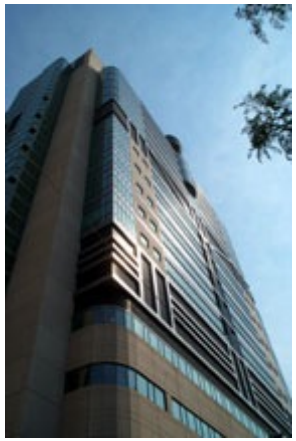
Finnish Testicular Cancer Meeting 2015
in collaboration with Finnish Oncology and Urology Associations

Treatment Strategies for Testicular Cancer in Canada



Michael A.S. Jewett

DEPARTMENT OF SURGICAL ONCOLOGY
PRINCESS MARGARET CANCER CENTRE
DIVISION OF UROLOGY
THE UNIVERSITY OF TORONTO

Toronto Multidisciplinary Testicular Cancer Clinic new patient volumes

YEAR	TOTAL	SEMINOMA				NON-SEMINOMA			
		Stage at Presentation				Stage at Presentation			
		I	II	III	Subtotal	I	II	III	Subtotal
2010	123	50	10	2	62	33	13	15	61
2011	121	37	5	2	44	24	25	28	77
2012	138	36	13	3	52	36	26	24	86
2013	135	53	13	5	71	38	15	11	64
2014	137	47	6	3	56	40	23	18	81
Subtotal		223 (78%)	47 (17%)	15 (5%)	**285 (44%)**	171 (46%)	102 (28%)	96 (26%)	**369 (56%)**
Total 2010-2014	**654 (100%)**								

Some of our milestones

- First and maybe only full multidisciplinary clinic in the world
- Description of nerve sparing RPLND technique
- Surveillance for CS I Seminoma in North America
- Prognostic grouping CSI Seminoma
- Surveillance for CS I Non-seminoma in North America
- Leader in reduction of risk – low dose CT scan, anticoagulation
- 88 publications; 1982-2015

Survivorship Care Plan

Testis Cancer

Type of plan: At end of treatment

Care plan date: 21-Aug-2014

Patient Information

Patient Name: Test Test	Date of Birth: 11-Jul-1991
Marital status: Single	Employment status: Student
Current Co-morbidities: Diabetes mellitus type 1 Sleep apnea	

Disease Background

Cancer type: Testis cancer	Date of diagnosis: 21-Jan-2014
Cancer location: Left testicle	Histology subtype: Non-Seminoma

Tumour markers

Initial:

	Date	Result	Units
BHCG:	20-Jan-2014	37	IU/L
AFP:	20-Jan-2014	1043.0	ug/L
LDH:	20-Jan-2014	421	U/L

Most recent:

	Date	Result	Units
BHCG:	27-May-2014	<1	IU/L
AFP:	27-May-2014	2.0	ug/L
LDH:	27-May-2014	252	U/L

Surgical Details

	Procedure Date	Procedure	Details	Prosthesis
1	21-Jan-2014	Orchiectomy	Tolerated procedure well.	Yes

Chemotherapy Details

	Regimen name	Start date	End date	Cycles	Completed	Reason for change
1	GERM-BEP 5 DAYS	18-Feb-2014	15-Apr-2014	3	Yes	

Getting Back on Track - Online Curriculum

Website	Details
http://www.theprincessmargaret.ca/gbot	

Persistent Treatment Effects Monitoring and Management Plan

Physical/Symptom Effects

Symptom	Provider/Management Plan	Attachments
Hearing loss, ringing in the ears	Pamphlet Referral to audiologist	Managing Concerns About Hearing Loss After Cancer Treatment
Fatigue	Pamphlet Referral to Fatigue Clinic Counselling on exercise - Survivorship exercise program	Managing cancer related fatigue
Neuropathy	Pamphlet Referral to pain clinic	Managing Neuropathy after Cancer Treatment
Sexual Health • Decreased sex drive • Erectile dysfunction • Ejaculation problems • Infertility • Lack of testosterone	Pamphlet Referral to GU sexual health program - http://www.prostatecentre.ca/wellness-and-survivorship/psychosocial-support/psych-support Referral to endocrinologist	Sexual Health After Testicular Cancer Sexuality and Cancer

Pesistent Treatment Effects Monitoring and Management Plan

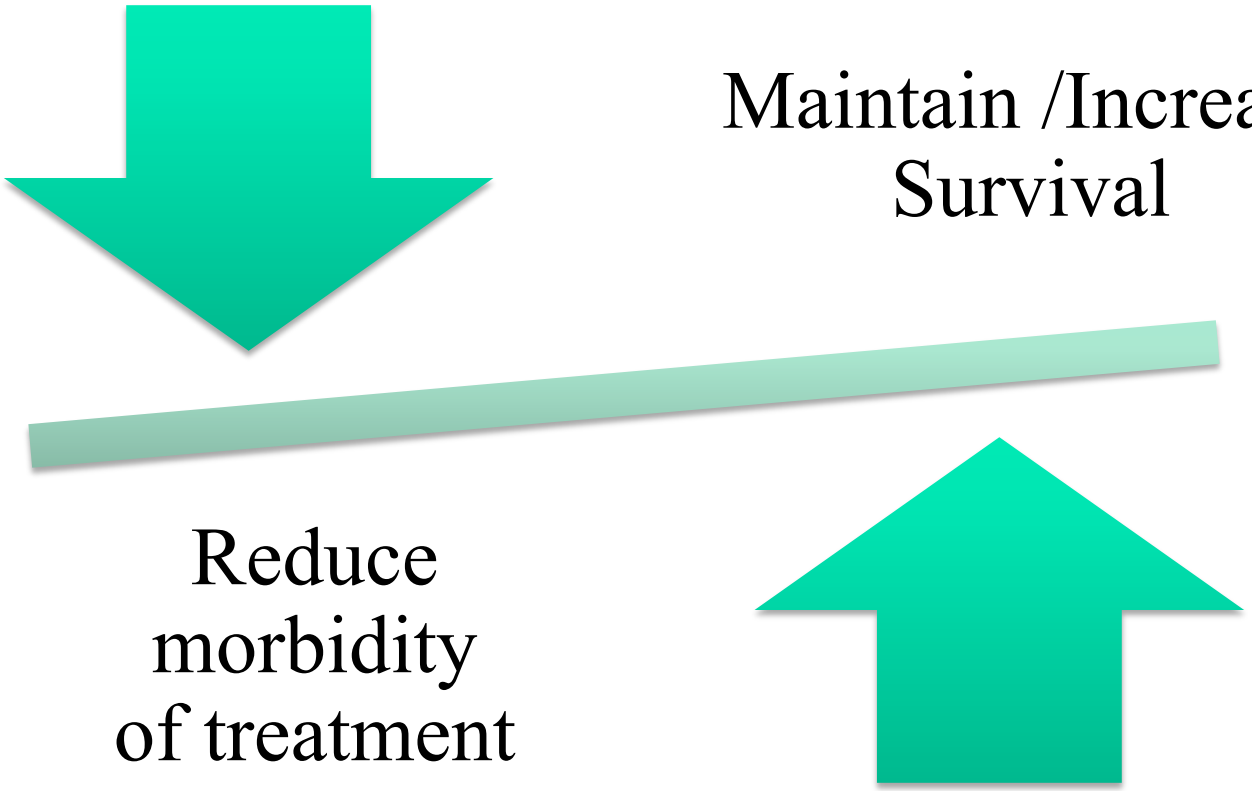
Psychosocial Effects

Symptom	Provider/Management Plan	Attachments

Seminoma and Non-Seminoma Post Chemotherapy with CR (no RPLND) Surveillance

Time Post Treatment	Approximate Date	Tests
3 months	Jun-2014	Blood Test (Tumor markers: HCG, AFP, LDH)
6 months	Sep-2014	Blood Test (Tumor markers: HCG, AFP, LDH) CT Scan of Thorax CT Scan of Abdomen and Pelvis
9 months	Dec-2014	Blood Test (Tumor markers: HCG, AFP, LDH)
1 year	Mar-2015	Blood Test (Tumor markers: HCG, AFP, LDH) Blood Test (Serum LH, FSH, Free & Total Testosterone) CT Scan of Thorax

Guiding Principles of Treatment Testicular Cancer



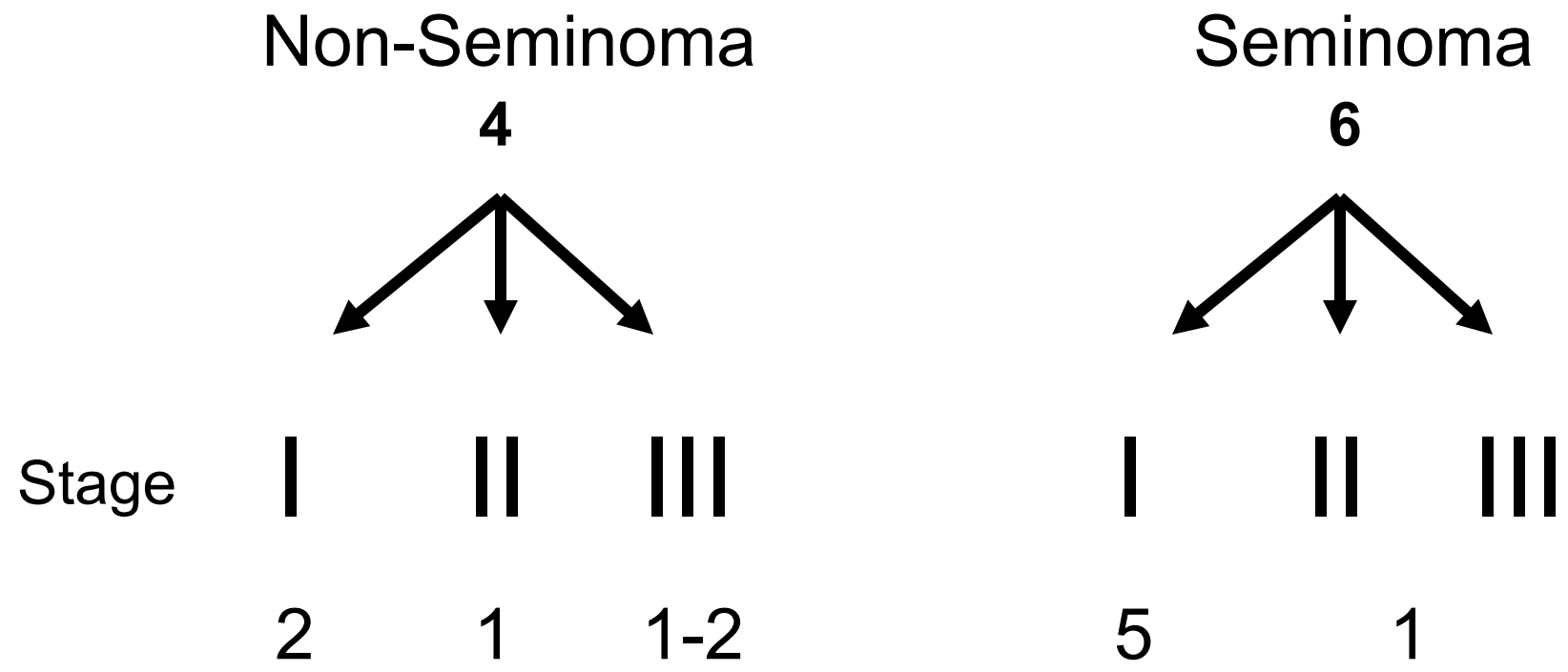
Guiding Principles of Treatment

Reduce morbidity of treatment

- Acute - treatment pain and disability, lost time, cost
- Late toxicities – infertility, radiation induced second malignancy/CVD

Maintain high survival rates

Next 10 Testis Tumors



CLINICAL STAGE I (pT1-4N0M0) GCT

NEGATIVE STAGING AFTER ORCHIECTOMY

- Normal history and physical examination
- Markers nadir to normal range-Recall $T^{1/2}$:
  - AFP 5 days (5 half-lives ≈ 3-4 weeks)
  - HCG 36 hrs (5 half-lives ≈ 1 week)
- Normal Chest X-ray or CT
- Normal CT Abdomen and Pelvis – timing?

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JOURNAL OF CLINICAL ONCOLOGY

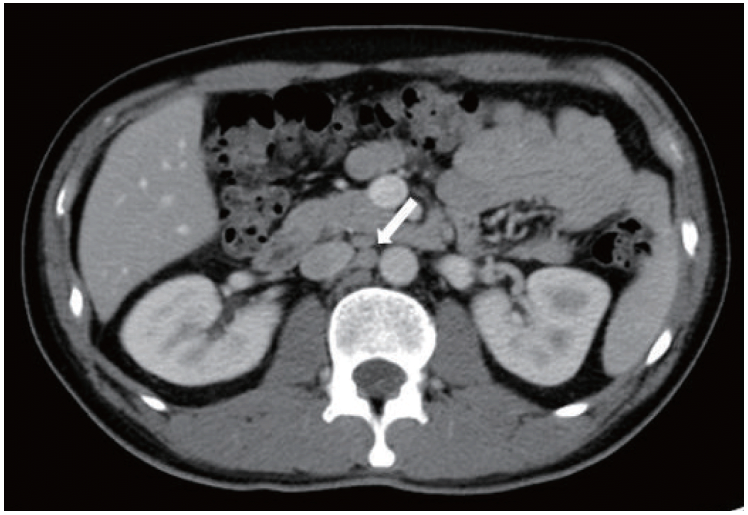
COMMENTS AND CONTROVERSIES

Active Surveillance Is the Preferred Approach to Clinical Stage I Testicular Cancer

Craig R. Nichols, *Virginia Mason Medical Center, Seattle, WA*
Bruce Roth, *Washington University School of Medicine, St Louis, MO*
Peter Albers, *University Hospital Heinrich-Heine, University of Düsseldorf, Düsseldorf, Germany*
Lawrence H. Einhorn and Richard Foster, *Melvin and Bren Simon Cancer Center, Indiana University School of Medicine, Indianapolis, IN*
Siamak Daneshmand, *Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA*
Michael Jewett and Padraig Warde, *Princess Margaret Hospital, University of Toronto, Toronto, Ontario, Canada*
Christopher J. Sweeney and Clair Beard, *Dana-Farber Cancer Institute, Brigham and Women's Hospital, Boston, MA*
Tom Powles, *Bart's Cancer Institute, St Bartholomew's Hospital, Queen Mary University of London, London, United Kingdom*
Scott Tyldesley and Alan So, *British Columbia Cancer Agency–Vancouver Cancer Centre, University of British Columbia, Vancouver, British Columbia, Canada*
Christopher Porter and Semra Olgac, *Virginia Mason Medical Center, Seattle, WA*
Karim Fizazi, *Institute Gustave Roussy, University of Paris Sud, Paris, France*
Brandon Hayes-Lattin, *Knight Cancer Institute, Oregon Health and Science University, Portland, OR*
Peter Grimison, *Royal Prince Alfred Hospital, Sydney Cancer Centre, University of Sydney, Sydney, New South Wales, Australia*
Guy Toner, *Peter MacCallum Cancer Center, University of Melbourne, Melbourne, Victoria, Australia*
Richard Cathomas, *Kantonsspital Graubuenden, Chur, Switzerland*
Carsten Bokemeyer, *University Medical Centre Eppendorf, Hamburg University, Hamburg, Germany*
Christian Kollmannsberger, *British Columbia Cancer Agency–Vancouver Cancer Centre, University of British Columbia, Vancouver, British Columbia, Canada*

Diagnosis and Staging

- Any nodes in landing zone(s) should be regarded with suspicion



Guiding Principles of Treatment

Reduce morbidity of treatment

- Acute - treatment pain and disability, lost time, cost
- Late toxicities – infertility, radiation induced second malignancy/CVD

Maintain high survival rates

Non-Risk Adapted
Active Surveillance (AS) for all CSI

- Equivalent outcomes to adjuvant treatment
- Lower overall morbidity
- Avoids overtreatment - only treat those that need treatment
- “Easy” and generalizable
- Requires compliance – patient AND MD

Canadian consensus guidelines for the management of testicular germ cell cancer

Can Urol Assoc J 2010;4(2):E19-E38

- Seminoma (Stage I)

  In a patient willing and able to adhere to a surveillance program, this approach should be considered as the management option of choice (Fig 1).

- Nonseminoma (Stage I)

  In a patient willing and able to adhere to a surveillance program, for all risk groups, surveillance should be considered as the management option of choice (Fig 2).

Non-Risk Adapted
Active Surveillance (AS) for all CSI

- Critics state:
  - Compliance an issue (loss to follow-up)
  - Diagnostic radiation exposure from surveillance imaging
  - Relapses require more aggressive treatment, in particular more chemotherapy
  - Increased risk of cancer death

Stage I Seminoma

- Stage I Seminoma represents 60% of GCTs
- Management Options
  - Surveillance
  - Adjuvant Radiation Therapy
  - Adjuvant Chemotherapy
- ~100% cure with all strategies

Adjuvant RT

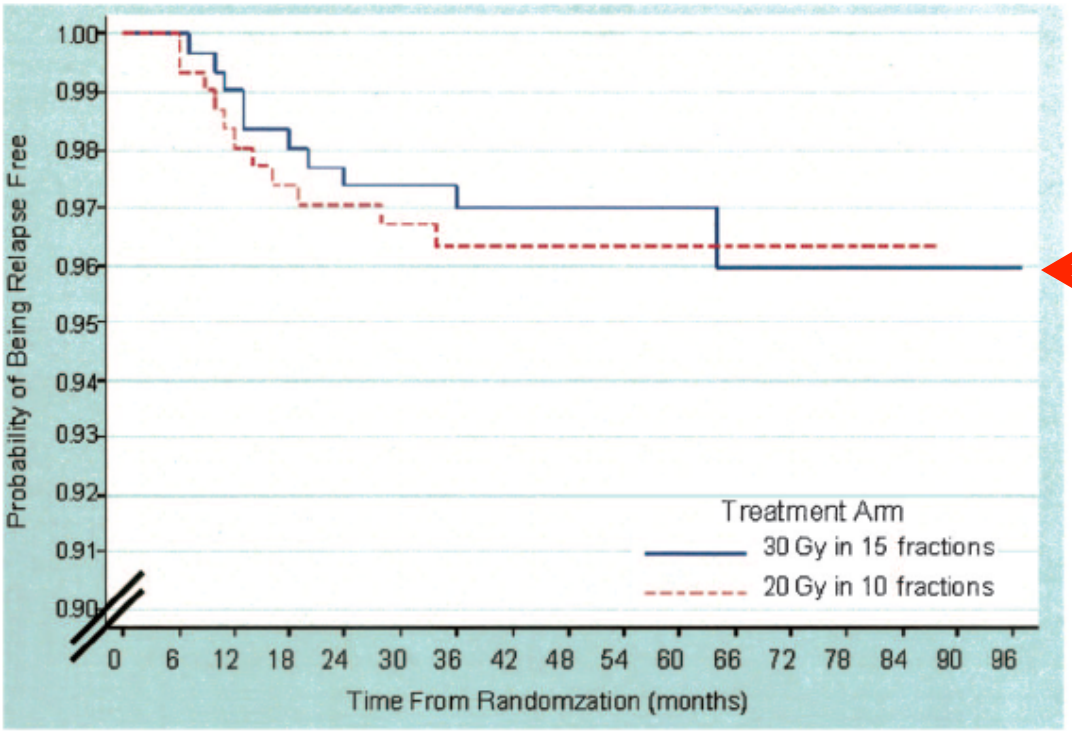
- Standard management for past 65 years
- Overall 10 yr survival in large series 95% - few deaths from Seminoma
- Relapse Rate 0.5% - 5%
  - Mediastinum, Lungs, supraclav fossa
    - Chemotherapy ~100% cure

Author	Yrs	# pts	% Relapse	CSS
Bayens	1975-85	132	4.5	99%
Coleman	1980-95	144	4.2	100%
Fossa	1989-93	478	3.8	100%
Jones	1995-98	625	3.5	99.6%
Santoni	1970-99	487	4.3	99.4%
Warde	1982-02	283	5	100%

Randomized Trial of 30 Versus 20 Gy in the Adjuvant Treatment of Stage I Testicular Seminoma: A Report on Medical Research Council Trial TE18, European Organisation for the Research and Treatment of Cancer Trial 30942 (ISRCTN18525328)

J Clin Oncol 23:1200-1208. © 2005

William G. Jones, Sophie D. Fossa, Graham M. Mead, J. Trevor Roberts, Michael Sokal, Alan Horwich, and Sally P. Stenning

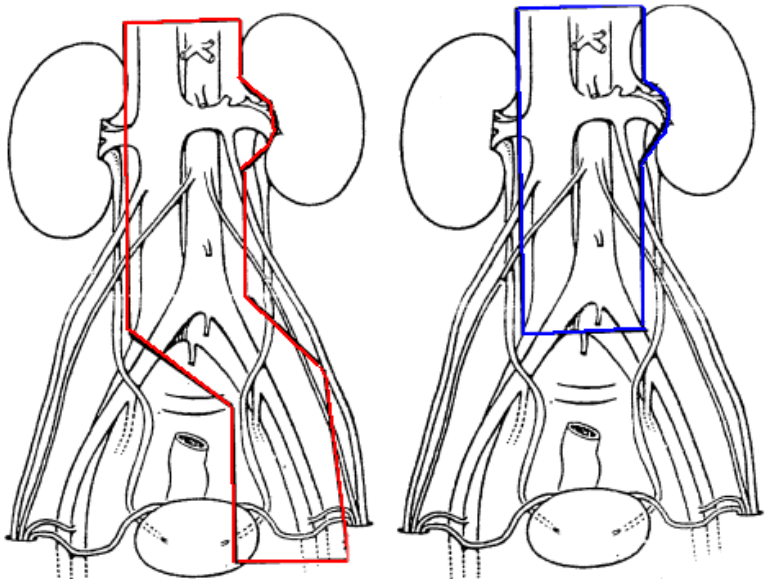


4% relapse

Radiation for CSI Seminoma

But…
2x Increased CV risk
2x Increased 2nd cancer

- Overall: 4% relapse rate
- Only 2 questions:
  - A) Dose 20, 25, 30Gy? (20 Gy is ok)
  - B) "D 'A is ok)



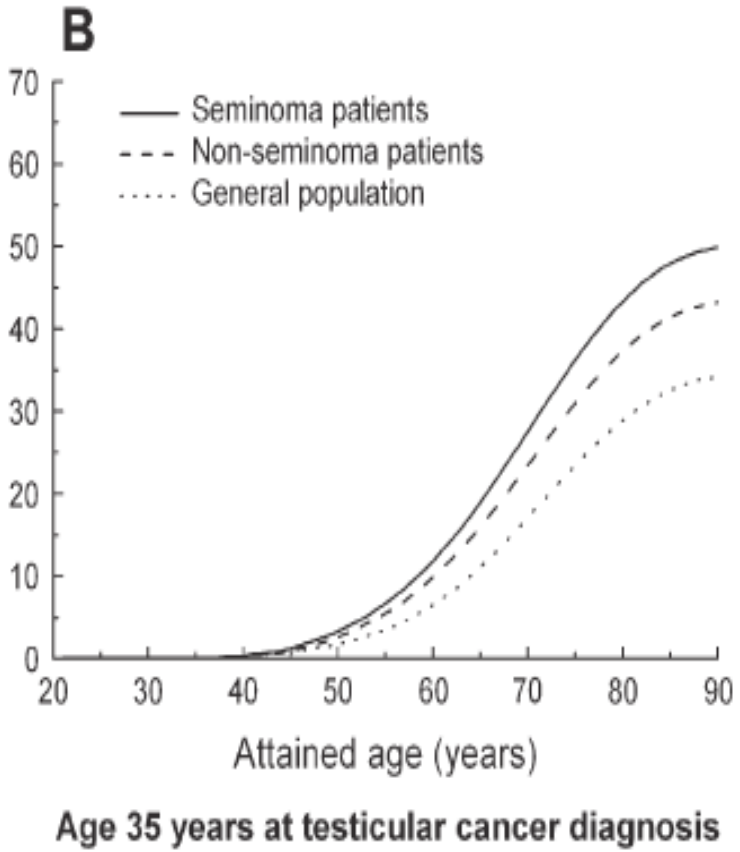
Fossa, JCO 1999; Jones, JCO 2005

Why Abandon Adjuvant RT

- Virtually no surgical data on incidence of occult nodal disease
- Improved Imaging
- Encouraging data from NSGCT surveillance
- Late Toxicity from Adjuvant RT
  - Second non-testicular malignancy
  - Cardiovascular disease
  - Fertility

Second Malignancy after RT for Seminoma

- NIH Study
  - 14 population based registries
  - 22,424 patients with Seminoma
  - For 35 yr patient with seminoma cumulative risk of 2nd Solid Tumour at age 75
    36% vs 23% in general population



Travis et al JNCI 97: 1354-67, 2005

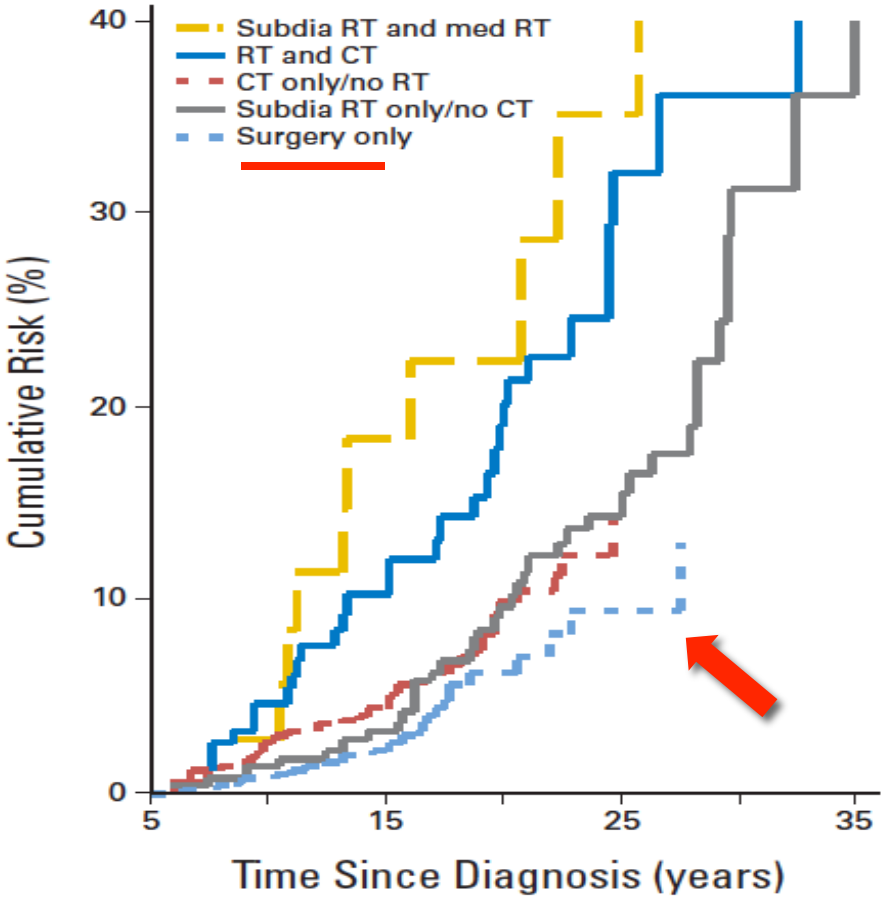
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Treatment-Specific Risks of Second Malignancies and Cardiovascular Disease in 5-Year Survivors of Testicular Cancer

J Clin Oncol 25:4370-4378. © 2007

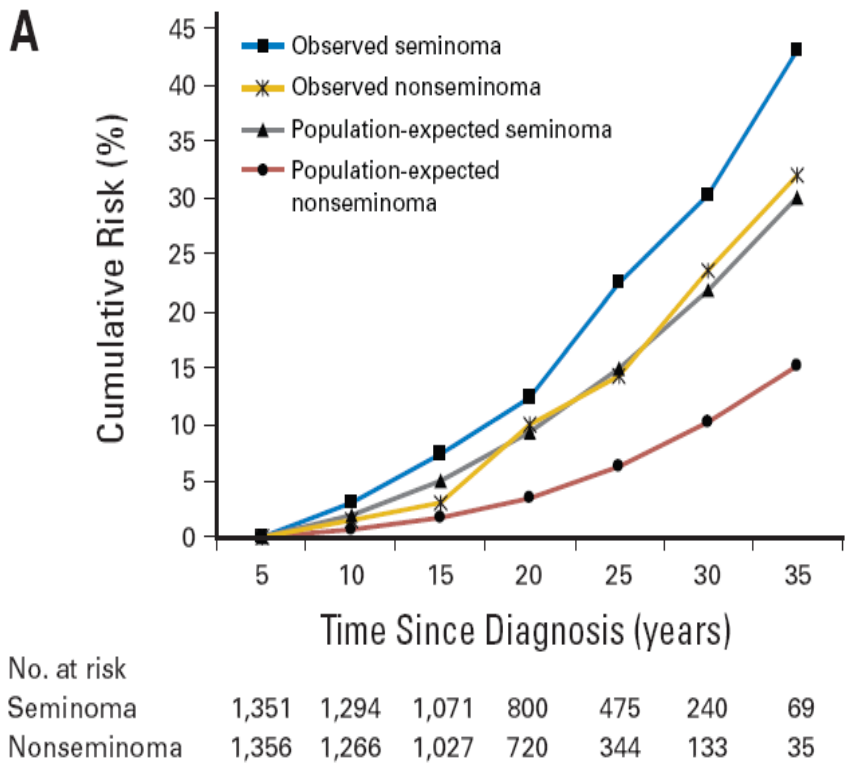
Alexandra W. van den Belt-Dusebout, Ronald de Wit, Jourik A. Gietema, Simon Horenblas, Marieke W.J. Louwman, Jacques G. Ribot, Harald J. Hoekstra, Gabey M. Ouwens, Berthe M.P. Aleman, and Flora E. van Leeuwen

- n=2700 survivors
- F/U: 17.6 yrs
- Outcomes:
  - Second neoplasm
  - Cardiovasc. disease



Second Malignancy after RT for Seminoma

- Dutch population based study
  - 2707 Testicular Cancer survivors
  - Median Follow-up 17.6 years
  - 2nd malignancy risk with subdiaphragmatic RT was 2.6 fold increased as compared to surgery alone
    - Mainly in-field or adjacent to RT field
    - Risk increase similar to that of smoking



Van den Belt-Dusebout et al J Clin Oncol 25:4370-4378, 2007

Long term RT morbidity Cardiovascular

- Royal Marsden Hospital Study
  - Relative risk of cardiac event 2.40 (95% CI 1.04-5.45)
    - Death from Myocardial Infarction
    - Documented Myocardial Infarction or history of Angina
    - Surgery for CAD
  - Increased Risk starts 5-8yrs after treatment
    - Actuarial risk of cardiac event at 10 years
      - Surveillance 1.4%
      - Radiotherapy 7.2%
      - Chemotherapy 3.43%

Huddart et al JCO 21:1513-1523, 2003

Cardiovascular morbidity

- MD Anderson
  - 477 pts treated RT 1951-1999
    - 453 never relapsed,
      - » 373 Stage I (93% subdiaphragmatic RT alone)
  - Median follow-up 13.3 years
  - Standardised Mortality Ratio
    - Cardiac death - 1.61
    - Retroperiteonal RT only (> 15 years F/U) 1.80

Zagars et al JCO 22:640-647, 2004

Surveillance

- 15% Relapse Rate
  - Para-aortic nodes
  - most patients treated successfully with RT
  - Actuarial risk of requiring chemotherapy at any time in management same as with Adjuvant RT

Author	# Patients	5-year Relapse	CSS
Horwich	103	17.3%	100%
Daugaard	394	17%	100%
Warde	638	17.7%	99.3%

Horwich et al Br J Cancer 65: 775-778, 1992
Daugaard et al APMIS 111:76-85, 2003
Warde et al. J Clin Oncol; 20:4448-4452 2002

BJUI
BJU International

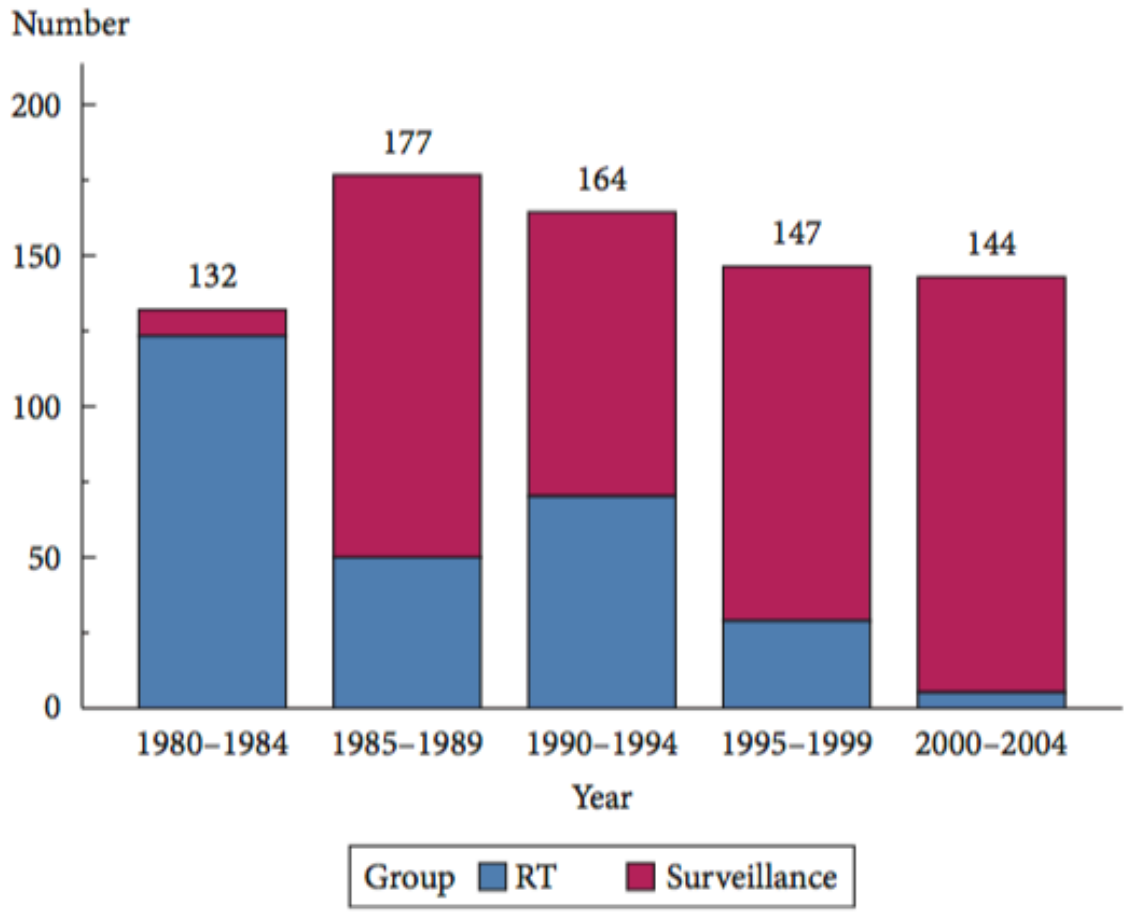
Treatment burden in stage I seminoma: a comparison of surveillance and adjuvant radiation therapy

Eric Leung[1,7], Padraig Warde[1,7], Michael Jewett[2,7], Tony Panzarella[3,7], Martin O'Malley[4,7], Joan Sweet[5,7], Malcolm Moore[6,7], Jeremy Sturgeon[8], Mary Gospodarowicz[1,7] and Peter Chung[1,7]

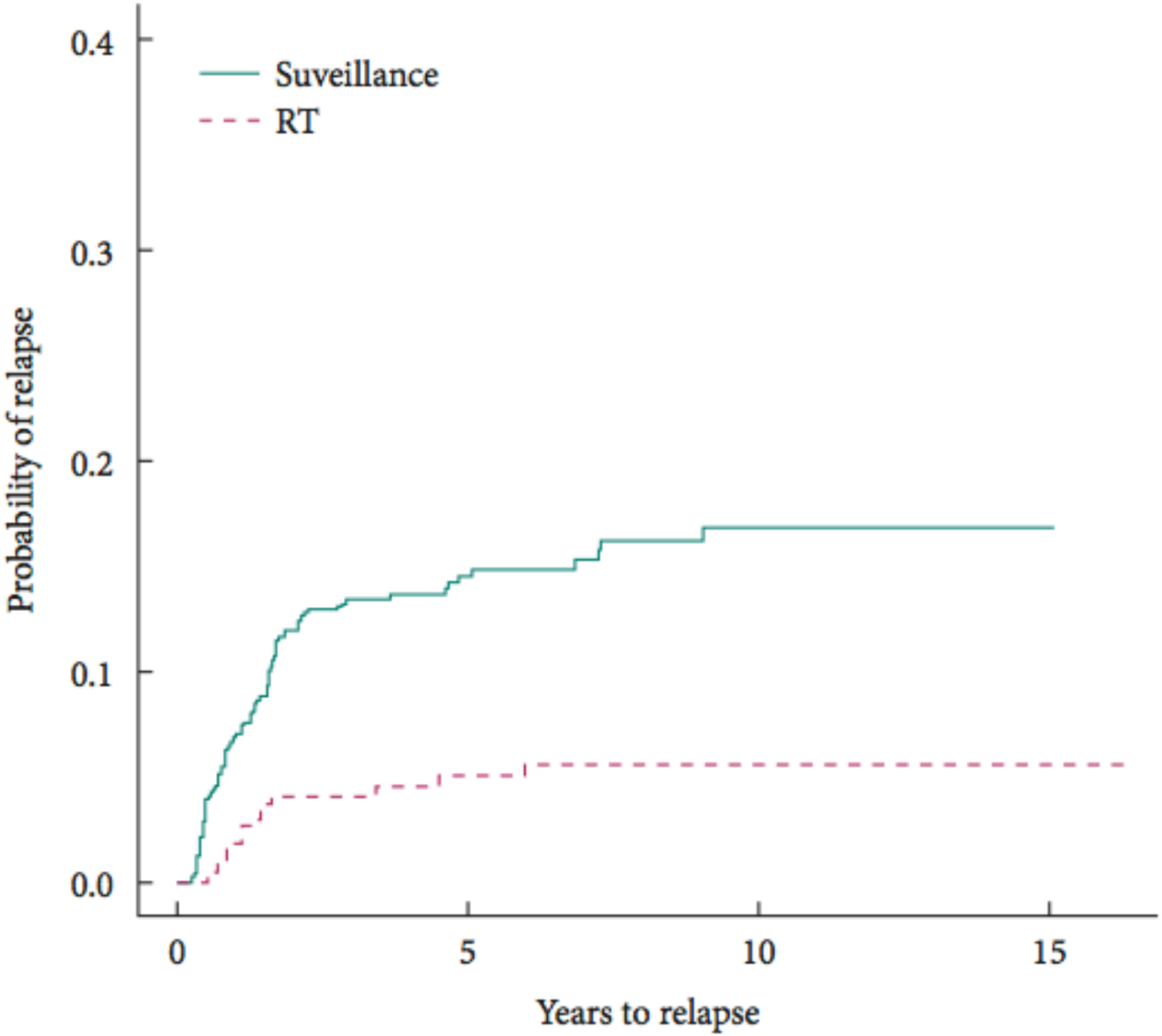
[1]Radiation Medicine Program, [2]Department of Surgical Oncology (Urology), [3]Department of Biostatistics, [4]Department of Medical Imaging, Princess Margaret Hospital, [5]Department of Pathology, University Health Network, [6]Department of Medical Oncology, Princess Margaret Hospital, [7]University of Toronto, Toronto, ON, and [8]Division of Medical Oncology, McGill University Health Centre, Montreal, QC, Canada

Presented at Annual Meeting of ASCO 2010.

BJU Int 2013; **112:** 1088–1095



- n=764, AS = 484, RT = 280
- 72 AS relapses: 56 RT, 15 chemo, 1 RPLND
- 14 RT relapses

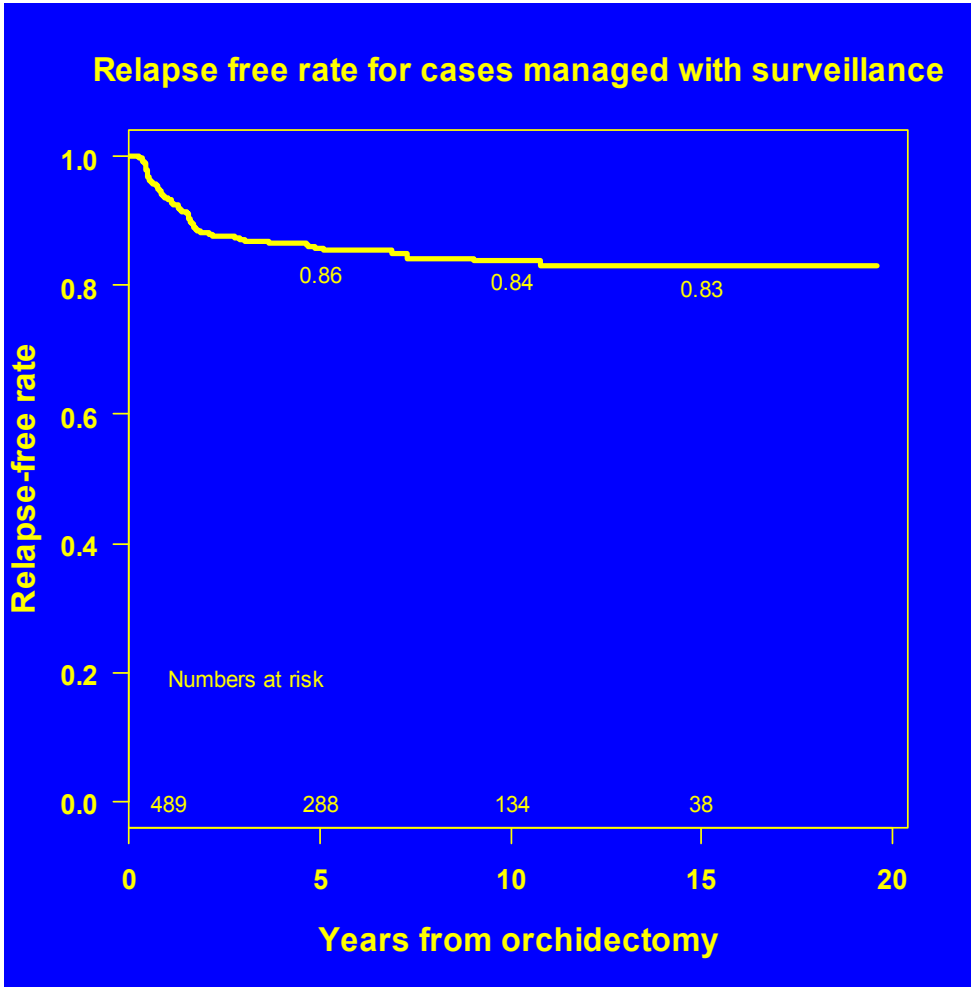

0.4
0.3
0.2
0.1
0.0
Probability of relapse
Suveillance
RT
0
5
10
15
Years to relapse

Stage I Seminoma PMH 1981-2004

- 776 Cases
  - Prospective data collection,
    - Phase II study of surveillance 1985 - 1994, patient choice since 1994
  - Follow-up - median 9.1 years (range 0.1-20.4)
    - 489 Surveillance - median f/u 8 years (0.1-19.8)
    - 287 Adjuvant RT - median f/u 10.1 years (0.2-20.4)
      - 4 monthly X 3 years, 6 monthly to yr 7, then annual to year 10
      - CT Abdomen/Pelvis if surveillance

Stage I Seminoma
PMH 1981-2004

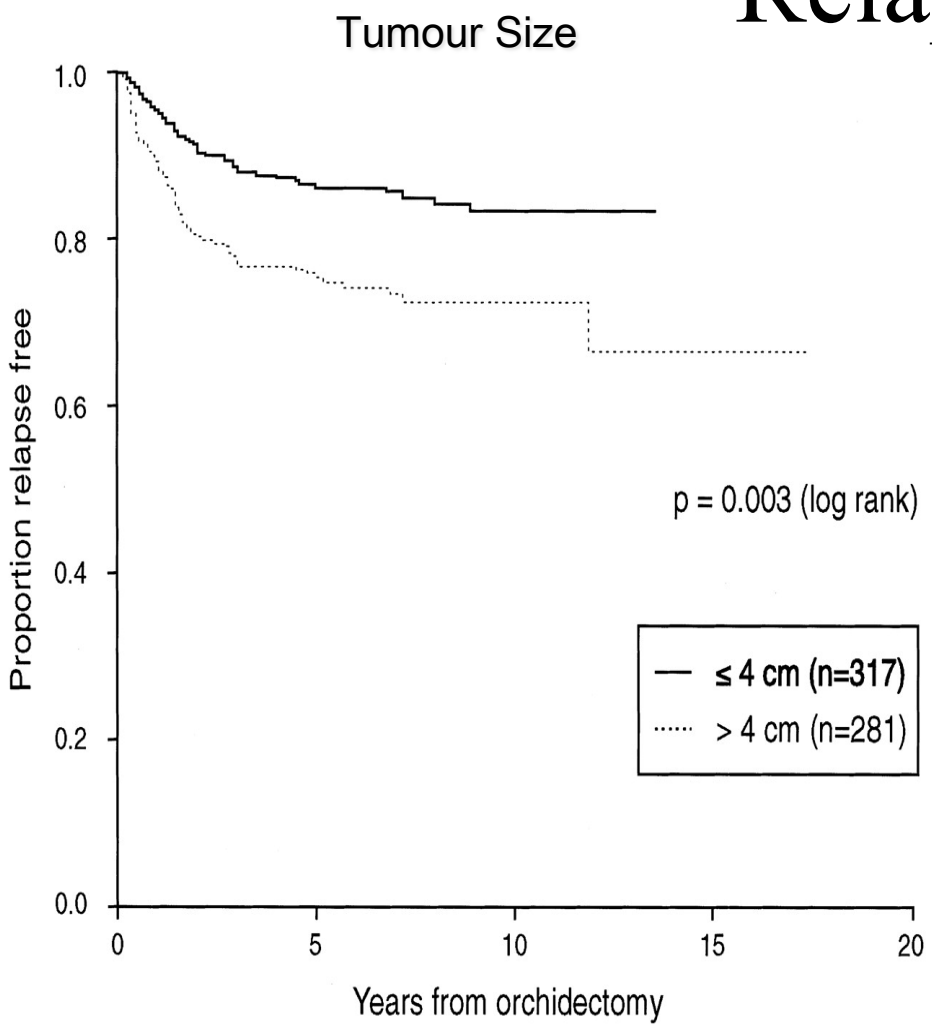
- Surveillance
  - 72 Relapses - 86% Relapse-Free Rate at 5 Years
  - Sites of Relapse
    - 64 (89%) Para-aortic nodes alone
    - 3 (4.2%) Para-aortic + Pelvic nodes
    - 4 (5.5%) Pelvic nodes alone
    - 1 (1.6%) Other

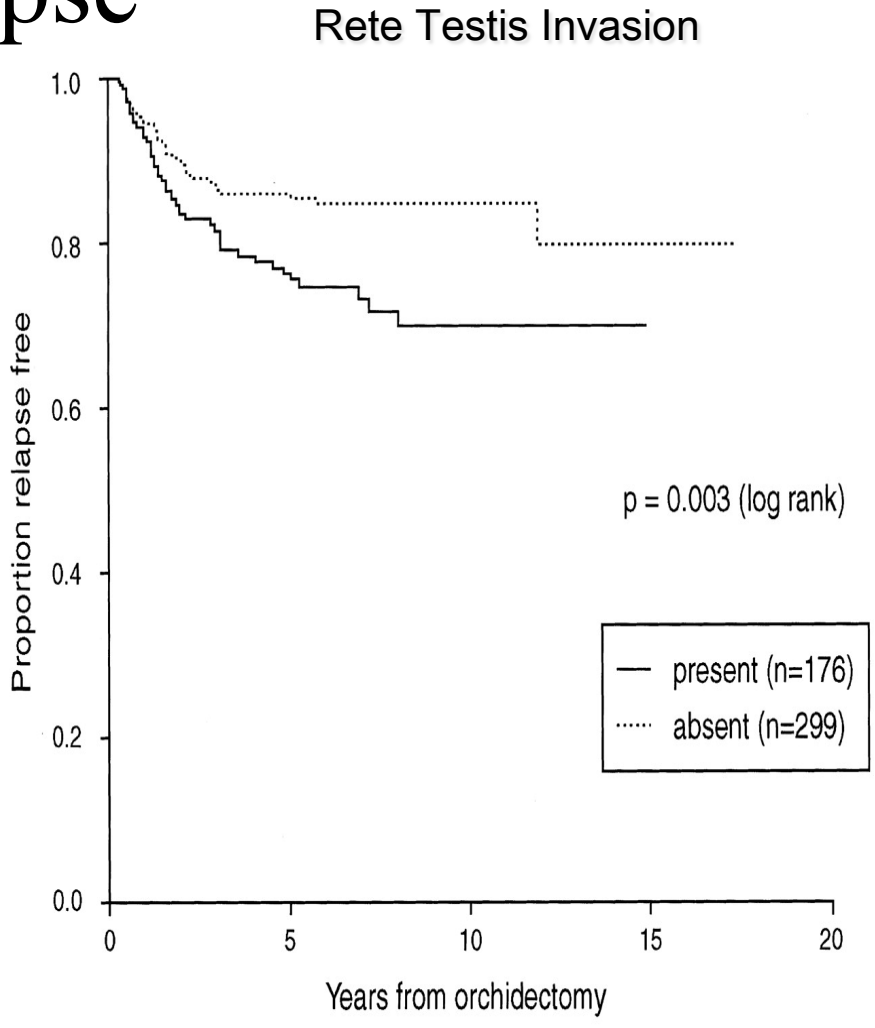


Stage I Seminoma
PMH 1981-2004

- Surveillance – treatment of relapse
  - 72 Relapses
    - 54 treated with RT
      - 5 second relapse all salvaged with chemotherapy
    - 16 Chemotherapy
    - 2 Surgery
  - 1 patient died from Seminoma

Surveillance Prognostic Factors for Relapse

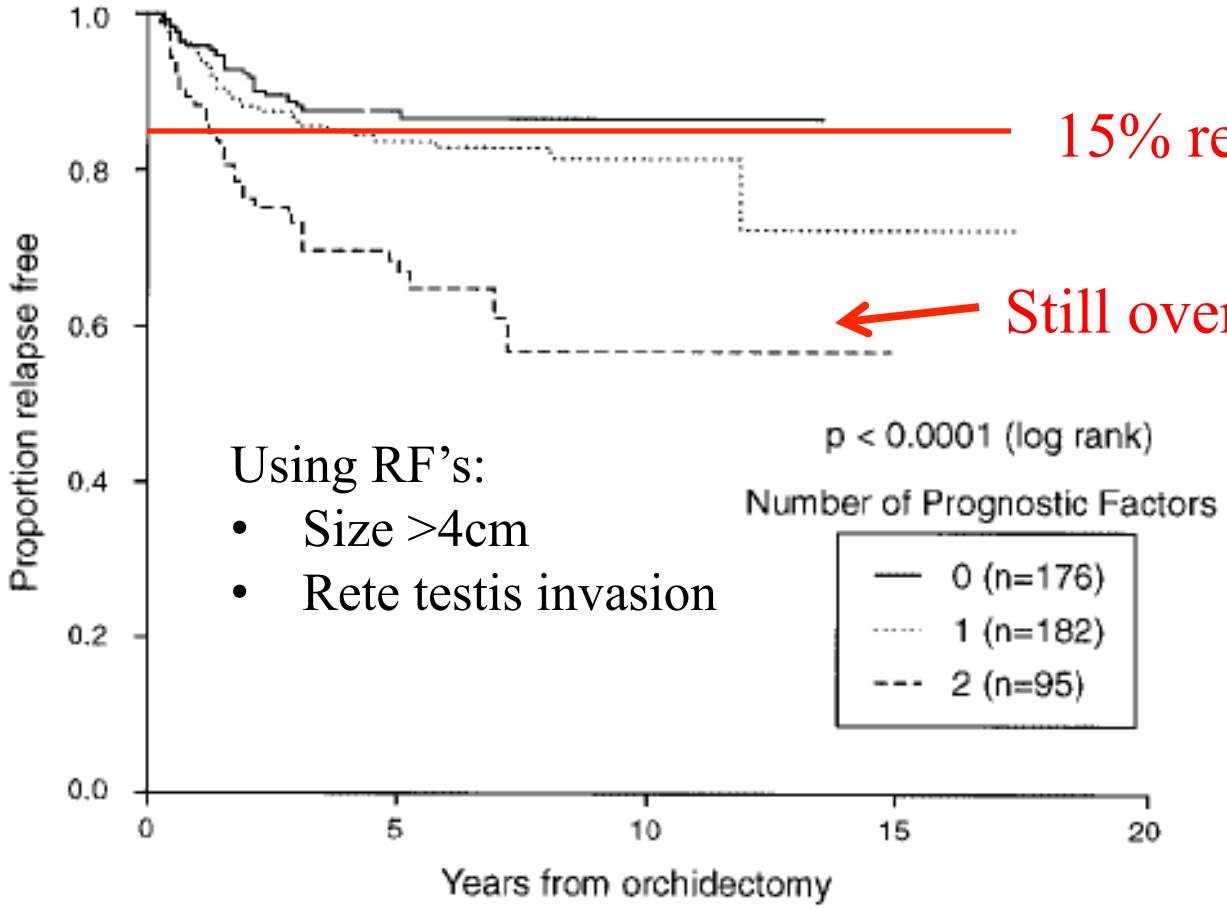




Warde et al. J Clin Oncol; 20:4448-4452 2002

Surveillance: Stage I Seminoma

- Risk adapted approach?



15% relapse overall

Still over treat 60% of time

Using RF's:

- Size >4cm
- Rete testis invasion

Warde et al., JCO, 2002

Should we risk stratify CS I Seminoma for adjuvant treatment? NO!

Cancer Medicine

Open Access

ORIGINAL RESEARCH

Evaluation of a prognostic model for risk of relapse in stage I seminoma surveillance

Peter Chung[1,2], Gedske Daugaard[3], Scott Tyldesley[4], Eshetu G. Atenafu[5], Tony Panzarella[5], Christian Kollmannsberger[4] & Padraig Warde[1,2]

[1]Radiation Medicine Program, Princess Margaret Cancer Centre, Toronto, Canada
[2]Department of Radiation Oncology, University of Toronto, Toronto, Canada
[3]Department of Oncology, Rigshospitalet, Copenhagen, Denmark
[4]British Columbia Cancer Agency, Vancouver, Canada
[5]Department of Biostatistics, Princess Margaret Cancer Centre, Toronto, Canada

Received: 20 May 2014; Revised: 22 June 2014; Accepted: 24 July 2014

Pooled analysis of 685 CS I Sem 1998-2005

Table 1. Patient characteristics.

Variable	Category	All (685)
Tumor size	≤4 cm	408
	>4 cm	161
	Missing	116 (16.9%)
Rete testis invasion	Absent	312
	Present	166
	Missing	207 (30.2%)
Age at surgery	≤36	361
	>36	323
	Missing	1 (0.15%)
Small vessels invasion	Absent	462
	Present	50
	Missing	173 (25.3%)

Table 1. Patient characteristics.

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Evaluation of a prognostic model for risk of relapse in stage I seminoma surveillance

Cancer Medicine E-pub Sept 2014

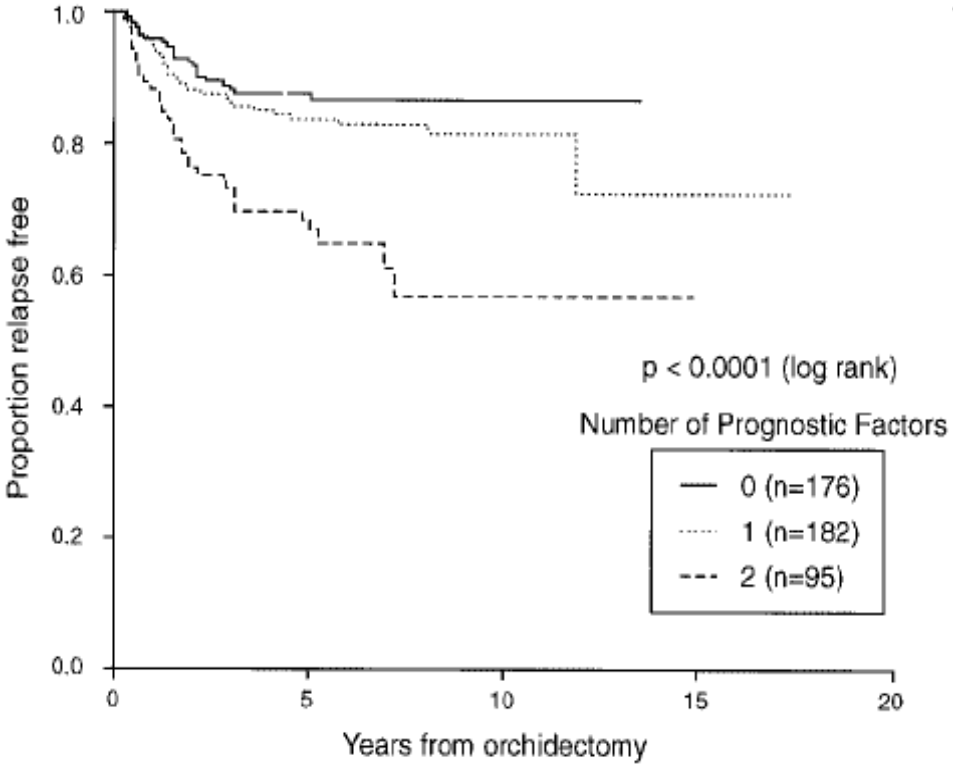
Peter Chung[1,2], Gedske Daugaard[3], Scott Tyldesley[4], Eshetu G. Atenafu[5], Tony Panzarella[5], Christian Kollmannsberger[4] & Padraig Warde[1,2]

- n = 685 CSI Seminomas
- 3 cancer centres
- 1998 – 2005
- Results:
  - Rete testis NOT validated
  - Tumour size did validate
- Conclusions:
  - "A clinically useful, highly discriminating prognostic model remains elusive in stage I seminoma"

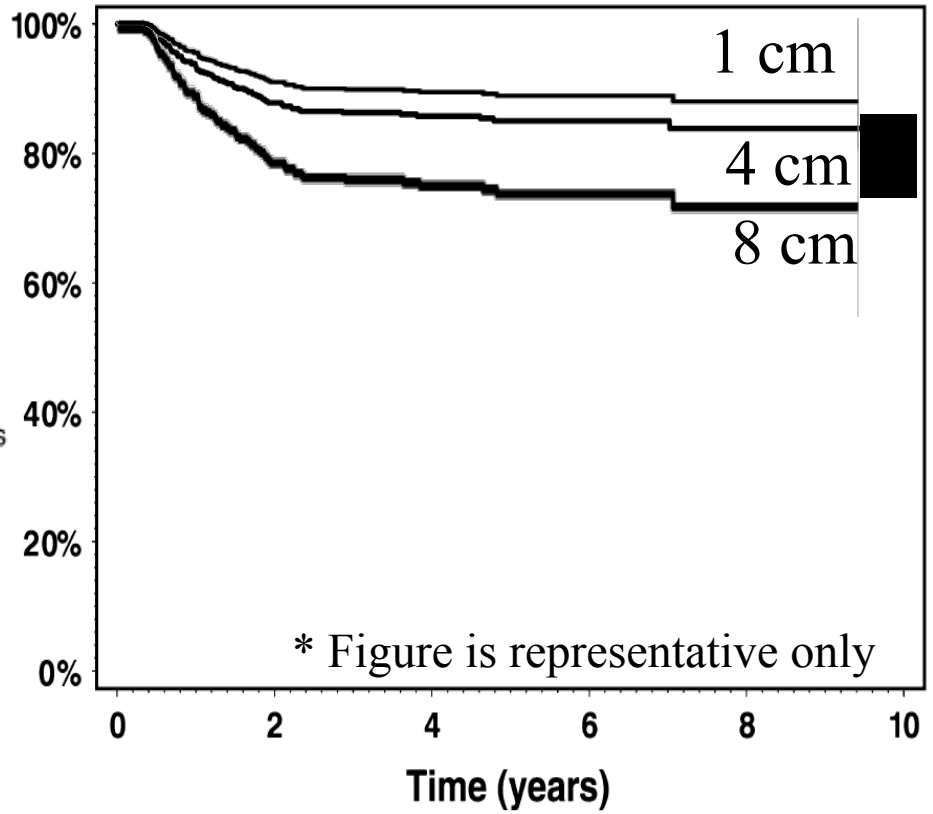
Primary tumor size*	Rate of relapse (%)
1 cm	9
2 cm	11
3 cm	13
4 cm	15
5 cm	17
6 cm	20
7 cm	23
8 cm	26

Seminoma: no good way to discriminate

Old



New*



Over treat 60%

Over treat 75%

For "high-risk" patients

Chemotherapy for CS I Seminoma

Randomized Trial of Carboplatin Versus Radiotherapy for Stage I Seminoma: Mature Results on Relapse and Contralateral Testis Cancer Rates in MRC TE19/EORTC 30982 Study (ISRCTN27163214)

R. Timothy D. Oliver, Graham M. Mead, Gordon J.S. Rustin, Johnathan K. Joffe, Nina Aass, Robert Coleman, Rhian Gabe, Philip Pollock, and Sally P. Stenning

- 1447 patients
- XRT(para-aortic) vs. 1 cycle Carbo
- 5 yr relapse rate: 4% vs. 5.3% (vs. 15% surveillance)
- Carbo: Proved “non-inferior” to XRT
- “Carboplatin can be regarded as a standard management option for stage I seminoma”

J Clin Oncol 29:957-962. © 2011

Carboplatin for Stage I Seminoma

- Advantages:
  - Reduces relapse from 15% to 5%
- Disadvantages:
  - Only reduces relapse from 15% to 5%
  - Short and long-term toxicity of chemo
    - Short: thrombocytopenia (GI-II: 12%, GIII-IV: 4%)
    - Long-term: not well known
      - One study: 199 pts with 9yrs follow-up
      - No increase in risk of overall mortality or second malignancy
      - But, non-significant increase in CV deaths (SMR 1.44)

SWENOTECA VII

GU ASCO 2014: Tandstad

- Carbo x 1 vs. Surveillance.
- Rete (HR 1.8) and Size >4cm (HR 2.7) as RFs.
  - No RFs: 97.1% RFR on surveillance
  - 1-2 RFs: 77.2% RFR on surveillance
  - No RFs: 97.7% RFR with carbo
  - 1-2 RFs: 90.6% RFR with carbo

Carboplatin for Stage I Seminoma

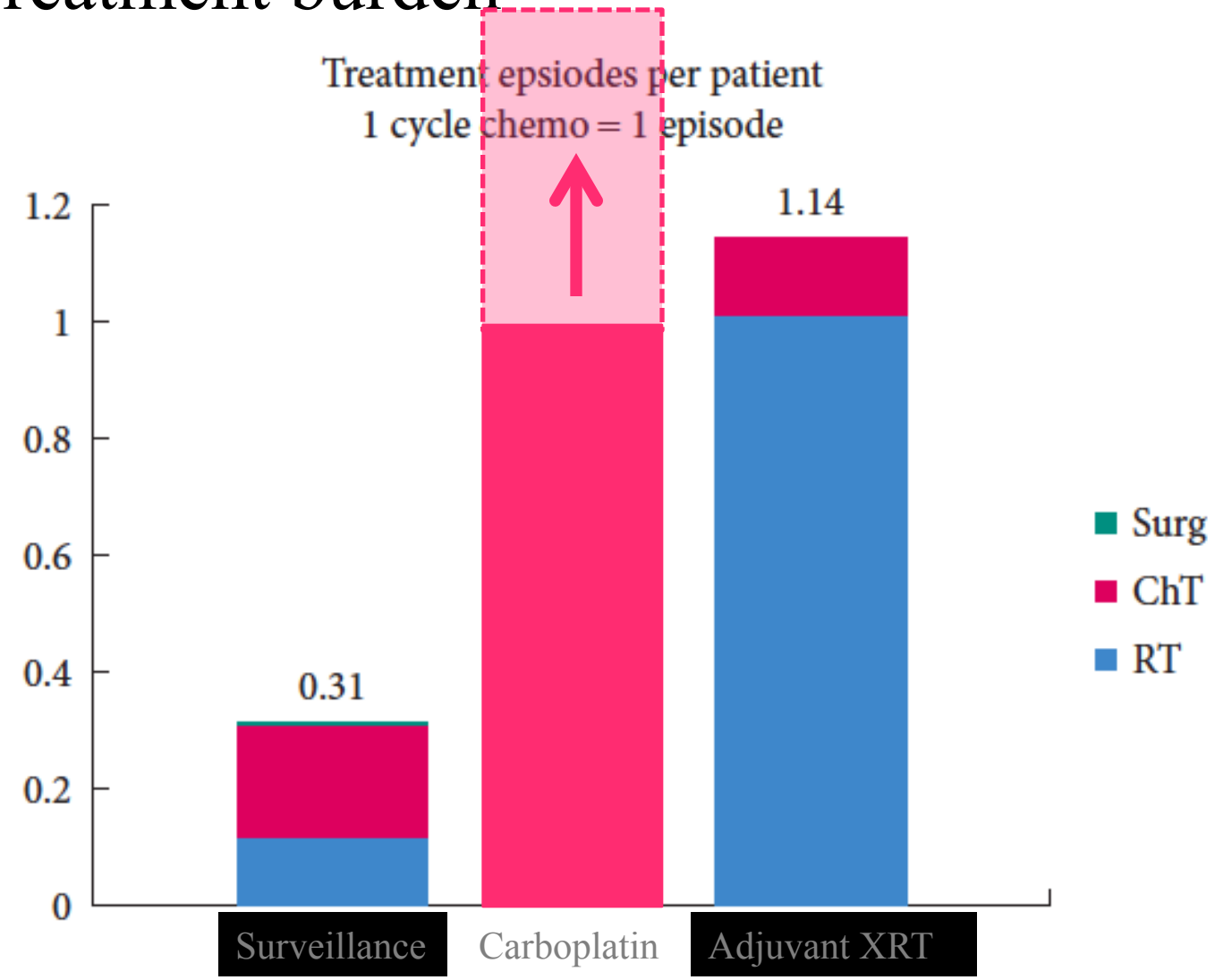
- Disadvantages:
  - Still need to image the retroperitoneum
    - Ideal follow-up schedule not known after carbo
    - But probably should be as frequent as surveillance of seminoma
    - THUS – Radiation exposure is the same
  - 85% are overtreated

Seminoma Stage 1: Surveillance, RT, and Carboplatin

	Surveillance	Radiation	Carbo x 1 or 2
Relapse	15%	4%	5%
Imaging Burden	Highest	Lowest	Highest
Treatment Burden	Lowest	Highest	Intermed?
Cancer specific Survival	99%	99%	99%

Surveillance: Stage I Seminoma

- Treatment burden



Leung, BJU Int, 2013

Adjuvant Chemotherapy

- 1 Course Carboplatin
  - At best reduces relapse rate from 15% to 5%
  - Unnecessary treatment in 85% cases
  - Late Relapse in seminoma is well recognised
    - Short Median Follow-up in MRC trial

Must continue to do Cross Sectional Imaging because of risk of Retroperiteonal Relapse if adjuvant chemotherapy chosen as management strategy

Oliver et al Lancet:366,293-300,2005

UHN Princess Margaret Cancer Centre

Approved 20-Apr-12

STAGE I SEMINOMA SURVEILLANCE PROTOCOL

Time Post Orchiectomy	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10	Month 11	Month 12
Year 1						**CT A&P***						**CT A&P** **CXR**** serum LH, FSH, free & total testosterone
Year 2						**CT A&P**						**CT A&P** **CXR** serum LH, FSH, free & total testosterone
Year 3						**CT A&P**						**CT A&P** **CXR** serum LH, FSH, free & total testosterone
Year 4												**CT Abdo*** ONLY** serum LH, FSH, free & total testosterone
Year 5												**CT Abdo ONLY** serum LH, FSH, free & total testosterone
Year 7												**CT Abdo ONLY** serum LH, FSH, free & total testosterone
Year 9												**CT Abdo ONLY** **CXR** serum LH, FSH, free & total testosterone

- 10 abdo CTs, 6 pelvis CTs, 4 CXR in 9 years
- low-dose CT (<1/2 dose of regular CT)

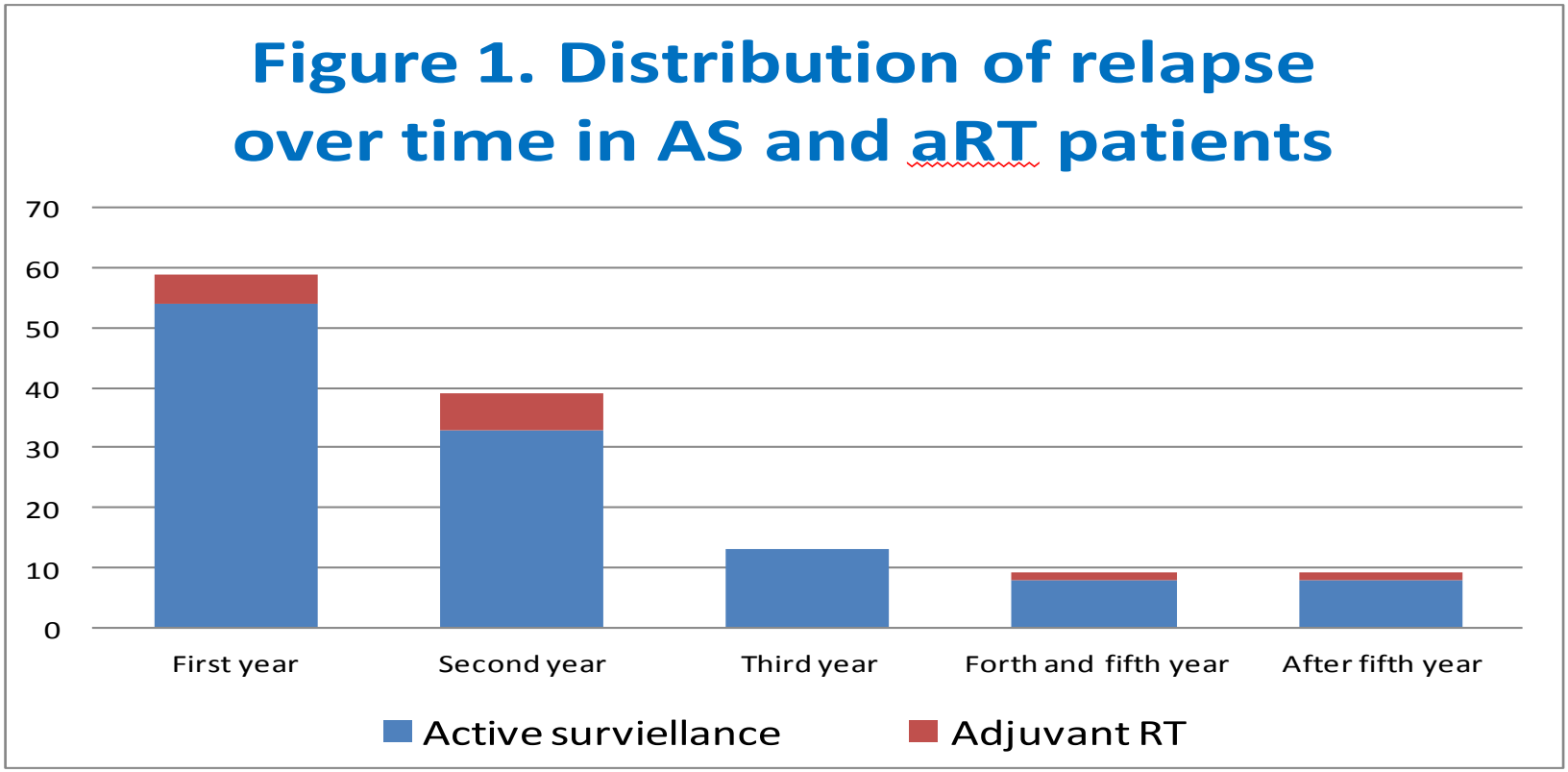
Seminoma Surveillance Summary: What to tell your patients

- 15% relapse rate
  - Yes…you can chose to have treatment to lower your relapse rate, but at what cost?
  - Survival is 99% no matter what you choose
- There is no good way to discriminate "low risk" from "high risk" seminoma
- Radiation – ↓relapse, but CV and 2nd cancer
  Carbo – …easy….sexy…but
  - Still need surveillance style imaging for relapse
  - Long-term toxicity not known

Clinical Outcomes of Late Relapse

CSI Seminoma

(1981-2011,n=129/1047,AS=753)



Para-aortic node(s) was the most common relapse site in AS patients either in LR (n=28, 97%; median size: 2.1 cm) or in ER (n=79, 92%; median size: 2 cm)

Recommendations
Stage I Seminoma 2010
Best way to minimise treatment and late effects

- Surveillance
  - allows > 80% of patients to avoid *any* postorchidectomy treatment
  - with no increase in % patients requiring chemotherapy
  - with no increase in cause specific mortality
  - should be *offered* to all patients

Outline

- Relapse after Initial Management Strategy
  - Surveillance 15%
    - Low bulk Para-aortic nodes -90% – **Main Focus**
    - Bulky Para-aortic nodes/Distant Metastases
      - BEP X 3 or EPX4
  - Adjuvant Carboplatin 5%
    - Low bulk Para-aortic nodes -66%– **Main Focus**
    - Bulky Para-aortic nodes/Distant Metastases
      - BEP X 3 or EPX4
  - Adjuvant RT
    - Pelvic/Inguinal nodes
      - RT or BEP X 3 or EPX4
    - Distant Relapse
      - BEP X 3 or EPX4

Treatment Options for Stage I Non-Seminoma

- Active Surveillance
  - Universal or Non-Risk Adapted for all with delayed Rx for relapse
  - Risk-adapted with adjuvant chemotherapy for high risk
- pRPLND for high risk or all

Active Surveillance Non-Seminoma

- **Strategy based on early detection of relapse by intense follow-up after orchidectomy**
- **Over 3000 patients in surveillance protocols**
- **Identification of prognostic factors of relapse**
  - **Lymphovascular Invasion (LVI)**
  - **Embryonal Carcinoma (EC)**
- **Risk-adapted policy?**

Read G et al. J Clin Oncol 1992; Albers P et al. J Clin Oncol 2003

Author	No. of Patients	Median Follow-up (years)	Relapses (Number/ %)	Median time to relapse (months-range)	Deaths (Number/%)	Overall Survival Rate
Read [2]	373	5	100 (27%)	NR	5 (2%)	98%
Daugaard [20]	301	5	86 (29%)	5 (1-171)	0 (0%)	98.6%
Colls [19]	248	4.5	70 (28%)	NR	3 (2%)	97%
Francis [22]	183	5.1	52 (28%)	6 (1-122)	2 (1%)	99%
Sharir [29]	170	6.3	48 (28%)	6.9	1 (1%)	99%
Gels [14]	154	7	42(27%)	4 (2-24)	2 (1%)	99%
Sogani [17]	105	11.3	27 (26%)	5 (2-24)	3 (3%)	97%
Roeleveld [23]	90	8	23 (26%)	7 (3-44)	1 (1%)	98.9%
Nicolai [15]	85	11	25 (29%)	7 (2-68)	3 (3.5%)	96%

EUROPEAN UROLOGY 59 (2011) 556–562

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

European Association of Urology

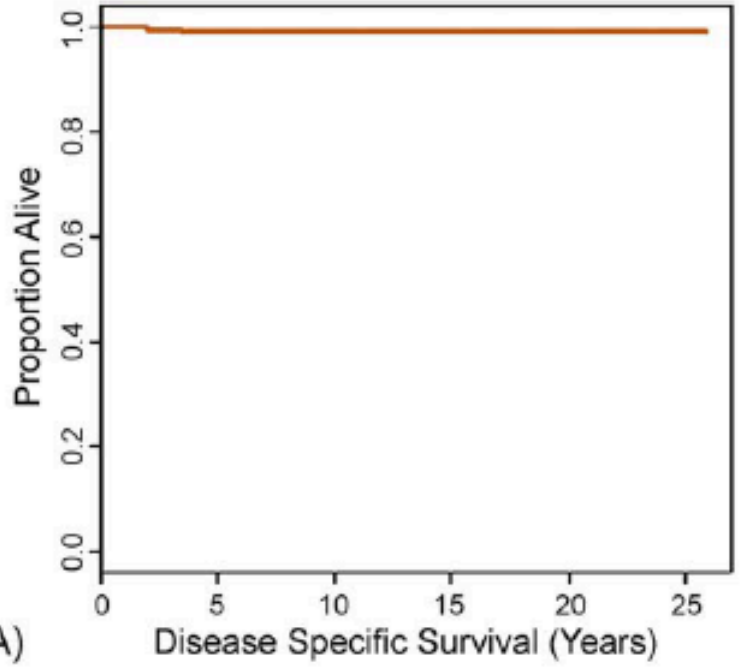
Platinum Priority – Testis Cancer

Editorial by Arthur I. Sagalowsky on pp. 563–565 of this issue

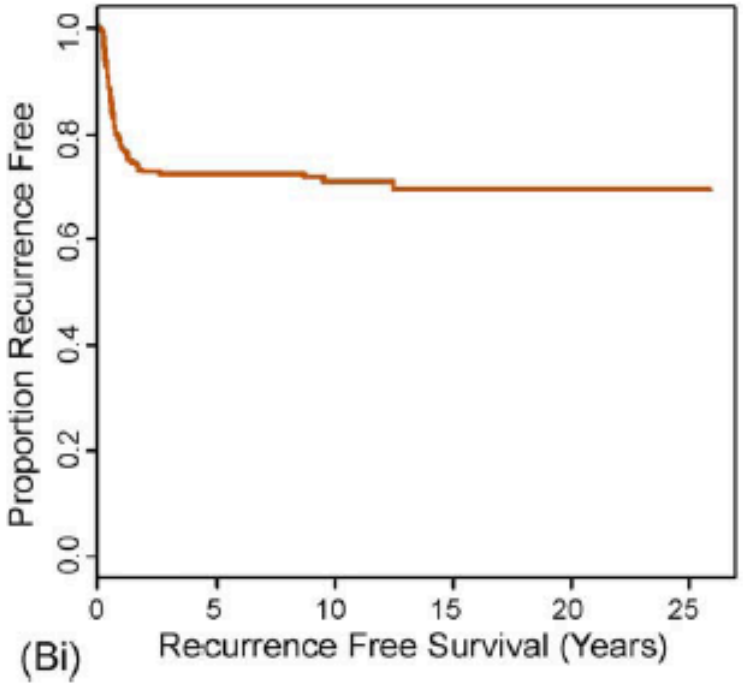
Non–Risk-Adapted Surveillance in Clinical Stage I Nonseminomatous Germ Cell Tumors: The Princess Margaret Hospital's Experience

Jeremy F. Sturgeon, Malcolm J. Moore, David M. Kakiashvili, Ignacio Duran, Lynn C. Anson-Cartwright, Dominik R. Berthold, Padraig R. Warde, Mary K. Gospodarowicz, Ruth E. Alison, Justin Liu, Clement Ma, Greg R. Pond, Michael A. Jewett *

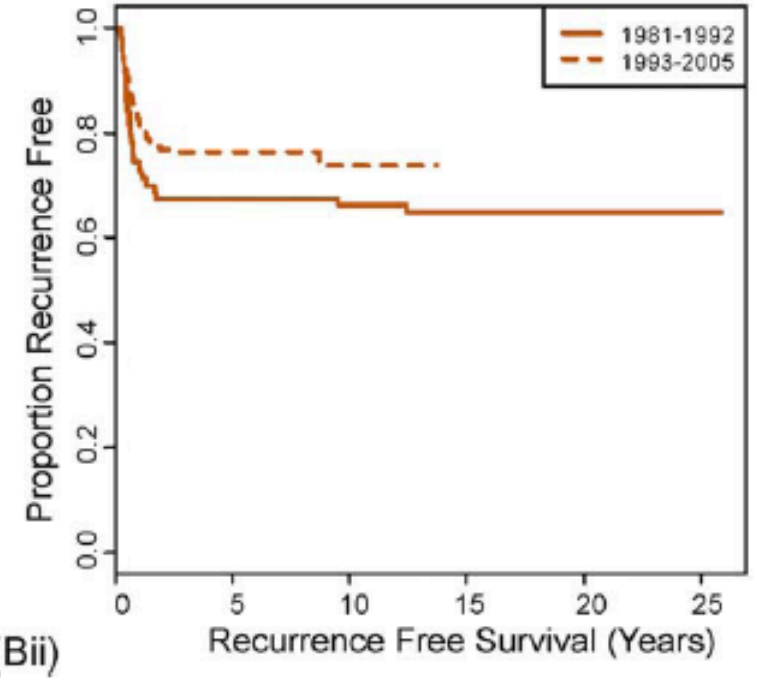
Departments of Medical, Surgical, and Radiation Oncology, Princess Margaret Hospital, University Health Network and Department of Surgery (Urology), University of Toronto, Toronto, Ontario, Canada


Proportion Alive
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
Disease Specific Survival (Years)

(A)

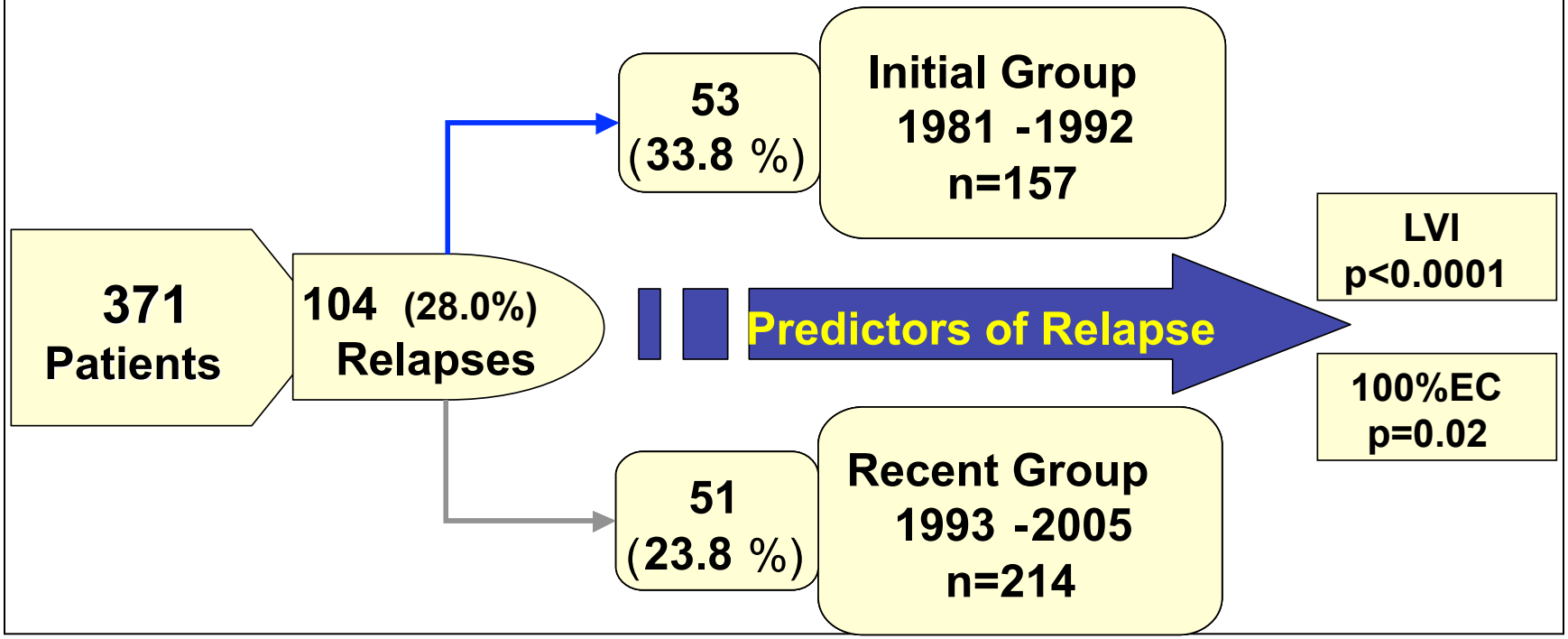

Proportion Recurrence Free
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
Recurrence Free Survival (Years)

(Bi)


1981-1992
1993-2005
Proportion Recurrence Free
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
Recurrence Free Survival (Years)

(Bii)

RELAPSE & PREDICTORS



RELAPSE RATE BY RISK

	High Risk	Relapses	Low Risk	Relapses
Initial Group n=157	66	36/66 (54.5%)	91	17/91 (18.7%)
Recent Group n=214	59	29/59 (49.2%)	155	22/155 (14.2%)
	125	65	246	39

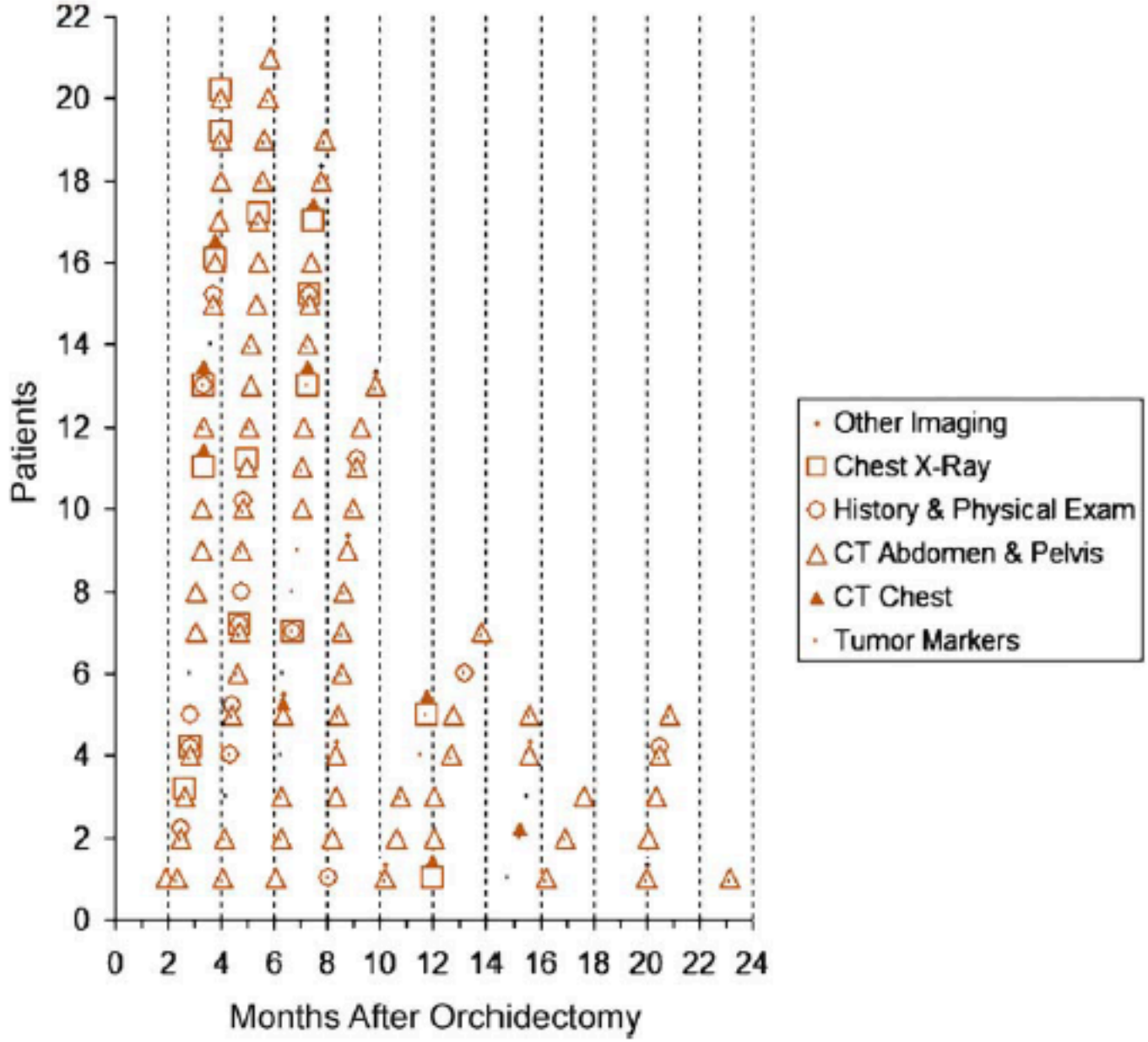


Fig. 1 – Diagnostic tools at detection of relapse.

Our Preferred Management of Clinical Stage I (pT1-4N0M0) NSGCT

- Non-Risk Adapted Active Surveillance
  - Universal surveillance
- In those not suitable for surveillance
  - Primary Chemotherapy, or
  - Nerve Sparing Retroperitoneal Lymphadenectomy
- Routine RPLND not recommended
- Marker +ve – treat as stage II with chemotherapy

Annals of Oncology Advance Access published October 29, 2009

original article

Annals of Oncology
doi:10.1093/annonc/mdp473

Non-risk-adapted surveillance for patients with stage I nonseminomatous testicular germ-cell tumors: diminishing treatment-related morbidity while maintaining efficacy

C. Kollmannsberger[1], C. Moore[2], K. N. Chi[1], N. Murray[1], S. Daneshmand[3], M. Gleave[4], B. Hayes-Lattin[5] & C.R. Nichols[2*]

[1]Division of Medical Oncology, Department of Medicine, British Columbia Cancer Agency-Vancouver Cancer Center, Vancouver, British Columbia, Canada; [2]Department of Medicine, Earle A. Chiles Research Institute, Providence Cancer Center; [3]Section of Urologic Oncology, Division of Urology and Renal Transplantation, Department of Medicine, Oregon Health & Science University, Portland, OR, USA; [4]Department of Urological Sciences, University of British Columbia, The Prostate Center at Vancouver General Hospital, Vancouver, British Columbia, Canada and [5]Division of Hematology and Medical Oncology, Department of Medicine, Oregon Health & Science University Knight Cancer Institute, Portland, OR, USA

n=223

59 (26%) relapse, 7 >2yrs

100% DSS

Clinical Stage I Non-seminoma

Canadian Consensus :

Clinical stage I Recommendations

- For appropriately selected patients, primary surveillance regardless of risk is recommended.
- For patients unsuitable for surveillance, or who prefer immediate treatment, adjuvant chemotherapy with BEP X 2 is recommended.
- RPLND is not recommended in the routine management of patients with clinical stage I nonseminoma.

EUROPEAN UROLOGY 53 (2008) 478–496

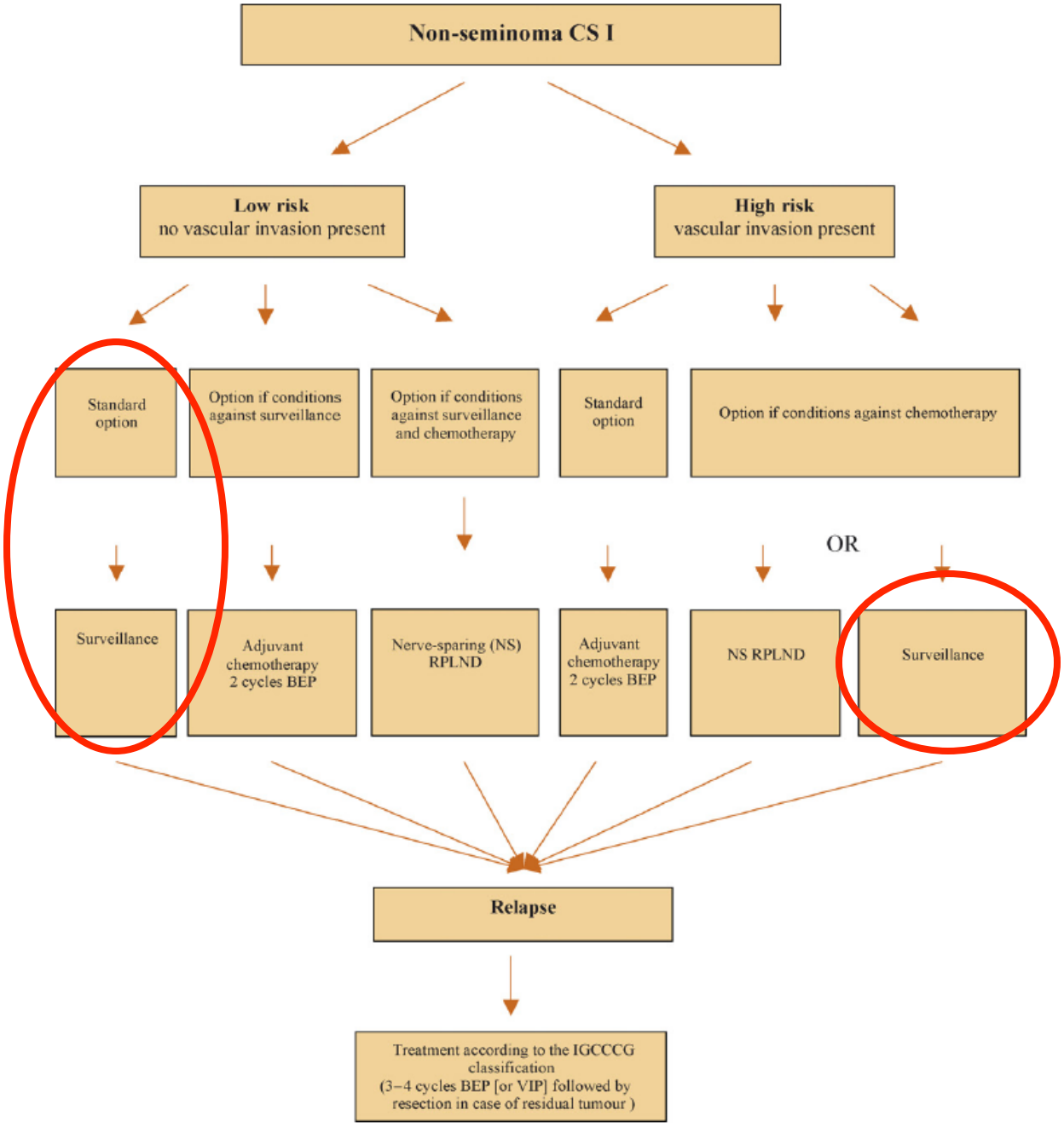
available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Review – Testis Cancer

European Consensus Conference on Diagnosis and Treatment of Germ Cell Cancer: A Report of the Second Meeting of the European Germ Cell Cancer Consensus group (EGCCCG): Part I

Susanne Krege[1,*], Jörg Beyer[2], Rainer Souchon[3], Peter Albers[4], Walter Albrecht[5], Ferran Algaba[6], Michael Bamberg[7], István Bodrogi[8], Carsten Bokemeyer[9], Eva Cavallin-Ståhl[10], Johannes Classen[11], Christoph Clemm[12], Gabriella Cohn-Cedermark[13], Stéphane Culine[14], Gedske Daugaard[15], Pieter H.M. De Mulder[16], Maria De Santis[17], Maike de Wit[18], Ronald de Wit[19], Hans Günter Derigs[20], Klaus-Peter Dieckmann[21], Annette Dieing[22], Jean-Pierre Droz[23], Martin Fenner[24], Karim Fizazi[25], Aude Flechon[26], Sophie D. Fossa[27], Xavier Garcia del Muro[28], Thomas Gauler[29], Lajos Geczi[30], Arthur Gerl[31], Jose Ramon Germa-Lluch[32], Silke Gillessen[33], Jörg T. Hartmann[34], Michael Hartmann[35], Axel Heidenreich[36], Wolfgang Hoeltl[37], Alan Horwich[38], Robert Huddart[39], Michael Jewett[40], Johnathan Joffe[41], William G. Jones[42], László Kisbenedek[43], Olbjørn Klepp[44], Sabine Kliesch[45], Kai Uwe Koehrmann[46], Christian Kollmannsberger[47], Markus Kuczyk[48], Pilar Laguna[49], Oscar Leiva Galvis[50], Volker Loy[51], Malcolm D. Mason[52], Graham M. Mead[53], Rolf Mueller[54], Craig Nichols[55], Nicola Nicolai[56], Tim Oliver[57], Dalibor Ondrus[58], Gosse O.N. Oosterhof[59], Luis Paz Ares[60], Giorgio Pizzocaro[61], Jörg Pont[62], Tobias Pottek[63], Tom Powles[64], Oliver Rick[65], Giovanni Rosti[66], Roberto Salvioni[67], Jutta Scheiderbauer[68], Hans-Ulrich Schmelz[69], Heinz Schmidberger[70], Hans-Joachim Schmoll[71], Mark Schrader[72], Felix Sedlmayer[73], Niels E. Skakkebaek[74], Aslam Sohaib[75], Sergei Tjulandin[76], Padraig Warde[77], Stefan Weinknecht[78], Lothar Weissbach[79], Christian Wittekind[80], Eva Winter[81], Lori Wood[82], Hans von der Maase[83]


Non-seminoma CS I
Low risk
no vascular invasion present
High risk
vascular invasion present
Standard option
Option if conditions against surveillance
Option if conditions against surveillance and chemotherapy
Standard option
Option if conditions against chemotherapy
OR
Surveillance
Adjuvant chemotherapy 2 cycles BEP
Nerve-sparing (NS) RPLND
Adjuvant chemotherapy 2 cycles BEP
NS RPLND
Surveillance
Relapse
Treatment according to the IGCCCG classification
(3–4 cycles BEP [or VIP] followed by resection in case of residual tumour)

Nonseminoma: Stage I

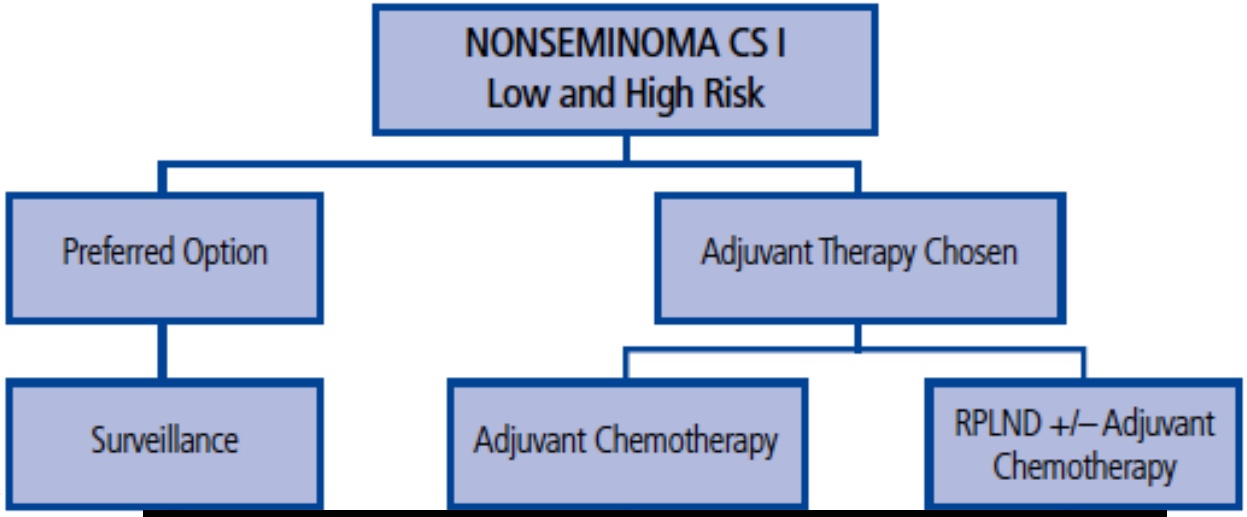
- Slightly more controversial than seminoma
- More discriminative risk factors available
  - All comers: 30% relapse
    - LVI -: 15% relapse (Stage IA)
    - LVI+: 50% relapse (Stage IB)
  - Only other risk factor advocated by some:
    - Pure Embryonal or Embryonal “predominant”
      - Confers about 1.7x risk of recurrence (vs. 3.2 for LVI)

Our Preferred Management of Clinical Stage I (pT1-4N0M0) NSGCT

- Non-Risk Adapted Active Surveillance
  - universal surveillance
- In those not suitable for surveillance
  - Primary Chemotherapy, or
  - Nerve Sparing Retroperitoneal Lymphadenectomy
- Routine RPLND not recommended
- Marker +ve – treat as stage II with chemotherapy

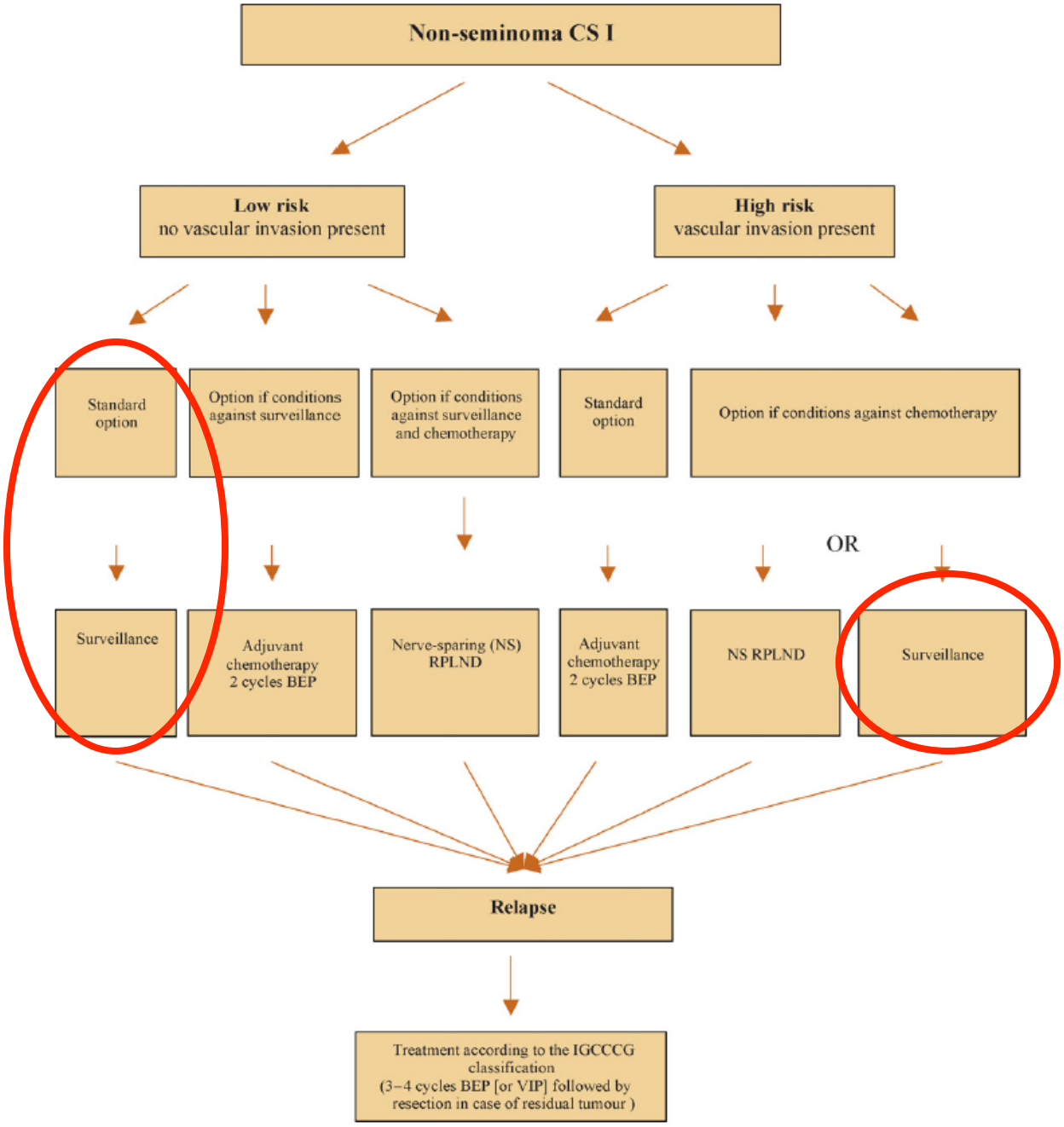
Nonseminoma: Stage I

- CUA Consensus Guidelines (2010)



Princess Margaret:
"Non-risk-adapated" surveillance

Not all guidelines agree……
NCCN – more emphasis on RPLND
ESMO – more emphasis on BEP x 1-2


Non-seminoma CS I
Low risk
no vascular invasion present
High risk
vascular invasion present
Standard option
Option if conditions against surveillance
Option if conditions against surveillance and chemotherapy
Standard option
Option if conditions against chemotherapy
OR
Surveillance
Adjuvant chemotherapy 2 cycles BEP
Nerve-sparing (NS) RPLND
Adjuvant chemotherapy 2 cycles BEP
NS RPLND
Surveillance
Relapse
Treatment according to the IGCCCG classification
(3–4 cycles BEP [or VIP] followed by resection in case of residual tumour)

Variable Recommendations for CS1 NSGCT

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2014
Testicular Cancer - Nonseminoma

CLINICAL STAGE	PRIMARY TREATMENT
Stage IA	Surveillance (preferred) or Nerve-sparing RPLND[O,I]
Stage IB	Nerve-sparing RPLND[O,I] or Primary chemotherapy:[I] BEP for 2 cycles or BEP for 1 cycle or Surveillance for T2 only (category 2B)

ESMO-Clinical Practice Guideline

	Stage I
First line	Vascular invasion absent [redacted] Preferred: • Surveillance Alternatively: ▪ 1-2xBEP ▪ RPLND (rarely) Vascular invasion present [redacted] Preferred: ▪ 1-2xBEP ▪ Surveillance Alternatively: ▪ RPLND (rarely)

Nonseminoma: Stage I

- Relapse and CSS by therapy

Option	Relapse	CSS
Primary RPLND	13% (0% @ PM*)	98-100% (99% @ PM)

- Sheinfeld and Hedenreich (Feldman editorial):
  - RPLND 5-7% recurrence for CS1B
  - Only 1-3% recurrence in the RP

Princess Margaret Hospital
University Health Network

Approved 20-Apr-12

STAGE I NON-SEMINOMA SURVEILLANCE GUIDELINE

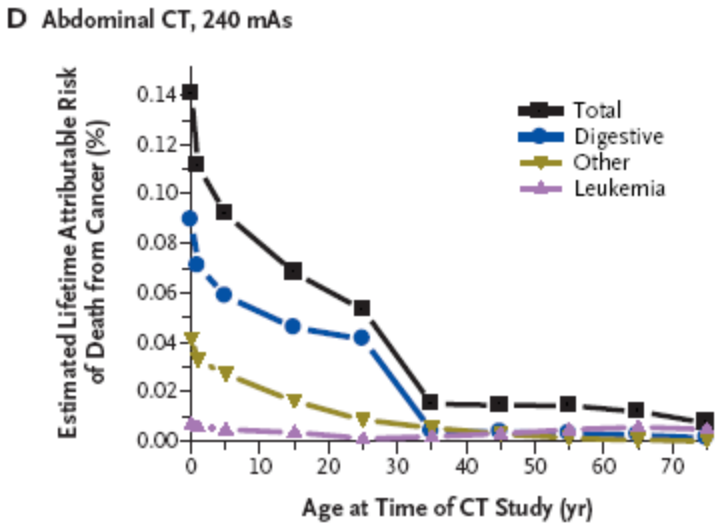
Time Post Orchiectomy	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10	Month 11	Month 12
Year 1	Markers*	Markers		Markers CT A&P*** CT Thorax		Markers		Markers CT A&P CT Thorax		Markers		Markers CT A&P CT Thorax Serum LH,FSH, free & total testosterone
Year 2		Markers		Markers		Markers		Markers		Markers		Markers CT A&P CT Thorax Serum LH,FSH, free & total testosterone
Year 3				Markers				Markers				Markers Serum LH,FSH, free & total testosterone
Year 4						Markers						Markers Serum LH,FSH, free & total testosterone
Year 5												Markers CT A&P CT Thorax Serum LH,FSH, free & total testosterone
	Transition to primary care after 5 years. No ongoing imaging/labs required. Physical surveillance of remaining testis.											

- 5 abdo-pelvis CTs, 5 Chest CTs, in 5 years
- low-dose CT (<1/2 dose of regular CT)

Risks of Diagnostic Radiatioin

Serial CT scanning

- cancer risk Lifetime risk Death from Ca with 1 CT Scan (Brenner & Hall, NEJM 2007;357:2277)



Rationale for RPLND for Clinical Stage I (pT1-4N0M0) NSGCT

- Accurate staging of retroperitoneum
- “Control the retroperitoneum” if pS II
- Reduce follow-up imaging of abdomen
- Reduce chemotherapy and its toxicity

VOLUME 26 · NUMBER 18 · JUNE 20 2008

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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

Peter Albers, Roswitha Siener, Susanne Krege, Hans-Uwe Schmelz, Klaus-Peter Dieckmann, Axel Heidenreich, Peter Kwasny, Maik Pichlmeier, Jan Lehmann, Sabine Kliesch, Kai-Uwe Köhrmann, Rolf Finnern, Lothar Weißbach, Volker Ley, Christian Wittekind, and Michael Hartmann

VOLUME 26 · NUMBER 19 · JUNE 20 2008

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

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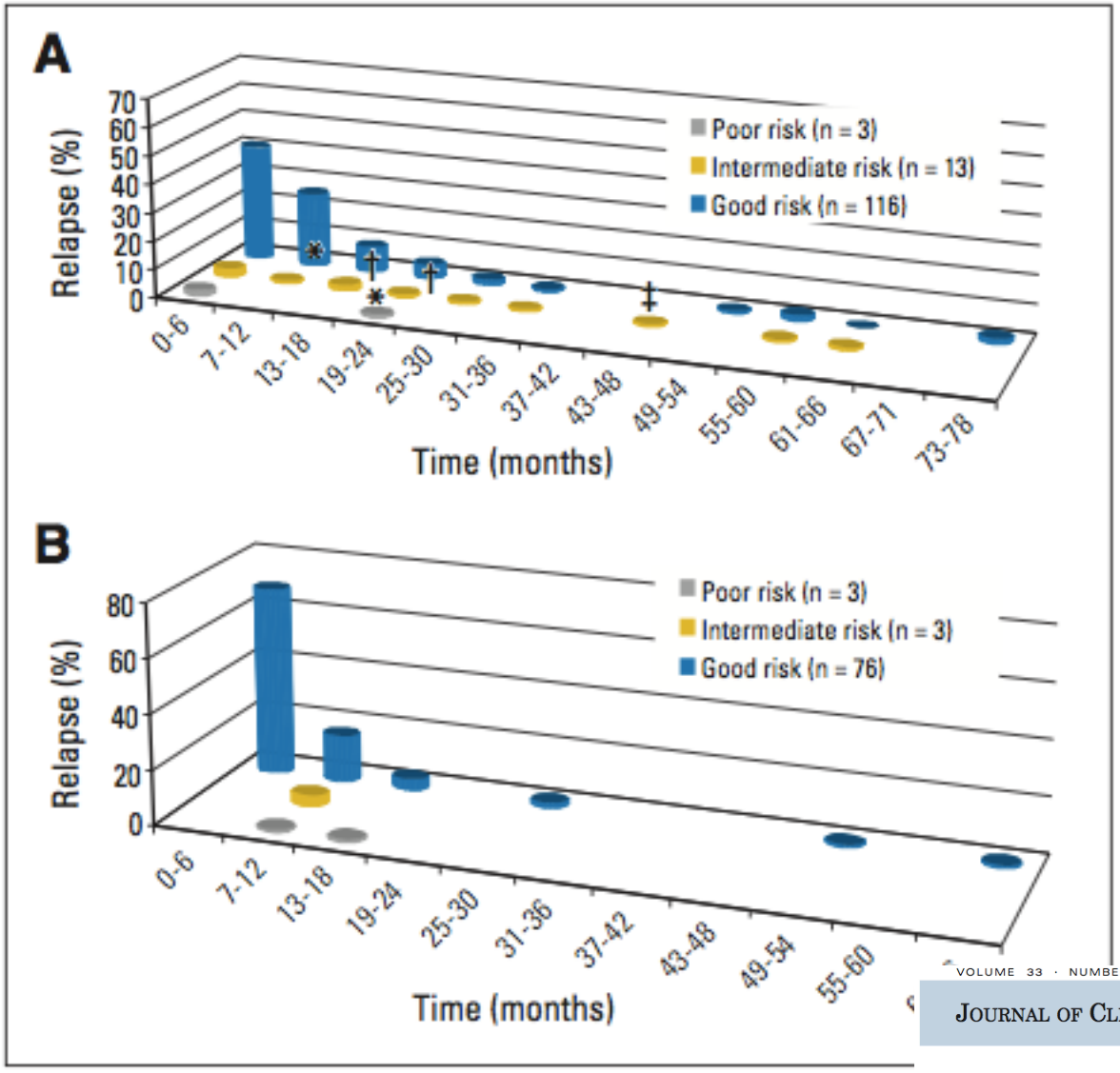
1 course BEP vs RPLND

- 61 centres performed 173 RPLND's
- 18% N+ (32/172) - adjuvant BEPx2 in 24
- 10% relapse (13/140 those no adjuvant chemo) – BEPx3, salvage surgery in some
- Approx 25% double therapy
- 7 retroperitoneal recurrences (mainly outside template)

Alternatives for Rx of Clinical Stage I NSGCT / 100 patients

	Toronto PMH	German Testicular Cancer Study Group AUO Trial AH 01/94	
	Surveillance	RPLND	Chemotherapy
High risk	28	42	42
Mortality (@2yrs)	0.5	3	0
Relapses (@ 2 yrs)	23	5	.5
No Therapy	77	0	0
Single Therapy	13	93	99
Multimodal Therapy	9	19	.5
Surveillance	100	0	0
RPLND	13	100	1
Chemotherapy	17	41	100
Chemotherapy cycles	69	59	122
1 &/or 2 cycles	1	38	122
3 or more	68	21	0

Pattern of & Risk Status @ Relapse of Clinical Stage I NSGCT



VOLUME 33 · NUMBER 1 · JANUARY 1 2015

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Patterns of Relapse in Patients With Clinical Stage I Testicular Cancer Managed With Active Surveillance

Christian Kollmannsberger, Torgrim Tandstad, Philippe L. Bedard, Gabriella Cohn-Cedermark, Peter W. Chung, Michael A. Jewett, Tom Powles, Padraig R. Warde, Siamak Daneshmand, Andrew Protheroe, Scott Tyldesley, Peter C. Black, Kim Chi, Alan I. So, Malcom J. Moore, and Craig R. Nichols

Peter C. Black and Alan I. So, University of British Columbia, The Vancouver

Trend to Chemotherapy in Clinical Stage II NSGCT

VOLUME 25 · NUMBER 35 · DECEMBER 10 2007

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Nonrandomized Comparison of Primary Chemotherapy and Retroperitoneal Lymph Node Dissection for Clinical Stage IIA and IIB Nonseminomatous Germ Cell Testicular Cancer

Andrew I. Stephenson, George J. Bosl, Robert J. Motzer, Dean F. Bajorin, Jason P. Stasi, and Joel Sheinfeld

Table 1. Primary Treatment Modality (overall and by clinical stage) for Patients Over Time

Modality	Period						*P*
	1989-1993		1994-1998		1999-2002		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Overall							< .001
RPLND	57	78	56	52	23	32	
Chemotherapy	16	22	52	48	48	68	
Clinical stage IIA							< .001
RPLND	44	98	52	84	23	55	
Chemotherapy	1	2	10	16	19	45	
Clinical stage IIB							< .001
RPLND	13	46	4	9	0	0	
Chemotherapy	15	54	42	91	29	100	

Abbreviation: RPLND, retroperitoneal lymph node dissection.

VOLUME 25 · NUMBER 35 · DECEMBER 10 2007

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ORIGINAL REPORT

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Table 4. Outcome Comparison for Patients Treated From 1989 to 1998 versus 1999 to 2002

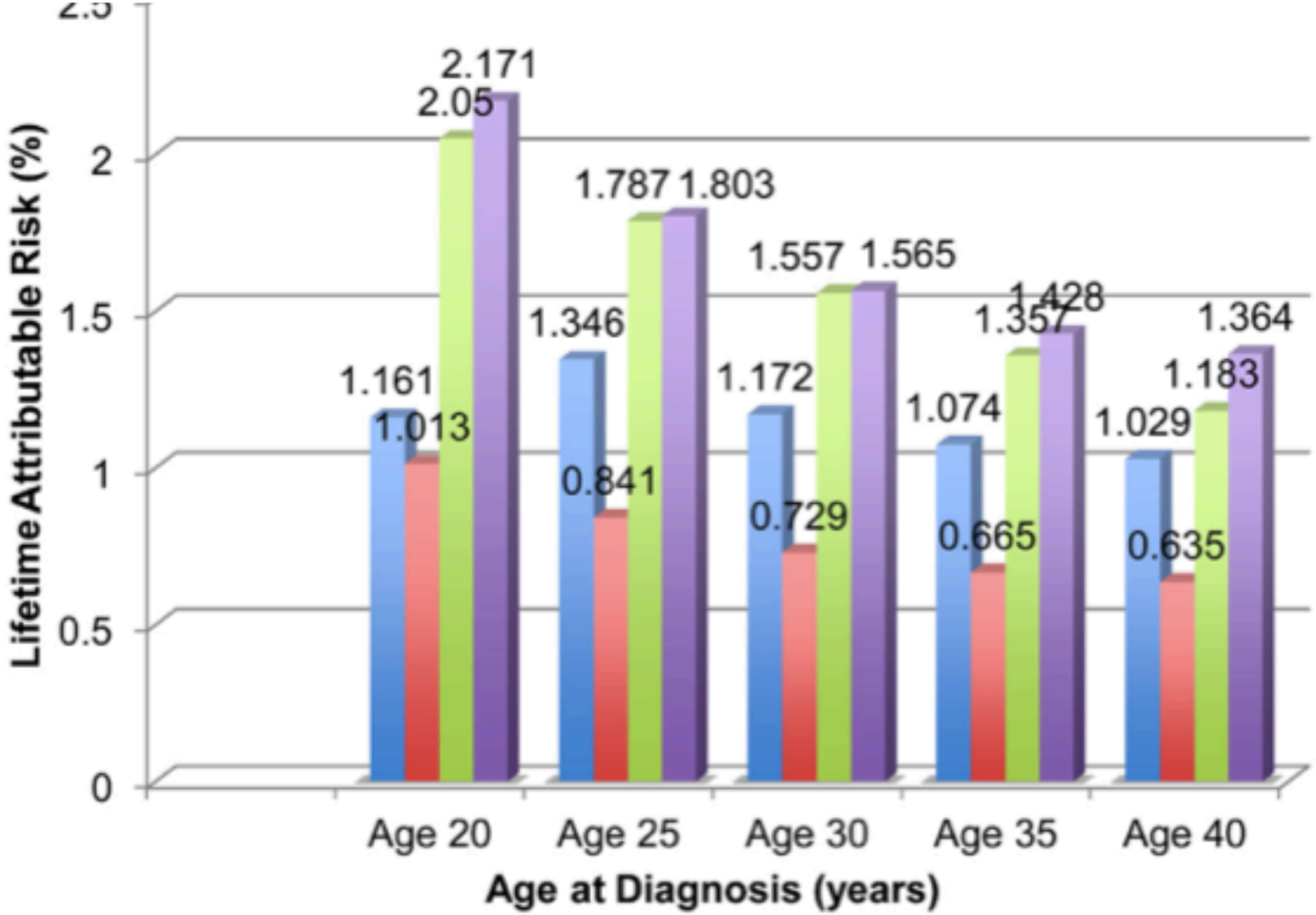
Outcome	Period				
	1989-1998		1999-2002		
	No. of Patients	%	No. of Patients	%	*P*
Patients	181		71		
Treatment					< .001
Primary RPLND	113	62	23	32	
Induction chemotherapy	68	38	48	68	
Progression events	26		1		
5-year relapse-free survival, %		84		98	.004
Patients receiving chemotherapy	127	70	56	79	.16
Mean chemotherapy cycles		2.5		3.1	.040
5-year disease-specific survival, %		99		100	.4

Abbreviation: RPLND, retroperitoneal lymph node dissection.

Comparative Analysis of the Risk of Radiation Exposure and Cost of Reduced Imaging Intensity For Surveillance of Early-stage Nonseminomatous Germ Cell Tumors

UROLOGY 85 (1), 2015

Daniel Su, Izak Faiena, Robert Tokarz, Mark Bramwit, and Robert E. Weiss



Comparative Analysis of the Risk of Radiation Exposure and Cost of Reduced Imaging Intensity For Surveillance of Early-stage Nonseminomatous Germ Cell Tumors

UROLOGY 85 (1), 2015

Daniel Su, Izak Faiena, Robert Tokarz, Mark Bramwit, and Robert E. Weiss

Table 1. 2012 and 2014 NCCN active surveillance protocol for clinical stage I NSGCT

	NCCN 2012				NCCN 2014			
Year	Months Between CXR	Months Between CTAP	CXR (Per Year) Min/Max	CTAP (Per Year) Min/Max	Month Between CXR	Month Between CTAP	CXR (Per Year) Min/Max	CTAP (Per Year) Min/Max
1	1-2	2-3	6/12	4/6	1-2	3-4	6/12	3/4
2	2	3-4	6	3/4	2	4-6	6	2/3
3	3	4	4	3	3	6-12	4	1/2
4	4	6	3	2	4	6-12	3	1/2
5	5	12	2	1	5	12	2	1
6+	6	12	2	1	6	12-24	2	0/1
Total	—	—	23/29	14/17	—	—	23/29	8/13

Table 2. CT abdomen and pelvis NCCN 2012 and 2014 risk comparison

Protocol	Number of CTAP	Total Effective Dose (mSv)	Risk at Age 20 y (%)	Risk at Age 25 y (%)	Risk at Age 30 y (%)	Risk at Age 35 y (%)	Risk at Age 40 y (%)	CT Cost ($369.30/ Study)	MRI Cost ($772.18/ Study)
NCCN 2014 (max)	13	182	1.16	1.35	1.17	1.07	1.03	4801	10,038.34
NCCN 2014 (min)	8	112	1.01	0.84	0.73	0.67	0.64	2954	6177.44
Auto EC	17	177.7	2.05	1.79	1.56	1.36	1.18	—	—
NCCN 2012	17	240.9	2.17	1.80	1.57	1.43	1.36	6278	13,127.06
Change (%) NCCN (max)	13	−24	−47	−25	−25	−25	−25	−24	−24
NCCN (min)	8	−54	−53	−53	−53	−53	−53	−53	−53
Auto EC	—	−26	−6	−1	−1	−5	−13	—	—

ELSEVIER

Urologic Oncology: Seminars and Original Investigations ▮ (2014) ▮▮▮–▮▮▮

UROLOGIC ONCOLOGY

Original article

Contemporary trends in postchemotherapy retroperitoneal lymph node dissection: Additional procedures and perioperative complications

Clint Cary, M.D., M.P.H.*, Timothy A. Masterson, M.D., Richard Bihrle, M.D., Richard S. Foster, M.D.

RPLND has low complication rate, even pcRPLND

Conclusion: The incidence of perioperative complications is low with no significant trend over the last decade. A substantial number of patients require additional intraoperative procedures during PC-RPLND, which has remained stable at our institution over time.

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

N ENGL J MED 371;21 NEJM.ORG NOVEMBER 20, 2014

Dan L. Longo, M.D., *Editor*

Testicular Cancer — Discoveries and Updates

Nasser H. Hanna, M.D., and Lawrence H. Einhorn, M.D.

E II NONSEMINOMATOUS GERM-CELL TUMOR

Patients with a low-volume stage II nonseminomatous germ-cell tumor (disease confined to the retroperitoneal lymph nodes, with the lymph nodes <3 cm in diameter) and normal β-hCG and AFP levels after orchiectomy are generally treated with retroperitoneal lymph-node dissection, although care must be individualized. Patients with higher-volume stage II disease or increasing levels of markers should receive chemotherapy (BEP for three cycles or etoposide and cisplatin for four cycles).[31] Cures are achieved in 95 to 99% of patients.

Retroperitoneal lymph-node dissection is the standard treatment after chemotherapy in patients with stage II or III disease who have had a sero-

Quote from these

VOLUME 26 · NUMBER 18 · JUNE 20 2008
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

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

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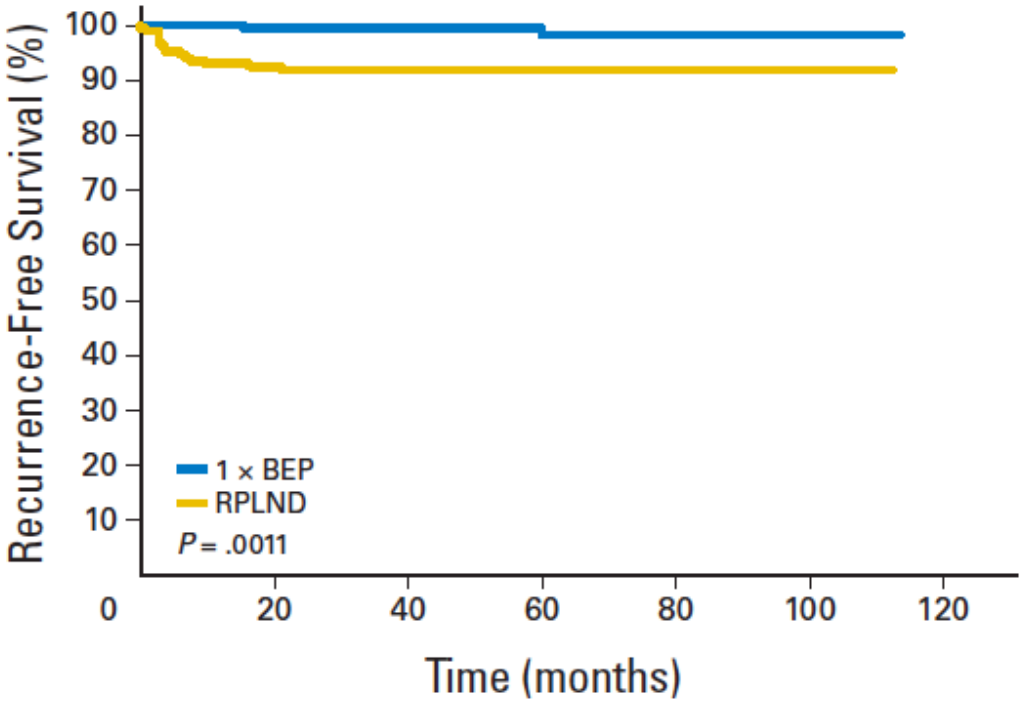
- BEP x 1 vs. RPLND
- 382 patients
- 5 year follow-up
- Recurrence:
  - HR 7.94 (p=0.001)!!



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- Flaws with this trial:
  - 60% were Stage IA: should survey these
  - Many centres doing few RPLNDs
    - 61 centres did the 173 RPLND's
    - Only ipsilateral template done
    - Bad Surgery?:
      - 7 (4%) RP recurrences; 2 (1.1%) inguinoscrotal recurrences
  - Only 2% relapse rate in chemo arm:
    - Suggests inadequate follow-up to see teratoma
  - Conclusion:
    - BEP x 1 is superior to bad surgery in a cohort that mostly should have been observed anyway

Comparison for CS1 NSGCT: For 100 Patients (at 2yrs follow-up)

	PMH Surveillance	German Testicular Cancer Study Group Trial	
	Surveillance	RPLND	Chemo
No therapy	77	0	0
Monotherapy	13	93	99
Multimodal	9	19	0.5
RPLND	13	100	1
Chemo	17	41	100
Chemo cycles	69	59	122
Relapses @ 2yrs	23	5	0.5
Mortality	0.5	3	0

VOLUME 33 · NUMBER 20 · JULY 10 2015

JOURNAL OF CLINICAL ONCOLOGY

CORRESPONDENCE

Primum Non Nocere: What Hurts in Clinical Stage I Testicular Cancer?

Torgrim Tandstad
The Cancer Clinic, St Olavs University Hospital, Trondheim, Norway

Gabriella Cohn-Cedermark
The Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden

Ann Oncol. 2015 Aug 11. pii: mdv328. [Epub ahead of print]

Chronic fatigue in 812 testicular cancer survivors during long-term follow up: increasing prevalence and risk factors.

Sprauten M[1], Haugnes HS[2], Brydøy M[3], Kiserud C[1], Tandstad T[4], Bjøro T[5], Bjerner J[6], Cvancarova M[1], Fosså SD[1], Oldenburg J[7].

Cardiovascular disease after RT and Cht for Germ Cell Tumours

Radiation Therapy

- RMH – 982 survivors
  - Actuarial risk of cardiac event at 10 years
    - Surveillance 1.4%
    - Radiotherapy 7.2%
    - Chemotherapy 3.43%
- Dutch study – population based – 2707 survivors
  - No Increased rate of CVD with RT

Chemotherapy

- Norwegian Study – 990 survivors
  - BEP was associated with 5.7 fold increase for CAD vs age matched controls
- Dutch study – population based – 2707 survivors
  - 1.7 fold Increased rate of CVD with ChT
- Raynauds 15-45% long term survivors treated with ChT

Haugnes et al J Clin Oncol 30:3752-3763, 2012

Pulmonary Disease after Cht for Germ Cell Tumours

- Pulmonary Toxicity
  - Fatal Bleomycin Toxicity in 1-3% of pts treated with Bleomycin
    - Predictive factors
      - Age >40, Decreased renal function, cumulative dose, advanced disease
- GCT patients cured with Chemotherapy after 1975
  - 2.5 fold risk of dying from a Resp infection as compared to normal population

Sullivan et al Annals Oncol 14:91-96, 2003
Fossa et al JNCI 99:533-44, 2007

Nonseminoma Surveillance Summary: What to tell your patients

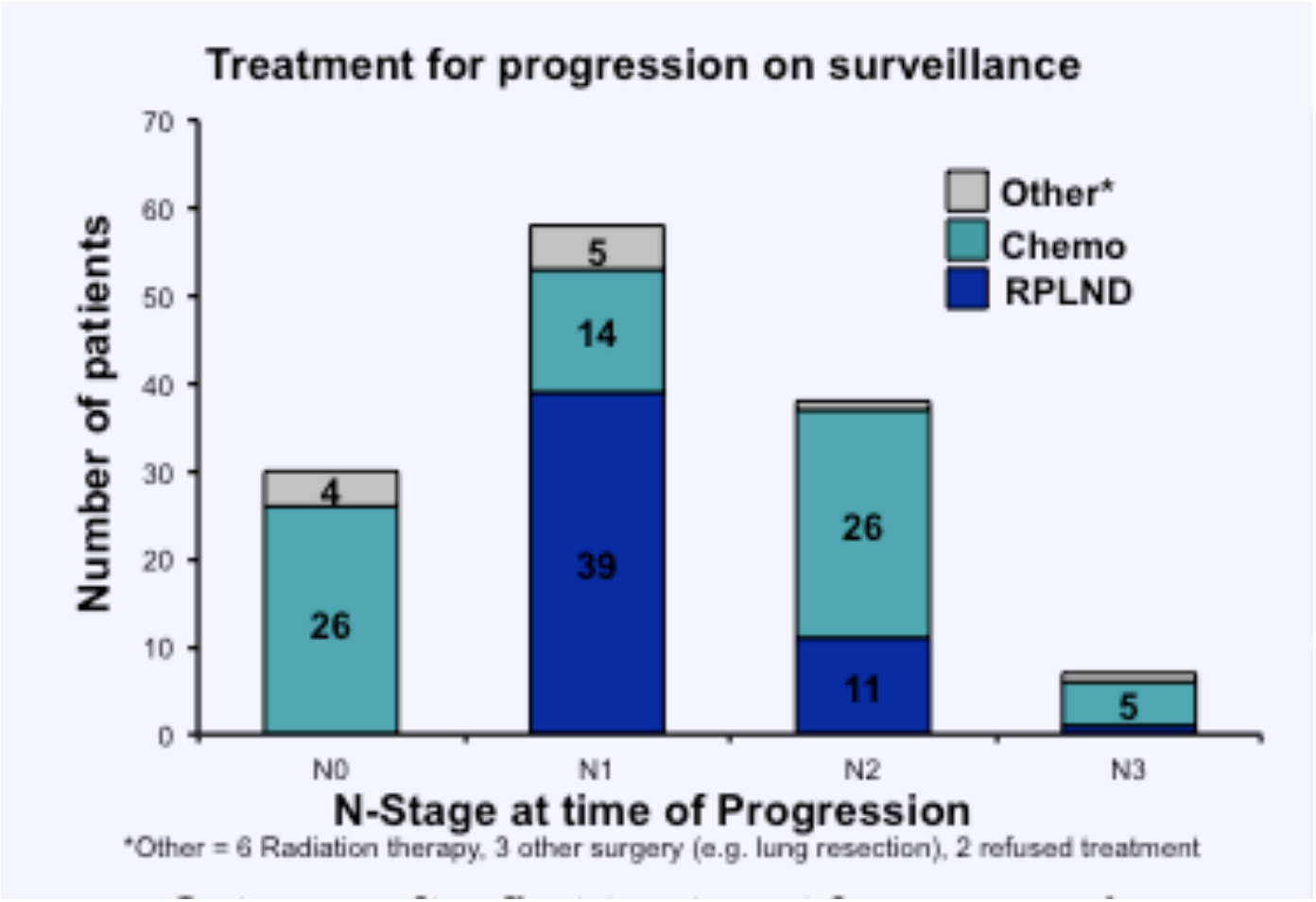
- 30% relapse rate
  - Yes…you can chose to have treatment to lower your relapse rate, but at what cost?
  - Survival is 99% no matter what you choose
- Can discriminate:
  - Low risk (LVI-): 15% relapse rate
  - High risk (LVI+): 50% relapse rate
- Even if restrict adjuvant treatment to high-risk: 50% never needed it
- Total treatment burden is less with surveillance

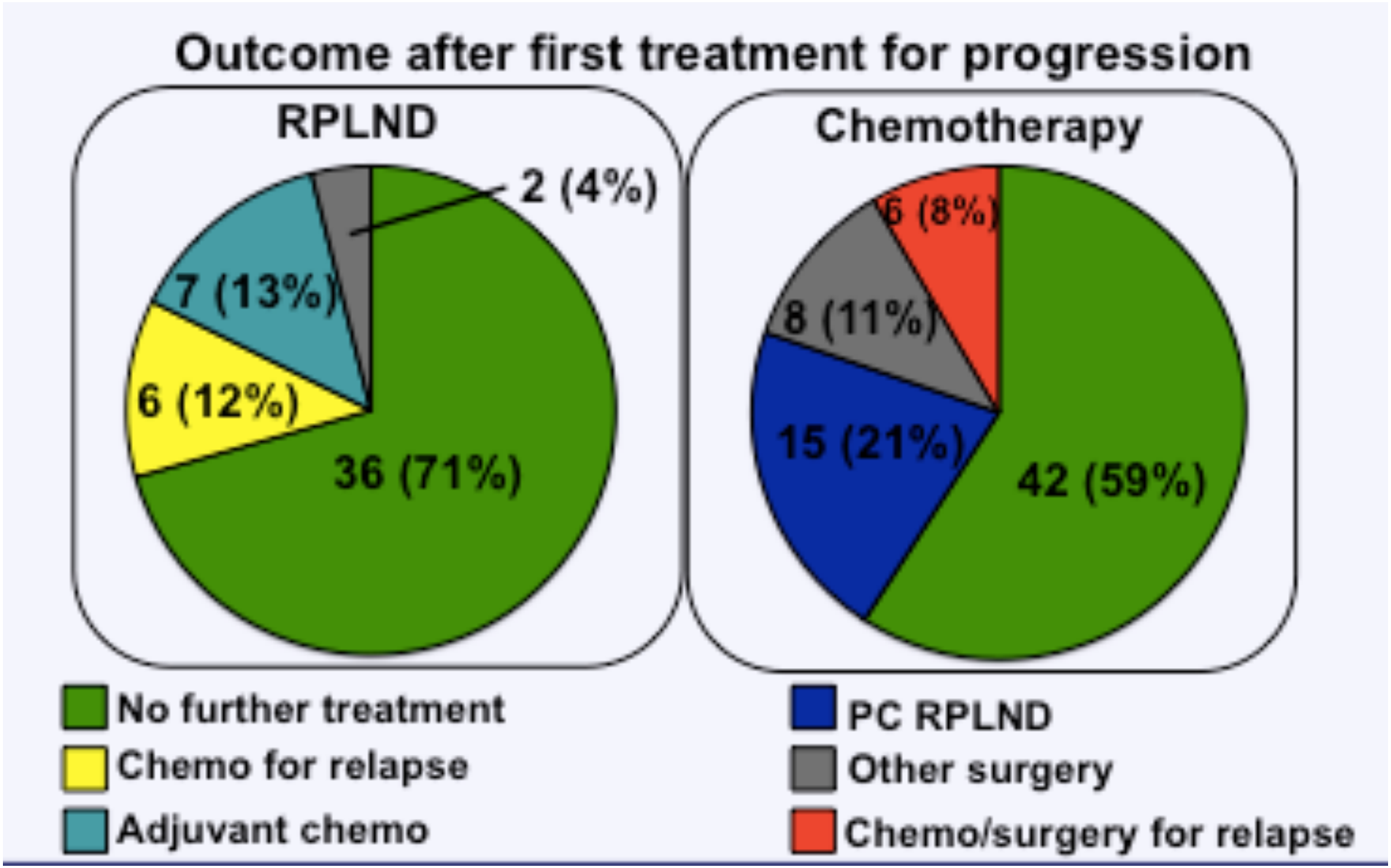
Addressing the "Loss to follow-up" criticism

- "21% lost to follow-up within 5 years"
  - That's the Ottawa experience *(Alomary et al., 2006)*
  - 5.4% at PMH (for NSGCT) *(Sturgeon et al., 2011)*
  - 3% at Sunnybrook *(Choo et al.,2005)*
  - *3% in Danish series just published (Daaguard JCO 2014 – can find in feldman)*
- Points about the 5.4%
  - Not all of them relapse (only 15%)
  - Likely the loss to follow-up is later in surveillance
    - Conditional survival teaches us the rate of relapse is lower for that group
  - Adjuvant treatment (chemo, rads, RPLND) doesn't reduce the relapse rate to zero; just lowers it.

Outcomes on Progression for Non-risk Adapted AS CSI-NS

n=466,1981-2011



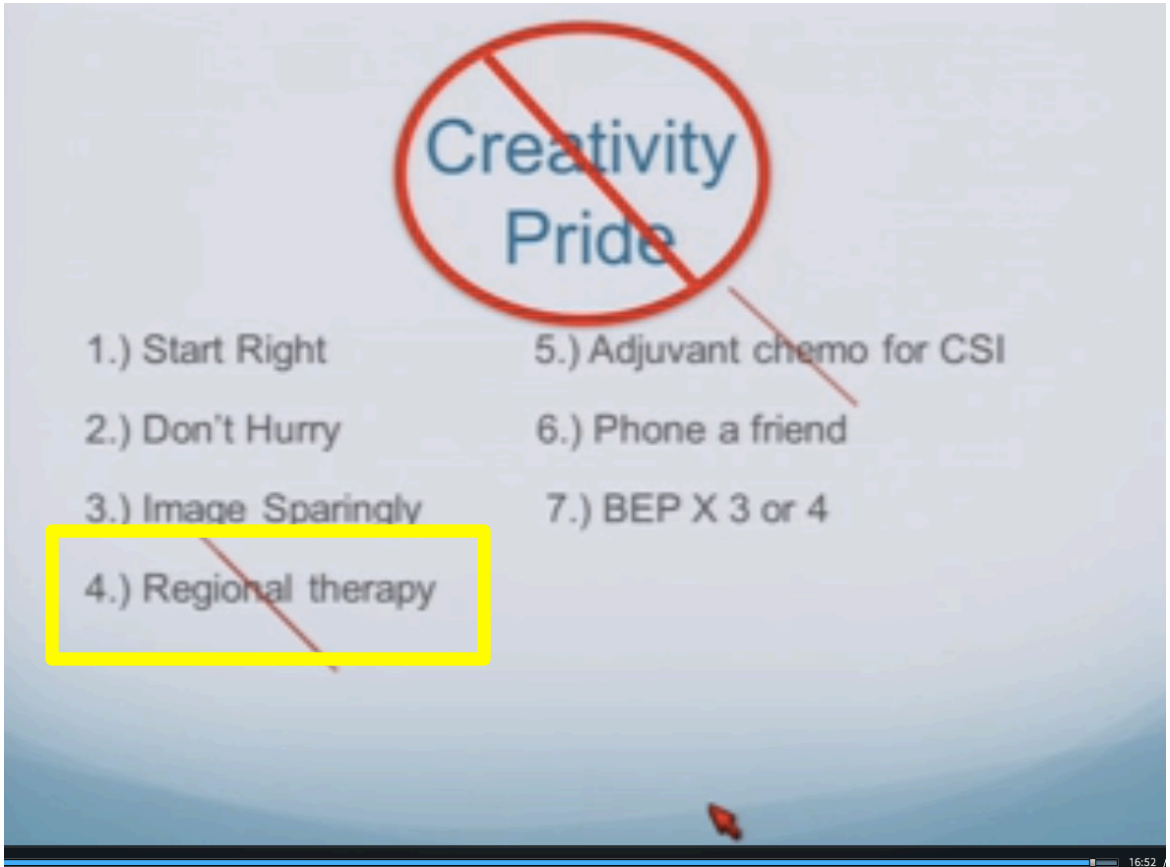

Outcome after first treatment for progression
RPLND
2 (4%)
7 (13%)
6 (12%)
36 (71%)
Chemotherapy
6 (8%)
8 (11%)
15 (21%)
42 (59%)
No further treatment
Chemo for relapse
Adjuvant chemo
PC RPLND
Other surgery
Chemo/surgery for relapse

Pitfalls in Surveillance

- 1) Beware the “Normal” report
- 2) Caution the suspicious node:
  - 7-9mm node in the primary landing zone is called “normal”
  - Recommend early (6 week) re-scan to ensure not a budding Stage II prior to starting surveillance
- 3) Treating relapse

Treatment of Surveillance Relapses

- GU ASCO 2013: Craig Nichols
  - Medical Oncologist at Virginia Mason
- "Can we optimize testis cancer outcomes by simply following the rules"



Treatment of Surveillance Relapses

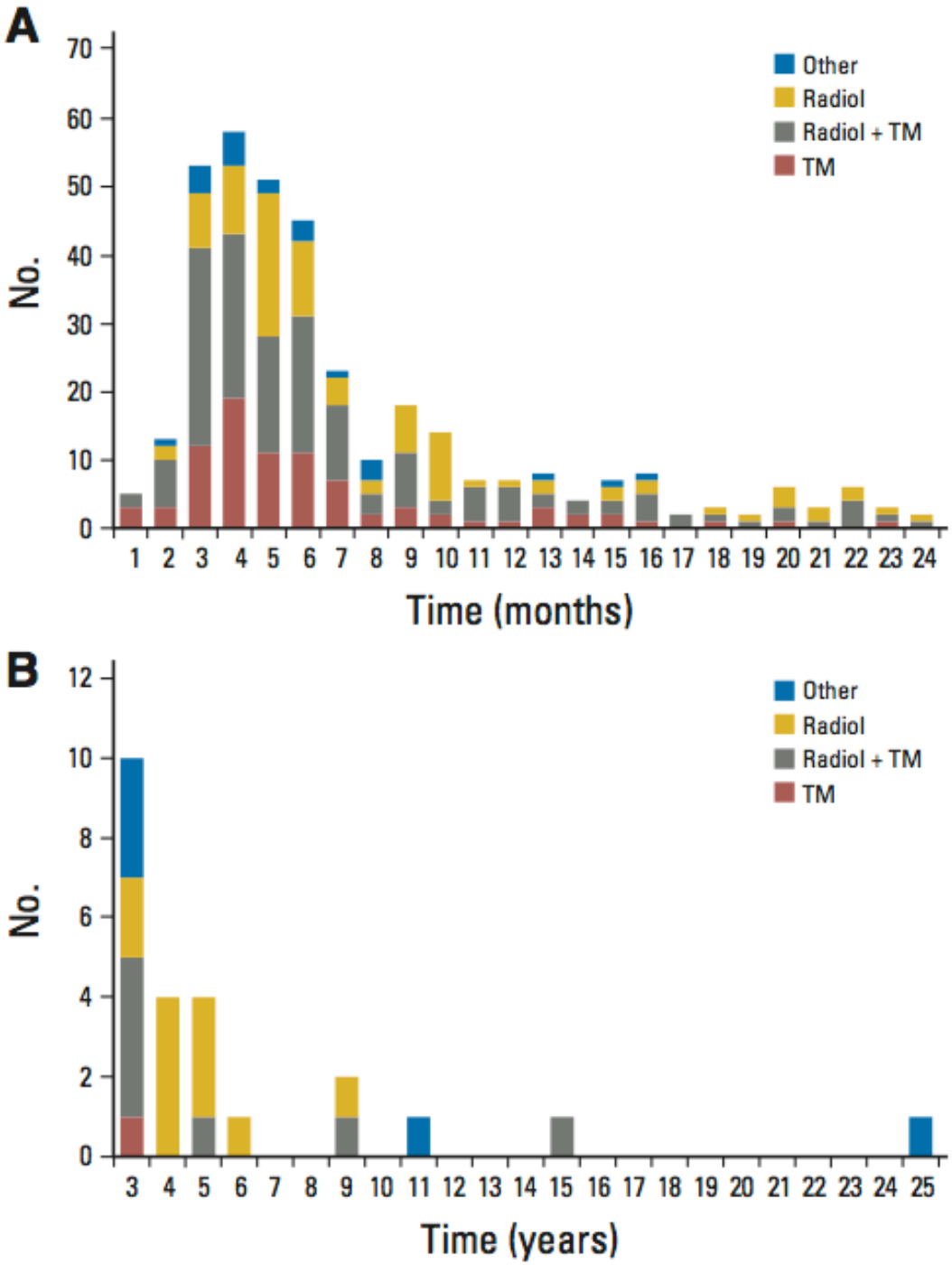
VOLUME 32 · NUMBER 34 · DECEMBER 1 2014

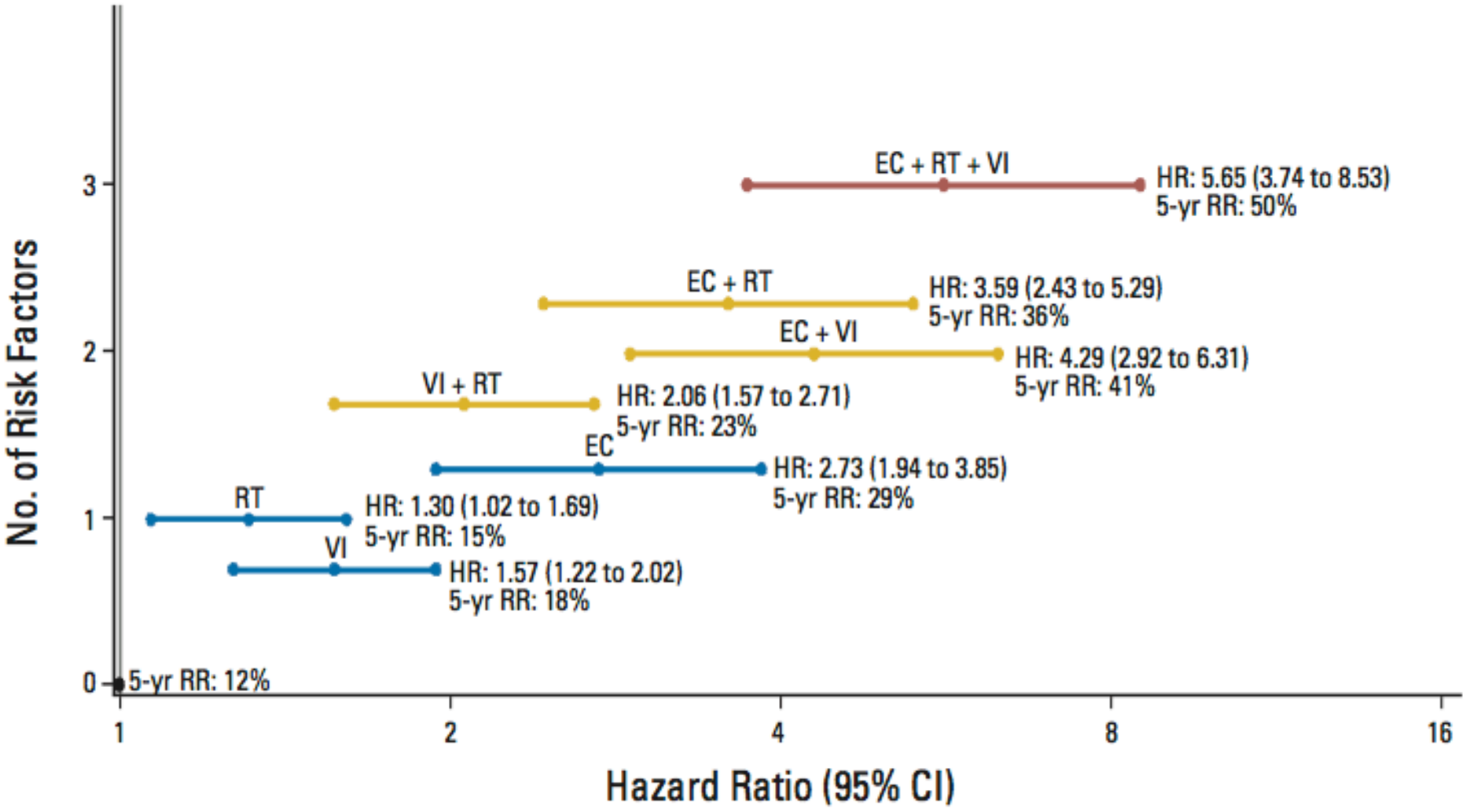
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Surveillance for Stage I Nonseminoma Testicular Cancer: Outcomes and Long-Term Follow-Up in a Population-Based Cohort

Gedske Daugaard, Maria Gry Gundgaard, Mette Saksø Mortensen, Mads Agerbæk, Niels Vilstrup Holm, Mikael Rørth, Hans von der Maase, Ib Jarle Christensen, and Jakob Lauritsen


A
70
60
50
40
30
20
10
0
No.
Other
Radiol
Radiol + TM
TM
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time (months)
B
12
10
8
6
4
2
0
No.
Other
Radiol
Radiol + TM
TM
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Time (years)


No. of Risk Factors
3
2
1
0
EC + RT + VI
HR: 5.65 (3.74 to 8.53)
5-yr RR: 50%
EC + RT
HR: 3.59 (2.43 to 5.29)
5-yr RR: 36%
EC + VI
HR: 4.29 (2.92 to 6.31)
5-yr RR: 41%
VI + RT
HR: 2.06 (1.57 to 2.71)
5-yr RR: 23%
EC
HR: 2.73 (1.94 to 3.85)
5-yr RR: 29%
RT
HR: 1.30 (1.02 to 1.69)
5-yr RR: 15%
VI
HR: 1.57 (1.22 to 2.02)
5-yr RR: 18%
5-yr RR: 12%
1
2
4
8
16
Hazard Ratio (95% CI)

Treatment of Surveillance Relapses

- Most common sites of relapse
  - Seminoma *(PMH: Leung et al., 2013)*

Site of Relapse	# (%)
Distant	2(3%)

  - Non-seminoma *(PMH: Sturgeon et al., 2011)*

Site of Relapse	# (%)
RP + Other	8 (8%)

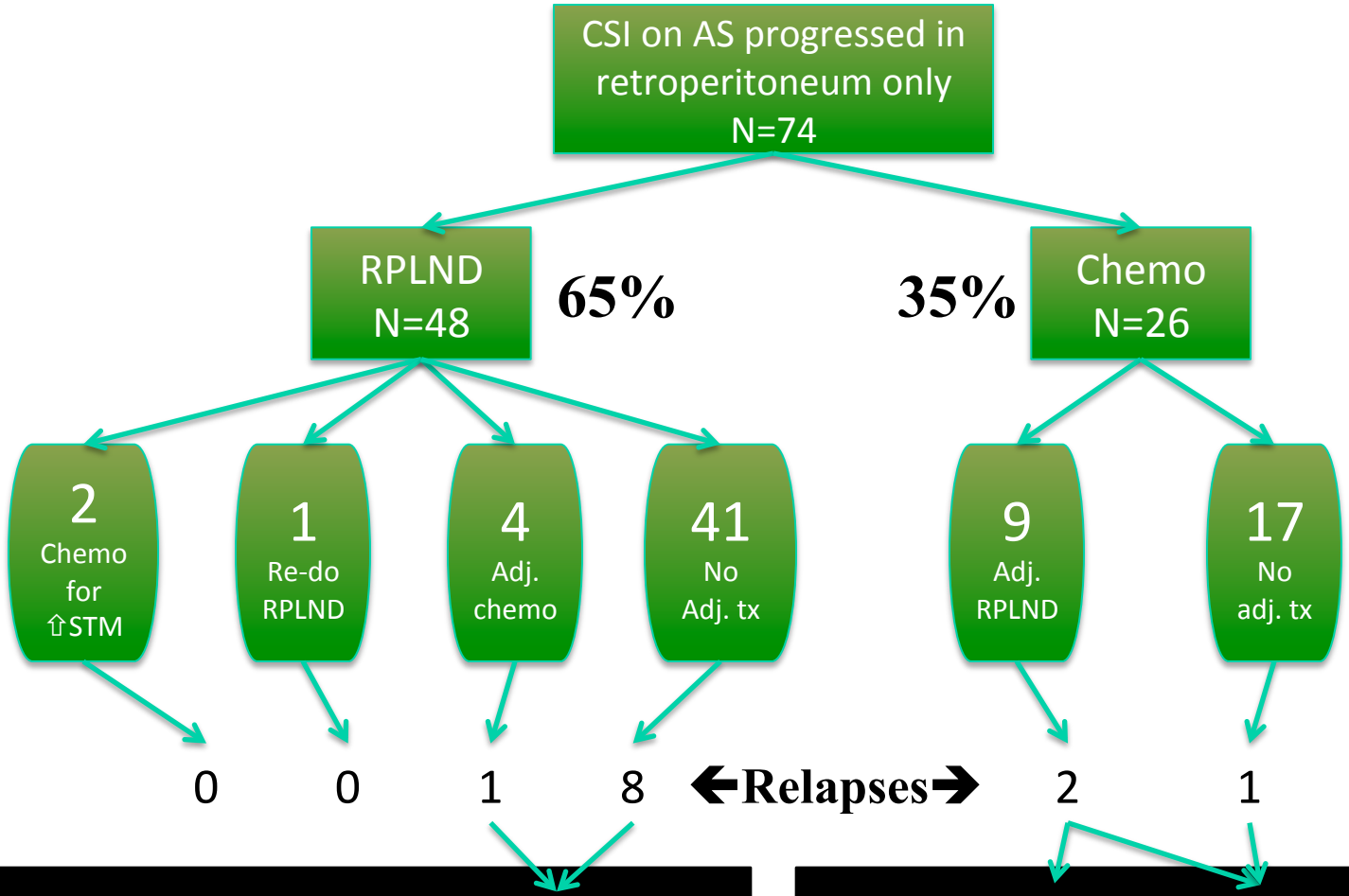
Treatment of Surveillance Relapses at PMH

- Seminoma:
  - 56/72 (78%) treated with XRT
  - Monotherapy: 91%
- Nonseminoma:
  - 71/133 (53%): Chemotherapy
  - 51/133 (38%): RPLND
  - Monotherapy: in 60%
    - **Chemotherapy only in 40/71 (56%)**
    - **RPLND only in 36/51 (71%)**

Leung, BJU Int, 2013

Nonseminoma relapses

PMH: Progression on AS



[redacted]

1 death
(other causes)

[redacted]

Methods

- Retrospective review
- December 1980 – August 2011
- N= 466 CS1 patients managed with AS
- 133 (28%): disease progression while on AS
- Logistic regression used to explore factors associated with further treatment after RPLND.

Methods

- Choice of treatment was multidisciplinary decision based on:
  - Site of progression
  - Bulk/multifocality of progression
  - Serum tumor marker kinetics
- Generally we offer RPLND if non-bulky, unifocal progression confined to the retroperitoneum and markers S0 or S1 with low doubling rate

Progressors on AS: Patient Characteristics (n=133)

Age at orchiectomy (Mean (SD))	28.9 (7.8)
Right-sided primary	65 (49%)
pT stage • T1 • T2 • T3	 73 (55%) 58 (43%) 2 (1.5%)
Overall stage at presentation • Stage 1A • Stage 1B	 73 (55%) 60 (45%)
EC in orchiectomy pathology	117 (88%)

Treatment of Progression on Surveillance for CS1 NSGCT

- Despite majority of progression occuring in the retroperitoneum
- Most of the world treats ALL progression on surveillance with chemotherapy

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Patterns of Relapse in Patients With Clinical Stage I Testicular Cancer Managed With Active Surveillance

Christian Kollmannsberger, Torgrim Tandstad, Philippe L. Bedard, Gabriella Cohn-Cedermark, Peter W. Chung, Michael A. Jewett, Tom Powles, Padraig R. Warde, Siamak Daneshmand, Andrew Protheroe, Scott Tyldesley, Peter C. Black, Kim Chi, Alan I. So, Malcom J. Moore, and Craig R. Nichols

J Clin Oncol 32. © 2014

- **90% of relapses treated with chemo**

Treatment of Progression on Surveillance for CS1 NSGCT

- Of 466 on surveillance: 133 (28%) progressed
- Progression occurred in the retroperitoneum alone in 65%
- First-line treatment following progression:
  - 71 (53%): Chemotherapy
  - 51 (38%): RPLND
  - 11 (8.3%): other therapy (6 radiation, 3 other surgery (1 brain, 1 lung, 1 completion orch), 2 refused further treatment)
- In 78 (59%), only one modality of treatment was required:
  - **Chemotherapy only in 40/71 (56%)**
  - **RPLND only in 36/51 (71%)**

Results

- Looking specifically at RPLND:
  - 51 patients underwent RPLND
    - 36 (71%): received no further therapy
    - 6 (12%): received adjuvant chemotherapy
      - (typically BEP x 2)
    - 7 (13%): received chemotherapy after relapse
      - (typically BEP x 3 or 4)
    - 2 (4%): underwent other surgery

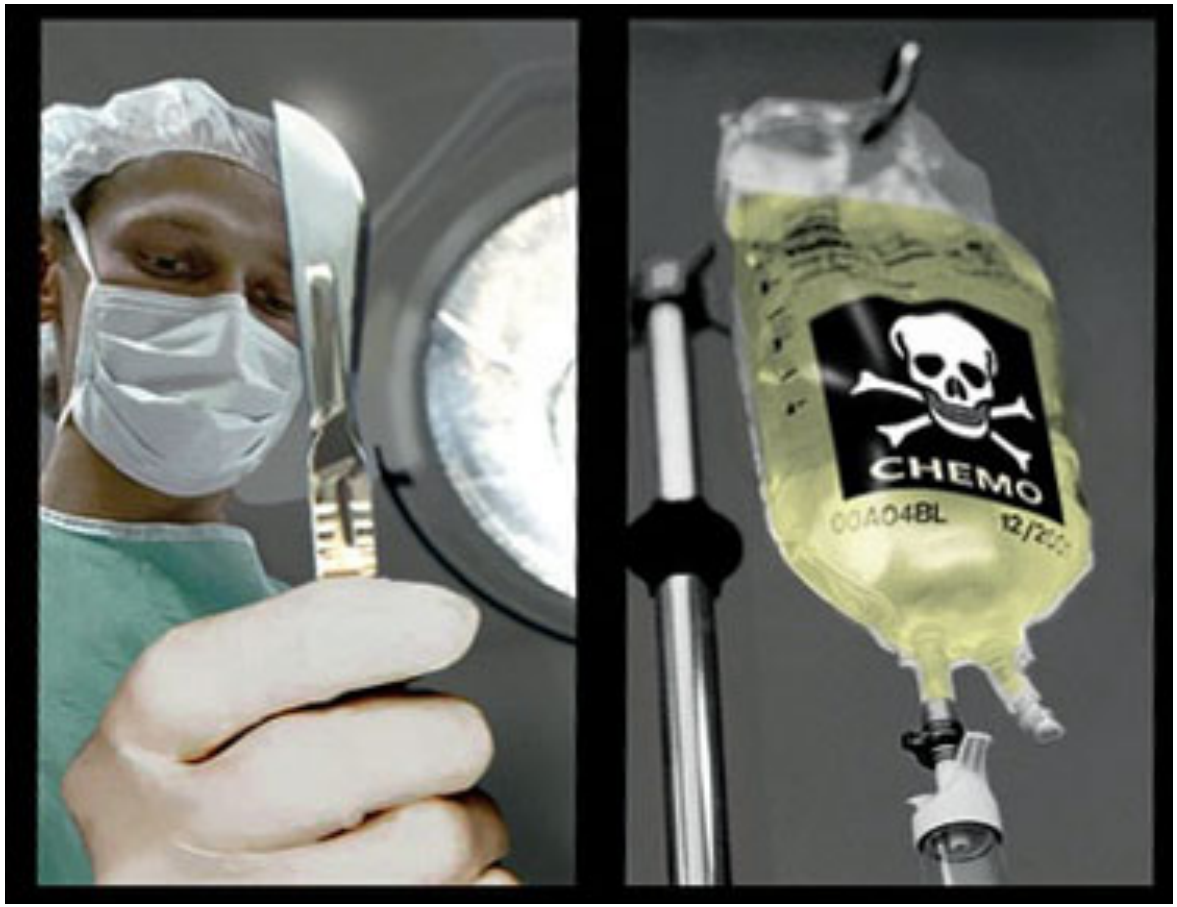
Predicting need for additional treatment AFTER RPLND

Variable	Univariate		Multivariate	
	OR (95% CI)	p value	OR (95% CI)	p value
Right-sided orch	0.78 (0.23-2.62)	0.691	0.63 (0.14-2.76)	0.541
Stage 1A vs. 1B	1.80 (0.53-6.06)	0.345	2.65 (0.54-12.9)	0.227
Time to progression (yrs)	1.16 (0.85-1.57)	0.352	1.07 (0.49-2.31)	0.865
Age at RPLND	1.03 (0.96-1.10)	0.414	1.04 (0.96-1.14)	0.338
Markers preRPLND (S0 vs. S1)	**6.67 (1.69-26.3)**	**0.007**	**7.68 (1.68-35.2)**	**0.009**
Node size(N1 vs N2)	1.04 (0.23-4.69)	0.964	1.47 (0.20-11.0)	0.709

Results – Long-term Outcomes

- Median follow-up of 7.9 years
- After initial treatment for AS progression:
  - Second relapse occurred in 25/133 (19%)
- 5 deaths
  - 3.8% of AS progressors from testis cancer
  - Still only 1.1% of the overall AS cohort

Discussion



Surgery vs. Chemo for progressors on AS?

Long-term Toxicity of RPLND vs. Chemo

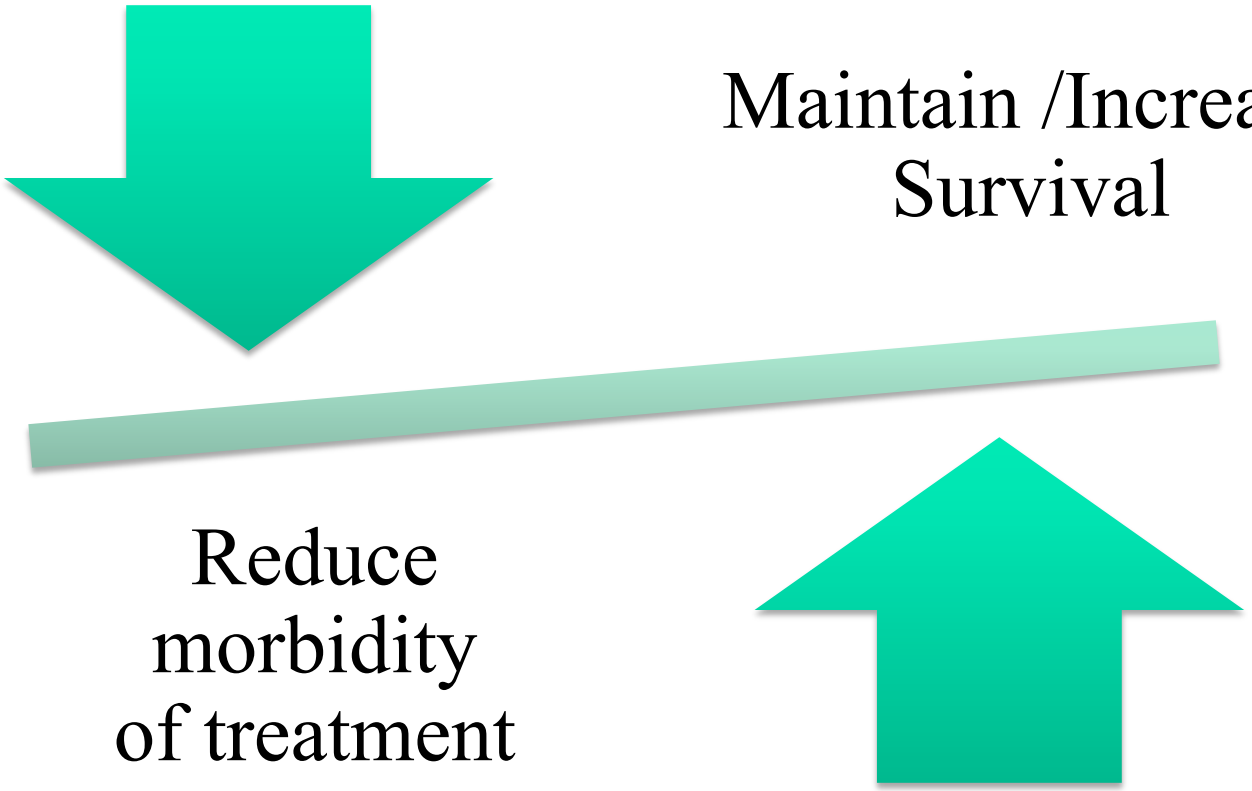
Chemotherapy	RPLND
• Cardiovascular • Cancer (Leukemia/Solid) • Ototoxicity • Neurotoxicity • Metabolic syndrome • Raynaud's • Pulmonary fibrosis • Nephrotoxicity • Hypogonadism • Infertility	• Loss of antegrade ejaculation • Scar • Ventral hernia • Bowel obstruction

Haugnes et al., JCO 2012; Fung et al., JCO 2013; Sprauten et al, JCO 2012; Travis et al., JNCI 2000
de Haas et al., Ann Oncol 2013; Jewett et al., J Urol 1988

Summary

- Active surveillance recommended as preferred option for CSI Seminoma & CSI Nonsem
- Equivalent survival vs. adjuvant treatment
- Lower treatment burden vs. adjuvant treatment
- Progression on surveillance does not mean automatic chemotherapy
  - Can use local/regional therapy as monotherapy in selected cases (XRT and RPLND)

Guiding Principles of Treatment Testicular Cancer



Rationale for RPLND for Clinical Stage I (pT1-4N0M0) NSGCT

- Accurate staging of retroperitoneum
- “Control the retroperitoneum” if pS II
- Reduce follow-up imaging of abdomen
- Reduce chemotherapy and its toxicity

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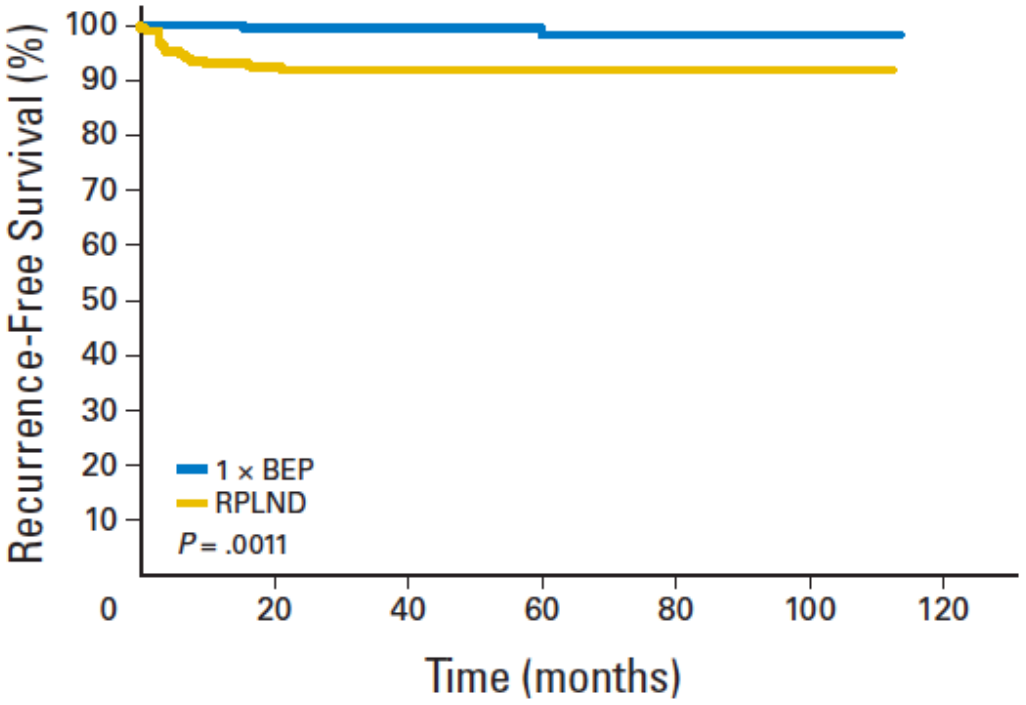

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1 course BEP vs RPLND

- 61 centres performed 173 RPLND's
- 18% N+ (32/172) - adjuvant BEPx2 in 24
- 10% relapse (13/140 those no adjuvant chemo) – BEPx3, salvage surgery in some
- Approx 25% double therapy
- 7 retroperitoneal recurrences (mainly outside template)

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Surgery (pRPLND, pc RPLND)

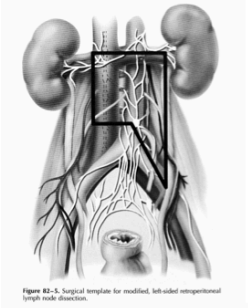
Primary RPLND

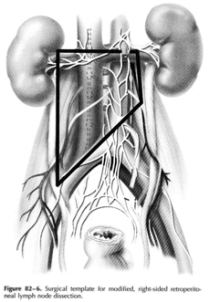
- Very limited role today
- Nerve sparing critical
- May have increased role in Stage I progression confined to the RP

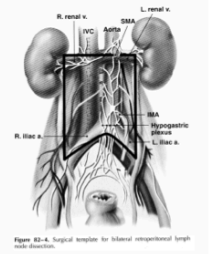
Surgery (pRPLND, pc RPLND)

Residual Mass

- Can not accurately predict histology
- Timing of surgery after chemotherapy
- Indication - >1 cm
- Template/extent of surgery







Role for Primary RPLND for NSGCTT

- cStage I progressors with RP limited progression
- cStage II at presentation with small volume disease and low/normal markers

Treatment of Surveillance Relapses at PMH

- Seminoma:
  - 56/72 (78%) treated with XRT
  - Monotherapy: 91%
- Nonseminoma:
  - 71/133 (53%): Chemotherapy
  - 51/133 (38%): RPLND
  - Monotherapy: in 60%
    - **Chemotherapy only in 40/71 (56%)**
    - **RPLND only in 36/51 (71%)**

Leung, BJU Int, 2013

Treatment of Progression on Surveillance for CS1 NSGCT

- Despite majority of progression occuring in the retroperitoneum
- Most of the world treats ALL progression on surveillance with chemotherapy

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Patterns of Relapse in Patients With Clinical Stage I Testicular Cancer Managed With Active Surveillance

Christian Kollmannsberger, Torgrim Tandstad, Philippe L. Bedard, Gabriella Cohn-Cedermark, Peter W. Chung, Michael A. Jewett, Tom Powles, Padraig R. Warde, Siamak Daneshmand, Andrew Protheroe, Scott Tyldesley, Peter C. Black, Kim Chi, Alan I. So, Malcom J. Moore, and Craig R. Nichols

J Clin Oncol 32. © 2014

- **90% of relapses treated with chemo**

Treatment of Progression on Surveillance for CS1 NSGCT

- Of 466 on surveillance: 133 (28%) progressed
- Progression occurred in the retroperitoneum alone in 65%
- First-line treatment following progression:
  - 71 (53%): Chemotherapy
  - 51 (38%): RPLND
  - 11 (8.3%): other therapy (6 radiation, 3 other surgery (1 brain, 1 lung, 1 completion orch), 2 refused further treatment)
- In 78 (59%), only one modality of treatment was required:
  - **Chemotherapy only in 40/71 (56%)**
  - **RPLND only in 36/51 (71%)**

Methods

- Retrospective review
- December 1980 – August 2011
- N= 466 CS1 patients managed with AS
- 133 (28%): disease progression while on AS
- Logistic regression used to explore factors associated with further treatment after RPLND.

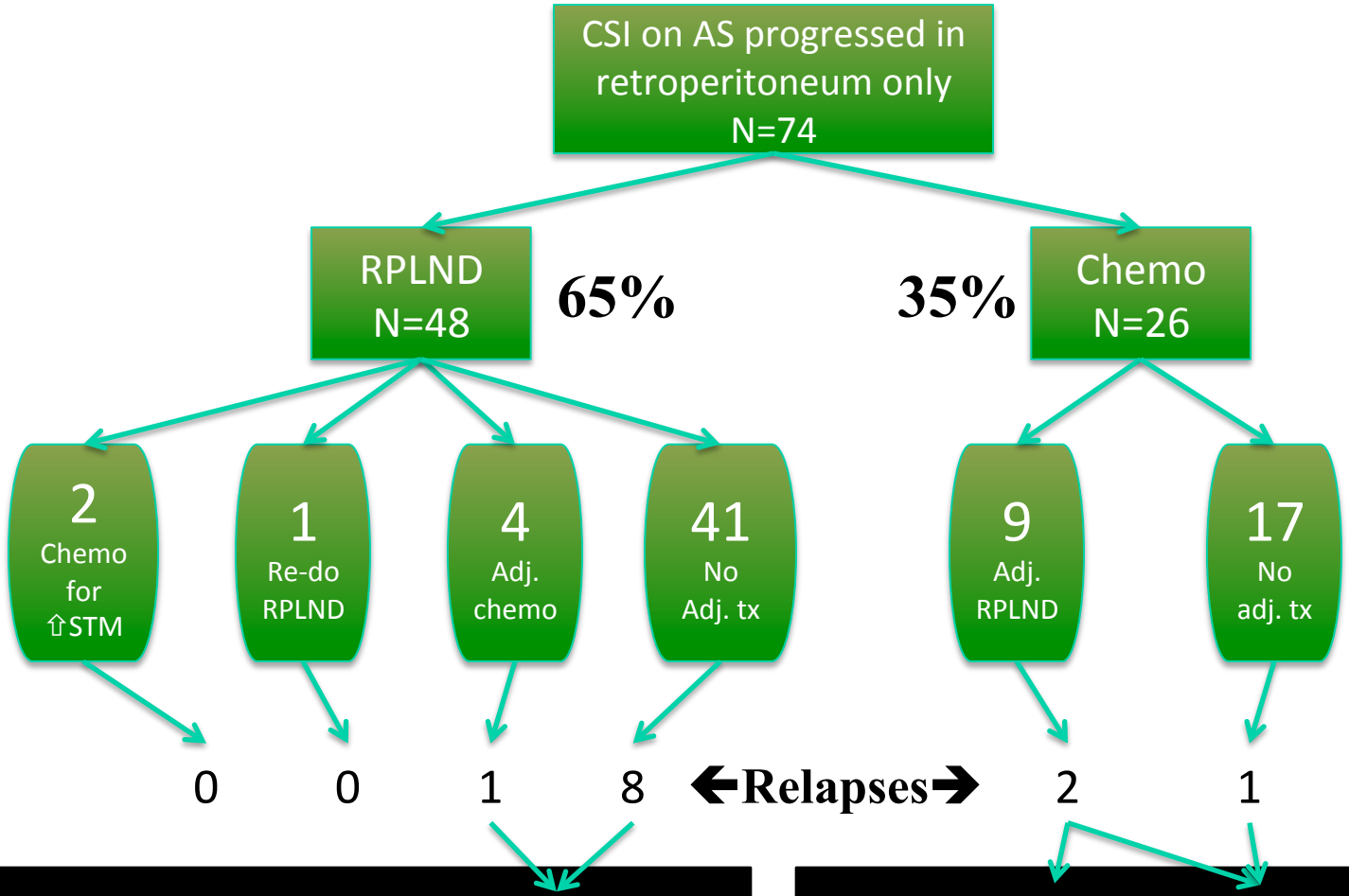
Methods

- Choice of treatment was multidisciplinary decision based on:
  - Site of progression
  - Bulk/multifocality of progression
  - Serum tumor marker kinetics
- Generally we offer RPLND if non-bulky, unifocal progression confined to the retroperitoneum and markers S0 or S1 with low doubling rate

Progressors on AS: Patient Characteristics (n=133)

Age at orchiectomy (Mean (SD))	28.9 (7.8)
Right-sided primary	65 (49%)
pT stage • T1 • T2 • T3	 73 (55%) 58 (43%) 2 (1.5%)
Overall stage at presentation • Stage 1A • Stage 1B	 73 (55%) 60 (45%)
EC in orchiectomy pathology	117 (88%)

PMH: Progression on AS



[redacted]

1 death
(other causes)

[redacted]

Results

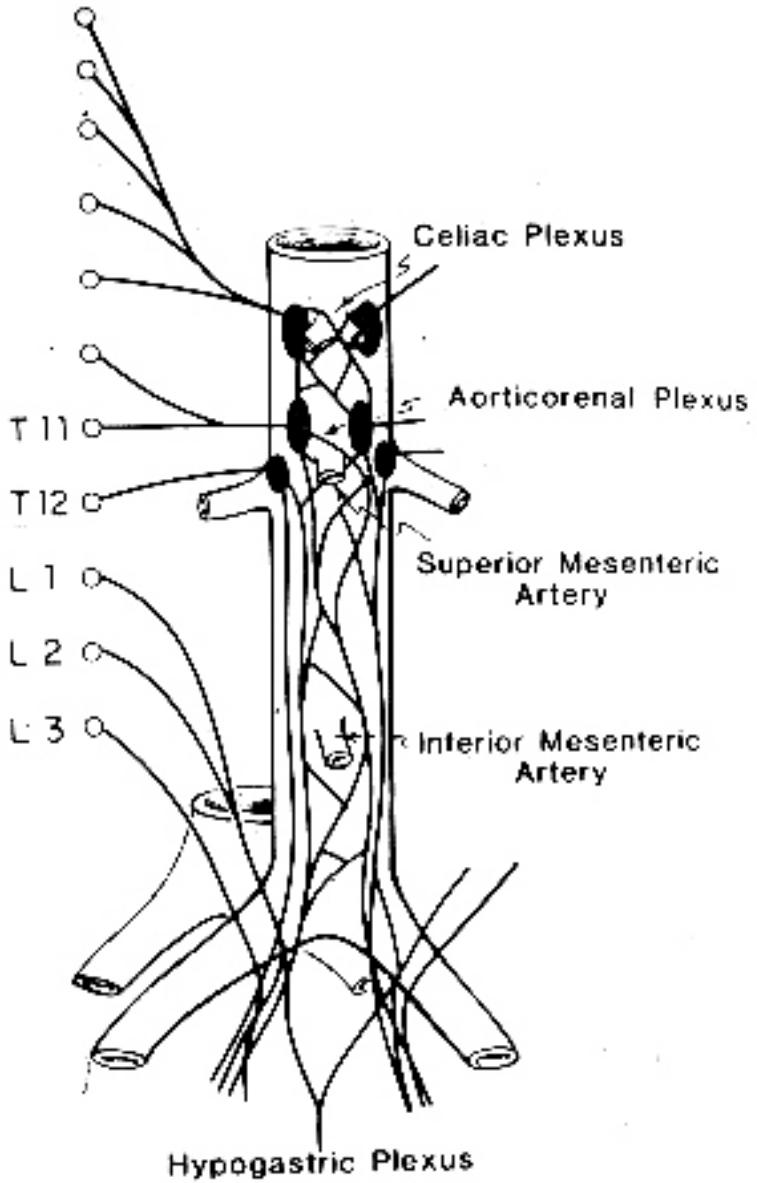
- Looking specifically at RPLND:
  - 51 patients underwent RPLND
    - 36 (71%): received no further therapy
    - 6 (12%): received adjuvant chemotherapy
      - (typically BEP x 2)
    - 7 (13%): received chemotherapy after relapse
      - (typically BEP x 3 or 4)
    - 2 (4%): underwent other surgery

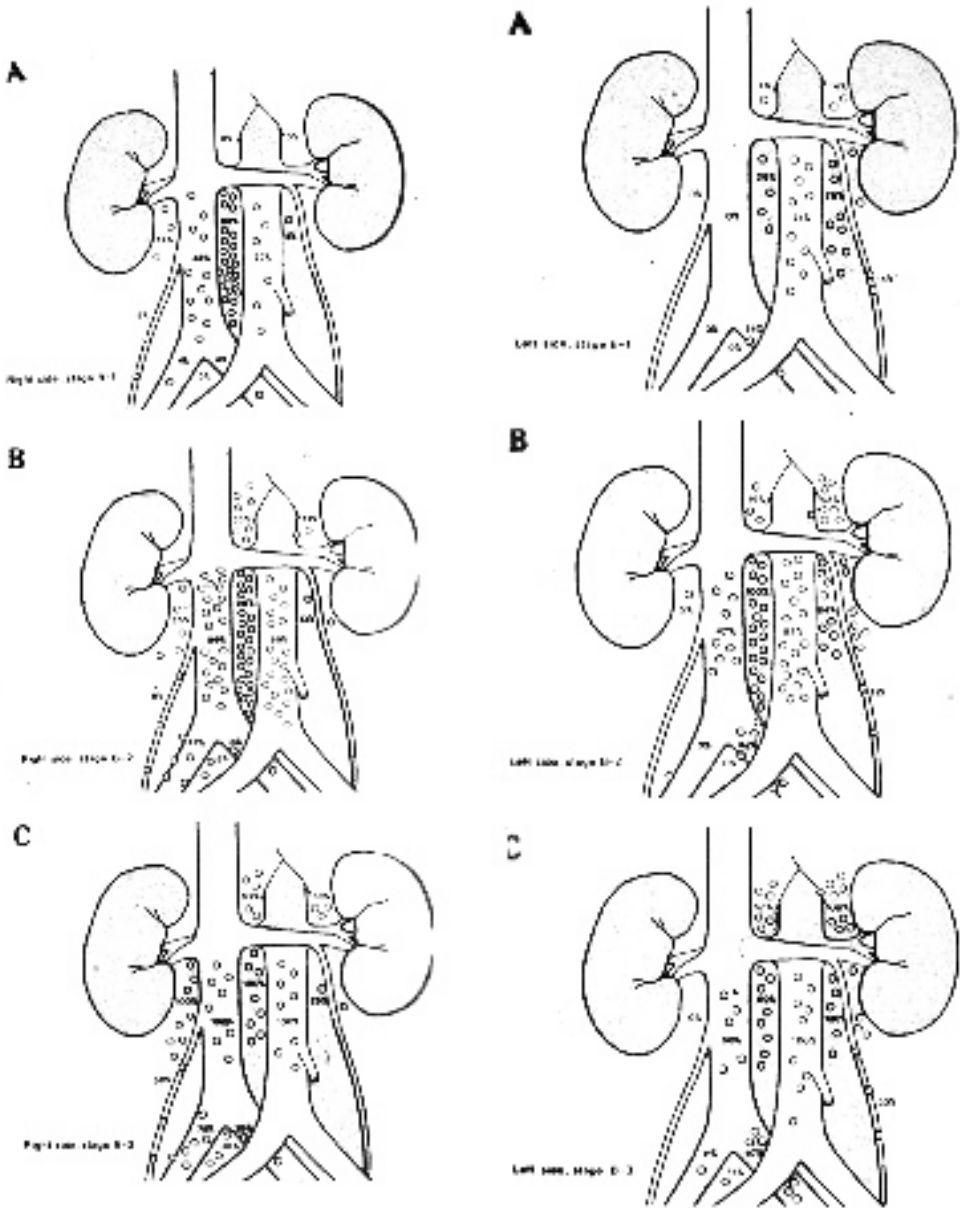
Predicting need for additional treatment AFTER RPLND

Variable	Univariate		Multivariate	
	OR (95% CI)	p value	OR (95% CI)	p value
Right-sided orch	0.78 (0.23-2.62)	0.691	0.63 (0.14-2.76)	0.541
Stage 1A vs. 1B	1.80 (0.53-6.06)	0.345	2.65 (0.54-12.9)	0.227
Time to progression (yrs)	1.16 (0.85-1.57)	0.352	1.07 (0.49-2.31)	0.865
Age at RPLND	1.03 (0.96-1.10)	0.414	1.04 (0.96-1.14)	0.338
Markers preRPLND (S0 vs. S1)	**6.67 (1.69-26.3)**	**0.007**	**7.68 (1.68-35.2)**	**0.009**
Node size(N1 vs N2)	1.04 (0.23-4.69)	0.964	1.47 (0.20-11.0)	0.709

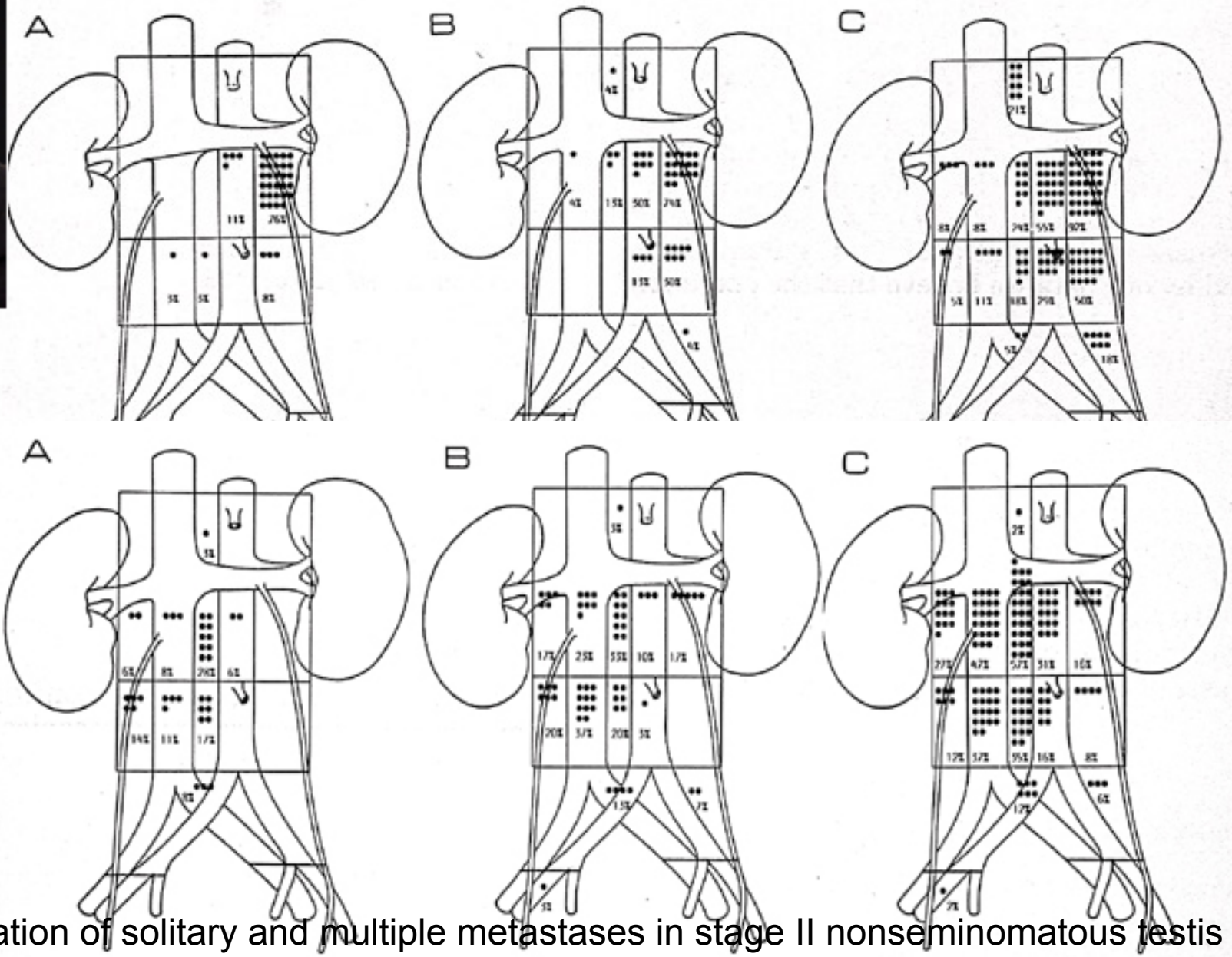
Results – Long-term Outcomes

- Median follow-up of 7.9 years
- After initial treatment for AS progression:
  - Second relapse occurred in 25/133 (19%)
- 5 deaths
  - 3.8% of AS progressors from testis cancer
  - Still only 1.1% of the overall AS cohort

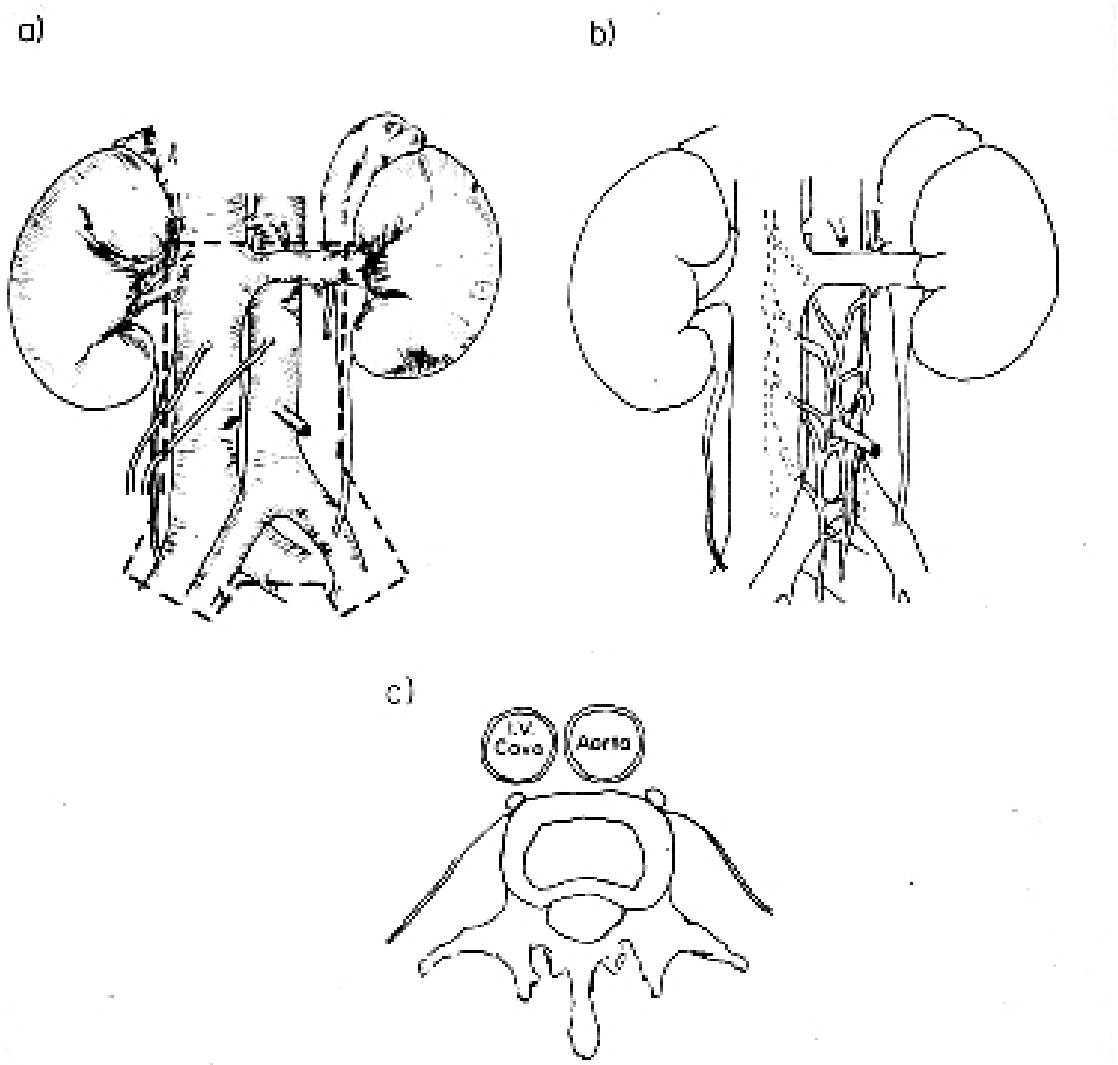

Celiac Plexus
Aorticorenal Plexus
T 11
T 12
L 1
L 2
L 3
Superior Mesenteric Artery
Inferior Mesenteric Artery
Hypogastric Plexus



Distribution of nodal metastases in nonseminomatous testis cancer.
Donohue JP,Zachary JM,Maynard BR
J Urol. 1982;128;315-320

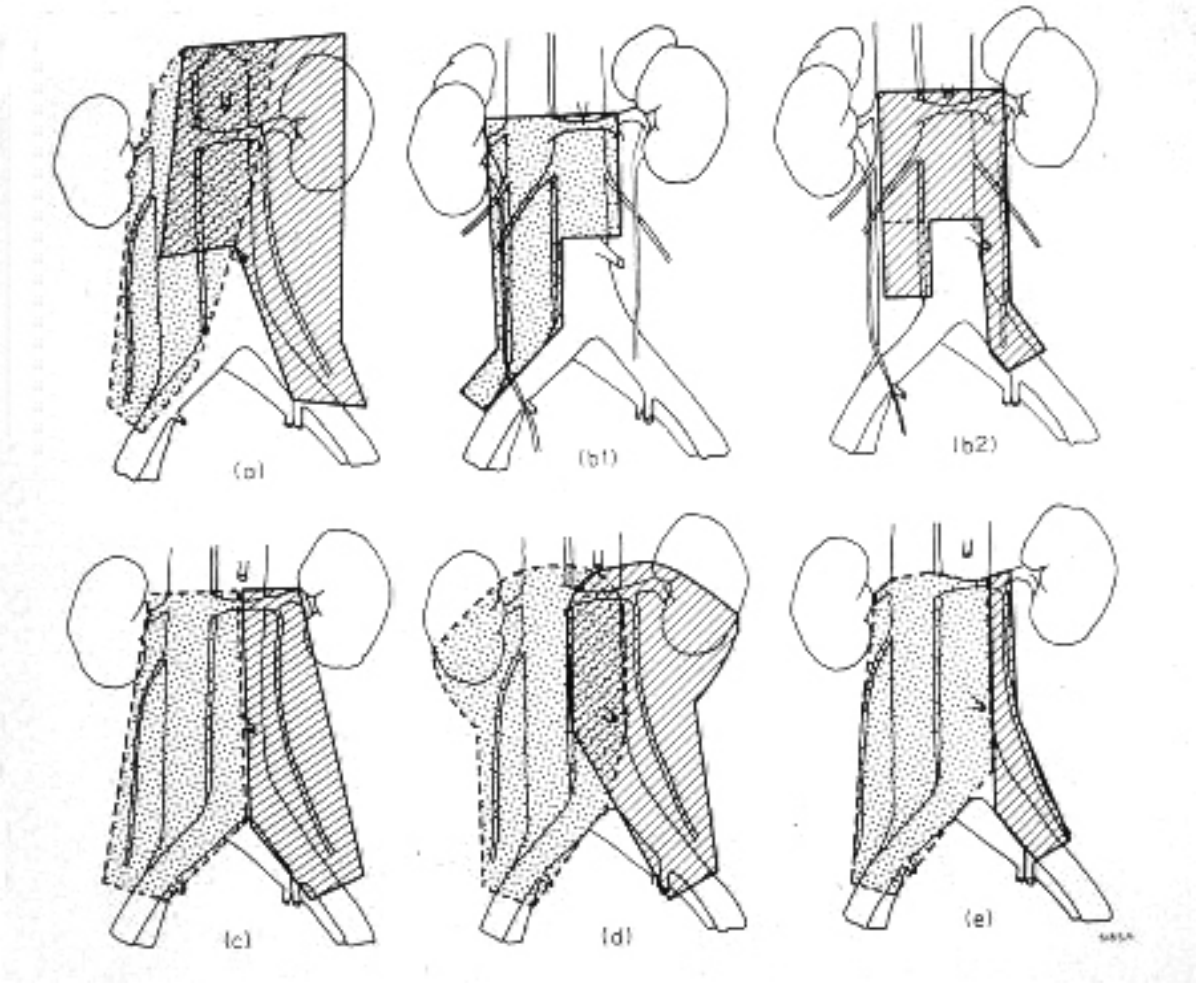


Localization of solitary and multiple metastases in stage II nonseminomatous testis tumor as basis for a modified staging lymph node dissection in stage I.
Weissbach L,Boedefeld EA.
J Urol 1987;138:77-82



Retroperitoneal lymphadenectomy for testis tumor with nerve sparing for ejaculation.
Jewett MA,Kong YS,Goldberg SD,Sturgeon JF,Thomas GM,Alison RE,Gospodarowicz MK
J Urol. 1988 Jun;139(6):1220-4

Nerve-sparing retroperitoneal lymphadenectomy with preservation of ejaculation.
Donohue JP,Foster RS,Rowland RG,Bihrle R,Jones J,Geier G
J Urol. 1990 Aug;144:287-91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(a)
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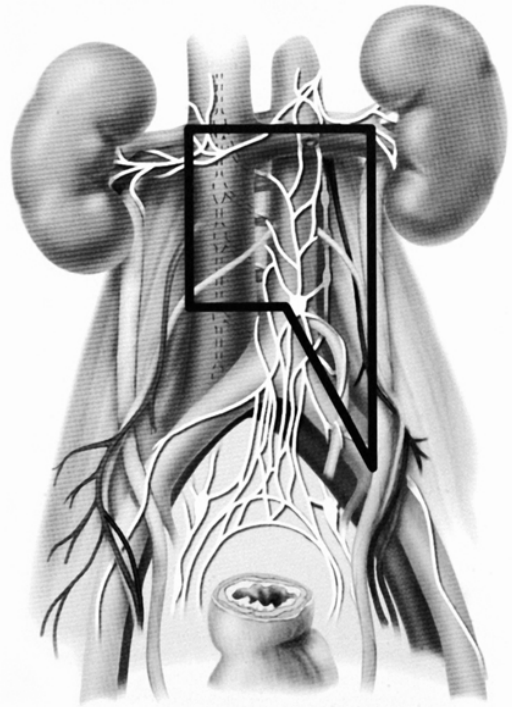


Figure 82–5. Surgical template for modified, left-sided retroperitoneal lymph node dissection.

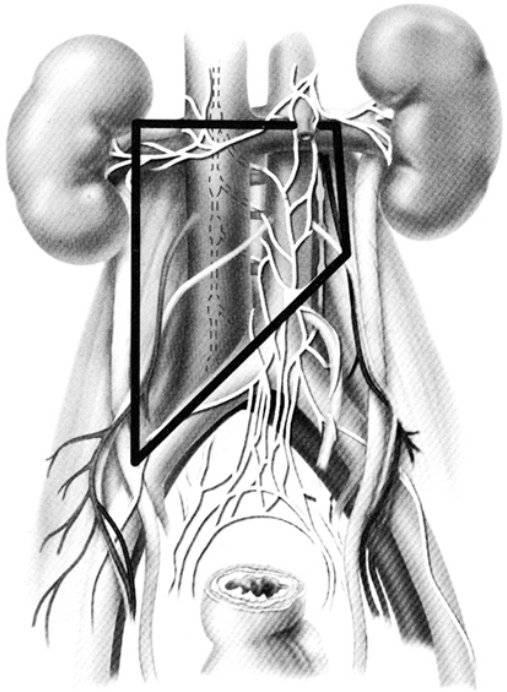


Figure 82–6. Surgical template for modified, right-sided retroperitoneal lymph node dissection.

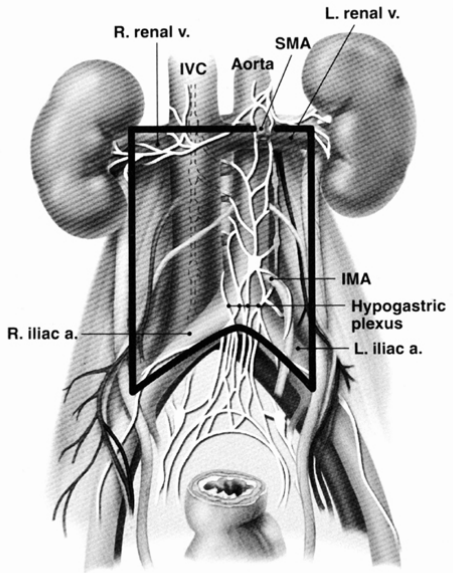


Figure 82–4. Surgical template for bilateral retroperitoneal lymph node dissection.

Loss of Antegrade Ejaculation after RPLND

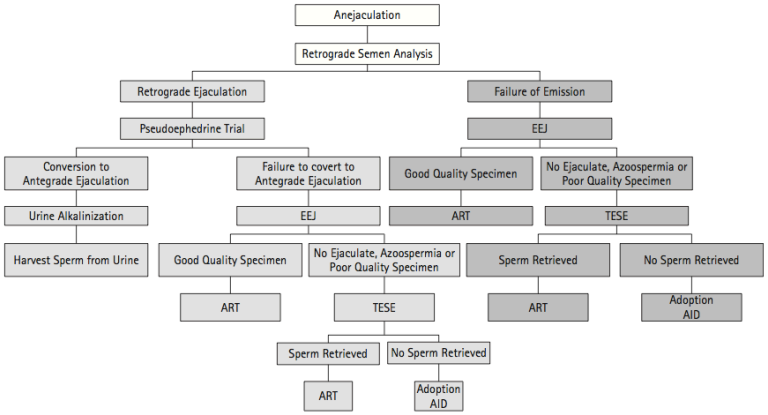
BJUI
BJU INTERNATIONAL

Outcomes of the management of post-chemotherapy retroperitoneal lymph node dissection-associated anejaculation

Wayland Hsiao*, Serkan Deveci and John P. Mulhall

*Memorial Sloan-Kettering Cancer Center, Department of Urology and Male Reproductive Medicine, and *Sexual and Reproductive Medicine Program, Department of Surgery, Division of Urology, Weill Cornell Medical College, New York, NY, USA*

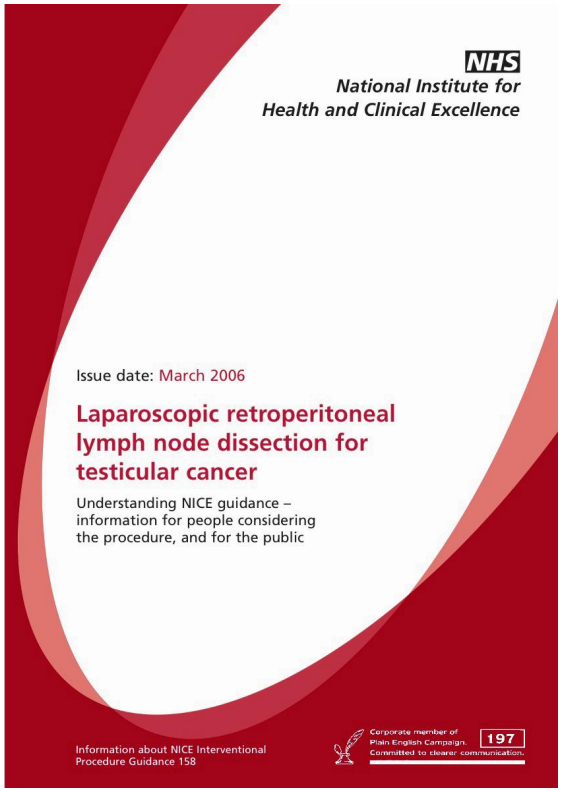
Accepted for publication 7 October 2011



Clinical Care Pathway

- Retrograde ejaculation (RE)
- Failure of emission (FOE)

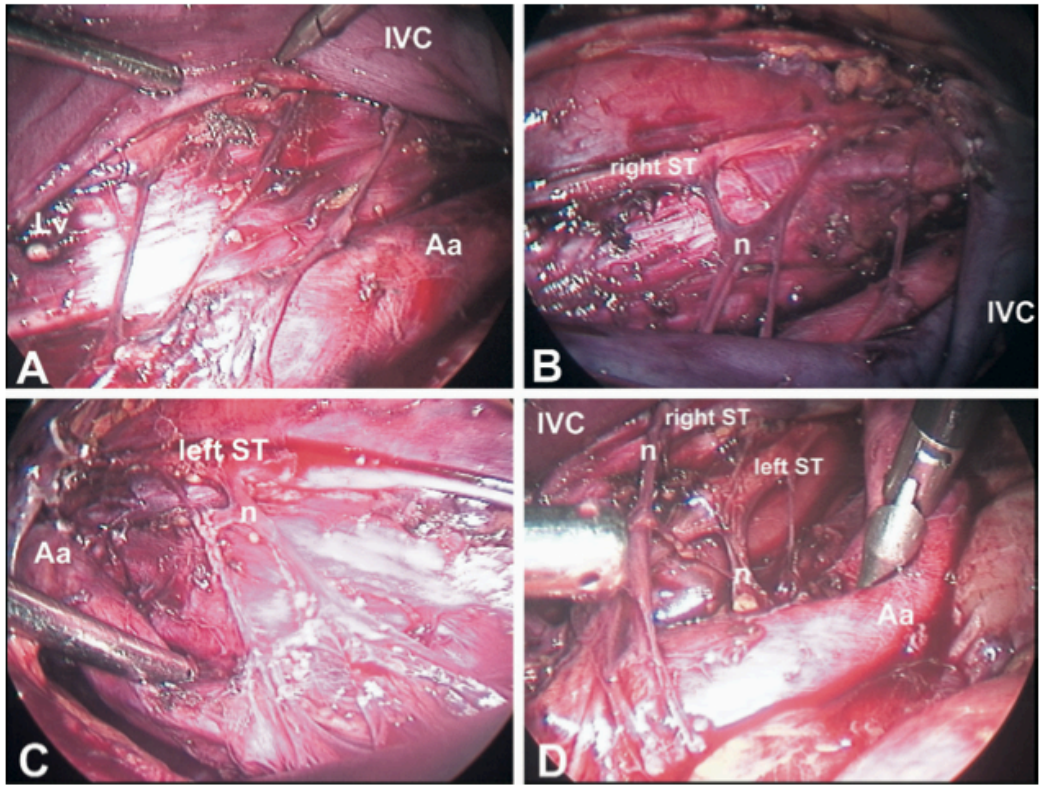
BJU International 2012;1196-2000



"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"

"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"

MIS Lap or RAL RPLND and Nerve Sparing



Innsbruck 42 cases – short followup

- 23 bilateral pRPLND, 19 pcRPLND
- 86% antegrade ejaculation

Steiner H,..Peschel R.
J Urol 2008;180:1348

Princess Margaret Hospital
University Health Network

Faculty of Medicine University of Toronto

Management of Residual Disease in NSGCT Testicular Cancer: Retroperitoneal Lymphadenectomy Can Be Performed Selectively

Michael A.S. Jewett

DIVISION OF UROLOGY

THE UNIVERSITY OF TORONTO

DEPARTMENT OF SURGICAL ONCOLOGY

PRINCESS MARGARET HOSPITAL

Management of Residual Disease in NSGCT Testicular Cancer

- Assessment of response to chemotherapy
- Timing of surgery
- Indications for surgery
- Extent of surgery
- Prediction of residual mass pathology
- Complications of surgery

Residual Disease in NSGCT Testicular Cancer

No accurate predictor of residual pathology

- embryonal in primary (Fossa JCO 1992)
- teratoma in primary (Donohue J Urol 1987)
- normal pretreatment markers (Fossa JCO 1992)
- >90% reduction in residual mass (Donohue J Urol 1987) rate of cancer and teratoma decreases as mass shrinks (Oldenburg Fossa JCO 2003)
- image characteristics of residual mass
- rate of cancer and teratoma decreases as mass decreases
- nomogram

Post – Chemotherapy(pc) RPLND RATIONALE

- Resection of carcinoma is therapeutic as drug resistant and allows adjuvant planning
- Resection of teratoma is therapeutic to prevent growing teratoma, malignant transformation and late relapse ,ie, “control the RP”
- Resection of necrosis is not therapeutic but provides staging information and follow - up regimen
- Advantages of above outweigh morbidity

Residual Disease in NSGCT Testicular Cancer

Complications of RPLND

- important to have experience assessing implications of location, size, adjacent organs, # renal vessels
- increase with extent of surgery, bilat>modified template (Beck Einhorn Cancer 2007;110:1235-40,)

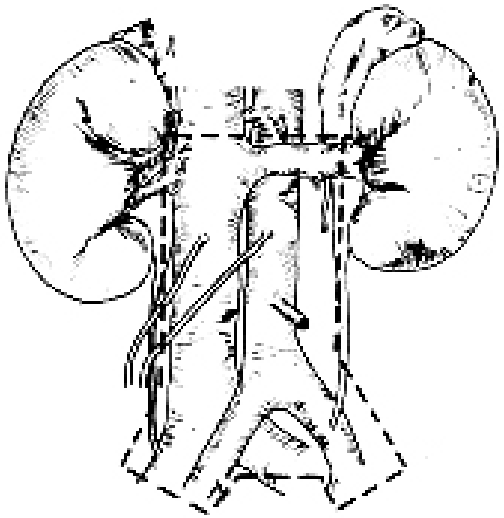
Management of Residual Disease in NSGCT Testicular Cancer Recommendations

- Observe RP if imaging “normal”
- Observe RP if residual disease is < 1 cm as the RP rarely becomes “normal”
- May consider observing some >1 cm

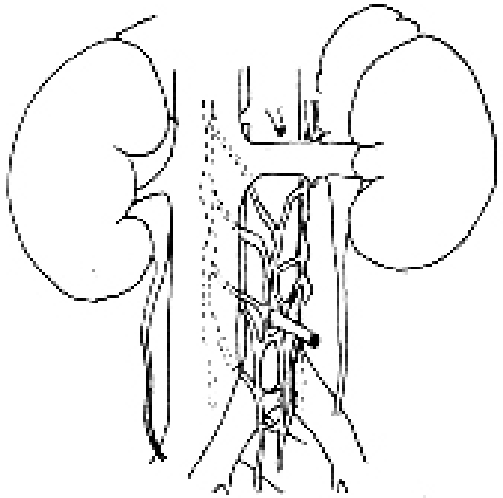
Personal Experience with pcRPLND for Residual Disease Princess Margaret Hospital, Toronto

- n = 226
- Residual mass 6.5 cm (0.5-21)
- Nerve-sparing in 52.8%
- Histology of the residual mass
  - Ca ± teratoma 16.6 % (last 134=13.4%)
  - teratoma 55.2%
  - necrosis/fibrosis 28.2%)
- Tumor outside lumpectomy or template
  21.4 and 4.7% of cases * 1982- 2004

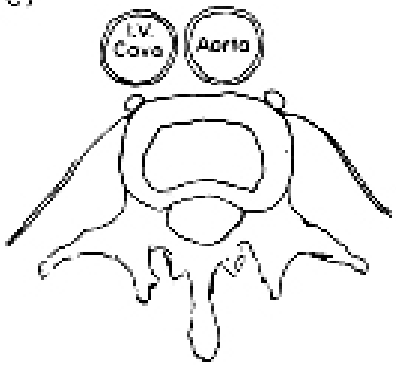
a)

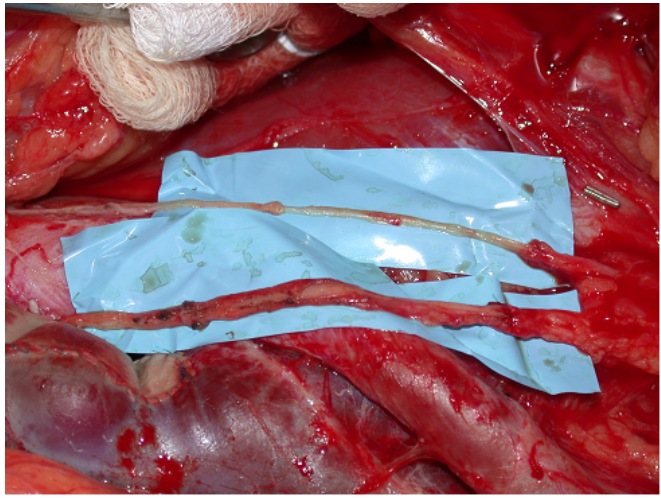


b)



c)





Post – Chemotherapy(pc) RPLND – is it always necessary

- The management of retroperitoneal nodal disease that achieves a complete response (CR), has been controversial – Observe vs pcRPLND
- We have retrospectively evaluated our experience with the management of patients who presented with retroperitoneal(RP) metastases and who underwent initial chemotherapy to determine if pcRPLND was indicated in those who achieved a complete response(CR) in the RP

VOLUME 28 · NUMBER 4 · FEBRUARY 1 2010

JOURNAL OF CLINICAL ONCOLOGY

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Christian Kollmannsberger, Siamak Daneshmand, Alan So, Kim N. Chi, Nevin Murray, Christie Moore, Brandon Hayes-Lattin, and Craig Nichols

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Christian Kollmannsberger, Siamak Daneshmand, Alan So, Kim N. Chi, Nevin Murray, Christie Moore, Brandon Hayes-Lattin, and Craig Nichols

- CR = 161
- 100% DSS
- 10 relapses (6.2%), 2 late

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Yaron Ehrlich, Mary J. Brames, Stephen D.W. Beck, Richard S. Foster, and Lawrence H. Einhorn

- CR = 141, median F/U 15.5 years
- 97% est. DSS
- 12 relapses (9%), 6 in RP, 5 late and all NED

Post – Chemotherapy(pc) RPLND – is it always necessary

- n = 296, presented with RP adenopathy and received initial chemotherapy (1997-2007)
  - 40(14%) were stage I on surveillance who progressed
  - 147(50%) residual disease & pcRPLND
  - 129(43%) achieved a CR in the RP
    - 10 (7.7%) later relapsed and 9 were salvaged

      (7 RPLND only, 3 salvage chemotherapy+RPLND)
- 20 NR initially or unknown and 50% DOD

Post – Chemotherapy(pc) RPLND – is it always necessary NO!

- Unique experience - outcomes of all men who present with RP adenopathy managed by initial chemotherapy and not just those who either undergo RPLND or are managed expectantly
- 43% (129) achieved a CR in the RP and were observed
- 7.7%(10) of these patients relapsed and all but 1 were salvaged
- Our experience strongly supports continuing surveillance as opposed to surgery in this population.

Management of Residual Disease in NSGCT Testicular Cancer Recommendations

- Observe RP if imaging “normal”
- Observe RP if residual disease is < 1 cm as the RP rarely becomes “normal”
- May consider observing some >1 cm

Residual Seminoma Mass after RT or Chemotherapy

Management is controversial

- Location, size, kinetics – observe vs surgery
- Value PET uncertain

SEMINOMA- RESIDUAL MASS

- Common post chemo for advanced seminoma
- Controversial topic
- Very uncommon to have teratoma (not impossible)
- CT/PET
- Surgery associated with desmoplasia
  - Surgical planes less well defined
  - Vascular catastrophe
  - Some cases virtually impossible

Residual Mass: Seminoma
PET Scans

- N=51; post-chemotherapy; SEMPET Trial

Largest Residual Mass	# Patients	TP	TN	FN	FP
> 3 cm	19	7	12	0	0
≤ 3 cm	37	1	34	2	0

- PPV = 100%; NPV = 96%
- Specificity = 100%; Sensitivity = 80%
- These results are more predictive than those previously published by Indiana University

de Santis et al. J Clin Oncol 2004; p1034-1039.
de Santis et al. J Clin Oncol 2001; p3740-3744.
Ganjoo et al. J Clin Oncol 1999; p3457-3460.

Residual Mass: Seminoma
PET Scans: Canadian Survey

- If a residual mass is PET positive after chemo, the appropriate management is
  - observe with CT scan (n=1)
  - biopsy or dissection and directed further therapy based on pathology (n=14)
  - irradiation (n=4)
  - further chemotherapy (n=1)

PUTTING IT ALL TOGETHER

- Mass < 3cm—observe
- Well defined > 3 cm—observe and operate if grows or operate up-front
  - We prefer later—6 cases at 15 years at PMH

SEMINOMA- RESIDUAL MASS

- Common post chemo for advanced seminoma
- Controversial topic
- Very uncommon to have teratoma (not impossible)
- Gallium/PET– not sucessful
- Surgery associated with desmoplasia
  - Surgical planes less well defined
  - Vascular catastrophe
  - Some cases virtually impossible

Centralization of Care

Evolving Story

- Advanced disease, >5 pts/year and better outcomes
- Referals for salvage therapy and RPLND outcomes also vary
- Multidisciplinary team, centralization, population based outcomes improved

Residual Mass: Seminoma
PET Scans: Canadian Survey

- If a residual mass is PET positive after chemo, the appropriate management is
  - observe with CT scan (n=1)
  - biopsy or dissection and directed further therapy based on pathology (n=14)
  - irradiation (n=4)
  - further chemotherapy (n=1)

PUTTING IT ALL TOGETHER

- Mass < 3cm—observe
- Well defined > 3 cm—observe and operate if grows or operate up-front
  - We prefer later—6 cases at 15 years at PMH