Received: 25 July 2022 | Accepted: 5 December 2022
DOI: 10.1111/jog.15524

ORIGINAL ARTICLE

Three-dimensional vs two-dimensional endoscopic approach in urogynecology: A retrospective cohort study of laparoscopic sacrocolpopexy

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Abstract

Aim: The gold standard to treat an apical pelvic organ prolapse is the abdominal route via a sacrocolpopexy, which is also reproduced by laparoscopic route. A laparoscopic sacrocolpopexy however, requires surgical expertise. Three-dimensional (3D) laparoscopy has been developed to overcome the lack of depth perception, that is a known disadvantage of conventional two-dimensional (2D) laparoscopy. This procedure can accelerate the learning curve and optimize the intra-, peri-, and postoperative outcomes. This study aims to compare 3D laparoscopy to traditional 2D laparoscopy for sacrocolpopexy.
Methods: Data from 132 patients who underwent a sacrocolpopexy with 2D or 3D laparoscopy in Department of Obstetrics and Gynecology, University Medical Center of the Johannes Gutenberg University, between June 2012 and September 2021, were collected retrospectively. Seventy-one laparoscopic sacrocolpopexy operations in 2D ($n = 23$) and 3D ($n = 48$) group were reviewed and compared regarding the duration of surgery, blood loss and the length of hospital admission as primary objectives.
Results: There were no differences in the baseline demographics between the two groups. The estimated blood loss (1.0 (±0.6) g/dL vs 1.7 (±1.0) g/dL, $p = 0.010$), and duration of surgery (115.4 (±34.7) min. vs 134.7 (±26.2) min., $p = 0.012$) was significantly better in favor of 3D laparoscopy. The length of hospital stay was comparable in both groups ($p = 0.833$). Furthermore, no differences were observed between the groups regarding other surgical outcomes.
Conclusion: 3D laparoscopy shows a significant benefit in terms of estimated blood loss and surgery duration among complex urogynecological surgeries compared to traditional 2D laparoscopy.

KEYWORDS
2-dimensional laparoscopy, 3-dimensional laparoscopy, laparoscopic sacrocolpopexy, laparoscopy, urogynecology

INTRODUCTION

Pelvic organ prolapse (POP) is one of the most common and bothersome clinical conditions, with a prevalence of up to %50 when based on symptoms and vaginal examination.[1] The apical prolapse, defined as Level 1 by DeLancey is often the main or the additional plain of pathology with a prevalence of 0.2%–43%.[1] By the age of 80, women have an estimated life time risk of 11.1% for undergoing a surgery for POP and nearly 30% risk for a repeat surgery.[2] Vaginal or abdominal routes are available to treat an apical prolapse. The gold standard abdominal route in means of abdominal sacrocolpopexy was first described in the 50 s and is the favored access route for this purpose, with higher success rates, lower recurrence rates and a better sexual function thereafter than vaginal route.[2,3] Despite relatively high success rates, morbidity is also high at 17%. A longer time to return to daily activities, longer operating time and higher costs are expected with the abdominal route.[1,4]

With the knowledge that laparoscopy avoids the need for large abdominal incisions, and leads to less postoperative pain, shorter recovery time and hospital stay,[5] Nezhat et al. reported the first laparoscopic sacrocolpopexy in 1994 which reproduced the abdominal procedure.[6] Meanwhile abdominal and laparoscopic procedures for POP have demonstrated similar success rates.[1,4]

The adoption of laparoscopy was especially limited for complex surgeries, mainly due to the surgical skills to perform suturing and knot tying and the ability to accurately determine the correct planes for safe dissection. Traditional laparoscopy with a 2-dimensional (2D) view has in fact a lacking depth perception, leading to spatial disorientation, as well as higher mental load and visual fatigue considering a monocular vision on a flat screen.[7]

With advances in technology, the industry developed various technologies that make surgery easier for surgeon. The United States Food and Drug Administration approved robot-assisted surgery for gynecological procedures in 2005. Robotic surgery has emerged as an alternative surgical route with a short learning curve, 3-dimensional (3D) view, camera stability, and tremor reduction, but at much higher costs.[5,8] Because of its lower cost than robotic surgery, the 3D vision system is increasingly used for conventional laparoscopic approaches.[9]

3D laparoscopy offers the surgeon a stereopsis in meanings of depth perception through a binocular view. This enables regardless of surgeon experience a better working speed, optical visualization, and better handling, leading to time saving and reducing mistakes by skills training in vitro.[10] In addition, in a clinical setting would 3D-vision lead to significantly shorter operating time, less blood loss, and shorter hospital stay, probably because of this to improved short- and long-term outcomes.[8,11]

Despite controversial data, the disadvantages of the 3D-laparoscopy include cognitive workload and adverse effects, such as headache, blurred vision, vertigo, and dizziness. Having a cognitive knowledge of intricate surgical tasks and the update in technology in the meanings of novel 3D-vision systems prevents adverse effects and leads to a better cognitive workload in favor of a 3D-vision.[12,13]

Laparoscopic sacrocolpopexy is hindered by the need for mastery of laparoscopic surgical techniques and perfect knowledge of pelvic organs and pelvic floor anatomy. The use of a 3D-vision system can facilitate the whole surgery and lead to better outcomes. In this study, we retrospectively compared the surgical outcomes of sacrocolpopexy with 3D- vs 2D-vision laparoscopic surgical systems and discussed the usefulness of 3D surgical systems.

METHODS

We conducted a retrospective review of all surgeries performed between 2012 and 2021 in the Department of Gynecology and Obstetrics, University Medical Center of the Johannes Gutenberg University, in Mainz. The first laparoscopic sacrocolpopexy performed in our department was in June 2012. First, we reviewed the data of 132 patients with POP who underwent laparoscopic sacrocolpopexy until September 2021. We defined the first 18 procedures for laparoscopic sacrocolpopexy and the first five procedures performed with a 3D-vision system as a learning curve referred to the literature.[2,9,14]

All laparoscopic sacrocolpopexies were performed by five expert surgeons who were also specialized in the field of urogynecology. After excluding the cases performed during the learning curves, we enrolled and analyzed finally 71 cases (48 in 3D group; 23 in 2D group) performed by just two expert surgeons who have performed over 200 laparoscopic surgeries. Figure 1 presents the cohort diagram of the study.

The primary outcome was the duration of the surgery in order to evaluate the efficacy of 3D-vision in the operating room. A secondary outcome was the estimated blood loss and the duration of hospitalization.

Demographic and clinical characteristics of the patients [age, parity, menopausal status, preoperative status of prolapse, history of prior surgery in meanings of hysterectomy, urogynecological surgeries, and other abdominal surgeries, body mass index (BMI), ASA (American Society of Anesthesiologists) classification], operation times, estimated blood loss, duration of hospitalization, intraoperative and postoperative complications were evaluated in both groups. We defined the pelvic organ prolapse stage above grade 3 regarding POP-Q system[15] as high grade prolapse.

Estimated blood loss was calculated as the difference between the preoperative and postoperative hemoglobin values, which were collected 1 day after surgery. The duration of surgery was calculated as the time interval between the first incision on the umbilicus and the last skin suture. The duration of hospital stay was calculated as the number of days between the day of the operation and the day of discharge from the hospital. We assessed only the major intraoperative complications by means of major hemorrhage requiring transfusion, bowel, ureter, or urinary bladder injury. Postoperative complications occurring within 30 days of surgery were concluded in the analysis and defined as "major" based on the Clavien-Dindo classification if they occurred above grade 3.[16]

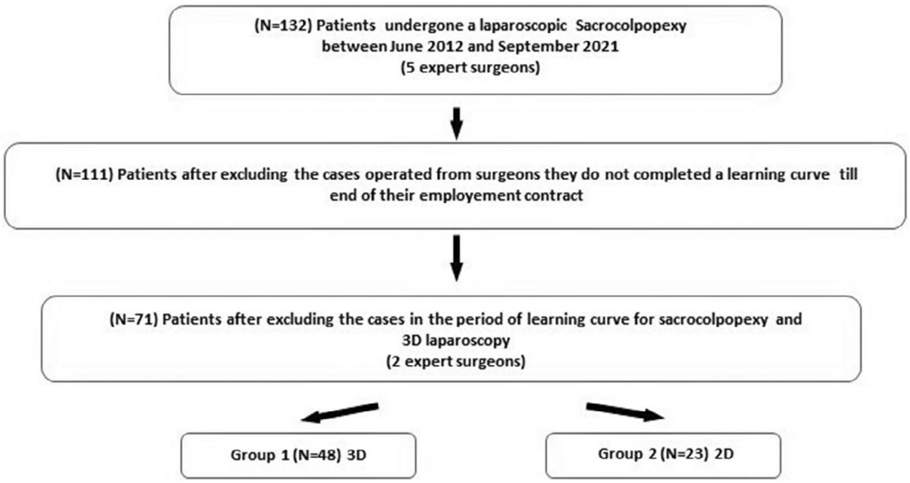

FIGURE 1 Flow diagram showing the recruitment of study population

Einstein 3D full HD Vision TM (Aesculap, Tuttlingen, Germany) was used for 3D laparoscopy in this study. The 3D-vision was installed in an operating room in September 2016 and from June 2021 in both operating rooms at our hospital. Between September 2016 and June 2021, both vision modalities were utilized in our operating rooms. Patients were randomly assigned to operating rooms by our operation management department, regardless of the surgeon's preferences or the type of vision system installed.

The surgical procedures were performed under general anesthesia. The patient was placed in a lithotomy position. For 2D- and 3D-laparoscopy, a 10-mm trocar was inserted as the camera port through a vertical incision in the umbilicus. A 5-mm trocar was placed in the right inguinal region, and another 10-mm trocar in the left inguinal region. A last 5-mm trocar was inserted as desired by the surgeon, either suprapubic or between the two trocars on the left side.

A simple intrauterine vaginal manipulator was used to manipulate the uterus or vaginal cuff so that the vesical-vagina fold and rectal-vagina fold could be easily exposed.

If hysterectomy was included, supracervical hysterectomy was performed as usual, with or without adnexectomy. Separately, the peritoneum was opened over the sacral promontory and caudally extended towards the Douglas pouch. The rectovaginal septum was dissected and pushed posteriorly, exposing the pararectal space. Similarly, the vesicovaginal space was dissected anteriorly towards the bladder neck.

The anterior and posterior polypropylene meshes were sutured to the anterior and posterior vaginal walls by using absorbable sutures. In case of uterine conservation, the anterior mesh was inserted through the right broad ligament before reaching the promontory. In case of subtotal hysterectomy, meshes were fixed on the cervix with sutures. The tail of the mesh was attached to the sacral promontory using a Protack™ 5-mm helical fastener (Covidien™ USA). The mesh was completely covered by peritoneum. A non-absorbable polypropylene mesh was used. There was no need for concomitant vaginal surgery in any of the cases.

It is a routine practice in our unit to invite these women for outpatient follow-up 8 weeks later, where a gynecologic examination is performed for objective/anatomical outcomes. Statistical data were analyzed using SPSS Statistics 25. Descriptive statistical methods (numbers, percentages, means, and standard deviations) were used to evaluate the study data. To define the differences between the two groups and to compare categorical variables, the Wilcoxon rank sum test, Fisher's exact test, and Pearson's chi-squared test were used. Results were evaluated with a 95% confidence interval with two-tailed p values of <0.05 considered statistically significant.

Due to the retrospective nature of the study, no ethics approval was required.

RESULTS

A total of 71 patients were evaluated in this study after excluding patients as part of the learning curve. 48 (67.6%) participants underwent 3D laparoscopy and 23 (32.4%) were treated with the traditional 2D laparoscopic approach. The two groups were comparable in terms of demographic and clinical characteristics (Table 1). The median age was 60 years (range, 54–67 years) in the 3D group and 61 years (range, 56–70 years) in the 2D group ($p = 0.6$). There were no statistically significant differences between the groups in terms of parity ($p = 0.655$), menopause status ($p = 1.000$), ASA classification ($p = 0.535$), body mass index (BMI) ($p = 0.370$), prior caesarean section ($p = 0.243$), and abdominal surgery ($p = 0.173$). The groups were comparable in terms of the types of surgical procedures performed ($p = 0.634$) (Table 2). The majority of the women underwent a sacrocolpopexy and a laparoscopic supracervical hysterectomy (LASH) with sacrocolpopexy in both groups (90% in 3D group and 82% in 2D group).

TABLE 1 Demographic and clinical characteristics

		Group 1 (3-dimensional laparoscopy)	Group 2 (2-dimensional laparoscopy)	*p*-value
Age (years)[a]	$n = 71$	61.5 (±9.6) (44.2–81.3)	62.3 (±10.6) (40.6–82.4)	0.649[b]
Parity[a]	$n = 68$ number of missing's	2.1 (±1.3) (0.0–8.0) $n = 2$	2.3 (±1.3) (1.0–6.0) $n = 1$	0.655[b]
BMI (kg/m^2)[a]	$n = 71$	25.9 (±3.3) (19.0–33.1)	27.3 (±5.2) (19.9–40.4)	0.370[b]
Menopausal status[c]	$n = 71$			1.000[d]
Premenopausal		7(15)	3(13)	
Postmenopausal		41(85)	20(87)	
Prior c-section[c]	$n = 68$ number of missing's	1 (2.2) $n = 2$	2 (9.1) $n = 1$	0.243[d]
Prior abdominal surgery[a]	$n = 69$ number of missing's	0.8 (±1.0) (0.0–3.0) $n = 2$	0.4 (±0.6) (0.0–2.0) $n = 0$	0.173[b]
Prior hysterectomy[c]	$n = 71$	23(48)	13(57)	0.497[e]
Abdominal		5(22)	2(15)	0.671[d,*]
Vaginal		14(61)	10(77)	
Laparoscopic		4(17)	1(7.7)	
Prior surgery for POP[c]	$n = 71$	21(44)	12(52)	0.505[e]
Prior surgery for UI[c]	$n = 71$	1(2.1)	0(0)	1.000[d]
ASA classification[c]	$n = 71$			0.535[d]
1		2(4.2)	1(4.3)	
2		40(83)	17(74)	
3		6(12)	5(22)	
Preoperative high grade prolapse (POP-Q ≥ 3)[c]	$n = 71$	16(33)	6(26)	0.537[e]

Abbreviations: BMI, body mass index; POP, pelvic organ prolapse; UI, urinary incontinence; POP-Q, pelvic organ prolapse quantification.
*Type of hysterectomy between groups did not differ statistically.
[a]Mean, standard deviation (SD) and range.
[b]Wilcoxon rank sum test.
[c]Number and percent.
[d]Fisher's exact test.
[e]Pearson's chi-squared test.

Regarding clinical characteristics in terms of a prior hysterectomy as well as the type of a prior hysterectomy [$n = 23$ (48%) ($n = 5/14/4$ respectively for abdominal/vaginal/laparoscopic route) in 3D group, $n = 13$ (57%) ($n = 2/10/1$, respectively, for abdominal/vaginal/laparoscopic route) in 2D group; $p = 0.497$ and 0.671], prior surgery for pelvic organ prolapse ($p = 0.505$), and prior surgery for urinary incontinence ($p = 1.000$), there were no statistically differences.

The level of the pelvic organ prolapse above grade 3 based on the pelvic organ quantification (POP-Q) system as clinical characteristic of the two groups was comparable and had no statistically difference [$n = 16$ (33%) in 3D group, $n = 6$ (26%) in 2D group; $p = 0.537$]. Furthermore, the level of prolapse of any compartment was comparable between the groups ($p > 0.050$).

No major postoperative complications occurred in either group. Two patients (4%) in the 3D group experienced an intraoperative complication: one patient had a bladder injury, and one patient had a bowel injury. In the 2D group one patient had bowel injury. All these complications were immediately identified and treated in the same procedure, without any further consequences. Conversion to laparotomy was performed for one patient in each of the two-study groups [1, (2.1%) in 3D group; 1 (4.3%) in 2D group] due to self-complication of surgery. There was no statistically significant difference between the two groups in terms of intraoperative complications or organ injuries ($p = 0.725$) (Table 2).

After excluding the cases with conversion to laparotomy, a significantly longer mean duration of surgery for all procedures was recorded for the 2D group [134.7 (±26.2) min] compared to the 3D group [115.4 (±34.7) min, $p = 0.012$] as primary outcome of this study. Blood loss, according to the difference between the preoperative and postoperative hemoglobin values, was significantly higher in the 2D group compared with the 3D group [1.7 (±1.0) and 1.0 (±0.6), $p = 0.010$].

TABLE 2 Peri-operative characteristics and outcomes

		Group 1 (3-dimensional laparoscopy)	Group 2 (2-dimensional laparoscopy)	*p*-value
Readmission[a]	$n = 71$	1(2.1)	–	–
Major postoperative complications	$n = 71$	–	–	
Intraoperative complications[a]	$n = 71$			0.725[b]
Major hemorrhage		–	–	
Bowel injury		1(2.1)	1(4.3)	
Bladder injury		1(2.1)	–	
Ureter injury		–	–	
Conversion to laparotomy		1(2.1)	1(4.3)	
Type of surgery performed[a]	$n = 71$			0.634[b]
Sacrocolpopexy		20(42.1)	10(43)	
LASH with sacrocolpopexy		23(48)	9(39)	
Sacrohysteropexy		2(4.2)	0(0)	
Abd.sacrocolpopexy		1(2.1)	1(4.3)	
Sacrocolpopexy with rectopexy		2(4.2)	2(8.7)	
LASH, sacrocolpopexy with rectopexy		0(0)	1(4.3)	
First follow-up (days)[d] number of missing's	$n = 59$	65.3 (±12.8) (44.0–97.0) $n = 9$	87.8 (±58.0) (13.0–216.0) $n = 3$	0.486[c]

Abbreviations: LASH, laparoscopic supracervical hysterectomy; abd., abdominal; UI, urinary incontinence.
[a]Number and percent.
[b]Fisher's exact test.
[c]Wilcoxon rank sum test.
[d]Mean, standard deviation (SD) and range.

TABLE 3 Main operative outcomes

		Group 1 (3-dimensional laparoscopy)	Group 2 (2-dimensional laparoscopy)	*p*-value
Duration of surgery (min)[a]	$n = 69$	115.4 (±34.7) (61.0–195.0)	134.7 (±26.2) (95.0–194.0)	0.012[b]
Length of hospital stay (days)[a]	$n = 71$	4.4 (±1.3) (2.0–8.0)	4.3 (±1.3) (2.0–8.0)	0.833[a]
Blood loss (g/l)[a]	$n = 63$	1.0 (±0.6) (0.0–2.7)	1.7 (±1.0) (0.0–3.5)	0.010[b]

[a]Mean, standard deviation (SD) and range.
[b]Wilcoxon rank sum test.

No significant difference was observed in the length of hospital stay between the 3D and 2D group (4.4 ± 1.3 vs 4.3 ± 1.3 days; $p = 0.833$) (Table 3).

The mean time for the first follow-up was 65 days (range, 44–97) in the 3D group and 88 days (range, 13–216) in the 2D group, without any significant difference ($p = 0.486$). One patient in the 2D group had a recurrence for prolapse grade 4 due to mesh detachment and underwent a reattachment. One patient in the 3D group was readmitted due to ileus and required an adhesiolysis.

DISCUSSION

It is rare that a laparotomy is performed for a gynecologic surgery, except in gynecologic oncology. Although minimally invasive surgery is advantageous, it may be challenging for both expert and novice surgeons because of the lack of depth perception and spatial disorientation. The mental load resulting from this, and visual fatigue are further challenges.[7]

Since the first report by Becker et al. in 1993[17] showed that the new 3D vision system facilitates complex surgical maneuvers such as mobilization of organs, preparation in the deep space, and suture techniques in the human body, various studies have been published showing advantages regarding the mean time to complete the tasks, rate of errors while completing the tasks, advanced surgical skills in meanings of suturing, towards 2D imaging systems by laparoscopically naïve subjects and laparoscopic novice surgeons in simulated settings.[18] Independent of the experience level of the surgeon, 3D laparoscopy leads in simulated settings also to time acceleration, increased accuracy, and a lower rate of errors.[10]

The reported increased cognitive workload and adverse effects such as headache, blurred vision, vertigo and dizziness with the 3D-vision system were addressed to lacking surgical knowledge of the participants in the studies.[12]

Differently Usta et al. reported also in different experienced participants in meanings of novice and up to resident surgeon's comparable results regarding adverse effects like eye fatigue, headache, facial discomfort in simulated settings. The authors concluded that these adverse results reported mainly in older studies might be due to the use of unfavorable old vision systems for 3D-laparoscopy different from novel 3D-HD systems.[13] We performed all the surgeries in this study, which performed with 3D-vision using a novel 3D view system. In a meta-analysis by Liang et al., in which the study population was relatively heterogeneous with a mix of laparoscopic and thoracoscopic surgeries, 3D laparoscopy showed no adverse effects in terms of dizziness, headache, eyestrain, and physical discomfort above surgeons. The authors also addressed the unfavorable old vision systems as a reason for the above-mentioned adverse effects on surgeons.[19] We did not report any results in our study concerning adverse effects, but we excluded the first five surgeries performed by expert surgeons with a 3D laparoscopy as the learning curve,[9] which might have impaired our results in this regard.

We showed that the mean operative time and blood loss were significantly better in the 3D group. Our results are consistent with those of previous studies.[7,8,20,21] In the field of gynecology, Yazawa et al. recently reported the results of a retrospective study comparing the surgical outcomes of total laparoscopic hysterectomy with 2D vs 3D laparoscopy. The 3D group tended to have less blood loss than the 2D group, although the difference between the two groups was not statistically significant ($p = 0.642$). The mean operative time in the 3D group was significantly shorter ($p < 0.05$).[20] Fanfani et al. reported the results of a randomized clinical trial comparing the surgical outcomes of 2D vs 3D laparoscopic hysterectomy and pelvic lymphadenectomy in patients with endometrial and cervical cancer. The authors reported no significant differences in the mean operative time and median blood loss for the entire procedure. However, significantly lower blood loss was observed in the 3D-group during lymphadenectomy. Additional subgroup analyses showed a significant reduction in operative time for hysterectomy performed by an expert surgeon compared to those performed by a novice surgeon ($p = 0.018$) and a significant reduction in operation time for lymphadenectomy performed by novice surgeons.[7] These results address the benefit of the 3D-vision for complex surgeries performed by novices as well as expert surgeons. In a retrospective study comparing 3D laparoscopy with 2D laparoscopy in total laparoscopic hysterectomy, Usta et al. reported a significantly shorter operative time in favor of 3D-laparoscopy. The mean blood loss was lower but not significantly different in the 3D group (1.4 ± 0.9 g/dL vs 1.7 ± 1.0 g/dL).[21] Ding et al. reported in their study whereby all patients underwent a radical hysterectomy performed by the same surgeon with the shortest operating time and lowest amount of blood loss in the 3D laparoscopy group compared with robotic and 2D laparoscopy.[8] Sinha et al. also reported in their retrospective study comparing the surgical outcomes of 2D vs 3D laparoscopic hysterectomy for large uteri (≥500 g) significant advantages regarding operative time and blood loss in favor of 3D laparoscopy.[22] All the authors concluded that the 3D laparoscopic system is useful for performing more precise and safer surgeries.

Controversially, Lara-Domínguez et al. reported different results regarding the surgery time and blood loss. However, the study group was quite heterogeneous, including non-complex gynecologic surgeries, such as cystectomy and salpingo-oophorectomy.[23] Lui et al. reported similar results without the benefits of 3D-laparoscopy for ovarian cystectomy.[24] Song et al. reported in their randomized controlled trial no significant difference between 2D and 3D laparoscopic myomectomy regarding blood loss and operative time.[25] All the studies above concluded either simple or moderately complex surgeries. In our opinion, this might be the reason for the comparable surgical outcomes between 2D and 3D laparoscopy.

The length of hospital stay in the present study was comparable in two groups. The length of hospital stay in our department is greatly influenced by clinic protocol respectively standards and healthcare.

In terms of sacrocolpopexy, robotic surgery with a high-definition three-dimensional (3D) visual field as a unique advantage was associated with significantly lower blood loss and lower conversion rate compared to traditional laparoscopic sacrocolpopexy.[26] The 3D-laparoscopy is a good alternative for robotic surgery with equal optical conditions but less setup time and costs.[9] The novel 3D-vision system shows also significant advantages in upper and lower abdominal surgery in the context of surgery time, blood loss, and error rates, especially in complex surgeries.[27,28]

Our study had several strengths and limitations. We excluded the first patients who underwent surgery in the period of the learning curve for 3D laparoscopy and sacrocolpopexy. However, many operations with 3D laparoscopy were performed more likely after 2D laparoscopy regarding installation of the novel 3D vision system first in September 2016 and then in June 2021 in our operating rooms, which possibly influenced the climbing effect of the learning curve[29] on our results. Estimated blood loss was calculated according to the difference between the preoperative and postoperative hemoglobin values, which were collected 1 day after surgery. An intraoperative quantitative blood loss count might have led to a better comparison between the groups. This study reported the results of well-experienced surgeons with extensive experience in the field of urogynecology and laparoscopy, which may also have contributed to the results favoring 3D laparoscopy. Therefore, our findings may not be applicable to surgeons with less experience.

In contrast, our results and the advantage of 3D laparoscopy could be generalized for a population with relative usual characteristics, such as postmenopausal non-obese women with pelvic organ prolapse treated by urogynecologists with extensive experience.

Fergo et al. showed that approximately one in 10 doctors is stereo-blind, which leads to missing benefits from the implementation of 3D laparoscopy. In this context, we did not examine the surgeons.[30]

In conclusion, our study is the first to compare the two laparoscopic vision types -2D or 3D, in the field of urogynecology. We showed significant advantages of 3D laparoscopy in terms of estimated blood loss and surgery duration among complex surgeries, which probably contributed to a better sense of space and depth. Therefore, we believe that 3D laparoscopic surgery should be considered a preferable option, especially for surgeries involving complex anatomical steps or difficult procedures. According to literature on this subject 3D laparoscopy might also improve the learning curve among novice surgeons and lead to better surgical outcomes for pelvic organ prolapse.

AUTHOR CONTRIBUTIONS

Yaman Degirmenci: project development, data collection, manuscript writing and editing. Markus Schepers: Data analysis; Joscha Steetskamp: project development; Annette Hasenburg: Supervision; Christine Skala: Supervision. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors have no relevant financial or non-financial interests to disclose. Informed consent is not applicable to the current study.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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How to cite this article: Degirmenci Y, Schepers M, Steetskamp J, Hasenburg A, Skala C. Three-dimensional vs two-dimensional endoscopic approach in urogynecology: A retrospective cohort study of laparoscopic sacrocolpopexy. J Obstet Gynaecol Res. 2023;49(3):1028–35. https://doi.org/10.1111/jog.15524