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Pelvic Organ Prolapse after Three Modes of Hysterectomy: Long-Term Follow Up

Iwona Gabriel MD, PhD[1,2], Anthony Kalousdian [1], Luiz Gustavo Brito MD, PhD [3], Talar Abdalian [1], Allison F Vitonis ScM [4], Vatche Arakel Minassian MD, MPH [1]

1. Division of Urogynecology, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Boston, MA
2. Department of Gynecology, Obstetrics and Gynecological Oncology, Medical University of Silesia, Bytom, Poland
3. Department of Obstetrics and Gynecology, University of Campinas, SP, Brazil
4. Department of Epidemiology, Brigham and Women's Hospital, Boston, MA

Corresponding author:
Vatche Minassian
Division of Urogynecology
Department of Obstetrics and Gynecology
Brigham and Women's Hospital
500 Brookline ave
Boston, MA 02415
Email: vminassian@bwh.harvard.edu

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Short title: Long-term Incidence of prolapse after hysterectomy

This study was presented during the 2019 AUGS/IUGA Joint Meeting in Nashville, TN.

Condensation

Risk of pelvic organ prolapse is similar after abdominal, vaginal or laparoscopic/robotic hysterectomy when adjusted for risk factors including hysterectomy indication in long-term follow up.

Short title

Long-term incidence of prolapse after hysterectomy

AJOG at a Glance

A. Why the study was conducted?

There is a lack of robust long-term data whether differences exist in the incidence of pelvic organ prolapse between different modes of hysterectomy, generating conflicting opinions.

B. What are the key findings?

The unadjusted risk of prolapse is highest for vaginal hysterectomy in up to 17-year follow up (17%); however, the adjusted risk is similar for abdominal, vaginal and laparoscopic/robotic hysterectomy after controlling for age, parity, body mass index, year and indication of surgery. About half of women with pelvic organ prolapse following hysterectomy receive treatment.

C. What does this study add to what is already known?

Most vaginal hysterectomies are performed for prolapse, which in turn are associated with the highest risk of prolapse recurrence. However, this risk is no different across all modes of hysterectomy when indication (such as prolapse, cancer, or other) is accounted for.

ABSTRACT

Background: There are various indications and approaches for hysterectomy; yet, the difference in long-term risk of subsequent prolapse after surgery is not well studied.

Objective: To assess the risk of prolapse after abdominal, vaginal and laparoscopic/robotic hysterectomy for up to 17 years from surgery.

Study design: A retrospective chart review study of women undergoing hysterectomy across all indications (benign and malignant) between 2001-2008 was conducted. An equivalent random sample of hysterectomy patients was selected each year. We compared demographic and other surgical characteristics data including age, race, parity, body mass index (BMI), indication and year of hysterectomy, blood loss, cervix removal, cuff suspension, and complications using Chi square, Kruskal- Wallis test, and Fisher's exact across the three groups. Presence and treatment of subsequent prolapse (based on patient symptoms, pelvic exam, ICD9 diagnosis, and CPT pessary or surgical codes) were compared with Kaplan Meier survival analysis and Cox proportional hazards regression.

Results: Of the 2,158 patients, 1459, 375 and 324 underwent open, vaginal and laparoscopic/robotic hysterectomy, respectively. The vaginal group (56) was older than the abdominal (52) or laparoscopic / robotic (49) groups, $p<0.05$. Most patients were white with a mean BMI of 30kg/m^2. The main indication was cancer for abdominal (33%) and laparoscopic/robotic hysterectomy (25%) and prolapse for vaginal hysterectomy (60%). . Time to prolapse was shortest after vaginal surgery (27 months) and longest after laparoscopic/robotic surgery (71 months). After controlling for confounders, including surgery indication, the hazard ratio (HR) for subsequent prolapse was no different among vaginal (HR=1.36 (0.77, 2.45)), laparoscopic/robotic (HR=1.47 (0.80, 2.69)), or open (reference) hysterectomy. Prolapse grade was similar across the three groups. About 50% of women with recurrent prolapse received physical therapy, pessary or surgical treatment.

Conclusion: At 17-year follow up, the route of hysterectomy is not associated with a difference in recurrence, grade or subsequent treatment of prolapse when the indication for hysterectomy is taken into account. Prolapse as an indication for hysterectomy, increases

97 risk for recurrence. Women planning a hysterectomy should be counseled appropriately
98 about risk of subsequent prolapse.

99 **Introduction**

100 Pelvic organ prolapse (POP) has an overall prevalence of 3-6%, and is even more
101 common in older women [1]. With the increase in prevalence of pelvic organ prolapse [1,2], the
102 need for reconstructive surgery is predicted to increase by 45% over the next three decades
103 associated with a predicted rise in costs to exceed one billion dollars per year [3,4]. POP has a
104 significant impact on quality of life where patients generally complain of feeling a vaginal
105 bulge and pressure, as well as voiding, defecatory and sexual dysfunction [5]. Risk factors for
106 POP include increasing age, parity, race and body mass index (BMI) [6,7,8,9].

107 Hysterectomy is the most common major gynecological surgery in the United States
108 [10,11] and is considered to be a potential risk factor for POP with an incidence of post-
109 operative vault prolapse varying from 2 to 43% [12,13]. One study estimated an incidence of
110 6.25% for post-hysterectomy vault prolapse requiring surgical correction [13]. In another study,
111 the incidence of prolapse requiring surgical correction after hysterectomy was 1.3 to 4.2 per
112 1000 women-years [14]. Although the American College of Obstetrics and Gynecology
113 (ACOG) recommends vaginal apex suspension such as a McCall culdoplasty to be
114 performed at the time of hysterectomy to reduce risk of subsequent POP [15], it is not known if
115 all gynecologists at our institution or elsewhere follow this recommendation routinely.
116 Furthermore, little is known whether different hysterectomy approaches have a different risk
117 factor profile regarding subsequent POP. Moreover, the effectiveness of prophylactic
118 measures at the time of surgery that reduce the risk of POP (such as uterosacral ligament
119 suspension) after different hysterectomy routes is unknown [16].

120 The goal of our study was to determine whether there exists a difference in
121 subsequent POP occurrence and treatment after different modes of hysterectomy
122 (abdominal, vaginal and laparoscopic/robotic), and whether the three groups differed by
123 timing of POP occurrence and by indication of hysterectomy.

124

Material and Methods

This was a retrospective chart review analysis of women who underwent hysterectomy for any indication at a tertiary care hospital in Boston from January 2001 through December 2008 to allow us to have at least 10-year follow-up data from the last year of the study period Electronic review of the medical records was completed through the end of 2018 for a total of up to 17 years of follow-up. We included all women who underwent hysterectomy regardless of indication. We excluded women who did not follow up within our healthcare system after the index surgery. The exposure was defined as hysterectomy (by type) and the primary outcome of interest was defined as symptomatic prolapse in any compartment subsequent to the index surgery. All surgeries between 2001 and 2008 with CPT code for hysterectomy were abstracted from the electronic system, and a random sample of all hysterectomies by route of surgery were included in the analysis.

Specifically, each third medical record number pooled by the system was included in the review. Based on our power calculations (see below), it was estimated we will have an adequate sample size by following this strategy to answer our study question. During the study period, since the majority of hysterectomies was performed abdominally, open hysterectomies were oversampled compared with the vaginal and laparoscopic / robotic cases to have equivalent and proportional representation. The hysterectomies were conducted by different gynecologists and gynecologic subspecialists with different practice standards with respect to post-operative follow-up care. To simplify, we considered women who had at least one gynecological follow-up exam post-operatively to be eligible for study inclusion. After the first 12 weeks post-operatively, most patients were followed up by their primary care physicians. There was a total of 172 women who did not follow up within the system or who had incomplete medical records that were excluded from the final analysis.

All charts were thoroughly reviewed from the date of the index surgery till the end of the study period, including all progress notes from primary care physicians, general gynecologists, gynecologic subspecialists, urologists and colorectal surgeons. Data abstracted from the medical records included: age at hysterectomy, race, parity, body mass

index (BMI), indication for hysterectomy, type of hysterectomy (abdominal, vaginal, laparoscopic/robotic), concomitant surgeries, removal of cervix, intra and peri-operative complications, estimated blood loss (EBL), vaginal apex suspension, presence of prolapse after hysterectomy (based on progress notes subsequent to the index surgery), time to prolapse occurrence, type of prolapse (cystocele, rectocele, vault prolapse), grade of prolapse (defined using the Baden-Walker grading system), and treatment of subsequent prolapse (none, pessary, surgery). The presence of POP after hysterectomy was based on documentation in the clinical progress notes (i.e., patient's subjective symptoms and/or physician's pelvic examination or diagnosis), pelvic floor physical therapy notes, ICD-9 POP diagnosis codes, and prolapse pessary or CPT codes. When available, POP by compartment was objectively measured using the Baden-Walker system (or inferred from the pelvic exam / POP-Q exam) because most surgeons performing the hysterectomies were not female pelvic medicine and reconstructive surgeons and as such they did not use the POP-Q system.

The null hypothesis was that there is no difference in the rate of post hysterectomy prolapse between the three hysterectomy routes. Considering the incidence of clinically significant post hysterectomy prolapse to be approximately 6.25% [13], assuming a 10% difference (6.25% versus 16.25%) in prolapse rates between the hysterectomy routes to be clinically relevant, and using an alpha value of 0.05, and a beta value of 80%, we estimated approximately 300 patients per group of hysterectomy are needed. With eight years of study period, we needed at approximately 40 patients each year per group to have a representative sample during the study period and meet the sample size requirements.

To compare patient characteristics and surgical details (e.g., estimated blood loss, complications, cuff suspension, cervix removed) by type of surgery, we used ANOVA for normally distributed variables (age, BMI), the Kruskal-Wallis test for non-normally distributed variables (EBL), chi-square tests for categorical variables, and Fisher's exact tests for categorical variables with small expected numbers. Among patients who experienced post-hysterectomy POP, we compared prolapse type, grade, and treatment method by surgery

type. The Kaplan–Meier method was used to estimate time to prolapse curves and log-rank tests were used to compare crude survival distributions. Additionally, Cox proportional hazard regression was used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for the associations between type of surgery and post-hysterectomy prolapse. To determine what factors might confound the association between surgery type and prolapse, we assessed the change in HRs when each patient demographic or surgical characteristic variable was added to the Cox proportional hazard model individually. Additionally, we decided to adjust for age (continuous) and BMI (<25, 25-29.9, 30-34.9, ≥35, missing) a priori. To verify the assumption of proportional hazards, we added an interaction term between log transformed time and each predictor. Interaction terms with p-values <0.05 indicated non-proportional hazards. A sensitivity analysis was run examining the association between surgery type and prolapse after excluding patients with cancer. All analyses were performed using SAS software version 9.4 (Cary, NC, USA). The study was approved by Partners Institutional Board Review (2014P001869).

Results

We reviewed 2,158 charts of women who underwent hysterectomy between 2001 and 2008 for any indication including 1,459 abdominal, 375 vaginal, and 324 laparoscopic/robotic cases with a mean age of 51.9 years, 56.3 years and 49.7 years, respectively. Over the years of the study period, there was a noticeable decline in open abdominal surgeries and an increase in laparoscopic/robotic surgeries. Most women were multiparous and white, with mean BMI approximately 30 kg/m^2 (Table I). The most common indication for abdominal hysterectomy was cancer (33%), followed by fibroids (24%). For laparoscopic/robotic surgery, the primary indication was cancer (25%) followed by abnormal uterine bleeding (25%). Prolapse was the indication for the index surgery in 60% of vaginal cases, and only 2% of abdominal and laparoscopic/robotic cases. The EBL was lowest for laparoscopic/robotic hysterectomy (median=100ml), and highest for abdominal surgery (median=250ml). Retention of cervix (subtotal hysterectomy) was more commonly

performed with laparoscopic/robotic hysterectomies (42.9%). Documentation of prophylactic vaginal cuff suspension in the operative note was present only in 10.1% of abdominal hysterectomies and 5.9% of laparoscopic/robotic hysterectomies. The majority of patients in the vaginal group had documentation of cuff suspension in the operative note (73.3%) (Table II).

The 172 cases who were excluded (versus those who were included) from the final analysis due to lack of follow-up or incomplete data were similar across all patient demographics and surgical characteristics except for indication for surgery (Table III). Of those patients included in the final analysis, 1,361 patients underwent open surgery, 325 had vaginal hysterectomy and 300 had laparoscopic/robotic surgery. The incidence of prolapse after hysterectomy was the lowest among abdominal (3.2%), followed by laparoscopic / robotic (5.6%) and then vaginal (17.2%) hysterectomies (Table IV).

The median (range) follow-up for the cohort was 84 (0.17-204) months. Time to prolapse occurred earliest after vaginal (median=27 months), followed by abdominal (median=69 months) and then laparoscopic/robotic (median=71 months) hysterectomy. The median follow-up time was shortest in the laparoscopic/robotic group because these surgeries were not being performed during the first half of our study period. The most common type of subsequent prolapse was a cystocele across after all types of hysterectomy. There was no difference in prolapse grade or subsequent treatment for prolapse among the three groups, with approximately 50% of women receiving treatment. Excluding the cancer cases had no significant effect on the incidence or timing of subsequent prolapse by route of hysterectomy (data not shown). In brief, there were eight fewer cases who had subsequent prolapse in the abdominal group, one fewer case in the vaginal group, and three fewer cases in the laparoscopic/robotic group when hysterectomies due to cancer were excluded.

Further, we performed survival analysis among the three groups with the crude hazard ratio (HR) for subsequent POP being 2.06 (95%CI:1.16,3.66) for laparoscopic/robotic and 4.98 (95%CI:3.35,7.42) for vaginal when compared to open hysterectomy (Table V). In

the multivariate model controlling for indication, laparoscopic/robotic surgery still had a significant HR. However, controlling for all significant demographic and surgical characteristics, the differences in the HR among the three groups for subsequent POP were no longer significantly different. Since documentation of cuff suspension was only available in some (but not most) operative notes, we further accounted for this variable. The association between cuff suspension and prolapse was found to vary by time and an interaction term between time and cuff suspension was also included in the model, and in doing so, the lack of significant difference in subsequent POP between the three groups persisted (Table V).

Lastly, the unadjusted Kaplan-Meier curve for time to prolapse by each surgery type was significantly different in favor of open, followed by laparoscopic/robotic and then vaginal hysterectomy, $p<0.001$. However, in the multivariate adjusted model, there was no significant difference between the three groups (figure 1).

Comment

Principal Findings

The overall incidence of post-hysterectomy POP across our sample of women, and who were not lost to follow-up after surgery was approximately 6%. Long-term observation after hysterectomy showed that incident POP differed by route of hysterectomy with the lowest rate favoring the abdominal approach, whether cancer cases were considered or not. However, indication for hysterectomy was a significant confounder. Prolapse more commonly occurred (or re-occurred) when the primary indication for hysterectomy was prolapse itself. Interestingly, after controlling for this and other significant confounders, there remained no significant difference in rates of subsequent prolapse between the three routes of hysterectomy. Time to outcome occurrence (symptomatic prolapse) was shortest after the vaginal approach and longest for laparoscopic/robotic hysterectomy (median=5.9 years), and of those with documented follow-up in our hospital system, only about half of women with post-hysterectomy POP received subsequent care within our health system. Lastly, the

trends of increasing laparoscopic/robotic hysterectomies and decreasing abdominal hysterectomies for benign and oncologic cases in the mid 2000's mirror national trends in the United States [17].

Results

Although most studies do not account for the indication for surgery, hysterectomy has been shown to be associated with subsequent pelvic organ prolapse with prevalence estimates of 5.4% in women with previous hysterectomy versus 2.3% in those without[18]. Post-hysterectomy rates in our study are consistent with other studies [13,18]. However, our study provides further detailed information on differences in incidence of prolapse after various modes of hysterectomy. With long-term follow up, the rate of subsequent prolapse is lowest after abdominal followed by laparoscopic/robotic and then vaginal hysterectomy. The impact of route of hysterectomy on subsequent prolapse has been previously debated, however it is still not well established. In a nationwide longitudinal study, Altman et al reported a rate of subsequent prolapse in 564 (per 100,000 person-years) women undergoing abdominal surgery, 679 after vaginal and 287 after laparoscopic hysterectomy [19]. Recently, a study using the Danish National Patient Registry with a 20-years of follow-up showed that the highest cumulative incidence of POP surgery was after vaginal hysterectomy (14%) with approximately 6% for laparoscopic or abdominal hysterectomy [209]. The data presented by those studies are limited only to women who had subsequent pelvic floor surgeries [19,20], as opposed to ours that considered all patients with POP symptoms regardless of repeat surgery or not. It should be underlined that our study demonstrated that of those with documented follow-up in our hospital system, as many as half of women with POP symptoms after hysterectomy did not seek (or receive) surgical treatment. Also importantly, our study demonstrated women who developed prolapse after hysterectomy were less likely to develop vaginal vault prolapse (versus cystocele or rectocele) when the vaginal vault was prophylactically suspended at the time of the hysterectomy.

Our study demonstrates that the route of hysterectomy has no impact of the risk of subsequent POP. Since the primary indication for most vaginal hysterectomies was POP,

the un-adjusted risk of subsequent prolapse appears to favor open and laparoscopic/robotics surgeries. Importantly however, when indication of surgery was accounted for, vaginal hysterectomy was no longer associated with increased prolapse risk. This information can be used to better counsel women prior to surgery by increasing awareness that the route of hysterectomy has little to no effect on subsequent prolapse. Previous studies on risk of post-hysterectomy prolapse have not compared all three modes of hysterectomy due to low number of laparoscopic surgeries [14], had a shorter observation period [21], did not include all hysterectomy indications [22], or used questionnaires [23] or registries [24] to determine risk of prolapse after hysterectomy.

The uniqueness of our study is that it represents a large cohort of women with a long-term follow-up of up to 17 years, and across all women who underwent hysterectomy for all indications. Most previous studies have focused on prolapse risk after benign hysterectomy indications [19,20,25,26]. Recently, a study by Higgs et al. [27] showed improvement in PFDI scores (Pelvic Floor Distress Inventory scores) six-months post-surgery for endometrial cancer. These patients were observed up to 4.5 years post-hysterectomy and they showed improvement in pelvic floor symptoms through the end of study [27]. One could argue that our study population may not be generalizable since we included women with both benign and malignant indications and the surgical practices along with possible peri-operative radiotherapy may significantly impact the subsequent development (or lack thereof) of our outcome of interest (prolapse). However, when we excluded cancer cases from our analysis, there was only a slight but non-significant increase in POP from for all women from 5.8% to 7.3%. Similarly, the time to prolapse after exclusion of cancer cases remained the same across the three routes of hysterectomy.

Vaginal cuff suspension such as the McCall culdoplasty has been shown to reduce the risk of subsequent prolapse in women undergoing vaginal hysterectomy [12]. Although most (70%) operative reports on vaginal hysterectomies reviewed indicated that a vaginal cuff suspension was performed at the time of closure, the converse was true for the open (10%) or laparoscopic / robotic (6%) cases. Because of this, we modeled the survival

analysis for three modes of hysterectomy with and without cuff suspension and found no difference in the HR of subsequent prolapse. We postulate that most surgeons performing a hysterectomy irrespective of the route prophylactically suspend the cuff to the uterosacral ligaments. However, we recognize that this may not be a universal practice and may influence the external validity of our conclusions. More research is needed in this area, such as interviewing surgeons performing hysterectomies, to further elucidate the true impact of cuff suspension by route of hysterectomy.

Clinical implications

Risk of prolapse subsequent to hysterectomy is approximately 6%. When all hysterectomy indications are considered, controlling for confounders (including indications), eliminates the differences in prolapse risk across the three hysterectomy groups. Importantly, the risk of de novo versus or recurrent prolapse is not associated with the route of hysterectomy. About 50% of women with subsequent prolapse after hysterectomy do not receive or seek care. These are important discussion points between the surgeon and the patient when planning a hysterectomy.

Strengths and limitations

The strengths of our study include long-term follow-up (at least 10 years for patients operated in 2008 and up to 17 years for patients who underwent hysterectomy in 2001); inclusion of all modes of hysterectomies namely vaginal, laparoscopic/robotic, and open cases; since over time it is possible that hysterectomy techniques could have evolved, we included an equivalent number of hysterectomies per year to account for temporal changes; and thorough review of all accessible electronic operative and progress notes. The design of our study allowed us not to rely solely on coding for prolapse. Rather, we identified all women with symptomatic prolapse within our health care system with the thorough review of all pertinent electronic medical records including progress notes of physicians and physical therapists, ICD9 diagnoses and CPT codes.

Our study had some limitations including the nature of our study population which was limited to a majority of white race limiting its generalizability to other populations with a

larger distribution of black, Hispanic or other races. Because of the retrospective nature of the study, selection bias could have played a role, but we would expect that it would be randomly distributed across the three groups with little effect on the outcomes of the study. Of note is that concomitant prolapse repairs were predominantly performed vaginally as they occurred primarily in patients undergoing vaginal hysterectomy. Moreover, we accounted for potential known prolapse risk factors. Another weakness is that we had some patients who were lost to follow-up, or with limited or no data after their index surgery. Therefore, we did not have information on their subsequent prolapse status or whether or not they sought care elsewhere. Baseline and operative characteristics between patients who were included versus excluded were not significantly different. However, it is possible that our study may have missed some patients with POP (false negative cases) such as those with mild POP with little to no symptoms, or those with no follow-up within our health care system who may have differentially had higher rates of POP. Another limitation is that we did not have data on the degree (or stage) of prolapse in women who underwent hysterectomy prior to the index surgery. It is possible that women with advanced prolapse had a higher rate of recurrent prolapse following hysterectomy. Finally, although we believe most surgeons performing hysterectomies via any route actually do suspend the cuff at the completion of the surgery, given the ACOG recommendations to do so, only a fraction of the operative reports related to the open or laparoscopic routes had documentation of doing so.

Research implications

Future studies should develop improved assessment tools of vaginal cuff suspension at the time of hysterectomy by route of surgery. Additionally, it is important to better understand patient and social determinants of health associated with those who seek (or receive) care for prolapse following hysterectomy versus those who do not.

Conclusions

Post-hysterectomy prolapse occurs after all types of hysterectomy. In-long term survival analysis, when adjusted for common risk factors including indication for surgery, the risk is no different between the different routes of hysterectomy. Women planning a

hysterectomy should be appropriately counseled about risk and treatment of subsequent prolapse.

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Table I. Demographic data of women who underwent hysterectomy between 2001-2008.

	Open (Abdominal) Hysterectomy (n= 1459)	Vaginal/ Lap-assisted Vaginal Hysterectomy (n=375)	Laparoscopic or Robotic Hysterectomy (n=324)	p-value*
Age (years) at time of hysterectomy, mean (SD)	51.9 (11.7)	56.3 (12.1)	48.8 (10.4)	<0.0001
Parity, n (%)				
Nulliparous	350 (27.4%)	12 (4.0%)	78 (25.0%)	<0.0001
1-2	610 (47.8%)	156 (51.5%)	151 (48.4%)	
>=3	316 (24.8%)	135 (44.5%)	83 (26.6%)	
Unknown (n=261)				
Race, n (%)				
White	1169 (83.5%)	301 (84.3%)	263 (84.6%)	0.86
Non white	231 (16.5%)	56 (15.7%)	48 (15.4%)	
Unknown (n=86)				
BMI, mean (SD)†	30.2 (8.7)	27.6 (6.1)	29.5 (8.6)	0.001
Year of hysterectomy, n (%)				
2001	196 (13.4%)	44 (11.7%)	5 (1.5%)	<0.0001
2002	190 (13.0%)	47 (12.5%)	2 (0.6%)	
2003	191 (13.1%)	49 (13.1%)	0 (0.0%)	
2004	192 (13.2%)	38 (10.1%)	9 (2.8%)	
2005	193 (13.2%)	37 (9.9%)	16 (4.9%)	
2006	231 (15.8%)	69 (18.4%)	106 (32.7%)	
2007	127 (8.7%)	38 (10.1%)	81 (25.0%)	
2008	139 (9.5%)	53 (14.1%)	105 (32.4%)	

*p-values from ANOVA for age and BMI and chi-square tests for parity, race, and year of hysterectomy.

†BMI missing for 686 open hysterectomy, 186 vaginal/laparoscopically assisted vaginal hysterectomy, and 139 total laparoscopic or robotic hysterectomy patients.

Table II. Peri-operative characteristics across hysterectomy routes.

	Open (Abdominal) Hysterectomy (n= 1459)	Vaginal/ Lap-assisted Vaginal Hysterectomy (n=375)	Laparoscopic or Robotic Hysterectomy (n=324)	p-value*
Indication for surgery, n (%)				
Abnormal uterine bleeding	175 (12.0%)	58 (15.5%)	77 (24.0%)	<.0001
Fibroids	356 (24.4%)	19 (5.1%)	71 (21.9%)	<.0001
Endometriosis/ Pelvic pain	176 (12.1%)	14 (3.7%)	55 (17.0%)	<.0001
Prolapse	34 (2.3%)	226 (60.3%)	7 (2.2%)	<.0001
Cancer	488 (33.4%)	29 (7.7%)	82 (25.3%)	<.0001
Cesarian hysterectomy	26 (1.8%)	0	0	0.0005
Gastrointestinal Involvement	13 (0.9%)	1 (0.3%)	0	0.14
Preneoplastic (EIN,CIN)	55 (3.8%)	18 (4.8%)	21 (6.5%)	0.09
Ovarian benign	117 (8.0%)	2 (0.5%)	6 (1.8%)	<.0001
Prophylactic	19 (1.3%)	8 (2.1%)	5 (1.5%)	0.44
EBL, median (IQR)†	250 (150 - 400)	200 (100 - 350)	100 (50 - 200)	<.0001
Cervix removed, n (%)				
Yes	1255 (86.0%)	374 (100.0%)	185 (57.1%)	<.0001
No	204 (14.0%)	0 (0%)	139 (42.9%)	
Complications (Any), n (%)				
Any Complication	85 (5.8%)	13 (3.5%)	11 (3.4%)	0.06
None	1374 (94.2%)	362 (96.5%)	313 (96.6%)	
Complications, n (%)				
None	1374 (94.2%)	362 (96.5%)	313 (96.6%)	0.02
Hemorrhagic	19 (1.3%)	1 (0.3%)	0 (0%)	
Bladder Injury	12 (0.8%)	2 (0.5%)	2 (0.6%)	
Ureteral Injury	4 (0.3%)	0 (0%)	1 (0.3%)	
Bowel Injury	20 (1.4%)	0 (0%)	0 (0%)	
Cardiopulmonary event	10 (0.7%)	1 (0.3%)	0 (0%)	
Other	20 (1.4%)	9 (2.4%)	8 (2.5%)	
Detailed cuff suspension, n (%)				
Yes	148 (10.1%)	275 (73.3%)	19 (5.9%)	<.0001
No	1311 (89.9%)	100 (26.7%)	305 (94.1%)	

*p-values from chi-square and Fisher's exact tests for categorical variables and Kruskal-Wallis test for EBL.

†EBL missing for 184 open hysterectomy, 38 vaginal/laparoscopically assisted vaginal hysterectomy, and 96 total laparoscopic or robotic hysterectomy patients.

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Table III. Demographic data of women who underwent hysterectomy between 2001-2008 and were included versus excluded from analysis

	Excluded (n=172)	Included (n=1,986)	p-value*
Age at time of hysterectomy, mean (SD)	50.9 (11.4)	52.3 (11.8)	0.15
Parity, n (%)			
Nulliparous	18 (19.6%)	422 (23.5%)	0.08
Parity(1 to 2)	55 (59.8%)	862 (47.9%)	
Grandmultipara (>=3)	19 (20.6%)	515 (28.6%)	
Unknown (n=261)			
Race, n (%)			
White	131 (80.4%)	1602 (84.1%)	0.22
Non white	32 (19.6%)	303 (15.9%)	
Unknown (n=86)			
BMI, mean (SD)†	29.9 (10.1)	29.6 (8.3)	0.91
Indication for surgery, n (%)			
Abnormal uterine bleeding	38 (22.1%)	272 (13.7%)	0.003
Fibroids	46 (26.7%)	400 (20.1%)	0.04
Endometriosis/ Pelvic pain	14 (8.1%)	231 (11.6%)	0.17
Prolapse	42 (24.4%)	225 (11.3%)	<.0001
Cancer	16 (9.3%)	583 (29.4%)	<.0001
Cesarean hysterectomy	6 (3.5%)	20 (1.0%)	0.01
Gastrointestinal Involvement	0 (0%)	14 (0.7%)	0.62
Preneoplastic (EIN, CIN)	6 (3.5%)	88 (4.4%)	0.56
Ovarian (benign)	4 (2.3%)	121 (6.1%)	0.04
Prophylactic	0 (0%)	32 (1.6%)	0.09
EBL, median (IQR)†	250 (100-400)	200 (100-400)	0.16
Complications (Any), n (%)			
Any Complication	164 (95.4%)	1885 (94.9%)	0.80
None	8 (4.6%)	101 (5.1%)	
Complications, n (%)			
None	164 (93.4%)	1885 (94.9%)	0.49
Hemorrhagic	2 (1.1%)	18 (0.9%)	
Bladder Injury	2 (1.1%)	14 (0.7%)	
Ureteral Injury	1 (0.6%)	4 (0.2%)	
Bowel Injury	2 (1.1%)	18 (0.9%)	
Cardiopulmonary event	0 (0%)	11 (0.6%)	
Other	1 (0.6%)	36 (1.8%)	

Table IV. Incidence of prolapse after different modes of hysterectomy by type and grade of prolapse

	Open (Abdominal) Hysterectomy (n=1361)	Vaginal/ Lap-assisted Vaginal Hysterectomy (n=325)	Laparoscopic or Robotic Hysterectomy (n=300)	P value
Prolapse				
- Yes	43 (3.2%)	56 (17.2%)	16 (5.3%)	<0.0001
- No	1318 (96.8%)	269 (82.8%)	284 (94.7%)	
Follow-up months among those with no prolapse				
- Median (IQR)	96 (24-132)	120 (48-144)	72 (6-114)	<0.0001
Prolapse	**n=43**	**n=56**	**n=16**	
Time to prolapse in months (median (IQR))	69 (24-108)	27 (12-76)	71 (24-96)	0.07
Type of prolapse				
- Cystocele				
Yes	29 (67.4%)	33 (58.9%)	11 (68.8%)	0.61
No	14 (32.6%)	23 (41.1%)	5 (31.2%)	
- Rectocele				
Yes	22 (51.2%)	23 (41.1%)	8 (50.0%)	0.57
No	21 (48.8%)	33 (58.9%)	8 (50.0%)	
- Vault prolapse				
Yes	12 (27.9%)	10 (17.9%)	4 (25.0%)	0.48
No	31 (72.1%)	46 (82.1%)	12 (75.0%)	
Grade of prolapse (Baden-Walker)* **				
- 1	8 (24.2%)	17 (39.5%)	2 (13.3%)	0.17
- 2	14 (42.4%)	12 (27.9%)	9 (60.0%)	
- 3	11 (33.3%)	14 (32.6%)	4 (26.7%)	
Prolapse treatment				
- None	19 (44.2%)	30 (53.6%)	9 (56.2%)	0.57
- Pessary	6 (14.0%)	11 (19.6%)	2 (12.5%)	
- Surgery	18 (41.9%)	15 (26.8%)	5 (31.2%)	

*Amongst women with known prolapse status

**P-values from log rank test for prolapse, Kruskal-Wallis test for time to prolapse, and chi-square and Fischer's exact tests for prolapse type, grade and treatment

*** There were 24 patients whose grade of prolapse was unknown

Table V. Survival analysis across three modes of hysterectomy with known prolapse status

Hysterectomy Type	Prolapse (n=115)	Crude HR (95% CI)	p-value	Adjusted 1 HR (95% CI)*	p-value*	Adjusted 2 HR (95% CI)†	p-value†	Adjusted 3 HR (95% CI)‡	p-value‡
Abdominal (n=1,361)	43	1.00 (ref)	ref	1.00 (ref)	ref	1.00 (ref)	---	1.00 (ref)	---
Lap/robotic (n=300)	16	2.06 (1.16, 3.66)	0.01	2.09 (1.17, 3.73)	0.01	1.47 (0.80, 2.69)	0.21	1.58 (0.86, 2.90)	0.14
Vaginal (n=325)	56	4.98 (3.35, 7.42)	<0.001	1.50 (0.82, 2.73)	0.19	1.36 (0.76, 2.44)	0.3	1.06 (0.59, 1.92)	0.83

*Adjusted for indication only (benign, prolapse, cancer).

†Adjusted for age (continuous), BMI (<25, 25-29.9, 30-34.9, ≥35, missing), parity (nulliparous, 1-2, 3+, missing), year of hysterectomy (continuous), and indication (benign, prolapse, cancer).

‡Additionally adjusted for cuff suspension and an interaction term (cuff suspension and log transformed time).

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505 FIGURE LEGEND

506 **Figure 1.** Prolapse survival curves by type of hysterectomy, adjusted for age (continuous), BMI (<25,
507 25-29.9,30-34.9, ≥35, missing), parity (nulliparous, 1-2, 3+, missing), year of hysterectomy
508 (continuous), and indication (benign, prolapse, cancer). Compared to abdominal hysterectomy, the
509 hazard ratios (95% CI) for laparoscopic/robotic and vaginal hysterectomy were 1.47 (0.80, 2.69) and
510 1.36 (0.76, 2.44), respectively.

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