Testicular Cancer: Non-Seminoma Evolving Role
Retroperitoneal Lymph Node Dissection

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PRINCESS MARGARET HOSPITAL
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THE UNIVERSITY OF TORONTO
To Discuss

RPLND in 2008 and its History

Primary RPLND
   Role in Stage I
   Role in Stage II

Post-chemotherapy RPLND and Management of Residual Masses
10 New Testis Tumors

Non-Seminoma: 5

Stage: I  II  III
2  1  2

Seminoma: 5

Stage: I  II  III
4  1  1

Residual Mass: 1
Classical Suprahilar Retroperitoneal Lymph Node Dissection for Testis Cancer
Celiac Plexus
Aorticorenal Plexus
Superior Mesenteric Artery
Hypogastric Plexus
T11
T12
L1
L2
L3
STRATEGIES FOR NERVE SPARING AND ADEQUATE RETROPERITONEAL LYMPHADENECTOMY

• BILATERAL LYMPHADENECTOMY WITH NERVE IDENTIFICATION AND SPARING

• TEMPLATE MODIFICATION +/- NERVE IDENTIFICATION
Figure 82-4. Surgical template for bilateral retroperitoneal lymph node dissection.

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.
Retroperitoneal Lymphadenectomy for Testis Tumor with Nerve Sparing for Ejaculation

Michael A.S. Jewett,* Young-Soo P. Kong, Susan D. Goldberg, Jeremy F.G. Sturgeon, Gillian M. Thomas, Ruth E. Alison and Mary K. Gospodarowicz

From the Department of Surgery (Urology), Medicine and Radiation Oncology, The Wellesley Hospital, The Ontario Cancer Institute and The University of Toronto, Toronto, Ontario, Canada
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

Canadian Consensus Guidelines for the Management of Testicular Germ Cell Cancer

Padraig Warde, Lori Wood, Michael Jewett, Christian Kollmannsberger, Peter Chung, Sebastian Hotte, Martin O’Malley, Joan Sweet, Lynn Anson-Cartwright, Scott North, Scott Tysldey, Jeremy Sturgeon, Roanne Segal, Peter Venner, Malcolm Moore
Clinical Stage I Non-seminoma

Management of Stage I Non-Seminomatous Testicular Cancer: A Clinical Practice Guideline
S. Hotte, L.A. Mayhew, E. Winquist, and Members of the Genitourinary Cancer Disease Site Group

Report Date: August 18, 2007

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 recommend
- RPLND is not recommended in the routine management of patients with clinical stage I nonseminoma.
ESMO Guidelines Working Group

clinical recommendations

Mixed or non-seminomatous germ-cell tumors: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

R. Huddart¹ & V. Kataja²
On behalf of the ESMO Guidelines Working Group*

¹Department of Academic Radiotherapy, Institute of Cancer Research, Royal Marsden Hospital, Sutton, UK; ²Department of Oncology, Kuopio University Hospital, Kuopio, Finland

<table>
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<tr>
<th>Category</th>
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<th>Alternative</th>
<th>Evidence grade</th>
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<td>&quot;High&quot; risk</td>
<td>Adjacent chemotherapy BEP⁶× 2 cycles or surveillance protocol</td>
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<td>Group: good prognosis</td>
<td>BEP⁶ × 3 cycles</td>
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<td>Group: intermediate or poor prognosis</td>
<td>BEP⁶ × 4</td>
<td>Entry into appropriate clinical trial protocols is encouraged</td>
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CLINICAL STAGE I (pT1-4N0M0) NSGCT

NEGATIVE STAGING AFTER ORCHIECTOMY

- Normal history and physical examination
- Normal Markers - hCG and AFP - levels after 1/2 life
- Normal Chest X-ray or CT
- CT Abdomen and Pelvis
Active Surveillance

- Strategy based on early detection of relapse by intense follow-up after orchidectomy
- Over 2000 patients in surveillance protocols
- Identification of prognostic factors of relapse
  - Lymphovascular Invasion (LVI)
  - Embryonal Carcinoma (EC)
- Risk-adapted policy?

Non-Risk Adapted Surveillance In Stage I Non-Seminomatous Germ Cell Tumors (NSGCT): Improved Recent Outcomes

Michael AS Jewett, Malcolm J Moore, Padraig R Warde, Lynn Anson-Cartwright, David Kakiashvili, Ingnacio Duran, Justin Liu, Clement Ma, Dominik R Berthold, Ruth E Alison, Gregory R Pond, Jeremy FG Sturgeon

Department of Surgical Oncology, Division of Urology, Princess Margaret Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada

Abstract

Introduction and Objectives: Since 1981 the Princess Margaret Hospital testicular cancer group has used surveillance as the preferred management option for all patients (pts) with clinical stage I NSGCT. In a report of the first 105 pts [Sturgeon et al. J Clin Oncol. 1992] the relapse rate was 35% and the disease specific 5-year survival 99%. Improvements in imaging technique over time could cause stage migration with an overall lower relapse rate in this patient population. We report our experience with surveillance over different time points.

Material and Methods: 371 patients of 399 seen with stage I NS-GCT were placed on an active surveillance protocol between 1981-2005. They were not stratified by risk and only received treatment on the event of a relapse. Recurrence rates, time to relapse, risk factors predictive for recurrence, disease specific and overall survival were determined. For the analysis by time period, patients were divided in two groups based on diagnosis date. (Bellafi-1981-1992) and Recent-1993-2005 (N=214).

Results: With a median follow-up of 6.3 years. 104/371 pts (28%) relapsed, 53/157 pts (33.8%) in the initial group and 51/214 (23.8%) in the recent. All but 4 (3.8%) relapses occurred within 2 years after orchidectomy with a median time to relapse of 7.1 months. A multivariate analysis established lymphovascular invasion (LVI) (p=0.001) and pure embryonal carcinoma (EC) (p=0.01) as independent predictors of recurrence. Overall 125/371 (33.7%) were designated as ‘high-risk’(HR) based on the presence of LVI +/or EC. In the initial group 66/157 (42%) were HR and 36 (54.5%) relapsed versus 17/91 (18.7%) low-risk (LR) (p<.0001). In the recent group, 59/214 (27.5%) pts were HR and 29 (49.2%) recurred, versus 22/155 (14.2%) others (p=0.001). There were 3 (0.8%) deaths due to testis cancer. The estimated 5-year disease specific survival was 99.8% in the initial group and 98.8% in the recent one. 28 patients either refused surveillance or were advised to undergo immediate treatment. One refused all treatment and survived. The other 27 were treated by RPLND (20), chemotherapy(2) and radiation (5).

Conclusions: Initial active surveillance is an effective strategy for the management of all stage I NSGCT. A risk-adapted policy would still result in the over treatment in 50% of the patients who may be unneccessarily treated. The overall relapse rate has decreased over time but the rate in the HR patients has not changed. Hence, the proportion of high risk population has not decreased leading to increased overall treatment burden among all patients resulting in decreased overall treatment efficacy.

Methods

STUDY DESIGN

Since 1981 the Princess Margaret Hospital Testicular Cancer Group has used surveillance as the preferred management option for all Stage I NS-GCT patients.

Is surveillance a valid treatment option for all Clinical Stage I NS-GCT patients?

Have our outcomes changed over time?


ANALYSIS

Study population was divided in two cohorts:

- Initial Group (1981-1992)
- Recent Group (1993-2005)

- Analyzed parameters in each cohort:
  - Recurrence rate
  - Time to relapse
  - Risk factors predictive for recurrence
  - Disease specific and overall survival

CONCLUSIONS

- Active Surveillance is an effective strategy for the management of all stage I NS-GCT patients
- A risk-adapted policy would still result in the over treatment in 50% of the patients
- The overall relapse rate has decreased over time, but the rate in the high risk population has not changed.
- The proportion of high risk population has not decreased leading to increased overall treatment burden.
RELAPSE & PREDICTORS

Initial Group 1981 -1992
n=157
53 (33.8%)

Recent Group 1993 -2005
n=214
51 (23.8%)

Predictors of Relapse

LVI
p<0.0001

100%EC
p=0.02

371 Patients
104 (28.0%) Relapses

Initial Group 1981 -1992
n=157
53 (33.8%)

Recent Group 1993 -2005
n=214
51 (23.8%)
# Relapse Rate by Risk

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<th>High Risk</th>
<th>Relapses</th>
<th>Low Risk</th>
<th>Relapses</th>
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<tr>
<td><strong>Initial Group</strong></td>
<td>66</td>
<td>36/66 (54.5%)</td>
<td>91</td>
<td>17/91 (18.7%)</td>
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<tr>
<td>n=157</td>
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<tr>
<td><strong>Recent Group</strong></td>
<td>59</td>
<td>29/59 (49.2%)</td>
<td>155</td>
<td>22/155 (14.2%)</td>
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<td>n=214</td>
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| Total            | 125       | 65           | 246      | 39           |
3 deaths (0.8%) due to testicular cancer

<table>
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<tr>
<th>Group</th>
<th>Number Deaths</th>
<th>Disease Specific Survival 5-Year</th>
<th>Overall Survival 5-Year</th>
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<tr>
<td>Initial Group</td>
<td>1</td>
<td>99.3%</td>
<td>98%</td>
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<tr>
<td>Recent Group</td>
<td>2</td>
<td>98.9%</td>
<td>97.3%</td>
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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
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.
PATTERN OF RELAPSE

Site of Relapse
n=104

- Retroperitoneum: 75%
- Markers: 9.6%
- Lung: 8.7%
- Other: 6.7%

78 (70 Retroperitoneum only)
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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<th>Month 2</th>
<th>Month 4</th>
<th>Month 6</th>
<th>Month 8</th>
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<td></td>
<td>Markers CXR</td>
<td>Markers CXR</td>
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<td>Markers CXR</td>
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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 Kroge, Hans-Uwe Schmelz, Klaus-Peter Dieckmann, Axel Heidenreich, Peter Kwaasny, Mark Pedrini, Jan Lehmann, Sabine Klasch, Kai-Uwe Kiklmann, Rolf Pirmann, Lothar Weißbach, Volker Ley, Christian Wittkopp, and Michael Hartmann
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

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<td>Mortality (@2yrs)</td>
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<tr>
<td>Relapses (@2 yrs)</td>
<td>23</td>
<td>5</td>
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<tr>
<td>No Therapy</td>
<td>77</td>
<td>0</td>
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<tr>
<td>Single Therapy</td>
<td>13</td>
<td>93</td>
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<td>Multimodal Therapy</td>
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<td>19</td>
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<tr>
<td>Surveillance</td>
<td>100</td>
<td>0</td>
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<tr>
<td>RPLND</td>
<td>13</td>
<td>100</td>
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<tr>
<td>Chemotherapy</td>
<td>17</td>
<td>41</td>
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<tr>
<td>Chemotherapy cycles</td>
<td>69</td>
<td>59</td>
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<tr>
<td>1 &amp;/or 2 cycles</td>
<td>1</td>
<td>38</td>
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<tr>
<td>3 or more</td>
<td>68</td>
<td>21</td>
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</table>
Every 10 New Testis Tumours

- Non-Seminoma
  - 5
  - Stage I: 2
  - Stage II: 1
  - Stage III: 2
  - Residual Mass: 1
  - 98% Survive

- Seminoma
  - 5
  - Stage I: 4
  - Stage II: 1

98% Survive
CT Scanning Axial Orientation

- Current standard
- Nodal morphology
  - size criteria
    - 8 mm round
    - 10 mm short axis oval
  - shape
  - central necrosis
  - location
- 8-10 mm = threshold for “macrometastases”
Staging Accuracy

- Stage II A = N1 \leq 2 \text{ cm}
- Stage II B = N 2 >2-5 \text{ cm}, S 0-1 \ AFP +/or \ \beta hCG <1000
- pStage – maximum dimension may not be the axial diameter
Role of Primary Pathology

• Primary teratoma predicts for residual teratoma in retroperitoneal nodes after induction chemotherapy
  – 20% of Stage II A/B at pc-RPLND (Carver..Sheinfeld JCO 2007)

• Primary embryonal predicts for systemic disease
  – Consider initial chemo
Primary RPLND for Stage II A

- Increasing rate pN1 – 67% MSKCC (Stephenson et al JCO 2007)
## Primary RPLND

<table>
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<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>Effective regional therapy</td>
<td>Risk 2\textsuperscript{nd} treatment – adjuvant, salvage with more chemo</td>
</tr>
<tr>
<td>Reduce risk overtreatment - pN0</td>
<td>Experienced surgeons required</td>
</tr>
<tr>
<td>Reduce followup imaging</td>
<td>Long term toxicity</td>
</tr>
<tr>
<td></td>
<td>• Infertility due to loss antegrade ejaculation</td>
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PRIMARY RETROPERITONEAL LYMPH NODE DISSECTION FOR CLINICAL LOW STAGE NONSEMINOMATOUS GERM CELL TESTICULAR TUMORS

David Kakiashvili, Lynn Anson-Cartwright, Malcolm Moore, Jeremy FG Sturgeon, Alvaro Zuniga, Padraig R Warde, Peter Chung, Justin Liu, Clement Ma, Michael AS Jewett

Department of Surgical Oncology, Division of Urology, Princess Margaret Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada

Abstract

**INTRODUCTION:** Non-risk adapted surveillance is our recommended management for clinical stage I nonseminomatous germ cell testicular tumors (NSGCTT) at the Princess Margaret Hospital Testis Clinic with clinical stage I NSGCTT who underwent primary NS-RPLND between November 1984, when NS was introduced, and October 2007 were reviewed. Adjuvant chemotherapy was offered if resected disease was extensive or pathological characteristics were adverse. Salvage chemotherapy was given for relapse after RPLND. Clinical staging(Technetium-99m) bone and retroperitoneal (RP) metastases and normal or retroperitoneal (RP) metastases and normal or low level markers were used. Surveillance was contraindicated for and for pathological characteristics were adverse.

**METHODS:** The charts of the 120 consecutive patients from the Princess Margaret Hospital Testis Clinic with clinical stage I NSGCTT who underwent primary NS-RPLND between November 1984, when NS was introduced, and October 2007 were reviewed. Adjuvant chemotherapy was offered if resected disease was extensive or pathological characteristics were adverse. Salvage chemotherapy was given for relapse after RPLND. Clinical staging(Technetium-99m) bone and retroperitoneal (RP) metastases and normal or retroperitoneal (RP) metastases and normal or low level markers were used. Surveillance was contraindicated for and for pathological characteristics were adverse.

**RESULTS:** The median age of diagnosis was 39.5 years. The median time of follow-up was 4 years (0.75-20.89 years) (42.5% stage I, 57.5% stage II patients). 61 (51%) had bilateral disease, 39 (33%) experienced relapse after RPLND, and 31 (25.8%) initial CS I who progressed on surveillance in the RP. The charts of the 120 consecutive patients from the Princess Margaret Hospital Testis Clinic with clinical stage I NSGCTT who underwent primary NS-RPLND between November 1984, when NS was introduced, and October 2007 were reviewed. Adjuvant chemotherapy was offered if resected disease was extensive or pathological characteristics were adverse. Salvage chemotherapy was given for relapse after RPLND. Clinical staging(Technetium-99m) bone and retroperitoneal (RP) metastases and normal or retroperitoneal (RP) metastases and normal or low level markers were used. Surveillance was contraindicated for and for pathological characteristics were adverse.

**OBJECTIVES:**

- To evaluate the Princess Margaret Hospital (PMH) experience with primary nerve sparing retroperitoneal lymphadenectomy by indication for:
  - Staging accuracy
  - Total treatment burden including the need for adjuvant chemotherapy
  - Preservation of antegrade ejaculation
  - Survival outcomes stratified to the clinical stage(CS)

**METHODS:**

- Initial surveillance is our recommended management for clinical stage I (CS I) nonseminoma at PMH
- From November 1984, when NS was introduced, to October 2007, 120 patients from the PMH Testis Tumor Clinic underwent primary bilateral NS-RPLND for:
  - CS I as an alternative to initial surveillance at patient request or when surveillance was contraindicated
  - CS I who progressed on surveillance with retroperitonal (RP) metastases and normal or low level markers
  - CSII with small volume retroperitoneal metastases and normal or low level markers
  - Salvage chemotherapy was given for relapse after RPLND
  - Adjuvant chemotherapy was given if resected disease was extensive or pathological characteristics were adverse

**FOLLOW-UP:**

- 120 patients underwent primary RPLND with the median follow-up of 4.8 years (range 0.50 - 20.89 years)
  - 20 (16.7%) CS I who did not undergo initial surveillance (group 1)
  - 31 (25.8%) initial CS I who progressed on surveillance in the RP (group 2)
  - 69 (57.5%) CS II (group 3)
  - Pathologic stage and treatment burden (adjuvant and/or salvage) by groups:
    - Group 1
      - pN0 - 13(65%); pN1 - 1(5%); pN2 - 4(20%); pN3 - 2(10%)
      - 2/7 (28.6%) had adjuvant and 3/18(16.7%) salvage treatment
    - Group 2
      - pN0 - 2(6.5%); pN1 - 14(45%); pN2 - 11(35.5%); pN3 - 4(13%)
      - 2/6(33.3%) had adjuvant and 6/23(26.1%) salvage treatment
    - Group 3
      - pN0 - 24(35%); pN1 - 11(16%); pN2 - 25(36%); pN3 - 8(11.5%)
      - 76/106 (71%) had adjuvant and 63(59%) had documented antegrade ejaculation

**CONCLUSIONS:**

- Primary NS-RPLND can be performed for different indications in CS I including as salvage for progression on surveillance as well as for low volume CS II with excellent survival.
- Total burden of treatment can be reduced by avoiding adjuvant chemotherapy with small volume completely resected nodal disease.
- Antegrade ejaculation is preserved in the majority of men, even those with +ve retroperitoneal nodes.

**INTRODUCTION:**

- Retropertineal lymphadenectomy (RPLND) for testicular cancer has been performed since the late 1940’s
- The retropertineum (RP) is the initial site of metastatic spread in 76% to 90% of patients with germ cell testicular cancer
- Approximately 70% of men diagnosed with nonseminomatous germ cell testicular tumor (NSGCTT) have CS I or low burden CS IIA-B disease at original manifestation
- Primary RPLND remains an integral part of the management for this group of patients

- **Follow-up:**
  - YEAR 1
  - MARKERS
  - YEAR 2
  - MARKERS
  - YEAR 3
  - MARKERS
  - YEAR 4
  - MARKERS

- **MONTH:**
  - MONTH 1
  - MONTH 3
  - MONTH 6
  - MONTH 12

**RESULTS:**

- Survival outcomes were similar for the 3 groups; 3 deaths from testicular cancer (2 in group 1 and 1 in group 3) with disease-specific and overall survival of 98.1% and 97.2%, respectively

**OVERALL:**

- No relapse occurred in the RPLND field
- Peri-operative complications after primary RPLND were rare (4 or 1.6%)
- The median maximum pathologic dimension of resected mass was 3.5 cm (range 1.2-14cm)
- 5/90(13%) pN0 patients relapsed and required salvage chemotherapy
- 26 (24.1%) experienced relapse after RPLND, with the median time to relapse of 0.4 years (0.1-10.6 years)
- 19 (33%) with N+ (pN1- 4; pN2-12; pN3-3) received salvage chemotherapy for recurrence and remained disease-free after 4/25(16%) of those who received adjuvant chemotherapy, needed further therapy

**CONCLUSIONS:**

- **Follow-up:**
  - YEAR 1
  - MARKERS
  - YEAR 2
  - MARKERS
  - YEAR 3
  - MARKERS
  - YEAR 4
  - MARKERS

- **MONTH:**
  - MONTH 1
  - MONTH 3
  - MONTH 6
  - MONTH 12
Primary RPLND in Stage II
Princess Margaret Hospital

- N=117 for Stage II including 32 RP progressors from CS I on surveillance
- pN0 (overstaged)
  - CS II 36% (30/83)
  - CS I progressors in RP 6% (2/32)
- Progression in pN1 without adjuvant - 31%
- All stage II
  - 88% successful NS-RPLND
  - 86% (evaluable) antegrade ejaculation
Adjuvant Chemotherapy pStage II

• Review OR, pathology & consider restaging
• Effective – 2 cycles BEP or EP (MSKCC JCO 2004)
  – Essentially no relapse vs 50% overall (Williams, Birch, Einhorn et al NEJM 1987, Kondagunta, Sheinfeld...Motzer JCO 2004)
  – pN3 – full dose BEP
  – pN2 – most would give adjuvant
  – pN1 and complete resection – relapse risk 25-30% so initial surveillance with salvage an option at the price of more therapy (3-4 cycles) with toxicity
• Issue of compliance
Recommendation Stage II A/B Non-Seminoma
According to Jewett

Stage IIA – normal markers after decay
  – Initial surveillance – reimage CT (not PET)
  – RPLND
Stage IIA/B – low level markers <100
  – Consider RPLND espec if 1°teratoma, limited nodal mets to primary landing zone
  – Chemotherapy with pc-RPLND for residual
Stage IIA/B – markers elevated
  – Chemotherapy with pc-RPLND for residual
Clinical stage IIA/B nonseminomas-Stage IIA without marker elevation

Canadian Consensus:

Clinical stage IIA patients without elevated tumor markers should undergo primary RPLND. In case of PS IIA/B adjuvant chemotherapy or surveillance are further options.

Close surveillance is an alternative to primary RPLND. If progression, further options are:
- primary RPLND ± adjuvant chemotherapy (marker negative progression)
- primary chemotherapy ± RPLND for residual masses (marker positive progression)
Clinical stage IIA/B nonseminomas-Stage IIA/B with marker elevation

Canadian Consensus suggestion:

Patients with clinical stage IIA / B with elevated tumor markers or patients with IIB disease should be treated with primary chemotherapy followed by resection of residual masses.

Chemotherapy should be given according to the chemotherapy for IGCCCG good prognosis patients either as 3 cycles of BEP or 4 cycles of EP

RPLND for residual masses should be performed as nerve-sparing RPLND
Management of Residual Disease in NSGCT Testicular Cancer: Retroperitoneal Lymphadenectomy Can Be Performed Selectively

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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
Management of Residual Disease in NSGCT Testicular Cancer

Presented with RP nodal disease
Normalized markers (or low plateau levels)

Stable extraperitoneal disease

• RPLND
  – modified template  (Beck Einhorn Cancer 2007;110:1235-40 no out of field Wood Herr J Urol 1992 8%
contralateral )
  – full bilateral lymphadenectomy  (even with contemporary series Sheinfeld JCO  2007
20%)

• Observation
Residual Mass NSGCT Post -Chemotherapy

- Necrosis 40 + % - prognosis excellent
  5 - year DFS 77 - 90 %

- Teratoma 40 + % - prognosis excellent
  5 - year DFS 80 - 90 %

- Carcinoma < 10 % - prognosis poor
  5 - year DFS 44 - 59 %
  2 cycles of adjuvant chemo

Fossa et al. J Clin Oncol 1995
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

Patients who achieve complete remission, that is, normalised tumour markers and no visible residual lesions after chemotherapy, postchemotherapy surgery is not required [EBM IIB: 87,88; EBM III: 89].
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
Residual Disease in NSGCT Testicular Cancer

No clinically useful predictor of residual pathology

Vergouwe Steyerberg Donohue J Urol 2001

Vergouwe Steyerberg Donohue Eur J Urol 2007
## Prediction Models – Predicting the Probability of Necrosis

<table>
<thead>
<tr>
<th>Patients</th>
<th>N</th>
<th>Model</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicenter(@)</td>
<td>556</td>
<td>Log regression 6 factors</td>
<td>ROC = 0.84</td>
</tr>
<tr>
<td>Multicenter(#)</td>
<td>716</td>
<td>Many different prediction rules</td>
<td>All rules lead to at least 5% or cancer NOT being resected</td>
</tr>
<tr>
<td>TE-20 pts(!)</td>
<td>105</td>
<td>Log regression 6 factors</td>
<td>ROC = 0.76</td>
</tr>
<tr>
<td>Multicenter(●)</td>
<td>1094</td>
<td>Log regression 6 factors</td>
<td>ROC = 0.81</td>
</tr>
</tbody>
</table>
| Multicenter(^) | 362 | Decision Analysis            | Resect 11-20 mm: 4.3% gain in 5YS  
Resect 0-10 mm: 2.7% gain in 5YS |

(@) Steyerberg et al. JCO 1995; p1177-1187.  
(!) Vergouwe et al. Br J Cancer; p843-847.  
Residual Disease in NSGCT Testicular Cancer

Rationale (cont’d)

• Complications of RPLND - skilled operator (s) and experienced centre for pcRPLND
• Morbidity & cost of followup - clinic visits, markers, imaging with chest Xray / CT
• Anxiety – MD, patient
• Serial CT abdomen/pelvis (low dose?) – will do baseline postop at least if pcRPLND, many do more
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 but pcRPLND if any significant disease
Personal Experience with pcRPLND
Princess Margaret Hospital, Toronto

- n = 235
- 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 in 21.4 and 4.7% of cases  
* 1982-2004
Personal Experience with pcRPLND
Princess Margaret Hospital, Toronto

• n = 332, presented with RP adenopathy and underwent chemotherapy
• 226 pc RPLND
• 106 observation-only AND no relapse observed

* 1982- 2004
Residual Mass: Seminoma
PET Scans

- N=51; post-chemotherapy; SEMPET Trial

<table>
<thead>
<tr>
<th>Largest Residual Mass</th>
<th># Patients</th>
<th>TP</th>
<th>TN</th>
<th>FN</th>
<th>FP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 3 cm</td>
<td>19</td>
<td>7</td>
<td>12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>≤ 3 cm</td>
<td>37</td>
<td>1</td>
<td>34</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

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

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
Acknowledgements – PMH Testis Group

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