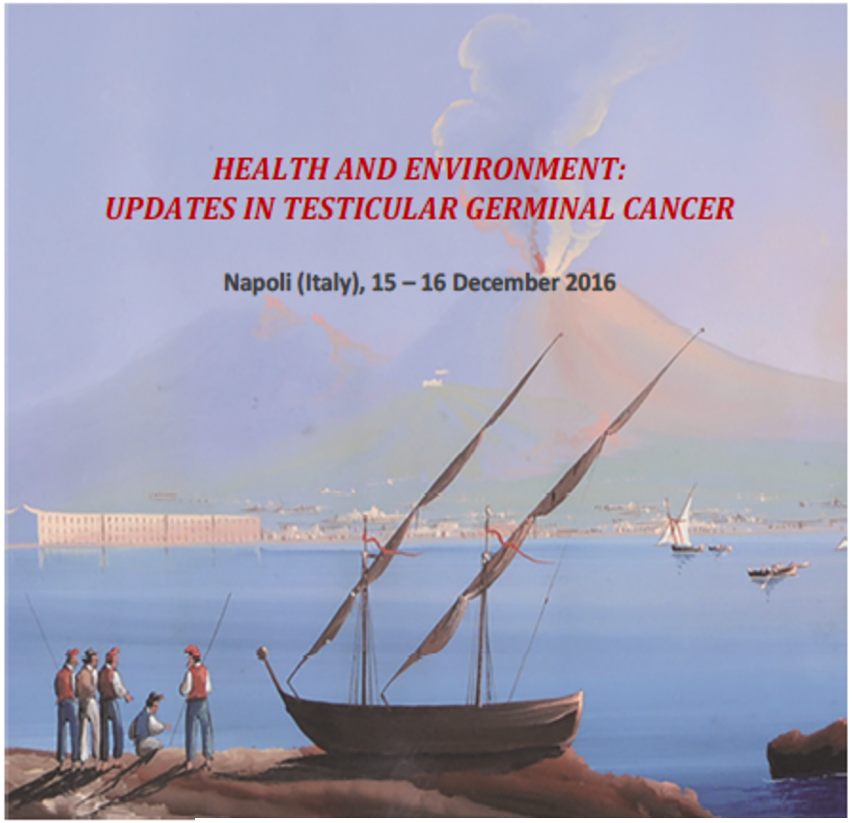
ISTITUTO NAZIONALE TUMORI
IRCCS - Fondazione Pascale



Role of Surgery in non seminoma

S.C. Urologia Oncologica

Sisto Perdonà

Session IV:

Focusing on advanced, poor prognosis and residual disease management

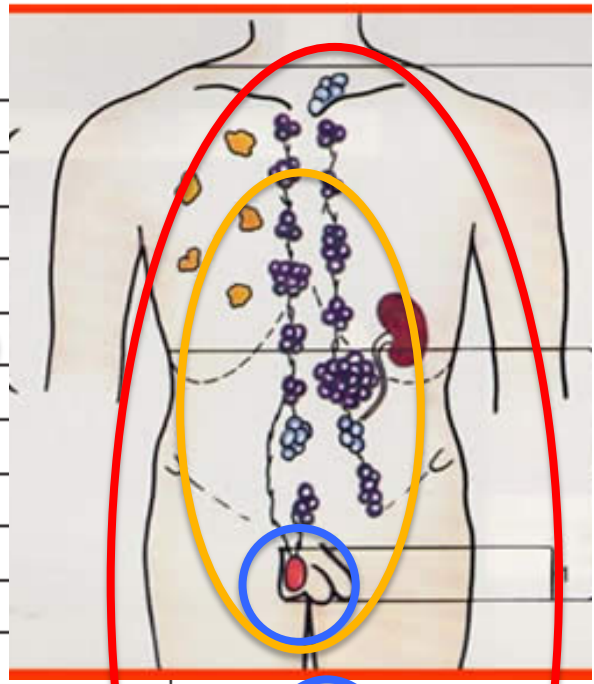
Chairmen: *Pignata S.*, Damiano R.

ISTITUTO NAZIONALE TUMORI
IRCCS - Fondazione Pascale

European Association of Urology

Role of Surgery in non seminoma

Stage 0	pTis	N0	M0	S0, SX
Stage I	pT1-T4	N0	M0	SX
Stage IA	pT1	N0	M0	S0
Stage IB	pT2 - pT4	N0	M0	S0
Stage IS	Any patientTX	N0	M0	S1-3
Stage II	Any patient/TX	N1-N3	M0	SX
Stage IIA	Any patient/TX	N1	M0	S0
	Any patient/TX	N1	M0	S1
Stage IIB	Any patient/TX	N2	M0	S0
	Any patient/TX	N2	M0	S1
Stage IIC	Any patient/TX	N3	M0	S0
	Any patient/TX	N3	M0	S1
Stage III	Any patient/TX	Any N	M1a	SX
Stage IIIA	Any patient/TX	Any N	M1a	S0
	Any patient/TX	Any N	M1a	S1
Stage IIIB	Any patient/TX	N1-N3	M0	S2
	Any patient/TX	Any N	M1a	S2
Stage IIIC	Any patient/TX	N1-N3	M0	S3
	Any patient/TX	Any N	M1a	S3
	Any patient/TX	Any N	M1b	Any S



NSGCT clinical stage I

Table 6.1: Risk factors for occult metastatic disease in stage I testicular cancer

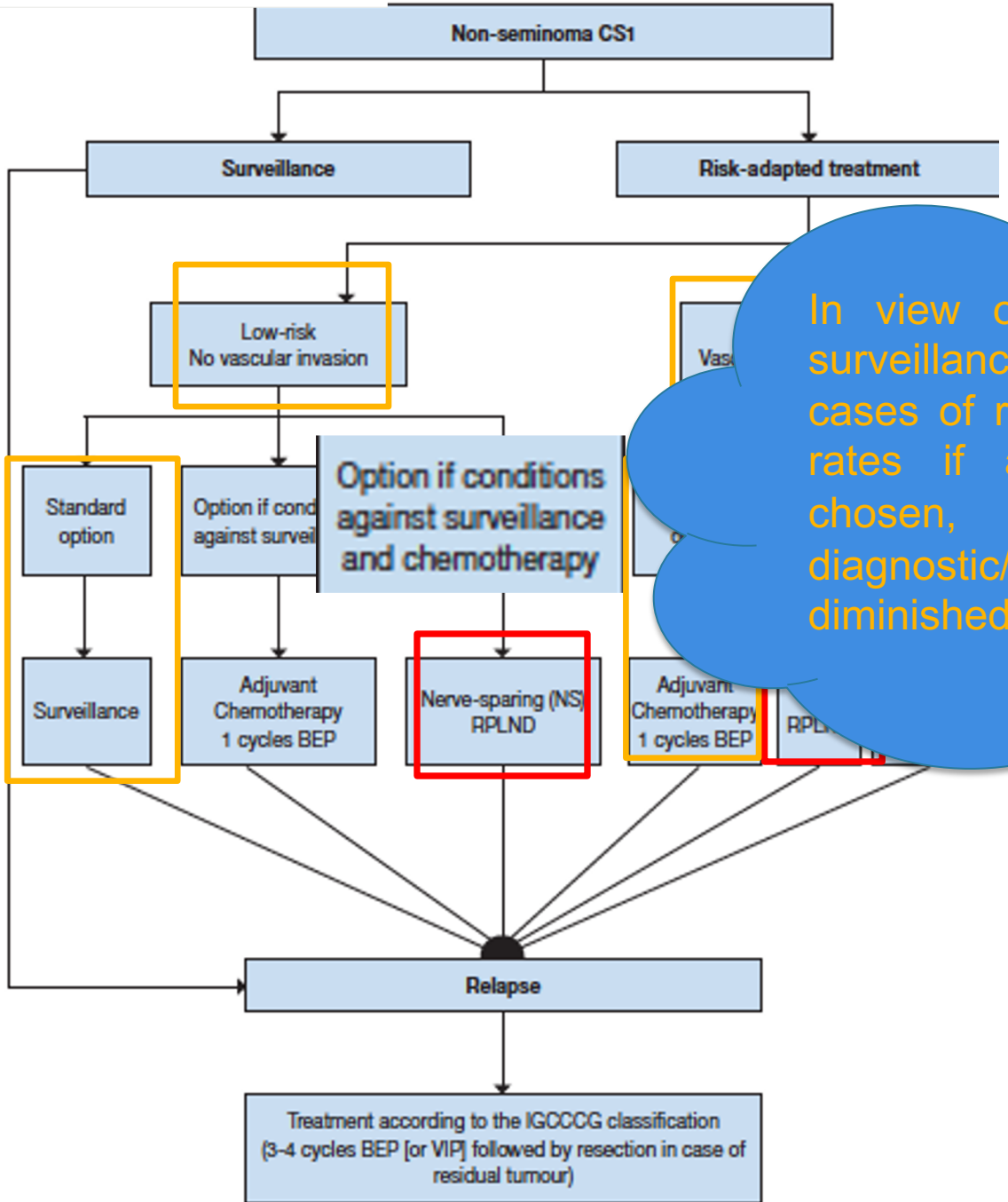
	For seminoma	For non-seminoma
Pathological (for stage I)		
Histopathological type	• Tumour size (> 4 cm) • Invasion of the rete testis	• Vascular/lymphatic in or peri-tumoural invasion • Proliferation rate > 70% • Percentage of embryonal carcinoma > 50%

Most Important predictor for occult metastatic disease

Additional predictors

Albers, P., et al. Risk factors for relapse in clinical stage I nonseminomatous testicular germ cell tumors: results of the German Testicular Cancer Study Group Trial. J Clin Oncol, 2003. 21: 1505.
Alexandre, J., et al.
Stage I non-seminomatous germ-cell tumours of the testis: identification of a subgroup of patients with a very low risk of relapse. Eur J Cancer, 2001. 37: 576.

Role of Surgery in non seminoma



In view of the high CSS rates of surveillance with salvage treatment in cases of relapse and the low relapse rates if adjuvant chemotherapy is chosen, role of primary diagnostic/therapeutic RPLND has diminished.

European Association of Urology

in NSGCT (RPLND) clinical stage I A/B

Up to ***30%*** of NSGCT patients with clinical stage I (CS1) disease ***have subclinical metastases*** and will relapse if surveillance alone is applied after orchiectomy.

Treatment choice should be based on:

- ✓ Multidisciplinary patient evaluation
- ✓ discussion with the patient, taking into account the described advantages and disadvantages
- ✓ individual situation of the patient

Kollmannsberger, C., et al. Non-risk-adapted surveillance for patients with stage I nonseminomatous testicular germ-cell tumors: diminishing treatment-related morbidity while maintaining efficacy. Ann Oncol, 2010. 21: 1296.

Nichols, C.R., et al. Active surveillance is the preferred approach to clinical stage I testicular cancer. J Clin Oncol, 2013. 31: 3490.

NSGCT clinical stage IS

ents

have

retro

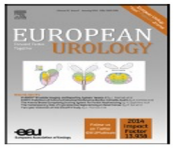
Da *tumors of the testis wit*

Piz *SGCT) of the testis. Which primary therapy? J Urol 1996; 155(Suppl):328A.*

EURURO-6823; No. of Pages 7
ARTICLE IN PRESS
EUROPEAN UROLOGY XXX (2016) XXX–XXX

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology



Surgery in Motion

Safety and Early Oncologic Effectiveness of Primary Robotic Retroperitoneal Lymph Node Dissection for Nonseminomatous Germ Cell Testicular Cancer

Shane M. Pearce [a,], Shay Golan [a], Michael A. Gorin [b], Amy N. Luckenbaugh [c], Stephen B. Williams [d], John F. Ward [d], Jeffrey S. Montgomery [c], Khaled S. Hafez [c], Alon Z. Weizer [c], Phillip M. Pierorazio [b], Mohamad E. Allaf [b], Scott E. Eggener [a]*

[a] Section of Urology, Department of Surgery, University of Chicago, Chicago, IL, USA; [b] Department of Urology, The Johns Hopkins School of Medicine, Baltimore, MD, USA; [c] Department of Urology, University of Michigan Health System, Ann Arbor, MI, USA; [d] Department of Urology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

SURGICALLY SAFE

Table 2 – Operative outcomes

Outcomes	All patients (*n* = 47)
Operative time (min)	235 (212–258)
Estimated blood loss (ml)	50 (50–100)
Node yield	26 (18–32)
Length of stay (d)	1 (1–1)

All variables displayed as median (interquartile range).

Table 3 – Intraoperative and postoperative complications

Type	Frequency (%)
Overall	6 (13)
Intraoperative	2 (4.3)
Open conversion	1 (2.1)
30-D postoperative	4 (8.5)
Chylous ascites	2 (4.3)
Ileus	1 (2.2)
Body wall hematoma	1 (2.2)
Late postoperative	
No	46 (98)
Yes	0 (0)
Unknown	1 (2)

Table 1 – Baseline patient and primary tumor characteristics

Characteristics (*n* = 47)	Median (IQR)/frequency
Age (yr)	30 (26–38)
BMI (kg/m^2)	28 (25–33)
Race	
White	42 (89)
Other	5 (11)
ASA	
1	18 (31)
2	33 (57)
3	7 (12)
Primary tumor laterality	
Right	22 (47)
Left	25 (53)
Clinical Stage	
I	42 (89)
IIA	5 (11)
Nodes on CT (if CS IIA)	2.5 (1.5–3)
Node diameter on CT (cm)	1.4 (1.2–1.5)
LVI	
No	28 (60)
Yes	19 (40)
>40% Embryonal	
No	19 (40)
Yes	27 (58)
Unknown	1 (2)
Risk factors if CS I	
None	13 (28)
LVI only	6 (13)
>40% Embryonal only	14 (29)
Both	13 (28)
Unknown	1 (2)
Teratoma present	
No	15 (32)
Yes	31 (66)
Unknown	1 (2)
Teratoma present if 0 risk factors	
No	2 (15)
Yes	11 (85)

ASA, American Society of Anesthesiologists; BMI = body mass ind
CS = clinical stage; CT = computed tomography; IQR = interquartile ran
LVI = lymphovascular invasion.

ONCOLOGICALLY SAFE? short Follow up!

Table 4 – Final pathologic outcomes

Outcomes	Frequency (%)
pN+	
All (n = 47)	8 (17)
CS I (n = 42)	6 (14)
CS IIA (n = 5)	2 (40)
Final pN stage	
pN0	39 (83)
pN1	7 (15)
pN2	1 (2)
pN+ among CS I	
No risk factors (n = 12)	1 (8)
LVI alone (n = 5)	1 (20)
>40% Embryonal alone (n = 18)	0 (0)
Both (n = 12)	4 (33)
–LVI (n = 25)	1 (4)
+LVI (n = 17)	5 (29)

CS = clinical stage; LVI = lymphovascular invasion; pN+ = pathologic node positive disease.

Table 5 – Early oncologic and functional outcomes

Outcome	Median (IQR)/frequency (%)
Mo of follow-up	
All	16 (9–23)
Pathologic Stage I	16 (9–24)
Pathologic Stage II	12 (8–16)
Pathologic Stage II (no chemo)	7 (2–10)
Adjuvant chemotherapy (if pN+)	
No	3 (38)
Yes	5 (62)
Number of positive nodes	
–Adjuvant chemotherapy	2 (1–2)
+ Adjuvant chemotherapy	3 (3–4)
Recurrence-free survival (95% CI)	
2 yr (all patients)	97% (82–100%)
2 yr (–adjuvant chemotherapy)	100% (N/A)
Normal ejaculation (unknown in n = 3)	
No	0 (0)
Yes	44 (100)

CI = confidence interval; IQR = interquartile range; N?A = not applicable; pN+ = pathologic node positive disease.

This multicenter experience supports R-RPLND as a **potential option at experienced centers in select patients with low-stage NSGCT.**

Comparing open and laparoscopic series suggests R-RPLND has an acceptably low morbidity, but oncologic efficacy requires further evaluation.

ISTITUTO NAZIONALE TUMORI
IRCCS - Fondazione Pascale

NSGCT Clinical stage IIA/B

Table 4.3: Prognostic-based staging system for metastatic germ cell cancer (International Germ Cell Cancer Collaborative Group [47])*

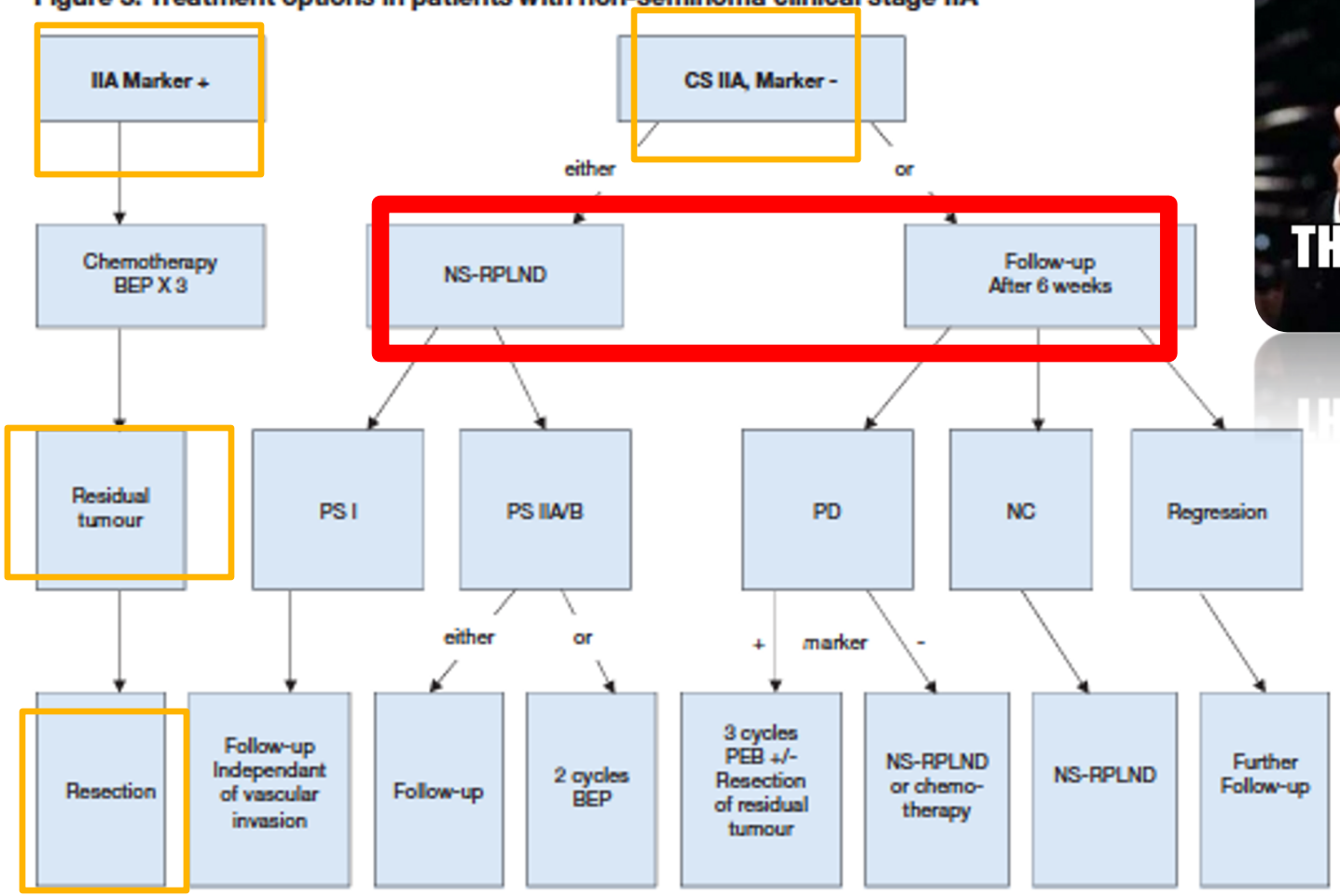
Good-prognosis group		
Non-seminoma (56% of cases) 5-year PFS 89% 5-year survival 92%	*All of the following criteria:* • Testis/retroperitoneal primary • No non-pulmonary visceral metastases • AFP < 1,000 ng/mL • hCG < 5,000 IU/L (1,000 ng/mL) • LDH < 1.5 x ULN	***M1a*** ***S1***

Intermediate prognosis group		
Non-seminoma (28% of cases) 5-year PFS 75% 5-year survival 80%	*All of the following criteria:* • Testis/retroperitoneal primary • No non-pulmonary visceral metastases • AFP 1,000 - 10,000 ng/mL or • hCG 5,000 - 50,000 IU/L or • LDH 1.5 - 10 x ULN	***M1a*** ***S2***

Poor prognosis group		
Non-seminoma (16% of cases) 5-year PFS 41% 5-year survival 48%	*Any of the following criteria:* • Mediastinal primary • Non-pulmonary visceral metastases • AFP > 10,000 ng/mL or • hCG > 50,000 IU/L (10,000 ng/mL) or • LDH > 10 x ULN	***M1b*** ***S3***

NSGCT clinical stage IIA/B

Figure 3: Treatment options in patients with non-seminoma clinical stage IIA



BEP = cisplatin, etoposide, bleomycin; NS = nerve-sparing; RPLND = retroperitoneal lymph node dissection; PS = pathological stage; PD = progressive disease; NC = no change.

European Association of Urology

RESIDUAL TUMOR RESECTION

Residual tumour resection is ***MANDATORY*** in all patients with a residual mass **> 1 cm** in the short axis at cross-sectional CT imaging.

Hartmann, J.T., et al. Comparison of histological results from the resection of residual masses at different sites after chemotherapy for metastatic non-seminomatous germ cell tumours. Eur J Cancer, 1997. 33: 843.

Sheinfeld, J. The role of adjunctive postchemotherapy surgery for nonseminomatous germ-cell tumors: currentconcepts and controversies. Semin Urol Oncol, 2002. 20: 262.

The role of surgery is ***debated*** in patients with retroperitoneal residual lesions **< 1 cm**. There is still a risk of residual cancer or teratoma although the vast majority of patients (> 70%) harbour fibro-necrotic tissue.

Carver, B.S., et al. Long-term clinical outcome after postchemotherapy retroperitoneal lymph node dissection in men with residual teratoma. J Clin Oncol, 2007. 25: 1033.

RESIDUAL TUMOR RESECTION

Following first-line BEP chemotherapy, only **6-10%** of residual masses contain viable cancer, **50%** contain mature teratoma, and *40%* contain necrotic-fibrotic tissue.

Carver, B.S., et al. Improved clinical outcome in recent years for men with metastatic nonseminomatous germ cell tumors. J Clin Oncol, 2007. 25: 5603.

In cases of ***complete remission*** after first line chemotherapy (no visible tumour), tumour ***resection is not indicated***.

Kollmannsberger, C., et al. Management of disseminated nonseminomatous germ cell tumors with risk-based chemotherapy followed by response-guided postchemotherapy surgery. J Clin Oncol, 2010. 28: 537.

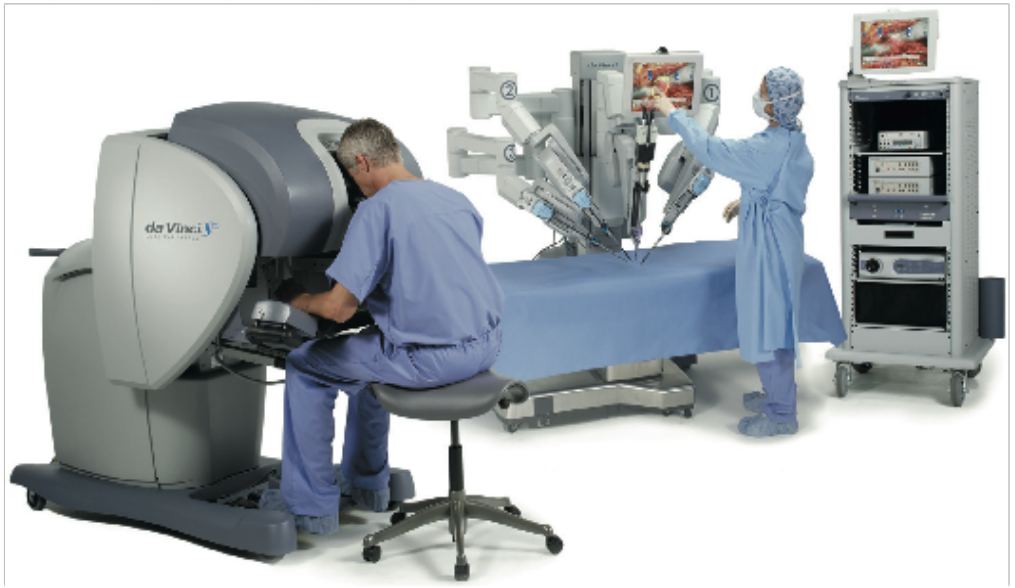
Ehrlich, Y., et al. Long-term follow-up of Cisplatin combination chemotherapy in patients with disseminated nonseminomatous germ cell tumors: is a postchemotherapy retroperitoneal lymph node dissection needed after complete remission? J Clin Oncol, 2010. 28: 531.

Our experience with Robot “da Vinci Si”

SINCE NOVEMBER 2012

ISTITUTO NAZIONALE TUMORI
IRCCS – Fondazione Pascale

- 650 robotic procedures
- 570 urologic surgery
- (RALP, RAPN, RARN, RANU,RARC, RA RPLND)



- **14 Ra-RPLND**

(4 procedures in 2016)

ISTITUTO NAZIONALE TUMORI
IRCCS – Fondazione Pascale

TRAINING: THE RIGHT WAY

European Association of Urology

Figure 1: EAU Robotic Urology Section (ERUS) proposed curriculum (Ahmed et al., 2014, Volpe et al., 2014)

3 VIDEOS PRESENTED @ ERUS 16
2 VIDEO PRESENTED @ EAU 16

ERUS16
13th Meeting of the EAU Robotic Urology Section
14-16 September 2016, Milan, Italy
www.erus16.org
erus
European Association of Urology

EAU ORIENTED *ROBOTIC TEAM:*

7 UROLOGISTS

4 NURSES

4 FOCUSED DATABASES
(RALP - RARC - RaRPLND - RAPN - RANU)

ISTITUTO NAZIONALE TUMORI
IRCCS – Fondazione Pascale

How do we do...

Review – Testis Cancer

Laparoscopic Retroperitoneal Lymph Node Dissection: Does It Still Have a Role in the Management of Clinical Stage I Nonseminomatous Testis Cancer? A European Perspective

Jens J. Rassweiler [a,*], *Walter Scheitlin* [a], *Axel Heidenreich* [b], *M. Pilar Laguna* [c], *Günter Janetschek* [d]

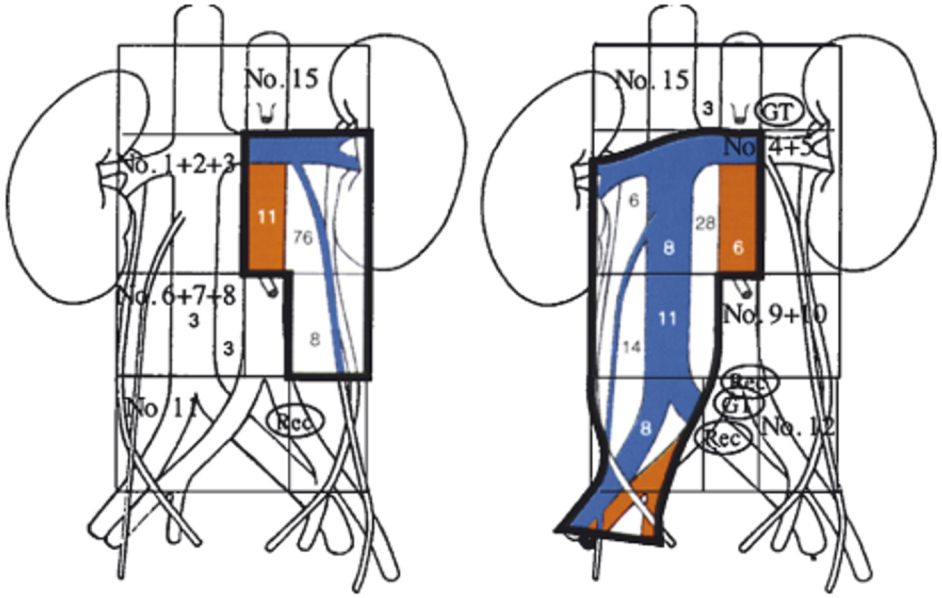
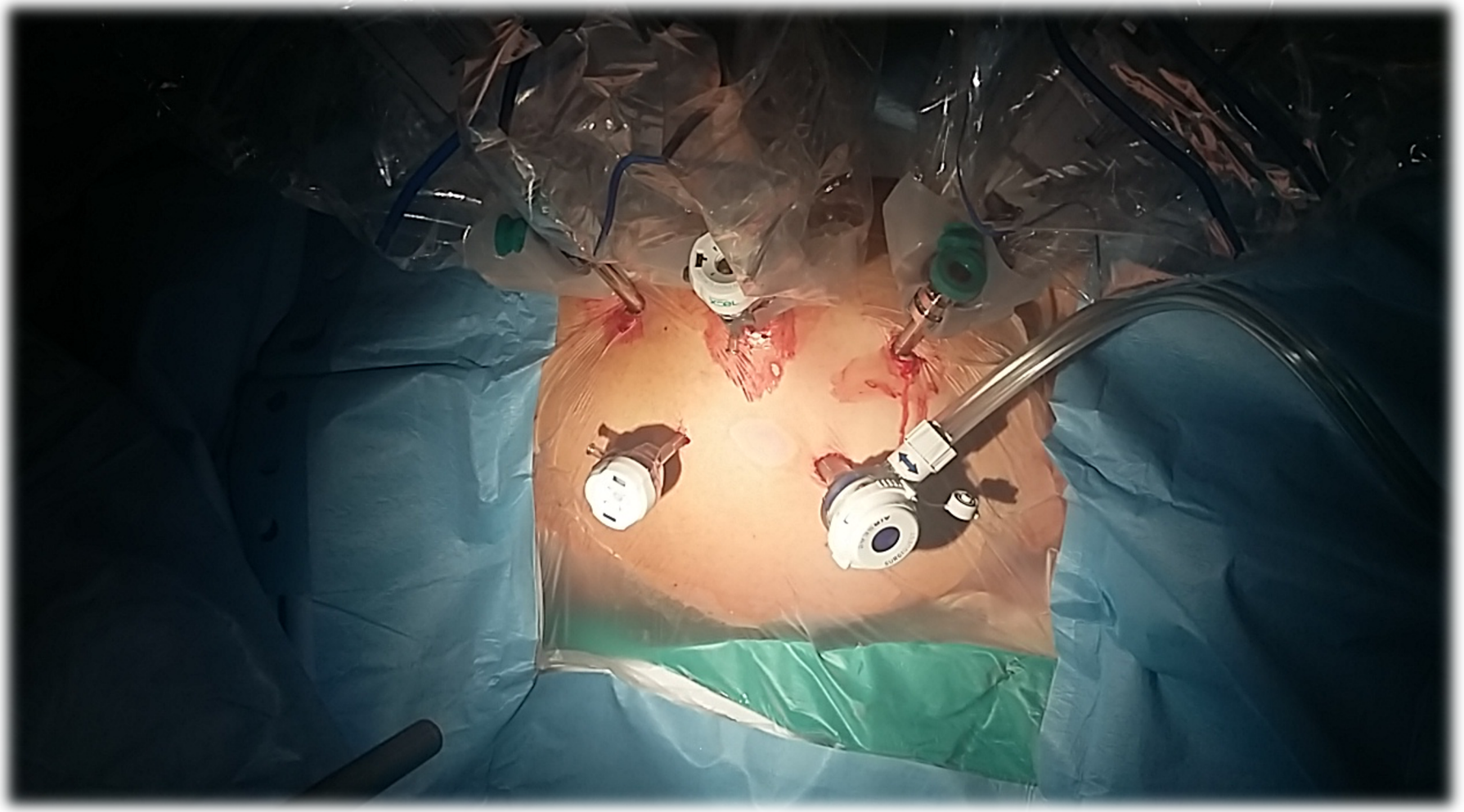


Fig. 1 – Modified templates of laparoscopic retroperitoneal lymph node dissection (L-RPLND) with percentage and site of pN+ in Weissbach study [49], including the definition and numbers of fields.
GT = site of growing teratoma (n = 1) in the Cresswell study [14]; Rec = sites of recurrent metastasis following pN0 at L-RPLND.

How do we do...



OUR EXPERIENCE: PRELIMINAR DATA

OPERATIVE OUTCOMES	
OPERATIVE TIME (MIN)	241 (205-315)
ESTIMATED BLOOD LOSS (ml)	147 (50 - 350)
NODE YELD	17 (10-25)
LENGHT OF STAY (D)	3,2 (3-4)

ONCOLOGIC OUTCOMES	
BIOCHEMICAL FAILURE	1 pt
IN-FIELD RELAPSE	0 pt
DISTANT RELAPSE	1 pt

COMPLICATIONS	
OVERALL	3
INTRAOPERATIVE	1 cava injury 1 epigastric artery injury
30-D POST-OPERATIVE - ILEUS - LINPHOCELE - HEMATOMA	 0 1 0
LATE POST-OPERATIVE	0

FUNCTIONAL OUTCOMES	
NORMAL EJACULATION	15/16 pt

Has mininvasive approach changed the indication??

Difference outcomes between open and mininvasive surgery

Laparoscopic Retroperitoneal Lymph Node Dissection: Does It Still Have a Role in the Management of Clinical Stage I Nonseminomatous Testis Cancer? A European Perspective

Jens J. Rassweiler [a,*], *Walter Scheitlin* [a], *Axel Heidenreich* [b], *M. Pilar Laguna* [c], *Günter Janetschek* [d]

Table 2 – Operative data from later series (2000–2008) of laparoscopic and open retroperitoneal lymph node dissection for stage I disease

Author	*n*	OR time (minutes)	Complication (%)	Conversion (%)	Reintervention (%)	Hospital stay (days)	No. of nodes
Laparoscopy							
Castillo [10], 2004 (Santiago, Chile)	96	138	14.6	4.2	1.0	1.8	14 (5–36)
Albqami [1], 2005 (Linz, Austria)	103	217	11.6	2.9	0	3.6	N/A
Romero [12], 2006 (Baltimore, MD, USA)	77	N/A	10.8	5.4	0	2.0	N/A
Neyer [13], 2007 (Innsbruck, Austria)	136	261	25.7	5.1	0.7	4.1	N/A
Cresswell [14], 2008 (Heilbronn, Germany)	87	177	9.4	1.1	5.7	5.0	14 (4–25)
Total	499	204	15.6	3.8	1.4	3.3	14
Open surgery							
Weissbach [15], 2000	109	N/A	41.0	N/A	0	N/A	N/A
Spermon [16], 2002 (The Netherlands)	101	158	40.0	N/A	13.0	6.0	N/A
Heidenreich [17], 2003 (Germany)	239	214	34.2	N/A	8.9	8.0	18.5 (9–57)
Beck [18], 2007 (Indianapolis, IN, USA)	75	132	16.1*	N/A	0	2.8	N/A
Total	524	186	33	N/A	6.6	6.6	19

OR = operating room; N/A = not available.

* No data on retrograde ejaculation (no nerve-sparing in 6.7%).

Laparoscopic Retroperitoneal Lymph Node Dissection: Does It Still Have a Role in the Management of Clinical Stage I Nonseminomatous Testis Cancer? A European Perspective

Table 3 – Long-term oncologic data from later series (2000–2008) of laparoscopic and open retroperitoneal lymph node dissection for stage I disease

Author	*n*	Positive nodes (%)	Retroperitoneal relapse (%)	In-field relapse (%)	Distant relapse (%)	Biochemical failure (%)	Secondary retroperitoneal surgery (%)	Follow-up (mo)
Laparoscopy								
Albqami [11], 2005 (Linz, Austria)	103	25	1.0	0	2.9	1.0	0	62
Neyer [13], 2007 (Innsbruck, Austria)	136	18	0.7	0	4.4	0.7	1.4	89
Castillo [19], 2007 (Santiago, Chile)	111	19	1.8	0	1.8	0.9	0	30
Nielsen [20], 2007 (United States)	120	38	1.6	0	4.1	1.6	3.3	36
Cresswell [14], 2008 (Heilbronn, Germany)	87	24	2.3	0	4.6	2.3	2.3	84
Total	557	25	1.4	0	3.3	0.9	1.1	63
Open surgery								
Spermon [16], 2002 (The Netherlands)	101	31	0	0	8.9	0	0	83
Heidenreich [17], 2003 (Germany)	239	28	1.3	0.8	4.2	1.2	0.8	44
Stephenson [21], 2005 (Memorial Sloan-Kettering Cancer Center, USA)	196	34*	1.5	0.45	4.5	N/A	3.1	53
Al-Tourah [7], 2005 (Canada)	52	40*	0	0	7.6	0	1.9	48
Albers [22], 2008 (Germany)	173	18.5	2.8	0.6	4.6	3.4	1.2	56
Total	761	28.5	1.3	0.45	6.1	1.1	1.5	54

N/A = not available.
* Only patients with predominant embryonal carcinoma and/or lymphovascular invasion.

Laparoscopic Retroperitoneal Lymph Node Dissection: Does It Still Have a Role in the Management of Clinical Stage I Nonseminomatous Testis Cancer? A European Perspective

Jens J. Rassweiler [a,*], *Walter Scheitlin* [a], *Axel Heidenreich* [b], *M. Pilar Laguna* [c], *Günter Janetschek* [d]

Table 4 – Comparative studies of laparoscopic versus open retroperitoneal lymph node dissection: operative data

Author	*n*	OR time (minutes)	Complication (%)	Reintervention (%)	Analgesics (hours)	Hospital stay (days)	Positive nodes (%)	Comments
Macedo [50], 1994	27							Antegrade ejaculatio
Laparoscopic	14	288	N/A	7.1	24	5.5	N/A	open vs laparoscopic
Open	13	309	N/A	7.7	72	12.4	N/A	(86% vs 93%)
Janetschek [51], 1996	59							Steep learning curve of
Laparoscopic	29	390	41.4	–	36	4.7	27.6	L-RPLND
Open	30	252	30	3.3	72	10,6	16.7	
Poulakis [52], 2006	50							Learning curve of
Laparoscopic	21	233	15.0	4.8	8	2	19	L-RPLND decreases
Open	29	203	86.2	6.9	30	7	24	OR time
Abdel-Aziz [53], 2006	28							More lymph nodes
Laparoscopic	22	313	22.8	–	N/A	1.2	32	removed by O-RPLN
Open	6	284	16.7	–	N/A	8.5	–	(33 vs 17)

OR = operating room; N/A = not available; L-RPLND = laparascopic retroperitoneal lymph node dissection; O-RPLND = open retroperitoneal lymph node dissection.

BJUI
BJU International

A comparative analysis of robotic vs laparoscopic retroperitoneal lymph node dissection for testicular cancer

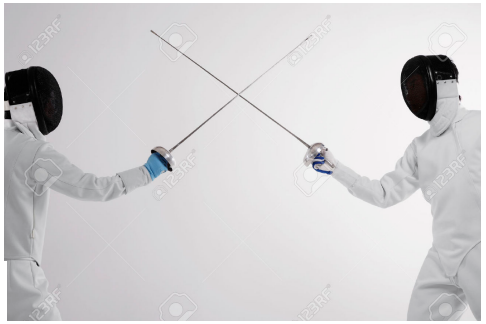


Table 2 Comparison of intraoperative, pathological and perioperative outcomes of R-RPLND vs L-RPLND.

Variable	L-RPLND (*N* = 21)	R-RPLND (*N* = 16)	*P*
RPLND template, *n* (%)			
Left	8 (38.1)	8 (50.0)	0.52
Right	13 (61.9)	8 (50.0)	
Median (IQR) operative time, min	294 (259–370)	270.5 (236–299)	0.13
Median (IQR) estimated blood loss, mL	125 (50–150)	75 (50–100)	0.16
Intraoperative complication, *n* (%)	0	1 (6.3)	0.43
Conversion, *n* (%)	1 (4.8)	1 (6.3)	1.00
Median (IQR) LN yield	22 (18–30)	30 (23–35.5)	0.13
pN Stage, *n* (%)			
pN0	17 (81.0)	14 (87.5)	1.00
pN1	3 (14.3)	2 (12.5)	
pN2	1 (4.8)	0	
RPLND pathology, *n* (%)			
Choriocarcinoma	0	0	
Embryonal	3 (14.3)	1 (6.3)	0.62
Seminoma	0	0	
Teratoma	1 (4.8)	1 (6.3)	1.00
Yolk sac	0	0	
Postoperative complication, *n* (%)	2 (9.5)	1 (6.3)	1.00
Clavien Grade, *n* (%)			
I–II	1 (4.8)	0	1.00
III–IV	1 (4.8)	1 (6.3)	
Antegrade ejaculation, *n* (%)			
Yes	16 (76.2)	16 (100)	0.16
No	2 (9.5)	0	
Unknown	3 (14.3)	0	
Median (IQR) follow-up, months	2.8 (0.2–31.0)	13.5 (5.8–20.1)	0.18

In conclusion, as an early checkpoint, R-RPLND appears ***comparable*** *to the laparoscopic approach in terms of* ***safety and perioperative outcomes****. It remains unclear if R-RPLND offers any tangible benefits over standard laparoscopy. However, larger studies are needed to more fully explore this question.*

TAKE HOME MESSAGES:

Mininvasive RPLND, performed by an experienced surgeon in specialised centres has become safe.

IS IT A SAFE PRIMARY APPROACH?

TAKE HOME MESSAGES:

SECONDARY RPLND (RESIDUAL MASS)

When RPLND is performed in a multicentre setting, higher rates of in-field recurrences and complications were reported.

Therefore nerve-sparing RPLND should be performed by an experienced surgeon in highly specialized centres.

Albers, P., et al. Randomized phase III trial comparing retroperitoneal lymph node dissection with one course of bleomycin and etoposide plus cisplatin chemotherapy in the adjuvant treatment of clinical stage I Nonseminomatous testicular germ cell tumors: AUO trial AH 01/94 by the German Testicular Cancer Study Group. J Clin Oncol, 2008. 26: 2966.

Neyer, M., et al. Long-term results of laparoscopic retroperitoneal lymph-node dissection for clinical stage I nonseminomatous germ-cell testicular cancer. J Endourol, 2007. 21: 180.

Follow us on Twitter and share your comments and experience!

URO-ONCOLOGY UNIT
@UROPascale