INCIDENCE OF ADVERSE EVENTS COMPARING ABDOMINAL VS. MINIMALLY INVASIVE RADICAL HYSTERECTOMY IN PATIENTS WITH EARLY-STAGE CERVICAL CANCER: LACC TRIAL

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QCGC research

Faculty Disclosure

	No, nothing to disclose
X	Yes, please specify:

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SurgicalPerformance.com				x		x		
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Cervical cancer

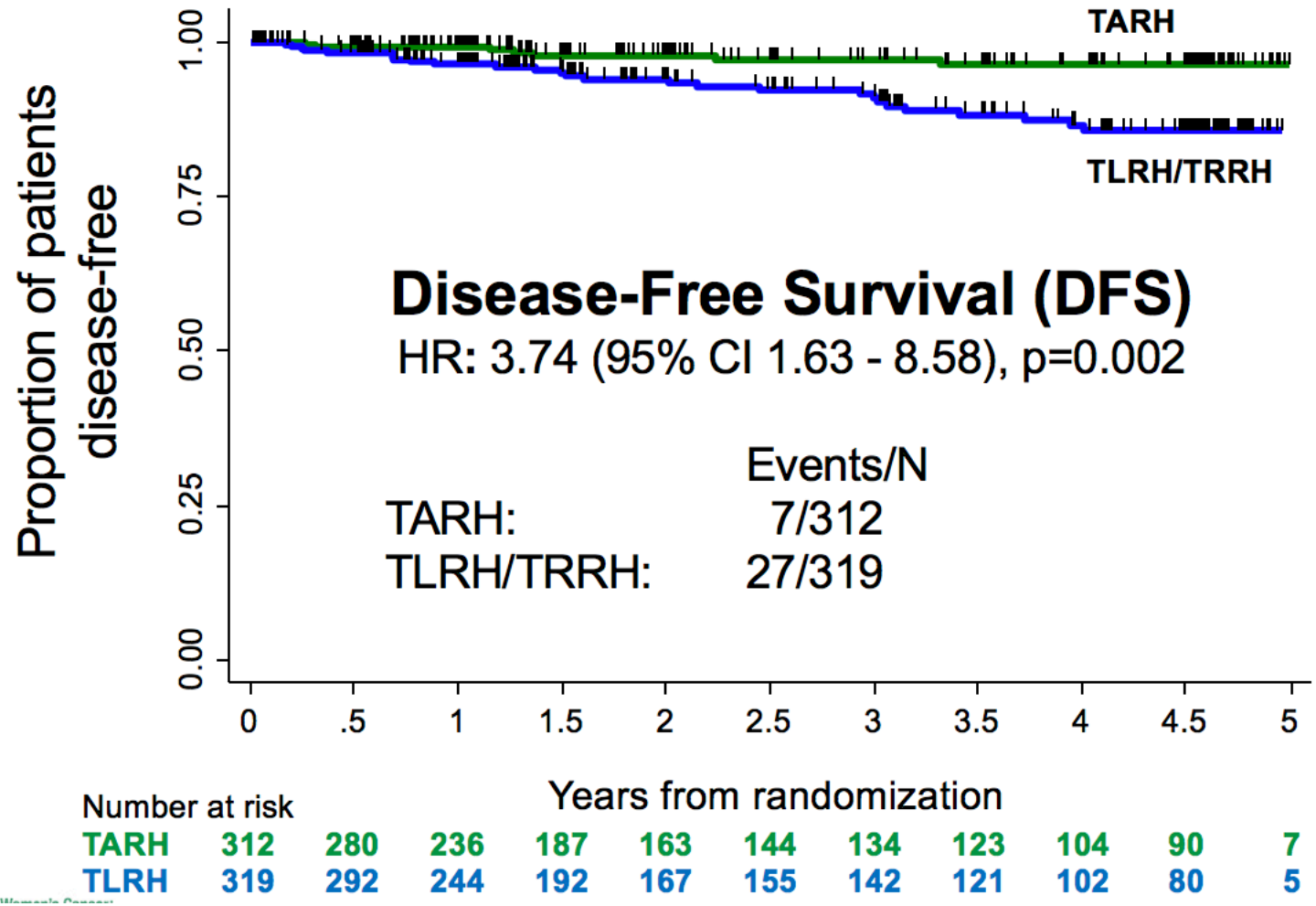
- More than 500,000 women per annum worldwide (WHO)
- Treatment of early stages is radical hysterectomy
- Increased uptake of Minimally Invasive Surgery (MIS) by surgeons
- Numerous retrospective studies or prospective case series suggested:
  - MIS associated with decreased treatment-related morbidity
  - Survival outcomes between open and MIS similar
- **No prospective controlled trial available until 2007**

  Laparoscopic **A**pproach to **C**arcinoma of the **C**ervix (LACC) trial

Primary objective

Disease-free survival at

4.5 years amongst patients who underwent a total laparoscopic or robotic radical hysterectomy (TLRH/TRRH) vs. a total abdominal radical hysterectomy (TARH).



Ramirez P et al.: SGO 2018

Secondary objectives

- **Compare treatment-associated morbidity (up to 6 months from surgery)**
- Quality of Life (QoL) between arms
- Compare patterns of recurrence between arms
- Compare the cost effectiveness of TLRH/TRRH vs. TARH
- Assess pelvic floor function
- Compare overall survival between arms
- Determine the feasibility of sentinel lymph node mapping

Trial design, inclusion criteria

International, multicenter, randomized, phase III trial to test for non-inferiority of Laparoscopic/Robotic radical hysterectomy vs. open radical hysterectomy.

Inclusion criteria

- Squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of uterine cervix
- FIGO stage IA1 (with LVSI), IA2, IB1
- Type II or III radical hysterectomy (Piver-Rutledge Classification)
- Performance status of ECOG 0-1
- Age 18 years or older
- Availability of assessment of adverse events up to 3 or 6 months post-surgery

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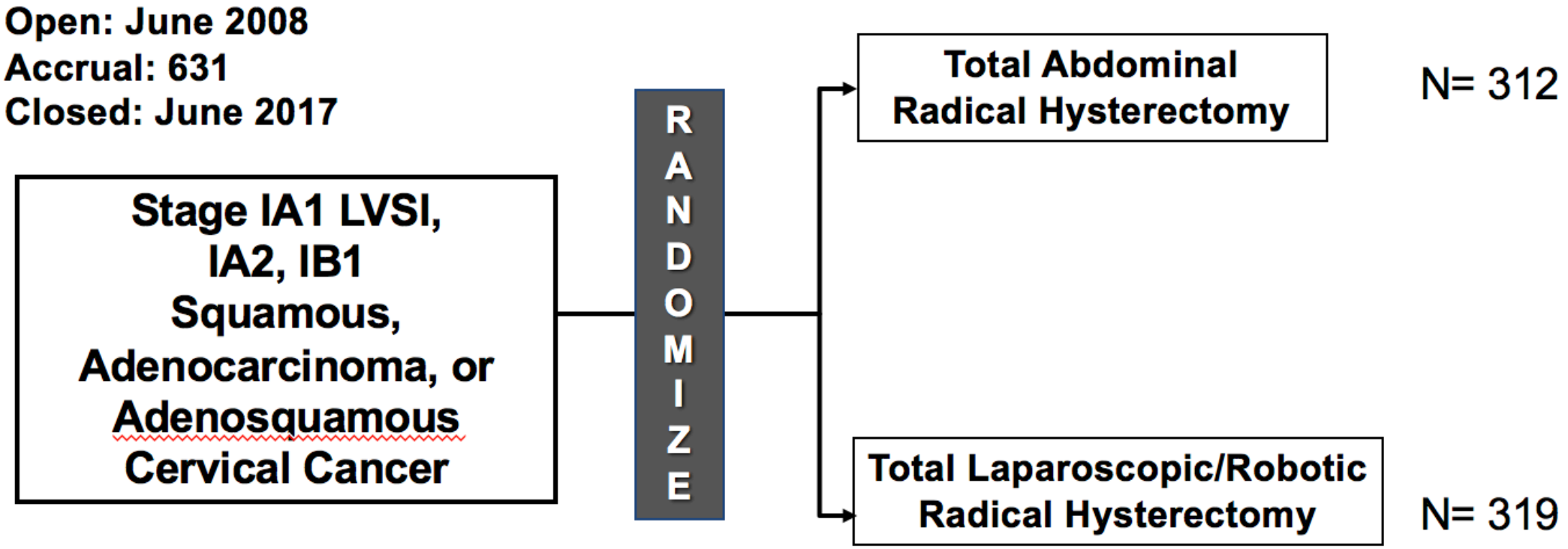
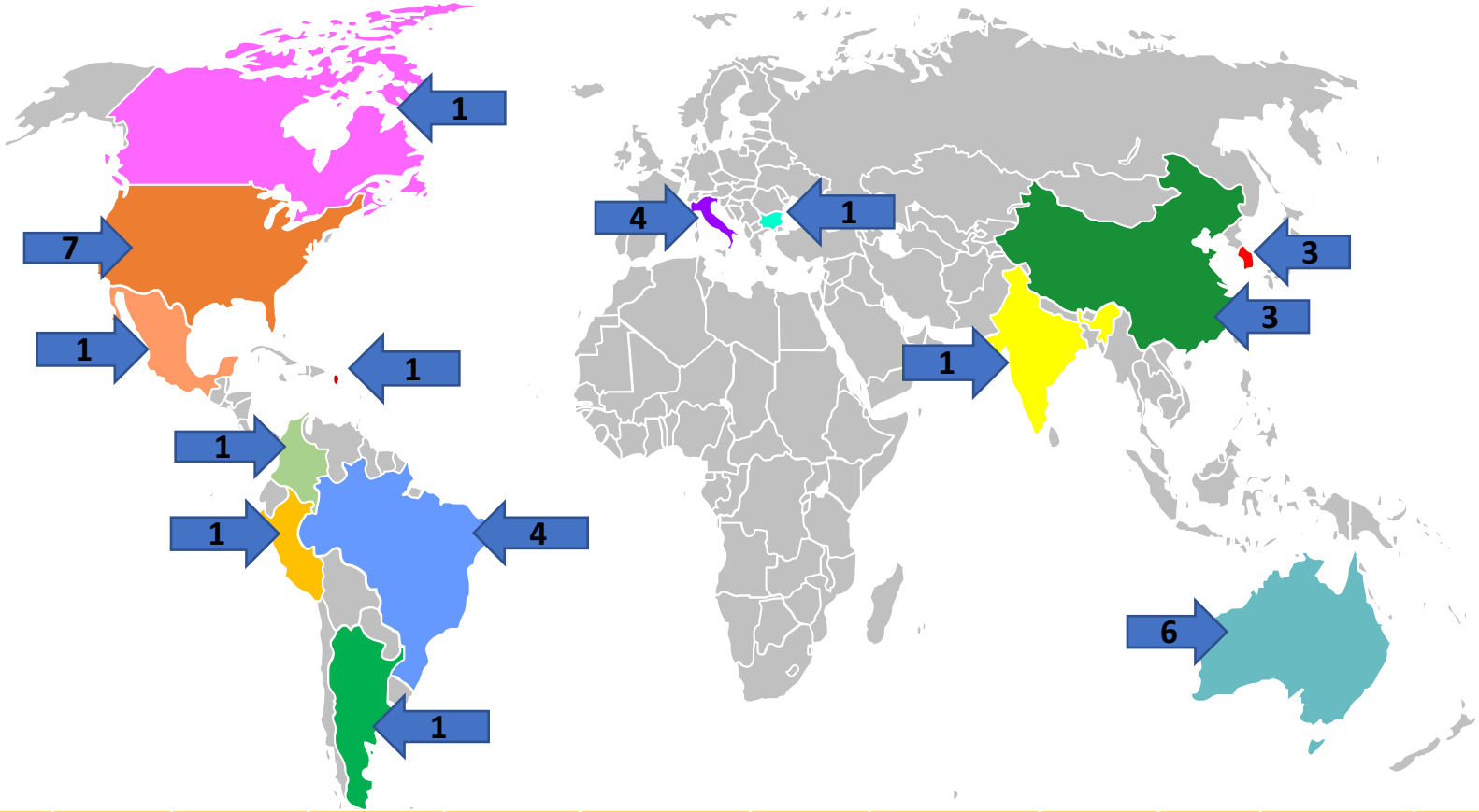
Trial schema



LACC trial enrolment was put on hold after recommendation by the DSMC in June 2017; Enrolment was stopped in September 2017. Follow up is ongoing.

LACC TRIAL (NCT00614211)
Open January 2008 – Closed to Recruitment June 2017 (631 pts)



Country/ Territories	Australia	USA	Puerto Rico	Canada	Mexico	Argentina	Brazil	Colombia	Peru	Italy	Bulgaria	China	South Korea	India
Recruited	94	58	5	14	22	3	128	47	75	47	12	89	36	1

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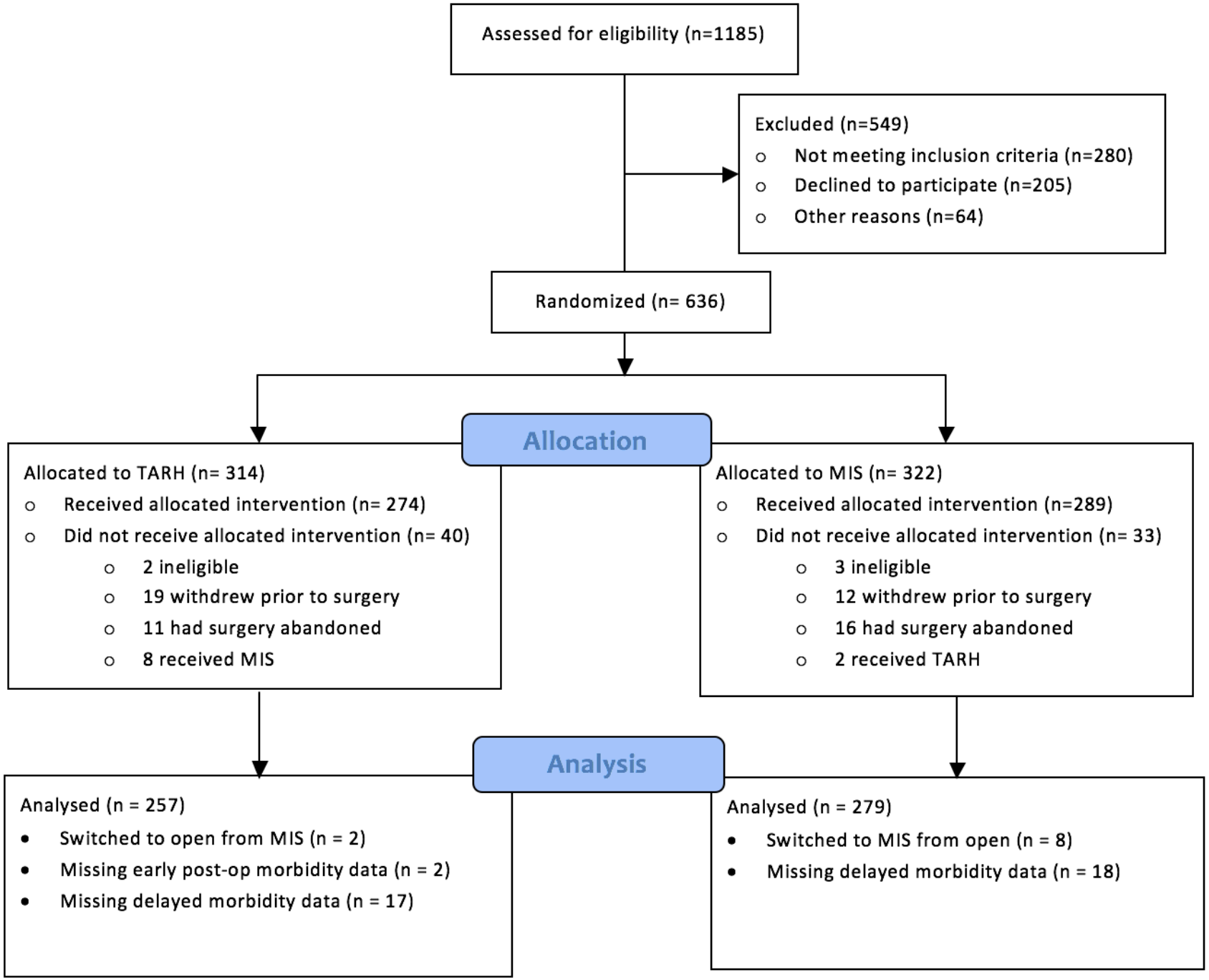
Surgeon proficiency

- Submission of **10 cases** of TLRH/TRRH 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 TLRH/TRRH
- Independent Review 2 members of Trial Management Committee


Assessed for eligibility (n=1185)
Excluded (n=549)
Not meeting inclusion criteria (n=280)
Declined to participate (n=205)
Other reasons (n=64)
Randomized (n= 636)
Allocation
Allocated to TARH (n= 314)
Received allocated intervention (n= 274)
Did not receive allocated intervention (n= 40)
2 ineligible
19 withdrew prior to surgery
11 had surgery abandoned
8 received MIS
Allocated to MIS (n= 322)
Received allocated intervention (n=289)
Did not receive allocated intervention (n= 33)
3 ineligible
12 withdrew prior to surgery
16 had surgery abandoned
2 received TARH
Analysis
Analysed (n = 257)
Switched to open from MIS (n = 2)
Missing early post-op morbidity data (n = 2)
Missing delayed morbidity data (n = 17)
Analysed (n = 279)
Switched to MIS from open (n = 8)
Missing delayed morbidity data (n = 18)

Patients' characteristics

		Open (n = 257)	MIS (n = 279)
Age at randomization (years)		45.8 (10.4)	46.2 (10.9)
Weight (kg)		66.3 (14.6)	68.5 (15.1)
Height (cm)		158.2 (7.5)	159.5 (6.9)
BMI (kg/m2)		26.5 (5.5)	26.9 (5.5)
Race	White/Caucasian	134 (52%)	143 (51%)
ECOG	0	236 (92%)	256 (92%)
	1	21 (8%)	23 (8%)
Stage	Stage IAI	4 (2%)	5 (2%)
	Stage IA2	18 (7%)	16 (6%)
	Stage IB1	235 (91%)	258 (92%)
Histology	Adenocarcinoma	69 (27%)	81 (29%)
	SCC	183 (71%)	193 (69%)
	Adenosquamous	5 (2%)	5 (2%)

Surgical outcomes

	Open (n = 257)	**MIS (n = 279)**	**P-value**
Length of Operation (minutes)	190 (61 – 425)	215 (75 – 441)	<.0001
Estimated blood loss (ml)	200 (0 - 2200)	100 (0 - 1500)	<.0001

Intraoperative complications

Intraoperative complications	Open (n=257)	MIS (n=279)	p-value
Any complication	**26 (10%)**	**34 (12%)**	**0.450**
Bladder injury	2 (1%)	7 (3%)	0.119
Blood transfusion	**12 (5%)**	**5 (2%)**	**0.057**
Bowel injury	1 (0%)	2 (1%)	0.611
Nerve injury*	**1 (0%)**	**6 (2%)**	**0.072**
Ureter injury	4 (2%)	5 (2%)	0.832
Uterus rupture	0	3 (1%)	0.095
Vaginal laceration	0	2 (1%)	0.173
Vascular injury	3 (1%)	4 (1%)	0.786
Other**	3 (1%)	5 (2%)	0.526

*Genitofemoral N (3); Obturator N (2); Femoral Cutaneous Lateral N (1); Femoral N (1)

**Bleeding; uterine perforation; PID

Postoperative complications (CTC grade 2+)

	Open (n = 257)	MIS (n = 279)	p-value
Wound complications	**16 (6.2%)**	**4 (1.4%)**	**0.003**
Surgical site infection	4 (1.6%)	5 (1.8%)	0.832
Incisional or port site hernia	1 (0.4%)	0 (0.0%)	0.297
Febrile morbidity	2 (0.8%)	6 (2.2%)	0.190
Vaginal vault complications*	**2 (0.8%)**	**11 (3.9%)**	**0.017**
Acute renal injury	1 (0.4%)	1 (0.4%)	0.953
Genitourinary fistula or stricture	7 (2.7)	10 (3.6%)	0.570
GI fistula	0 (0.0%)	1 (0.4%)	0.336
GI obstruction	1 (0.4%)	3 (1.1%)	0.356
Ileus	2 (0.8%)	0 (0.0%)	0.139
Neuropathy	2 (0.8%)	7 (2.5%)	0.119
DVT/PE	0 (0.0%)	1 (0.4%)	0.336
Lymphocele formation	3 (1.2%)	0 (0.0%)	0.070
Pain	24 (9.3%)	19 (6.8%)	0.281
Nausea	9 (3.5%)	8 (2.9%)	0.675
Lymphedema	2 (0.8%)	1 (0.4%)	0.515
Anaemia	16 (6.2%)	16 (5.7%)	0.810
Anxiety	3 (1.2%)	2 (0.7%)	0.587
Any other AE	86 (33.5%)	95 (34.1%)	0.885

*Vault infection, bleeding/spotting and dehiscence

Postoperative complications (cont'd) (CTC grade 2+)

	Open (n = 257)	MIS (n = 279)	p-value
Any pulmonary complications	3 (1.2%)	5 (1.8%)	0.551
Any cardiac complications	**10 (3.9%)**	**2 (0.7%)**	**0.013**
Any urinary complications*	46 (17.9%)	63 (22.6%)	0.178
Any sepsis	2 (0.8%)	2 (0.7%)	0.934
Any GI complications	36 (14.0%)	44 (15.8%)	0.567
Any Serious Adverse Event**	28 (10.9%)	39 (14.0%)	0.280

*Including bladder dysfunction

**Death; Immediately life threatening; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability/incapacity

Summary of complications

	Open (n = 257)	MIS (n = 279)	P value
Any complication	118 (46%)	145 (52%)	0.161
Intra-operative complications	26 (10%)	34 (12%)	0.447
Early post-operative morbidity (CTC grade 2+; <6 weeks)	84 (33%)	99 (35%)	0.494
Delayed morbidity (CTC grade 2+; 3 to 6 months)	44 (17%)	55 (20%)	0.439

Complications by groups

	Open (n = 257)	**Lap (n = 238)**	**Robotic (n=41)**
Any complication (any grade)	118 (46%)	124 (52%)	21 (51%)
Intra-operative complications	26 (10%)	30 (13%)	4 (10%)
Early post-operative morbidity (CTC grade 2+; <6 weeks)	84 (33%)	84 (35%)	15 (37%)
Delayed morbidity (CTC grade 2+; 3 to 6 months)	44 (17%)	48 (20%)	7 (17%)

Conclusions

- Anticipated benefits of laparoscopic/robotic radical hysterectomy over open radical hysterectomy were not demonstrated
- Length of surgery greater in laparoscopic/robotic group
- Estimated blood loss less in laparoscopic/robotic group
- Intraoperative, postoperative and serious adverse events are similar in both groups.

Discussion

STRENGTHS

- Prospective capture of AEs
- Robust trial design
- Appropriately powered
- Multicentre & international collaboration
- Surgeon proficiency requirements

LIMITATIONS

- Allowed laparoscopic and robotic surgery
- Documentation of AEs higher than clinically relevant
    - Numbness, vault spotting, vaginal laceration, bladder serosal tear

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