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Single Incision Laparoscopic Surgery: Review of Pros and Cons

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Abstract

Despite huge advances in minimally invasive surgeries, efforts still continue for finding less invasive methods of surgery. Patients desire less postoperative pain as well as better cosmetic outcomes. This may be achieved by decreasing the number of laparoscopic ports in which all the surgical maneuvers are performed through a single incision. However, surgeons should be also equipped to act well while avoiding adverse events of the new practicing approach. Along with increasing trends in performing of single incision laparoscopic surgery (SILS) in routine practice, the number of assessing the pros and cons of this new modality is also on the rise. Although it has been claimed that SILS is able to make the dream of invisible laparoscopy true for patients and surgeons, consecutive studies regarding postoperative outcomes questioned the benefits of the new evolved technique. Subsequent meta-analysis also revealed equal outcomes for SILS in comparison to the standard laparoscopy. Our review aimed to outline the pros and cons of SILS.

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Introduction

The history of endoscopy dates back to 500 B.C., when Hippocrates used the first rectal speculum, and primitive gynecologic endoscopy also dates to the same era (1,2). Direct observation of internal cavities through a metal tube was replaced by semi-flexible endoscopes to watch the internal organs via an existing passage into the human body. Finally, newer laparoscopes emerged to allow view access to the abdominopelvic cavity to diagnose the pathology and to perform therapeutic intervention (2,3). Although the guiding tube to observe the interior of the human body has evolved extensively in shape and material, it was the light sources and lens systems restricting super advancement of laparoscopy during these centuries (2,4). Ultimately, with the interaction of multidisciplinary medicine and modern technology, laparoscopic surgeries are performed routinely throughout the world for a wide range of surgically manageable diseases. However, laparoscopy has blossomed during recent years due to the explosion of modern advances in video-assisted techniques, novel and super-flexible instruments, and natural orifice access point (5,6).

Today, laparoscopy has found its place in all fields of surgery and wherever surgeons try to operate by this mean. However, it seems surgeons have not been satisfied with the minimally invasive nature of laparoscopic surgeries and have attempted to use less invasive approaches and diminished port number techniques. For this reason, single port laparoscopic surgery (SILS) has emerged which is also referred to as single wound laparoscopic surgery or single port access laparoscopy. Despite the increasing number of studies assessing the cost-effectiveness of SILS in many areas of surgery, it seems that the practical application of this novel approach has been slow as compared to the rapid growth of the number of studies evaluating its outcomes. This is probably another barrier to the second revolution of laparoscopic surgeries after its initial one within the past decades thanks to the modern light, lens, video, and flexible instrumentation technologies (2,4). Although this might be due to the infancy of SILS, existing evidences regarding final outcomes and associated complications of SILS are

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heterogeneous and inconclusive, and the quest to find the cost-effectiveness of these new super minimally invasive surgeries remain robust. In this review, we aim to discuss the pros and cons of SILS to allow the readers to draw their own judgment.

Materials and Methods

We searched MEDLINE, SCOPUS, Embase, and Google Scholar databases using the key terms "single incision laparoscopic surgery", "single port laparoscopic surgery", "single wound laparoscopic surgery", and "single site laparoscopic surgery" in order to retrieve existing studies regarding SILS with no filter for our search criteria. Studies the full texts of which were unavailable were excluded, while the references of all the obtained full texts were searched. Inclusion criteria were comparing at least one feature of SILS with conventional laparoscopic surgery (CLS), and clearly described the technique as well as the outcome measure. The included studies were reviewed by three authors while 2 independent authors confirmed the accuracy of the extractions. The below mentioned outcomes were then reviewed and interpreted by authors of the current study.

Single incision laparoscopic surgery (SILS)

With the advancement of flexible instruments and bending optic devices, all within a single multi-port system, today laparoscopic procedures can be performed by accessing the critical view through a single incision on the surface of the human body. Moreover, called single port laparoscopic surgery (SPLC), the preferred site to provide the access port is turning between small incisions on the abdominal quadrants or even preferably the umbilicus. On the one hand, technology is offering more feasible multi-port systems and much more flexible instruments that are able to bend sufficiently not only to provide the critical view, but also to let the surgeons operate within the field. On the other hand, surgeons throughout the world are becoming familiar with this newly adopted technique and performing further procedures on more complicated cases will lead to proficiency in surgeries, a phenomenon referred to as "learning curve". This is why it is too early to draw a meaningful decision about its role in daily surgeries. Nevertheless, some authors have shown that the potential benefits of SILS do not compensate for its huge costs and adverse intraoperative and postoperative outcomes. The results of numerous studies investigating the safety and feasibility of SILS are consecutively published; however, it seems that mid-term outcomes have not been conclusive and there is still work to do.

Single incision laparoscopic cholecystectomy

It was back in 1883 when the first open cholecystectomy was performed by Langenbecks on a 43 years old man with cholelithiasis pain (7). Then, over a century passed until the first laparoscopic cholecystectomy (LC) emerged (8,9). Today, LC is the gold standard for stone-related diseases of the gallbladder (10). Although slightly evolved during the last decades, mainly in terms of video-assisted techniques, conventional LC has been performed routinely using 4 laparoscopic ports (4,11,12). In order to reduce postoperative pain while providing faster recovery and improving cosmetic outcomes, surgeons have tried to lower the number of ports during LC (13-15). This has led to the evolution of conventional 4 ports LC to 3 ports LC, and finally 2 trocars (13,14). One step further, some authors have reported the possibility of conducting an endoscopic surgery via natural orifice which means having access to the peritoneum or other target organs through natural lumens in the human body called natural transluminal endoscopic surgery (NOTES) (6,16). However, despite its limited experimental application, transluminal surgery has not been prevalently practiced in daily surgeries (17).

LC by a single port of entry was first introduced in 1997 by Navarra et al. (15). Since its inception, numerous authors have reported their experiences with single incision laparoscopic cholecystectomy (SILC) and more recently several randomized clinical trials (RCTs) have also been conducted to compare intraoperative adverse events and postoperative outcomes following SILC with conventional multiport LC (5,18-24). However, the results are varying as much as the study type varies itself. While there has even been special selection of inserting site (i.e., umbilicus for placing the sole remaining port to perform SILC), it seems that its benefits have come to the balance with the accompanied costs preventing this possibly scarless, potentially attractive, and extremely harmless procedure from being widely practiced (5,18,19).

Single incision laparoscopic gastrointestinal surgeries

SILS has received extensive attention in surgical management of disease of gastrointestinal tract especially those of colorectal pathologies from appendectomy by single wound laparoscopy in children, and gastric, pancreatic, and colorectal resections in GI malignancies, and finally targeting morbidly obese patients to perform bariatric surgery (27-31). By decreasing the number of ports, researchers have tried to reduce the probability of damage to the internal organs, port site hernia, bleeding, scar formation, and infection while improving cosmetic outcomes (32,33). However, despite the satisfactory performance of SILS techniques in gastrointestinal surgeries, early outcomes did not differ with conventional laparoscopic methods and later outcomes are to be assessed in upcoming RCTs (32-35).

Surgical Oncology

Application of laparoscopic techniques in surgical oncology has not been growing much rapidly due to the increased number of studies against its efficacy to provide sufficient margin free tumor resection and metastases at the port site (36). However, in several RCTs investigating these concerns, it has been noted that the recurrent rate in SILS port site is around 0.62%, comparable to that of 0.6% in open surgeries (37). Hence, surgeons have begun to adopt laparoscopy in a higher pace in surgical oncology. This includes investigating laparoscopy for diagnosis and staging purposes along with surgical procedures to resect tumors, excise lymph nodes, and perform metastasectomy (34,38). While the recurrence rate has been documented to remain as reasonable as oncologic laparotomies, laparoscopy offer improved recovery, shorter hospitalization, and less stress response following surgery (36,37). Despite early results of a recent RCT showing SILS to be a feasible and safe procedure in resection of colorectal tumors, short outcomes have been similar to traditional multiport laparoscopic surgeries (39).

Gynecologic Surgeries

Minimally invasive surgery has become the standard treatment in many benign gynecologic diseases, pelvic masses, and oncologic risk reducing surgeries (i.e., salpingo-oophorectomy/total laparoscopic hysterectomy) (40,41). Like other fields of surgery, proficiency in performing surgical techniques has been achieved following the completion of 15-20 procedures (40). Several studies have weighed surgical outcomes following BSO/THA, colposuspension for stress incontinence, benign adnexal cystectomy, appendectomy during pregnancy, and even ectopic pregnancy by single site laparoscopy against conventional methods of this minimally invasion surgical procedure (40-45). Existing evidences are in favor of single-site laparoscopy as an alternative technique to gynecologic pathologies (38,40-45). However, no single report has certainly considered SILS as a routine practice and the decision rests with future studies to determine the impact of the ongoing interaction between modern medicine and advanced technology.

Urology

Urologists have been at the forefront of adopting SILS and NOTES (46). In this filed, combination of NOTES and conventional laparoscopic techniques has necessitated the reevaluation of these already practiced approaches. This is because this new combinative modality although documented to be diagnostically valuable, still lacks therapeutic efficacy (46). However, similar to the field of colorectal surgeries, where assessment of recently established techniques occurs at the highest pace, a wide range of urological conditions are now treated by SILS. While a series of urologic procedures including radical cystectomy, prostatectomy, urologic reconstructing surgeries, and even donor kidney harvesting have been performed by the combination of SILS and other endoscopic techniques, efforts to rank SILS in urology continues as newer laparo-endoscopic hybrids are going to emerge (41,47-50).

Advantage of SILS over traditional laparoscopic surgery

Despite many advances in laparoscopic surgeries, the new adopted technique should receive remarkable benefits over the conventional laparoscopic surgery (CLS) before it can be rewarded the routine practice. Some of the proposed advantages of SILS are discussed below.

Lower postoperative pain

Beside cosmesis, “lower postoperative pain” has been one of the main fantasies of SILS. This may occur as a result of decreased number of ports which is associated with fewer painful points after surgery, and subsequent fewer potential locations for wound complications including bleeding, and infection (19). However, those who oppose it bring up the larger trocar site for SILS port. Meta-analysis on pooled data has revealed no significant difference between SILC and CLS for patients’ postoperative pain measured by visual analogue scale (5,19). This is probably due to the fact that there are several determinants for postoperative pain rather than the incisions in the abdominal wall including visceral pain, larger port systems at a single site, and maybe higher trauma to the abdominal wall due to the decreased angle of freedom. The controversy may also arise from the heterogeneity of the literatures that is a result of variation in the method of pain assessment and recording and which makes the combined analysis challenging. However, there may be an explanation for reduced postoperative pain in some studies and that can be due to the changing of the location of ports from upper abdomen to the umbilicus (especially in surgeries in the upper abdomen). In fact, incisions in the upper abdomen produce more pain due to respiratory movement (51,52).

Length of Hospital Stay

While it seemed that SILS is associated with reduced length of hospitalization due to the potentially lower complication rate, the reporting studies show a range of 1 to 3 days for hospital stay with no significant difference between SILS and CLS groups (19,53,54).

Time to Return to Work

There is limited contribution in the literature comparing the time period until the patient returns to work between SILS and traditional laparoscopic surgery. Some authors have declared that faster recovery following SILS leads to a reduced time of returning to work (54,55). However, combined analyses are not in favor of either group due to the difficulty in interpretation of heterogeneous data (5,19,53).

Cosmesis
SILS surgeries were developed with the aim of improving cosmetic outcomes. Reduced number of ports causes fewer scars. Although SILS port needs a 2 cm incision, it is usually concealed in the umbilicus. Therefore, in some cases the minimally invasive surgery may even be virtually scarless (56). However, in reality the results are different to some extent. Cosmesis have been reported to be satisfactory in urological and gynecologic procedures, even when adjusted for some predicting variables in meta-analysis without considering the random model (5,19,38,43,46,49,53,54). However, other studies investigating the cosmetic outcomes have not reported a significant difference between SILS and CLS in abdominal procedures (5,19,53). Therefore, it seems that cosmetic results are not significantly better and are related to type of surgery.

Patients' Satisfaction
This is one of the most important but also challenging to assess parameters when comparing two different surgical techniques. Although there are some reports regarding improved patients' satisfaction after SILS cholecystectomy, other studies have not contributed to this issue yet (5,19,53,57,58). Unintentionally neglected, patients' satisfaction is an important determinant in selecting criteria for the most appropriate surgical technique (53). Nevertheless, patients' satisfaction is reflective of many other components including what a patient expects from his/her surgery, how it would be if the other technique was performed on the patient, and how the patient is treated during the process of the disease either at the surgical ward or after discharge at follow up visits. Standardized methods of measuring patients' satisfaction should be used in large sample size RCTs to compare satisfaction between SILS and CLS groups.

Less immunological stress
Interleukin-6 (IL-6), total white cell counts, and acute phase reactant C-reactive protein (CRP) have been shown to be directly proportional to the extent of injury occurring during surgery (10,59-61). Indeed, following surgical traumatic injury, increase in CRP due to mediation of IL-6 is detectable in peripheral blood (60,61). It has been shown that open surgeries produce more severe stress response compared to laparoscopic approaches (59,62). On the other hand, IL-6 has been directly related to postoperative complications; hence, the assessment of stress responses could be indicative of the level of injury during each surgical technique (60,63-65). However, the results of a recent study revealed no significant difference between SILC and CLS for serum levels of CRP and IL-6, nor any correlation between systemic stress response and surgical parameters (66).

Disadvantages of SILS versus CLS

Learning Curve
To adopt a new surgical technique as a routine practice, there is a necessity for the practicing surgeons to acquire proficiency (40,67,68). Although the first cholecystectomy was introduced in 1997, there has not been an increasing trend in its performance in daily surgeries for years (15,19). Beside the resistance of surgeons to accept great changes in the practice, this kind of delay in accepting new surgical techniques could be due to the required learning curve for carrying out a new technique. Even after passing the learning curve, it takes time to reach mastery with least complications. By performing more cases, the operation time begins to decrease until it reaches a plateau.

There is a difference between the numbers of procedures needed to be performed before a surgeon can acquire proficiency in a surgical technique. This difference is obviously associated with the type of procedure and the surgeons' experience and expertise in similar procedures (69). For laparoscopic cholecystectomy, it is reported to be between 20 and 40 procedures by a single surgeon (70). Similarly the operative time to learn the SILS procedures varies between the types of surgeries as well as the surgeons.

Operative Time
However, when compared to the CLS technique, it has been reported that SILS procedures last longer than the conventional laparoscopic surgeries (5,19,57,58). It is notable that as surgeons gain more experience and the instruments become more advanced the learning curve could vanish.

Feasibility and Technical challenges
The main technical challenge in SILS is reduced number of port sites and subsequent loss of ergonomics and triangulation (71). As multiple trocars are inserted through a single port, they diminish the flexibility of the surgeon to perform maneuvers with the laparoscopic instrument. Crowding ports within a single incision makes the surgeon experience interference of instruments with one another, compromising the position of hand-sided device to the left-sided one and vice versa. Furthermore, even flexible instruments with sufficient articulation would reduce the surgeon's performance when crossed over at the entry point necessitating higher maneuverability of the surgeon's hands (19,53,70). All of these may prevent "critical views" in each type of surgery.

Intraoperative adverse events and postoperative complications

Although SILS is often performed worldwide by highly experienced surgeons in conventional laparoscopy, it is thought that this technique could lead to more adverse events intraoperatively. For this reason, adoption of SILS occurred slowly since its introduction to the laparoscopist until sufficient reports of its feasibility along with development of more flexible devices would be available. There are some evidences that do not support the higher rate of intraoperative adverse events including internal organ damage, vascular or intestinal leakage, and bleeding or fistula formation following SILS procedures when compared to CLS, but there are also other evidences (5,19,53,70). On the other hand, most common postoperative complications are wound infection, abscess formation, bile duct injury, bile leakage, and in some cases internal bleeding (68,72). Nevertheless, the difference in rate of complications between SILS and CLS has not been reported to be significant in the literature. This could occur as a result of the fact that most SILS procedures are still performed on uncomplicated surgical cases leaving much more complicated patients to be treated by CLS, mini-laparoscopy, or open surgeries (5,19,38,53,57,58). There is also a fear of more incisional hernia because of the larger trocar site (73). For this reason, we should wait till more expert surgeons report their experience with SILS on challenging cases.

Need for additional ports and conversion to multiport CLS

Whether as a result of intraoperative adverse events, lack of critical view, or long operative time, it may be needed to add trocars and increase the number of port sites or even change the technique to an open surgery to continue the operation all of which is referred to as "conversion". Conversion rate has been reported to vary between 0 and 33% in SILS procedures based on the type of surgery with some cases needing reoperation in some circumstances (53). However, there is an inverse relationship between surgeon's experience and complexity of the cases with the conversion rate, with the most experienced surgeons performing excellently in uncomplicated surgeries. Results of combined analyses on the pooled data of existing studies revealed that the conversion rate from SILS to CLS or open surgery, or from CLS to open surgery is not significantly different between these 2 groups (5,19). As already mentioned, the more the SILS is practiced, the less the conversion is subject to occur.

Multi-port systems and modern laparoscopic instruments and associated costs

There are limited data on the cost associated with SILS procedure; however, there are harsh data on similar costs between these 2 groups. It should be noted that while modern multi-port systems are more expensive than conventional laparoscopic ports, other secondary outcomes of SILS such as time away from work, diminished number of applied ports, and shorter hospitalization length should all be taken into account when comparing SILS associated costs with CLS. Nevertheless, while some surgeons use modern laparoscopic instruments to perform SILS, others still use conventional laparoscopic ports due to intolerability of associated costs or unavailability of modern technology, or enjoy some novel ideas such as application of surgical glove as a port system. For this reason, future studies investigating the cost-effectiveness of SILS versus CLS procedures must consider this inequality between studies and standardize their techniques.

NOTES: Is it a new horizon to move to?

The term "*NOTES*" was first used by the NOSCAR working group, a multidisciplinary joint committee of gastroenterologists and surgical endoscopists, referring to a minimally invasive modality with purposed access to the internal organs through natural orifices on the body surface including mouth, vagina, and rectum (74). This evolving technique builds on a multidiscipline of medicine and technology aiming to offer the least possible level of pain theoretically, improving postoperative outcomes, and reducing surgical site complications while at the same time avoiding any visible scar on body surface (75). Although SILS is also performed through an embryonic natural orifice (i.e., umbilicus (E-NOTES)), the NOTES has been considered to be potentially associated with invisible scars, faster recovery, shorter hospitalization, and reduced postoperative complications such as hernia, bleeding, and pain (76,77). However, some authors have recently discussed risks and complications associated with NOTES as with unfamiliarity with endoscopic visual approaches, ineffective existing instruments, and challenges in adequate closure of the incised organ for peritoneal access, which is the GI tract or vagina in many cases. As a result, SILS has regained huge attention as it is the only easy developing laparoscopic procedure at this time. Finally, it seems too soon to decide whether improved cosmesis in NOTES is worth the associated risk, complications, and costs.

However, performing SILS can make surgeons ready for future techniques like NOTES to be in practice.

Conclusion

SILS seems to offer some potential benefits in selected patients including possible reduced pain in early postoperative period, possible improved cosmetic outcomes, and a way toward NOTES. Patients should be aware to choose the benefits of SILS over the potential risks and costs such as longer operation time, possible higher complication rate, need to the learning curve to be achieved by the surgeon. There is a need to further high-power RCTs to provide more high-level evidence regarding this advanced technique. It is suggested that future studies be designed and established with standard protocol to reduce heterogeneity and make pooling analysis more reliable.

References

1. Bonner TN. American Doctors and German Universities. Lincoln, NE: University of Nebraska Press; 1963.
2. Duffy J. From Humors to Medical Science: A History of American Medicine. Champaign, IL: University of Illinois Press; 1993.
3. Lau WY, Leow CK, Li AK. History of endoscopic and laparoscopic surgery. World J Surg 1997; 21(4): 444-53.
4. Kaiser AM, Corman ML. History of laparoscopy. Surg Oncol Clin N Am 2001; 10(3): 483-92.
5. Markar SR, Karthikesalingam A, Thrumurthy S, Muirhead L, Kinross J, Paraskeva P. Single-incision laparoscopic surgery (SILS) vs. conventional multiport cholecystectomy: systematic review and meta-analysis. Surg Endosc 2012; 26(5): 1205-13.
6. de la Fuente SG, Demaria EJ, Reynolds JD, Portenier DD, Pryor AD. New developments in surgery: Natural Orifice Transluminal Endoscopic Surgery (NOTES). Arch Surg 2007; 142(3): 295-7.
7. Bittner R. The standard of laparoscopic cholecystectomy. Langenbecks Arch Surg 2004; 389(3): 157-63.
8. Reynolds W, Jr. The first laparoscopic cholecystectomy. JSLS 2001; 5(1): 89-94.
9. Muhe E. [Laparoscopic cholecystectomy--late results]. Langenbecks Arch Chir Suppl Kongressbd 1991; 416-23.
10. Gallstones and laparoscopic cholecystectomy. NIH Consens Statement 1992; 10(3): 1-28.
11. Schirmer BD, Edge SB, Dix J, Hyser MJ, Hanks JB, Jones RS. Laparoscopic cholecystectomy. Treatment of choice for symptomatic cholelithiasis. Ann Surg 1991; 213(6): 665-76.
12. Prasad A, Mukherjee KA, Kaul S, Kaur M. Postoperative pain after cholecystectomy: Conventional laparoscopy versus single-incision laparoscopic surgery. J Minim Access Surg 2011; 7(1): 24-7.
13. Mori T, Ikeda Y, Okamoto K, Sakata K, Ideguchi K, Nakagawa K, et al. A new technique for two-trocar laparoscopic cholecystectomy. Surg Endosc 2002; 16(4): 589-91.
14. Slim K, Pezet D, Stencl J, Jr., Lechner C, Le RS, Lointier P, et al. Laparoscopic cholecystectomy: an original three-trocar technique. World J Surg 1995; 19(3): 394-7.
15. Navarra G, Pozza E, Occhionorelli S, Carcoforo P, Donini I. One-wound laparoscopic cholecystectomy. Br J Surg 1997; 84(5): 695.
16. Kalloo AN, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, et al. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc 2004; 60(1): 114-7.
17. Park PO, Bergstrom M, Ikeda K, Fritscher-Ravens A, Swain P. Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos). Gastrointest Endosc 2005; 61(4): 601-6.
18. Garg P, Thakur JD, Garg M, Menon GR. Single-incision laparoscopic cholecystectomy vs. conventional laparoscopic cholecystectomy: a meta-analysis of randomized controlled trials. J Gastrointest Surg 2012; 16(8): 1618-28.
19. Sajid MS, Ladwa N, Kalra L, Hutson KK, Singh KK, Sayegh M. Single-incision laparoscopic cholecystectomy versus conventional laparoscopic cholecystectomy: meta-analysis and systematic review of randomized controlled trials. World J Surg 2012; 36(11): 2644-53.
20. Leung D, Yetasook AK, Carbray J, Butt Z, Hoeger Y, Denham W, et al. Single-incision surgery has higher cost with equivalent pain and quality-of-life scores compared with multiple-incision laparoscopic cholecystectomy: a prospective randomized blinded comparison. J Am Coll Surg 2012; 215(5): 702-8.
21. Phillips MS, Marks JM, Roberts K, Tacchino R, Onders R, DeNoto G, et al. Intermediate results of a prospective randomized controlled trial of traditional four-port laparoscopic cholecystectomy versus single-incision laparoscopic cholecystectomy. Surg Endosc 2012; 26(5): 1296-303.
22. Pisanu A, Reccia I, Porceddu G, Uccheddu A. Meta-analysis of prospective randomized studies comparing single-incision laparoscopic cholecystectomy (SILC) and conventional multiport laparoscopic cholecystectomy (CMLC). J Gastrointest Surg 2012; 16(9): 1790-801.
23. Sinan H, Demirbas S, Ozer MT, Sucullu I, Akyol M. Single-incision laparoscopic cholecystectomy versus laparoscopic cholecystectomy: a prospective randomized study. Surg Laparosc Endosc Percutan Tech 2012; 22(1): 12-6.
24. Solomon D, Shariff AH, Silasi DA, Duffy AJ, Bell RL, Roberts KE. Transvaginal cholecystectomy versus single-incision laparoscopic cholecystectomy versus four-port laparoscopic cholecystectomy: a prospective cohort study. Surg Endosc 2012; 26(10): 2823-7.
25. Abdelaziz Hassan AM, Elsebae MM, Nasr MM, Nafeh AI. Single institution experience of single incision trans-umbilical laparoscopic cholecystectomy using conventional laparoscopic instruments. Int J Surg 2012; 10(9): 514-7.
26. Luo C, Yang Q, Liu B, Ji X. Difficulties and countermeasures of transumbilical single incision laparoscopic cholecystectomy. J Am Coll Surg 2012; 214(5): e35-e38.
27. Chandler NM, Danielson PD. Single-incision laparoscopic appendectomy vs multiport laparoscopic appendectomy in children: a retrospective comparison. J Pediatr Surg 2010; 45(11): 2186-90.
28. Gopall J, Shen XF, Cheng Y. Current status of laparoscopic total mesorectal excision. Am J Surg 2012; 203(2): 230-41.
29. Huang CK. Single-incision laparoscopic bariatric surgery. J Minim Access Surg 2011; 7(1): 99-103.
30. Raman SR, Franco D, Holover S, Garber S. Does transumbilical single incision laparoscopic adjustable gastric banding result in decreased pain medicine use? A case-matched study. Surg Obes Relat Dis 2011; 7(2): 129-33.
31. Tacchino RM, Greco F, Matera D, Diflumeri G. Single-incision laparoscopic gastric bypass for morbid obesity.

Obes Surg 2010; 20(8): 1154-60.
32. Leggett PL, Churchman-Winn R, Miller G. Minimizing ports to improve laparoscopic cholecystectomy. Surg Endosc 2000; 14(1): 32-6.
33. Leroy J, Cahill RA, Asakuma M, Dallemagne B, Marescaux J. Single-access laparoscopic sigmoidectomy as definitive surgical management of prior diverticulitis in a human patient. Arch Surg 2009; 144(2): 173-9.
34. Jerby BL, Milsom JW. Role of laparoscopy in the staging of gastrointestinal cancer. Oncology (Williston Park) 1998; 12(9): 1353-60.
35. Yeo D, Mackay S, Martin D. Single-incision laparoscopic cholecystectomy with routine intraoperative cholangiography and common bile duct exploration via the umbilical port. Surg Endosc 2012; 26(4): 1122-7.
36. Lundberg O, Kristoffersson A. Port site metastases from gallbladder cancer after laparoscopic cholecystectomy. Results of a Swedish survey and review of published reports. Eur J Surg 1999; 165(3): 215-22.
37. Reilly WT, Nelson H, Schroeder G, Wieand HS, Bolton J, O'Connell MJ. Wound recurrence following conventional treatment of colorectal cancer. A rare but perhaps underestimated problem. Dis Colon Rectum 1996; 39(2): 200-7.
38. Zullo F, Falbo A, Palomba S. Safety of laparoscopy vs laparotomy in the surgical staging of endometrial cancer: a systematic review and metaanalysis of randomized controlled trials. Am J Obstet Gynecol 2012; 207(2): 94-100.
39. Huscher CG, Mingoli A, Sgarzini G, Mereu A, Binda B, Brachini G, et al. Standard laparoscopic versus single-incision laparoscopic colectomy for cancer: early results of a randomized prospective study. Am J Surg 2012; 204(1): 115-20.
40. Escobar PF, Starks DC, Fader AN, Barber M, Rojas-Espalliat L. Single-port risk-reducing salpingo-oophorectomy with and without hysterectomy: surgical outcomes and learning curve analysis. Gynecol Oncol 2010; 119(1): 43-7.
41. Fader AN, Escobar PF. Laparoendoscopic single-site surgery (LESS) in gynecologic oncology: technique and initial report. Gynecol Oncol 2009; 114(2): 157-61.
42. Gumus II, Surgit O, Kaygusuz I. Laparoscopic single-port Burch colposuspension with an extraperitoneal approach and standard instruments for stress urinary incontinence: early results from a series of 15 patients. Minim Invasive Ther Allied Technol 2013; 22(2): 116-21.
43. Ulker K, Huseyinoglu U, Kilic N. Management of benign ovarian cysts by a novel, gasless, single-incision laparoscopic technique: keyless abdominal rope-lifting surgery (KARS). Surg Endosc 2013; 27(1): 189-98.
44. Koh AR, Lee JH, Choi JS, Eom JM, Hong JH. Single-port laparoscopic appendectomy during pregnancy. Surg Laparosc Endosc Percutan Tech 2012; 22(2): e83-e86.
45. Marcelli M, Lamourdedieu C, Lazard A, Cravello L, Gamerre M, Agostini A. Salpingectomy for ectopic pregnancy by transumbilical single-site laparoscopy with the SILS system. Eur J Obstet Gynecol Reprod Biol 2012; 162(1): 67-70.
46. Gettman MT, Box G, Averch T, Cadeddu JA, Cherullo E, Clayman RV, et al. Consensus statement on natural orifice transluminal endoscopic surgery and single-incision laparoscopic surgery: heralding a new era in urology? Eur Urol 2008; 53(6): 1117-20.
47. Horstmann M, Kugler M, Anastasiadis AG, Walcher U, Herrmann T, Nagele U. Laparoscopic radical cystectomy: initial experience using the single-incision triangulated umbilical surgery (SITUS) technique. World J Urol 2012; 30(5): 619-24.
48. Caceres F, Cabrera PM, Garcia-Tello A, Garcia-Mediero JM, Angulo JC. Safety study of umbilical single-port laparoscopic radical prostatectomy with a new DuoRotate system. Eur Urol 2012; 62(6): 1143-9.
49. Khoder WY, Schlenker B, Trottmann M, Stief CG, Becker AJ. Single-Incision Laparoscopic Surgery (SILS) in Reconstructive Urological Cases. Surg Technol Int 2011; XXI: 35-40.
50. Wang GJ, Afaneh C, Aull M, Charlton M, Ramasamy R, Leeser DB, et al. Laparoendoscopic single site live donor nephrectomy: single institution report of initial 100 cases. J Urol 2011; 186(6): 2333-7.
51. Hughes R, Gao F. Pain control for thoracotomy. Contin Educ Anaesth Crit Care Pain 2005; 5(2): 56-60.
52. Desai PM. Pain management and pulmonary dysfunction. Crit Care Clin 1999; 15(1): 151-66, vii.
53. Ahmed K, Wang TT, Patel VM, Nagpal K, Clark J, Ali M, et al. The role of single-incision laparoscopic surgery in abdominal and pelvic surgery: a systematic review. Surg Endosc 2011; 25(2): 378-96.
54. Gill IS, Canes D, Aron M, Haber GP, Goldfarb DA, Flechner S, et al. Single port transumbilical (E-NOTES) donor nephrectomy. J Urol 2008; 180(2): 637-41.
55. Visnjic S. Transumbilical laparoscopically assisted appendectomy in children: high-tech low-budget surgery. Surg Endosc 2008; 22(7): 1667-71.
56. Cuesta MA, Berends F, Veenhof AA. The "invisible cholecystectomy": A transumbilical laparoscopic operation without a scar. Surg Endosc 2008; 22(5): 1211-3.
57. Song T, Liao B, Liu J, Yin Y, Luo Q, Cheng N. Single-incision versus conventional laparoscopic cholecystectomy: a systematic review of available data. Surg Laparosc Endosc Percutan Tech 2012; 22(4): e190-e196.
58. Hall TC, Dennison AR, Bilku DK, Metcalfe MS, Garcea G. Single-incision laparoscopic cholecystectomy: a systematic review. Arch Surg 2012; 147(7): 657-66.
59. Glaser F, Sannwald GA, Buhr HJ, Kuntz C, Mayer H, Klee F, et al. General stress response to conventional and laparoscopic cholecystectomy. Ann Surg 1995; 221(4): 372-80.
60. Lin E, Calvano SE, Lowry SF. Inflammatory cytokines and cell response in surgery. Surgery 2000; 127(2): 117-26.
61. Menger MD, Vollmar B. Surgical trauma: hyperinflammation versus immunosuppression? Langenbecks Arch Surg 2004; 389(6): 475-84.
62. Vittimberga FJ, Jr., Foley DP, Meyers WC, Callery MP. Laparoscopic surgery and the systemic immune response. Ann Surg 1998; 227(3): 326-34.
63. Vander VG, Penninckx F, Kerremans R, Van DJ, Arnout J. Interleukin-6 and coagulation-fibrinolysis fluctuations after laparoscopic and conventional cholecystectomy. Surg Endosc 1994; 8(10): 1216-20.
64. Grande M, Tucci GF, Adorisio O, Barini A, Rulli F, Neri A, et al. Systemic acute-phase response after laparoscopic and open cholecystectomy. Surg Endosc 2002; 16(2): 313-6.
65. Kimura F, Shimizu H, Yoshidome H, Ohtsuka M, Kato A, Yoshitomi H, et al. Increased plasma levels of IL-6 and IL-8 are associated with surgical site infection after

pancreaticoduodenectomy. Pancreas 2006; 32(2): 178-85.
66. McGregor CG, Sodergren MH, Aslanyan A, Wright VJ, Purkayastha S, Darzi A, et al. Evaluating systemic stress response in single port vs. multi-port laparoscopic cholecystectomy. J Gastrointest Surg 2011; 15(4): 614-22.
67. Joseph M, Phillips M, Farrell TM, Rupp CC. Can residents safely and efficiently be taught single incision laparoscopic cholecystectomy? J Surg Educ 2012; 69(4): 468-72.
68. Joseph M, Phillips M, Rupp CC. Single-incision laparoscopic cholecystectomy: a combined analysis of resident and attending learning curves at a single institution. Am Surg 2012; 78(1): 119-24.
69. Tokunaga M, Hiki N, Fukunaga T, Miki A, Ohyama S, Miyata S, et al. Learning curve of laparoscopy-assisted gastrectomy using a standardized surgical technique and an established educational system. Scand J Surg 2011; 100(2): 86-91.
70. Qiu Z, Sun J, Pu Y, Jiang T, Cao J, Wu W. Learning curve of transumbilical single incision laparoscopic cholecystectomy (SILS): a preliminary study of 80 selected patients with benign gallbladder diseases. World J Surg 2011; 35(9): 2092-101.
71. Morandeira-Rivas A, Millan-Casas L, Moreno-Sanz C, Herrero-Bogajo ML, Tenias-Burillo JM, Gimenez-Salillas L. Ergonomics in laparoendoscopic single-site surgery: survey results. J Gastrointest Surg 2012; 16(11): 2151-9.
72. Lau KN, Sindram D, Agee N, Martinie JB, Iannitti DA. Bile duct injury after single incision laparoscopic cholecystectomy. JSLS 2010; 14(4): 587-91.
73. Lajer H, Widecrantz S, Heisterberg L. Hernias in trocar ports following abdominal laparoscopy. A review. Acta Obstet Gynecol Scand 1997; 76(5): 389-93.
74. Rattner D, Kalloo A. ASGE/SAGES Working Group on Natural Orifice Translumenal Endoscopic Surgery. October 2005. Surg Endosc 2006; 20(2): 329-33.
75. Isariyawongse JP, McGee MF, Rosen MJ, Cherullo EE, Ponsky LE. Pure natural orifice transluminal endoscopic surgery (NOTES) nephrectomy using standard laparoscopic instruments in the porcine model. J Endourol 2008; 22(5): 1087-91.
76. Baron TH. Natural orifice transluminal endoscopic surgery. Br J Surg 2007; 94(1): 1-2.
77. Flora ED, Wilson TG, Martin IJ, O'Rourke NA, Maddern GJ. A review of natural orifice translumenal endoscopic surgery (NOTES) for intra-abdominal surgery: experimental models, techniques, and applicability to the clinical setting. Ann Surg 2008; 247(4): 583-602.