Advances in Minimally Invasive Gynaecological Surgery

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Laparoendoscopic single-site surgery, robotic-assisted laparoscopic surgery, and natural orifice transluminal endoscopic surgery are major innovations in minimally invasive surgery. These techniques have the potential to improve patient outcomes such as quicker recovery, less postoperative pain, and better cosmetic results. Moreover, complicated laparoscopic procedures can be facilitated with the robotic surgical system. Current available data suggest that these techniques are feasible, safe, and effective, with similar perioperative outcomes to conventional laparoscopic techniques. Nonetheless, robotic-assisted surgery is more costly and may preclude its use in financially constrained areas. There is no good-quality evidence to support the use of these new techniques over conventional laparoscopy, and the purported benefits of better patient outcome are yet to be confirmed. Further prospective trials and randomised controlled trials with long-term data are required to determine their effectiveness and safety.

Hong Kong J Gynaecol Obstet Midwifery 2018; 18(1):43-51

Keywords: Minimally invasive surgical procedures; Natural orifice endoscopic surgery; Robotic surgical procedures

Introduction

Since Professor Kurt Semm, a German gynaecologist and a pioneer in operative laparoscopy, performed the first laparoscopic appendectomy in 1981[1], laparoscopic surgery has developed rapidly. Laparoscopic surgery is minimally invasive and superior to laparotomy in terms of less intraoperative blood loss, less postoperative pain, less postoperative fever, fewer wound complications, shorter hospital stay, and a faster return to normal activities[2-5]. Minimally invasive surgery is now considered to be the standard of care for the treatment of many benign and malignant gynaecological conditions.

The early-phase development of minimally invasive surgery was hampered by a lack of advanced instruments and good-quality imaging system to facilitate complex surgical procedures. With advances in technologies (three-dimensional image system, ergonomic instruments, instruments to cater special operative needs, and advanced energy sources to allow quick and secure haemostasis), many complex procedures can now be accomplished. This study reviews the major advances in minimally invasive surgery, namely laparoendoscopic single-site surgery (LESS), robotic-assisted laparoscopic surgery, and natural orifice transluminal endoscopic surgery (NOTES).

Laparoendoscopic Single-site Surgery

Conventional laparoscopic surgery typically requires one camera port at the umbilicus and two to three assistant ports at the lower abdomen. LESS was originated in a consortium at The Cleveland Clinic in 2010[6]. It is also known as single-port access surgery, single-incision laparoscopic surgery, and embryonic NOTES. The concept of single-incision laparoscopic surgery can be dated back to the 1960s. The first report of single-incision laparoscopic female sterilisation (by cauterisation and excision of a 5-mm segment of the fallopian tubes) was published in 1969[7]. In the 1970s, single-incision laparoscopy was limited to simple sterilisation procedures only. By reducing the number of incisions to one, LESS can potentially reduce postoperative pain and enable better cosmetic results, shorter hospital stay, faster recovery, and fewer port-related complications (e.g. hernia, vascular injury, nerve injury)[8].

In LESS, there are two common approaches to access the abdominal cavity and maintain the pneumoperitoneum during the procedure. The first approach is to make an initial single umbilical incision of 2-3 cm and then move off the underlying fascia of the umbilical skin and soft tissue flap. Multiple small incisions are then made in the fascia to insert two or three 5- to 10-mm trocars[9]. The second approach is to make a single 2- to 3-cm incision at the umbilicus from the skin down to the fascia to enter the abdominal cavity directly. Specialised access ports

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with different channels on top are then introduced for insertion of laparoscopic instruments. These access ports are commercially available but costly. A Korean group described a more economic approach by using a glove-port system, in which an Alexis wound retractor (Applied Medical, Rancho Santa Margarita [CA], USA) is inserted transumbilically with the outer rim covered with a surgical glove[10]. Holes are cut in the glove fingers through which trocars of different sizes can be placed and secured to the glove fingers with sutures, allowing insertion of a camera and other laparoscopic instruments[10].

There are several technical challenges to LESS. Instrument crowding can be a problem; in such a confined space, instruments are close together and range of movement is limited. Instrument collision inside the abdominal cavity or hand collision outside the ports is common. In addition, triangulation is not feasible. Triangulation enables approaching the surgical targets with two instruments in two directions to facilitate traction-countertraction and dissection. To overcome these technical challenges, a larger outer cap is used to increase the instrument distance outside the abdomen, and curved or articulating instruments are developed to restore the loss of triangulation. Nonetheless, LESS remains technically demanding and requires a long learning curve[11].

A number of gynaecological procedures can use the LESS approach, including adnexal surgery, hysterectomy, myomectomy, sacrocolpopexy, and lymphadenectomy, but the most common ones are LESS hysterectomy and adnexal surgery. In a meta-analysis of six randomised controlled trials that involved 624 women who underwent single-port versus multiport laparoscopic hysterectomy for benign indications, the single-port approach resulted in a longer operative time by 13 minutes, and there was no significant difference in intra- or post-operative complication rates, pain score, estimated blood loss, or length of hospital stay between the two groups[12]. The conversion rate was higher (but not significantly) in the single-port group (3.6% vs. 1.2%). The reason for conversion was dense adhesions or inadequate visualisation. Most conversions in the single-port group required only placement of an additional laparoscopic port. For cosmetic outcome, the results were inconsistent: two studies reported better cosmetic satisfaction for the single-port approach[13,14], but others failed to confirm this[15].

In another meta-analysis of six randomised controlled trials comparing single-port laparoscopy with conventional laparoscopy for benign adnexal diseases, single-port surgery was associated with a longer operative time, but there was no significant difference in postoperative pain, blood loss, mean length of hospital stay, or cosmetic results[16]. No case required conversion to laparotomy.

There were two randomised controlled trials comparing single-port with conventional laparoscopic myomectomy[17,18]. One study randomised 100 patients to either the single-port or the conventional laparoscopy groups and reported that the two groups were comparable in terms of the mean suturing time to close the uterine defect and surgical outcomes including operative time, blood loss, haemoglobin change, postoperative pain scores, operative complications, and length of hospital stay[17]. The other study randomised 66 patients to either single-port or conventional laparoscopic myomectomy and reported that the single-port group achieved a more favourable cosmetic outcome and better patient satisfaction; other surgical outcomes such as operation time, estimated blood loss, and complications were similar in both groups[18].

Studies of LESS in the treatment of gynaecological malignancies are limited. No randomised controlled trial could be identified. In one case series of 13 patients, LESS was feasible in the treatment of gynaecological cancer in selected patients[19].

In a retrospective case series of 110 patients who underwent single-port laparoscopic full staging (including pelvic and para-aortic lymphadenectomy) for endometrial cancer, the single-port approach was considered safe and feasible and comparable with other minimally invasive modalities in terms of operative time, complication rates, and length of hospital stay[20]. The conversion rate was 6.3% (7/110), six cases of which required laparotomy due to complications arising from the procedure. The mean number of pelvic lymph nodes harvested was 30, whereas that of para-aortic lymph nodes was 15.

In a study that compared a prospective group of 37 patients with endometrial cancer who underwent LESS hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymphadenectomy with a historical group of 74 patients who underwent the same procedure using a 4-port conventional laparoscopic approach, the LESS group had significantly lower postoperative pain scores and analgesic requirements[21]. There were no significant differences in the operating time, estimated blood loss, need for transfusion, postoperative hospital stay, or intra- or post-operative complications between the two groups. No patients required conversion, and the number of pelvic or para-

aortic lymph nodes retrieved in both groups was similar. Respectively in the LESS and conventional laparoscopy groups, the mean number of pelvic nodes harvested was 24.6 and 23.3, and that of para-aortic nodes was 4.9 and 6.9.

One retrospective case series compared the perioperative outcomes of LESS radical hysterectomy with the mini-laparoscopic approach in 46 patients with stage 1A2-1B1/IIA1 cancer according to the International Federation of Gynecology and Obstetrics[22]. For the mini-laparoscopic group, one 5-mm umbilical camera port with three additional 3-mm secondary ports were used. The LESS group was associated with longer operative time but shorter hospital stay; the two groups were comparable in term of the number of lymph nodes removed, perioperative outcome, and oncological outcome. After a median follow-up of 27 months, only one patient in the mini-laparoscopic group died of pelvic recurrence.

The current evidence suggests that LESS is a feasible approach for treatment of benign and malignant gynaecological diseases; it is safe and as effective as conventional laparoscopic surgery. LESS is associated with a longer operative time, but the proposed advantages of less postoperative pain and higher cosmetic satisfaction have not been consistently demonstrated. Therefore, the benefit of LESS over conventional laparoscopic surgery has yet to be confirmed. Incisional herniation is a potential drawback of LESS and has been poorly examined. In one retrospective study of 211 women who underwent LESS, umbilical herniation occurred in 2.4% of patients after a median follow-up of 16 months[23]. When women with additional risk factors for herniation were excluded (e.g. obesity, connective tissue diseases), the rate of umbilical herniation was 0.5%, which is comparable to that after the conventional laparoscopic route. For the treatment of malignant diseases, oncological outcomes seem to be comparable between LESS and conventional laparoscopy. Nonetheless, data are limited and follow-up periods are short. More long-term data are required to establish the oncological safety of LESS.

Robotic-assisted Laparoscopic Surgery

The da Vinci Surgical System (Intuitive Surgical, Sunnyvale [CA], US) was the first robotic surgical system approved by the US Food and Drug Administration for general laparoscopic surgery in 2000 and for gynaecological procedures in 2005. It has been extensively used for performing hysterectomy and other complex laparoscopic procedures (myomectomy, sacrocolpopexy), and staging for gynaecological cancers. The laparoscopic trocars are docked to robotic arms to which surgical instruments are attached. The surgeon sits at the console to perform the surgery by remotely controlling the movement and function of different robotic arms using hand and foot controls.

The major advantages of robotic surgery over conventional laparoscopic surgery include improved visualisation through three-dimensional stereoscopic vision, wider range of motions and improved dexterity with robotic-wristed instruments, improved surgical precision by eliminating hand tremor, and better ergonomics to improve surgeon comfort during the procedure. These features potentially enable easier and more precise complex laparoscopic procedures and may lead to shortening of the learning curve. Nonetheless, its drawback is the loss of tactile feedback during surgery, reduced flexibility, longer operative time, and increased cost.

Although there has been a florid growth in the number of robotic procedures since its introduction in the 2000s, clinical trials that compare the performance of robotic-assisted surgery with conventional laparoscopic surgery in gynaecology are limited and involve only a small number of patients.

In a meta-analysis of four randomised trials that encompassed 326 women undergoing total hysterectomy in the robotic-assisted group (n=162) or conventional group (n=164), the two groups were comparable in terms of rates of major or minor complications, length of hospital stay, operating time, rate of conversion to laparotomy, and estimated blood loss[24]. Only two of the four trials reported quality of life[25,26], but results were inconsistent owing to heterogeneity of metrics used, and thus pooling of results was not possible.

Laparoscopic sacrocolpopexy is a procedure that requires advanced laparoscopic skills and demanding suturing and knot-tying techniques, with a steep learning curve and long operating time. The robotic system can facilitate such procedures. Only two randomised trials (each with a sample size of 78) have compared robotic-assisted with conventional laparoscopic sacrocolpopexy[27,28]. One study included patients with post-hysterectomy vaginal prolapse and reported that the robotic route was associated with a significantly longer operative time (suturing time and sacrocolpopexy time), with a mean difference of 67 minutes[27]. Patients in the robotic group had more pain at rest and during activity from weeks 3 to 5 and required

analgesics for a longer duration[27]. The cost incurred by the robotic route was also significantly higher, with a mean difference of US$1936. Both robotic and laparoscopic groups were equally effective in improving vaginal support and functional outcomes.

Another study included patients with pelvic organ prolapse grade II or greater, with 58% of patients undergoing concomitant hysterectomy[28]. When the initial costs of robot purchase and maintenance were excluded, the robotic route and laparoscopic route did not differ significantly in terms of initial day of surgery costs or hospital costs over 6 weeks. Nonetheless, the robotic system was associated with longer operative time; the rate of adverse events was similar between the two groups.

There is no randomised controlled trial to compare robotic with laparoscopic myomectomy. In a systematic review of robotic-assisted versus laparoscopic and/or open myomectomy, there were no significant differences in operative time, estimated blood loss, need for transfusion, length of hospital stay, complication rate, or postoperative fertility outcomes between the two groups[29].

Robotic-assisted surgery has been widely used in treatment of gynaecological malignancies. In a systematic review that comprised 24 comparative non-randomised studies comparing robotic-assisted laparoscopic hysterectomy with laparoscopic hysterectomy for endometrial cancer, the robotic route was associated with a shorter length of stay, less estimated blood loss, fewer conversions to laparotomy, and less postoperative pain, as well as fewer intra-operative complications, urinary tract injuries, and cystotomy incidence[30]. The postoperative complications and the numbers of pelvic lymph nodes and para-aortic lymph nodes retrieved were similar between the two groups[30]. Three of the studies reported oncological outcomes up to 36 months; there was no significant difference in the overall survival, disease-free survival, or recurrence rate between the two groups[31-33].

One randomised controlled trial compared robotic-assisted (n=50) with conventional (n=49) laparoscopy surgery for endometrial cancer, the robotic group achieved a shorter operation time, shorter total time spent in the operating room, and lower rate of conversion to laparotomy[34]. The two groups were comparable in terms of the number of lymph nodes retrieved, blood loss, length of hospital stay, and intra- and post-operative complications.

In a systematic review that included 11 studies that compared robotic-assisted with laparoscopic radical hysterectomy for early-stage cervical cancer, robotic-assisted surgery was associated with shorter length of hospital stay and less need for transfusion[35]. The two groups were similar in terms of operation time, estimated blood loss, intra- and post-operative complication rates, number of lymph nodes removed, rate of positive margin, and overall and disease-free survival.

The evidence for robotic-assisted radical trachelectomy and staging surgery for ovarian tumour is even more limited. Overall, the robotic approach is deemed safe and feasible, with results comparable to those of the laparoscopic approach[36-38].

For the treatment of benign gynaecological conditions, the available evidence suggests that robotic surgery is safe and effective with similar perioperative outcomes in terms of complication rates, conversion rates, blood loss, and length of hospital stay. Operative time is significantly longer in robotic-assisted laparoscopic sacrocolpopexy. For the treatment of gynaecological malignancies, the evidence is very limited. Patients with endometrial cancer may benefit from robotic-assisted surgery with advantages of shorter operative time and lower conversion rates. Robotic-assisted radical hysterectomy is better than the conventional laparoscopic route in terms of shorter hospital stay and less need for blood transfusion, with similar oncological survival data.

Robotic-assisted Laparoendoscopic Single-site Surgery

Robotic-assisted LESS can potentially have the benefits of less postoperative pain, better cosmetic results, and fewer port-related complications. The robotic surgical platform may help overcome the technical challenges associated with conventional LESS. Robotic-assisted LESS is feasible in many gynaecological procedures such as adnexal surgery, hysterectomy, sacrocolpopexy, myomectomy, radical hysterectomy, lymph node removal, and ovarian staging surgery. There is no randomised or prospective trial that compares robotic-assisted LESS with conventional LESS or multiport robotic-assisted surgery. Most studies are small retrospective cohort studies or case series to demonstrate the feasibility and safety.

Four retrospective cohort studies have compared robotic-assisted LESS with robotic-assisted multiport surgery for (mostly) early endometrial cancer (Table 1)[39-42]. Robotic-assisted LESS is associated with less operating blood loss and is less costly than multiport robotic surgery.

Six retrospective studies have compared robotic-assisted LESS with LESS (Table 2)[43-48]. The robotic route is associated with longer operative time and is more costly although surgical outcomes were similar.

Natural Orifice Transluminal Endoscopic Surgery

In the 1940s, culdoscopy was performed by gynaecologists to view the pelvic organs using an endoscope through the recto-uterine pouch for diagnostic pelvic examinations and sterilisation procedures[49]. Subsequent development of NOTES was impeded by the lack of appropriate technology to facilitate more complex procedures. The first human NOTES is believed to be the transgastric appendectomy performed in India in 2006[50]. It was presented but has not been published. The

Table 1. Comparative studies of robotic-assisted laparoendoscopic single-site surgery (RA-LESS) versus robotic-assisted multiport surgery (RA-MP)[39-42]

Study	Study type	Surgery	No. of patients	Results
Moukarzel et al[39], 2017	Retrospective cohort	Hysterectomy and sentinel lymph node mapping	RA-LESS=14; RA-MP=13	RA-LESS is associated with lower costs; no difference in operative time, console time, blood loss, or complication rates
Corrado et al[40], 2016	Retrospective case-control	Hysterectomy	RA-LESS=23; RA-MP=46	RA-LESS is associated with less blood loss, fewer hospital stay; RA-MP is associated with higher costs; no difference in operative time or complication rate
Bogliolo et al[41], 2016	Retrospective cohort	Hysterectomy	RA-LESS=45; RA-MP=59	RA-LESS is associated with less blood loss and shorter hospital stay; RA-MP is associated with shorter docking time and higher costs; no difference in console time, surgical complication rate, conversion rate, or postoperative pain
Khafagy et al[42], 2015	Retrospective cohort	Pelvic lymph node	RA-LESS=10; RA-MP=41	RA-LESS is feasible for pelvic lymph node dissection

Table 2. Comparative studies of robotic-assisted laparoendoscopic single-site surgery (RA-LESS) versus laparoendoscopic single-site surgery (LESS)[43-48]

Study	Study type	Surgery	No. of patients	Results
Gungor et al[43], 2017	Retrospective cohort	Hysterectomy	RA-LESS=20; LESS=25	No difference in conversion rate, operative time, blood loss, operative and post-operative complications, length of hospital stay
Hachem et al[44], 2016	Retrospective case-control	Adnexal surgery, hysterectomy, pelvic lymph node dissection	RA-LESS =33; LESS=59	8 cases in RA-LESS were aborted or converted to laparotomy (due to adhesions or technical difficulty); RA-LESS is associated with longer operative time and higher costs; no difference in blood loss, length of stay, or complication rates
Paek et al[45], 2016	Retrospective cohort	Adnexal surgery	RA-LESS =20; LESS=228	RA-LESS has longer operative time and lower complication rate (0% vs. 1.3%)
Lopez et al[46], 2016	Retrospective cohort	Hysterectomy	RA-LESS =50; LESS=50	No difference in conversion rate, complication rate, estimated blood loss; RA-LESS has shorter length of stay (by 8.12 hours) but longer operative time (by 24.9 minutes)
Paek et al[47], 2016	Retrospective cohort	Hysterectomy	RA-LESS =25; LESS=442	No difference in conversion; RA-LESS has longer operative time but less blood loss and lower major complication rate (0% vs. 1.4%)
Akdemir et al[48], 2015	Retrospective cohort	Hysterectomy	RA-LESS =24; LESS=34	RA-LESS has longer operative time; intraoperative outcomes and postoperative pain scores are similar

first published NOTES was a transvaginal endoscopy cholecystectomy performed in Brazil in 2007[51]. Vaginal hysterectomy is a traditional natural orifice surgery. It is superior to laparoscopic or abdominal hysterectomy with faster recovery[2]. Nonetheless, it can be difficult in nulliparous patients with a non-descent uterus or patients with a large uterus or with pelvic adhesions. Concomitant salpingo-oophorectomy can be challenging because of a limited operative field and difficulty in inspecting the entire abdominal and pelvic cavity. Other potential advantages of transvaginal NOTES include better cosmetic results, less incisional herniation, less postoperative pain, less postoperative wound infection, and a shorter hospital stay[52].

Approaches of NOTES include transgastric, transvaginal, transcolonic, and transvesical. The transvaginal route has the advantage of fewer complications arising from wound closure or leakage, compared with other routes. For transvaginal NOTES, prophylactic antibiotics and disinfection of the vagina are required. It typically starts with a 2- to 3-cm posterior colpotomy. The pouch of Douglas is opened and a vaginal NOTES port is inserted vaginally. The commercially available ports and the more economic glove-port system for LESS can be used as a NOTES port. A standard laparoscope (rigid or flexible, 0° or 30°) and conventional laparoscopic instruments can be inserted through the NOTES port. The NOTES port is removed at the end of procedure and the specimen is retrieved via the colpotomy wound. The wound is then closed with absorbable sutures. NOTES is technically challenging and can have the same problems of instrument crowding, hand collision, and loss of triangulation as encountered in LESS.

In pure NOTES, natural body orifices (mouth, urethra, anus, vagina) are used to access the peritoneal cavity without the need for an abdominal incision. In hybrid NOTES, natural body orifices are used in addition to transabdominal laparoscopic port. In vaginal-assisted NOTES hysterectomy, the first part of the operation is a vaginal procedure to dissect the caudal part of the uterus under direct vision. After that, the procedure is completed with transvaginal NOTES. In total vaginal NOTES hysterectomy, the whole procedure is performed by means of transvaginal NOTES with laparoscopic instruments.

Since the first published case of the NOTES in 2004, NOTES in gynaecology has remained limited. NOTES has been reported to be feasible and safe for adnexal surgery, hysterectomy, myomectomy, and sacrocolpopexy. Most reports are small case series with <20 patients; no randomised controlled trial for gynaecological NOTES has been published. In a case series of 137 patients who underwent NOTES hysterectomy, the success rate was 94.9% (130/137) and seven patients required conversion to conventional laparoscopy (two due to intraoperative complications of unintended cystotomy and bleeding, and five due to failure as a result of a narrow vagina, location of pathology obstructing the route of entry, or adhesions)[53]. Postoperative febrile morbidity and urinary tract infection occurred in five patients, but all resolved with conservative treatment.

In one retrospective matched case-control study that compared NOTES hysterectomy (n=147) with laparoscopic-assisted vaginal hysterectomy (LAVH) [n=365], NOTES was associated with less operative time, less blood loss, less need for blood transfusion, and shorter postoperative stay[54]. There was no conversion to laparotomy in either group. The overall complication rate was comparable between groups, but if the uterine weight was >500 mg, LAVH was associated with more complications (4.3% vs. 0%). NOTES resulted in higher hospital charges[54].

In another retrospective matched case-control study that compared NOTE hysterectomy (n=16) with single-port LAVH (n=32), NOTES was associated with shorter operative time (70.6 vs. 93.2 min) and shorter hospital stay (3.5 vs. 4 days)[55]. There was no conversion to laparotomy in either group and no significant difference in perioperative outcomes (estimated blood loss, amount of analgesic drugs used, postoperative visual analogue scale pain score, and febrile complications).

In a retrospective matched case-control study that compared NOTES salpingo-oophorectomy (n=33) with conventional laparoscopic approach (n=203), NOTES was associated with shorter operative time and shorter hospital stay, but higher hospital charges[56]. There was no conversion in either group.

In a similar case-controlled study that compared NOTES-assisted ovarian cystectomy (n=34) with laparoscopic ovarian cystectomy (n=243), NOTES had shorter operative time and shorter hospital stay but higher hospital charges[57].

In an on-going randomised controlled trial comparing transabdominal laparoscopic hysterectomy with NOTES in patients with a non-prolapsed uterus and benign gynaecological diseases, the primary outcome was the success rate and secondary outcomes included perioperative

outcomes, postoperative pain, sexual function, costs, and health-related quality of life[58].

It is proposed that the robotic platform may help overcome the difficulties associated with NOTES. In the first robotic-assisted NOTES for hysterectomy, all four patients with benign disease were successfully treated, with no intra- or post-operative complications[59]. Nonetheless, patients were highly selected due to the lack of appropriate instruments. Further development of surgical instruments are required to facilitate its implementation. For the treatment of benign disease, NOTES is associated with shorter operative time and shorter hospital stay but higher costs; the postoperative pain score does not seem to decrease.

Conclusion

The robotic system may help solve some technical challenges associated with LESS or NOTES. Nonetheless, the evidence to support the use of these minimally invasive techniques over conventional laparoscopic surgery remains limited. The available evidence suggests that LESS, robotic-assisted laparoscopic surgery, and NOTES are safe and effective for different gynaecological diseases. More prospective randomised controlled trials with long-term follow-up are needed to determine whether they enable better patient outcomes in terms of less pain, better cosmetic results, and faster recovery.

Declaration

The author has disclosed no conflicts of interest.

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