

# Cognitive Impairment in Long-Term Survivors of Testicular Cancer More Than 20 Years after Treatment

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## 1. Supplementary methods

### 1.1. Cognitive tests

The AVLT was used as an alternative for the Hopkins Verbal Learning Test – Revised (HVLT-R). The Dutch AVLT is based on the Rey AVLT (Rey, 1964) and measures learning and memory capabilities. Five presentations of a 15-word list are given, each followed by an attempted direct recall. Approximately 20 minutes after the direct recall an attempted delayed recall of the 15-word list takes place. Lastly, during the recognition test, the participant is presented with 30 words and asked to recognize which words were part of the 15-word list and which were not.[28] The fluency tests (LFT and CFT) measure aspects of language and executive function. The LFT is a validated Dutch version of the Controlled Word Association Test and uses three letters.[29] Individuals are given one minute to name as many words as possible beginning with one of the letters. This procedure is then repeated for the remaining two letters. During the CFT, participants have to produce as many words as possible from a category—animals (CFT-A) and professions (CFT-P)—during one minute. The TMT measures information processing speed and aspects of executive function.[30] It consists of two parts in which the subject is instructed to connect a set of 25 dots as quickly as possible. Cognitive test performance of our study participants were compared to the normative data from the normative database of Advanced Neuropsychological Diagnostics Infrastructure (ANDI). The number of individual control measurements included in the ANDI is large, varying from 1855 to 7583 per cognitive test. This provides robust control data for our analyses.

**Table S1.** Raw Scores on Cognitive Tests per Group.

| Characteristic              | Testicular Cancer Survivors (TCS) |              |              |                                 | CT vs. RT<br>vs. Orchie-<br>tomy Only | Healthy Controls   |                     |
|-----------------------------|-----------------------------------|--------------|--------------|---------------------------------|---------------------------------------|--------------------|---------------------|
|                             | All TCS<br>N = 185                | CT<br>N = 66 | RT<br>N = 53 | Orchiec-<br>tomy Only<br>N = 65 |                                       | controls<br>N = 70 | TCS vs.<br>Controls |
|                             |                                   |              |              |                                 | P-value†                              |                    | P-value†            |
| RAVLT<br>median<br>range    | 38<br>11–60                       | 39<br>22–60  | 37<br>11–59  | 39<br>24–55                     | 0.83                                  | 42<br>24–64        | < 0.01              |
| RAVLT DR<br>median<br>range | 7<br>0–14                         | 8<br>2–14    | 7<br>2–14    | 7<br>0–13                       | 0.31                                  | 9<br>0–14          | 0.08                |
| LFT<br>median<br>range      | 33<br>15–65                       | 31<br>15–59  | 33<br>15–60  | 36<br>15–65                     | 0.32                                  | 36<br>17–78        | 0.09                |
| CFT<br>median<br>range      | 40<br>17–67                       | 39<br>17–67  | 40<br>23–61  | 40<br>19–63                     | 0.68                                  | 42<br>25–83        | < 0.01              |
| TMT-A<br>median             | 30<br>13–122                      | 33<br>16–95  | 30<br>13–122 | 27<br>13–75                     | 0.04                                  | 30<br>15–76        | 0.46                |

| range  |        |        |        |        |      |        |      |
|--------|--------|--------|--------|--------|------|--------|------|
| TMT-B  | 68     | 72     | 64     | 63     |      | 67     |      |
| median | 27–294 | 36–294 | 32–219 | 27–172 | 0.26 | 24–184 | 0.22 |
| range  |        |        |        |        |      |        |      |

Abbreviations: TCS, testicular cancer survivors; CT, chemotherapy group; RT, radiotherapy group; AVLTL, auditory verbal learning test; AVLTL DR, auditory verbal learning test delayed recall; LFT, letter fluency test; CFT, category fluency test; TMT, trail making test; † Comparison of three groups was made with an ANOVA if normally distributed, or Kruskal Wallis if not. Comparison of two groups with students' T test or Mann-Whitney U Test.

**Table S2.** Proportion Impaired Scores on Cognitive Tests per Group.

| Characteristic                     | Testicular Cancer Survivors (TCS) |              |              |                            | CT vs. RT<br>vs. Orchiectomy Only | Healthy Controls   |                     |
|------------------------------------|-----------------------------------|--------------|--------------|----------------------------|-----------------------------------|--------------------|---------------------|
|                                    | All TCS<br>N = 185                | CT<br>N = 66 | RT<br>N = 53 | Orchiectomy Only<br>N = 65 |                                   | controls<br>N = 70 | TCS vs.<br>Controls |
|                                    |                                   |              |              |                            |                                   |                    | P-value†            |
| AVLT<br>proportion impaired (%)    | 2                                 | 2            | 4            | 2                          | 0.64                              | 0                  | 0.58                |
| AVLT DR<br>proportion impaired (%) | 6                                 | 3            | 2            | 11                         | 0.06                              | 7                  | 0.59                |
| LFT<br>proportion impaired (%)     | 2                                 | 3            | 2            | 2                          | 0.83                              | 0                  | 0.58                |
| CFT<br>proportion impaired (%)     | 3                                 | 3            | 0            | 5                          | 0.30                              | 0                  | 0.16                |
| TMT-A<br>proportion impaired (%)   | 2                                 | 3            | 4            | 0                          | 0.32                              | 1                  | 1.00                |
| TMT-B<br>proportion impaired (%)   | 2                                 | 3            | 2            | 0                          | 0.39                              | 1                  | 1.00                |

Abbreviations: TCS, testicular cancer survivors; CT, chemotherapy group; RT, radiotherapy group; AVLTL, auditory verbal learning test; AVLTL DR, auditory verbal learning test delayed recall; LFT, letter fluency test; CFT, category fluency test; TMT, trail making test; † Proportions were compared using  $\chi^2$ -test.

**Table S3.** All Subscales of the Cognitive Failure Questionnaire per Study Group.

| Characteristic            | Testicular cancer survivors (TCS) |              |              |                            | CT vs. RT<br>vs. Orchiectomy only | Healthy controls   |                     |
|---------------------------|-----------------------------------|--------------|--------------|----------------------------|-----------------------------------|--------------------|---------------------|
|                           | All TCS<br>N = 185                | CT<br>N = 66 | RT<br>N = 53 | Orchiectomy only<br>N = 65 |                                   | controls<br>N = 70 | TCS vs.<br>controls |
|                           |                                   |              |              |                            |                                   |                    | P-value†            |
| CFQ total score<br>median | 24<br>0 –65                       | 29<br>2 –49  | 22<br>0 –53  | 25<br>0 –65                | 0.12                              | 27<br>0 –53        | 0.87                |

|                      |       |       |       |       |      |       |      |
|----------------------|-------|-------|-------|-------|------|-------|------|
| range                |       |       |       |       |      |       |      |
| CFQ –memory          | 6     | 7     | 5     | 7     | 0.12 | 6     | 0.76 |
| median               | 0 –20 | 0 –17 | 0 –16 | 0 –20 |      | 0 –18 |      |
| range                |       |       |       |       |      |       |      |
| CFQ –distractibility | 10    | 10    | 8     | 10    | 0.36 | 10    | 0.86 |
| median               | 0 –24 | 0 –22 | 0 –21 | 0 –24 |      | 0 –18 |      |
| range                |       |       |       |       |      |       |      |
| CFQ –social blun-    |       |       |       |       | 0.39 |       | 0.23 |
| ders                 | 6     | 7     | 6     | 7     |      | 6     |      |
| median               | 0 –19 | 0 –14 | 0 –13 | 0 –19 |      | 0 –14 |      |
| range                |       |       |       |       | 0.26 |       | 31   |
| CFQ –forgetting      |       |       |       |       |      |       |      |
| names                | 4     | 4     | 3     | 4     |      | 4     |      |
| median               | 0 –8  | 0 –7  | 0 –7  | 0 –8  |      | 0 –8  |      |
| range                |       |       |       |       |      |       |      |

Abbreviations: TCS, testicular cancer survivors; CT, chemotherapy group; RT, radiotherapy group; CFQ, cognitive functioning index; † Comparison of three groups was made with an ANOVA if normally distributed, or Kruskal Wallis if not. Comparison of two groups with students' T test or Mann-Whitney U Test.