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Australia and New Zealand Horizon Scanning Network

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AND THE GOVERNMENT OF NEW ZEALAND

Horizon scanning technology prioritising summary

Natural orifice transluminal endoscopic surgery (NOTES): cholecystectomy

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**Australian
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PRIORITISING SUMMARY

REGISTER ID S000101

NAME OF TECHNOLOGY NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC SURGERY (NOTES): TRANSVAGINAL CHOLECYSTECTOMY

PURPOSE AND TARGET GROUP PATIENTS WITH SYMPTOMATIC CHOLELITHIASIS

STAGE OF DEVELOPMENT (IN AUSTRALIA)

- | | |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- Yes
 No
 Not applicable

INTERNATIONAL UTILISATION

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United States	✓		
United Kingdom	✓		
India	✓		
Germany	✓		

IMPACT SUMMARY

Natural orifice transluminal endoscopic surgery (NOTES) is an emerging surgical procedure which may potentially be less invasive than laparoscopic surgery.

BACKGROUND

In the last few years, minimally invasive surgical access techniques have garnered substantial interest among patients and the medical community, due to the promise of less pain, shorter hospital stays, lower complication rates and better cosmetic results. It is not

surprising therefore that there has been substantial research into the development of new techniques to further reduce the invasiveness of surgery. NOTES represents a new approach to access the peritoneum that is being evaluated as a complement to, or even a replacement for, laparoscopic and open abdominal procedures. Recently, NOTES has attracted widespread interest and in some cases has been claimed to be a defining paradigm shift in modern surgery (McGee et al 2006). The procedure was first described in 2005, where a flexible endoscope is passed through a natural orifice, such as the mouth, vagina or rectum to perform intra-abdominal procedures. The technique has been touted as less invasive than laparoscopic surgery by virtually eliminating incision-related complications such as scars, hernias, pain, adhesions and surgical site infections (McGee et al 2006, Merrifield et al 2006). To date, the best portal for access is not yet determined, but all have been evaluated in various animal studies (Box et al 2009). However, despite the enthusiasm among its proponents, there are major concerns with regards to transgastric approaches to NOTES as improper gastric closure may lead to postoperative leakage and peritonitis. Currently, there are substantial efforts to develop a safe closure device to improve the safety profile of transgastric NOTES.

In contrast to transgastric NOTES, transvaginal NOTES has the potential advantages of easy access and closure under direct vision. The experience gained from experimental settings has suggested that with current available technology, procedures involving in the upper part of the abdomen are better undertaken via natural orifices located in the pelvis (Pearl and Ponsky 2008). Furthermore, transvaginal access to the abdominal cavity is not a new concept to surgeons, as it has been used occasionally by general surgeons to extract large specimens and by gynaecologists to perform diagnostic and therapeutic procedures. At the time of writing, one of the most common applications of transvaginal NOTES is cholecystectomy, which will be discussed further in this summary.

The first transvaginal cholecystectomy in a human being was carried out in 2003 at the Mount Sinai Hospital by Dr. Tsin, utilising rigid laparoscopic instruments and minimal abdominal assistance. From 2007, several research groups have described different techniques for transvaginal cholecystectomy using flexible endoscopes with minimal laparoscopic assistance (Pugliese 2009). In virtually all human trials to date, a hybrid procedure was adopted where the operators utilised a fusion of minilaparoscopy and NOTES (Noguera et al 2009).

CLINICAL NEED AND BURDEN OF DISEASE

Cholecystectomy is one of the most common hospital procedures in Australia, with a total of 46,816 cholecystectomy procedures performed between 2005 and 2006 (all hospitals). Of these, laparoscopic cholecystectomy accounted for 40,557 procedures (Australian Institute of Health and Welfare 2008). The Medicare Benefits Schedule claims for services that are performed by a registered provider, but not including services provided by hospital doctors to public patients in public hospitals, indicated that laparoscopic procedures were performed more commonly than open procedures, with 19207 claims for laparoscopic cholecystectomy (item number 30445) and 1026 claims for

open cholecystectomy (item number 1026) between 2007 and 2008 (Medicare Australia 2009). The average length of hospital stay for public or private hospital patients undergoing laparoscopic cholecystectomy (without closed common duct exploration or catastrophic or severe complications or comorbidities) was 1.8 days (Australian Institute of Health and Welfare 2008).

DIFFUSION

Transvaginal cholecystectomy is currently at the investigational stage and has been conducted on a few patients in different centres, including Spain, the United States, Germany and Italy. In practically all of these cases, the operation was performed with the help of at least one abdominal trocar. The German Society of General and Visceral Surgery has registered over 300 NOTES operations, almost all are transvaginal cholecystectomies (Zornig et al 2009). There is no indication that this procedure is being performed in Australia or New Zealand.

Our searches revealed 8 planned/ongoing clinical trials on transvaginal cholecystectomy. Brief details of these trials are provided below:

- Transvaginal cholecystectomy versus laparoscopic cholecystectomy in patients with biliary colic (ClinicalTrials.gov identifier: NCT00963950). Enrolling participants by invitation only, estimated completion date: August 2012.
- Natural orifice transluminal endoscopic surgery (NOTES) transvaginal cholecystectomy (ClinicalTrials.gov identifier: NCT00984100). Currently recruiting patients, estimated completion date: January 2011.
- Natural orifice transluminal endoscopic surgery: Laparoscopic-assisted transvaginal cholecystectomy (ClinicalTrials.gov identifier: NCT00910325). Currently recruiting patients, estimated completion date: December 2009.
- NOTES transvaginal cholecystectomy and appendectomy (ClinicalTrials.gov identifier: NCT00552162). Not yet open for patient recruitment, estimated completion date: July 2009.
- Trial comparing laparoscopic cholecystectomy and hybrid natural orifice transluminal surgery (ClinicalTrials.gov identifier: NCT00835250). Currently recruiting patients, estimated completion date: June 2010.
- Minimally invasive surgery: using natural orifices (NOTES) (ClinicalTrials.gov identifier: NCT00530998). Currently recruiting patients, estimated completion date: September 2010.
- Laparoscopic transvaginal hybrid cholecystectomy: a prospective data collection (ClinicalTrials.gov identifier: NCT00940264). Currently recruiting patients, estimated completion date: not stated.

- A trial to evaluate natural orifice transvaginal endoscopic cholecystectomy with laparoscopic assistance (NOTES) (ClinicalTrials.gov identifier: NCT00889928). Currently recruiting patients, estimated completion date: January 2010.

COMPARATORS

The comparative procedures for transvaginal cholecystectomy are:

- open cholecystectomy (now reserved for special situations only);
- small-incision open cholecystectomy;
- conventional laparoscopic cholecystectomy;
- single incision laparoscopic cholecystectomy.

SAFETY AND EFFECTIVENESS ISSUES

Study description

Three case series studies have been selected for inclusion in this summary based on cohort size and quality of the study.

The retrospective case series study by Zornig et al (2009) reported on the safety and effectiveness of transvaginal NOTES in 68 patients treated for symptomatic cholecystolithiasis from June 2007 to June 2008. Eleven of these patients had acute or chronic inflammation of the bladder. The mean age was 50 years (range: 16-76 years) and mean BMI was 25.4 kg/m² (range: 16-35 kg/m²). A total of 26 patients (38%) have had previous abdominal operations. Patients were interviewed 3 to 10 months after surgery (mean: 5 months). It is important to note that a hybrid NOTES procedure was utilised, as an abdominal trocar was used during the operation.

The second case series study was performed by Pugliese et al (2009) between July 2007 and May 2009 and involved 18 patients (mean age: 54 years; range: 32-67 years) with symptomatic cholelithiasis. Mean BMI was 28 kg/m², however four patients had BMIs >30 kg/m². Unlike Zornig et al (2009), patients with previous major abdominal surgery were excluded. In addition, patients had to be free of gynaecologic disease, not pregnant and have no intention to plan a pregnancy in the early postoperative period. Patients with ultrasonographic features of cholecystitis were also excluded. As with Zornig et al (2009), a hybrid procedure was utilised (Pugliese et al 2009). It is unclear if patients were enrolled in a consecutive manner. Dissection was conducted in the first 4 cases by a round tip unipolar electrode introduced through an endoscope from the vagina. The last 14 cases underwent dissection with an ultrasonic scalpel introduced via the 5mm abdominal port. Mean follow up duration was 12 months (Pugliese et al 2009).

The final study was conducted by Noguera et al (2009), where a prospective series of 15 consecutive patients underwent a hybrid transvaginal NOTES procedure for symptomatic cholelithiasis. The mean age of patients was 39.7 years (range 22-47 years); no data on BMI was presented. Patients selected for inclusion had to fulfil several criteria: no gynaecological conditions that could complicate the procedure, perforated hymen and

agreement to abstain from sex for 2 weeks after the procedure. Patients were followed-up for a mean of 62 days (range: 30-90 days)

Safety and Effectiveness

Zornig et al (2009) noted that three patients had severe adhesions in the lesser pelvis during diagnostic laparoscopy. These patients were converted to conventional laparoscopic cholecystectomy. There were no intraoperative complications, but in three cases (4.4%) an additional abdominal trocar was necessary. The in-hospital postoperative course was uneventful in all patients. The authors reported that patients complained of well-known consequences of pneumoperitoneum, but no specific examples were presented. None of the patients reported pain as a result of vaginal manipulation. At 1-week follow up (n=59), none of the patients had any complaints, and physical examination including vaginal endosonography revealed no pathological findings. However, one patient who did not undergo the 1-week follow up examination presented with an abscess in the pouch of Douglas 3 weeks after surgery. When patients were interviewed 3 to 10 months after surgery (mean: 5 months; n=68), there were no complaints regarding the procedure. A total of 48 patients (70.5%) had sexual intercourse after the operation (mean time not stated) and did not notice any changes (Zornig et al 2009).

Pugliese et al (2009) reported no intraoperative complications and no conversions to open or laparoscopic cholecystectomy. The hybrid transvaginal NOTES technique was successfully employed in four obese patients (BMI>30). However, the performance of colpotomy was difficult in these patients due to the thickness of the properitoneal fat layer. There were no cases of rectal injury or colpotomy-related complications. There was one case of biliary leak (4th patient in series, BMI=45) after dissection with the unipolar electrode. This complication required endoscopic retrograde pancreaticholangiography. Complete healing was achieved in 7 days and the patient was discharged 11 days after surgery. In contrast, there were no biliary complications when dissection was performed with the ultrasonic scalpel. Analysis revealed that patient morbidity was significantly higher for those who underwent unipolar electrode dissection compared with those who received ultrasonic scalpel dissection (p<0.005), however the validity of this was limited by the small patient cohort. No patient referred pain at the vaginal level. Meanwhile, the mean values for abdominal pain were 3 (range: 1-4), 2 (range: 0-3), 1 (range: 0-2) and 0 at 4, 12, 24 and 48 hours after surgery, respectively. Several patients experienced shoulder pain that resolved spontaneously within 12 hours. Oral feeding resumed the evening of the operation and the use of pain relievers was minimal (no data provided). No specific treatment was required for colpotomy and there were no colpotomy-related problems or discomfort during the postoperative period. In addition, there were no complaints of dyspareunia or genital infections after intercourse. At a mean follow up of 12 months (range: 1-22 months), there were no cases of sexual or vaginal discomfort.

Noguera et al (2009) reported that 2 patients (2/15, 13%) had adhesions that needed to be severed, while 2 other patients (13%) had ovarian cysts that were not suspected preoperatively but did not complicate the procedure. The only complication was mild

haematuria that resolved spontaneously within 12 hours. No surgical wound infections were observed.

Zornig et al (2009) reported that the overall mean operative time was 51 minutes (range: 30-100 minutes). The mean operative time for the last 40 cases was 47 minutes (range: 30-85 minutes). This did not appear to be substantially different to the investigators' previous experience with conventional laparoscopic cholecystectomy (mean 43 minutes; n=430). Pugliese et al (2009) reported that the average duration for the whole NOTES procedure was 75 minutes (range: 40-190 minutes). When conducted with unipolar electrode dissection, mean operating time was 148 minutes (range: 140-190 minutes). This was substantially longer compared with patients who underwent ultrasonic scalpel dissection, with a mean operating time of 53 minutes (range: 40-60 minutes) (p<0.01). Overall hospital stay was 2.2 days (range: 1-11 days). Noguera et al (2009) reported that all patients (n=15) were discharged within 36 hours after surgery, with 2 patients returning home on the same day. Mean length of stay was 0.8 days and mean procedure duration was 89.62 minutes (range 48-121 minutes).

COST IMPACT

There are no cost effectiveness studies on transvaginal cholecystectomy. However, the evidence to date suggests that the overall operative time can match conventional laparoscopic cholecystectomy (Zornig et al 2009). There are no strict requirements for the use of new devices during the procedure; however, it is likely that new technologies will be introduced to perform NOTES more efficiently as the technique matures, which will add to the overall cost. No clear comparisons with regards to patient recovery and discharge time have been performed.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

As NOTES is a rapidly evolving technique, there are no standardised approaches for the procedure. As a result of this, it is difficult to perform valid comparisons between studies.

Surgeons attempting this technique must be experienced with performing biliary laparoscopic surgery and familiar with the use of minilaparoscopic instruments.

SUMMARY OF FINDINGS

The overall evidence on NOTES transvaginal cholecystectomy remains limited. The evidence retrieved indicates that the procedure is feasible; however, there is insufficient data to determine if it is comparable to conventional laparoscopic cholecystectomy. In addition, it is important to note that in all three included studies, the investigators performed hybrid NOTES techniques which utilised an abdominal trocar. Transvaginal

cholecystectomy appears to be safe and does not appear to affect sexual function after a 2 week recovery period.

Hybrid cholecystectomy is becoming the only viable and safe clinical application at this time for a NOTES approach to the gallbladder. In addition, hybrid techniques also provide a bridge between laparoscopy and pure NOTES, that allows researchers and clinicians to expand their experience before pure transluminal techniques are utilised. Our search indicates that interest in transvaginal NOTES is likely to increase over time and this is reflected by the number of clinical trials due for completion in 2010.

HEALTHPACT ACTION

Additional studies are required before transvaginal NOTES can be performed routinely. Considering the interest and the potentially rapid diffusion of this technique, it is recommended that transvaginal cholecystectomy is monitored for 12 months for new evidence.

NUMBER OF STUDIES INCLUDED

Total number of studies	3
Level IV intervention evidence	3

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SEARCH CRITERIA TO BE USED

Natural orifice cholecystectomy, transvaginal OR trans vaginal, NOTES cholecystectomy.