# 자궁경부암 치료의 최신지견

Staging and Treatment plan

세종충남대학교병원 신원교

# Disclosure

- **Source of Materials:** The part of slides in this presentation were provided by MSD
- Slide design 일부 : Gemini

- **Conflict of Interest:** The presenter has no other financial conflicts of interest to disclose.

자궁경부암 최신 치료 지견

# Introduction

- 다양한 new molecule 들의 등장
  - Specific receptor target molecule, IO drug, ADC
  - Bevacizumab, Pembrolizumab,

- Endometrial cancer : Molecular classification, sub-categorization

- Ovarian cancer : Paclitaxel / PARPi

- Cervical cancer
  - Radical Hysterectomy

- **[ASCO 2025]** KEYNOTE-A18 Final Analysis Results
- **[ESMO 2025]** KEYNOTE-A18 Post Hoc (Subgroup: High-Risk LACC) data
- **[ESMO 2025]** TroFuse-001 Phase 1/2 Cervical Cancer data (Sac-TMT mono, 2L+)
- **[IGCS 2025]** KEYNOTE-826 5yr Outcome
- **[SGO 2026]** TroFuse-002 Phase 2 Cervical Cancer data (Sac-TMT + Pem, 2-3L)
- **[ESMO Gyn 2026]** KEYNOTE-A18 East Asia OS analysis
- TroFuse 관련 참고사항*
- TroFuse-022 (OC, 2L, maint) Part1, Part2 TiP

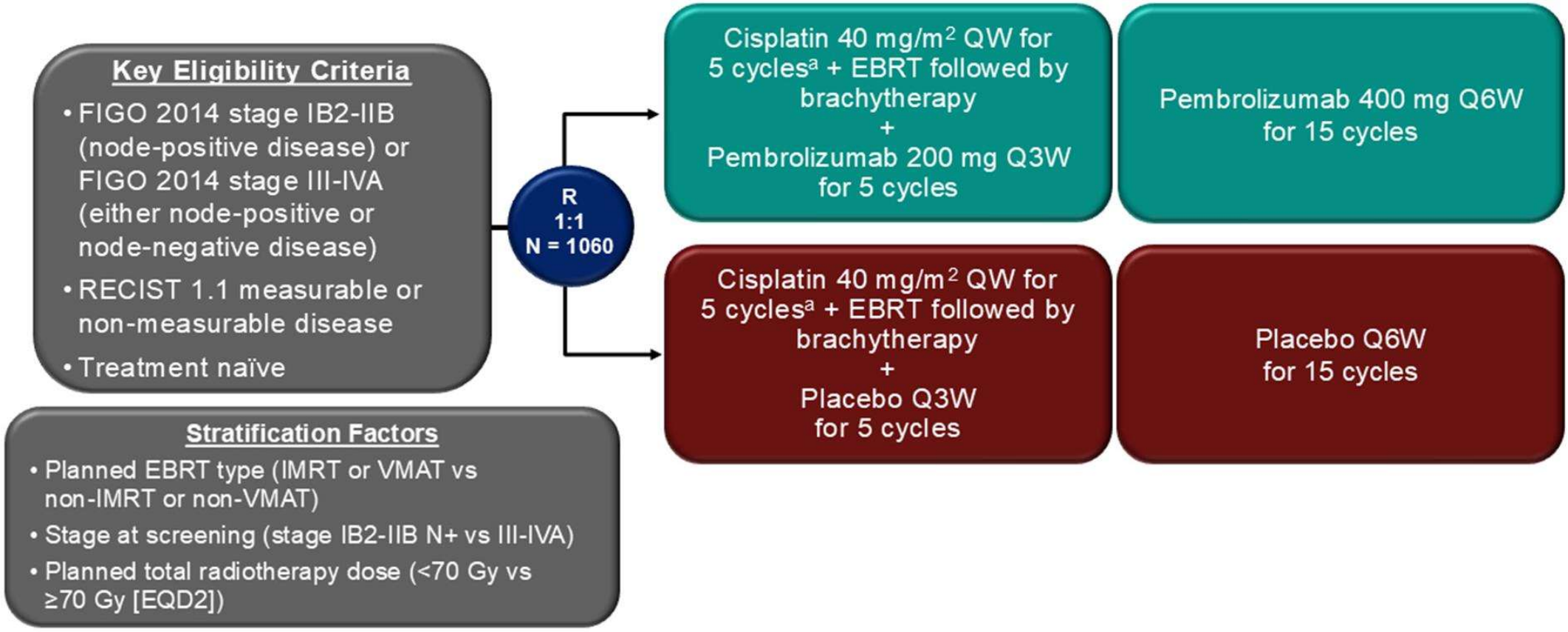
* 현재 TroFuse 이름으로 진행되는 Sac-TMT (Sacituzumab Tirumotecan) 임상 3상 시험은 자궁경부암에서 TroFuse-020, 036이 있습니다.
2026년 10월 19일 기준, TroFuse-036은 TiP가 외부에 공개되지 않은 터라, TiP 공개된 020만 말미에 TiP 첨부하였습니다.

# Pembrolizumab with Concurrent Chemoradiotherapy in Participants with High-Risk Locally Advanced Cervical Cancer: A Descriptive Analysis of Final Survival from the Phase 3, Randomized, Double-Blind ENGOT-cx11/GOG-3047/KEYNOTE-A18 Study

Linda R. Duska,[1] Yang Xiang,[2] Kosei Hasegawa,[3] Pier Ramos-Elias,[4] Paolo Rodolfo Valdez Barreto,[5] Alejandro Acevedo,[6] Felipe José Silva Melo Cruz,[7] Valeriya Saevets,[8] Rudolf Lampé,[9] Limor Helpman,[10] Jalid Sehouli,[11] Flora Zagouri,[12] Yong Man Kim,[13] Peng Liu,[14] Karin Yamada,[14] Sarper Toker,[14] Sandro Pignata,[15] Domenica Lorusso,[16] on behalf of the ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators

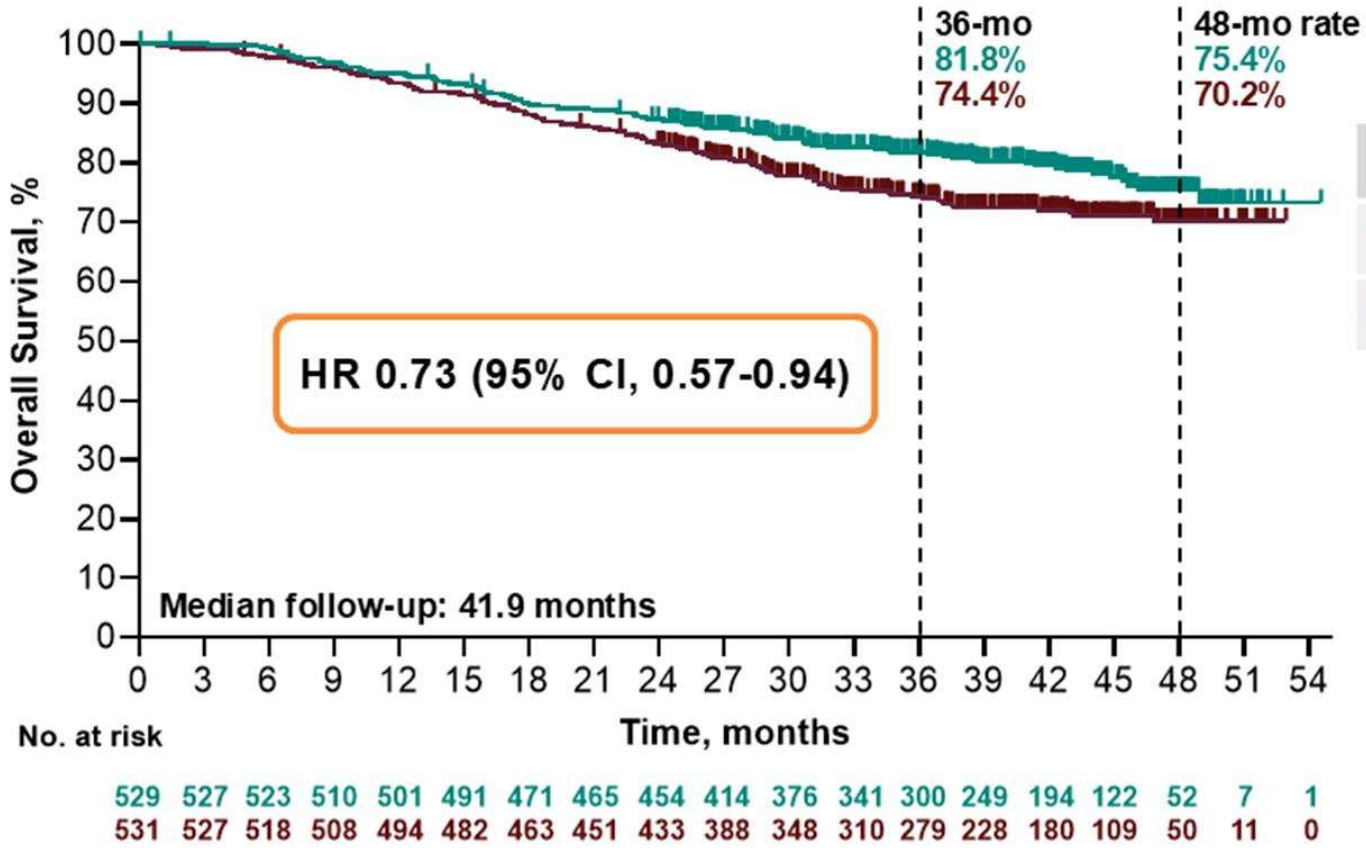
[1]University of Virginia School of Medicine, Charlottesville, VA, USA; [2]Department of Obstetrics and Gynecology, National Clinical Research Center for Obstetric & Gynecologic Diseases, Peking Union Medical College Hospital, Beijing, China; [3]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [4]Integra Cancer Institute, Edificio Integra Medical Center, Guatemala City, Guatemala; [5]Hospital de Alta Complejidad de La Libertad Virgen de La Puerta, Trujillo, Peru; [6]Oncocentro, Valparaiso, Chile; [7]Instituto Brasileiro de Controle do Câncer, São Paulo, Brazil; [8]Chelyabinsk Regional Clinical Center of Oncology and Nuclear Medicine, Chelyabinsk, Russia; [9]University of Debrecen, Faculty of Medicine, Department of Obstetrics and Gynecology, Debrecen, Hungary; [10]Sheba Medical Center, Tel Aviv University Faculty of Medical and Health Sciences, Ramat Gan, Israel; [11]Charite Universitaetsmedizin, Berlin, Germany and North-Eastern German Society of Gynecological Oncology (NOGGO); [12]Alexandra Hospital, Athens, Greece; [13]Asan Medical Center, University of Ulsan, Seoul, South Korea; [14]Merck & Co., Inc., Rahway, NJ, USA; [15]Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy; [16]Gynaecology Oncology Unit, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome and Humanitas San Pio X, Milan, Italy

# ENGOT-cx11/GOG-3047/KEYNOTE-A18: Randomized, Double-Blind, Phase 3 Study




[a]A 6th cycle was allowed per investigator discretion. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

# Descriptive Overall Survival at Final Analysis




| | Pts w/ Event | Pts Censored |
|---|---|---|
| Pembro Arm | 20.2% | 79.8% |
| Placebo Arm | 26.4% | 73.6% |

Data cutoff date: January 7, 2025.

# Overall Survival in Protocol-Specified Subgroups at Final Analysis

| Subgroup | No. of Events/ No. of Patients | HR (95% CI) |
|---|---|---|
| Overall | 247/1060 | 0.73 (0.57-0.94) |
| Age | | |
| <65 years | 217/927 | 0.69 (0.52-0.90) |
| ≥65 years | 30/133 | 1.18 (0.58-2.43) |
| Race | | |
| White | 132/518 | 0.96 (0.68-1.36) |
| All others | 114/539 | 0.55 (0.38-0.80) |
| ECOG PS score | | |
| 0 | 183/778 | 0.71 (0.53-0.96) |
| 1 | 64/282 | 0.80 (0.49-1.30) |
| Planned EBRT | | |
| IMRT/VMAT | 220/939 | 0.76 (0.58-0.99) |
| non-IMRT/-VMAT | 27/121 | 0.60 (0.28-1.32) |
| FIGO 2014 stage | | |
| IB2 to IIB | 95/459 | 0.92 (0.62-1.38) |
| III to IVA | 152/601 | 0.64 (0.46-0.88) |
| Planned total RT dose | | |
| <70 Gy | 19/93 | 0.60 (0.24-1.52) |
| ≥70 Gy | 228/967 | 0.75 (0.58-0.97) |




Data cutoff date: January 7, 2025.

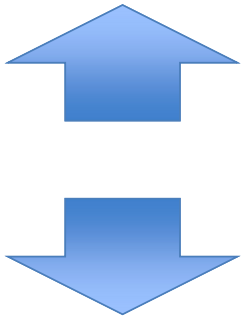
자궁경부암 최신 치료 지견

# 2018 FIGO staging

TABLE 1 FIGO staging of cancer of the cervix uteri (2018).

| Stage | | | Description |
|---|---|---|---|
| I | | | The carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded) |
| | IA | | Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion ≤5 mm[a] |
| | | IA1 | Measured stromal invasion ≤3 mm in depth |
| | | IA2 | Measured stromal invasion >3 mm and ≤5 mm in depth |
| | IB | | Invasive carcinoma with measured deepest invasion >5 mm (greater than Stage IA); lesion limited to the cervix uteri with size measured by maximum tumor diameter[b] |
| | | IB1 | Invasive carcinoma >5 mm depth of stromal invasion and ≤2 cm in greatest dimension |
| | | IB2 | Invasive carcinoma >2 cm and ≤4 cm in greatest dimension |
| | | IB3 | Invasive carcinoma >4 cm in greatest dimension |
| II | | | The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall |
| | IIA | | Involvement limited to the upper two-thirds of the vagina without parametrial involvement |
| | | IIA1 | Invasive carcinoma ≤4 cm in greatest dimension |
| | | IIA2 | Invasive carcinoma >4 cm in greatest dimension |
| | IIB | | With parametrial involvement but not up to the pelvic wall |
| III | | | The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or para-aortic lymph nodes |
| | IIIA | | The carcinoma involves the lower third of the vagina, with no extension to the pelvic wall |
| | IIIB | | Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause) |
| | IIIC | | Involvement of pelvic and/or para-aortic lymph nodes (including micrometastases),[c] irrespective of tumor size and extent (with r and p notations)[d] |
| | | IIIC1 | Pelvic LNM only |
| | | IIIC2 | Para-aortic LNM |
| IV | | | The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to Stage IV |
| | IVA | | Spread of the growth to adjacent pelvic organs |
| | IVB | | Spread to distant organs |

Radical Suegery

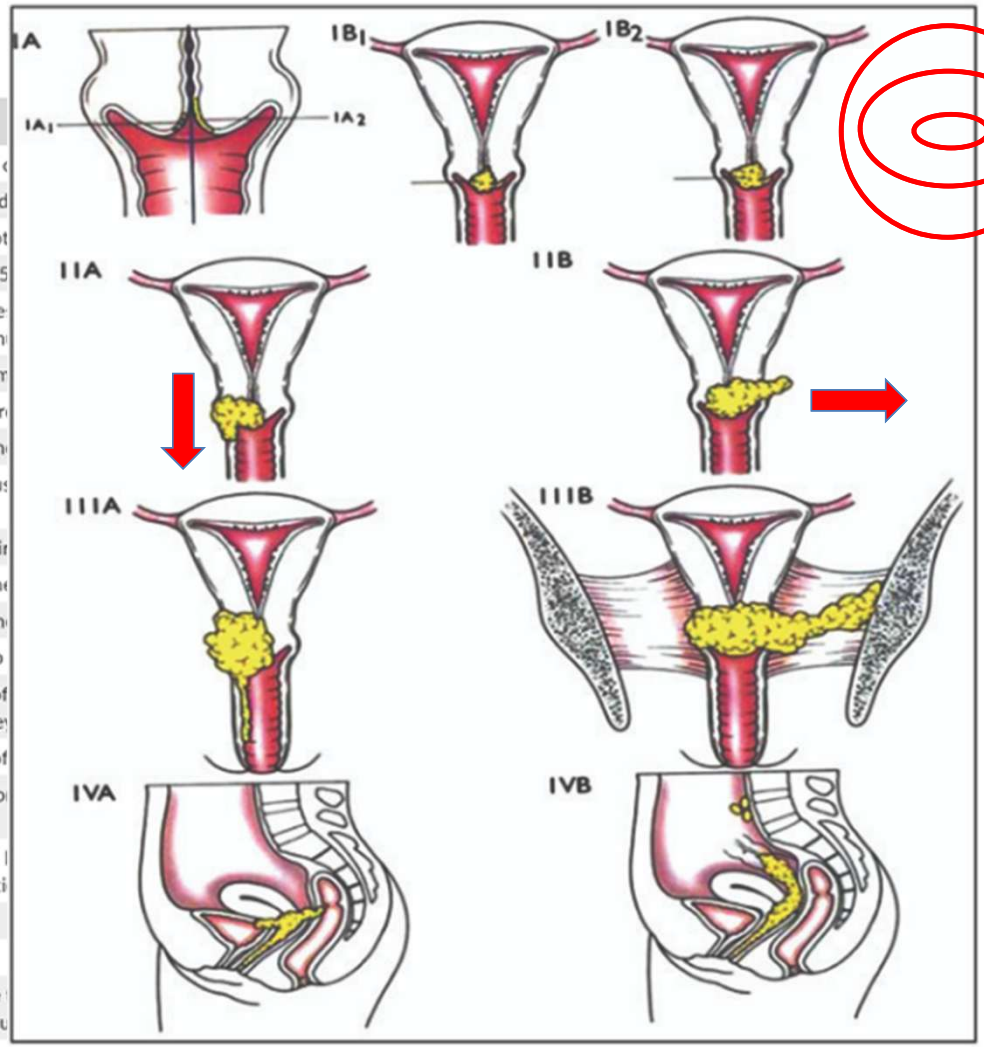


CCRT
Systemic treatment

# 2018 FIGO staging

TABLE 1 FIGO staging of cancer of the cervix uteri (2018).

| Stage | | | Description |
|---|---|---|---|
| I | | | The carcinoma is strictly confined to the c |
| | IA | | Invasive carcinoma that can be diagnosed |
| | | IA1 | Measured stromal invasion ≤3 mm in dept |
| | | IA2 | Measured stromal invasion >3 mm and ≤5 |
| | IB | | Invasive carcinoma with measured deepe cervix uteri with size measured by maxim |
| | | IB1 | Invasive carcinoma >5 mm depth of stron |
| | | IB2 | Invasive carcinoma >2 cm and ≤4 cm in gr |
| | | IB3 | Invasive carcinoma >4 cm in greatest dim |
| II | | | The carcinoma invades beyond the uterus to the pelvic wall |
| | IIA | | Involvement limited to the upper two-thi |
| | | IIA1 | Invasive carcinoma ≤4 cm in greatest dim |
| | | IIA2 | Invasive carcinoma >4 cm in greatest dim |
| | IIB | | With parametrial involvement but not up |
| III | | | The carcinoma involves the lower third of hydronephrosis or non-functioning kidne |
| | IIIA | | The carcinoma involves the lower third of |
| | IIIB | | Extension to the pelvic wall and/or hydro to another cause) |
| | IIIC | | Involvement of pelvic and/or para-aortic l tumor size and extent (with r and p notati |
| | | IIIC1 | Pelvic LNM only |
| | | IIIC2 | Para-aortic LNM |
| IV | | | The carcinoma has extended beyond the bladder or rectum. A bullous edema, as su |
| | IVA | | Spread of the growth to adjacent pelvic organs |
| | IVB | | Spread to distant organs |




3
2
1

LN metastasis 가 확인되면,
original tumor 의 크기과는
상관없이 IIIC

scientific reports

Check for updates

OPEN

# Comparing survival outcomes for cervical cancer based on the 2014 and 2018 International Federation of Gynecology and Obstetrics staging systems

Wonkyo Shin[1], Tae Young Ham[2], Young Ran Park[2], Myong Cheol Lim[1,3,4,5] & Young-Joo Won[2,5]✉

The International Federation of Gynecology and Obstetrics (FIGO) cervical cancer staging system was modified in 2018, introducing new stage IB subdivisions and new lymph node status considerations in stage IIIC. We compared cervical cancer survival outcomes according to the 2014 and 2018 FIGO staging systems. We selected 10% of cervical cancer cases (2010–2015) from the Korean national cancer registry (2010–2015) through a systematic sampling method. We collected information using a collaborative stage data collection system and evaluated the results according to both staging systems. The log-rank test was used to analyze overall survival differences. No significant difference in survival was observed between 2018 subdivisions IB1/IB2/IB3 (P = 0.069), whereas a considerable difference was observed between these subdivisions according to histological subtypes. In the 2018

scientific reports

Check for updates

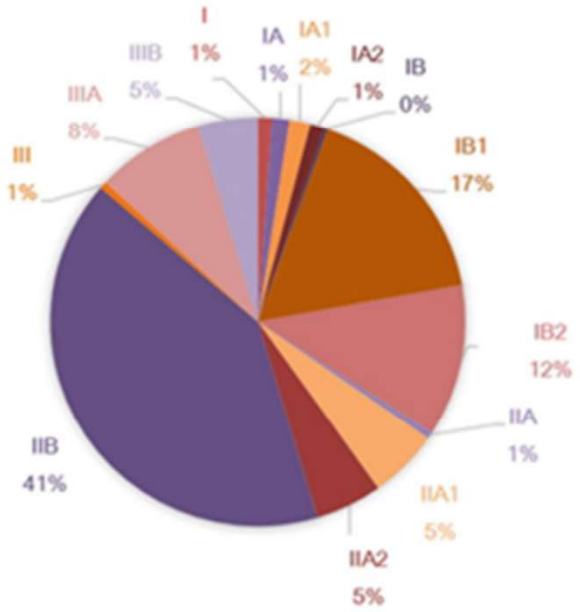
OPEN

# Comparing survival outcomes fo or Fe ar

Won
Your

The l
modi
in sta
stagi
cance
a coll
syste
in sur
differ

a) The 2014 FIGO stages in 2018 FIGO stage IIIC1




b) The 2014 FIGO stages in 2018 FIGO stage IIIC2

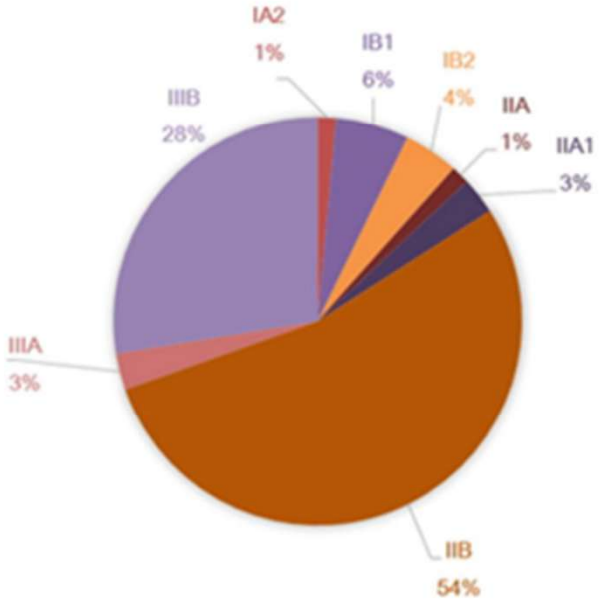



**Figure 3.** Distribution of 2014 FIGO stages in the 2018 FIGO stages IIIC1 (**a**) and IIIC2 (**b**).

scientif

OPEN

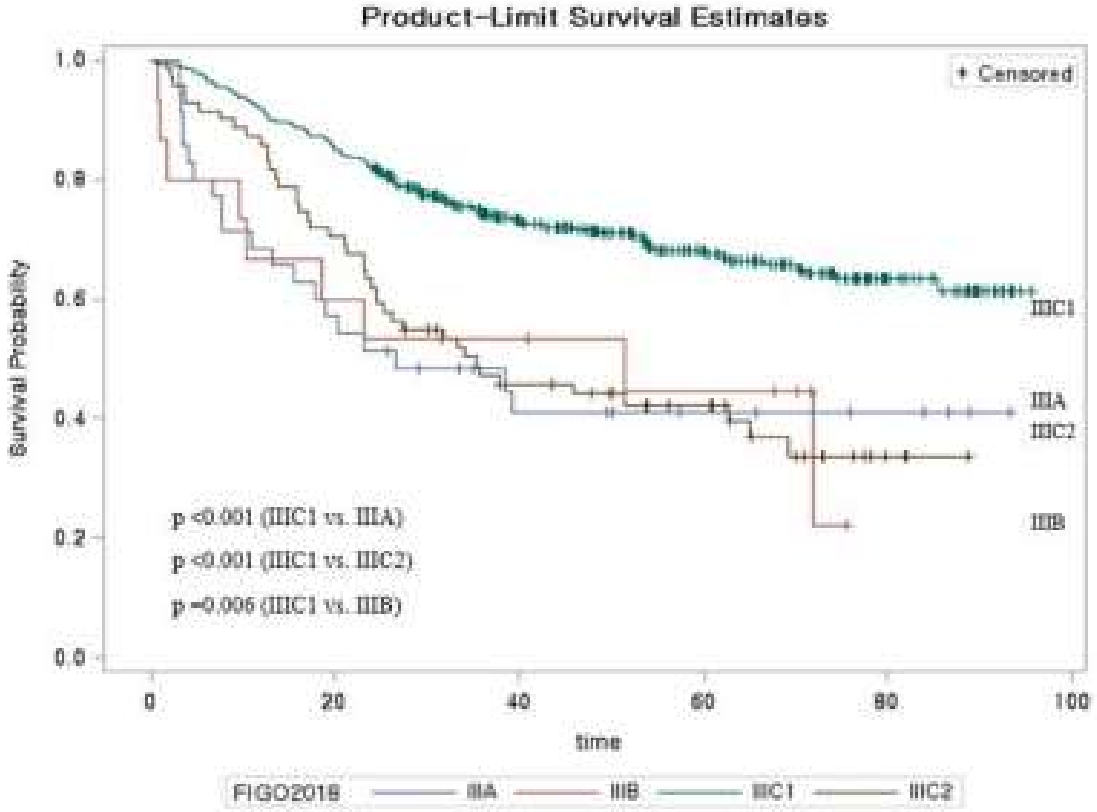



**Figure 2.** Kaplan–Meier analysis of survival for 2018 FIGO stage III.

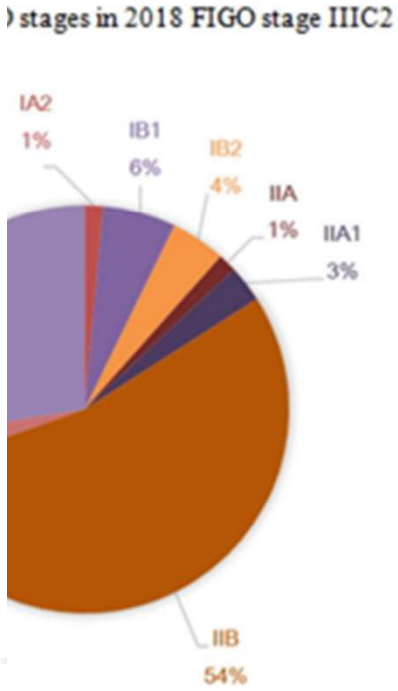



**Figure 3.** Distribution of 2014 FIGO stages in the 2018 FIGO stages IIIC1 (**a**) and IIIC2 (**b**).

자궁경부암 최신 치료 지견

# 전통적인 자궁경부암 치료의 기준: IIB →→ IB3 ?

- FIGO IIB 치료의 이분법적 접근 방식 : RH vs CCRT
  - 완치율은 유사하나 중복 치료 시 골반 내 합병증 극대화' 위험성
  - Lymph node metastasis 가 stage 에 들어가지 않던 시절의 구분법
  - 개복 수술 또는 Primary CCRT 중 하나를 선택

- 환자 개별적 tumor 상태와 림프절 상태를 유연하게 반영하지 못한 과거

Articles

Radical surgery vs CCRT

# Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer

*Fabio Landoni, Andrea Maneo, Alessandro Colombo, Franco Placa, Rodolfo Milani, Patrizia Perego, Giorgio Favini, Luigi Ferri, Costantino Mangioni*

## Summary

**Background** Stage Ib and IIa cervical carcinoma can be cured by radical surgery or radiotherapy. These two procedures are equally effective, but differ in associated morbidity and type of complications. In this prospective randomised trial of radiotherapy versus surgery, our aim was to assess the 5-year survival and the rate and pattern of complications and recurrences associated with each treatment.

**Methods** Between September, 1986, and December, 1991, 469 women with newly diagnosed stage Ib and IIa cervical carcinoma were referred to our institute. 343 eligible patients were randomised: 172 to surgery and 171 to radical radiotherapy. Adjuvant radiotherapy was delivered

**Interpretation** There is no treatment of choice for early-stage cervical carcinoma in terms of overall or disease-free survival. The combination of surgery and radiotherapy has the worst morbidity, especially urological complications. The optimum therapy for each patient should take account of clinical factors such as menopausal status, age, medical illness, histological type, and cervical diameter to yield the best cure with minimum complications.

*Lancet* 1997; **350:** 535–40
*See Commentary page 532*

## Introduction

Stage Ib and IIa carcinoma of the cervix can be cured by radical surgery or radiotherapy with similar effectiveness

# Radical Surgery vs. Primary Radiotherapy (RT)

Clinical comparison of treatment strategies for early invasive cervical cancer (Based on Landoni et al., 1997)

| | Radical Surgery | Primary Radiotherapy (RT) |
|---|---|---|
| **5-Year Survival & Local Control** | • Identical (83%) to RT group<br>• Suggests no single treatment of choice regarding local control | |
| **Patient Demographics & Eligibility** | • Highly advantageous for younger / middle-aged women | • Easier to deliver for obese, elderly, or severely ill patients<br>• Avoids major surgical contraindications |
| **Quality of Life & Organ Preservation** | • Saves ovarian gonadal function (avoids early menopause)<br>• Vaginal shortening/fibrosis limited if sexually active | • High risk of early menopause (cannot save gonadal function)<br>• Complications are often permanent |
| **Complication Profiles** | • Arise early but easily corrected<br>• Operative mortality & urological risks reduced past 20 years | • Arise later than surgery<br>• Avoids anesthesia risks & laparotomy scars; iatrogenic mortality rare |
| **Salvage Treatment (After Relapse)** | • Pelvic relapses can be successfully cured by RTx | • Salvage surgery after primary RT carries a high rate of failure and severe morbidity |
| **Prognostic Assessment** | • Accurate pathological assessment of lymph nodes | • Does not allow accurate, direct pathological assessment of lymph node status |
| **The Combined Risk (Worst Morbidity)** | • **Surgery + Adjuvant RT carries the worst morbidity (hydroureteronephroses, lower limb edema, bowel/vesical complications)**<br>• RT alone is well-tolerated with low major complication rate (12%) | |

# Radical Surgery vs. Primary Radiotherapy (RT)

Clinical comparison of treatment strategies for early invasive cervical cancer (Based on Landoni et al., 1997)

| | Radical Surgery | Primary Radiotherapy (RT) |
|---|---|---|
| **5-Year Survival & Local Control** | • Identical (83%) to RT group<br>• Suggests no single treatment of choice regarding local control | |
| **Patient Demographics & Eligibility** | • Highly advantageous for younger / middle-aged women | • Easier to deliver for obese, elderly, or severely ill patients<br>• Avoids major surgical contraindications |
| **Quality of Life & Organ Preservation** | • Saves ovarian gonadal function (avoids early menopause)<br>• Vaginal shortening/fibrosis limited if sexually active | • High risk of early menopause (cannot save gonadal function)<br>• Complications are often permanent |
| **Complication Profiles** | • Arise early but easily corrected<br>• Operative mortality & urological risks reduced past 20 years | • Arise later than surgery<br>• Avoids anesthesia risks & laparotomy scars; iatrogenic mortality rare |
| **Salvage Treatment (After Relapse)** | • Pelvic relapses can be successfully cured by RTx | • Salvage surgery after primary RT carries a high rate of failure and severe morbidity |
| **Prognostic Assessment** | • Accurate pathological assessment of lymph nodes | • Does not allow accurate, direct pathological assessment of lymph node status |
| **The Combined Risk (Worst Morbidity)** | • **Surgery + Adjuvant RT carries the worst morbidity (hydroureteronephroses, lower limb edema, bowel/vesical complications)**<br>• RT alone is well-tolerated with low major complication rate (12%) | |

CCRT vs Radiation only

The New England Journal of Medicine

© Copyright, 1999, by the Massachusetts Medical Society

VOLUME 340 APRIL 15, 1999 NUMBER 15

# PELVIC RADIATION WITH CONCURRENT CHEMOTHERAPY COMPARED WITH PELVIC AND PARA-AORTIC RADIATION FOR HIGH-RISK CERVICAL CANCER

MITCHELL MORRIS, M.D., PATRICIA J. EIFEL, M.D., JIANDONG LU, PH.D., PERRY W. GRIGSBY, M.D., CHARLES LEVENBACK, M.D., RANDY E. STEVENS, M.D., MARVIN ROTMAN, M.D., DAVID M. GERSHENSON, M.D., AND DAVID G. MUTCH, M.D.

## ABSTRACT

***Background and Methods*** We compared the effect of radiotherapy to a pelvic and para-aortic field with that of pelvic radiation and concurrent chemotherapy with fluorouracil and cisplatin in women with advanced cervical cancer. Between 1990 and 1997, 403 women with advanced cervical cancer confined to the pelvis (stages IIB through IVA or stage IB or IIA with a tumor diameter of at least 5 cm or involvement of pelvic lymph nodes) were randomly assigned to receive either 45 Gy of radiation to the pelvis and para-aortic lymph nodes or 45 Gy

OF the estimated 13,700 women in the United States in whom invasive cervical cancer was diagnosed in 1998,[1] nearly 5000 will ultimately die of the disease because of the inadequacies of current treatment. In the United States, cervical cancer disproportionately affects women who are members of minority groups and women of low socioeconomic status, partly because such women tend to have insufficient access to and knowledge of screening programs for cervical cancer. The nationwide use of such screening pro-

The New England
Journal of Medicine

© Copyright, 1999, by the Massachusetts Medical Society

VOLUME

PELVIC R
PELVIC A

MITC
CHARLES L

**ABSTRACT**

***Background***
fect of radioth
with that of p
therapy with
with advance
1997, 403 wo
confined to t
stage IB or IIA
or involvemer
domly assign
to the pelvis a

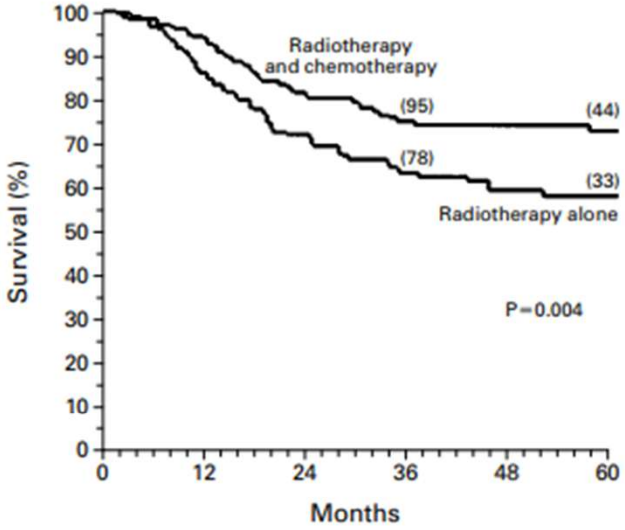



**Figure 1.** Kaplan–Meier Estimates of Survival among Patients Assigned to Receive Radiotherapy and Concurrent Chemotherapy and Those Assigned to Receive Radiotherapy Alone.
Numbers in parentheses are the numbers of patients alive and included in a follow-up assessment at three and five years.

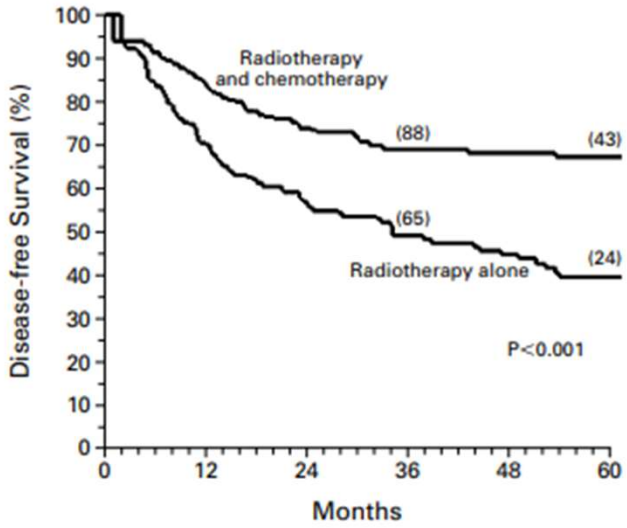



**Figure 2.** Kaplan–Meier Estimates of Disease-free Survival among Patients Assigned to Receive Radiotherapy and Concurrent Chemotherapy and Those Assigned to Receive Radiotherapy Alone.
Numbers in parentheses are the numbers of patients at risk at three and five years.

Early stage

Radical surgery vs Radiation

# Radical hysterectomy or radiotherapy for Stage I cervical cancer

## A prospective comparison with 5 and 10 year follow-up

MICHAEL NEWTON, M.D.

*Chicago, Illinois*

*A prospective study of the treatment of 119 patients with Stage I carcinoma of the cervix by radical hysterectomy alone (58 patients) or radiotherapy alone (61 patients) was undertaken between Jan. 1, 1956, and May 31, 1966. Eighty-one per cent of the patients treated by radical hysterectomy survived 5 years as compared with 74 per cent of those treated by radiotherapy. The 10 year survival rates were 75 and 65 per cent, respectively. These differences were not statistically significant. Complications of treatment were relatively few except for a greater incidence of urinary tract problems after surgical treatment; most of these were resolved with restoration of normal function. When recurrence occurred in the surgical series further treatment by radiotherapy offered a reasonable prospect of survival. Failure of radiotherapy left relatively little opportunity for later treatment by operation.*

SELECTION of the best treatment for early invasive carcinoma of the cervix is important because the disease is relatively curable at this stage. In the first 25 years of the century the only possible treatment was by operation. From 1925 to 1950 radiotherapy, because of primary treatment was limited to radical hysterectomy alone or radiotherapy alone. Treatment was confined to those patients who were judged operable, who had Stage I disease, and in whom no specific indications for either method were present. Furthermore, the type of

*Michael N. Am. J. Obstet. Gynecol. Vol 123(5) 535. 1975*

# Radical hysterectomy or radiotherapy for Stage I cervical cancer

## A prospective comparison with 5 and 10 year follow-

**Table IV.** Carcinoma of cervix—stage I;
5 year cumulative survival rate

| | *No.* | *Alive* | *Dead* | *Lost to follow-up* | *Cumulative survival (%)* |
|---|---|---|---|---|---|
| Operation | 58 | 46 | 11 | 1 | 81 |
| Radiotherapy | 61 | 42 | 15 | 4 | 74 |

**Table V.** Carcinoma of cervix—stage I;
10 year cumulative survival rate

| | *No.* | *Alive* | *Dead* | *Lost to follow-up* | *Cumulative survival (%)* |
|---|---|---|---|---|---|
| Operation | 43 | 24 | 14 | 5 | 75 |
| Radiotherapy | 50 | 21 | 19 | 10 | 65 |

*ırcinoma of the cervix*
*1 patients) was*
*per cent of the*
*d with 74 per cent of*
*nd 65 per cent,*
*plications of treatment*
*roblems after surgical*
*nction. When*
*therapy offered a*
*ly little opportunity*

y treatment was limited
r radiotherapy alone. T
e patients who were juc
disease, and in whom n
nethod were present. F

The difficulty of carrying through a study such as this over a period of years is considerable. It is hard to maintain consistency in diagnosis and treatment even with the same personnel in charge. Staging systems change: for example, a new International Staging classification was introduced by the International Federation of Gynecology and Obstetrics in 1961. Surgical and radiotherapeutic methods change and improve. Also, adequate follow-up, especially in a mobile population, is very difficult.

In spite of the complexities of this study and the problems of interpretation, it is reasonable to extrapolate the results to the present and to conclude (1) that there is relatively little difference in end-results between the two methods of treating Stage I carcinoma of the cervix and (2) that the differences noted in the complication rate may not be as great at this time.

Can additional information be obtained from similar studies in the future? Certainly it would be valuable to carry through to their conclusion investigations such as that begun by Roddick and Greenelaw.[22] Two points are worth considering in any future approach.

# Historical Evolution of Cervical Cancer Treatment

The shifting paradigms of management for early invasive carcinoma (1900-1955)

## 1900 ~ 1925

### The Surgical Era

- Only Possible Treatment
- Early invasive carcinoma was exclusively managed by surgical operation.

## 1925 ~ 1950

### The Radiotherapy Era

- Technological Leap
- Great improvements in RT techniques.
- Became the primary method for all stages in the US.

## 1944 ~ 1955

### The Clash of Paradigms

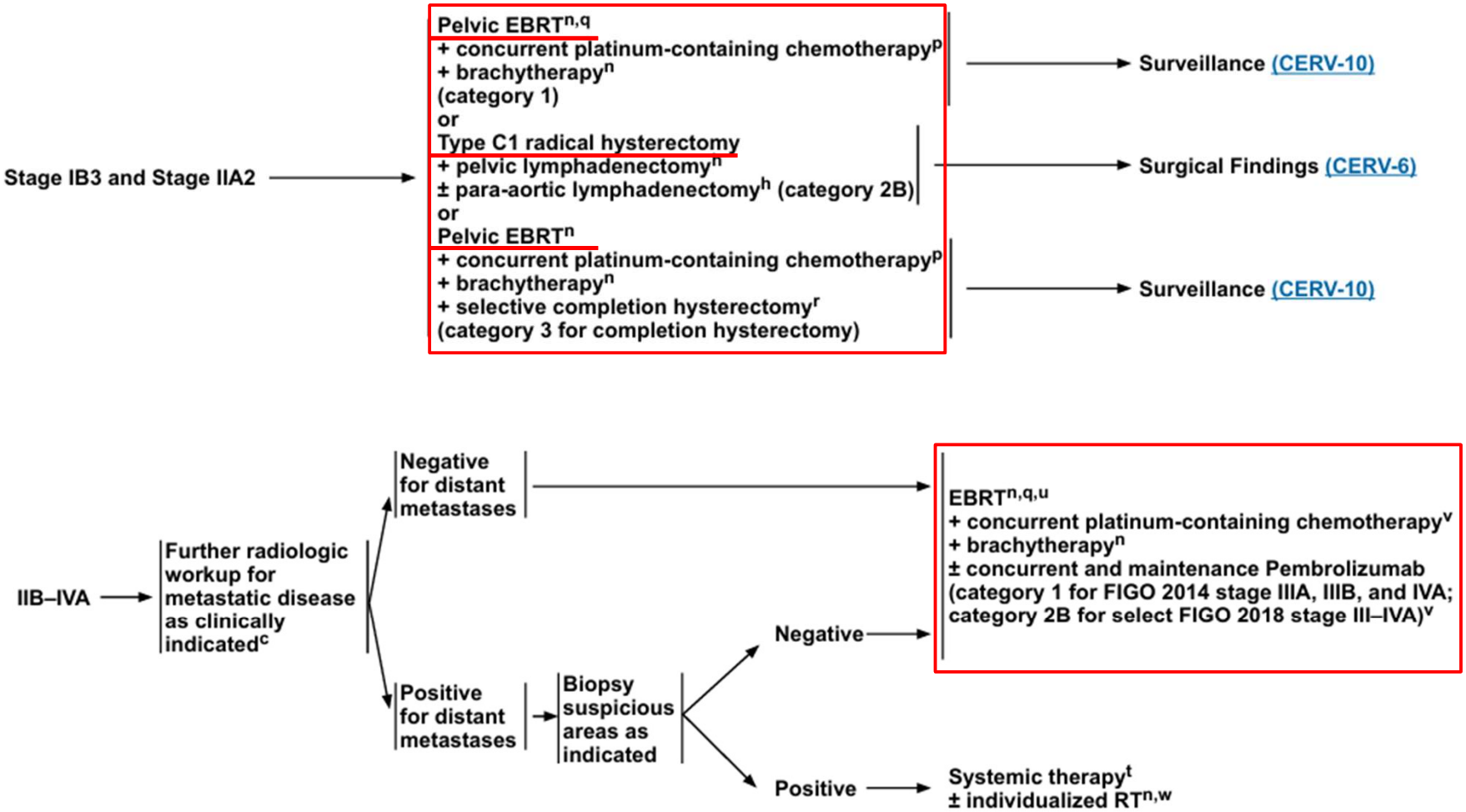
- Meigs (1944): Reintroduced the surgical approach.
- Controversy: Intense debate between exponents of operation vs. RT.

### Approaches to Resolve the Controversy (Until 1955)

01. Institutional Comparisons: Evaluating historical series of cases from different institutions.
02. Matched-Pairs Analysis: Comparing pairs of cases treated by different methods in the same institution.
03. Alternation of Modalities: Alternating RT or radical hysterectomy followed by RT for Stage I and II lesions.

자궁경부암 최신 치료 지견

# 전통적인 자궁경부암 치료의 기준: IIB →→ IB3 ?



자궁경부암 최신 치료 지견

# 2026년 현재

- 초기암 (≤2cm): 과도한 광범위 수술 범위(Radical Hysterectomy, LND)를 축소 Less Invasive (De-escalation)
  - SHAPE, PHENIX, Concerv & GOG-278
- Locally advanced : Radical surgery 유지, MIS 반대
  - LACC

# Less Invasive Surgical Trials in Early Cervical Cancer

Timeline of 4 major clinical trials shaping the de-escalation of surgical radicality

## 2018

### LACC Trial

**Surgical Approach (MIS vs. Open)**

- **Warning on MIS approach**
- Minimally invasive radical hysterectomy showed higher recurrence & lower OS vs. open surgery.
- Standard returned to open RH.

## 2021

### ConCerv

**Fertility saving**

- **Validated Fertility Sparing**
- Evaluation of oncological safety in tumors <=2cm after simple hysterectomy or cone biopsy.
- Demonstrated low recurrence and high pregnancy rate.

## 2024

### SHAPE Trial

**Parametrial Resection Scale**

- **Shift to Simple Hysterectomy**
- Simple hysterectomy (SH) proved non-inferior to radical hysterectomy (RH) in low-risk patients.
- Reduced surgical morbidity.

## 2025

### PHENIX Trial

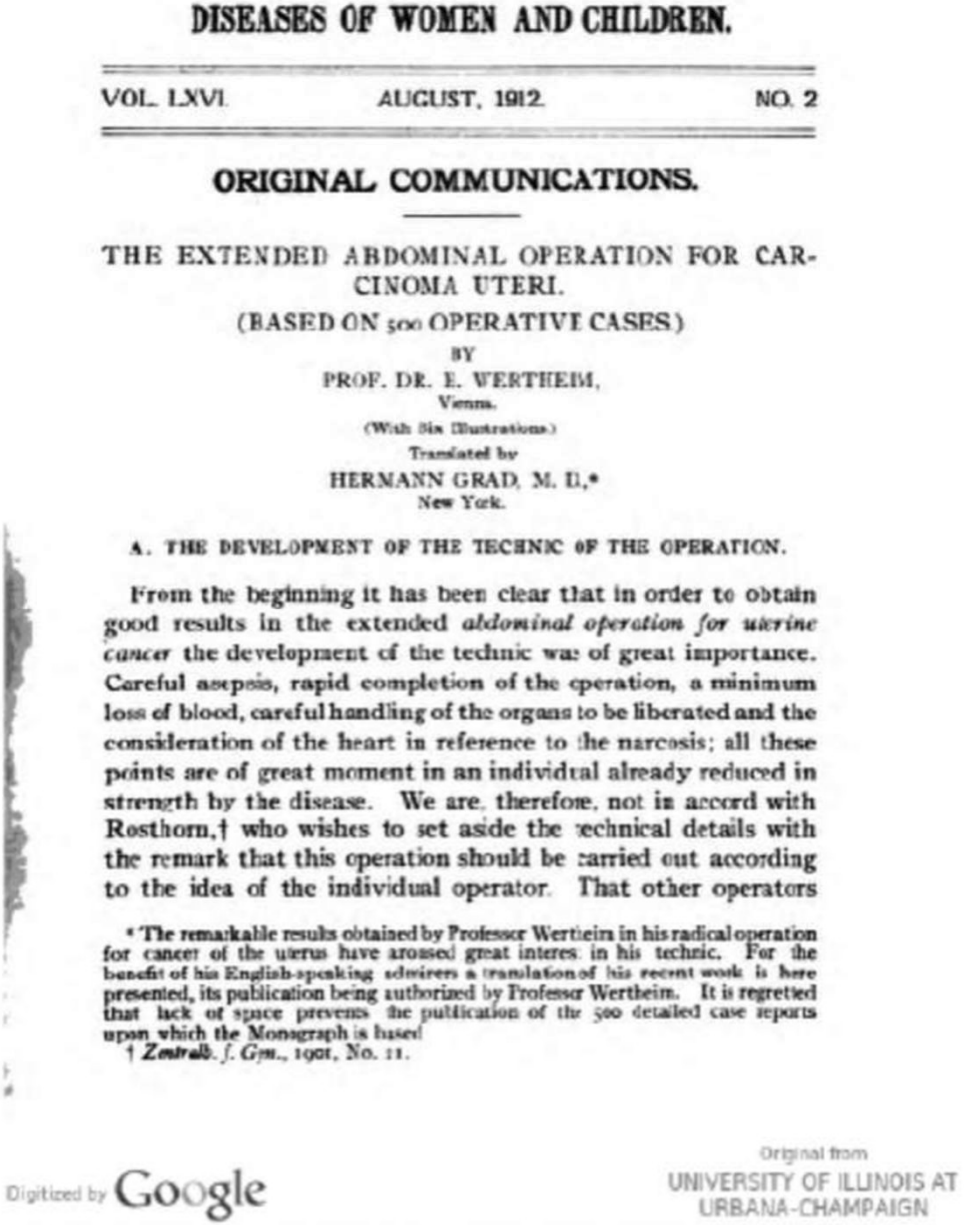
**Lymph Node De-escalation**

- **Omission of PLND**
- Safely omitted pelvic lymph node dissection (PLND) in early-stage patients with negative SLN.
- Reduced lymphedema.

자궁경부암 최신 치료 지견

# [Early stage] Less invasive surgery

- SHAPE trial
  - RH 수술은 100년전에 도입, 제대로 된 검증이 없었다
- PHENIX trial
  - Full LND 가 정말 필요한가에 대한 검증이 없었음
- LACC trial
  - MIS 도입이 가능한가
- Concerv trial
  - 자궁경부의 보존 or simple hysterectomy



DISEASES OF WOMEN AND CHILDREN.

VOL. LXVI. AUGUST, 1912. NO. 2

ORIGINAL COMMUNICATIONS.

THE EXTENDED ABDOMINAL OPERATION FOR CARCINOMA UTERI.

(BASED ON 500 OPERATIVE CASES)

BY

PROF. DR. E. WERTHEIM,

Vienna.

(With Six Illustrations.)

Translated by

HERMANN GRAD, M. D.,*

New York.

A. THE DEVELOPMENT OF THE TECHNIC OF THE OPERATION.

From the beginning it has been clear that in order to obtain good results in the extended *abdominal operation for uterine cancer* the development of the technic was of great importance. Careful asepsis, rapid completion of the operation, a minimum loss of blood, careful handling of the organs to be liberated and the consideration of the heart in reference to the narcosis; all these points are of great moment in an individual already reduced in strength by the disease. We are, therefore, not in accord with Rosthorn,† who wishes to set aside the technical details with the remark that this operation should be carried out according to the idea of the individual operator. That other operators

* The remarkable results obtained by Professor Wertheim in his radical operation for cancer of the uterus have aroused great interest in his technic. For the benefit of his English-speaking admirers a translation of his recent work is here presented, its publication being authorized by Professor Wertheim. It is regretted that lack of space prevents the publication of the 500 detailed case reports upon which the Monograph is based.

† *Zentralb. f. Gyn.*, 1901, No. 11.

Digitized by Google

Original from UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

ORIGINAL ARTICLE

# Simple versus Radical Hysterectomy in Women with Low-Risk Cervical Cancer

Marie Plante, M.D., Janice S. Kwon, M.D., Sarah Ferguson, M.D., Vanessa Samouëlian, M.D., Gwenael Ferron, M.D., Amandine Maulard, M.D., Cor de Kroon, M.D., Willemien Van Driel, M.D., John Tidy, M.D., Karin Williamson, M.D., Sven Mahner, M.D., Stefan Kommoss, M.D., Frederic Goffin, M.D., Karl Tamussino, M.D., Brynhildur Eyjólfsdóttir, M.D., Jae-Weon Kim, M.D., Noreen Gleeson, M.D., Lori Brotto, Ph.D., Dongsheng Tu, Ph.D., and Lois E. Shepherd, M.D., for the CX.5 SHAPE investigators*

## ABSTRACT

### BACKGROUND

Retrospective data suggest that the incidence of parametrial infiltration is low in patients with early-stage low-risk cervical cancer, which raises questions regarding the need for radical hysterectomy in these patients. However, data from large, randomized trials comparing outcomes of radical and simple hysterectomy are lacking.

### METHODS

We conducted a multicenter, randomized, noninferiority trial comparing radical hysterectomy with simple hysterectomy including lymph-node assessment in patients with low-risk cervical cancer (lesions of ≤2 cm with limited stromal invasion). The primary outcome was cancer recurrence in the pelvic area (pelvic recurrence) at 3 years. The prespecified noninferiority margin for the between-group difference in pelvic recurrence at 3 years was 4 percentage points.

The authors' affiliations are listed in the Appendix. Dr. Plante can be contacted at marie.plante@crhdq.ulaval.ca or at L'Hôtel-Dieu de Québec, 11 Côte du Palais, Quebec City, QC G1R 2J6, Canada.

*A list of the CX.5 SHAPE investigators is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Tu and Shepherd contributed equally to this article.

N Engl J Med 2024;390:819-29.
DOI: 10.1056/NEJMoa2308900
Copyright © 2024 Massachusetts Medical Society.

ORIGINAL ARTICLE

# Simple versus Radical Hysterectomy in Women with Low-Risk C

Marie Plante, M.D., Janice S. Kwon, M.D., Vanessa Samouëlian, M.D., Gwenael Ferron, M.D., Cor de Kroon, M.D., Willemien Van Driel, Karin Williamson, M.D., Sven Mahner, M.D., Frederic Goffin, M.D., Karl Tamussino, M.D., Br Jae-Weon Kim, M.D., Noreen Gleeson, M.D., Lori Bro and Lois E. Shepherd, M.D., for the CX.5

ABSTRACT

**BACKGROUND**

Retrospective data suggest that the incidence of para tients with early-stage low-risk cervical cancer, whic need for radical hysterectomy in these patients. How ized trials comparing outcomes of radical and sim

**METHODS**

We conducted a multicenter, randomized, noninf hysterectomy with simple hysterectomy including lyr with low-risk cervical cancer (lesions of ≤2 cm with primary outcome was cancer recurrence in the pelvic a The prespecified noninferiority margin for the bet recurrence at 3 years was 4 percentage points.

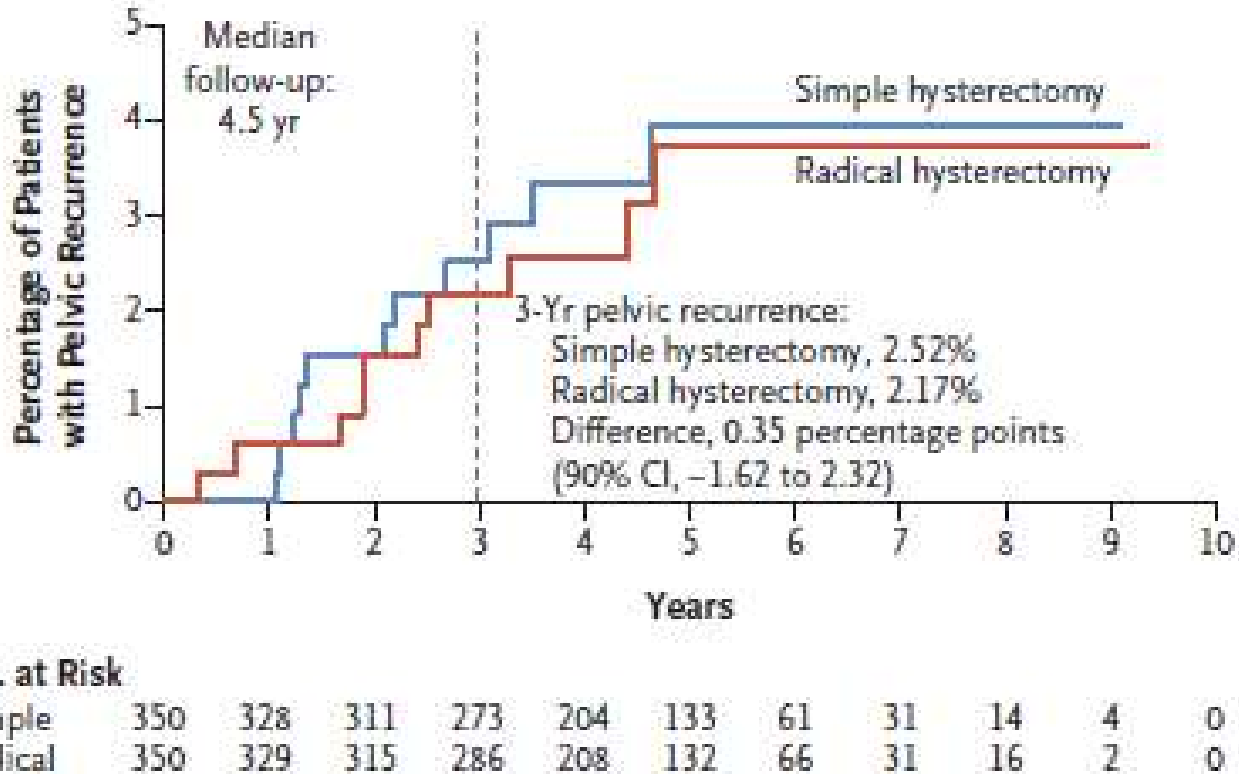



**Figure 1. Kaplan–Meier Curves for Pelvic Recurrence.**

ORIGINAL ARTICLE

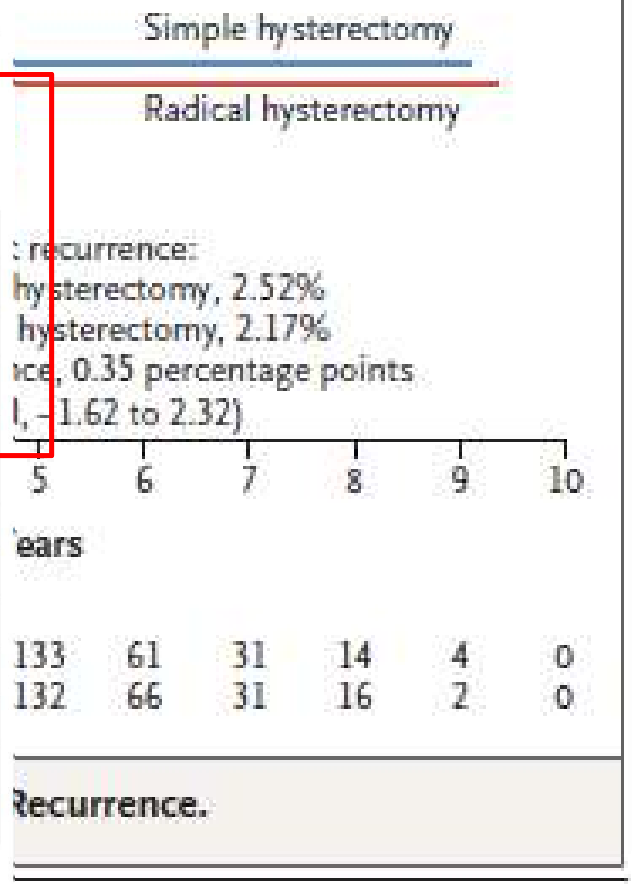
# Simple versus Radical Hysterectomy in Women with Low-Risk C

Marie Plante, M.D., Janice S. Kwon, M.D.

Table S2 Post Surgical Adjuvant Treatments

| | Number of Subjects (%) | |
|---|---|---|
| | Simple Hysterectomy N = 338 | Radical Hysterectomy N = 344 |
| Adjuvant treatment following surgery | 31 (9.2) | 29 (8.4) |
| Type of treatment | | |
| Chemotherapy only | 1 | 0 |
| Radiation therapy only | 15 | 11 |
| Chemoradiation | 15 | 18 |
| Indications for treatment* | | |
| Lesion size is > 2cm | 7 | 10 |
| Lymphovascular space invasion | 10 | 8 |
| Positive margins in the hysterectomy specimen | 4 | 6 |
| Non sentinel lymph node metastasis | 6 | 7 |
| Sentinel lymph node metastasis | 1 | 4 |
| Other | 7 | 3 |
| Missing | 2 | 2 |

*A patient may have more than one reason.

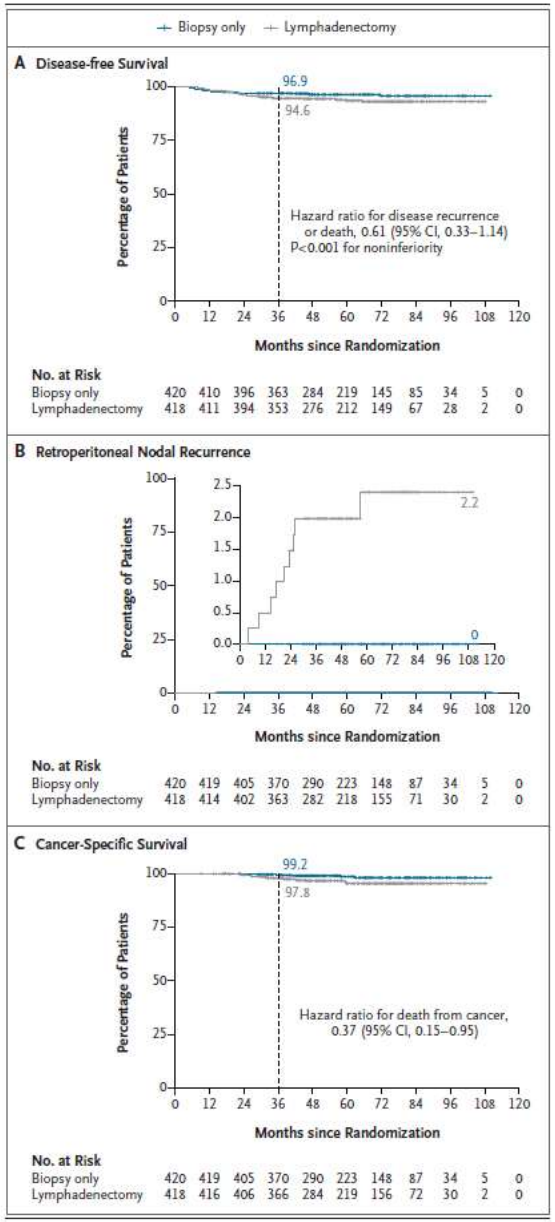


자궁경부암 최신 치료 지견

# [Stage IB1 (≤2cm)] 저위험군 초기암의 수술 축소: SHAPE Trial

- SHAPE : 종양 크기 2cm 이하, 기질 침윤 50% 미만의 저위험군 정의
  - Simple Hysterectomy(단순 자궁절제술)가 Radical 대비 골반 내 재발률 및 생존율에서 열세 없음
  - 수술 후 부작용의 획기적 감소: 급성/만성 방광 기능 부작용 및 성기능 합병증을 유의미하게 감소시킴

- 한계점 : Surgical approach, post-OP adjuvant treatment 에 제한이 없음.
  - 정말 수술의 효과인건지, adjuvant treatment(chemoradiation) 효과인건지 증명이 어려움




The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 16, 2025 VOL. 393 NO. 15

# Sentinel-Lymph-Node Biopsy Alone or with Lymphadenectomy in Cervical Cancer

H. Tu,[1] H. Huang,[1] Y. Li,[1] X. Chen,[2,3] C. Wang,[4] M. Zheng,[1] Y. Zhang,[1] W. Zhao,[5] Y. Feng,[1] T. Wan,[1] Y. Huang,[1] A. Yu,[6] W. Lu,[7] J. Xiao,[8] W. Shan,[2] P. Zhang,[6] C. Zhu,[7] D. Wang,[4] H. Zhou,[5] Jibin Li,[9] B. Kong,[10] W. Feng,[11] X. Wang,[12] R. Luo,[13] X. Huang,[1] Jundong Li,[1] Z. Lin,[1] S. Yao,[14] and J. Liu,[1] for the PHENIX Investigators*

## ABSTRACT

### BACKGROUND

Limited data are available on survival outcomes after sentinel-lymph-node biopsy alone as compared with lymphadenectomy in cervical cancer.

### METHODS

In this multicenter, randomized, noninferiority trial, we enrolled patients with cervical cancer that was stage IA1 (with lymphovascular invasion), IA2, IB1, or IIA1 according to 2009 International Federation of Gynecology and Obstetrics criteria. Sentinel-lymph-node biopsy was performed at the time of surgery and was followed by examination of frozen sections. Patients who had negative sentinel lymph nodes were intraoperatively assigned in a 1:1 ratio not to undergo pelvic lymphadenectomy (the biopsy-only group) or to undergo lymphadenectomy (the lymphadenectomy group). All the patients underwent hysterectomy, and adjuvant therapy was provided according to a unified protocol. The primary end point was disease-free survival at 3 years, with a prespecified noninferiority margin of 5 percentage points in the upper limit of the confidence interval for the difference between the lymphadenectomy group and the biopsy-only group. Secondary end points included retroperitoneal nodal recurrence, cancer-specific survival, and surgical complications.

The authors' full names, academic degrees, and affiliations are listed at the end of the article. Jihong Liu can be contacted at liujih@mail.sysu.edu.cn or at the Department of Gynecologic Oncology, Sun Yat-sen University Cancer Center, No. 651 Dongfeng Rd. E., Guangzhou 510060, China.

*A list of the PHENIX investigators is provided in the Supplementary Appendix, available at NEJM.org.

Hua Tu, He Huang, Yanfang Li, Xiaojun Chen, and Chunyan Wang contributed equally to this article.

N Engl J Med 2025;393:1463-74.
DOI: 10.1056/NEJMoa2506267
Copyright © 2025 Massachusetts Medical Society.

CME

**Table S9. Characteristics of Postoperative Pathological Findings.**

| | Intention-to-treat population | | Per-protocc |
|---|---|---|---|
| | Sentinel Biopsy (N = 420) | Lymphadenectomy (N = 418) | Sentinel Biopsy (N = 389) |
| **Tumor Size on Postoperative Specimen (%)*** | | | |
| Max diameter≤2 cm | 254 (60.5) | 251 (60.0) | 240 (61.7) |
| 2<Max diameter≤3 cm | 128 (30.5) | 125 (29.9) | 117 (30.1) |
| 3<Max diameter≤4 cm | 22 (5.2) | 25 (6.0) | 20 (5.1) |
| 4<Max diameter≤5 cm | 12 (2.9) | 15( 3.6) | 12 (3.1) |
| Max diameter>5 cm | 4 (1.0) | 2 (0.5) | 0 |
| **Pathological Factors (%)** | | | |
| Deep stromal invasion† | 128 (30.5) | 113 (27.0) | 110 (28.3) |
| Lymphovascular space invasion | 141 (33.6) | 131 (31.3) | 131 (33.7) |
| Parametrial involvement | 4 (1.0) | 3 (0.7) | 4 (1.0) |
| Positive vaginal margin | 7 (1.7) | 8 (1.9) | 7 (1.8) |
| Positive lymph node‡ | 8 (1.9) | 16 (3.8) | 7 (1.8) |
| Vaginal surgical margin<1cm | 8 (1.9) | 11 (2.6) | 7 (1.8) |

**Table S10. Adjuvant Treatments after Surgery.**

| | Sentinel Lymph Node Biopsy (N = 420) | Lymphadenectomy (N = 418) |
|---|---|---|
| **Adjuvant treatments*** | | |
| Chemoradiotherapy | 100 (23.8) | 88 (21.6) |
| EBRT+chemotherapy | 79 (18.8) | 69 (16.5) |
| VBT+chemotherapy | 6 (1.4) | 5 (1.2) |
| EBRT+VBT+chemotherapy | 15 (3.6) | 14 (3.3) |
| Radiotherapy alone | 46 (11.0) | 49 (11.7) |
| EBRT | 32 (7.6) | 37 (8.9) |
| VBT | 9 (2.1) | 7 (1.7) |
| EBRT+VBT | 5 (1.2) | 5 (1.2) |
| Chemotherapy alone | 58 (13.8) | 61 (14.6) |
| **No adjuvant treatment** | 216 (51.4) | 220 (52.6) |
| **Median days to adjuvant treatment** (range) | 28 (6-139) | 29 (5-93) |

*EBRT = External Beam Radiotherapy, VBT = Vaginal Brachytherapy

# Sentinel Lymph Node (SLN) Biopsy, PHENIX

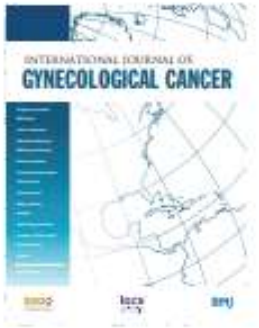
- Full LND 로 인한 다양한 수술후 삶의 질 저하문제
- SLN 만 시행해도 survival 에는 차이가 없고, 수술후 부작용이 현저히 적은 결과

- False Negative (위음성) 위험성: 미세 전이(Micrometastasis)나 Low-volume 병변을 놓칠 경우
- 장기 생존율 데이터 부재
  - Full Lymphadenectomy를 완전히 생략해도 장기 예후에 안전하다는 결과 필요
- Adjuvant treatment 의 적용을 임상의사가 결정하도록 설계되어, SLN vs Full LND 의 비교가 어려움
  - 전체환자의 50% 에서 adjuvant treatment(CCRT or radiation) 시행

# SLN biopsy

- 자궁경부암 림프 흐름(Lymphatic drainage)의 심한 개별 변이성
- 종양 비대로 인한 림프관 폐쇄: 추적제(ICG 등)가 차단되어 엉뚱한 림프절을 감시림프절로 오인할 위험 내포
- 전문가 사회의 합의
  - 종양학적 안전성이 완벽히 담보되지 않은 상태,
  - 병기 설정 오류 유발 가능
    - Surgical staging : incomplete

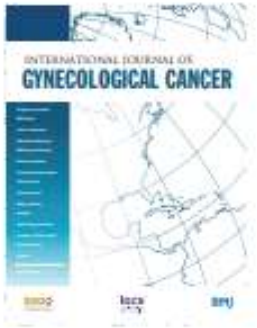
Original research




# Consensus on surgical technique for sentinel lymph node dissection in cervical cancer

Nicolò Bizzarri ,[1] Andreas Obermair ,[2] Heng-Cheng Hsu ,[3] Enrique Chacon ,[4] Anna Collins ,[5] Irina Tsibulak,[6] Alex Mutombo ,[7] Nadeem R Abu-Rustum ,[8] Vincent Balaya,[9] Alessandro Buda ,[10] David Cibula,[11] Allan Covens,[12] Francesco Fanfani ,[1] Gwenaël Ferron,[13] Michael Frumovitz ,[14] Benedetta Guani ,[15] Roman Kocian,[11] Christhardt Kohler ,[16,17] Eric Leblanc,[18] Fabrice Lecuru,[19] Mario M Leitao Jr ,[8] Patrice Mathevet,[20] Michael D Mueller,[21] Andrea Papadia,[22,23] Rene Pareja ,[24,25] Marie Plante,[26] Denis Querleu ,[1] Giovanni Scambia ,[1] Edward Tanner,[27] Ignacio Zapardiel ,[28] Jaime R Garcia,[29] Pedro T Ramirez [30]

*Bizzarri N, et al. Int J Gynecol Cancer 2024;34:504–509. doi:10.1136/ijgc-2023-005151*




# Consensus on surgical technique for sentinel lymph node dissection in cervical cancer

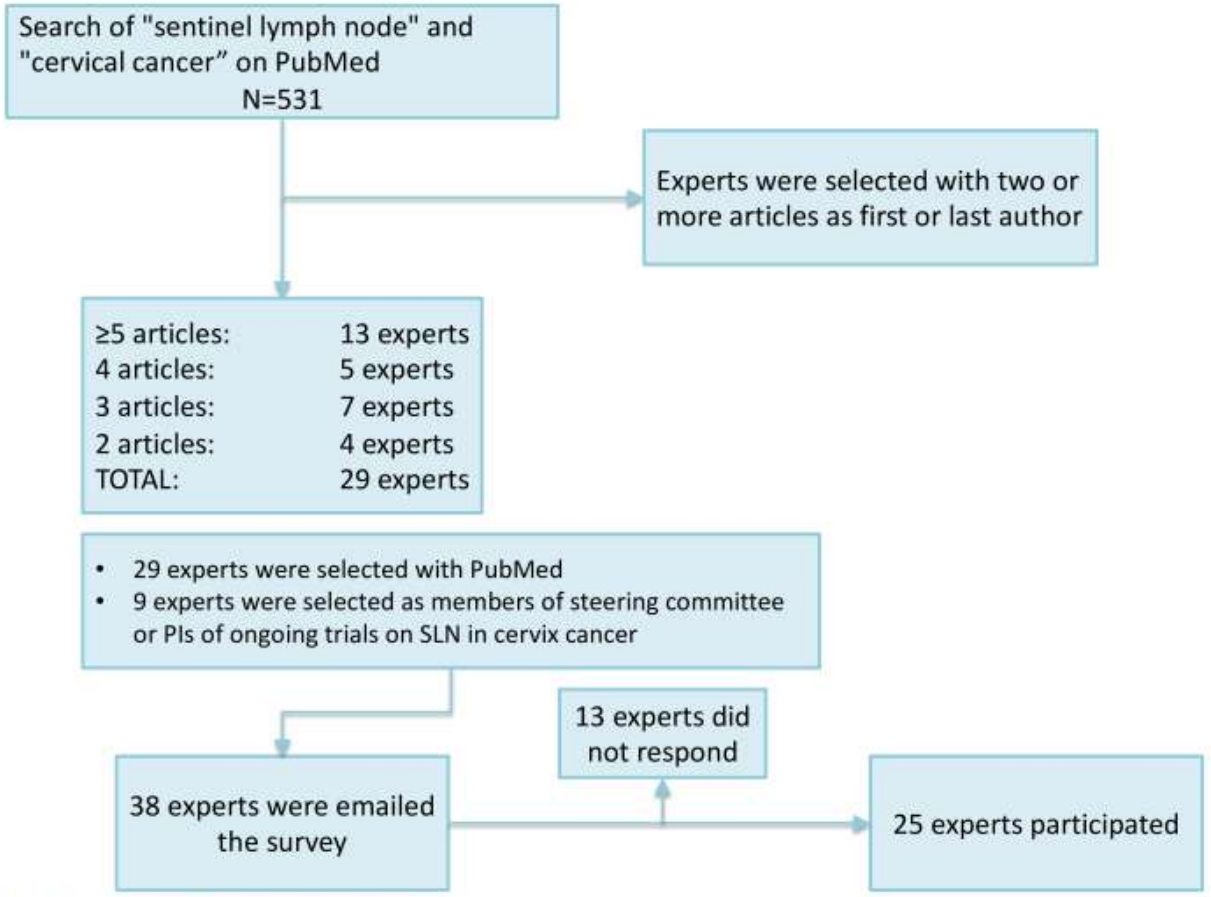



**Figure 1** Flowchart of inclusion process of experts.

**Box 1 Recommended, optional and non-recommended steps (experts agreement % in parenthesis)**

**Surgical step (% agreement)**

**Recommended steps**

Use indocyanine green (100%)

Inject at 3 and 9 o'clock (72%)

Superficial (with or without deep) injection (100%)

Grasp cervix with forceps only if part of cervix is free of tumor (88%)

Inject at the margins of uninvolved mucosa avoiding vaginal fornices (88%)

In case of simple trachelectomy/conization: minimally invasive surgery for SLN (88%)

Identification of following structures before SLN excision:

⇒ Ureter (88%)

⇒ Obliterated umbilical artery (80%)

⇒ External iliac artery and vein (88%)

Direction of dissection: start at uterine artery and continue laterally away from the uterus (88%)

Dissection/excision should be completed in one hemi-pelvis before proceeding to contralateral side (80%)

Parametrial SLN can be found medial to obliterated umbilical artery (80%)

Grasp the node only at the afferent/efferent channels (not at the center) (80%)

Labeling of specimens: obturator, internal iliac, external iliac, common iliac, aortic/caval, and presacral (88%)

Pathologic assessment: hematoxylin–eosin first and then ultrastaging if macrometastases not found (92%)

What to do in case of mapping failure: perform a side specific lymphadenectomy (84%)

If empty lymph node: reoperate with lymphadenectomy only if cervical factors/retrieved SLN (in one side) are not sufficient to define adjuvant treatment (84%)

**Optional/acceptable steps**

Blue dye (76%) or radiotracer (92%)

Hemostatic clips could be used during SLN excision (72%)

Perform frozen section to avoid empty lymph node packets (but only if there is a suspect of SLN metastasis) (72%)*

**Non-recommended steps**

Inject at 6 and 12 o'clock (76%)

Injection in the tumor in case of tumor completely replacing cervix (88%)

Removal of nodes through port without protective maneuvers (88%)

Pathologic assessment: hematoxylin–eosin only (88%)†

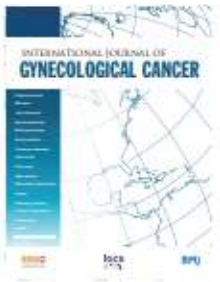
Modify concentration of tracer at time of reinjection in case of mapping failure (72%)

*This question did not reach consensus to be recommended.
†This question did not reach consensus to be recommended or optional.
SLN, sentinel lymph node.

자궁경부암 최신 치료 지견

# ConCerv : Non-radical surgery to Early stage cervical cancer

- IA2, IB1 을 대상으로 Conization or simple hysterectomy + PLND




Original research

## ConCerv: a prospective trial of conservative surgery for low-risk early-stage cervical cancer

Kathleen M Schmeler ,[1] Rene Pareja ,[2] Aldo Lopez Blanco,[3] Jose Humberto Fregnani,[4] Andre Lopes,[5] Myriam Perrotta,[6] Audrey T Tsunoda,[7] David F Cantú-de-León,[8] Lois M Ramondetta,[1] Tarinee Manchana,[9] David R Crotzer,[10] Orla M McNally,[11] Martin Riege,[12] Giovanni Scambia,[13] Juan Manuel Carvajal,[14] Julian Di Guilmi,[15] Gabriel J Rendon ,[16] Preetha Ramalingam,[17] Bryan M Fellman,[18] Robert L Coleman,[19] Michael Frumovitz ,[1] Pedro T Ramirez[1]

For numbered affiliations see end of article.

**Correspondence to**
Dr Kathleen M Schmeler, Gynecologic Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77230, USA; KSchmele@mdanderson.org

**HIGHLIGHTS**

- Conservative surgery was associated with a 3.5% recurrence rate in women with low-risk cervical cancer.
- The rate of positive lymph nodes was 5%, with lymph node assessment recommended in this low-risk population.
- Further study is needed to determine long-term outcomes and optimal pathologic criteria for conservative surgery.

**ABSTRACT**

**Objective** The objective of the ConCerv Trial was to prospectively evaluate the feasibility of conservative surgery in women with early-stage, low-risk cervical cancer.

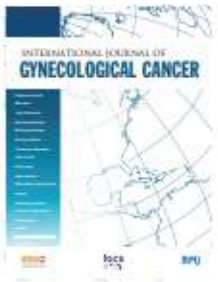
**Discussion** Our prospective data show that select patients with early-stage, low-risk cervical carcinoma may be offered conservative surgery.

INTRODUCTION

- **Histology & Grade Requirements**
  - Squamous cell carcinoma (any grade)
  - Adenocarcinoma (grade 1 or 2 only)
- **Tumor Size & Depth of Invasion**
  - Tumor size < 2 cm (by physical exam / imaging)
  - Depth of invasion < 10 mm
- LVSI Negative
- Negative Imaging for Metastatic Disease
  - Clear scans via CT, MRI, and/or PET
- **Pre-operative Evaluation**
  - Conization margins negative for malignancy
  - Endocervical curettage (ECC) negative for malignancy & high-grade dysplasia

# ConCerv : Non-radical surgery to Early stage cervical cancer

- IA1, IA2, IB1 을 대상으로 Conization or sim




## ConCerv: a prospective trial ( surgery for low-risk early-st cervical cancer

Kathleen M Schmeler ,[1] Rene Pareja ,[2] Aldo Lopez Blan Andre Lopes,[5] Myriam Perrotta,[6] Audrey T Tsunoda,[7] David F ( Tarinee Manchana,[9] David R Crotzer,[10] Orla M McNally,[11] Mart Juan Manuel Carvajal,[14] Julian Di Guilmi,[15] Gabriel J Rendon Bryan M Fellman,[18] Robert L Coleman,[19] Michael Frumovitz

For numbered affiliations see end of article.

**Correspondence to**
Dr Kathleen M Schmeler, Gynecologic Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77230, USA; KSchmele@mdanderson.org

**HIGHLIGHTS**

- Conservative surgery was associated with a 3.5% recurrence rate in w
- The rate of positive lymph nodes was 5%, with lymph node assessmen
- Further study is needed to determine long-term outcomes and optimal

**ABSTRACT**

**Objective** The objective of the ConCerv Trial was to prospectively evaluate the feasibility of conservative surgery in women with early-stage, low-risk cervical cancer.

**Discussio**
patients wit
be offered c

**Original research**

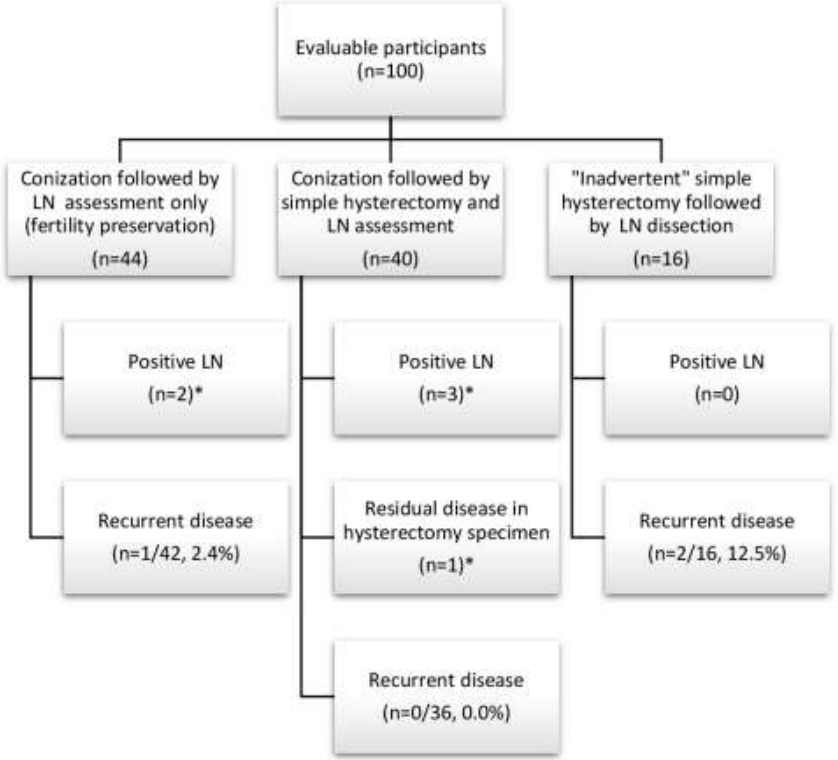



**Figure 1** Study results by treatment type. Lymph node (LN), pelvic lymph node assessment with sentinel lymph node biopsy and/or full pelvic lymphadenectomy. *Patients with positive lymph nodes or residual disease in the hysterectomy specimen were excluded from further analyses for rates of recurrent disease.

MIS(Laparoscopy or Robot)
Vs.
Open Laparotomy

연구에서 밝히고 싶은것은,
: MIS 가 non-inferior 하다

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 15, 2018 VOL. 379 NO. 20

# Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer

Pedro T. Ramirez, M.D., Michael Frumovitz, M.D., Rene Pareja, M.D., Aldo Lopez, M.D., Marcelo Vieira, M.D., Reitan Ribeiro, M.D., Alessandro Buda, M.D., Xiaojian Yan, M.D., Yao Shuzhong, M.D., Naven Chetty, M.D., David Isla, M.D., Mariano Tamura, M.D., Tao Zhu, M.D., Kristy P. Robledo, Ph.D., Val Gebski, M.Stat., Rebecca Asher, M.Sc., Vanessa Behan, B.S.N., James L. Nicklin, M.D., Robert L. Coleman, M.D., and Andreas Obermair, M.D.

## ABSTRACT

### BACKGROUND

There are limited data from retrospective studies regarding whether survival outcomes after laparoscopic or robot-assisted radical hysterectomy (minimally invasive surgery) are equivalent to those after open abdominal radical hysterectomy (open surgery) among women with early-stage cervical cancer.

### METHODS

In this trial involving patients with stage IA1 (lymphovascular invasion), IA2, or IB1 cervical cancer and a histologic subtype of squamous-cell carcinoma, adenocarcinoma, or adenosquamous carcinoma, we randomly assigned patients to undergo minimally invasive surgery or open surgery. The primary outcome was the rate of disease-free survival at 4.5 years, with noninferiority claimed if the lower boundary of the two-sided 95% confidence interval of the between-group difference (minimally invasive surgery minus open surgery) was greater than −7.2 percentage points (i.e., closer to zero).

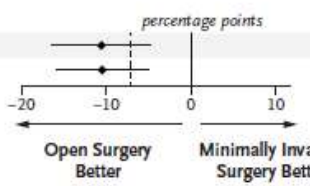
The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Ramirez at the Department of Gynecologic Oncology and Reproductive Medicine, Unit 1362, University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, or at peramire@mdanderson.org.

This article was published on October 31, 2018, at NEJM.org.

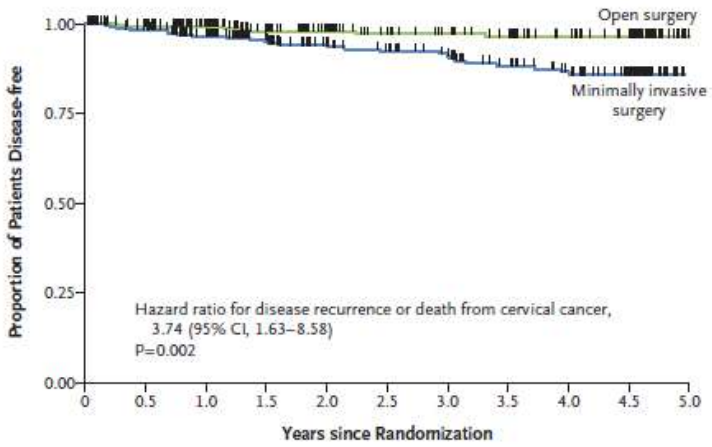
N Engl J Med 2018;379:1895-904.
DOI: 10.1056/NEJMoa1806395
Copyright © 2018 Massachusetts Medical Society.

A

| Population | Disease-free Survival Rate at 4.5 Yr (95% CI) | | Difference (95% CI) | P Value for Noninferiority |
|---|---|---|---|---|
| | Minimally Invasive Surgery | Open Surgery | | |
| | *percent* | | *percentage points* | |
| Intention-to-treat population | 86.0 (79.7–90.4) | 96.5 (92.7–98.4) | | 0.87 |
| Per-protocol population | 87.1 (81.0–91.3) | 97.6 (94.1–99.0) | | 0.88 |



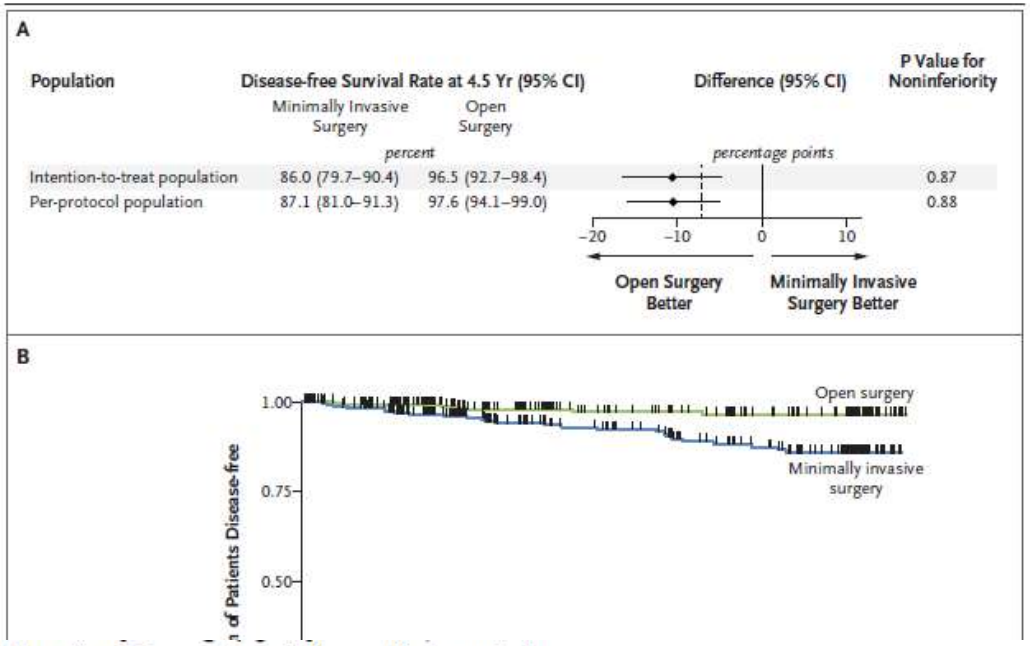

B




| No. at Risk | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Open surgery | 312 | 280 | 236 | 187 | 163 | 144 | 134 | 123 | 104 | 90 | 7 |
| Minimally invasive surgery | 319 | 292 | 244 | 192 | 167 | 155 | 142 | 121 | 102 | 80 | 5 |

**Figure 1. Estimates of Disease-free Survival.**

Minimally invasive surgery indicates laparoscopic or robot-assisted radical hysterectomy, and open surgery indicates open abdominal radical hysterectomy. Panel A shows the difference in disease-free survival rates between surgical groups at 4.5 years after surgery for both the intention-to-treat and per-protocol populations. The dashed line denotes the noninferiority margin of −7.2 percentage points. Noninferiority of minimally invasive surgery would be declared if the lower boundary of the two-sided 95% confidence interval were above this margin (i.e., to the right of this line). The P value for noninferiority is two-sided. Panel B shows the Kaplan–Meier disease-free survival curves for the surgical groups. The hazard ratio, 95% confidence interval, and corresponding P value were estimated with the use of Cox proportional-hazards models. Tick marks indicate censored data. Disease recurrence or death from cervical cancer occurred in 27 of 319 patients in the minimally invasive surgery group and 7 of 312 patients in the open-surgery group.




for the surgical groups. The hazard ratio, 95% confidence interval, and corresponding P value were estimated with the use of Cox proportional-hazards models. Tick marks indicate censored data. Disease recurrence or death from cervical cancer occurred in 27 of 319 patients in the minimally invasive surgery group and 7 of 312 patients in the open-surgery group.

others[10-12] have found 5-year rates of disease-free survival among patients who underwent open radical hysterectomy that range from 93.3 to 94.4%. These rates are consistent with the 4.5-year rate of disease-free survival of 96.5% reported in our prospective trial. Peters et al.[10] found a 4-year rate of progression-free survival of only 80% among patients undergoing chemotherapy and radiation after open radical hysterectomy. However, in that study, patients were required to have positive pelvic nodes, positive margins, or positive parametrial involvement to be enrolled. Rotman et al.[11] evaluated the recurrence-free interval and overall survival among

analysis.

Our trial has several limitations in that it did not reach its final intended enrollment, owing to the safety alert raised by the data and safety monitoring committee on the basis of the higher rates of recurrence and death in the minimally invasive surgery group than in the open-surgery group. The initial power was based on the assumption that there would have been a 4.5-year follow-up period for all the patients. However, at the time of analysis, 59.7% of the patients had reached the 4.5-year time point (median follow-up, 2.5 years). Even so, the trial did reach 84% power to declare noninferiority for our primary

# LACC trial : MIS 의 배제

- 종양 크기가 2cm를 초과하는 Locally advanced cancer
- 골반 림프절(Pelvic LN) 전이율의 동반 상승으로 인한 예후 악화 우려?
- Parametrial invasion 에 대한 대처가 어려움. Uterine manipulator 로 인해 micro dissemination?
- Skilled surgeon? 실력양성할때까지 치료받는 환자의 억울함?

자궁경부암 최신 치료 지견

# Surgical De-escalation 요약

- SHAPE / PHENIX
  - 2cm 이하 저위험군: Simple Hysterectomy로 축소 (QoL 극대화) +/- Adjuvant treatment
  - SLN 한계인정
    - No LND vs full LND 연구
    - Tumor specific antigen 을 활용한 microimetastasis detection 방법 연구

- 종양 크기 및 위험도 스펙트럼에 따른 선별적 치료 체계 구축 필요
  - 수술 vs CCRT 가 아닌, 적절한 수술과 적절한 adjuvant treatment 의 추가
  - Simple or Modified etc + adjuvant treatment 의 QoL 연구 동반

# 마지막 Slide

- FIGO 2018 stage 의 정리가 필요
  - LN metastasis 에 의한 예후의 차이분석,
  - Original tumor 와 LN metastasis 두가지 factor 중 어느것이 예후에 직접적인 영향을 주는지
  - IIA 와 IIB 의 진행방향성

- Radical surgery VS CCRT

→ 적절한 수술 + 적절한 adjuvant treatment

→ Micrometastasis 를 확인하는 new technique 연구