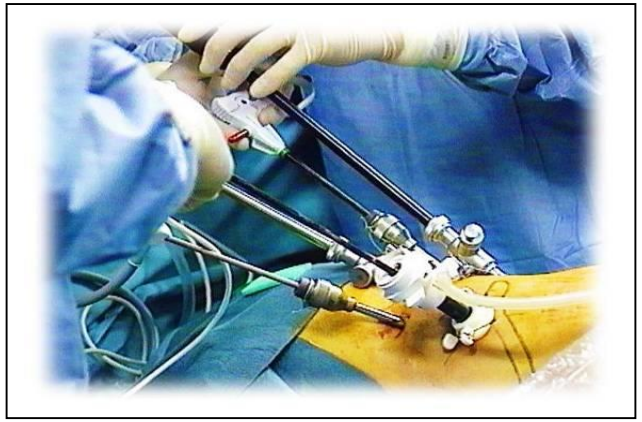
Chirurgia Mini-Invasiva: Quale Ruolo nel Trattamento della Neoplasia Cervicale?

Luca Bocciolone, MD

Ginecologia Chirurgica Oncologica

IRCCS Ospedale San Raffaele – Milano

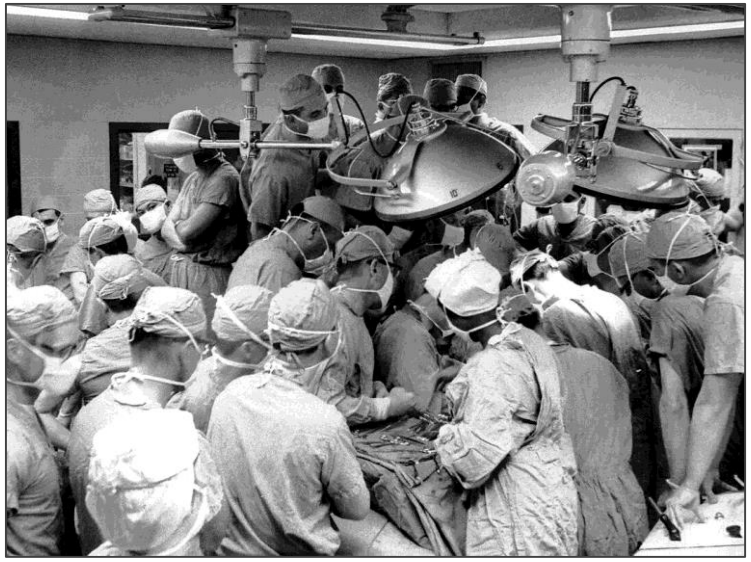
Unanswered Question:
Surgical Approach
Early Clinical Stage Cervical Cancer



Minimally Invasive Surgery

What shall we do?

Open Surgery



The Flipside of the Coin

Feasible & Safe Procedure
Less Morbidity
Better Peri-operative Outcomes

Shorter hospital stay
Less post-op pain
Less blood loss
Lower transfusion rates
Early recovery
Better cosmetic result
Improved QoL

Survival
Oncologic
Outcomes

PFS / DFS
OS

Pros

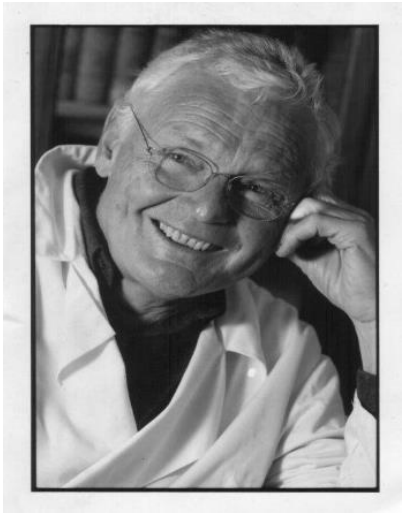
Minimally
Invasive Surgery

Cons

CERVICAL CANCER - LAPAROSCOPY

"A new future for Schauta operation through presurgical retroperitoneale pelviscopy"

D. Dargent — EUR J GYNECOL ONCOL 1987



D. DARGENT

RADICAL VAGINAL HYSTERECTOMY:

1880 Novak
1908 Schauta
1031 Stoeckel
1934 Peham & Amreich

TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY

- 1992 M. Canis
- 1995 D. Querleu

M. CANIS

D. QUERLEU

Wang et al. BMC Cancer (2015) 15:928
DOI 10.1186/s12885-015-1818-4

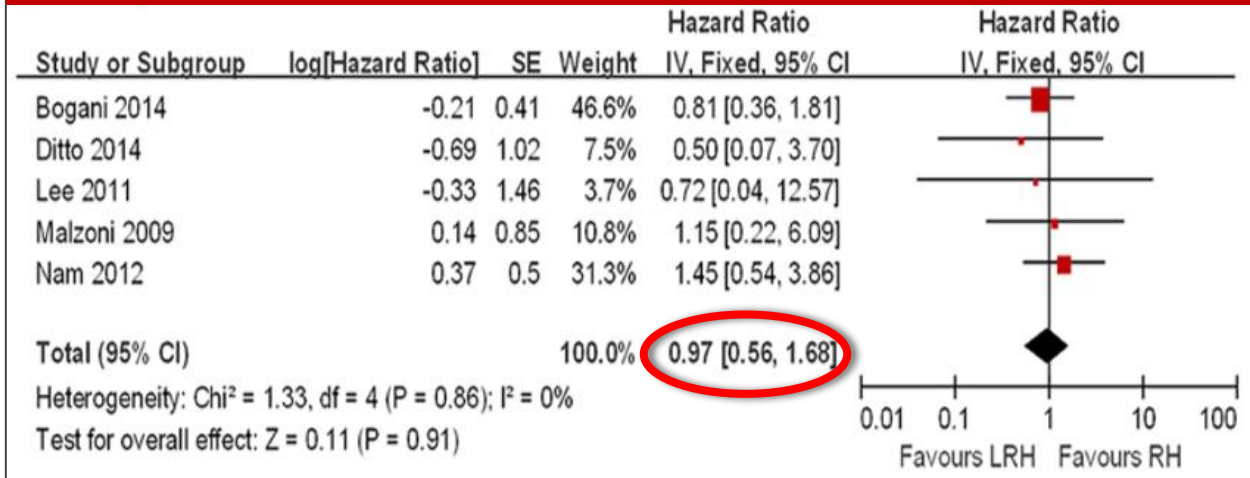
BMC Cancer

RESEARCH ARTICLE Open Access

Laparoscopy versus laparotomy for the management of early stage cervical cancer

Yan-zhou Wang[1], Li Deng[1], Hui-cheng Xu[1], Yao Zhang[2*†] and Zhi-qing Liang[1*†]

5-yrs Disease-Free Survival



Overall Survival

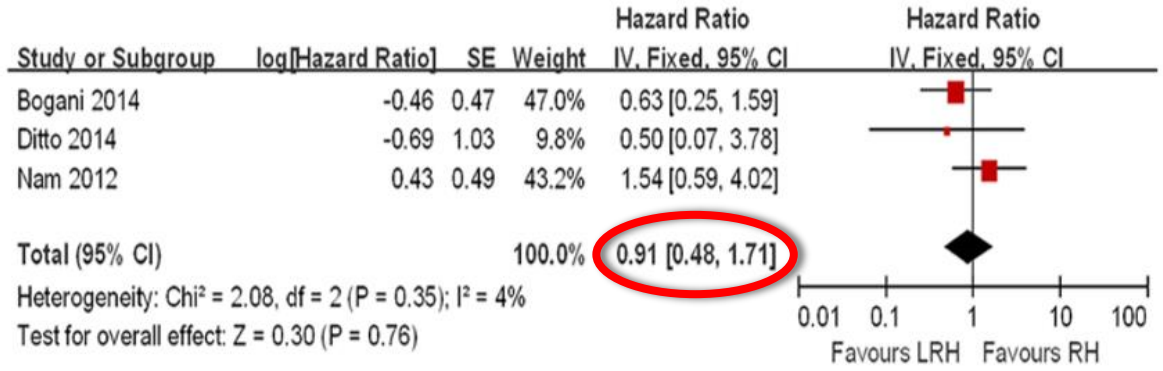
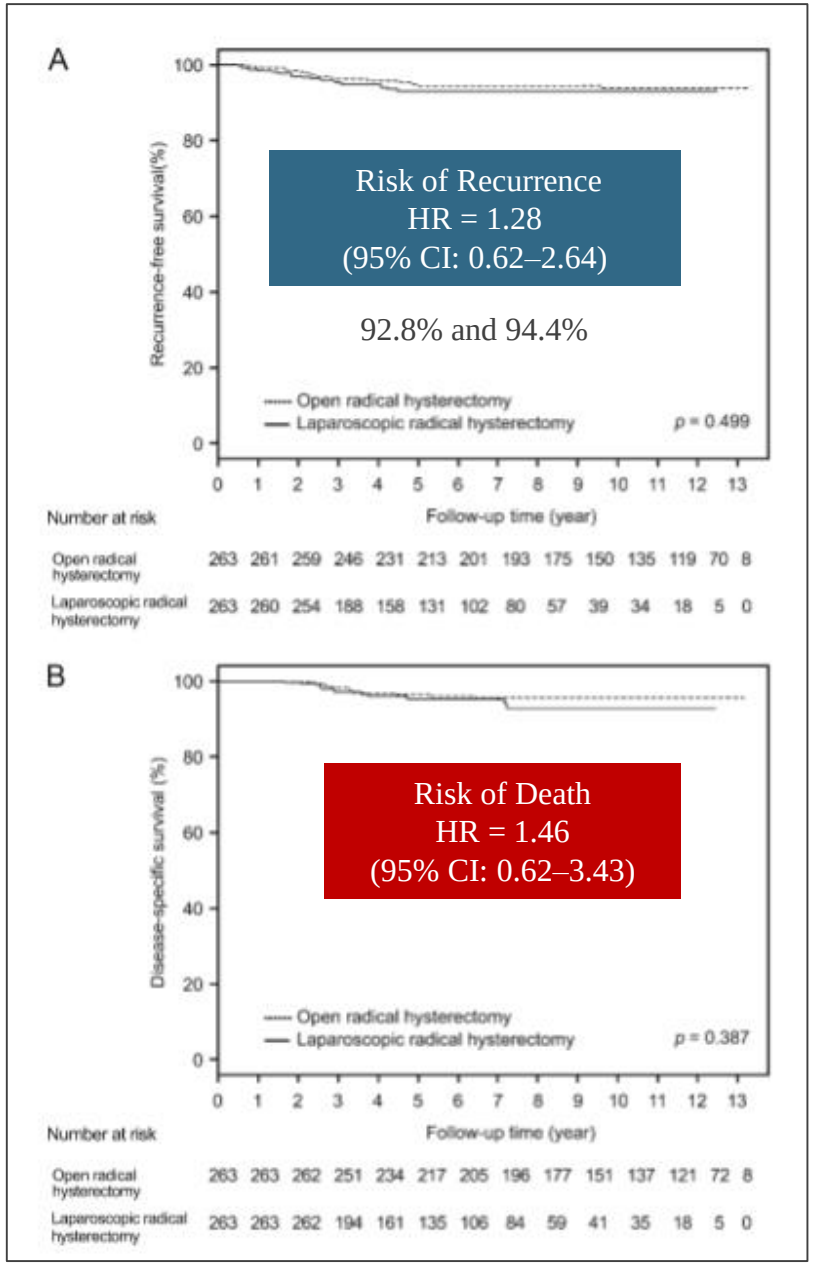


Table 3 Study outcomes

References	Approach	Number	Operative time (min)	Blood loss (ml)	Transfusion rate (%)	Nodal counts	Duration of hospital stay	Removal of foley catheter	Surgical margins positive	5-years disease free survival, (%)	5-years overall survival, (%)
Bogani et al. [31]	Laparoscopic	65	245 ± 72.2	200 ± 297.5	4 (6)	23.2 ± 8.2	4 ± 3.3	–	–	83 %	89 %
	Open	65	259.5 ± 69.6	500 ± 475	14 (22)	27.4 ± 17.2	8 ± 1.8	–	–	80 %	83 %
Chen et al. [20]	Laparoscopic	32	292.8 ± 65.2	225.0 ± 164.1	8 (25.0)	29.7 ± 15.4	9.0 ± 2.7	–	–	–	–
	Open	44	302.9 ± 76.4	1139.0 ± 656.8	33 (75.0)	27.8 ± 11.0	11.2 ± 3.3	–	–	–	–
Ditto et al. [25]	Laparoscopic	60	215.9 ± 61.6	50 ± 112.5	1 (2)	25.4 ± 10.0	4 ± 2	–	–	–	–
	Open	60	175.2 ± 32.1	200 ± 112.5	3 (5)	34.6 ± 13.5	6 ± 2.8	–	–	–	–
Frumovitz et al. [26]	Laparoscopic	35	–	319.0 ± 492.0	11 (31.4)	–	–	13.5 ± 4.5	3 (8.6)	–	–
	Open	54	–	548.0 ± 387.5	15 (27.8)	–	–	13 ± 9.3	2 (3.7)	–	–
Ghezzi et al. [27]	Laparoscopic	50	–	–	0	21 ± 10.3	6 ± 2.8	–	3 (6.0)	–	–
	Open	48	–	–	4 (8)	23 ± 10.8	10 ± 7.0	–	3 (6.2)	–	–
Lee et al. [21]	Laparoscopic	24	334.8 ± 52.4	414.3 ± 69.2	5 (20.8)	26.3 ± 11.8	–	–	0	90.5	–
	Open	48	326.8 ± 53.8	836.0 ± 315.8	23 (47.9)	26.8 ± 13.6	–	–	0	93.3	–
Li et al. [22]	Laparoscopic	90	263.0 ± 67.6	369.8 ± 249.9	–	21.3 ± 8.4	–	10.7 ± 7.2	–	–	–
	Open	35	217.2 ± 71.6	455.1 ± 338.1	–	18.8 ± 9.5	–	8.6 ± 6.8	–	–	
Lim et al. [23]	Laparoscopic	18	308.0 ± 66.0	425 ± 225	–	17 ± 7.5	5.5 ± 1.5	19.5 ± 10.3	–	–	
	Open	30	240.0 ± 90.0	500 ± 1455	–	21.0 ± 11.8	6 ± 6.5	21.0 ± 11.8	–	–	
Malzoni et al. [28]	Laparoscopic	65	196.0 ± 14.5	55.0 ± 12.5	–	23.5 ± 5.1	–	10 ± 2	–	92.4	–
	Open	62	152.0 ± 19.8	145.0 ± 41.3	–	25.2 ± 6.2	–	13 ± 2.5	–	93.6	–
Nam et al. [24]	Laparoscopic	263	246.8 ± 84.8	379.6 ± 350.0	76 (28.9)	–	–	7.2 ± 1.5	1 (0.4)	92.8	95.2
	Open	263	247.2 ± 86.3	541.1 ± 730.0	106 (40.3)	–	–	7.5 ± 4.3	2 (0.8)	94.4	96.4
Toptas et al. 2014	Laparoscopic	22	–	–	–	–	–	–	1 (4.5)	–	–
	Open	46	–	–	–	–	–	–	1 (2.2)	–	–
Zakashansky et al. [30]	Laparoscopic	30	318.5 ± 66.0	200.0 ± 125.0	0	31.0 ± 12.8	–	–	–	–	–
	Open	30	242.5 ± 69.5	520.0 ± 375.0	5 (16.7)	21.8 ± 8.5	–	–	–	–	–

No. 12

Wang et al. BMC Cancer 2015

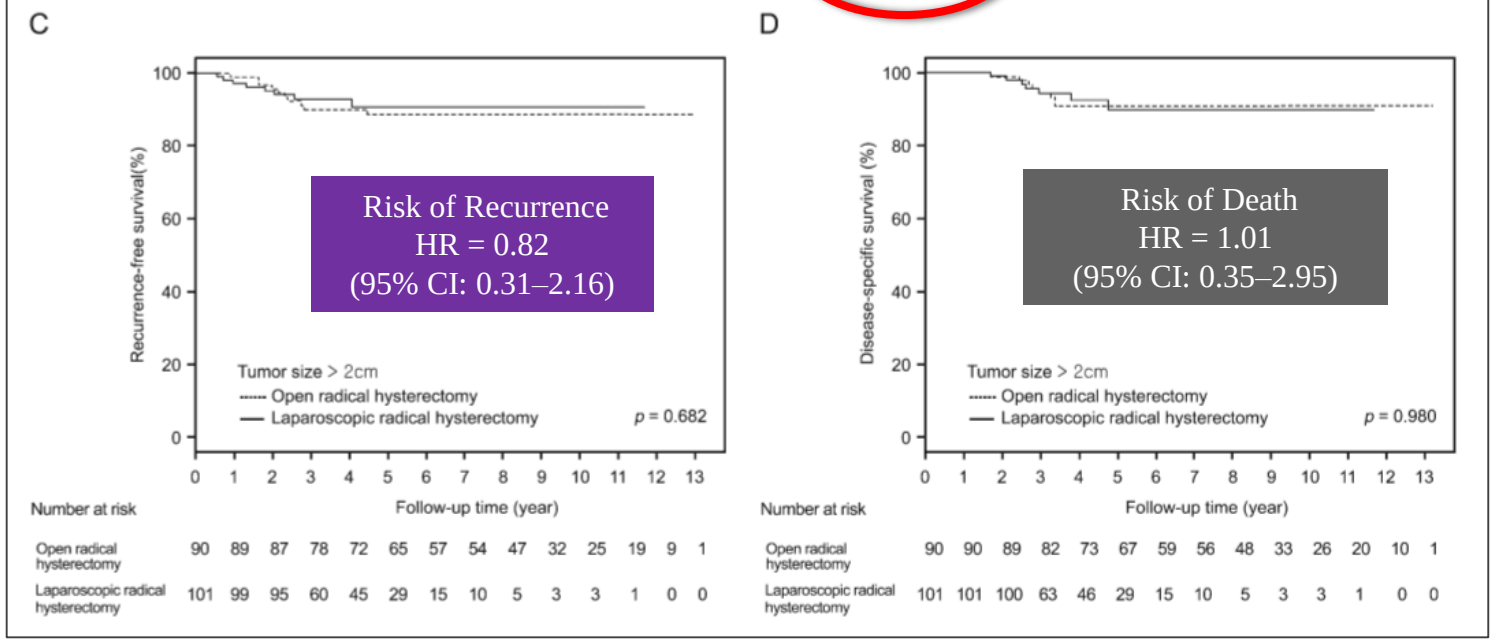


Annals of Oncology 23: 903–911, 2012
doi:10.1093/annonc/mdr360
Published online 12 August 2011

Laparoscopic versus open radical hysterectomy in early-stage cervical cancer: long-term survival outcomes in a matched cohort study

J.-H. Nam†*, J.-Y. Park†, D.-Y. Kim, J.-H. Kim, Y.-M. Kim & Y.-T. Kim

Tumor Size > 2 cm

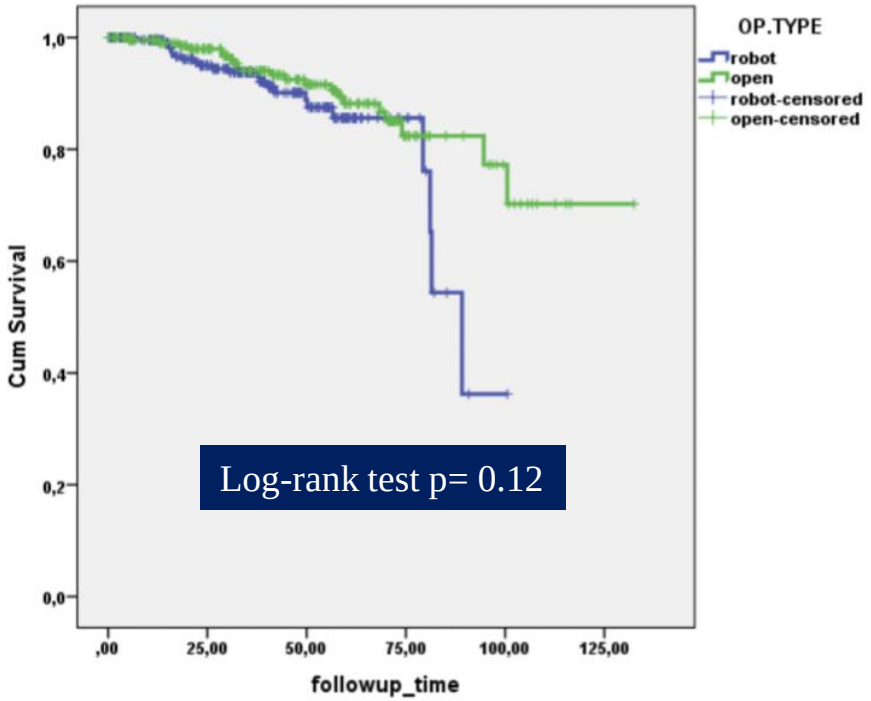


Available online at www.sciencedirect.com
ScienceDirect
EJSO
the Journal of Cancer Surgery
EJSO 42 (2016) 513–522
www.ejso.com

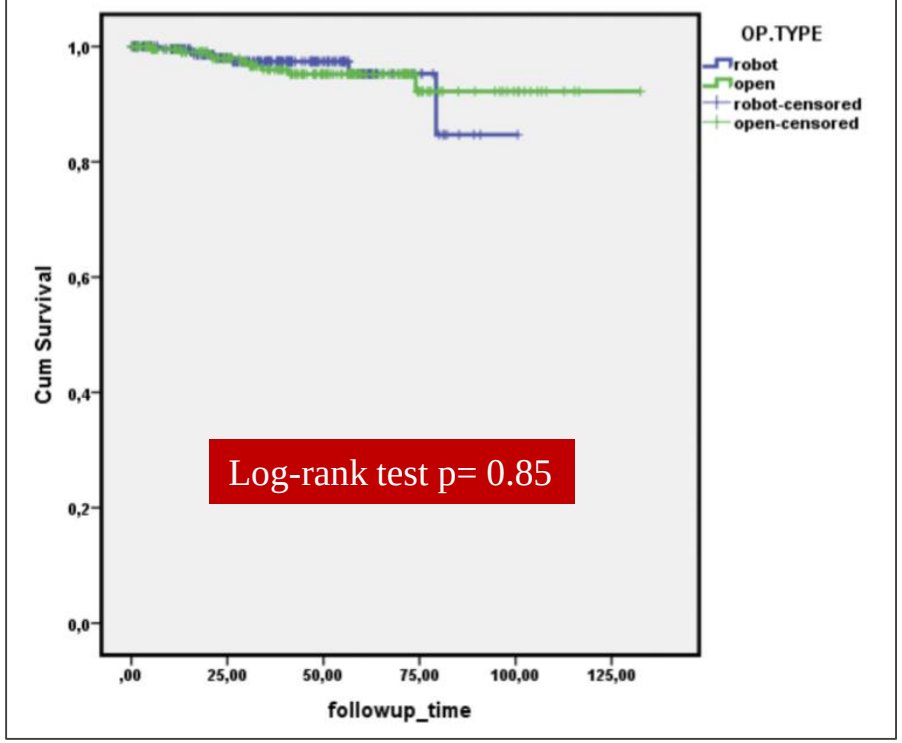
Robot-assisted versus open radical hysterectomy: A multi-institutional experience for early-stage cervical cancer☆

B.M. Sert [a,*], J.F. Boggess [b], S. Ahmad [c], A.L. Jackson [b,f], N.M. Stavitzski [c], A.A. Dahl [d,e], R.W. Holloway [c]

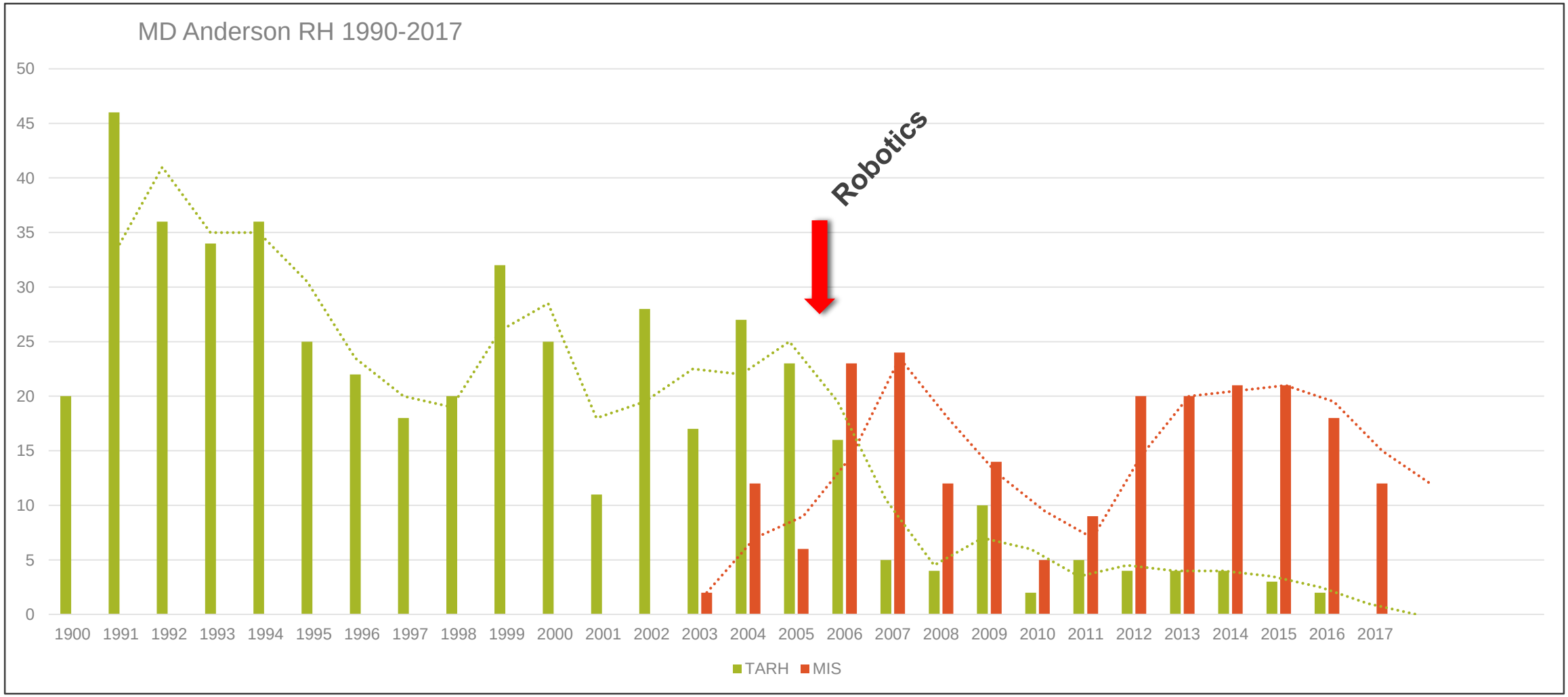
Recurrence in RRH vs OPH



Deaths in RRH vs OPH



MD Anderson Experience



Journal of Minimally Invasive Gynecology
(2008) 15, 584–588

THE JOURNAL OF MINIMALLY INVASIVE GYNECOLOGY

A Phase III Randomized Clinical Trial Comparing Laparoscopic or Robotic Radical Hysterectomy with Abdominal Radical Hysterectomy in Patients with Early Stage Cervical Cancer

Andreas Obermair, MD*, Val Gebski, MD, Michael Frumovitz, MD, MPH, Pamela T. Soliman, MD, MPH, Kathleen M. Schmeler, MD, MPH, Charles Levenback, MD, and Pedro T. Ramirez, MD

From the University of Queensland, School of Medicine, Herston, Brisbane, Queensland, Australia (Dr. Obermair); Department of Gynecological Oncology, Royal Brisbane and Women's Hospital, Herston, Brisbane, Queensland, Australia (Dr. Obermair); National Health and Medical Research Council Clinical Trials Center, Camperdown, New South Wales, Australia (Dr. Gebski); and the Department of Gynecologic Oncology, University of Texas M.D. Anderson Cancer Center, Houston, Texas (Drs. Frumovitz, Soliman, Schmeler, Levenback, and Ramirez).

Study Design
LACC Trial

- **International, multicenter, randomized, phase III trial** to test for **non-inferiority** of MIS vs. standard care (open)
- Therefore, the **primary intent** to demonstrate that minimally invasive surgery was within 7.2% of the DFS rate of the standard care (open) arm
- Test for non-inferiority was based upon a 97.5% one-sided confidence interval. Based on exponential survival times, for a 4.5-year follow-up, a total of **740 patients (370 per arm)** was determined to have at least 90% power for non-inferiority

- FIGO 2009 Stage IA1 LVSI, IA2, IB1
- Squamous, Adenocarcinoma, or Adenosquamous Cervical Cancer
- Type II or III radical hysterectomy
- PS of **ECOG 0-1**
- Age **18 years or older**
- Signed an approved Informed Consent

RANDOMIZE

Total Abdominal Radical Hysterectomy
No. 370

Total Laparoscopic/Robotic Radical Hysterectomy
No. 370

Objective
LACC Trial

Primary

- Compare **Disease-Free Survival at 4.5 years** amongst patients who underwent a total **Laparoscopic or Robotic Radical hysterectomy (MIS)** vs. a **Total Abdominal Radical Hysterectomy (open)** for early stage cervical cancer

Secondary

- Compare **Overall Survival**
- Compare patterns of **Recurrence**
- Compare treatment-associated **Morbidity** (< 6 mos)
- Evaluate **Quality of Life (QoL)**
- Assess **Pelvic Floor Function**
- Determine the **Feasibility of Sentinel Node Mapping**

Inclusion Criteria - Study Schema

The NEW ENGLAND JOURNAL of MEDICINE

Open: June 2008
Accrual: 631
Closed: June 2017*

- **FIGO 2009 Stage IA1 LVSI, IA2, IB1**
- **Squamous, Adenocarcinoma, or Adenosquamous Cervical Cancer**
- Type II or III radical hysterectomy
- Performance Status of **ECOG 0-1**
- Age **18 years or older**
- Signed an approved Informed Consent

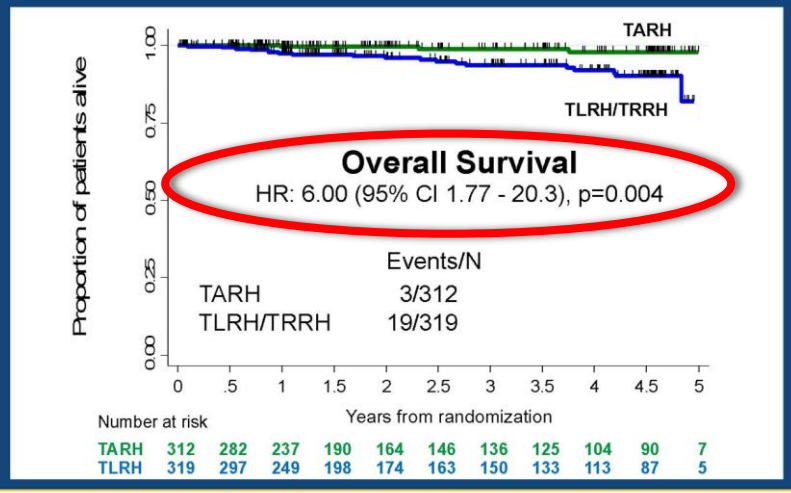
RANDOMIZE

Total Abdominal Radical Hysterectomy — **N= 312**

Total Laparoscopic/Robotic Radical Hysterectomy — **N= 319**

***Recommendation of study termination by DSMC**

MIS in Early Stage Cervical Cancer – LACC Trial



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PRESENTED BY: Ginger J. Gardner, MD

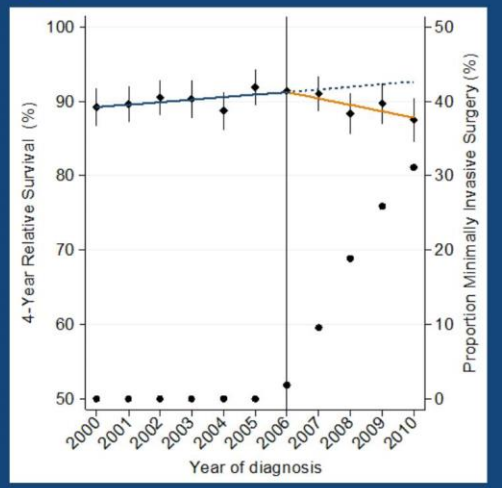
Ramirez P et al. SGO, 2018

American Society of Clinical Oncology (ASCO) Annual Meeting Chicago - June 2018

Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer New Orleans - March 2018

MIS Rates and Outcomes in Early Stage Cervical Cancer

- National Cancer Database
- Stage IA2-IB2
- 1166 RH, 1055 MIS
- 79% MIS - Robotic
- MIS rate increasing
- 4Yr Survival decreasing 1%/yr



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Chen ML...Rauh-Hain JA, SGO 2018

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.

J Gynecol Oncol. 2018 Jul;29(4):e73
https://doi.org/10.3802/jgo.2018.29.e73
pISSN 2005-0380-eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Expert Opinion

Check for updates

Unexpected result of minimally invasive surgery for cervical cancer

Hiroyuki Kanao, Yoichi Aoki, Nobuhiro Takeshima

Department of Gynecologic Oncology, Cancer Institute Hospital, Tokyo, Japan

OPEN ACCESS

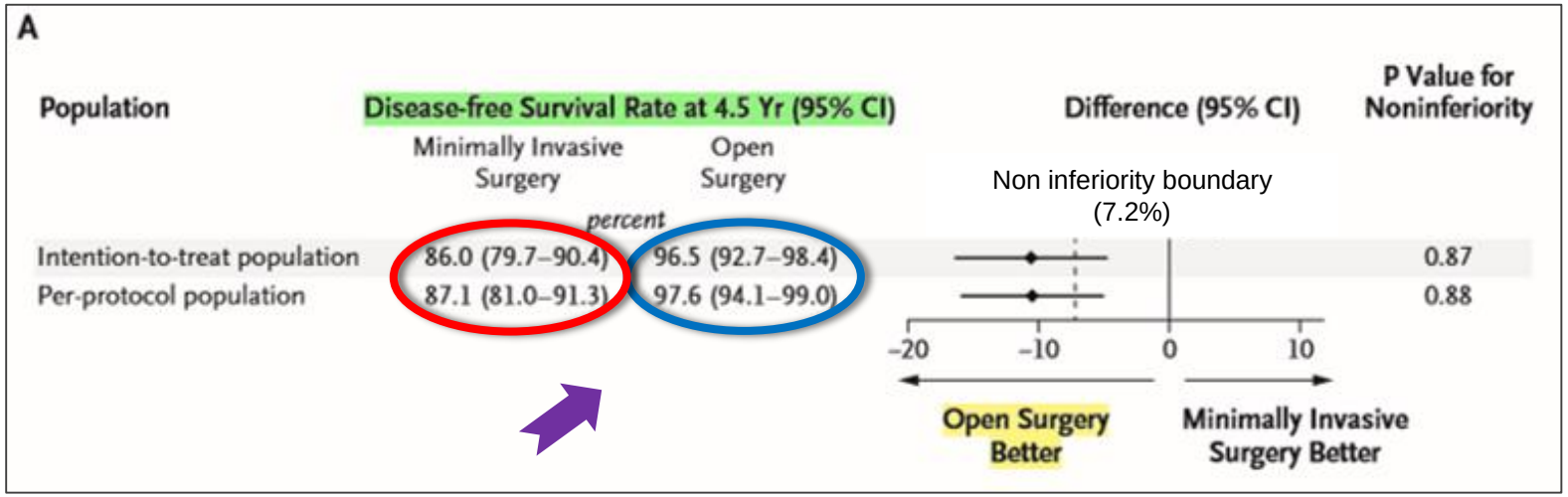
'None of us expected this': New research warns against minimally invasive cervical cancer surgery

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Survival after Minimally Invasive Radical Hysterectomy for Early-Stage Cervical Cancer

Alexander Melamed, M.D., M.P.H., Daniel J. Margul, M.D., Ph.D., Ling Chen, M.D, M.P.H., Nancy L. Keating, M.D., M.P.H., Marcela G. del Carmen, M.D., M.P.H., Junhua Yang, M.S., Brandon-Luke L. Seagle, M.D., Amy Alexander, M.D., Emma L. Barber, M.D., Laurel W. Rice, M.D., Jason D. Wright, M.D., Masha Kocherginsky, Ph.D., Shohreh Shahabi, M.D., E.M.H.A., and J. Alejandro Rauh-Hain, M.D., M.P.H.



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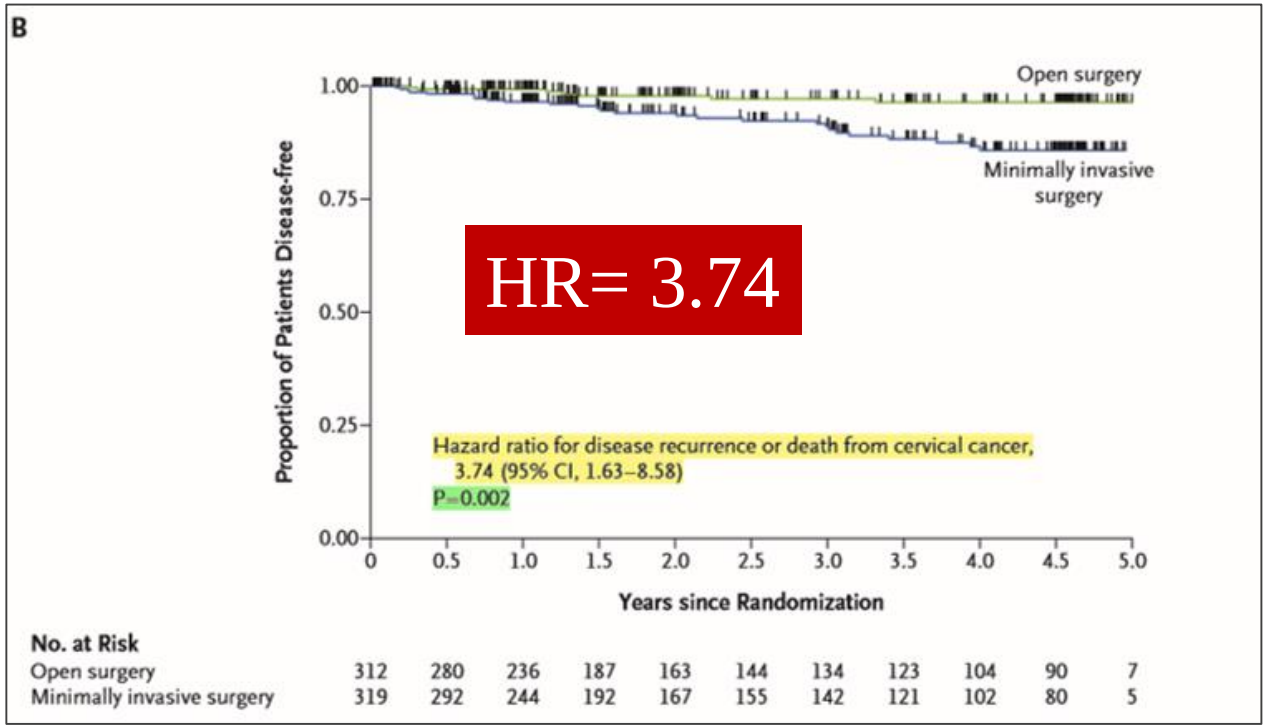
LACC Trial Results

Primary Outcome: DFS at 4.5 years



Results: Overall Surival

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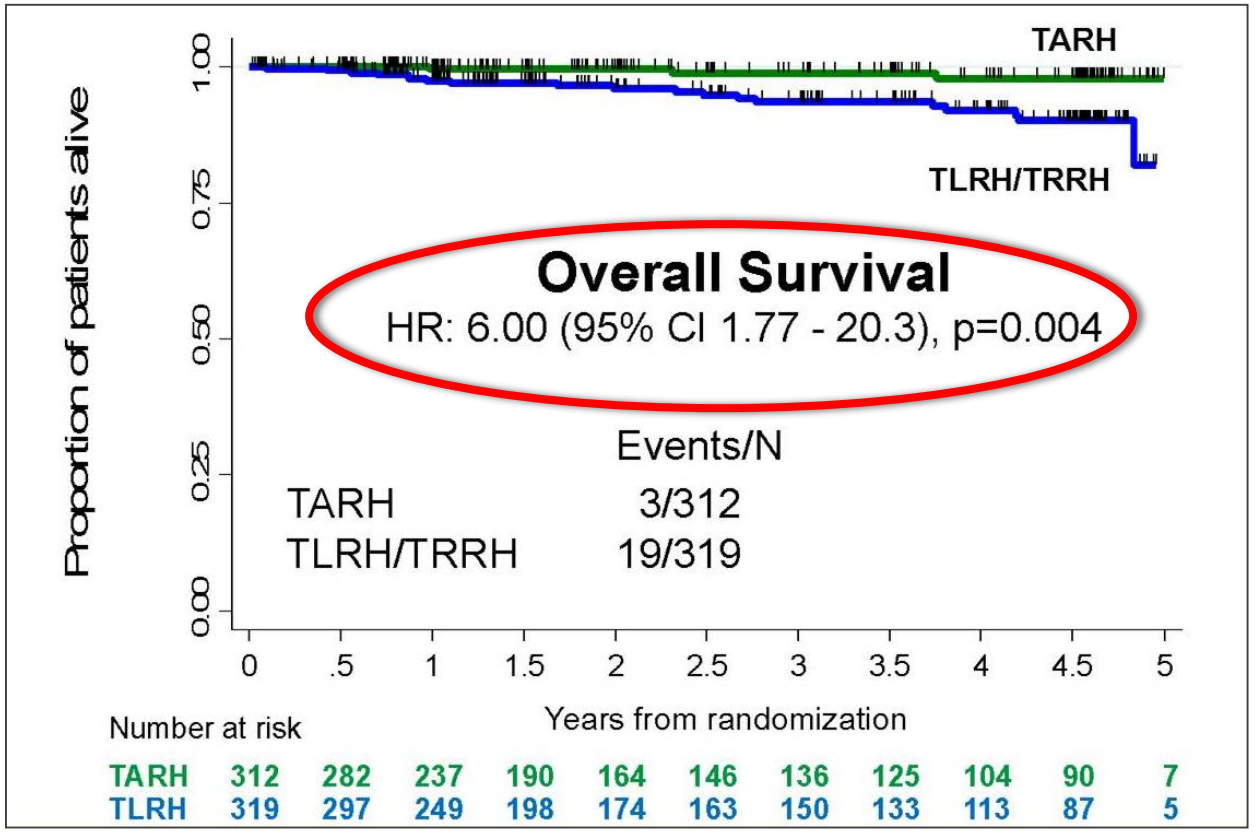

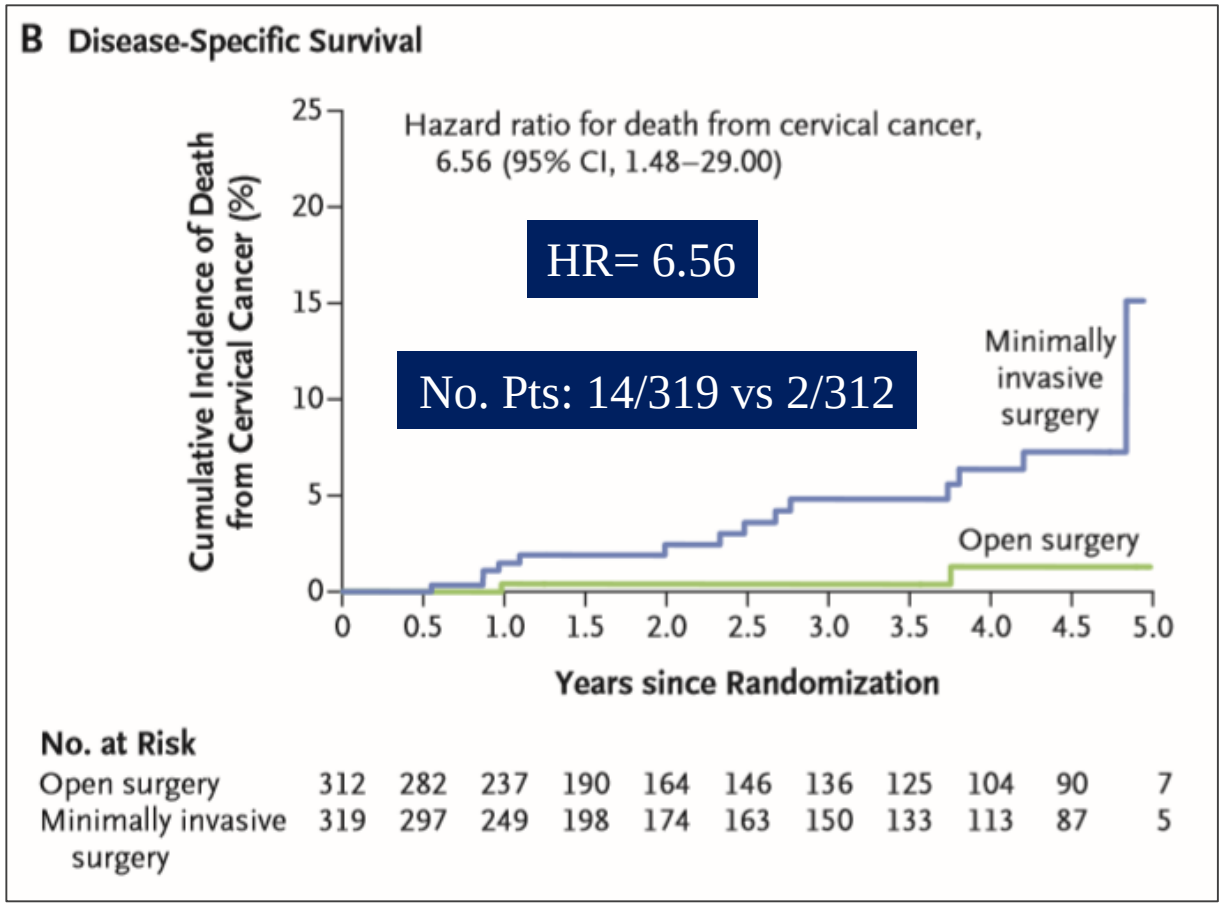

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ORIGINAL ARTICLE

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A retrospective cohort study

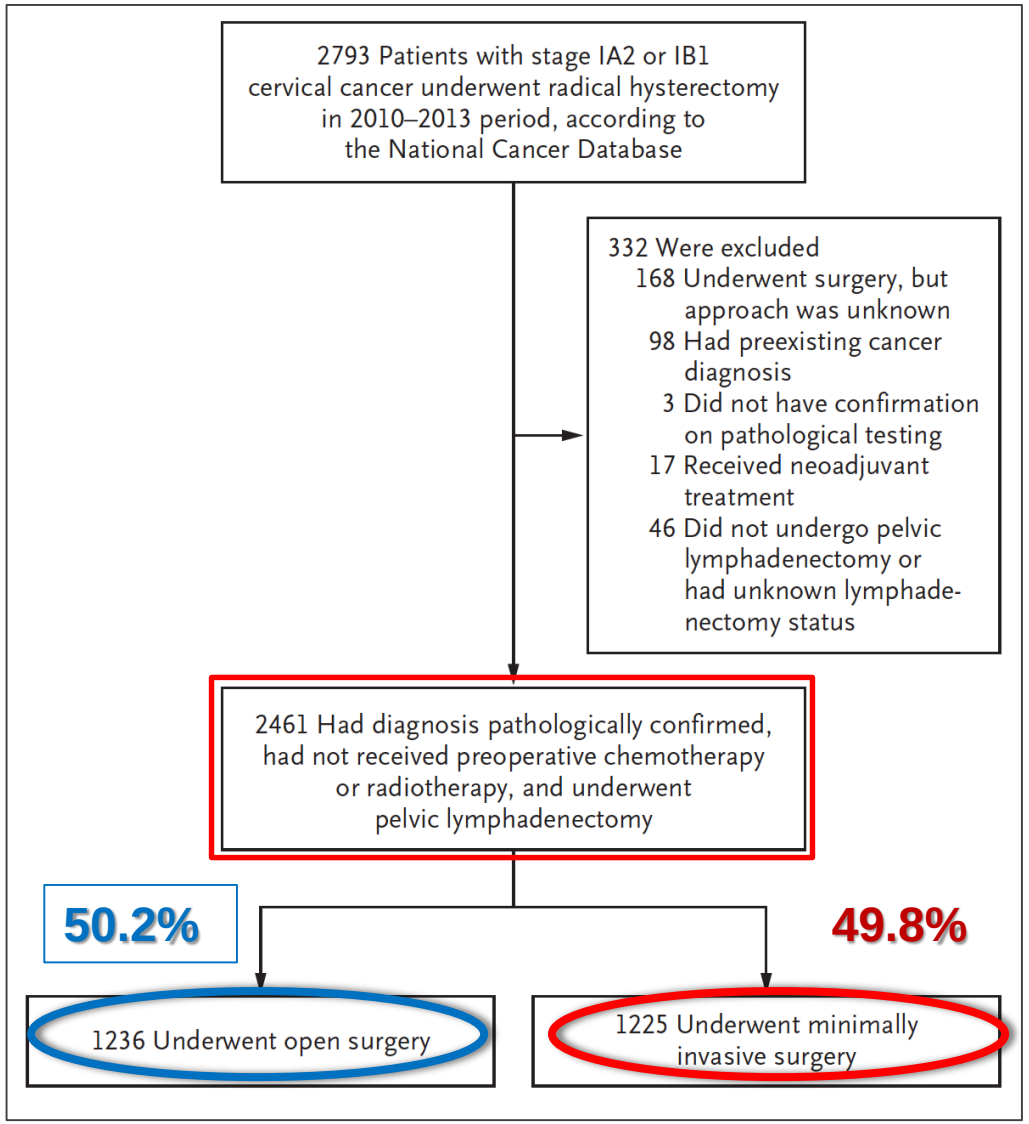
Data from: the National Cancer Database (NCDB)

the Surveillance, Epidemiology, and End Results (SEER) database

FIGO Stage (2009) IA2 or IB1 cervical cancer

Period: 2010 and 2013

The Primary Outcome:
Time to Death



Melamed et al. NEJM 2018

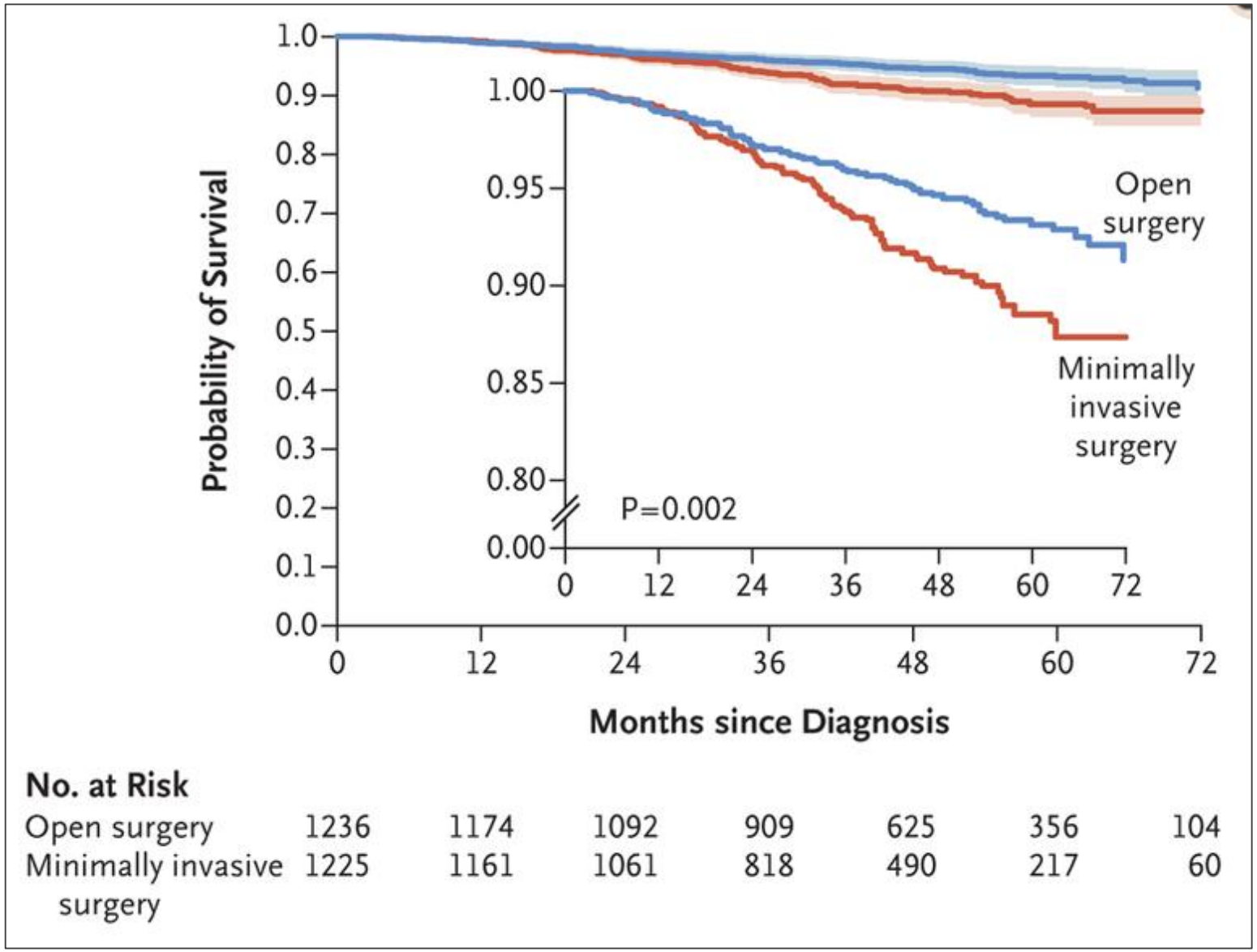
MIS **48% higher hazard of death** from any cause compared with laparotomy

(HR 1.48; 95% CI 1.10-1.98)

Adjusted probability of death within 4-years:

MIS (8.4%) vs. Open (5.8%)

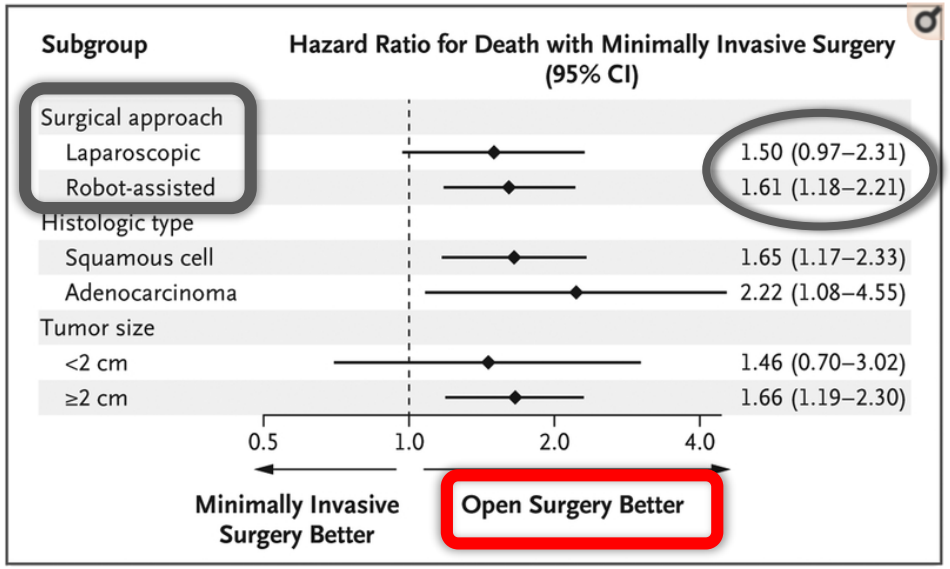
Median follow-up: 45 mos

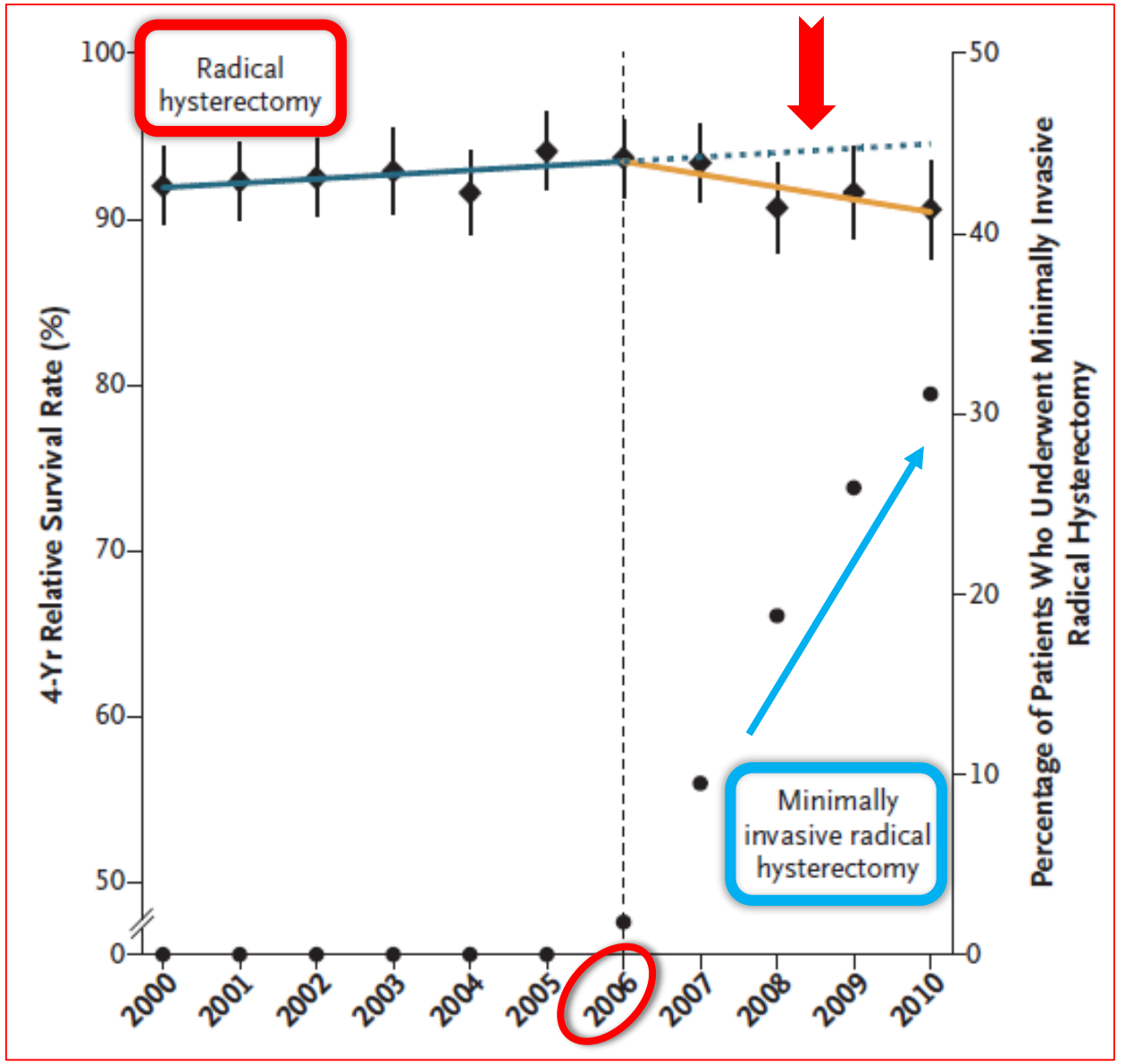


Melamed et al. NEJM 2018

Time Interrupted Series (SEER Data)

Adoption of MIS was associated with a significant change of temporal trend, with **4-year survival declining by 1.0%** (95%CI 0.3-1.6 per year annually after 2006)





Melamed et al. NEJM 2018

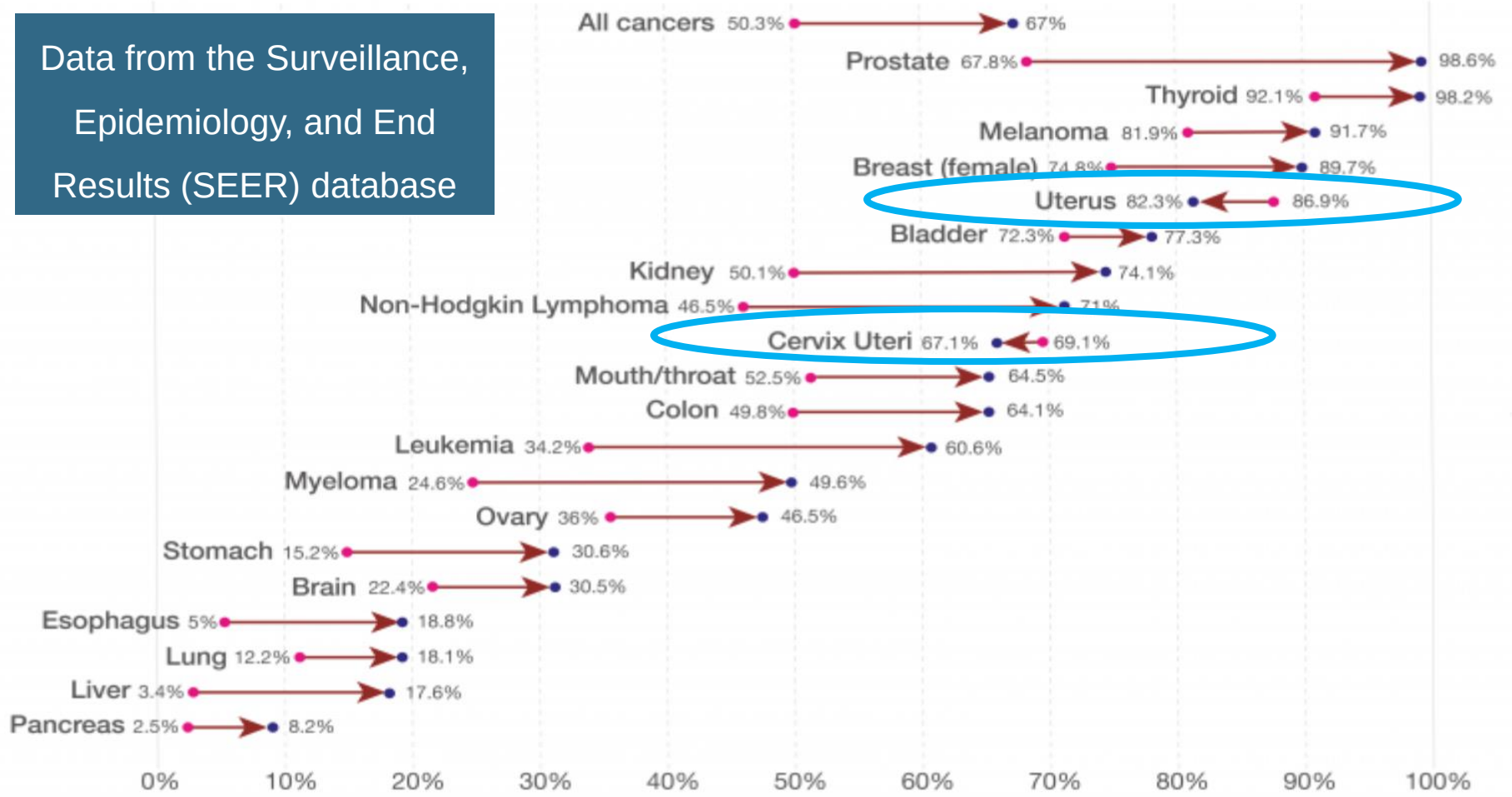
Five-year cancer survival rates in the USA

Average five-year survival rates from common cancer types in the United States, shown as the rate over the period 1970-77 [●] and over the period 2007-2013 [●]: 1970-77 → 2007-2013

This five-year interval indicates the percentage of people who live longer than five years following diagnosis.

Our World in Data

Data from the Surveillance, Epidemiology, and End Results (SEER) database



Based on data by Journal of the National Cancer Institute; Surveillance, Epidemiology and End Results Program.
The data visualization is available at OurWorldinData.org. There you find research and more visualizations on this topic.

Conclusions

- **Disease-free survival** at 4.5 years **for minimally invasive** radical hysterectomy was **inferior (86%)** compared to the open surgery **(96.5%)**
- **The 4-year mortality was 9.1%** among women who underwent minimally invasive radical hysterectomy among those who underwent open surgery. (p=0.002) **and 5.3%**
- Adoption of MIS coincided with **a decline in 4-year relative survival rate of 1% per year after 2006**

Studies Warn Against Minimally Invasive Surgery for Cervical Cancer
The New York Times
"At M.D. Anderson, we have completely stopped performing minimally invasive surgery for cervical cancer," said Dr. Pedro T. Ramirez, a leading expert in minimally invasive surgery for gynecologic cancers, and the lead author of one study. "Throughout the gynecologic oncology community, we're seeing a transition back to the predominance of open surgery."
link

Minimally Invasive Surgery Is Standard for Cervical Cancer. But A New Study Shows It's Not Effective
TIME
"We learned that people in the minimally invasive surgery arm had a four times higher likelihood of having a recur
potentially dying than with t
approach [after four to five
Pedro Ramirez, director of r
surgery at MD Anderson an
one of the studies.
link

More deaths seen for less invasive cervical cancer surgery
Associated Press (appeared in over 250 additional outlets)
"We immediately as a department changed our practice and changed completely to the open approach," said Dr. Pedro Ramirez of the University of Texas MD Anderson Cancer Center in Houston.
link

Keyhole surgery may be riskier for cervical cancer, studies find
NBC News
The results were so startling that the University of Texas MD Anderson Cancer Center has stopped offering minimally invasive surgery for most women with early stage cervical cancer, and several of the researchers at other institutions said they were advising their patients to opt for more invasive surgery.
link

In cervical cancer surgery, minimally invasive is worse than open, study says
CNN
Small studies of minimally invasive radical hysterectomy had "shown that it was safe," though most "just focused on what happen
in the short term," explained Dr. Jose Alejan
Rauh-Hain, senior author of one of the new studies and an assistant professor of gynecologic oncology and reproductive medicine at the University of Texas
MD Anderson Cancer Center in Houston.
link

For Cervical Cancer Patients, Less Invasive Surgery Is Worse For Survival
NPR
"Patients who underwent the minimally invasive surgery had four times greater likelihood of [cancer] recurrence than when they had the surgery through the open approach," says Dr. Pedro Ramirez at the MD Anderson Cancer Center in Houston.
link

Minimally invasive surgery for cervical cancer may cause it to return
NBC Nightly News
Two major studies in the New England Journal of Medicine find a minimally invasive surgery for early-stage cervical cancer nearly doubles the risk of death compared to traditional surgery.
link

Less-radical surgery may pose higher death risk in early cervical cancer
Reuters
"You have a four-times greater likelihood of recurrence" with the less-invasive technique, whether or not a robot is used in the operation, said Dr. Pedro Ramirez of the University of Texas MD Anderson Cancer Center in Houston, who led a randomized comparison of the procedures published in the New England Journal of Medicine.
link

HEALTHNEWSREVIEW.ORG
IMPROVING YOUR CRITICAL THINKING ABOUT HEALTH CARE

Minimally invasive surgery may not be best treatment for cervical cancer, studies show
ABC News Radio
It's believed that minimally invasive surgery using laparoscopy or robotic assisted surgery can decrease recovery time in the hospital and post-operative complications. However, at the University of Texas MD Anderson Cancer Center, two studies found that women with early stage cervical cancer actually had worse outcomes after a minimally invasive radical hysterectomy than those who underwent a traditional open abdominal hysterectomy.
link

Less-Invasive Surgery for Cervical Cancer May Bring More Risks, Studies Find
HealthDay
"Minimally invasive surgery was adopted as an alternative to open radical hysterectomy before high-quality evidence regarding its impact on survival was available," said Dr. Jose Alejandro Rauh-Hain of the University of Texas
MD Anderson Cancer Center in Houston, who helped lead the study.
link

Minimally invasive surgery for cervical cancer carries higher risk of recurrence and death, MD Anderson studies find
Houston Chronicle (page one)
"The takeaway is simple: stop doing minimally invasive surgery for radical hysterectomy," said Dr. Pedro Ramirez, an MD Anderson professor of gynecologic oncology and reproductive medicine and the primary investigator of one of the studies. "It results in more cancer than open surgery."
link

Is Less-Invasive Cervical Cancer Surgery Riskier?

By Robert Preidt

Research finds open hysterectomy may be less risky option for cervical cancer surgery

More deaths seen with less-invasive cervical cancer surgery

Studies: Less invasive cervical cancer treatment is also less effective

Open Hysterectomy Has Better Outcomes Than Minimally Invasive Surgery in Cervical Cancer

Should we abandon minimally invasive surgery for cervical cancer?

Recent data infer that, as a specialty, we should consider an open surgical approach

Mary M. Mullen, MD, and David G. Mutch, MD

Studies warn against minimally invasive surgery for cervical cancer

December 21, 2018

Cancer Reports and Reviews

oat open access text

Short Communication ISSN: 2513-9290

End of the minimal invasion surgery in cervical cancer?

Víctor Manuel Vargas Hernández*

Gynecology Department of Hospital Juárez of México, Mexico

J Gynecol Oncol. 2018 Jul;29(4):e73
https://doi.org/10.3802/jgo.2018.29.e73
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Expert Opinion

Check for updates

Unexpected result of minimally invasive surgery for cervical cancer

Hiroyuki Kanao, Yoichi Aoki, Nobuhiro Takeshima

Department of Gynecologic Oncology, Cancer Institute Hospital, Tokyo, Japan

OPEN ACCESS

LETTER TO THE EDITOR

The LACC Trial *Has Minimally Invasive Surgery for Early-Stage Cervical Cancer Been Dealt a Knockout Punch?*

International Journal of Gynecological Cancer • Volume 28, Number 7, September 2018

J Gynecol Oncol. 2018 Jul;29(4):e74
https://doi.org/10.3802/jgo.2018.29.e74
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Expert Opinion

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How should gynecologic oncologists react to the unexpected results of LACC trial?

Jeong-Yeol Park, Joo-Hyun Nam

Department of Obstetrics and Gynecology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

OPEN ACCESS

GebFra Science | Statement

Thieme

Comment on the LACC Trial Investigating Early-stage Cervical Cancer by the Uterus Commission of the Study Group for Gynecologic Oncology (AGO) and the Study Group for Gynecologic Endoscopy (AGE) of the German Society for Gynecology and Obstetrics (DGGG)

Stellungnahme zur LACC-Studie bei frühem Zervixkarzinom der Kommission Uterus der Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) und der Arbeitsgemeinschaft Gynäkologische Endoskopie (AGE) der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)

J Gynecol Oncol. 2018 Jul;29(4):e75
https://doi.org/10.3802/jgo.2018.29.e75
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Expert Opinion

Check for updates

Minimally invasive surgery for cervical cancer: consequences for treatment after LACC Study

Rainer Kimmig,[1] Thomas Ind[2,3]

[1]Department of Obstetrics and Gynaecology, West German Cancer Center, University Hospital of Essen, Essen, Germany
[2]Department of Gynaecological Oncology, Royal Marsden Hospital, London, UK
[3]St. George's University of London, London, UK

OPEN ACCESS

J Gynecol Oncol. 2019 Mar;30(2):e43
https://doi.org/10.3802/jgo.2019.30.e43
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Correspondence

Check for updates

Rethinking the next step after unexpected results associated with minimally invasive radical hysterectomy for early cervical cancer

Seung Yeon Pyeon,[1,2] Yun Jung Hur,[2] Jong-Min Lee[1]

LACC Trial: Pros - Cons

The NEW ENGLAND JOURNAL of MEDICINE

The strengths:

- ✓ **A prospective, randomized trial**
- ✓ **A large number of centers** throughout the world
- ✓ All centers were required to demonstrate proficiency in MIS

The limitations:

- ✓ It did **not reach** its final intended **enrollment**
  (Safety alert: higher rates of recurrence and death in MIS
  4.5-year follow-up period: 59.7% (**median follow-up: 2.5 yrs**)
- ✓ It did not reach **84% power** to declare non-inferiority for primary outcome
- ✓ **Missing data** in selected patients, with respect to race and ethnic group
- ✓ **Lack of follow-up**
- ✓ **Not Standardization of adjuvant treatment**
- ✓ **Failure to review the pathology**

Analysis of Published Literature Comparison to LACC Results

Flaws of retrospective data

- Sequential comparisons
- Unbalanced groups
- Lack of focus on oncologic outcomes

EDITORIAL

Surgery in Cervical Cancer

Amanda N. Fader, M.D.

but rather the better-than-expected results with open surgery (in contrast to previous randomized trials involving similar patients, with disease-free survival rates of 80 to 94.6%).[8-10] How-

hysterectomy in women with early-stage cervical cancer.[4] Midway through the trial, the data and safety monitoring committee called for early closure of the trial after an interim analysis

limitations that may warrant future study include the imperfect assessments of cervical-cancer stage, the lack of follow-up data and missing data in select patients, the lack of data regarding patient race and ethnic group, nonstandardization of adjuvant treatment, and nonperformance of central pathology review. How-

Data Completeness

Primary outcome (DFS)	
Median Follow-up time (min-max)	2.5 years (0.0 - 6.3)
Completeness* at 4.5 years (%)	219/558 (39.2%)
Information available at 4.5 years (%)	59.7%
Overall survival	
Median Follow-up time (min- max)	2.5 years (0.0 - 6.3)
Completeness* at 4.5 years (%)	208/558 (37.3%)
Information available at 4.5 years (%)	54.3%

*Completeness is proportion of patients with the event of interest, or with follow-up to 4.5 years, out of the total patients that we can achieve data at 4.5 years (excluding withdrawals and LTFU)

Postoperative Histopathology

Histopathology		Open 282	MIS 291	p-value
Histology	Squamous	146 (52%)	152 (52%)	0.99
	Adenocarcinoma	58 (21%)	59 (20%)	
	Adenosquamous	12 (4%)	12 (4%)	
	No residual disease	59 (21%)	60 (21%)	
	Other	7 (2%)	8 (3%)	
Grade	1	29 (10%)	32 (11%)	0.96
	2	111 (40%)	115 (40%)	
	3	61 (22%)	61 (21%)	
	Not Reported	81 (29%)	83 (29%)	
Invasion	Superficial	61 (22%)	83 (29%)	0.03
	Middle	72 (26%)	50 (17%)	
	Deep	56 (20%)	64 (22%)	
	Not Reported	94 (33%)	94 (32%)	

Postoperative Histopathology

Histopathology		Open 282	MIS 291	p-value
Tumor size	<2cm	147 (52%)	150 (52%)	0.82
	≥2cm	121 (43%)	123 (42%)	
	Not Reported	14 (5%)	18 (6%)	
LVSI	Negative	185 (66%)	195 (67%)	0.26
	Positive	81 (29%)	70 (24%)	
	Not Reported	16 (5%)	26 (9%)	
Parametria	Negative	250 (89%)	253 (87%)	
	Positive	11 (4%)	19 (7%)	0.35
	Not Reported	21 (7%)	19 (6%)	
Vaginal margins	Negative	248 (88%)	257 (88%)	
	Positive	6 (2%)	5 (2%)	0.40
	Not reported	28 (10%)	29 (10%)	

How should gynecologic oncologists react to the unexpected results of LACC trial?

Jeong-Yeol Park, Joo-Hyun Nam

Editorial Comments

The first problem is that the survival rate of the open surgery group was too good and much higher than that reported previously. Only 7 of 319 (2.2%) patients in open surgery group had recurrence in the LACC trial. In previous large studies with long term follow-up, the

Second, the high recurrence rate of the MIS group may be due to surgical technique or carelessness of the operator, not because of the MIS itself. In the case of cervical cancer, the

Third problem is the surgeon proficiency for MIS RH in LACC trial.

How should gynecologic oncologists react to the unexpected results of LACC trial?

Jeong-Yeol Park, Joo-Hyun Nam

Editorial Comments

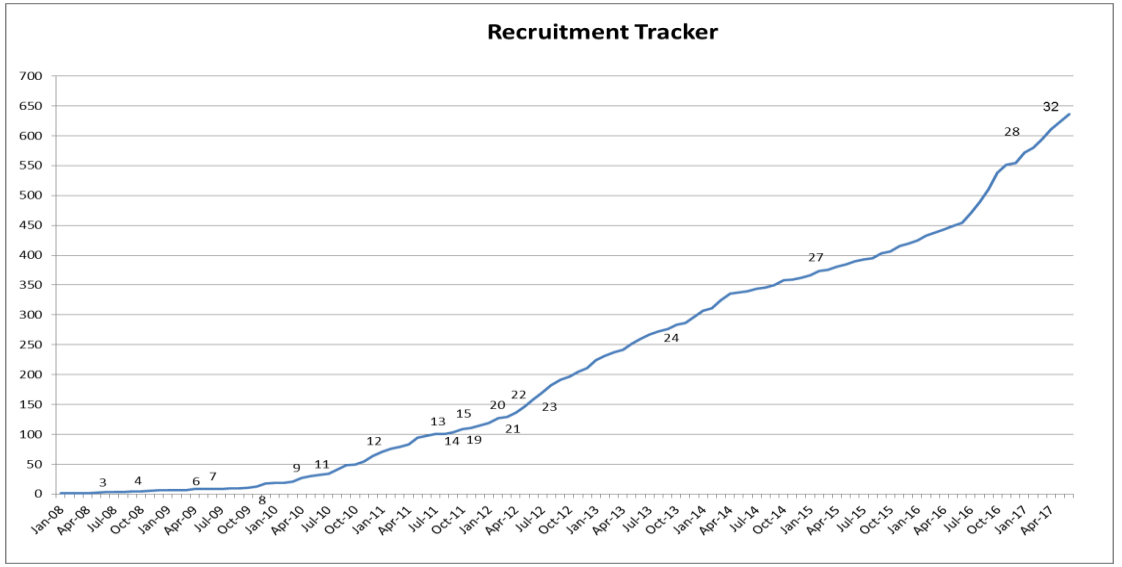
Fourth problem is that the results of subgroup analysis have not been reported. This analysis should be performed to determine which group has higher recurrence rate after MIS RH. This should include tumor size, stage, histology, surgery type (type II vs. III radical hysterectomy), surgeons' experience, and nationality or ethnicity, etc.

Fifth problem is that the participation in countries where MIS RH has become surgery of choice has been low. In countries where MIS RH has already been recognized as an

Editorial Comments

Minimally invasive surgery for cervical cancer: consequences for treatment after LACC Study

Rainer Kimmig,[1] Thomas Ind[2,3]



The number of eligible patients not recruited is unknown

outcome data from ten minimal access cases and 2 unedited videos. Many feel that this was not enough supporting evidence that properly trained surgeons were participating in the minimally invasive arm. Furthermore, the minimal access arm recruited an average of only 2 patients per center per year raising the question as to whether all surgeons had the chance to maintain sufficient experience during the decade of accrual. The number of

Inclusion Criteria
Participating Sites

The NEW ENGLAND JOURNAL of MEDICINE

- Submission of **10 cases** of MIS to Trial Management Committee
  - Age
  - BMI
  - Stage
  - OR time
  - EBL
  - LOS
  - Intraop and postop complications (<30 days)
  - Transfusion rates
- Total of **2 un-edited videos** of MIS
- Independent Review 2 members of Trial Management Committee

All cancer recurrences in the LACC trial were grouped

14 of the 33 participating cancer centers

Minimally invasive surgery for cervical cancer: consequences for treatment after LACC Study

Rainer Kimmig [1], Thomas Ind [2,3]

Editorial Comments

the chance to maintain sufficient experience during the decade of accrual. The number of eligible patients not recruited is unknown. However, it is not that the minimally invasive arm performed so much worse in the LACC study but that the control arm (open surgery) performed unexpectedly well. There were only seven recurrences in 312 (2.2%) women. This is an extremely low result for recurrences. On the other hand, 27 (8.4%) recurrences in the

Gynecologic Oncology 115 (2009) 56–59

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

A novel technique for the management of the vesicouterine ligament during radical hysterectomy

Eiji Kobayashi *, Tadashi Iwamiya, Masanori Isobe, Takahito Miyake, Yasuhiko Shiki, Masato Yamasaki

Department of Obstetrics and Gynecology, Osaka Rosai Hospital, 1179-3 Nagasone, Kita-ku, Sakai City, Osaka 591-8025, Japan

All the patients underwent radical abdominal hysterectomy (type III) and bilateral pelvic lymphadenectomy as described by Piver et al.

3.5. A positive lymph node in the pelvis was observed in 7 patients (20%). 18 patients received concurrent chemoradiotherapy, for lymph node involvement ($n=7$), deep stromal invasion ($n=5$) or lymphovascular involvement ($n=11$). The median follow-up period was 35.3 ± 11.6 months. Both overall survival and disease-free survival were 100%. At the latest follow-up, all patients were doing well and showed no signs of recurrent malignancy.

Gynecologic Oncology 151 (2018) 438–443

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

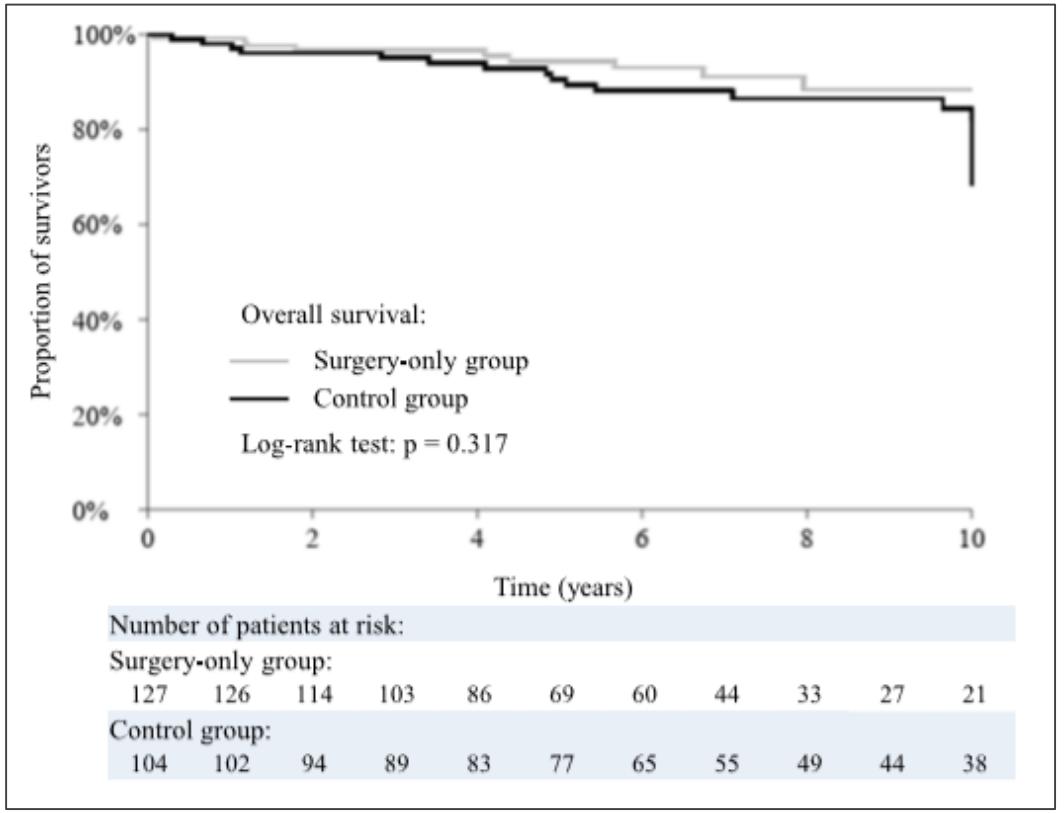
Surgical treatment of "intermediate risk" lymph node negative cervical cancer patients without adjuvant radiotherapy—A retrospective cohort study and review of the literature

David Cibula [a,*], Nadeem R. Abu-Rustum [b], Daniela Fischerova [a], Selvan Pather [c], Katie Lavigne [b], Jiri Slama [a], Kaled Alektiar [b], Lin Ming-Yin [d], Roman Kocian [a], Anna Germanova [a], Filip Frühauf [a], Lukas Dostalek [a], Ladislav Dusek [e], Kailash Narayan [d]

Kaplan-Meier estimate of **disease-specific survival** in patients who received a combined treatment (Control group) or radical surgery only (Surgery only group).

Disease-specific survival	Surgery only group ($N = 127$)	Control group ($N = 104$)	P[a]
1-year	99.2% (97.7%; 100.0%)	99.0% (97.1%; 100.0%)	0.745
5-year	95.7% (91.9%; 99.4%)	94.6% (90.0%; 99.2%)	
10-year	91.0% (83.7%; 98.3%)	90.4% (83.9%; 96.9%)	

[a] *P*-value of log-rank test.



Unexpected result of minimally invasive surgery for cervical cancer

Hiroyuki Kanao, Yoichi Aoki, Nobuhiro Takeshima

Department of Gynecologic Oncology, Cancer Institute Hospital, Tokyo, Japan

Editorial Comments

In the LACC study, a fair amount of data, including the use of uterine manipulators and the precise colpotomic approach, are unknown. We must judge the usefulness of MIS for early-stage cervical cancer dispassionately and objectively on the basis of all pertinent data.

Potential reasons for the inferior oncologic outcomes in MIS group:

Surgical Technique:

The routine use of a **uterine manipulator:** Increased the propensity for tumor spillage

Vaginal vs **Intracorporeal colpotomy** under pneumoperitoneum with CO2

An effect of the **insufflation gas** (CO2) on tumor-cell growth or spread (Potential risk of positive surgical margins in the vaginal vault and intraperitoneal tumor dissemination)

The patterns of recurrence differ in MIS or open surgery
(Vaginal Vault & Pelvic Recurrence: The most common site of relapse)

Meeting Abstracts

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

Attend this session at the 2019 ASCO Annual Meeting!

Session: Gynecologic Cancer

Type: Oral Abstract Session

Time: Monday June 3, 1:15 PM to 4:15 PM

Location: S406

Retrospective Multi-Istitutional Review
Jan 2010 – Dec 2017
FIGO Stage: IA1 – IA2 – IB1
No. Pts 185 (26%) vs 519 (74%) Open vs MIS

Recurrence (MIS)		
No Manipulator:	**0%**	**(0/26)**
Vaginal Manipulator:	**11%**	**(22/210)**
Uterine Manipulators:	**7%**	**(19/270)**

Role of Manipulators in increasing recurrence should be further studied

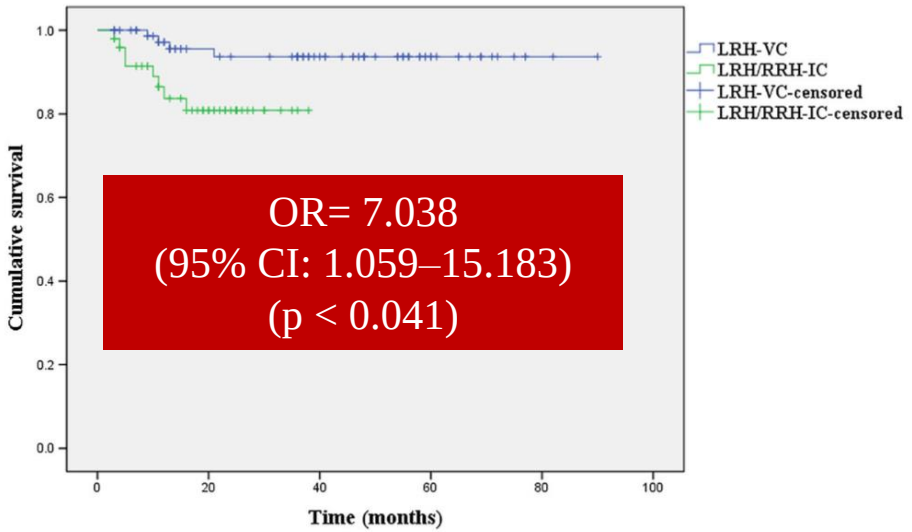
THE JOURNAL OF
Obstetrics and Gynaecology Research
doi:10.1111/jog.12840
J. Obstet. Gynaecol. Res. Vol. 42, No. 1: 77–86, January 2016

Patterns of recurrence and survival after abdominal versus laparoscopic/robotic radical hysterectomy in patients with early cervical cancer

Tae-Wook Kong[1,2], Suk-Joon Chang[1,2], Xianling Piao[6], Jiheum Paek[1,2], Yonghee Lee[1,3], Eun Ju Lee[1,4], Mison Chun[1,5] and Hee-Sug Ryu[1,2]

Laparoscopic Intracorporeal Colpotomy: a strong prognostic factor related relapse

16% vs 5%
p = 0.057



OR= 7.038
(95% CI: 1.059–15.183)
(p < 0.041)

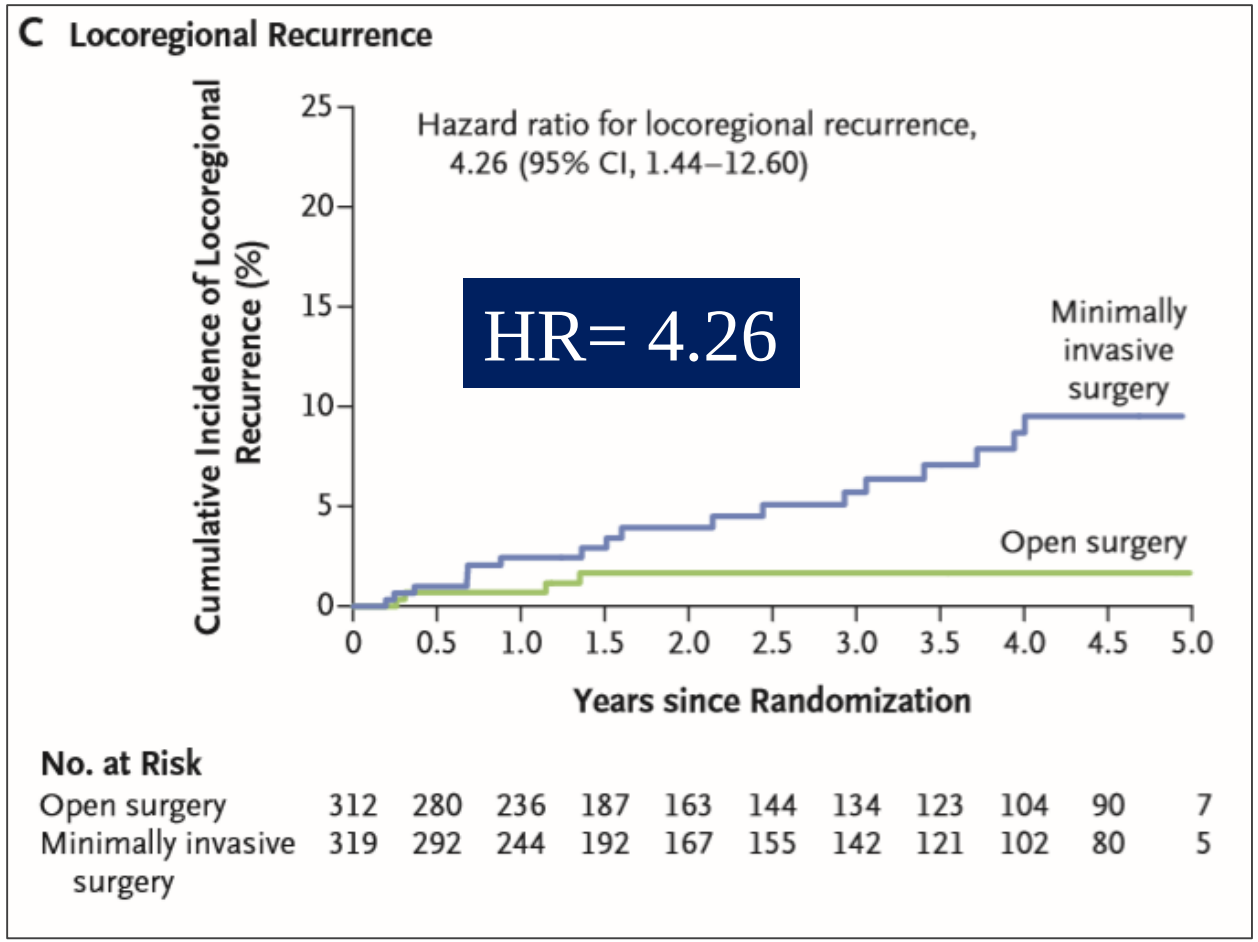
	Colpotomy	
	Vaginal	Intracorporeal
NO Relapse	75 (94.9)	41 (83.7)
Sites of relapse:		
Local	2 (2.5)	1 (2.0)
Distant	1 (1.3)	2 (4.1)
Intraperitoneal	1 (1.3)	5 (10.2)

Table 5 Clinicopathologic characteristics of patients with intraperitoneal recurrence

Patients	1	2	3	4	5	6
Sites of recurrence	Right paracolic gutter	Right paracolic gutter	Subhepatic area	Splenic hilar surface (Splenectomy)	Bowel serosa (Colectomy)	Peritoneal & omental mass
Recurrence (months)	3	4	10	12	16	9

LLAC Trial Results

The NEW ENGLAND JOURNAL of MEDICINE



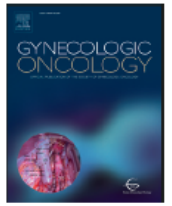
No. Pts: 18/319 vs 4/312

Gynecologic Oncology 153 (2019) 3–12

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Comparison of survival outcomes between minimally invasive surgery and conventional open surgery for radical hysterectomy as primary treatment in patients with stage IB1–IIA2 cervical cancer

Se Ik Kim, Jae Hyun Cho, Aeran Seol, Young Im Kim, Maria Lee *, Hee Seung Kim, Hyun Hoon Chung, Jae-Weon Kim, Noh Hyun Park, Yong-Sang Song

Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Republic of Korea

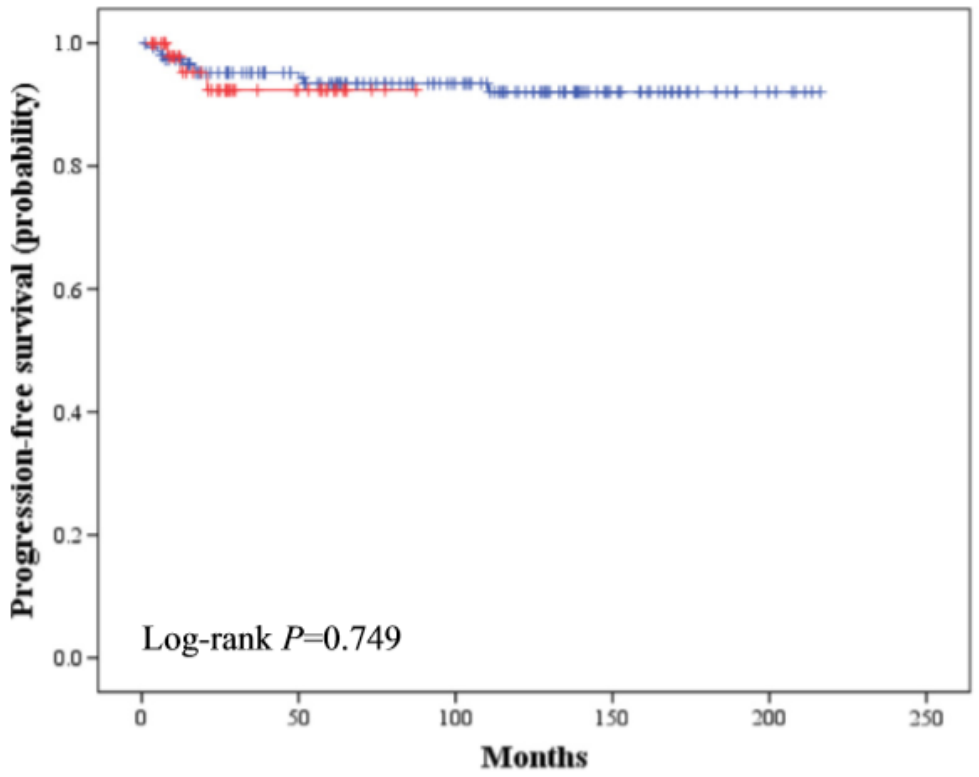
HIGHLIGHTS

- We investigated survival outcome of radical hysterectomy (RH) by laparoscopic surgery in early-stage cervical cancer.
- Compared to open RH, minimally invasive surgery (MIS) was associated with higher recurrence rates.
- MIS RH was not a poor prognostic factor in patients with stage IB1 and cervical mass size ≤2 cm on pre-operative MRI.

Conclusions. Overall, MIS RH was associated with higher recurrence rates than open RH in patients with early-stage CC. However, MIS was not a poor prognostic factor among those with stage IB1 and cervical mass size ≤2 cm on pre-operative MRI.

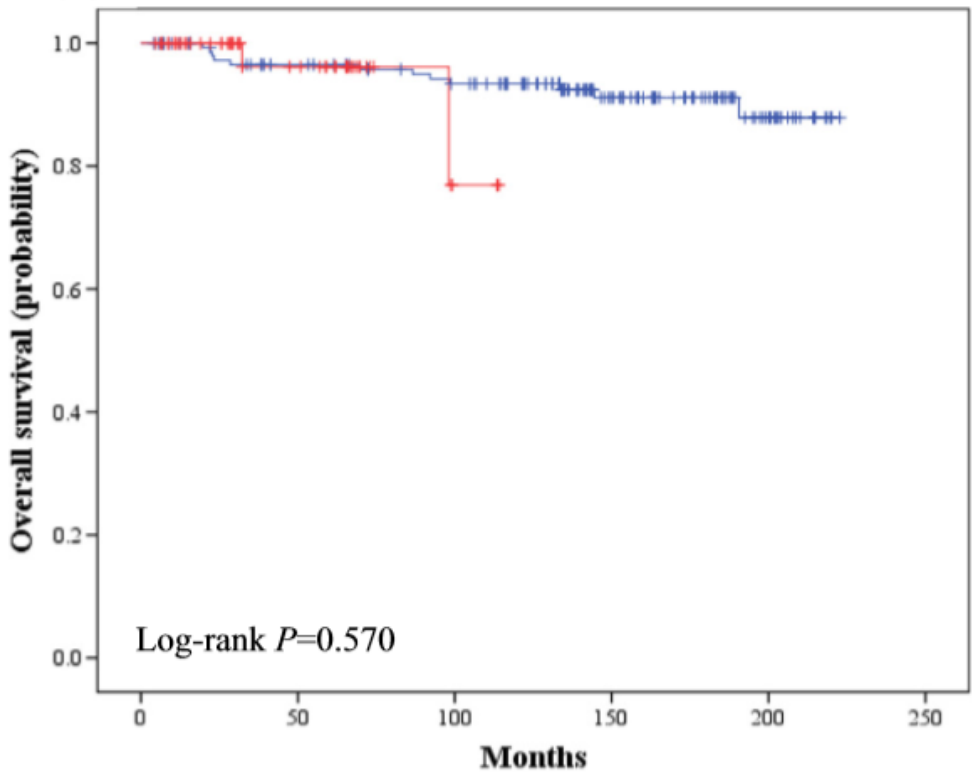
Cervical mass size ≤2 cm on MRI

(A)



	N	Events	5-year progression-free survival rate
Open surgery	153	10	93.5%
MIS	54	3	92.4%

(B)



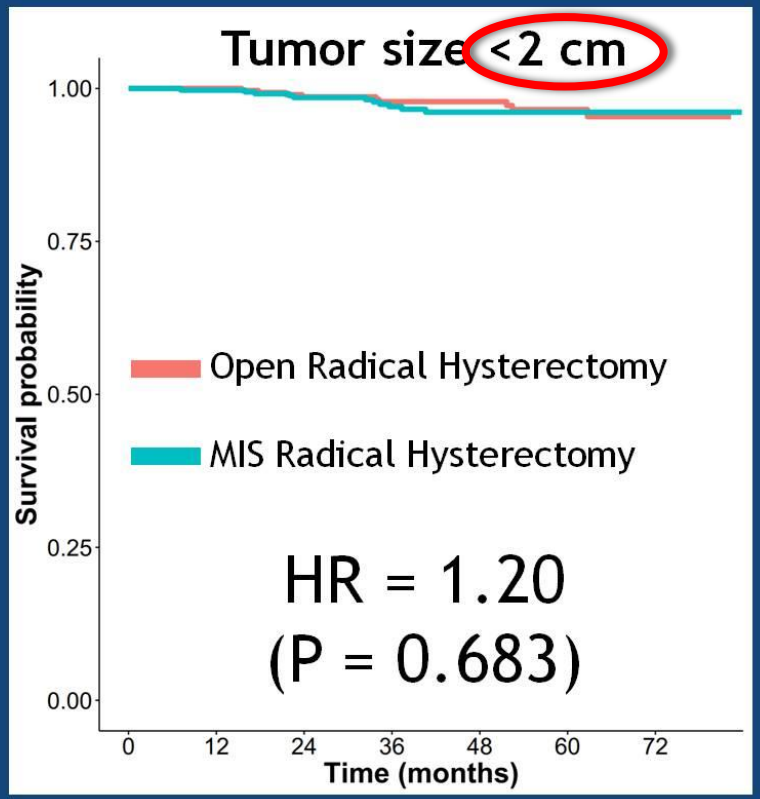
	N	Events	5-year overall survival rate
Open surgery	153	12	96.5%
MIS	54	2	96.2%

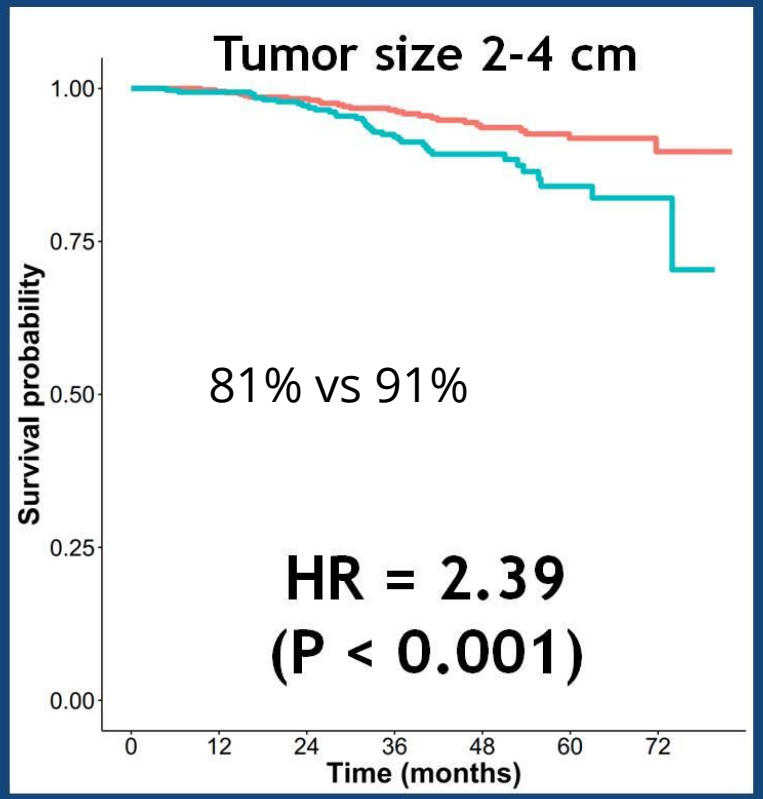
S.I. Kim et al. Gynecol Oncol (2019)

Outcomes and Costs of Open, Robotic, and Laparoscopic Radical Hysterectomy for Stage IB1 (FIGO 2009) Cervical Cancer

Overall Survival by Tumor Size

2010-2013 National Cancer Database
Retrospective cohort Syudy
Open vs MIS: 982 vs 910





PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

PRESENTED BY: Daniel Margul MD PhD

Margul DJ et al, Proc ASCO Abst 5502, 2018

Meeting Abstracts

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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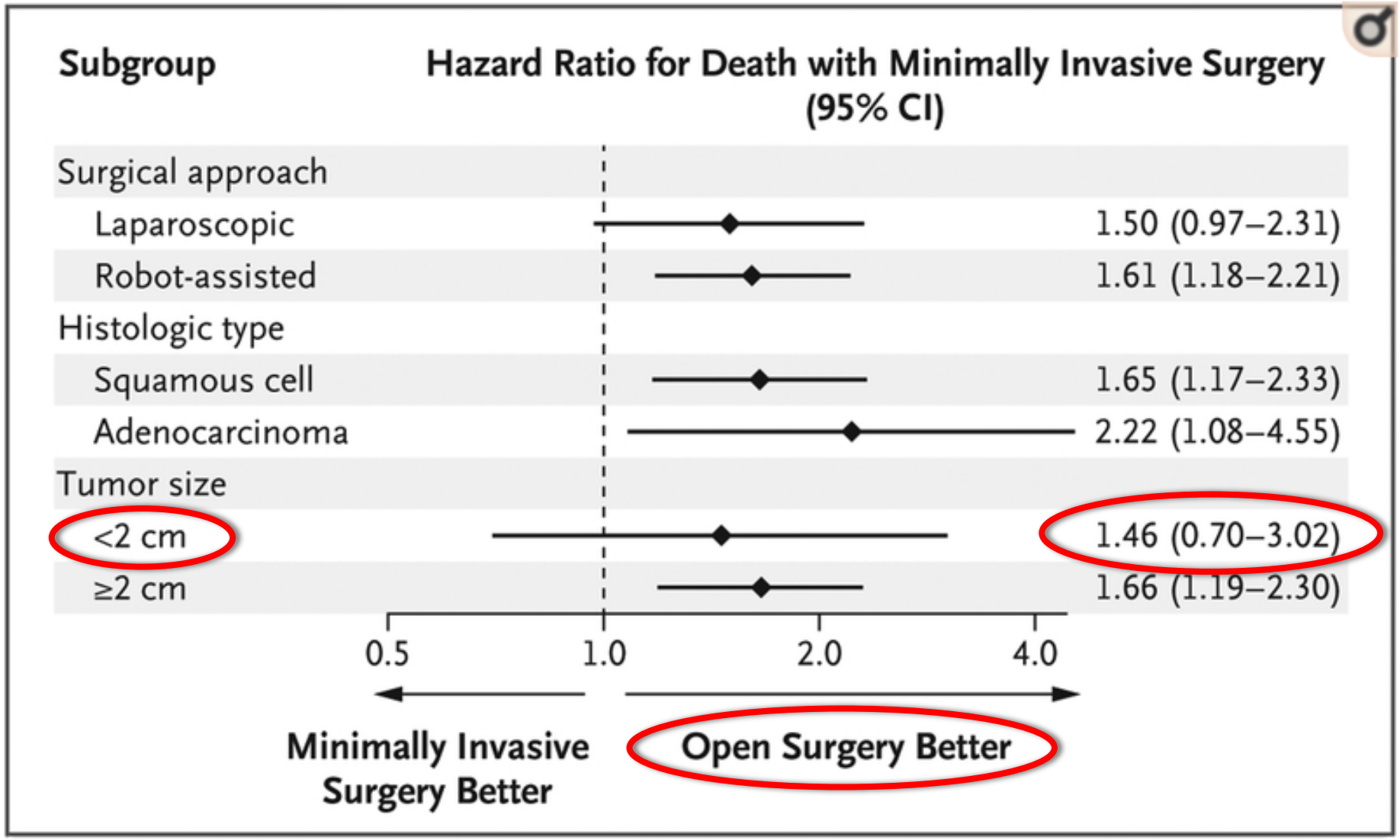
Retrospective Multi-Istitutional Review
Jan 2010 – Dec 2017
FIGO Stage: IA1 – IA2 – IB1
No. Pts 185 (26%) vs 519 (74%) Open vs MIS

Multivariate Analysis

Recurrence Rate MIS vs Open
OR= 2.37 (95% CI 1.1-5.1)
p = 0.031

Pre-operativeTumor Size ≤2 cm

Recurrence Rate MIS vs Open
6% (25/415) vs 4.1% (5/121)
p = 0.34



Melamed et al. NEJM 2018

Take-home points:

1) The evidence is the evidence

Consider this latest evidence **in your surgical planning**

We can attempt to explain away the findings, but despite arguments against these studies, these data are the most reliable evidence we have to date regarding outcomes for cervical cancer with MIS versus open approaches. These data demonstrate that **MIS may be harming our patients** and so we must take this into careful consideration during surgical planning

2) MIS radical hysterectomy may still be the **best approach** for patients with tumors less than 2 cm in size

The LACC study is **not powered** to evaluate oncologic outcomes in this subset of patients but retrospective studies suggest no difference in survival in this cohort

SUGGESTED CRITERIA TO OFFER TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY

INCLUSION CRITERIA:

- Newly diagnosed untreated invasive cervical cancer
- FIGO stage IA1 (with LVSI) to IB1 **(≤ 2 cm) lesions**
- Squamous, adenocarcinoma & adenosquamous histology
- Quetelet body mass index ≤ 35
- Desire for laparoscopic approach
- Karnofsky performance ≥ 90
- Signed informed consent

ABU-RUSTUM et al. GYNECOL ONCOL 2003

New guidelines are to come

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2019
Cervical Cancer

NCCN Guidelines Index
Table of Contents
Discussion

- Radical hysterectomy with bilateral pelvic lymph node dissection (with or without SLN mapping) is the preferred treatment for FIGO stage IA2, IB1, and select IB2/IIA1 lesions when fertility preservation is not desired. Radical hysterectomy results in resection of much wider margins compared with a simple hysterectomy, including removal of parts of the cardinal and uterosacral ligaments and the upper 1–2 cm of the vagina; in addition, pelvic and sometimes para-aortic nodes are removed. Radical hysterectomy procedures may be performed either via laparotomy or laparoscopy, and the laparoscopy approach may be with either conventional or robotic techniques. However, given recently presented findings of significantly poorer survival outcomes with the laparoscopic approach compared to the open approach in a randomized controlled trial of women with early-stage cervical cancer, women should be carefully counseled about the risks and benefits of the different surgical approaches until more data become available.[1,2] The Querleu and Morrow classification system[3] is a modern surgical classification that describes degree of resection and nerve preservation in three-dimensional (3D) planes of resection.[4] Procedural details for the most commonly used types of hysterectomy are described in Table 1 (see CERV-C 5 of 7).
- Para-aortic lymph node dissection for staging is typically done to the level of the inferior mesenteric artery (IMA). The cephalad extent of dissection can be modified based on clinical and radiologic findings.

A new international randomised controlled study is also ongoing

A Swedish study will be published soon in the *European Journal of Cancer*

Robot-assisted Approach to Cervical Cancer (RACC)

RACC Trial

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03719547

Recruitment Status : Recruiting
First Posted : October 25, 2018
Last Update Posted : May 31, 2019

See Contacts and Locations

Sponsor:
Karolinska Institutet

Information provided by (Responsible Party):
Henrik Falconer, Karolinska Institutet

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description

Go to

Brief Summary:
The purpose of the RACC trial is to compare the oncologic outcome defined as recurrence-free survival (RFS) between robot-assisted and open radical hysterectomy for the treatment of early stage cervical cancer.

Condition or disease	Intervention/treatment	Phase
Cervical Cancer	Procedure: Abdominal radical hysterectomy Procedure: Robot-assisted radical hysterectomy Diagnostic Test: Sentinel lymph node biopsy	Not Applicable

ESGO | European Society of Gynaecological Oncology

The European Voice of Gynaecological Oncology

European Society of Gynaecological Oncology: Newsflash

Message from the ESGO President

Laparoscopic radical hysterectomy: An ESGO statement

D. QUERLEU

LAPAROSCOPIC RADICAL HYSTERECTOMY: AN ESGO STATEMENT

D Querleu, D Cibula, N Concin, A Fagotti, A Ferrero, C Fotopoulou, P Knapp, D Kurdiani, J Ledermann, M Mirza, P Morice, J Ponce, E van der Steen, C Taskiran, P Wimberger, C Sessa

Updated recommendation regarding the approach for Radical Hysterectomy for Cervical cancer:

«Minimal invavise approach is favoured»

Is no is no longer valid and should be removed and replaced by

«Open approach is the gold standard»

ESGO Reccommandations for MIS:

- Prospectively recorded, including tumour characteristics and technical details
- Performed **only in highly specialised centres** by appropriately **trained surgeons**
- efforts should be made to **avoid spillage of tumour cells** in the peritoneal cavity

(e.g., avoiding crushing lymph nodes, banning vaginal or uterine manipulators, and closing the vaginal cuff in order to avoid any contact between tumour and peritoneal cavity)

- **Patients must be informed** about the available prospective and retrospective evidence on survival, complications, and QoL

May 27, 2019

Studies Find Open Surgery Safer For Early Cervical Cancer

Two studies compare open hysterectomy to minimally invasive hysterectomy

Nov 6, 2018

For Early Cervical Cancer, Open Hysterectomy is Safer than Minimally Invasive Surgery

October 31, 2018

PUBLIC RELEASE: 31-OCT-2018

Minimally invasive surgery for early-stage cervical cancer may increase risk of death

MASSACHUSETTS GENERAL HOSPITAL

News > Medscape Medical News > Oncology News

Worse Survival With Minimal Invasive Surgery for Cervical Cancer

Roxanne Nelson, BSN, RN
November 01, 2018

HEALTH

More deaths seen for less invasive cervical cancer surgery

By ASSOCIATED PRESS / OCTOBER 31, 2018

More deaths seen for less invasive cervical cancer surgery

For cervical cancer, open surgery is better than minimally invasive surgery

Is Less-Invasive Cervical Cancer Surgery Riskier?

By Robert Preidt

For Cervical Cancer Patients, Less Invasive Surgery Is Worse For Survival

Minimally invasive surgery lowers survival in cervical cancer, new studies show

By Matthew Bin Han Ong

Minimally invasive surgery less effective than open surgery for cervical cancer

COVER STORY

Minimally invasive cervical cancer surgery may promote disease recurrence; professionals urge patience

HemOnc Today, February 10, 2019

Keyhole surgery may be riskier for cervical cancer, studies find

The modern treatment for early-stage cervical cancer seems to be less effective than older methods