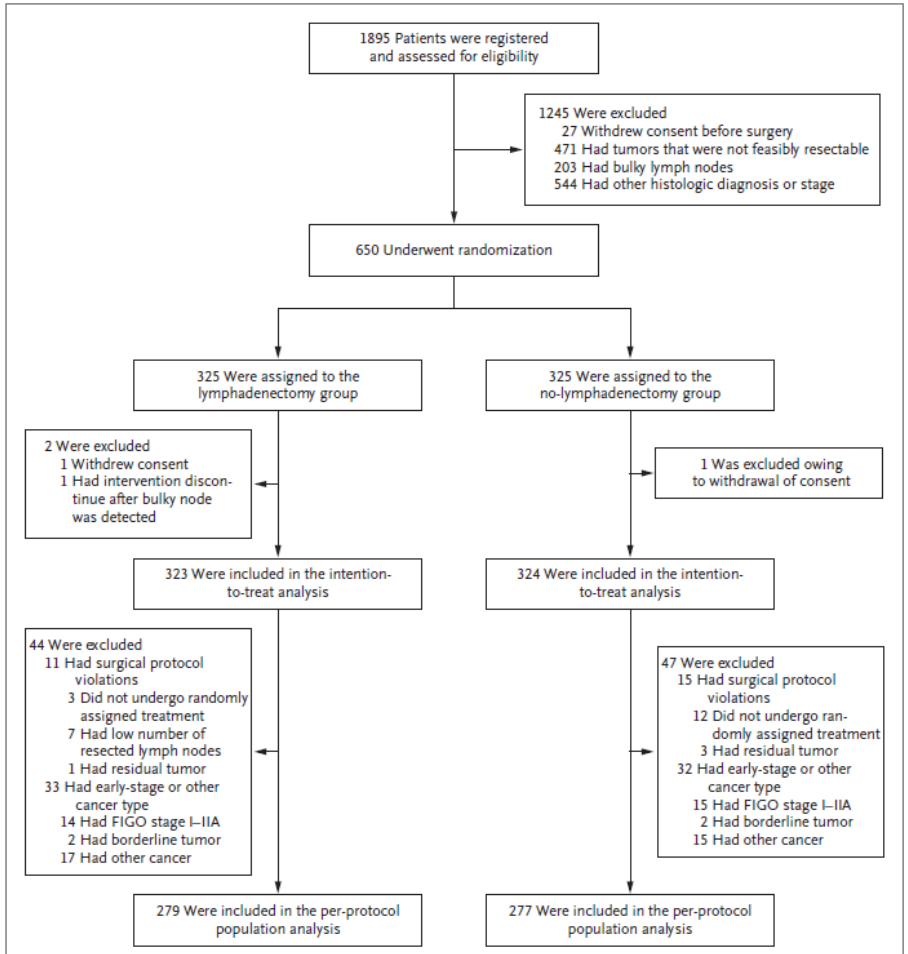
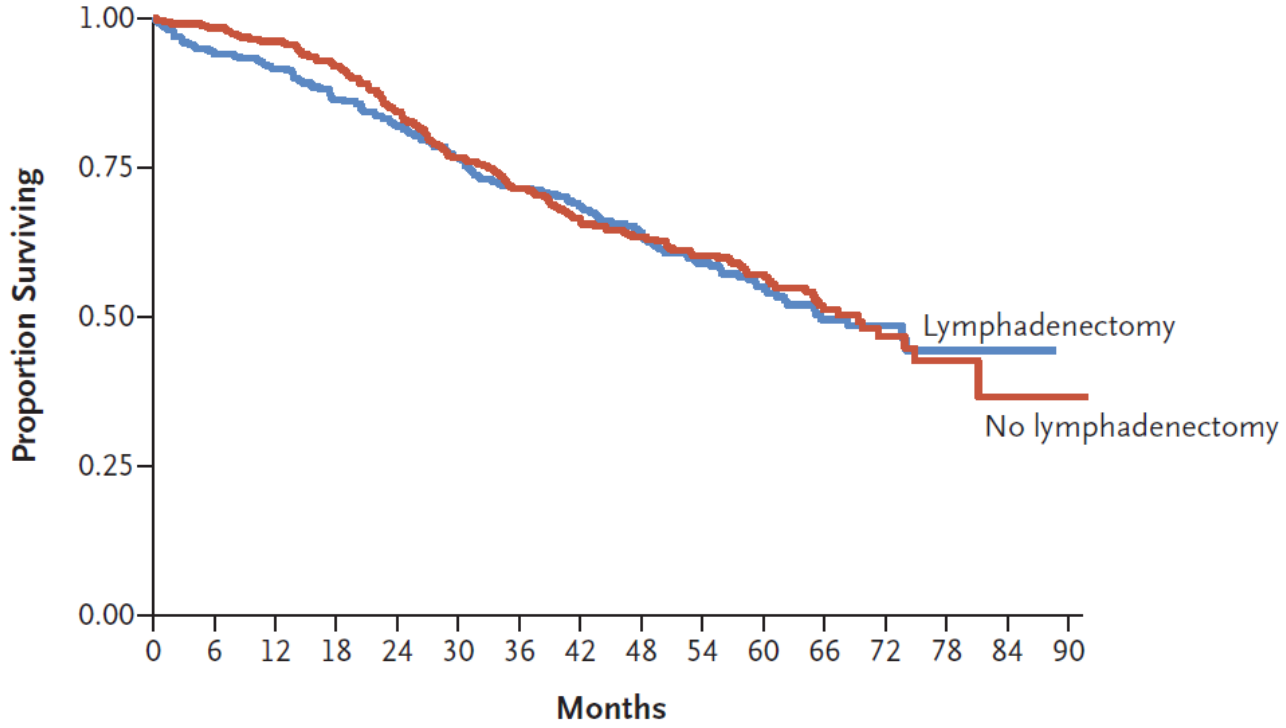



**Figure 1.** **Enrollment, Randomization, and Treatment.**

| Characteristic | Lymphadenectomy Group (N = 323) | No-Lymphadenectomy Group (N = 324) |
|---|---|---|
| Median age (range) — yr | 60 (21–83) | 60 (23–78) |
| Median CA-125 level before surgery (IQR) — U/ml | 416 (138–1276) | 347 (122–1025) |
| ECOG performance status score — no. (%)† | | |
| 0 | 272 (84.2) | 280 (86.4) |
| 1 | 51 (15.8) | 44 (13.6) |
| Histologic diagnosis available before registration — no. (%) | 106 (32.8) | 106 (32.7) |
| Final histologic diagnosis — no. (%) | | |
| Ovarian, fallopian tube, or peritoneal cancer | 306 (94.7) | 307 (94.8) |
| Other diagnosis, including borderline tumor | 17 (5.3) | 17 (5.2) |
| Final FIGO stage — no. (%)‡ | | |
| I to IIA | 15 (4.6) | 17 (5.2) |
| IIB to IIIA | 41 (12.7) | 52 (16.0) |
| IIIB to IV§ | 261 (80.8) | 244 (75.3) |
| Missing data | 6 (1.9) | 11 (3.4) |

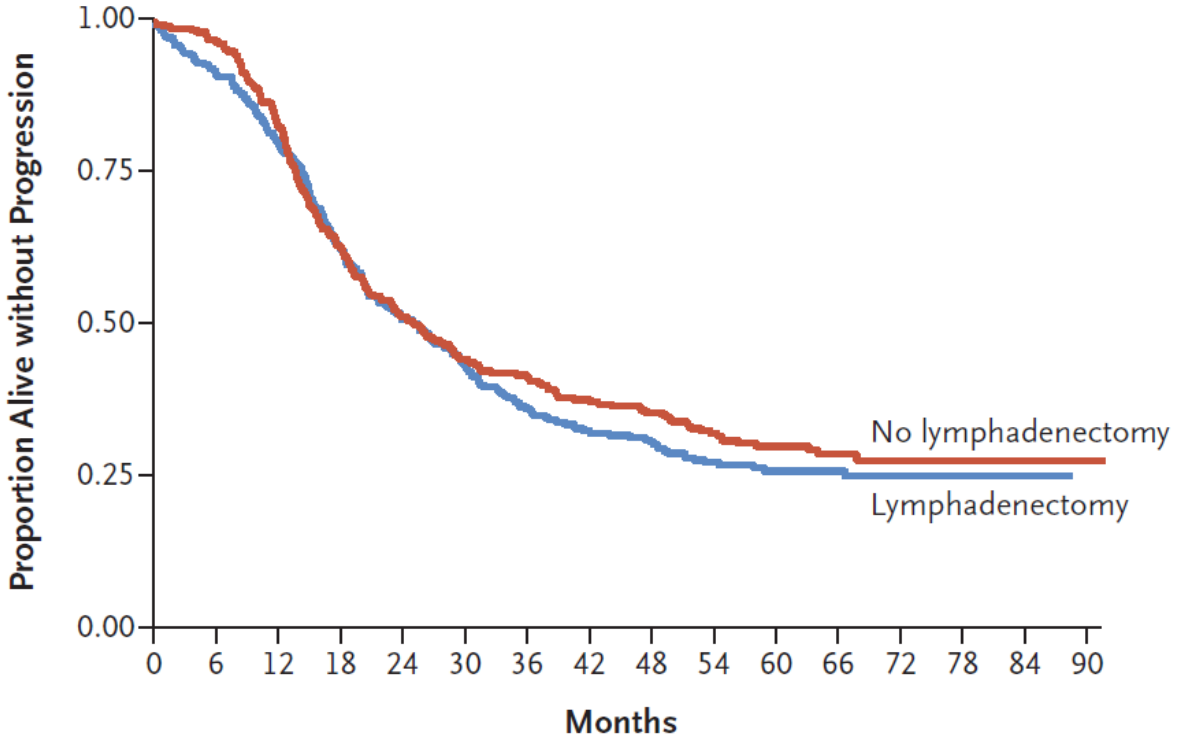
**A** **Overall Survival**



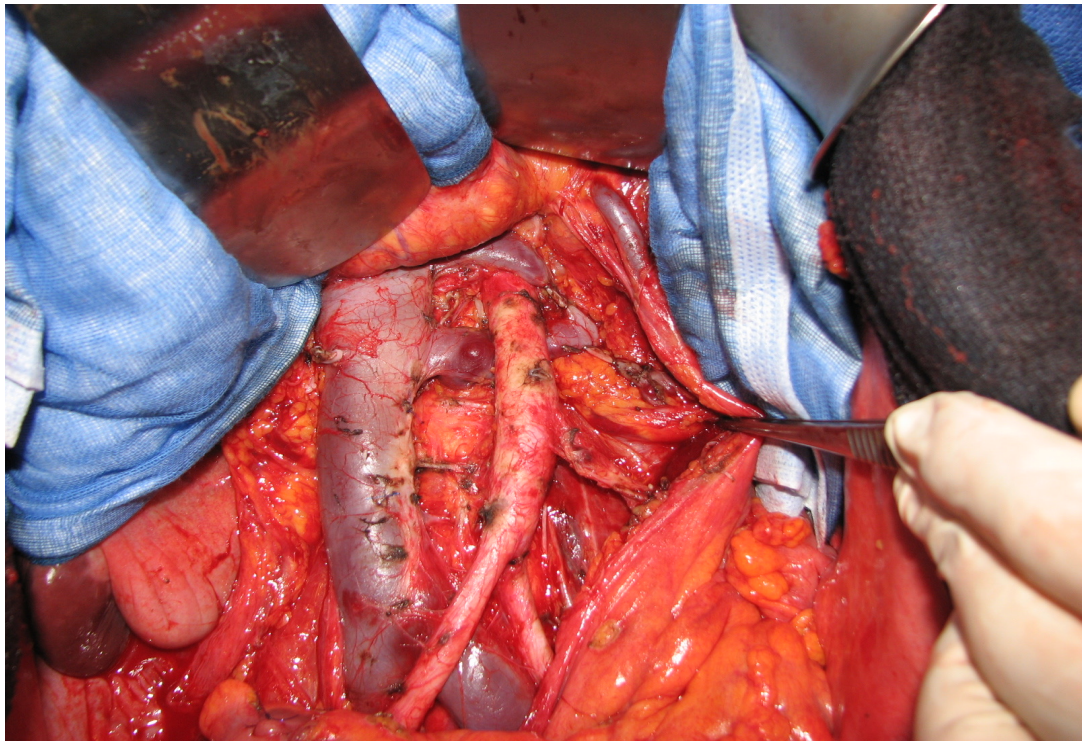

**No. at Risk**

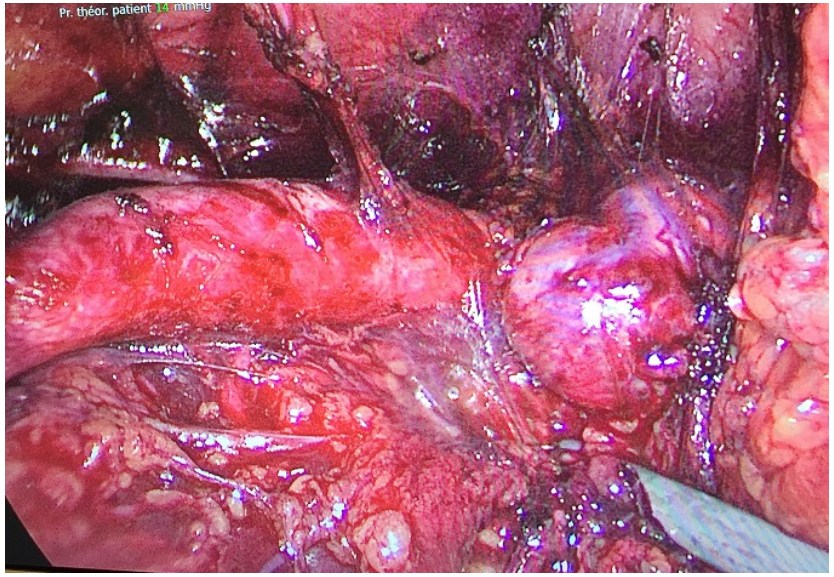
| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lymphadenectomy | 323 | 289 | 271 | 248 | 227 | 210 | 194 | 184 | 167 | 135 | 93 | 55 | 28 | 11 | 3 | 0 |
| No lymphadenectomy | 324 | 308 | 297 | 282 | 252 | 228 | 208 | 187 | 170 | 144 | 105 | 66 | 30 | 10 | 4 | 3 |

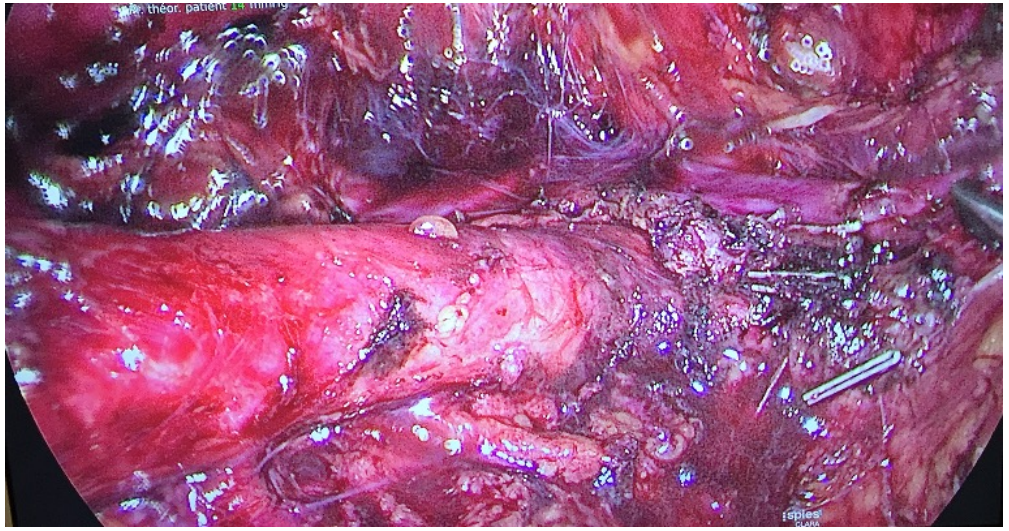
**B** **Progression-free Survival**




| No. at Risk | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lymphadenectomy | 323 | 282 | 239 | 183 | 143 | 120 | 100 | 89 | 82 | 65 | 45 | 31 | 14 | 6 | 2 | 0 |
| No lymphadenectomy | 324 | 303 | 256 | 193 | 155 | 133 | 122 | 109 | 97 | 78 | 55 | 33 | 14 | 5 | 2 | 2 |




Pr. théor. patient 14 mmHg

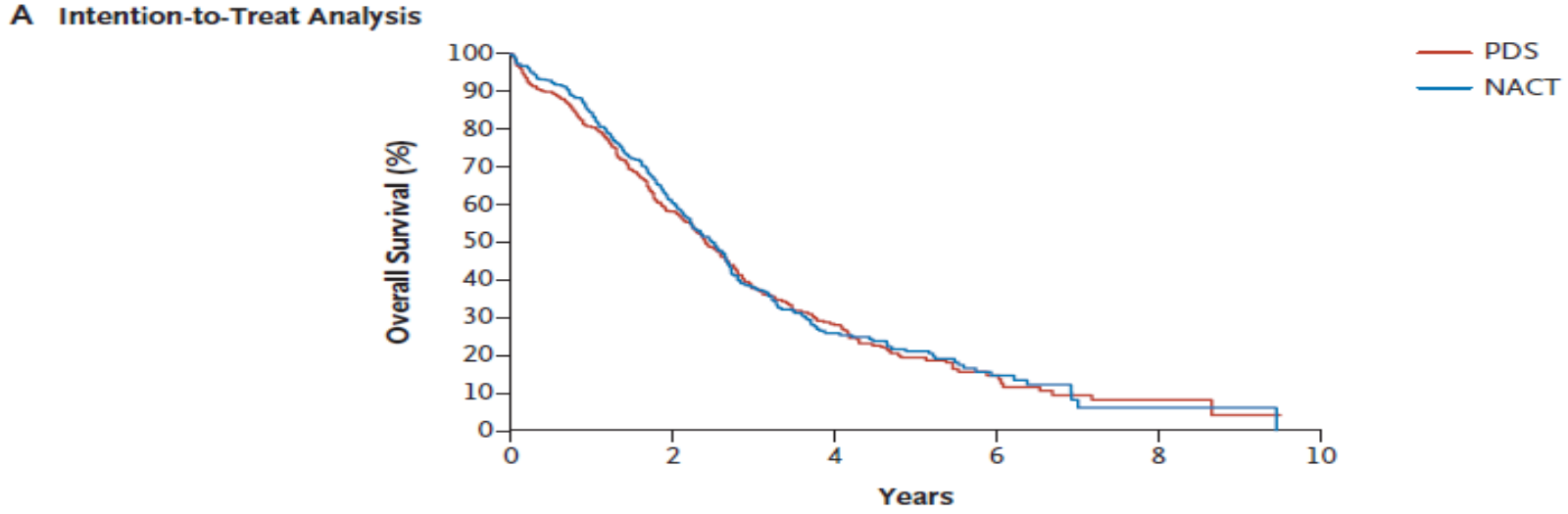


# 5. Is Interval debulking surgery  an acceptable option?

## Neoadjuvant Chemotherapy or Primary Surgery in Stage IIIC or IV Ovarian Cancer

Ignace Vergote, M.D., Ph.D., Claes G. Tropé, M.D., Ph.D., Frédéric Amant, M.D., Ph.D., Gunnar B. Kristensen, M.D., Ph.D., Tom Ehlen, M.D., Nick Johnson, M.D., René H.M. Verheijen, M.D., Ph.D., Maria E.L. van der Burg, M.D., Ph.D., Angel J. Lacave, M.D., Pierluigi Benedetti Panici, M.D., Ph.D., Gemma G. Kenter, M.D., Ph.D., Antonio Casado, M.D., Cesar Mendiola, M.D., Ph.D., Corneel Coens, M.Sc., Leen Verleye, M.D., Gavin C.E. Stuart, M.D., Sergio Pecorelli, M.D., Ph.D., and Nick S. Reed, M.D., for the European Organization for Research and Treatment of Cancer–Gynaecological Cancer Group and the NCIC Clinical Trials Group* — a Gynecologic Cancer Intergroup Collaboration

N Engl J Med 2010;363:943-53.

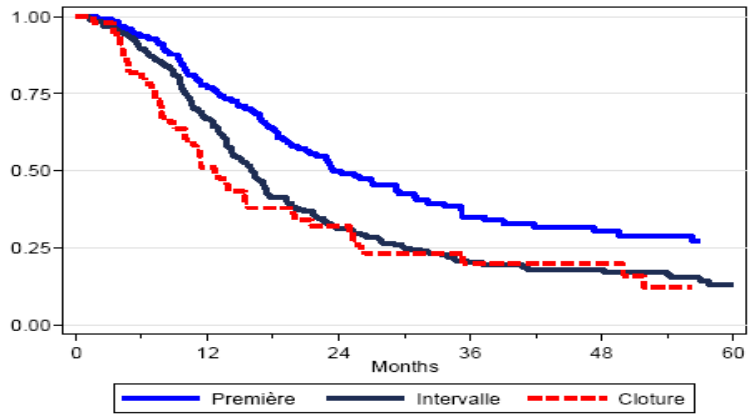


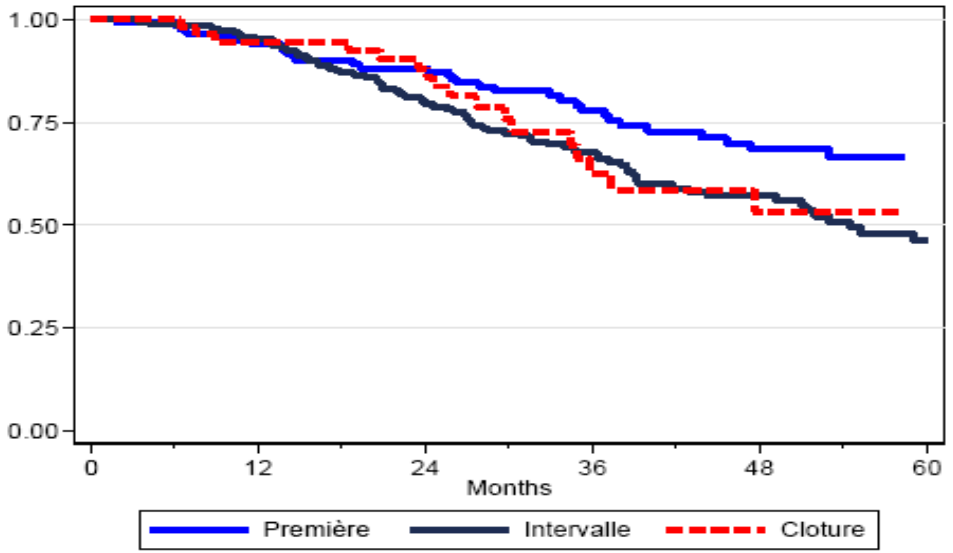
# 5. Is Interval debulking surgery  an acceptable option?

Maximal Cytoreduction in Patients With FIGO Stage IIIC to Stage IV Ovarian, Fallopian, and Peritoneal Cancer in Day-to-Day Practice

*A Retrospective French Multicentric Study*

*Mathieu Luyckx, MD,*† Eric Leblanc, MD, PhD,‡ Thomas Filleron, PhD,* Philippe Morice, MD, PhD,§ Emile Darai, MD, PhD,|| Jean-Marc Classe, MD, PhD,¶ Gwenaël Ferron, MD,* Eberhard Stoeckle, MD, PhD,# Christophe Pomel, MD, PhD,** Bénédicte Vinet, MD,* Elisabeth Chereau, MD,|| Cécile Bergzoll, MD,** and Denis Querleu, MD, PhD*††*




*International Journal of Gynecological Cancer* • Volume 22, Number 8, October 2012

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

# Unsolved issues

- (1) What is a « resectable » disease ?
  - There are technically no limits but retraction of the small bowel mesentery and massive involvement of most of small bowel length
  - In the real world, resecability is a trade-off between the objective of complete surgery and the risks of surgery
    - Postoperative mortality
    - Complication rate
    - Definitive alteration of quality of life

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

# Unsolved issues

- (2) How to integrate intraperitoneal chemotherapy
  - Ample evidence that IP chemo improves the results – however in patients with less than ideal surgery
  - Low acceptance in clinical practice
  - Competition with drug clinical trials

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

Van Driel et al NEJM 2018;378:230
Randomized study Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer

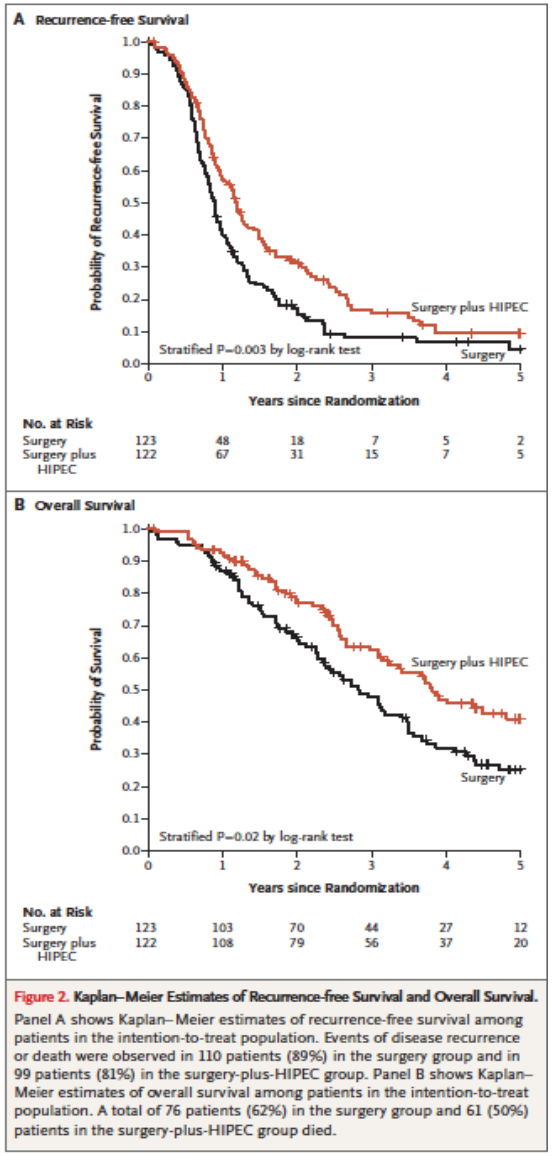



**Figure 2. Kaplan–Meier Estimates of Recurrence-free Survival and Overall Survival.**
Panel A shows Kaplan–Meier estimates of recurrence-free survival among patients in the intention-to-treat population. Events of disease recurrence or death were observed in 110 patients (89%) in the surgery group and in 99 patients (81%) in the surgery-plus-HIPEC group. Panel B shows Kaplan–Meier estimates of overall survival among patients in the intention-to-treat population. A total of 76 patients (62%) in the surgery group and 61 (50%) patients in the surgery-plus-HIPEC group died.

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar

J Clin Oncol. 2019 Jun 1;37(16):1380-1390. doi: 10.1200/JCO.18.01568. Epub 2019 Apr 19.

# Randomized Trial of Intravenous Versus Intraperitoneal Chemotherapy Plus Bevacizumab in Advanced Ovarian Carcinoma: An NRG Oncology/Gynecologic Oncology Group Study.

Walker JL[1], Brady MF[2], Wenzel L[3], Fleming GF[4], Huang HQ[2], DiSilvestro PA[5], Fujiwara K[6], Alberts DS[7], Zheng W[8], Tewari KS[3], Cohn DE[9], Powell MA[10], Van Le L[11], Davidson SA[12], Gray HJ[13], Rose PG[14], Aghajanian C[15], Myers T[16], Alvarez Secord A[17], Rubin SC[18], Mannel RS[1].

**Author information**

1 1 University of Oklahoma Health Sciences Center, Oklahoma City, OK.
2 2 Roswell Park Cancer Institute, Buffalo, NY.
3 3 University of California, Irvine, Medical Center, Orange, CA.
4 4 The University of Chicago Medicine, Chicago, IL.
5 5 Women and Infants Hospital, Providence, RI.
6 6 Saitama Medical University International Medical Center, Hidaka-Shi, Japan.
7 7 The University of Arizona Cancer Center, Tucson, AZ.
8 8 The University of Arizona, Tucson, AZ.
9 9 The Ohio State University, Columbus, OH.
10 10 Washington University in St Louis, St Louis, MO.
11 11 University of North Carolina at Chapel Hill, Chapel Hill, NC.
12 12 University of Colorado, Aurora, CO.
13 13 University of Washington School of Medicine, Seattle, WA.
14 14 Cleveland Clinic Foundation, Cleveland, OH.
15 15 Memorial Sloan Kettering Cancer Center, New York, NY.
16 16 University of Connecticut, Storrs, CT.
17 17 Duke University Health System, Durham, NC.
18 18 University of Pennsylvania, Philadelphia, PA.

# Advanced Ovarian cancer surgery : take home messages

- The 0 residue is the target
- Can be achieved in 80% of patients
- Can be completed as primary treatment or after neoadjuvant chemotherapy
- Involves major visceral surgery – if the overall estimated risk is acceptable
- No surgeon should undertake such a surgery without the skills to perform en bloc radical oophorectomy and upper abdominal procedures

Institut du Sein
NICE SANTA MARIA

Weill Cornell Medicine-Qatar