New minimally invasive approaches for cholecystectomy: Review of literature

Martin Gaillard, Hadrien Tranchart, Panagiotis Lainas, Ibrahim Dagher

Laparoscopic cholecystectomy is the most commonly performed abdominal intervention in Western countries. In an attempt to reduce the invasiveness of the procedure, surgeons have developed single-incision laparoscopic cholecystectomy (SILC), minilaparoscopic cholecystectomy (MLC) and natural orifice transluminal endoscopic surgery (NOTES). The aim of this review was to determine the role of these new minimally invasive approaches for elective laparoscopic cholecystectomy in the treatment of gallstone related disease. Current literature remains insufficient for the correct assessment of emerging techniques for laparoscopic cholecystectomy. None of these procedures has demonstrated clear benefits over conventional laparoscopic cholecystectomy. SILC cannot be currently recommended as it can be associated with an increased risk of bile duct injury and incisional hernia incidence. NOTES cholecystectomy is still experimental, although hybrid transvaginal cholecystectomy is gaining popularity in clinical practice. As it is standardized and almost identical to the standard laparoscopic technique, MLC could lead to limited benefits without exposing patients to increased postoperative complications, being therefore adoptable for routine elective cholecystectomy. Technical challenges of SILC and NOTES cholecystectomy could be addressed with the evolution of new surgical tools that need to catch up with the innovative minds of surgeons. Regardless the place of these approaches in the future, robotization may be necessary to impose them as standard treatment.

Key words: Cholecystectomy; Laparoscopy; Single-incision laparoscopic surgery; Minilaparoscopy; Natural orifice transluminal endoscopic surgery; Review

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: In an attempt to reduce the invasiveness of laparoscopic cholecystectomy, surgeons have developed single-incision laparoscopic cholecystectomy (SILC), minilaparoscopic cholecystectomy (MLC) and natural orifice transluminal endoscopic surgery (NOTES), which are hereby evaluated. SILC cannot be recommended as...
it can be associated with an increased risk of bile duct injury. NOTES cholecystectomy is still experimental, although hybrid transvaginal cholecystectomy is gaining popularity. As it is standardized and almost identical to the standard laparoscopic technique, MLC could lead to limited benefits without exposing patients to increased postoperative complications, being therefore adoptable for routine elective cholecystectomy.

INTRODUCTION

Laparoscopic cholecystectomy has become the procedure of choice for routine gallbladder removal and is currently the most commonly performed abdominal intervention in Western countries[11]. Compared to open cholecystectomy, laparoscopic cholecystectomy decreases postoperative pain and the need for postoperative analgesia, shortens hospital stay and return to full activity, with improved cosmesis and patient satisfaction[2]. The laparoscopic approach has gained acceptance not through organized and carefully conceived clinical trials but through commendation. Prospective randomized trials were late and irrelevant because advantages were already clear at the moment of their conception. Thus, laparoscopic cholecystectomy has received universal acceptance and is now considered the gold standard for the treatment of symptomatic cholecystolithiasis[3]. Moreover, trials have shown that day-case laparoscopic cholecystectomy was safe and successful, indicating that it should be offered to most patients in an outpatient basis[4].

Conventional laparoscopic cholecystectomy (CLC) is traditionally carried out with four ports (two 10-mm and two 5-mm ports). Since its introduction, investigators have attempted to achieve further improvements to the established technique, aiming to reduce the invasiveness of the procedure by decreasing the number and the size of the operating ports. The use of smaller incisions to complete the standard 4-port technique is broadly referred to as minilaparoscopic cholecystectomy (MLC). Needlescopic surgery is a subcategory of minilaparoscopic surgery using ports and instruments that are less than or equal to 3 mm in diameter[5]. In reduced trocar surgery, cholecystectomy is performed with less than 4 incisions, up to single incision laparoscopic cholecystectomy (SILC)[7]. More recently, in an attempt to eliminate all skin incision, surgeons have described cholecystectomy with an endoscope through a natural orifice then through internal incision of a intraperitoneal viscus, so-called natural orifice transluminal endoscopic surgery (NOTES)[8].

The aim of the current review is to determine the role of these new minimally invasive approaches for elective laparoscopic cholecystectomy in the treatment of gallstone related disease.

FOREWORD TO LITERATURE REVIEW

CLC is a well-established technique, with minimal conversion to open surgery and low incidence of complications[9], allowing day-case surgery as a standard procedure[4]. Therefore, it is unlikely that the trials assessing minimally invasive approaches can be powered to measure either reduction in the complication rate or in the length of hospital stay. Use of pain as the primary outcome can also be misleading, as the clinical significance of reduction in pain scores measured by visual analogue scale is unknown for laparoscopic cholecystectomy[9]. Moreover, patient’s perception of the cosmetic outcome after CLC is excellent[10,11], and improvements in cosmesis seems difficult to achieve when high rates of satisfaction exist with the established technique.

Another issue on the evaluation of these new minimally invasive approaches is the low quality of the existing studies[12,13], reporting mostly low samples with lack of blinding. There appears to be no standardization of the emerging techniques, limiting the relevance of a meta-analysis for comparison with CLC. In addition, a large majority of studies described follow-up of less than 12 mo, avoiding adequate interpretation of cosmetic outcome or incisional hemia rate[14,15].

It must be mentioned that existing studies comparing CLC to either SILC, MLC or NOTES cholecystectomy describe selected patients, including only uncomplicated cholecystolithiasis without previous upper abdominal laparotomy. At this time, no selection criteria for the optimal choice of minimally invasive technique have been defined in the literature.

SINGLE-INCISION LAPAROSCOPIC CHOLECYSTECTOMY

The first SILC was described in 1997 by Navarra et al[7] in a report on 30 selected patients with favorable outcomes. The technique spread slowly until more recent years, with publication of numerous prospective randomized controlled trials. However, these randomized control trials had several drawbacks[16], most reporting small sample size. Moreover, there is significant heterogeneity amongst surgical procedures defined as single-incision surgery. A wide variation of techniques is described with regard to the use of multiport device or separate trocars in one incision, the instrumentation, the method of gallbladder anchorage and the exposure of Calot’s triangle. Thus, there appears to be no standardization of the technique and comparison of SILC with standard multiport laparoscopic cholecystectomy suffers from this heterogeneity and lack a firm evidence base.
Proximity of instruments when used through a single incision results in inadequate retracting abilities and loss of triangulation, which may lead to suboptimal exposure of Calot’s triangle. Furthermore, clashing of instruments is common and complicates a smooth and meticulous dissection. In the literature, SILC is associated with a longer operative time than the standard technique. The addition of at least one instrument is necessary in 5% to 8.4% of SILC procedures.\(^\text{[12,17]}\)

Potential advantages of SILC were that it could reduce postoperative pain, allow earlier return to work, result in greater patient satisfaction, and especially improve cosmetic results. A total of 16 meta-analysis have compared the outcomes of SILC to conventional 4-ports laparoscopic cholecystectomy.\(^\text{[9,12,16–29]}\) The majority of these studies observed comparable postoperative pain\(^\text{[17,19,21–28]}\) and time to return to normal activities\(^\text{[16,29]}\), although 3 meta-analysis describe better postoperative pain scores within 24 h following SILC.\(^\text{[12,16,20]}\) Likewise, SILC does not seem to provide a better quality of life.\(^\text{[9,28]}\) Ten meta-analyses showed that SILC offered a better cosmetic score than CLC, three reported no difference, but all report short-time evaluation.\(^\text{[9,12,16,17,19,20,22–28]}\) Interestingly, recent studies assessed long-term cosmesis after 4-port laparoscopic cholecystectomy, showing excellent cosmetic outcome with this standardized technique.\(^\text{[10,11]}\) Moreover, these studies suggest that the umbilical port is the most related to wound-related issues such as pain, infection, or cosmesis dissatisfaction, problems that will not be eradicated with the use of a single-port approach.

Complication rates are low after laparoscopic cholecystectomy, thus no meta-analysis found statistical differences between single-incision and CLC. However, Allemann et al.\(^\text{[18]}\) specifically assessed the risk of bile duct injuries following these two procedures and observed a non statistically significant increase in the rate of bile duct injury (0.4%) and other biliary complications (1.6%) after SILC (0% and 0.5% respectively for CLC). A possible increased risk of port-site hernia after SILC is also difficult to evaluate, firstly because it is underestimated due to the lack of long-term results and secondly because of its low incidence. One meta-analysis\(^\text{[22]}\) showed a higher risk of incisional hernia after SILC, while others observed a trend towards a higher rate of incisional hernia after SILC without reaching statistical significance.\(^\text{[16,17,19]}\)

Moreover, although data regarding cost-effectiveness is scarce, a longer average operative time and the need for advanced surgical supplies could lead to potential added costs.\(^\text{[30,31]}\)

Finally, it appears that SILC is at present unable to preserve the well-established safe principles of laparoscopic cholecystectomy and could thus be associated with an increased risk of complications. No distinct benefit of SILC over CLC has been identified to date, with the arguable exception of cosmesis. Therefore, until further trials demonstrate the safety of SILC, it cannot currently be recommended as a routine procedure for laparoscopic cholecystectomy. Technical challenges of SILC could be eradicated with the evolution of novel instrumentation. Regardless the role of this approach in the future, robotization may be necessary in order to propose it as standard treatment.

**MINILAPAROSCOPIC CHOLECYSTECTOMY**

The benefits, safety and feasibility of MLC were established in small series at the late 1990s.\(^\text{[5,6,32,33]}\) Several prospective randomized controlled trials comparing MLC with CLC were published in the past decade, gathered in two systematic reviews\(^\text{[34,35]}\) and three meta-analyses\(^\text{[13,36,37]}\), although the latter include studies reporting less than 3-port laparoscopic cholecystectomy as minilaparoscopic approach.

By definition, MLC is carried out with the use of smaller diameter instruments than the 5-mm instruments used for CLC, a range of 1.7 to 3.5 mm being described. Most surgeons perform dissection of Calot’s triangle with a 10-mm laparoscope in the umbilical site, only reverting to a 2- or 3-mm laparoscope for clipping the cystic duct and cystic artery.\(^\text{[13,38–40]}\) Others reported using the 10-mm umbilical port for instrumental introduction and a 2- or 3-mm laparoscope.\(^\text{[34]}\) The only difference between MLC and CLC being the size of the incisions made and the instruments used, the surgical technique remains almost identical, offering satisfactory triangulation and retraction. In our experience, MLC can be easily standardized, with a relatively short learning curve. In our experience, MLC can be completed successfully in more than 80% of patients, the remaining being mostly converted to CLC.\(^\text{[34]}\) In addition, the rate of conversion to open approach is similar for minilaparoscopic and CLC.\(^\text{[13,35]}\)

Operative time can be increased when performing MLC, but various studies did not observe a statistically significant difference.\(^\text{[13,34,35]}\)

The available data in the literature suggest that the advantages of MLC over CLC are limited. There appears to be no advantage of MLC over CLC regarding postoperative pain, length of hospital stay and return to professional activities.\(^\text{[34–36]}\) The impact of minilaparoscopic approach on cosmetic outcomes is inconsistent, the evaluation being challenged by the heterogeneity of the studies,\(^\text{[13,34,37]}\) the excellent results of the conventional laparoscopic approach\(^\text{[10,11]}\) and the absence of a reliable objective evaluation scale. Postoperative morbidity is not affected by the minilaparoscopic approach,\(^\text{[34,35,37]}\) demonstrating that MLC is a safe alternative to CLC. Additional cost related to the acquisition of minilaparoscopic instruments and ports is not assessed in the literature. However, instruments and ports are reusable and can be employed routinely for other laparoscopic procedures, such as hernia repair.\(^\text{[41]}\)

Finally, it seems that the use of smaller incisions in selected patients could lead to limited benefits (mainly cosmetic), without exposing them to increased
occurrence of adverse events. MLC appears as a standardizable and safe procedure, suitable for routine elective cholecystectomy.

**NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC CHOLECYSTECTOMY**

A new evolution in the history of gallbladder surgery occurred in the past few years with the first cases of cholecystectomy by NOTES. After several reports in animal models\[42\], Marescaux et al\[8\] performed the first NOTES cholecystectomy in a patient using transvaginal access and a single 2-mm abdominal entry port. Subsequently, several teams joined the development of NOTES cholecystectomy. Pure NOTES techniques have been described, using transvaginal access in humans or transgastric and transcolonic approaches in animal models\[43-45\]. However, in clinical practice, the hybrid technique is widely used, aiming to further add benefits of decreased invasiveness. Hybrid transgastric cholecystectomy has been reported in small case series\[46\], but the procedure is still technically challenging with the currently existing instrumentation. To date, due to the established safety of colpotomy, the majority of clinical NOTES cholecystectomy is performed through hybrid transvaginal access (TVC), which is hereby analyzed.

The novelty of the technique and the lack of operative standardization lead to heterogeneity between the studies in the literature. However, a trend towards standardization appeared in the last years, as the majority of studies use a 5-mm umbilical incision for initial laparoscopic visualization and deployment of instrumentation, and a transvaginal incision for insertion of a laparoscope along with a grasping forceps and for extraction of the specimen. This technique is associated with longer operative time than CLC, and the conversion rate of TVC to CLC is estimated at 10%\[47\].

To date, three randomized control trials have been published, comparing transvaginal hybrid cholecystectomy to conventional\[47,48\] or needlescopic\[49\] laparoscopic cholecystectomy, along with one meta-analysis\[50\]. The proponents of NOTES cite reduced postoperative pain as an advantage of TVC over CLC. However, a recent meta-analysis showed a non-significant reduction in postoperative pain but a significant decrease in time for return to normal activities\[50\]. Another clear benefit of TVC is improved cosmesis. Importantly, there appears to be no significant difference in postoperative complications or rate of bile duct injury between TVC and CLC in these trials, conducted in centers of excellence and on selected patients\[50\]. Moreover, several studies reported no dyspareunia or difference in return to sexual activity between TVC and CLC groups after short-term follow-up\[47-49\].

Therefore, the hybrid transvaginal technique is a promising minimally invasive approach for cholecystectomy, though it demands further standardization. Despite the lack of high-powered studies, TVC seems safe in selected patients when performed by skilled surgeons. Furthermore, it has a similar morbidity to CLC and may be associated with decreased postoperative pain and time for return to normal activities. The major drawback of TVC is its applicability to only half of the patients with symptomatic cholecystolithiasis. In addition, even among women, the use of the transvaginal approach should be evaluated with regards to potential risks on subsequent fertility and discomfort during sexual intercourse.

Impediments for the adoption of other types of NOTES cholecystectomy include skepticism on transgressing and closing mucosal barriers\[51\], but also the lack of technological evolution of surgical tools and platforms that need to catch up with the innovative minds of surgeons.

**CONCLUSION**

Technical innovation within surgery is laudable and the progress that results is generally a consequence of the quest to achieve optimum outcomes for patients. To date, current literature remains insufficient for the correct assessment of new minimally invasive approaches for laparoscopic cholecystectomy. None of these emerging techniques has demonstrated clear benefits over CLC. SILC cannot be currently recommended as it appears to be associated with an increased risk of bile duct injuries and a potential for increased incisional hema incidence. NOTES cholecystectomy is still experimental, although hybrid TVC is gaining popularity in clinical practice. As it is standardized and almost identical to the conventional technique, MLC could provide limited benefits without exposing patients to increased postoperative complications, and is therefore suitable for routine elective cholecystectomy.

**REFERENCES**

1. Litwin DE, Cahan MA. Laparoscopic cholecystectomy. Surg Clin North Am 2008; 88: 1295-1313, ix [PMID: 18992596 DOI: 10.1016/j.suc.2008.07.005]
2. McMahon AJ, Russell IT, Baxter JN, Ross S, Anderson JR, Morran CG, Sunderland G, Galloway D, Ramsay G, O’Dwyer Pj. Laparoscopic versus minilaparotomy cholecystectomy: a randomised trial. Lancet 1994; 343: 135-138 [PMID: 7904002 DOI: 10.1016/S0140-6736(94)90932-6]
3. Gallstones and laparoscopic cholecystectomy. NIH Consens Statement 1992; 10: 1-28 [PMID: 1301217]
4. Gurusamy K, Jumankar S, Farouk M, Davidson BR. Meta-analysis of randomized controlled trials on the safety and effectiveness of day-case laparoscopic cholecystectomy. Br J Surg 2008; 95: 161-168 [PMID: 18196561 DOI: 10.1002/bjs.6105]
5. Yuan RH, Lee WJ, Yu SC. Mini-laparoscopic cholecystectomy: a cosmetically better, almost scarless procedure. J Laparoendosc Adv Surg Tech A 1997; 7: 205-211 [PMID: 9448114 DOI: 10.1089/ lap.1997.7.205]
6. Ngoi SS, Goh P, Kok K, Kum CK, Cheah WK. Needlescopic or minislit cholecystectomy. Surg Endosc 1999; 13: 303-305 [PMID: 10064772 DOI: 10.1007/s004649900971]
7. Navarra G, Pozza E, Oechtonorelli S, Carcoforo P, Donini I. One-
wound laparoscopic cholecystectomy. Br J Surg 1997; 84: 695 [PMID: 9171771]

Mareault J, Dallermagne B, Perretta S, Wattiez A, Mutter D, Cournaras D. Surgery without scars: report of transluminal cholecystectomy in a human being. Surg Endosc 2007; 112: 823-826; discussion 826-827 [PMID: 17875836 DOI: 10.1001/archsurg.142.9.823]

Gurusamy KS, Vaughan J, Rossi M, Davidson BR. Fewer-than-four ports versus four ports for laparoscopic cholecystectomy. Cochrane Database Syst Rev 2014; 2: CD007109 [PMID: 24558020 DOI: 10.1002/14651858.CD007109.pub2]

Bignell M, Hindmarsh A, Nageswaran H, Mothe B, Jenkins K, Mahon D, Rhodes M. Assessment of cosmetic outcome after laparoscopic cholecystectomy among women 4 years after laparoscopic cholecystectomy: is there a problem? Surg Endosc 2011; 25: 2574-2577 [PMID: 21424204 DOI: 10.1007/s00464-011-1589-1]

Monkhouse SJ, Court EL, Beard LA, Bunni J, Burgess P. A retrospective wound review of standard four-port laparoscopic cholecystectomy: is there need for single-port laparoscopic surgery? Surg Endosc 2012; 26: 255-260 [PMID: 21858572 DOI: 10.1007/s00464-011-1863-2]

Arezzo A, Scozzari G, Famiglietti F, Passera R, Morino M. Is single-incision laparoscopic cholecystectomy safe? Results of a systematic review and meta-analysis. Surg Endosc 2013; 27: 2293-2304 [PMID: 23355161 DOI: 10.1007/s00464-012-2763-9]

Thakur V, Schlactha CM, Jayaraman S. Minilaparoscopic versus conventional laparoscopic cholecystectomy: a systematic review and meta-analysis. Ann Surg 2011; 253: 244-258 [PMID: 21138348 DOI: 10.1097/SLA.0b013e318207f52]

Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. Nature 2008; 453: 314-321 [PMID: 18480812 DOI: 10.1038/nature06703]

Bunting DM. Port-site hernia following laparoscopic cholecystectomy. JSLS 2010; 14: 490-497 [PMID: 21605509 DOI: 10.4293/108680810xs12924466007728]

Geng L, Sun C, Bai J. Single incision versus conventional laparoscopic cholecystectomy outcomes: a meta-analysis of randomized controlled trials. PLoS One 2013; 8: e76530 [PMID: 24098752 DOI: 10.1371/journal.pone.0076530]

Trastulli S, Cicori R, Desiderio J, Guarino S, Santoro A, Parisi A, Noya G, Boselli C. Systematic review and meta-analysis of randomized clinical trials comparing single-incision versus conventional laparoscopic cholecystectomy. Br J Surg 2013; 100: 191-208 [PMID: 23161281 DOI: 10.1002/bjs.8937]

Allemann P, Demartines N, Schäfer M. Remains of the day: biliary complications related to single-port laparoscopic cholecystectomy. World J Gastroenterol 2014; 20: 843-851 [PMID: 24574757 DOI: 10.3748/wjg.v20.i3.843]

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: 1618-1628 [PMID: 22588041 DOI: 10.1007/s11605-012-1906-6]

Hao L, Liu M, Zhu H, Li Z. Single-incision versus conventional laparoscopic cholecystectomy in patients with uncomplicated gallbladder disease: a meta-analysis. Surg Laparosc Endosc Percut Tech 2012; 22: 487-497 [PMID: 23283374 DOI: 10.1097/SLQ.0b013e3182685d0a]

Markar SR, Karthikesalingam A, Thrumurthy S, Muirhead L, Kinross J, Paraseva P. Single-incision laparoscopic surgery (SILS) vs. conventional multiport cholecystectomy: systematic review and meta-analysis. Surg Endosc 2012; 26: 1205-1213 [PMID: 22173546 DOI: 10.1007/s00464-011-2051-0]

Milas M, Devedija S, Tkaljulja V. Single incision versus standard multiport laparoscopic cholecystectomy: up-dated systematic review and meta-analysis of randomized trials. Surgeon 2014; 12: 271-289 [PMID: 24525971 DOI: 10.1016/j.surge.2014.01.009]

Pisano 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;
Gaillard M et al. Minimally invasive cholecystectomy

[PMID: 15791373 DOI: 10.1007/s00464-003-8247-1]

40 Saad S, Strassel V, Sauerland S. Randomized clinical trial of single-port, minilaparoscopic and conventional laparoscopic cholecystectomy. Br J Surg 2013; 100: 339-349 [PMID: 23188563]

41 Wada H, Kimura T, Kawabe A, Sato M, Miyaki Y, Tochikubo J, Inamori K, Shiyama N. Laparoscopic transabdominal preperitoneal inguinal hernia repair using needlescopic instruments: a 15-year, single-center experience in 317 patients. Surg Endosc 2012; 26: 1898-1902 [PMID: 22223115 DOI: 10.1007/s00464-011-2122-2]

42 Park PO, Bergström M, Ikeda K, Fritscher-Ravens A, Swain P. Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos). Gastrointest Endosc 2005; 61: 601-606 [PMID: 15812420 DOI: 10.1016/S0016-5107(04)02774-9]

43 Gumbs AA, Fowler D, Milone L, Evanko JC, Ude AO, Stevens P, Bessler M. Transvaginal natural orifice transluminal endoscopic surgery cholecystectomy: early evolution of the technique. Ann Surg 2009; 249: 908-912 [PMID: 19474690 DOI: 10.1097/SLA.0b013e3181e3802c2]

44 Asakuma M, Perretta S, Allmann P, Cahill R, Duflémagne B, Tanigawa N, Marescaux J. Multimedia article. Peroral dual scope NOTES cholecystectomy in porcine model (with video). Surg Endosc 2010; 24: 2624-2625 [PMID: 20354867 DOI: 10.1007/s00464-010-0992-3]

45 Auyang ED, Hungness ES, Vaiziri K, Martin JA, Soper NJ. Natural orifice transluminal endoscopic surgery (NOTES): dissection for the critical view of safety during transcolonic cholecystectomy. Surg Endosc 2009; 23: 1117-1118 [PMID: 19263107 DOI: 10.1007/s00464-009-0407-5]

46 Salinas G, Saavedra L, Agurto H, Quispe R, Ramirez E, Grande J, Tamayo J, Sánchez V, Málaga D, Marks JM. Early experience in human hybrid transgastric and transvaginal endoscopic cholecystectomy. Surg Endosc 2010; 24: 1092-1098 [PMID: 19997754 DOI: 10.1007/s00464-009-0733-7]

47 Borchert DH, Fedelein M, Fritz-Büttnner F, Burghardt J, Liersch-Löhn B, Atas Y, Müller V, Rückbeil O, Wagenpfeil S, Gräber S, Gellert K. Postoperative pain after transvaginal cholecystectomy: single-center, double-blind, randomized controlled trial. Surg Endosc 2014; 28: 1886-1894 [PMID: 24464385 DOI: 10.1007/s00464-013-3409-2]

48 Noguera JF, Cuadrado A, Dolz C, Olea JM, García JC. Prospective randomized clinical trial comparing laparoscopic cholecystectomy and hybrid natural orifice transumbilical endoscopic surgery (NOTES) (NCT00835250). Surg Endosc 2012; 26: 3435-3441 [PMID: 22648123 DOI: 10.1007/s00464-012-2359-4]

49 Bulian DR, Knuth J, Cerasani N, Sauerwald A, Lefering R, Heiss MM. Transvaginal/transumbilical hybrid--NOTES--versus 3-trocar needleless cholecystectomy: short-term results of a randomized clinical trial. Ann Surg 2015; 261: 451-458 [PMID: 24108196 DOI: 10.1097/SLA.0000000000000218]

50 Sodergren MH, Markar S, Pucher PH, Badran IA, Jiao LR, Darzi A. Safety of transvaginal hybrid NOTES cholecystectomy: a systematic review and meta-analysis. Surg Endosc 2015; 29: 2077-2090 [PMID: 25424364 DOI: 10.1007/s00464-014-3915-x]

51 Sodergren MH, Pucher P, Clark J, James DR, Sackett J, Matar N, Teare J, Yang GZ, Darzi A. Disinfection of the Access Orifice in NOTES: Evaluation of the Evidence Base. Diagn Ther Endosc 2011; 2011: 245175 [PMID: 21785559 DOI: 10.1155/2011/245175]

P- Reviewer: Sandblom G  S- Editor: Qiu S  L- Editor: A  E- Editor: Lu YJ
