NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endoscopic radical inguinal lymphadenectomy

Treating cancer using keyhole removal of lymph nodes in the groin

Inguinal lymph nodes are removed in the routine management of genital or anal cancer, and melanoma of the leg. This procedure aims to reduce discomfort, scarring and complications associated with the procedure by using an endoscopic device and small incisions. Robotic control may also be used.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in September 2010.

Procedure name

- Endoscopic radical inguinal lymphadenectomy

Specialty societies

- British Association of Urological Surgeons
- British Association of Surgical Oncology
- British Association of Plastic Reconstructive and Aesthetic Surgeons

Description

Indications and current treatment

Patients with penile, vulval, or anal cancer, or melanoma of the leg may require resection of inguinal lymph nodes as part of their management.

The standard method for inguinal lymph node resection (lymphadenectomy) is an open procedure requiring an incision in the groin. An endoscopic approach has the theoretical advantages of reduced postoperative pain, morbidity and recovery time compared with the open procedure.

What the procedure involves

The procedure is performed with the patient under general anaesthesia and in the supine position. Ultrasound guidance may be used as part of the procedure to help anatomical landmark and lymph node identification. Three to four 5-mm ports are inserted into the femoral triangle using small incisions. The working space is insufflated with CO_2. Endoscopic instruments, including a camera, are used to visualise main landmarks such as the saphenous vein, the femoral vein and artery, the spermatic cord, the medial adductor longus muscle, the lateral sartorius muscle and the superior inguinal ligament. Instruments are used to dissect the required lymph nodes. Resected nodes are placed in an impermeable sac and removed through one of the port sites. Resection of the saphenous vein may also be required. A suction drain is normally inserted at the end of the procedure.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endoscopic radical inguinal lymphadenectomy. Searches were conducted of the following databases, covering the period from their commencement to 24 September 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with cancer
Intervention/test	Endoscopic radical inguinal lymphadenectomy
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 30 patients from 1 non-randomised controlled trial[1], 2 case series[2,3] and 2 case reports[4,5].

Table 2 Summary of key efficacy and safety findings on endoscopic radical inguinal lymphadenectomy

Abbreviations used: ml, millilitre

Study details

Tobias-Machado M (2008)[1]

Non-randomised comparative study

Brazil
Recruitment period: 2003–6

Study population: patients with penile cancer who had undergone penectomy 1 month previously.

n =**15 patients (30 limbs [20 vs 10])**
Age: not reported
Sex: 100% male (15/15)

Patient selection criteria: The first 10 patients were those with non-palpable lymph nodes and high risk pathologic features observed in penectomy specimen. These patients had an endoscopic procedure on one side and the open procedure on the other side. The inclusion criteria were then expanded to include patients with small volume, clinically node-positive disease. These last 5 patients had the endoscopic procedure on both sides.

Technique: video endoscopic inguinal lymphadenectomy vs open lymphadenectomy

Follow-up: **31.93 months**

Conflict of interest/source of funding: not reported

Key efficacy findings

Number of patients analysed: **30 limbs (20 vs 10)**

	Endoscopic group (n = 20)	Open group (n = 10)	p value
Mean operative time (minutes)	120	92	0.0002
Mean time drainage system used (< 50ml per day)	4.9 days	6.4 days	0.008
Mean number of inguinal lymph nodes retrieved	10.75	9.7	0.3
% histologically positive nodes	1.9% (4/215)	1.03% (1/97)	0.509

	Endoscopic only patients (n = 5)	Endoscopic + open patient (n = 10)	p value
Mean length of hospital stay	24 hours	6.4 days	< 0.001
Mean time to return to usual activities	14 days	21 days	0.032

Key safety findings

	Endoscopic group (n = 20)	Open group (n = 10)	p value
Any complication	20% (4/20)	70% (7/10)	0.015
Skin related events	5% (1/20) (small skin necrosis)	50% (5/10)* 3 patients had limited skin necrosis with no need for skin graft ,1 wound infection and 1 area of cellulitis	0.009
Lymphatic complications	10% (2/20)‡ 1 patient with lymphorrhoea and 1 patient with unilateral limited lymphocele requiring 3 evacuation punctures	20% (2/10) 1 patient with chronic lymphoedema and 1 patient with lymphocele with spontaneous regression in 2 months.	0.58
Haematoma (clinical resolution after 10 days)	5% (1/20)	0	1.00

No information on timing or treatment of complications was reported unless otherwise stated.

Comments

Follow-up issues:

- Completeness of follow-up was not reported.

Study design issues:

- Single-centre prospective study.

Study population issues:

- All patients with positive lymph nodes underwent subsequent laparoscopic extended pelvic lymphadenectomy.
- No conversions from the endoscopic to the open procedure were required.

Abbreviations used: ml, millilitre

Study details	Key efficacy findings	Key safety findings	Comments
Sotelo R (2007)[2] **Case series** Brazil, Ecuador and Canada (?) Recruitment period: not reported Study population: patients with clinical stage $T_2N_{0-3}M_0$ penile carcinoma who have had a partial penectomy. n = **8** Age: 56 years (mean) Sex: 100% (8/8) male Patient selection criteria: see above. Technique: endoscopic inguinal lymphadenectomy (including removal of lymph nodes along the saphenous vein and arch) Follow-up: **not reported** Conflict of interest/source of funding: not reported	Number of patients analysed: **8** Median operative time: 91 minutes Mean number of lymph nodes retrieved: 9	Lymphoceles: 3 patients (all had undergone saphenous vein ligation). No information on timing or treatment of complications was reported unless otherwise stated.	**Study design issues**: • Unclear if it was a multicentre study. • Doppler ultrasound mapping of inguinal lymph nodes and the saphenous vein was undertaken before the procedure was performed. • All patients received a 4-week course of antibiotics before surgery. • No information on follow-up, recurrence or length of stay in hospital was given.

Abbreviations used: ml, millilitre

Study details	Key efficacy findings	Key safety findings	Comments
Delman KA (2010)[3] **Case series** USA Recruitment period: not reported Study population: patients with metastatic melanoma n = **5** Age: 57 years (median) Sex: 40% (2/5) male Patient selection criteria: patients with sentinel node-positive disease or clinically detected metastases. Technique: endoscopic inguinal lymphadenectomy. Follow-up: **not reported** Conflict of interest/source of funding: not reported	Number of patients analysed: **5** Median operative time: 180 minutes Mean number of lymph nodes retrieved: 9 Median length of stay in hospital: 1 day* Length of time drainage system used: 8 days *one patient had concurrent pelvic lymphadenectomy and remained in hospital for 5 days. Recurrence: 2 patients. 1 patient had recurrence with multiple visceral metastases after the procedure. Another patient had recurrence in the limb outside of the nodal basin in an in-transit node, which was subsequently resected.	Estimate blood loss of < 100ml for each procedure Cellulitis: 2 patients. 1 of these patients had a severe infection in the site of prior sentinel node biopsy. No information on timing or treatment of complications was reported unless otherwise stated.	**Follow-up issues**: • All patients completed follow-up to discharge. **Study design issues**: • Single-centre study. **Study population issues**: • 60% (3/5) had ulcerated melanoma.

Abbreviations used: ml, millilitre

Study details	Key efficacy findings	Key safety findings	Comments
Josephson DY (2009)[4] **Case report** USA Recruitment period: not reported Study population: patient with Stage T3 moderate to poorly differentiated squamous cell carcinoma of the penis who had undergone a partial penectomy. Palpable and radiographic bilateral adenopathy persisted at 1 month postpenectomy and antibiotic therapy. n = **1** Age:37 years Sex: male Patient selection criteria: see above Technique: Robotic-assisted endoscopic inguinal lymphadenectomy (using the da Vinici S robotic system). Surgical stockings worn after procedure. 2 procedures were performed with a 3-week gap between them. Follow-up: **2 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **1** See table below	Estimated blood loss: 1st procedure:100 ml 2nd procedure: 50 ml At 2 months the patient had not experienced any wound complications or lower extremity lymphoedema.	

	1st procedure	2nd procedure (contralateral extremity)
Operative time	120 minutes	130 minutes
Number of lymph nodes retrieved	10 (6 superficial, 4 deep) None showed metastatic involvement	9 (5 superficial, 4 deep)
Mean drainage output per day	< 50 ml	< 50 ml
Length of time drainage system used	10 days	2 weeks
Discharge details	Patient was discharged the morning after the procedure with 1 week course of antibiotic therapy.	Patient was discharged on day 1.

Abbreviations used: ml, millilitre

Study details	Key efficacy findings	Key safety findings	Comments
Tobias-Machado M (2006)[5] **Case report** Brazil Recruitment period: not reported Study population: patient with grade 3 squamous cell carcinoma of the penis without palpable nodes who had undergone a partial penectomy. Pathology revealed pT2NxMo with corpus cavernosum invasion. n = **1** Age: 40 years Sex: male Patient selection criteria: see above Technique: prophylactic bilateral inguinal lymphadenectomy. Video endoscopic inguinal lymphadenectomy was used on at the right side and open inguinal lymphadenectomy on t he left side. Follow-up: **25 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **1** See table below Patient was discharged after 10 days with antibiotic therapy. No disease progression noted at 25 months follow-up. When asked about how he felt about both surgeries, the patient chose the endoscopic approach as the less morbid of the 2 procedures.	No complications reported on the endoscopic side. A small area of skin necrosis occurred on the open side which was managed conservatively with debridement and ceftriaxon without the need for a skin graft. No information on timing or treatment of complications was reported unless otherwise stated.	First case of video endoscopic inguinal lymphadenectomy. It is unclear if this patient was included in the later Tobias-Machado (2008) case series reported in table 2.

	Endoscopic (right side)	Open (left side)
Operative time	130 minutes	90 minutes
Number of lymph nodes retrieved	8 (0 showed positivity on pathology)	7 (0 showed positivity on pathology)
Mean drainage output	80 ml	120 ml
Length of time drainage system used	5 days	6 days

Efficacy

Lymph nodes removed

The non-randomised study of 30 limbs (comparing 20 endoscopic procedures with 10 open procedures) reported a similar mean number of lymph nodes were removed in each group (10.75 vs 9.7 respectively, p = 0.3). Of these, 2% (4/215) of nodes in the endoscopic group and 1% (1/97) of nodes in the open group were histologically positive (p = 0.509) within a 32-month follow-up[1].

Recurrence

A case series of 5 patients reported recurrence in 2 patients. One patient had recurrence with multiple visceral metastases after the procedure. The other patient had recurrence in the limb outside of the nodal basin in an in-transit node, which was subsequently resected (follow-up not reported)[3].

Length of hospital stay

The non-randomised study of 30 limbs reported a significantly longer mean length of hospital stay in the group of patients who had both endoscopic and open procedures (n = 10) compared with the group of patients who had bilateral endoscopic procedures (n = 5) (6.4 days vs 24 hours, p < 0.001)[1].

Recovery

The non-randomised study of 30 limbs reported a significantly longer mean time to return to usual activities in the group of patients who had both endoscopic and open procedures (n = 10) compared with the group of patients who had bilateral endoscopic procedures (n = 5) (21 days vs 14 days, p = 0.032)[1].

Operating time

The non-randomised study of 30 limbs reported a significantly longer mean operating time for the endoscopic procedure compared with the open procedure (120 minutes vs 92 minutes, p = 0.0002)[1].

Duration of required post-operative drainage

The non-randomised study of 30 limbs reported a significantly longer drainage time for the open procedure compared with the endoscopic procedure (6.4 days vs 4.9 days, p = 0.008)[1].

Safety

Lymphatic complications

The non-randomised study of 30 limbs reported a similar level of lymphatic complications in both the endoscopic and open procedure groups (10% [2/20] vs 20% [2/10] respectively, p = 0.58) with a 32-month follow-up. This included 1 patient with chronic lymphedema and 1 patient with lymphocele with

spontaneous regression in 2 months in the open group; and 1 patient with lymphorrhea and 1 patient with unilateral limited lymphocele requiring 3 evacuation punctures in the endoscopic group[1].

A case series of 8 patients reported 3 patients with lymphoceles. All patients had undergone saphenous vein ligation during the procedure (follow-up not reported)[2].

Skin complications

The non-randomised study of 30 limbs reported a significantly higher proportion of skin-related complications in the open group (50% [5/10] vs 5% [1/20], p = 0.009) with a 32-month follow-up. These included 1 small skin necrosis in the endoscopic group and 3 patients who had limited skin necrosis with no need for skin graft, 1 wound infection and 1 area of cellulitis in the open group[1].

A case series of 5 patients reported cellulitis in 2 patients. One of these patients had a severe infection in the site of prior sentinel node biopsy (follow-up not reported)[3].

Validity and generalisability of the studies

- Studies were available for penile cancer and melanoma. No studies using this technique in patients with vulval or anal cancer were reported.
- No randomised studies were reported.
- No long term follow-up data were reported (most of the evidence is about the short-term, and the maximum reported follow-up in studies included in Table 2 is 32 months), therefore very limited evidence on oncological outcomes has been reported.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Laparoscopic retroperitoneal lymph node dissection for testicular cancer. NICE interventional procedures guidance 158 (2006). Available from www.nice.org.uk/guidance/IPG158

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr David Dickerson and Mr Nicholas A Watkin (British Association of Urological Surgeons); and Mr Charlie Chan (British Association of Surgical Oncology).

- None of the Specialist Advisers have performed the procedure or been involved in the selection or referral of a patient for the procedure. However, 1 of the Specialist Advisers regularly performs open inguinal lymphadenectomy for patients with malignant melanoma. This adviser also states that the open procedure has a significant morbidity (50–70% reported in the literature).
- One of the Specialist Advisers stated that this is a minor variation on an existing procedure. The 2 remaining Specialist Advisers considered this to be a novel procedure of uncertain safety and efficacy. One of them stated that while using endoscopy makes this a variant of an existing well-established procedure, there is a significant difference to the open procedure.
- Comparator: open inguinal lymphadenectomy.
- Theoretical adverse events: damage to femoral vessel or femoral nerve, port site metastasis, gas embolus, lymph leak, lymphoedema, lymphocele, seroma and skin necrosis.
- Key efficacy outcomes: conversion to open procedure, length of hospital stay and time to full recovery, adequate clearance of lymph nodes and recurrence of cancer.
- Training and facilities: requires standard laparoscopic instrumentation. One of the Specialist Advisers stated that there is no direct training facility in the UK. Another stated that this procedure has a significant learning curve. The third Specialist Adviser stated that few surgeons in the UK will have significant experience of this procedure but training could be accelerated by cross-specialty working. This technique is likely to be adopted by urologists, general surgeons, gynaecologists and plastic surgeons.

- One specialist adviser stated that this is likely to be an increasing clinical issue with the rise in incidence of melanoma. This Specialist Adviser also stated that surgeons currently performing open lymphadenectomy may convert to this endoscopic procedure in the next 5–10 years (subject to suitable longer-term data on larger series). There are currently a relatively small number of surgeons performing open lymphadenectomy.
- Another Specialist Adviser indicated that this will only be useful in a small number of cases as endoscopic clearance will probably be unfeasible after dynamic sentinel node biopsy (which is likely to become the norm for non–clinical or impalpable nodes) and that bulky nodes will probably be unsuitable too. Therefore it is likely to only be indicated for small volume, mobile, palpable nodes where dynamic sentinel node biopsy is not possible or indicated.
- The third Specialist Adviser indicated that the number of penile cancer patients is likely to be 200 per year (assuming that none have sentinel biopsy).

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

None

References

1. Tobias-Machado M, Tavares A, Silva MN et al. (2008) Can video endoscopic inguinal lymphadenectomy achieve a lower morbidity than open lymph node dissection in penile cancer patients? Journal of Endourology 22:1687-1691.

2. Sotelo R, Sanchez-Salas R, Carmona O et al. (2007) Endoscopic lymphadenectomy for penile carcinoma. Journal of Endourology 21:364-367.

3. Delman KA, Kooby DA, Ogan K et al. (2010) Feasibility of a novel approach to inguinal lymphadenectomy: minimally invasive groin dissection for melanoma. Ann Surg Oncol 2010:731-737.

4. Josephson DY, Jacobsohn KM, Link BA et al. (2009) Robotic-assisted endoscopic inguinal lymphadenectomy. Urology 73:167-170.

5. Tobias-Machado M, Tavares A, Molina WR, Jr. et al. (2006) Video endoscopic inguinal lymphadenectomy (VEIL): initial case report and comparison with open radical procedure. Archivos Espanoles de Urologia 59:849-852.

Appendix A: Additional papers on endoscopic radical inguinal lymphadenectomy

There were no additional papers identified.

Appendix B: Related NICE guidance for endoscopic radical inguinal lymphadenectomy

Guidance	Recommendations
Interventional procedures	**Laparoscopic retroperitoneal lymph node dissection for testicular cancer. NICE interventional procedures guidance 158 (2006)** **1 Guidance** 1.1 Current evidence on the efficacy of laparoscopic retroperitoneal lymph node dissection is limited and there are safety concerns about the procedure. It should therefore not be used without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake laparoscopic retroperitoneal lymph node dissection for testicular cancer should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the potential serious complications associated with this procedure and provide them with clear written information. In addition, use of the Institute's *Information for the public* is recommended (available from www.nice.org.uk/IPG158publicinfo). • Audit and review clinical outcomes of all patients having laparoscopic retroperitoneal lymph node dissection for testicular cancer. 1.3 This procedure is technically demanding and should only be performed in units with experience in open and laparoscopic techniques, and in the context of a multidisciplinary team. 1.4 Publication of safety and efficacy outcomes will be useful. The Institute may review the procedure upon publication of further evidence.

Appendix C: Literature search for endoscopic radical inguinal lymphadenectomy

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	24/09/2010	Sept 2010
Database of Abstracts of Reviews of Effects – DARE (CRD website)	24/09/2010	Sept 2010
HTA database (CRD website)	24/09/2010	Sept 2010
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	24/09/2010	Sept 2010
MEDLINE (Ovid)	23/09/2010	1950 to September Week 2 2010
MEDLINE In-Process (Ovid)	23/09/2010	September 22, 2010
EMBASE (Ovid)	23/09/2010	1980 to 2010 Week 37
CINAHL (NLH Search)	24/09/2010	Sept 2010
BLIC (Dialog DataStar)	27/09/2010	Sept 2010

Trial sources searched on 23/09/2010

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched on 23/09/2010

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Lymph Node Excision/
2	Inguinal Canal/
3	(Lymph adj3 node* adj3 (dissection* or excision* or resection*)).tw.

4	(Inguinal* adj3 (dissection* or excision* or resection* or canal)).tw.
5	lymphadenectom*.tw.
6	1 or 2 or 3 or 4 or 5
7	Endoscopy/
8	Laparoscopy/
9	Robotics/
10	(endoscop* or laparoscop* or robot*).tw.
11	(peritoneoscop* or celioscop*).tw.
12	7 or 8 or 9 or 10 or 11
13	6 and 12
14	Penile Neoplasms/
15	((Penis* or penile*) adj3 (cancer* or neoplasm* or tumo?r* or carcinoma* or malignan*)).tw.
16	((Penis* or Penile*) adj3 (squamous cell carcinoma* or squamous-cell carcinoma*)).tw.
17	Anus Neoplasms/
18	((anal or anus) adj3 (cancer* or neoplasm* or tumo?r* or carcinoma* or malignan*)).tw.
19	Vulvar Neoplasms/
20	((vulva* or vagina*) adj3 (cancer* or neoplasm* or tumo?r* or carcinoma* or malignan*)).tw.
21	Melanoma/
22	Leg/
23	21 and 22
24	(melanoma* adj3 leg*).tw.
25	23 or 24
26	14 or 15 or 16 or 17 or 18 or 19 or 20 or 25
27	13 and 26

28	Animals/ not Humans/
29	27 not 28