Introduction
Introduction

Only 25 years ago, disseminated testicular cancer was the leading cause of cancer death in men between 15 and 45 years of age. After the introduction of cisplatinum into the chemotherapeutic regimen in the late 1970s, testicular cancer has become a curable disease for approximately 90% of the patients [1;2]. Because of the young age at diagnosis, testicular cancer survivors have an additional life expectancy of up to 50 years and, consequently, they have to face possible sequel of diagnosis and treatment for the rest of their lives. At the University Medical Center Groningen (UMCG), in The Netherlands, a tertiary referral center for patients with testicular cancer, considerable institutional research has been performed into the epidemiology, genetic susceptibility, and short- and long-term medical and sexual sequel of testicular cancer [3-10]. However, the possible impact of the experience with testicular cancer on the quality of life of survivors has not received empirical attention yet. This thesis addresses the quality of life of testicular cancer survivors treated at the UMCG between 1977 and 2003. This introductory chapter starts with an elaboration on the concept of quality of life and the possible effects of cancer on the quality of life of patients and survivors. After that, factors that may influence quality of life will be discussed. Lastly, the aim of the thesis and an overview of the chapters will be presented.

Quality of life

Calman [11] defines quality of life as the gap between the hopes, expectations, and desires of persons during a particular period of time and their present life experiences. In the same tenor, Cella [12] refers to quality of life as the patient's appraisals of and satisfaction with their current level of functioning compared with what they perceive to be possible or ideal. The greater the gap between the actual and the ideal situation, the lower a person's quality of life will be. The perception of a person's quality of life varies between individuals. This means that people with different expectations will report a different quality of life, even when they have the same objective health status. Therefore, insight into a patient's quality of life can only be obtained by asking a patient's perspective.

Quality of life encompasses several life domains, usually physical, psychological and social well-being [13-15]. Recently, investigators have started to include spirituality as a separate domain, because they have recognized that the experience of life as meaningful and the need to find meaning in life events may be important in determining a person's quality of life [16;17].

Ferrell and Dow [18] have defined the domains for cancer survivors as follows:

- **Physical well-being** is the control or relief of symptoms and the maintenance of function and independence.
- **Psychological well-being** is the attempt to maintain a sense of control in the face of life-threatening illness characterized by emotional distress, altered life priorities, and fear of the unknown as well as positive life changes.
- **Social well-being** is the effort to deal with the impact of cancer on individuals, their roles and relationships.
• *Spiritual well-being* is the ability to maintain hope and derive meaning from the cancer experience which is characterized by uncertainty.

Research has found that sequel from cancer diagnosis and treatment may affect all these domains in survivors, months or even years after successful completion of treatment. For example, the cancer experience has been found to induce fatigue [19-21], infertility [22-25], cardiovascular diseases [26;27], posttraumatic stress disorder, and fear for recurrence and death [28-30], and to negatively affect social support systems [31], marital relationships [32], job performance [33-35], and outlook on life [36]. The specific combination of clinical features of testicular cancer may make the population of testicular cancer survivors especially vulnerable for an impaired quality of life. Testicular cancer strikes at an age when health is taken for granted and life-threatening illnesses and the possibility of dying do not fit their outlook on life [2;37;38]. It assaults an organ associated with sexuality and reproduction at a time of life when sexual desire and performance, sense of masculinity, body image, and fertility are central themes [5;39]. And it mostly occurs in a period of life characterized by major social life changes. Between the ages of 15 and 45, important decisions about marriage, starting a family and a professional career are generally made [14]. Thus, the life stage in which testicular cancer occurs has its specific developmental tasks and social roles, and therefore it may make testicular cancer a particularly distressing experience. The confrontation with testicular cancer may continue to influence the well-being of the survivors months or even years after treatment completion, when sequel of the cancer experience continue to interfere with involvements in valued activities, interests, and desires.

**Factors that may affect quality of life**

The effect of a disease on people’s lives is generally examined by measuring the outcomes as well as the predictors of outcomes [17]. Quality of life as an outcome has been studied quite extensively in psychosocial oncology. Increasingly, research focuses on risk and resilience factors associated with quality of life. It is important to identify factors predictive of an impaired quality of life, because it may help health care providers to detect distressed individuals at an early stage and refer them for psychosocial care [40].

Based on the stress-coping literature, Holland and colleagues have developed a research model for the field of psycho-oncology [16], in which they have identified variables that may influence quality of life. In this model, cancer is the stressful life event and the disease- and treatment-related variables are the measurable characteristics of the event that may affect the patient’s functioning. The personal variables and life stresses represent the resources of a patient that may be relevant for the outcome of the adjustment process (e.g., quality of life). Figure 1 is a schematic representation of the model of Holland [16] and summarizes the specific variables that were identified as possibly relevant predictors of (domains of) quality of life in the cancer population. The effect of these variables on quality of life will be investigated in the current thesis.

**Disease and treatment variables**

Time since treatment, type of treatment, and the experience of a second cancer event will be studied in the present thesis. There is some evidence that cancer patients who have been diagnosed more recently, who have been treated with more extensive treatment, or who
have experienced a recurrence are at a higher risk for an impaired quality of life and cancer-related stress [28;40]. Furthermore, hemoglobin and testosterone levels will be examined in relation to fatigue during the first year after the diagnosis of testicular cancer. Chemotherapy can lower the levels of hemoglobin (mainly a short-term effect) and testosterone (mainly a long-term effect) which can cause excessive tiredness [27;41-43]. Associations between hemoglobin and testosterone levels and fatigue in testicular cancer patients have never received attention before.

**Personal variables**

Sociodemographic characteristics (e.g., age, educational level, marital status, employment status) have been found to be associated to some extent with how well people adjust to having (had) cancer [40], and should thus be included in studies that aim to elucidate factors that affect quality of life.

In general, having a sense of meaning has been identified as an important contributor to a person’s quality of life [16;17]. Stressful life events, such as testicular cancer, may threaten the belief that life is meaningful and this may have a negative effect on well-being. Therefore, it may be relevant to assess meaning and its relationship with psychosocial well-being and cancer-related distress in testicular cancer survivors.

Trait anxiety will be investigated in relation to cancer-related fatigue. Little research has focused on this relationship, but there are indications that cancer patients with an anxious disposition pay more attention to physical sensations than less anxious patients [44;45]. So, it might be that this personality trait increases the sensitivity to fatigue.

**Life stresses**

The main focus of this thesis is on the quality of life of testicular cancer survivors who have been treated over a period of 25 years (1977-2003). This large range in time since treatment is associated with a methodological problem, because in long-term survivors it is more difficult to distinguish effects caused by cancer and its treatment, from those attributable to other factors, such as additionally experienced life events and comorbidities [46]. The probability of experiencing additional major life events and of developing a functional limitation or chronic disease increases with advancing age, and this may influence the quality of life more than the earlier experience with cancer.

**Aims of the thesis**

The general aims of the thesis are:

1. To study the quality of life of testicular cancer survivors;
2. To investigate the extent to which characteristics of the disease and treatment, personal variables, and additional life stresses affect (domains of) quality of life of testicular cancer survivors.

*Chapter 2* offers a review of the literature on the quality of life of testicular cancer survivors. The aims of this review are (1) to gain insight into the current state of knowledge on the physical, psychological, and social well-being of testicular cancer survivors, and (2) to assess the impact of disease and treatment characteristics on these domains of quality of life. The
study that is presented in chapter 3, describes the quality of life (physical, psychological and social domains) of testicular cancer survivors in comparison to a reference group of Dutch men. Furthermore, relationships between quality of life and disease-and treatment-related variables, sociodemographic characteristics, concurrent chronic diseases and recently experienced life events are examined to identify testicular cancer survivors at risk for an impaired quality of life. In chapter 4, a study is presented that examines meaning among testicular survivors and describes the relative contribution of meaning in the prediction of psychosocial well-being and cancer-related distress, in addition to sociodemographics, disease- and treatment-related variables, concurrent chronic disease and recently experienced life events. The primary goal of the study described in chapter 5, is to investigate the prevalence of cancer-related stress symptoms among survivors of testicular cancer. The second goal is to gain insight into the relationships between such stress symptoms and disease- and treatment-related variables and sociodemographics, and to examine whether objective and subjective aspects of cancer diagnosis and treatment are associated with posttraumatic stress symptoms. Chapter 6 describes the levels of and changes in fatigue among testicular cancer patients at three time points during the first year after diagnosis. Also, relationships between fatigue on the one hand and sociodemographics, hemoglobin- and testosterone levels, and trait anxiety on the other hand are examined. In chapter 7 testicular cancer survivors recruited through the UMCG database are compared with survivors recruited through a patient association on sociodemographic and disease- and treatment-related characteristics and quality of life to investigate heterogeneity and differences in the quality of life between individuals recruited through different sources. Finally, in chapter 8, a discussion of the findings of the present study is presented.

Figure 1. Schematic representation of the model of research in psycho-oncology of Holland and colleagues [16]

<table>
<thead>
<tr>
<th>Testicular cancer</th>
<th>Related variables</th>
<th>Outcome variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal variables</td>
<td>sociodemographic characteristics</td>
<td>Quality of life (multidimensional)</td>
</tr>
<tr>
<td></td>
<td>meaning</td>
<td>Cancer-related stress symptoms</td>
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<tr>
<td></td>
<td>trait anxiety</td>
<td>Meaning</td>
</tr>
<tr>
<td>Life stresses</td>
<td>concurrent chronic disease</td>
<td>Satisfaction with life</td>
</tr>
<tr>
<td></td>
<td>recently experienced life events</td>
<td>Fatigue (multidimensional)</td>
</tr>
</tbody>
</table>

- Disease and treatment variables
  - time since treatment
  - type of treatment
  - second cancer event
  - hemoglobin level
  - testosterone level
Reference List


