Specific Rehabilitation Needs in Testicular Cancer Survivors (TCSs)

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Disposition

- Background
- Long-term Adverse Effects (AEs)
- Quality of Life
- Rehabilitation needs/tasks

Sources

- Literature
- Own experience (1400 TCSs surveyed in ~2000 and ~2008)
Background

- Testicular Cancer (TC): Peak incidence age 20-40 years
- Overall long-term survival: >95%
- Today several risk-adapted treatment options with a different risk profile of AEs to be discussed with the patient pre-treatment (start of rehabilitation)

Method

- Group-wise evaluation
- General population comparison
Domains at risk

Life-threatening:

• Cardiovascular
• Second cancer

Quality of Life affecting

• Neuro-ototoxicity
• Gonadotoxicity (fertility/hormones)
• Psycho-social/Cognitive/Life style/Quality of Life
Cumulative risk (%) of developing a second solid non-germ cell cancer for seminoma or non-seminoma and the general male population.

Travis/Fosså JNCI 2005
Bilateral metachronous invasive testicular cancer

Influence of chemotherapy


No Chemotherapy

Chemotherapy

Probability of contralateral test.ca.

Months since unilateral test.ca.

P: 0.02
Treatment for TC and risk of cardiovascular diseases (CVD)
(Surgery only as reference)

<table>
<thead>
<tr>
<th></th>
<th>CVD</th>
<th>Infarctus cordis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemotherapy only</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PVB</td>
<td>1.9 (1.2-2.9)</td>
<td>1.9 (1.7-2.0)</td>
</tr>
<tr>
<td>BEP</td>
<td>1.5 (1.0-2.2)</td>
<td>1.2 (0.7-2.1)</td>
</tr>
<tr>
<td><strong>Radiotherapy only</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediastinal</td>
<td>3.0 (2.0-4.5)</td>
<td>3.7 (2.2-6.2)</td>
</tr>
<tr>
<td>Infradiaphragmatic</td>
<td>1.2 (0.8-1.7)</td>
<td>1.1 (0.7-1.7)</td>
</tr>
</tbody>
</table>

van den Belt-Dusebout AW, et al. JCO 2006; 3, 467
Odds Ratio of having hypertension
age-adjusted

N: 1289  Norwegian Testicular cancer survivors

Follow-up: Median 11 years


Sagstuen, ESMO 2004
Cancer testis: CRP >1.5 tatt 10 år etter behandling predikerer ny kreft eller CVD 10 år deretter

Non-germ cell cancer

Cardiovascular events

Wethal, EJC, in press
Second Cancer / Cardio-vascular disease  

and  

Treatment modality

van den Belt-Dusebout AW, et al. JCO 2007
# Initial treatment and risk of second cancer / CVD

van den Belt-Dusebout (2007)

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery only</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Subdiaph. RT only*</td>
<td>2.6</td>
<td>1.7-4.0</td>
</tr>
<tr>
<td>Subdiaph. + mediast. RT*</td>
<td>3.6</td>
<td>2.1-6.0</td>
</tr>
<tr>
<td>Cispl. based chemoth. only</td>
<td>2.1</td>
<td>1.4-3.1</td>
</tr>
<tr>
<td>SMOKING</td>
<td>1.8</td>
<td>1.4-3.1</td>
</tr>
</tbody>
</table>

*Tendency for dose-effect relationship (p:0.055)
Quality of Life aspects
Prevalence of self-reported typical post-treatment symptoms (11 year)

<table>
<thead>
<tr>
<th>AE</th>
<th>SURV(^1)</th>
<th>RPLND(^2)</th>
<th>RAD(^3)</th>
<th>CHEM(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy</td>
<td>10%</td>
<td>11%</td>
<td>16%</td>
<td>21%</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>16%</td>
<td>14%</td>
<td>13%</td>
<td>22%</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>21%</td>
<td>25%</td>
<td>29%</td>
<td>29%</td>
</tr>
<tr>
<td>Impaired sexual function</td>
<td>13%</td>
<td>20%</td>
<td>23%</td>
<td>24%</td>
</tr>
</tbody>
</table>

\(^1\)Surveillance, \(^2\)Retrop. lymph node dissection only, \(^3\)Radiotherapy only, \(^4\)Chemotherapy +/- Surgery/Radiotherapy

Mykletun, JCO, 23:3061 (2005)
Prevalence of patients with clinically relevant worsening (≥10% of a scale 1-100) after chemotherapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>2 year</th>
<th>11 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy</td>
<td>22%</td>
<td>18%</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>26%</td>
<td>22%</td>
</tr>
<tr>
<td>Difficulty hearing</td>
<td>21%</td>
<td>21%</td>
</tr>
<tr>
<td>Sexual interest ↓</td>
<td>12%</td>
<td>24%</td>
</tr>
<tr>
<td>Sexual activity ↓</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Relapse anxiety</td>
<td>17%</td>
<td>24%*</td>
</tr>
</tbody>
</table>

→ No improvement of AEs after 2 years

*Skaali, Psycho-oncology 2009;18:580*
### 11 year TCSs: Risk factors for poor Quality of life (multivariate analysis compared with gen.pop.)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence TCSs</th>
<th>Prevalence Norm</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not working</td>
<td>10%</td>
<td>9%</td>
<td>4.08</td>
</tr>
<tr>
<td>Musculo-skeletal probl.</td>
<td>35%</td>
<td>41%</td>
<td>2.55</td>
</tr>
<tr>
<td>Anxiety/Depression</td>
<td>22%</td>
<td>18%</td>
<td>2.77</td>
</tr>
<tr>
<td>Low-self esteem</td>
<td>21%</td>
<td>18%</td>
<td>2.35</td>
</tr>
<tr>
<td>Neurotoxic symptoms</td>
<td></td>
<td></td>
<td>2.26</td>
</tr>
<tr>
<td>Fatigue</td>
<td>28%</td>
<td>10%</td>
<td>7.13</td>
</tr>
</tbody>
</table>

Falk Dahl, JCS, in press
OTOTOXICITY\(^1\) due to cisplatin-based chemotherapy (4 cycles)

Influence of days per cycle during 4 cycles cisplatin-based chemotherapy
1. Equally effective; 2. More ototoxicity during 2 days; 3. **Chemotherapy** to be given during 5 days

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\(^1\)Self-reported
Audiometry

chi kvadrat p<0.001

Brydøy et al., in preparation
Proportion of Testicular Cancer patients with self-reported COGNITIVE COMPLAINTS during the first post-orchiektomy year and using EORTC QL C-30

BEP chemotherapy x 3-4 (N = 276)

Radiotherapy only (N = 71)

Skaali, submitted
Predictive factors for the development of self-reported cognitive complaints among 122 orchiectomized testicular cancer patients undergoing neuropsychological tests before and 1 year after treatment:

- Chemotherapy
- Low level of education
- Mental problems prior to TC
- Fatigue after 1 year
- Raynaud-like symptoms

No relation between cognitive complaints and neuropsychological tests at 1 year

Skaali, submitted
Gonadal function and fertility

Hypogonadism in long-term TCSs

- Treatment- and cancer-related biochemical hypogonadism in 10-16%
- Clinical relevance? Metabolic Syndrome
- Clinical hypogonadism in 4-5%
- Optimal substitution?

Nord, Eur.Urol.(2003),44,322
Fertility: Post-treatment paternity in patients attempting fatherhood

1. Treatment-and cancer-related sub-fertility, but 70-80% father a child post-treatment if attempted, dose-effect relation

BUT
Possibly increased risk of slight malformations of the first child born after cancer in pre-diagn.childless men

2. Limited use (30/430) of frozen semen
16 pregnancies

QUALITYof LIFE (QoL) and SEXUALITY in Testicular cancer survivors (after 11 yrs) and the General male population (<40yrs old)

Quality of life

Sexual life

SF-36 scores

PF Physical Functioning, RP Role Physical, BP Bodily Pain, GH General Health, VT Vitality, SF Social Functioning, RE Role Emotional, MH Mental Health, PCS Physical composite score, MCS Mental Composit Score. Norm-data are age-adjusted to match the TCS.

* p<.05

Number of patients with major problems (%)

DRIVE Probl.
Ecaculation

Phys. QoL
Mental QoL

Dahl/Fosså (2005/2007)
Life style
Self-reported **Physical Activity** in ≤5 year Testicular Cancer Survivors

### Pre-treatment

- **Inactive**: 60 (43%)
- **Active**: 79 (57%)

### Post-treatment

- **Inactive**: 49 (82%)
- **Active**: 11 (18%)
  - + Active 55 (70%)
  - + Inactive 24 (30%)
- **Active**: 66 (47%)
- **Inactive**: 73 (53%)

**Overall development**

- Inactivity: 43% → 53%
- Activity: 57% → 47%

Gjerset, in prep.
Specific rehabilitation tasks in individual TCSs

**Second cancer:** Testicular self-examination / ultrasound in high-risk patients. Early specialist referral if symptoms suspicious of new cancer

**Cardiovascular:** Regular check-ups by family doctor (Lipids, blood pressure, weight, lifestyle)

**Gonadal:** Cautious testosterone substitution Assisted reproduction, Testicular prosthesis?? (→ bilateral TC)

**Neuro-/ototoxicity:** 5-days BEP, evtl. change of occupation

**Life style:** Physical activity
Conclusion

Specific therapeutic rehabilitation task needed in the minority of TCSs (15-20%?)

Prevention of second cancer and cardiovascular disease necessary
Thank you
Cisplatin-based chemotherapy delays the development of invasive cancer, but does not abolish the risk completely.

**Invasive test.cancer from CIS:**
Influence of chemotherapy (NRH: 1980-2001)

![Graph showing the probability of invasive testicular cancer development over months since diagnosis of testicular CIS with and without chemotherapy.](image)

- **No Chemotherapy**
- **Chemotherapy**
Relative risk of second solid cancer after treatment of testicular cancer at an age of 35 years (~ 40 000 patients, 1943-2002)

1. Stomach
2. Pancreas
3. Bladder
4. Kidney
5. Colon
6. Rectum
7. Mal.melanoma
8. Lung

Travis/Fosså, JNCI 2005
Quality of life (SF-36) in 1409 Norwegian males treated for testicular cancer 1980-1994 (median obs.time ~11 years)

SF-36 scores

PF Physical Functioning, RP Role Physical, BP Bodily Pain, GH General Health, VT Vitality, SF Social Functioning, RE Role Emotional, MH Mental Health, PCS Physical composite score, MCS Mental Composite Score. Norm-data are age-adjusted to match the TCS.

* p<.05

there was no difference in the proportion of cognitively impaired patients in the chemotherapy group (5.6%) compared to the nonchemotherapy group (8.3%) (chi2 = 0.22, p = .64).

20-30% have complaints
Cumulative risk (%) of developing a second solid non-germ cell cancer at age 70 years for seminoma, and the general male population.

A) 20yr
2nd. ca: 70yr ca. 40% vs 20%

B) 35year
2nd. ca: 70 yr 30% vs 15%
Second germ cell malignancy
(Contralateral Testicular Cancer [CTC])

Testicular dysgenesis syndrome (TDS) during embryonal life (Week 4-8)
→ Testicular cancer in situ

Other manifestations and clinical risk groups for CTC:
- Hypospadia
- Cryptorchidism
- Infertility
- Contralateral cancer in situ (5% of unilat.TC, 30% of extragonadal germ cell cancer)
### Testicular ca. in situ → Crude % of invasive CTC\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synocharonuous:</td>
<td>0.5%</td>
<td>0.2-0.8%</td>
</tr>
<tr>
<td>Metachronuous:</td>
<td>1.2%</td>
<td>0.8-2.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>SIR</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>1.9% (1.7%-2.1%)</td>
</tr>
<tr>
<td></td>
<td>2.4% (1.4%-3.9%)</td>
</tr>
<tr>
<td></td>
<td>3.9% (2.8%-5%)</td>
</tr>
<tr>
<td>20</td>
<td>5.2% (3.7%-6.7%)</td>
</tr>
</tbody>
</table>

Highest risk during the first 5 years

**Risk factors:** SEMINOMA (No chemotherapy)
Age <30 years at first TC

\(^{1}\)Contralateral Testicular Cancer, Large geographical differences

Fossa , JNCI (2005), 97;1056