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ORIGINAL RESEARCH ARTICLE

Decline in surgeon volume after successful implementation of advanced laparoscopic surgery in gynecology: An undesired side effect?

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Abstract

Introduction: The implementation of advanced minimally invasive surgical (MIS) techniques has broadened. An extensive body of literature shows that high hospital and surgeon volumes lead to better patient outcomes. However, no information is available regarding volume trends in the post-implementation phase of MIS. This study investigated these trends and poses suggestions to adjust these developments. This knowledge can provide guidance to optimize patient safe performance of new surgical techniques.

Material and methods: A national retrospective cohort study in the Netherlands. The number of advanced laparoscopic (level 3 and 4) and robotic procedures and the number of gynecologists performing them were collected through a web-based questionnaire to determine hospital and gynecological surgeon volume. These volumes were compared with our previously collected data from 2012.

Results: The response rate was 85%. Hospitals produced larger volumes for advanced laparoscopic and robotic procedures. However, still 63% of the hospitals perform low-volume level 4 laparoscopic procedures. Additionally, gynecological surgeon volumes appeared to decrease for level 3 procedures, as the group of gynecologists performing fewer than 20 procedures expanded (64% vs. 44% in 2012), with 15% of the gynecologists performing fewer than ten procedures. Despite an increase in surgeon volumes for level 4 laparoscopy and robotic surgery, volumes continued to be low, as still 49% of gynecologists performed fewer than 10 level 4 procedures per year and 41% performed fewer than 20 robotic procedures per year.

Conclusions: The broad implementation of advanced MIS procedures resulted in an increasing number of these procedures with increasing hospital volumes. However, as a side-effect, a disproportionate rise in number of gynecologists performing these procedures was observed. Therefore, surgeon volumes remain low and even decreased for some procedures. Centralization of complex procedures and training of specialized MIS gynecologists could improve surgeon volumes and therefore consequently enhance patient safety.

KEYWORDS
gynecological surgeon volume, hospital volume, hysterectomy, minimally invasive surgery, robotic surgery

1 | INTRODUCTION

Worldwide, the acceptance of the minimally invasive surgical (MIS) approach in gynecology has increased.[1–4] Indications have broadened and in addition to laparoscopy, robotic surgery is on the rise since its approval by the US Food and Drug Administration for gynecological procedures in 2005.[5] With further development of these techniques and improvement of surgical skills, a shift towards a minimally invasive approach as opposed to conventional surgery is observed, leading to beneficial patient outcomes, especially for laparoscopy.[6–11]

To master a new surgical technique, one has to go through a procedure-specific learning curve until a plateau is reached.[12] Additionally, to assure maintenance of quality and patient safety, both hospital and surgeon volumes are often used as a quality indicator. Volume itself does not necessarily guarantee safe surgery,[13] but it is often used as a proxy measure for conditions for skills and experience, both important factors for the quality of surgical outcomes. It is debatable if low volumes provide those optimal conditions, as evidence shows that a higher annual surgeon volume relates to fewer complications, lower costs, fewer strategic conversions, and less perioperative morbidity in gynecological surgery.[14–17] This is supported by outcomes in other surgical fields.[18–21] Surprisingly, previous studies showed that a large proportion of gynecologists still perform low volumes of advanced laparoscopic procedures,[22] including laparoscopic hysterectomies.[23,24]

In addition, because of the rapid adaptation by early adapters of new (surgical) techniques, a shift towards other techniques is observed. The abdominal hysterectomy shifted towards the laparoscopic (LH) approach. As a side-effect, also the vaginal approach (VH) shifted towards the LH,[1,2,22] despite VH still being the preferred approach.[7,25] Furthermore, the introduction of robotic surgery has had its effect on the changes of approaches. Creating multiple techniques for the same indication, inherently has effects on both hospital and surgeon volumes, and it is debatable what side-effect this fragmentation of approaches has on patient-safe surgery.

One could expect that full implementation of MIS would result in a higher number of procedures, including more hospitals offering the procedure. Additionally, the number of surgeons performing MIS should increase. Therefore, the effect of full implementation on surgeon volume is uncertain. Despite an extensive body of literature regarding the relation between volume and patient outcome, no information is available regarding volume trends in the post-implementation phase of MIS. We investigated the effects of implementing advanced laparoscopy and robotic surgery in daily practice correlated to both hospital and gynecological surgeon volumes. Additionally we make suggestions to adjust these developments. This knowledge can provide guidance to optimize patient-safe performance of new surgical techniques.

Key message

Rising numbers of advanced minimally invasive surgery procedures resulted in larger hospital volumes. Surgeon volumes unfortunately remained low as the number of gynecologists performing these procedures grew rapidly. Efforts must be made to improve surgeon volumes.

2 | MATERIAL AND METHODS

To obtain the data for this inquiry, a web-based questionnaire (SurveyMonkey) was sent to all Dutch hospitals (n = 81), including questions regarding advanced MIS procedures, robotic procedures, and hysterectomies performed in 2017 (Supplementary material, Appendix S1). Hospitals can be either teaching or non-teaching hospitals, depending on whether they train residents. Laparoscopy is divided into four levels of difficulty according to an international classification,[22,26] of which level 3 and 4 procedures are considered advanced laparoscopic procedures (Supplementary material, Appendix S2). The number of procedures was collected by the local gynecologists, extracted from the local electronic database, theater lists or annual reports, together with the number of consultant gynecologists performing these procedures. If it was not possible to fill out the questionnaire themselves, the information was sent to the researcher. Additionally, the effect of performing opportunistic salpingectomies for ovarian cancer risk reduction on the choice of hysterectomy route was collected. Reminders were sent by email or telephone to increase response rates. Data were compared with previously acquired data by our research group from 2002,[27] 2007,[28] and 2012.[22] As the result of mergers, hospital numbers differed over the years. Previous data from merging hospitals were combined to create a proper comparison with 2017. All data were anonymized before analysis was started. Vaginal hysterectomies involving pelvic organ prolapse were excluded, to provide an adequate comparison with our previous data. Gynecologist and hospital volumes were calculated using the number of procedures and the number of consultant gynecologists performing these procedures. Hospital volume was stratified into three groups: low volume (0–19 procedures), medium volume (20–59 procedures), and high volume (≥60 procedures). Gynecologist volume was stratified into four groups: very low

volume (0–9 procedures), low volume (10–19 procedures), medium volume (20–59 procedures), and high volume (≥60 procedures).[22]

2.1 | Statistical analyses

IBM SPSS Version 25 was used for statistical analysis. Histograms, Q-Q plots and Shapiro–Wilk test were used to evaluate normality. Mean and standard deviation (SD) were used to assess normal distributed descriptive data, and median and interquartile range (IQR) for non-normal distributed data. Paired *t* tests were used for assessment of normal distributed paired data and Wilcoxon signed rank test was used for non-normal distributed paired data. McNemar test was used to assess paired dichotomous data and chi-squared test or Fisher's exact test was used for non-paired dichotomous data. Values of *p* less than 0.05 were considered statistically significant.

2.2 | Ethical approval

According to the Dutch Medical Research Involving Human Subjects Act this study did not require evaluation by an ethics committee. The Ethics Committee Leiden Delft The Hague provided an IRB Exemption on November 14, 2019.

3 | RESULTS

The requested data were provided by 85% ($n = 69$) of all hospitals. Of them, 58% were teaching hospitals and 42% were non-teaching hospitals, which corresponds to the national distribution (54% vs. 46%).

3.1 | Advanced laparoscopic and robotic procedures

The 69 responding hospitals in 2017 performed a total of 6131 advanced laparoscopic procedures (median 78, IQR 47.5–109 per hospital). As 77 hospitals (95% response rate) in 2012 performed 4979 procedures (median 63.5, IQR 33–91), 2017 showed a significant increase over 2012 ($p < 0.001$). This increase was also visible after comparing the 66 hospitals that responded in both years (4459 in 2012 vs. 5965 in 2017). Laparoscopic hysterectomies showed a significant increase in 2017 (Table 1). The median number of abdominal hysterectomies (AH) and VH significantly decreased compared with 2012. The total number of robotic surgeries showed an increase from 384 in 2012 (median 20.5 per hospital, IQR 9.5–61.5) to 660 in 2017 (median 33.5 per hospital, IQR 24–62.75). Both level 3 and level 4 laparoscopic removal of endometriosis increased since 2012 (Table 1), as did the hospitals that offered removal of level 3 endometriosis (56% to 76% in 2017, $p = 0.004$, Table 2).

Significantly more hospitals offered LH compared with 2012 (99% vs. 91%, $p = 0.001$, Table 2). This is largely explained by the significant increase in non-teaching hospitals offering this procedure (93% vs. 62%, $p = 0.002$). Furthermore, significantly more hospitals offered robotic surgery, mostly explained by the rise in hospitals offering robotic hysterectomy. All hospitals now offer level 3 surgery, whereas this was 91% in 2012 because of initially slower implementation in non-teaching hospitals. The amount of hospitals offering level 4 surgeries showed an increasing trend (39% to 46%), but this was not statistically significant. In 2017, level 4 and robotic procedures remained to be offered in more teaching than non-teaching hospitals (respectively, 63% vs. 22%, $p = 0.002$ for level 4 and 35% vs. 11% for robotic procedures, $p = 0.044$, Table 2).

3.2 | Hospital and gynecological surgeon volumes

Hospitals produced larger volumes for level 3 and level 4 surgery, as the percentage of low-volume hospitals slightly decreased (Figure 1). Nevertheless, level 4 surgery is still often performed in low-volume hospitals. The group of gynecologists performing fewer than 20 level 3 surgeries per year expanded (64% in 2017 vs. 40% in 2012, respectively, $p < 0.001$), with 15% of the gynecologists performing fewer than 10 level 3 surgeries. For level 4 surgery, the low-volume group decreased ($p = 0.01$), although 79% of the gynecologists performed fewer than 20 surgeries per year and 49% performed fewer than 10 surgeries. Robotic surgery is now performed in larger volumes by gynecologists (low-volume proportion from 78% in 2012 to 41% in 2017, $p = 0.007$) and in larger volumes by hospitals (low-volume from 42% to 19%, $p = 0.250$).

3.3 | Hysterectomy approach

Table 1 showed a significant decrease in median numbers of VH and AH per hospital in favor of LH. This is confirmed by the trend in surgical approaches for hysterectomy, as 22% of all hysterectomies were performed via the abdominal route in 2017, compared with 40% in 2012 ($p < 0.001$). The vaginal approach decreased from 25% in 2012 to 19% in 2017 ($p < 0.001$). Laparoscopic and robotic approaches showed an increase (+22%, $p < 0.001$ and +2%, $p = 0.052$, respectively). Figure 2 shows the surgical trends over the last 15 years. The approaches did not differ between teaching or non-teaching hospitals.

4 | DISCUSSION

The implementation of advanced laparoscopic and robotic surgical procedures in gynecology in the Netherlands has continued in the last 5 years, confirming previous observations.[22] With the increasing numbers of procedures, hospital volume also rose. However, for all procedures still a large proportion of gynecologists perform

TABLE 1 Number of laparoscopic and robotic procedures and hysterectomies in 2012 and 2017

	2012				2017				
Procedure	**Total**	**Mean (SD)**	**Median**	**IQR**	**Total**	**Mean (SD)**	**Median**	**IQR**	***p* value[a]**
Laparoscopy—level 3									
LH, all	3518	50.3 (33.8)	42	24–75	4400	64.7 (35.2)	54	40.7–83.8	<0.001
TLH	2471	41.1 (26.3)	38.5	20–57	3928	60.4 (33.6)	52	37–83.50	<0.001
LAVH	289	11.6 (13.7)	6	2–18.5	252	22.9 (25.9)	10	2–41	0.345
SLH	606	16.4 (20.5)	10	3.5–20.5	220	13.8 (23.8)	5	2–11.5	0.006
Myomectomy	128	4.0 (5.5)	2	1–4	115	5.8 (6.7)	3.5	1.25–7	0.314
Adhesiolysis	383	8.5 (8.4)	5	2.5–12	262	10.1 (11.1)	6.5	4–12	0.831
Endometriosis	425	10.1 (10.0)	6	3–4	697	18.8 (29.0)	11	7.5–18	0.222
Laparoscopy—level 4									
Sacrocolpopexy	226	11.9 (10.1)	10	4–17	221	11.1 (15.1)	8	4–11	0.201
Lymphadenectomy/ staging	135	11.3 (10.2)	7.5	2–22	108	15.4 (14.0)	11	3–33	0.686
Rectovaginal and extensive endometriosis	164	10.3 (10.0)	4.5	3–20	328	19.3 (18.9)	16	4.5–34	0.009
Robotic surgery									
Robotic hysterectomy total	163	23.3 (21.5)	17	2–47	339	24.2 (14.7)	24.5	9.75–30.75	0.465
Robotic hysterectomy	NA	NA	NA	NA	270	22.5 (15.2)	24.5	9.25–29.75	NA
Robotic radical hysterectomy	NA	NA	NA	NA	69	17.3 (9.1)	20.5	7.75–23.5	NA
Robotic endometriosis (level 3)	6	6 (0)	6	6–6	14	4.7 (3.1)	4	2-X	NA
Robotic extensive and rectovaginal endometriosis	0	0	0	0–0	2	2 (0)	2	2–11	NA
Robotic sacrocolpopexy	166	23.7 (27.7)	17	8–26	246	24.6 (23.9)	16.5	8.5–34.25	0.715
Robotic lymphadenectomy	7	2.3 (1.2)	3	1-X	59	19.7 (16.0)	21	3-X	NA
Hysterectomy—other									
AH	4120	53.5 (33.8)	45	27–75.50	1787	26.3 (20.6)	21	10.25–33.5	<0.001
VH	2620	34.9 (29.1)	30	15–45	1516	23.0 (17.7)	20.5	10.75–29	<0.001
Total									
Laparoscopy—level 3	4454	63.6 (43.9)	52.5	29.5–84	5474	79.3 (56.2)	72	45–97.5	0.007
Laparoscopy—level 4	525	17.5 (14.3)	15.5	4.75–26.25	657	21.9 (23.4)	10.5	4.75–36.25	0.082
Laparoscopy—level 3 and level 4	4979	71.1 (50.6)	63.5	33–91	6131	88.9 (67.6)	78	47.5–109	0.003
Robotic	384	32.0 (29.0)	20.5	9.5–61.5	660	41.3 (26.3)	33.5	24–62.75	0.128

Abbreviations: AH, abdominal hysterectomy; IQR, interquartile range; LAVH, laparoscopically assisted vaginal hysterectomy; LH, laparoscopic hysterectomy; NA, not applicable; SD, standard deviation; SLH, supracervical laparoscopic hysterectomy; TLH, total laparoscopic hysterectomy; VH, vaginal hysterectomy.

[a]Statistical test is performed for hospitals performing the procedure in both years.

low volumes (<20 advanced procedures/year), especially for level 3 laparoscopy. A continuing national increase in LH was observed at the expense of VH and AH, conforming to international trends.[1–4]

Advantageous effects of fewer complications, lower costs and lower perioperative morbidity are reported for high-volume hospitals.[14–16,29-31] Despite the increase in hospital volumes, the proportion of low-volume level 4 hospitals is still large. To improve hospital volume, criteria for centralization might be formulated and indicated for complex procedures,[32] such as level 4 laparoscopy. Internationally, centers of expertise for endometriosis surgery are recommended.[33–35]

Although the hospital volumes increased, gynecological surgeon volumes did not follow in the same direction or at the same pace. With the rise in level 3 laparoscopic procedures, there was an even greater increase in gynecologists performing them. The increase resulted in a considerable amount of gynecologists performing fewer than 20 procedures and even in a great proportion (15%) performing fewer than 10 procedures per year. Our data imply that awareness of gynecological surgeon volume is already slightly more

TABLE 2 Percentage of hospitals performing procedures in 2012 and 2017

Procedure	Total 2012, % (*n*)	2017, % (*n*)	Non-teaching hospitals 2012, % (*n*)	Non-teaching hospitals 2017, % (*n*)	Teaching hospitals 2012, % (*n*)	Teaching hospitals 2017, % (*n*)
Laparoscopy—level 3						
LH, all	91 (70)	99 (68)*	81 (30)	97 (28)*	100 (40)	100 (40)
TLH	80 (61)	97 (67)*	62 (23)	93 (27)*	97 (38)	100 (40)
LAVH	34 (26)	24 (13)	43 (16)	30 (7)	26 (10)	19 (6)
SLH	50 (38)	34 (19)*	41 (15)	38 (9)	59 (23)	31 (10)*
Myomectomy	42 (32)	33 (21)	35 (13)	26 (7)	48 (19)	38 (14)
Adhesiolysis	60 (46)	49 (31)	49 (18)	48 (13)	70 (28)	50 (18)
Endometriosis	56 (42)	76 (48)*	44 (16)	70 (19)*	67 (26)	81 (29)
Laparoscopy—level 4						
Sacrocolpopexy	25 (19)	30 (20)	5 (2)	15 (4)	43 (17)	41 (16)**
Lymphadenectomy/ staging	16 (12)	14 (9)	8 (3)	4 (1)	23 (9)	21 (8)
Rectovaginal and extensive endometriosis	21 (16)	26 (17)	5 (2)	11 (3)	35 (14)	37 (14)**
Robotic surgery						
Robotic hysterectomy total	9 (7)	22 (15)*	0 (0)	11 (3)	18 (7)	30 (12)*
Robotic hysterectomy	NA	18 (12)	NA	11 (3)	NA	23 (9)
Robotic radical hysterectomy	NA	8 (5)	NA	0 (0)	NA	13 (5)
Robotic level 3 endometriosis	1 (1)	5 (3)	0 (0)	4 (1)	3 (1)	5 (2)
Robotic extensive and rectovaginal endometriosis	0 (0)	2 (1)	0 (0)	0 (0)	0 (0)	3 (1)
Robotic sacrocolpopexy	9 (7)	15 (10)	3 (1)	7 (2)	15 (6)	21 (8)
Robotic lymphadenectomy	5 (4)	6 (4)	0 (0)	4 (1)	10 (4)	8 (3)
Hysterectomy—other						
AH	100 (77)	100 (67)	100 (37)	100 (28)	100 (40)	100 (39)
VH	97 (75)	99 (66)	95 (35)	100 (28)	100 (40)	97 (38)
Total						
Laparoscopy - level 3	92 (69)	100 (69)*	83 (30)	100 (29)*	100 (39)	100 (40)
Laparoscopy - level 4	39 (30)	46 (30)	11 (4)	22 (6)	65 (26)	63 (24)**
Robotic	16 (12)	25 (17)*	5 (2)	11 (3)	25 (10)	35 (14)**

Abbreviations: AH, abdominal hysterectomy; LAVH, laparoscopically assisted vaginal hysterectomy; LH, laparoscopic hysterectomy; NA, not applicable; SLH, supracervical laparoscopic hysterectomy; TLH, total laparoscopic hysterectomy; VH, vaginal hysterectomy.

Statistical tests are performed only for the hospitals providing data in both years.

*$p < 0.05$ between 2012 and 2017.; **$p < 0.05$ between teaching and non-teaching hospitals in 2017.

embedded for level 4 laparoscopy, as the number of performers decreased. However, 79% of them are low-volume performers. Whereas research indicates that surgeon volume might even be more important than hospital volume,[36,37] one should additionally focus on gynecological surgeon volume, as the positive effect of increased hospital volume might be nullified by a small gynecological surgeon volume.

A decrease in gynecological surgeon volume might be affected by several factors. In our cohort however, the total number of gynecologists remained stable[38] and no new residency programs or working hour restrictions were introduced in recent years. Therefore, the increase is mainly the effect of the disproportionate increase of gynecologists adding these new techniques to their surgical palette. This is reinforced by new gynecologists already being exposed to these techniques during their residency. Despite the reason for the decrease, one should focus on optimizing gynecological surgeon volumes.

Although an optimal volume load is still unknown,[39] research indicates the beneficial effects of more than 10–20 surgeries per gynecologist.[14,16,31,40] However, our study, together with other research, shows that those numbers are not easily attained worldwide.[23,24,31] To increase gynecological surgeon volumes for advanced procedures, especially avoiding very low volumes (<10), the total number of gynecologists performing these procedures should be decreased. Internationally, the problem of low-volume

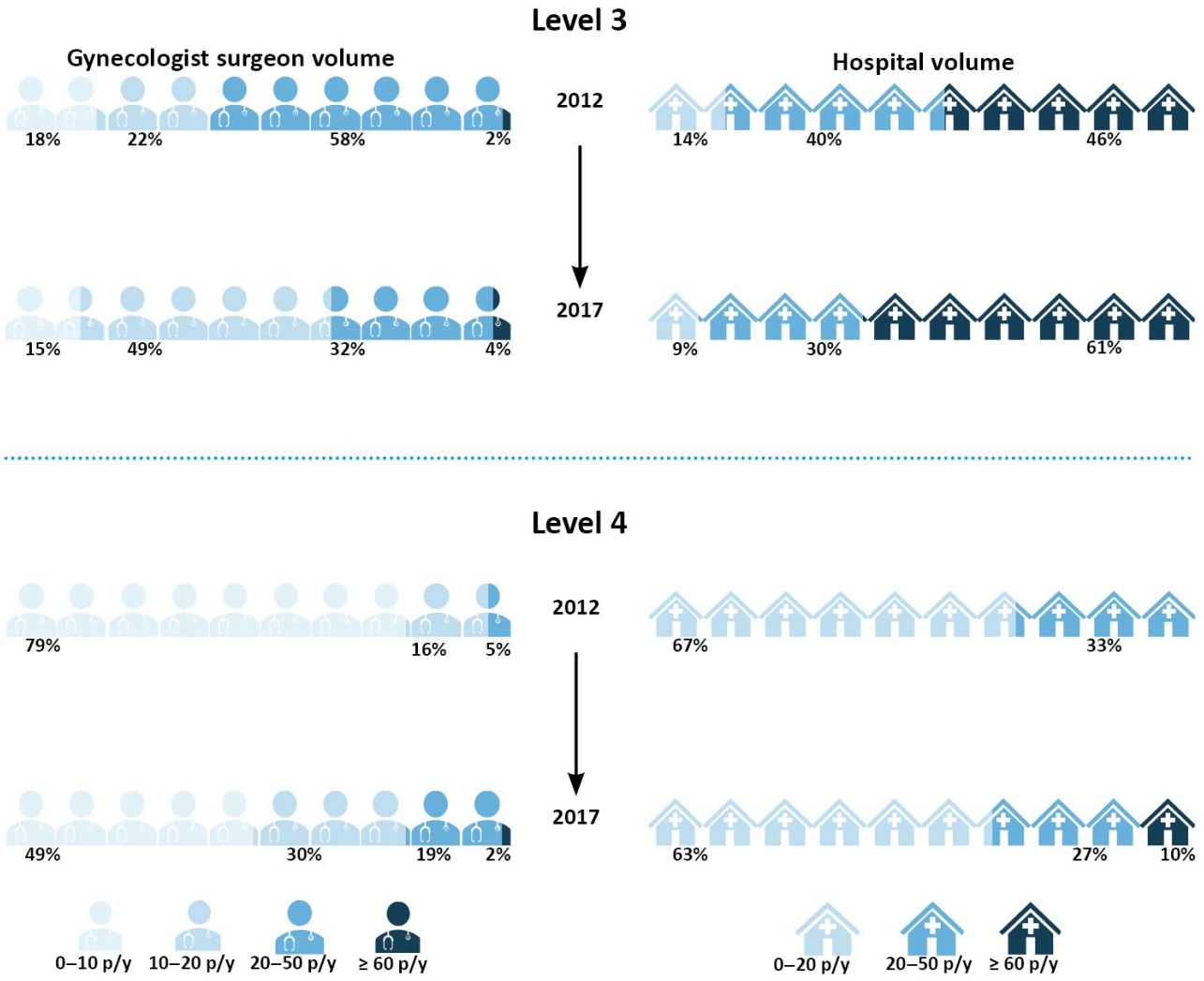
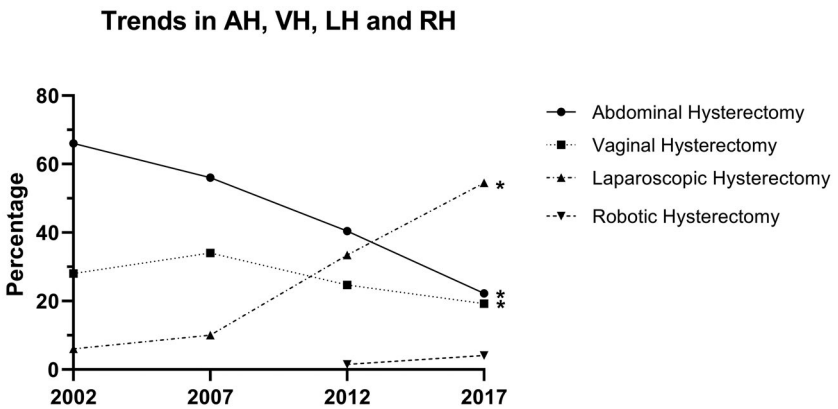


FIGURE 1 Hospital and gynecological surgeon volumes in 2012 and 2017. The number of procedures was stratified by volume into three groups for hospitals: low volume (0–19 procedures), medium volume (20–59 procedures) and high volume (≥60 procedures). The number of procedures was stratified by volume into four groups for gynecologists: very low volume (0–9 procedures), low volume (10–19 procedures), medium volume (20–59 procedures), and high volume (≥60 procedures)

FIGURE 2 Trends in abdominal hysterectomy, vaginal hysterectomy, laparoscopic hysterectomy and robotic hysterectomy. *$p < 0.05$ between 2012 and 2017



gynecologists is acknowledged, though an optimal way to decrease the performers is not yet addressed.[31,41]

To decrease the number of gynecologists performing advanced procedures, appointing specialized gynecologists might be an option.[24] However, it is advisable to appoint not only a single gynecologist per center to perform these procedures. First, because this ensures continuity of care, and second it results in the possibility of performing complex level 4 procedures with more surgeons at a

time. The profession should consider whether these procedures are registered for both surgeons. The specialization could start already during residency.[31] An alternative might be to change skills training programs, by facilitating basic laparoscopic (level 1 and 2) skills for everyone, but advanced skills for a few. Every gynecologist should therefore be able to perform basic laparoscopic procedures, but advanced procedures are only performed by specialized MIS-trained gynecologists. This is supported by fellowship-trained MIS specialists performing LH in less time on more difficult patients, with shorter length of stay, lower costs,[42] and with higher skills.[43] Specialization might also help surgeons to gain confidence for complex MIS procedures,[44] as residents often feel uncomfortable with MIS procedures on completion of residency training.[45,46] Different programs showed that fellowships or specialization tracks led to higher volumes.[47,48]

For robotic surgery, our study showed that both hospital and gynecological volumes increased, which shows a good first implementation of this new technique. Although, the volumes are still relatively low. One should be aware of possibly decreasing gynecological surgeon volumes if broader implementation of this technique results in more gynecologists performing this, as laparoscopy initially also showed rising volumes. Additionally, the discussion regarding implementation of robotic surgery is still ongoing, Though not yet researched sufficiently, robotic surgery could be beneficial for complex cases, such as obese patients, who would otherwise need a conventional abdominal approach. However, superiority over straight-stick laparoscopy is not proven regarding patient outcomes,[49] and robotic surgery is less cost-effective.[50]

The implementation of new surgical techniques also leads to changing volumes in hysterectomy approach. In particular, VH is decreasing, while still being the reference standard.[7,25] The decrease of VH volumes will inherently lead to less experience for gynecologists and less exposure during residency.[51] Additionally, despite a decrease in gynecologists performing VH, the mean number of VH performed per gynecologist still declined. One should be aware that with a further decrease in VH, desired case volumes are difficult to attain and VH will be liable to disappear from the surgical palette. Additionally, 50% of our cohort would change the vaginal route to laparoscopic route if opportunistic salpingectomy was preferred, which would lead to a further decrease in VH in the future. Besides the approaches mentioned in the questionnaire, new alternative approaches of advanced MIS procedures are being introduced (i.e. laparoendoscopic single-site surgery, Transvaginal natural orifice transluminal endoscopic surgery).[52,53] It is worrisome that implementing these new techniques dilutes the volumes and influences surgical outcomes even more than is now observed. Their impact on patient safety is therefore questionable.

The main strength of this study is the high and consecutive representation of all Dutch hospitals. There is a high response rate with all types of hospitals included, therefore the study is generalizable outside the Netherlands. A limitation of this study is the lack of patient outcomes. However, this study shows the effect of implementation of MIS techniques on case volumes and literature supports the benefits of high volumes for complex surgeries. To optimize the statements regarding surgeon volume and patient outcome, additional evidence regarding individual surgeon volume and patient outcomes is necessary. Attempts are being made to provide these individual outcomes.[54] Another potential limitation is the exclusion of VH with pelvic organ prolapse indication from analysis. This might underestimate the absolute numbers of VH in the Netherlands. However, as previous studies included the same indications, the observed trend regarding hysterectomies for indications other than prolapse is adequate.

5 | CONCLUSION

The broad implementation of advanced MIS procedures resulted in an increasing number of these procedures with increasing hospital volumes. However, hospital volumes for complex procedures are still low. As a side-effect of the broad implementation of advanced procedures, a disproportionate rise in number of gynecologists performing these procedures was observed. Therefore, gynecological surgeon volumes remain low and even decreased for some procedures. It is advised to consider measures to increase these volumes. Centralization of complex procedures and training of specialized MIS gynecologists could be taken into consideration to improve these volumes and therefore consequently enhance patient safety.

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AUTHOR CONTRIBUTIONS

FHMPT, FWJ, and ARHT contributed to protocol/project development, data collection, data analysis, and manuscript writing. JH contributed to data collection, data analysis, and manuscript writing. SRCD contributed to protocol/project development and to manuscript writing.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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