NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of laparoscopic retroperitoneal lymph node dissection for testicular cancer

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making 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 May 2005.

Procedure name

• Laparoscopic retroperitoneal lymph node dissection (L-RPLND).

Specialty society

• British Society of Urological Surgeons.

Description

Indications

Patients with testicular cancer who have had the cancerous testicle removed surgically may require resection of lymph nodes, depending on the type and extent of the cancer as defined by computed tomography and blood markers.

Current treatment and alternatives

The standard method for retroperitoneal lymph node dissection is an open procedure requiring an incision in the abdomen. A modification to the standard approach is nerve-sparing retroperitoneal lymph node dissection, in which the lumbar postganglionic nerves are prospectively identified and preserved in order to preserve antegrade ejaculation. A laparoscopic approach has the theoretical advantages of reduced morbidity and shorter recovery time.

What the procedure involves

Under general anaesthesia, and with the patient on his side, 4-5 small keyhole incisions are made on the abdomen. Using a small telescope and other instrumentation the lymph tissue that drains the testicle is removed. The number of nodes removed can vary from fewer than 10 to over 50 and the limits of excision are defined by a predetermined template. After all lymph nodes are dissected, they are

placed in a plastic bag and removed from one of the keyhole incisions, and the small incisions are closed.

Efficacy

In an historically controlled study the mean operative time for the first 14 patients undergoing L-RPLND was 9.3 hours, for right side tumours and 5.8 hours for left side tumours. For the following 15 cases (to allow for the learning curve) the operating time was 5.9 and 4.0 hours respectively, which was similar to the 4.3 and 4.1 hours in 30 cases having open retroperitoneal lymph node dissection¹. In other case series mean operative time for L-RPLND varied from 3.7, through 4.0, to 6.0 hours, and varied according to operator experience and stage of cancer.

Post operative hospitalisation time was found to 4.0 days for patients undergoing L-RPLND which was 6.6 days (166%) shorter than with open surgery in a comparative trial¹, and in case series length of stay varied between 3.0^2 and 4.1^3 days. The rate of conversion to open surgery in case series varies from 3% (5/185)³ to 10% (2/20)² and was necessary because of bleeding, or renal artery injury.

No local cancer recurrence was reported in a case series of 20 patients followed up for 10 months². Elsewhere contralateral retroperitoneal recurrence was reported in 2% (1/65) of cases with stage I cancer at 45 months, but no relapse was recorded among 47 cases with stage II disease at 35 months⁴. After 58 months of follow up in a case series of patients undergoing L-RPLND local recurrence was reported in 3% (2/80) of cases and distant metastases in 3% (2/80) of patients⁵. Finally, in another case series 97% (179/185) of cases were relapse free at 54 to 58 months follow up³.

Safety

In an historically controlled study major bleeding occurred during L-RPLND in 3% (1/29) of cases, and 13% (4/30) of open retroperitoneal lymph node dissections, however a new method of bipolar coagulation was introduced during the period of laparoscopic procedures¹. In case series Intraoperative haemorrhage occurred in between 5% (1/20)² and 18% (9/49)⁴ of L-RPLND cases in patients with stage I and stage II disease respectively.

Retrograde ejaculation was reported in between 0% (0/29 and 0/20)¹ and 2% $(3/185)^3$ of cases following L-RPLND. Among the controlled study and case series the incidence of lymphocele was between 4% $(3/76)^4$ and 9% (16/185): in most cases this was minor and asymptomatic.

Other complications reported across the studies include pressure sores $14\% (2/14)^1$, gonadal vessel injury $10\% (2/20)^2$, subcutaneous lymphoedema $7\% (1/15)^1$, chylous ascites 5% (9/185) (no cases were reported following the introduction of a new dietary regimen)³, injury to the inferior mesenteric artery $5\% (1/20)^2$, either renal artery or colon injury $1\% (2/185)^3$ and transient irritation of the genitofemoral nerve $1\% (1/76)^4$

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to laparoscopic retroperitoneal lymph node dissection Searches were conducted via the following databases, covering the period from their from commencement to 7 December 2004: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index. Trial registries and the Internet were also searched. No language restriction was applied to the searches.

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

Characteristic	Criteria
Publication type	Clinical studies 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, laboratory or animal study.
	Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with testicular or ovarian cancer.
Intervention/test	Laparoscopic retroperitoneal lymph node dissection.
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.

Table 1 Inclusion criteria for identification of relevant studies

List of studies included in the overview

This overview is based on one historically controlled study and four case series.

Existing reviews on this procedure

There were no systematic reviews or evidence-based guidelines on laparoscopic retroperitoneal lymph node dissection found during literature searches.

Abbreviations used: Nonseminomatous germ cell tumour – NSGCT			
Study details	Key efficacy findings	Key safety findings	Comments
Janetschek G (1996) ¹ Controlled study (historical control)	Outcomes for dissection to the left and right sides were analysed separately owing to the different fields to be cleared. In addition the first 14 (group 1) and second 15 (group 2) laparoscopic cases were	ComplicationsComplicationLaparoscopicOpenRetrograde0%7% (2/30)ejaculation0%0%	All laparoscopic procedures carried out by the same surgeon. Laparoscopic procedures
Austria n = 59 (laparoscopic retroperitoneal lymphadenectomy, = 29, open surgery = 30) Patients with histologically confirmed clinical stage L ponseminomatous	analysed separately to demonstrate the learning curveOperative timeMean time and range in hours techniquetechniqueRight tumoursLeft tumoursGroup 19.3 (7.0 to 10.5)5.8 (4.0 to 6.5)Group 25.9 (3.75 to 7.5)4.0 (3.0 to 5.5)	Minor21% (6/29)notbleedingrecordedMajor3% (1/29)13% (4/30)bleedingBlood0%10% (3/30)transfusionPressure14% (2/14)soresGroup 1	followed up prospectively, 30 consecutive open surgery patients evaluated retrospectively from case notes. Patients selection was not based on histological findings or risk factors
Age = 28 years All lymph nodes including those dorsal	Open 4.3 (3.5 to 5.0) 4.1 (3.5 to 5.) The operative time for right tumours was 3.3 hours (37%) less in group 2 than group 1, the operative time for open surgery was 1.6 hours (27%) shorter for open surgery than group 2	Transient7% (1/14)oedemaGroup 1Lymphocele7% (1/14)asymptomaticGroup 1Lymphocele3% (1/30)symptomaticSubcutaneousSubcutaneous7% (1/15)	The first 15 laparoscopic patients were given high dose antibiotics, all other patients received low dose antibiotics.
aorta and vena cava were removed. The extent of dissection was the same for both laparoscopic and open procedures	(31%) less in group 2 than group 1, the operative time for open surgery was 0.1 hours (2.5%) longer for open surgery than group 2	lymphoedema Group 2 lleus 3% (1/30) Fever 7% (2/30)	If positive nodes were encountered chemotherapy was initiated.
Follow-up = 54 months for open surgery, and 16 months for laparoscopic surgery (historical open surgery controls were treated prior to the instigation of laparoscopic technique)	As defined by decrease in haemoglobin level mean and range in mg/dl technique Right tumours Left tumours Group 1 4.5 (2.8 to 7.1) 2 (0.2 to 4.2) Group 2 2.2 (0.7 to 4.0) 1.2 (0 to 2.5) Open 2.6 (0.7 to 4.5) 2.3 (1.1 to 4.9) The decrease during dissection of right tumours was 2.3 mg/dl (51%) less in group 2 than group 1, the decrease for open surgery was 0.4 mg/dl (18%) greater for open surgery than group 2 The decrease during dissection of right tumours was 0.8 mg/dl (40%) less in group 2 than group 1, the decrease for open surgery was 1.1 mg/dl (92%) greater for open surgery than group 2	noted in either group	coagulation was developed during the laparoscopic procedures, not clear whether this was available in open surgery.

Table 2 Summary of key efficacy and safety findings on laparoscopic retroperitoneal lymph node dissection

Abbreviations used: Nonseminomatous germ cell tumour – NSGCT			
Study details	Key efficacy findings	Key safety findings	Comments
Janetschek G (1996) cont.	Length of stay Post operative hospitalisation time, mean in days technique Right tumours Left tumours Group 1 4.9 6.6 Group 2 4.0 4.0 Open 10.4 11.0 The length of stay for all tumours was 1.5 days (27%) less in group 2 than group 1, the length of stay for open surgery was 6.6 days (166%) longer for open surgery than group 2 Analgesic requirement Analgesics were required for a mean 1.5 days following laparoscopic interventions and 3 days following open surgery		

Abbreviations used: Nonseminomatous	germ cell tumour – NSGCT		
Study details	Key efficacy findings	Key safety findings	Comments
Study details Steiner H (2004) ³ Case series Austria n = 185 (188 procedures) Patients with stage I NSGCT, or low volume stage II disease	Key efficacy findings Procedure success Mean operative time was 256 minutes (range 115 to 570 minutes) in stage I, and 243 minutes (120 to 570) for stage II patients Comparing the initial and last 20 patients the mean operative time fell from 399 to 179 minutes in stage I patients, and from 284 to 181 minutes in stage II patients Conversion to open procedure was necessary in 3%	Key safety findingsComplications MajorRenal artery / colon injury1% (2/185)Minor Lymphoceles9%(16/185)Chylous ascites5% (9/185)(after introduction of a dietary regimen this was not encountered) Retrograde ejaculation2%(3/185)	Comments Two surgeons carried out all procedures reported. Patient selection not determined by body habitus or testicular pathologic findings. No details given of demographic or clinical characteristics at baseline.
Stage I = 113 Stage IIa (tumour marker negative) = 4 Stage IIa (marker positive) = 10 Stage IIb = 43 Stage IIc = 15 Follow-up by physical examination and blood count, CT scan twice in first year, radiograph and ultrasonography at	 (5/185) of cases, for bleeding (n = 3), renal artery injury (1), positive lymph nodes (1) The mean blood loss was 159 ml (range 10 to 3000 ml) in stage I patients and 78 ml (10 to 1600) in stage II patients Mean postoperative length of stay was 4.1 and 3.7 days for patients with stage I and stage II disease 		Analysis based on denominator of cases for some outcomes and procedures for others. Authors comment that there is a steep learning curve with this procedure. The number of ports used for the
subsequent visits Follow-up = 54 months stage I, 58 months stage II (mean)	Diagnostic outcomes In stage I patients active tumour was found in 19% (22/114) of procedures Active tumour was found in 50% (2/4) cases with tumour marker negative stage IIa disease. Active tumour was found in 7% (1/15) cases with stage IIc disease Mature teratoma was found in 38% (26/68) patients following chemotherapy Long term follow-up Active follow-up		procedure was not standardised across the series.
	At final follow-up 97% (179/185) of cases were relapse free. No patient died of tumour progression		

Abbreviations used: Nonseminomatous germ cell tumour – NSGCT			
Study details	Key efficacy findings	Key safety findings	Comments
Study details Rassweiler J (2003) ⁵ Case series – 89 retroperitoneal lymph node dissections reported among a total of 1089 laparoscopic procedures for urological malignancy Germany n = 79 (80 procedures) Age = 52 years (across all laparoscopic procedures) NSGCT = 68, Leydig cell tumours = 3, seminoma = 4, dissection for staging purposes = 4 Specimen retrieval was undertaken with or without a bag, and intact or morcellated Follow-up = 58 months (median) across all laparoscopic procedures	Key emcacy moings Long term follow-up Follow-up period in laparoscopic retroperitoneal lymph node dissection patients alone was not specified. Overall median follow up was 58 months Local recurrence was reported in 3% (2/80) of procedures Distant metastases were recorded following 3% (2/80) procedures, one in peritoneum, and one in lymph node	Complications Port site metastases 1% (1/80)	Comments Retrospective assessment. Specimen extraction method not standardised across all laparoscopic retroperitoneal lymph node dissections. It is not possible to define demographic or clinical characteristics of lymph node resection cases, from the total patient series. No details given of operator experience. Loss to follow-up not stated or justified.

Abbreviations used: Nonseminomatous germ cell tumour – NSGCT			
Study details	Key efficacy findings	Key safety findings	Comments
Janetschek G (2001) ⁴ Case series Austria n = 125 Clinical stage I disease n = 76 • Age = 30 years • Right side tumour = 71% Left side tumour = 29% Clinical stage II disease (IIc = 14, IIb = 35) n=49 • Age =29 years • Right side tumour =55% • Left side tumour =45% Surgery undertaken following chemotherapy All patients received low dose antibiotics Dissection using templates described by Weissbach. In first 29 cases luber vessels were transected to remove the tissue behind them Follow-up =45 months stage I, 35 months stage II	 Procedure success The procedure was converted in open surgery in 3% (2/76) of stage I cases, but none of 49 stage II cases To 47 months there was one case 2% (1/65) of retroperitoneal recurrence contralaterally, outside the surgical field in a stage I patient. The tumour in the landing site was removed at surgery but missed on histological analysis. No relapse was recorded (0/47) in the stage II patients Operative time For stage I patients the mean operative time was 219 minutes in the most recent 10 cases. For stage II patients the mean operative time was 226 minutes in stage IIb and 298 minutes in stage IIc Blood loss In stage I the mean blood loss was 152 ml (range 10 to 350 ml) excluding one patient who lost 2600 ml and the operation was converted to open surgery Length of stay The mean postoperative length of stay was 3.3 days and 3.5 days for stage I and stage II patients respectively 	Complications Complication Stage I Not Retrograde 1% (1/74) Not reported Intraoperative 1% (1/76) irritation of the genitofemoral nerve Lymphocele 4% (3/76) 8% (4/49) asymptomatic	Some of the patients in this series are those included in Janetschek (1996). Not stated if single or multiple surgeons undertaking the procedures. Patient selection not based on histological findings or risk factor assessment. A low fat diet for 1 week preoperatively and 2 weeks postoperatively was introduced during the series. Some loss to follow-up, and only cases with at least 6 months follow-up are included.
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Abbreviations used: Nonseminomatous germ cell tumour – NSGCT				
Study details	Key efficacy findings	Key safety finding	IS	Comments
Gerber G S (1994) ²	Procedure success	Complications		Specific aspects of the surgical
Case series	The procedure was converted in open surgery in 10% (2/20) of cases, due to failure to control bleeding	Complication Retrograde	rate 0% (0/20)	technique may have been different across the five institutions included.
USA	To a median 10 months (range 2 to 25 months) there	Gonadal vessel	10% (2/20)	
n = 20	was no case of retroperitoneal recurrence	injury Intraoperative	5% (1/20)	No details on case selection procedure.
Patients with nonseminomatous testicular tumours	Of the patients who completed laparoscopic intervention the 17% (3/18) provided positive nodes	Subscapular monecrosis Lymphocele	5% (1/20) 5% (1/20) 5% (1/20)	Authors state that longer follow- up in large groups is required to evaluate patient selection criteria
Age=29 years	Operative time	mesenteric artery	578 (1/20)	on factors associated with
Stage I disease (normal serum markers) = 19 Mixed seminoma and embryonal	10 hours). No inter-site analysis undertaken			increased risk of stage II disease.
carcinoma = 1	Blood loss			The potential need for abdominal
Right side tumour = 40% Left side tumour = 60%	The median estimated blood loss was 250 cc (range 30 to 3000 cc			incision to repair intraoperative injuries requires needs to be discussed with the patient.
The limits of dissection were the renal	3 patients (2 laparoscopic procedure) required blood			·
hilus, the ureter, medial aspect of the vena cava or aorta, level of the origin of	transfusion			No differentiation in analysis of left of right side procedures.
the interior mesenteric artery. Also extended to the bifurcation of the common iliac vessels on the ipsilateral side and the stump of the spermic cord was excised. The interaortocaval nodes were removed	Length of stay Total hospital length of stay was 3 days			Very few cases from each site, with no details of experience of operators.
A median of 14.5 nodes were removed				
Follow-up =10 months				

Validity and generalisability of the studies

- Efficacy, particularly relating to operative time may vary between procedures to right and left sides.
- Studies included in the overview used different operative techniques or templates for dissection.
- Outcomes of local recurrence or disease recurrence at any site are not well described.

Specialist advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Mr T Christmas, Mr A Dickinson, Mr G Sibley

All advisors suggested that this procedure was novel and of uncertain safety and efficacy.

The potential benefits of a laparoscopic approach are reduced bleeding and morbidity.

Theoretical adverse events reported include vascular injury, bowel perforation, incomplete resection, haemorrhage, and local or port site recurrence. Reported events include incomplete resection and subsequent concern regarding prognosis, and the need to convert to open surgery

There may be increased safety concerns when dissecting large nodal masses that encircle the aorta or vena cava.

Operators require experience or training in both laparoscopic surgery and retroperitoneal lymph node dissection.

Only 100 retroperitoneal dissections are carried out each year in the UK so the impact on the NHS of the new procedure is likely to be small. The procedure will probably be carried out in specialist centres with the greatest experience.

There is some controversy about whether this procedure should be used for diagnosis in early stage cancer, or with curative intent as an alternative to open surgery.

Issues for consideration by IPAC

There is diagnostic utility in the potential to find active tumour in stage IIa markernegative patients.

In the UK the procedure is rarely performed in patients with stage I testicular cancer, but for instances of recurrence following chemotherapy.

The procedure is also used for staging in prostate cancer, prior to therapy

References

1 Janetschek G, Hobisch A, Holtl L, Bartsch G. Retroperitoneal lymphadenectomy for clinical stage I nonseminomatous testicular tumor: laparoscopy versus open surgery and impact of learning curve. Journal of Urology 1996; 156(1):89-93.

2 Gerber GS, Bissada NK, Hulbert JC, Kavoussi LR, Moore RG, Kantoff PW et al. Laparoscopic retroperitoneal lymphadenectomy: multi-institutional analysis. Journal of Urology 1994; 152(4):1188-1191.

3 Steiner H, Peschel R, Janetschek G, Holtl L, Berger AP, Bartsch G et al. Long-term results of laparoscopic retroperitoneal lymph node dissection: a single-center 10-year experience. Urology 2004; 63(3):550-555.

4 Janetschek G, Peschel R, Hobisch A, Bartsch G. Laparoscopic retroperitoneal lymph node dissection. Journal of Endourology 2001; 15(4):449-453.

5 Rassweiler J, Tsivian A, Ravi Kumar AV, Lymberakis C, Schulze M, Seeman O et al. Oncological safety of laparoscopic surgery for urological malignancy: Experience with more than 1,000 operations. Journal of Urology Vol. 169(6):01.

Appendix A: Additional papers on laparoscopic retroperitoneal lymph node dissection therapy not included in the summary tables

Article title	Number of patients/ follow-up	Comments	Direction of conclusions
Bianchi G, Beltrami P, Giusti G, Tallarigo C, et al. Unilateral laparoscopic retroperitoneal lymph node dissection for clinical stage I nonseminomatous germ cell testicular neoplasm. <i>European Urology</i> 1998; 33(2):190–4.	n = 6 Follow- up = 21 months	Case series where larger series are included in table 2	Mean operative time = 325 minutes, length of stay = 4.8 days, blood loss < 50ml, relapses = 0%
Zhuo Y, Klaen R, Sauter TW, Miller K. Laparoscopic retroperitoneal lymph node dissection in clinical stage I nonseminomatous germ cell tumor: a minimal invasive alternative. <i>Chinese Medical</i> <i>Journa</i> l 1998; 111(6):537–41.	n = 13 Follow-up = 15 months	Case series where larger series are included in table 2	Mean operative time = 292 minutes, length of stay = 6.4 days, conversion to open surgery = 8% (1/13), retrograde ejaculation = 0% (0/10)

Appendix B: Literature search laparoscopic

retroperitoneal lymph node dissection

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in EMBASE, Current Contents, PredMedline and all EMB databases.

For all other databases a simple search strategy using the key words in the title was employed.

Procedure Number: 284	Procedure Name: Laparoscopic retroperitoneal lymph		
Detabases Madline	node dissection		
Database: Medline	Date searched: 7/12/04		
1966 to November Week 3			
2004>			
1 exp LAPAROSCOPY/ (33140)			
2 laparoscop\$.tw. (35895)			
3 telescop\$.tw. (1783)			
4 video camera.tw. (1157)			
5 or/1-4 (44118)			
6 exp Retroperitoneal Space/ (4641)			
7 retroperitoneal.tw. (13571)			
3 retro pertioneal.tw. (0)			
9 or/6-8 (15110)			
10 (lymph\$ adj2 nod\$ adj2 (dissect\$ or excis\$)).tw. (6329)			
exp Lympn Node Excision/ (18440)			
2 10 or 11 (21156)			
3 9 and 12 (12/6)			
14 RPLND.tw. (193)	KPLND.tw. (193)		
15 L-RPLIND.W.(1)			
16 13 0F 14 (1292)	5 13 or 14 (1292)		
17 - 5 and 16 (116)	(5 and 16 (116)		
10 17 01 13 (110)	5 - 1/101 (11b)		
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