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Testicular Cancer and the Importance of Early Diagnosis

Serife Zehra Altunkurek

Abstract

Prevalence of cancers is growing rapidly in all parts of the world. Testicular cancer (TC) is one of the greatest threats to health among 15- to 34-year-old males. Since testicular cancer peaks in incidence among young men of reproductive age, it is an important type of cancer for men. Risk factors for testicular cancer include cryptorchidism (i.e., undescended testicles), family history, infertility, tobacco use, and white race. Therefore increasing awareness in this regard, a joint effort that encourages risk factors and preventive measures, must be shown. The treatments are very effective, which greatly increases the 5-year survival rate by approximately 98%. Prevention is the best option to tackle TC. Secondary preventive measures, the most important testicular self-examination (TSE), are well known and are encouraged to them. TSE helps prevent the diagnosis of late-stage TSE. Because the treatment of testicular cancer detected early is often associated with very positive results, routine screening and monthly self-examination in young men have been suggested. Although testicular cancer is rare, it is very effective to treat symptoms when they are diagnosed by TSE. As with breast cancer, early detection of TC is best done through self-examination.

Keywords: testicular cancer, men's health, early diagnosis, self examination

1. Introduction

Cancer is the second leading cause of death globally and is responsible for an estimated 9.6 million deaths in 2018 [1]. A number of malignancies can be prevented through screening; an example is predominantly affecting males between 15 to 35 years of age and a relatively rare testicular malignancy that is a treatable cancer [2, 3]. However, TC incidence has risen worldwide in the past two decades [4]. Advances in the treatment of TC over the last 25 years have resulted in survival figures of 80–90%. Since TC peaks in incidence among young men of reproductive age, it is an important type of cancer for men [5]. Early diagnosis and treatment of TC is very important. TC is completely cured when detected at an early stage. Early diagnosis and 5-year survival rate is 99% [6–8]. Ninety to ninety-five percent of testicular tumors are caused by germinal tissue [9]. In this group, seminoma is the most common tumor with 40% [10]. The rate of cure with radiotherapy following orchiectomy in stage I seminoma is 99% [11]. Risk factors for TC include cryptorchidism (undescended testicles), abnormal development of testicles, adolescent and young adult age, family history, infertility, and white race [12–14]. Treatment is highly effective even when the diagnosis is made through

examination or because of symptoms [15]. As with breast cancer, early detection of TC is best done through self-examination [16]. Although routine screening and monthly self-examination in young men have been recommended, studies have not shown that they improve outcomes [17].

This chapter explains the epidemiology, etiology, stages, treatment of TC, and importance of early diagnosis for TC as well as TSE, as far as possible, with special considerations for adolescent and young adult populations.

2. Epidemiology

TC incidence is increasing worldwide, but the reasons for this increase are not fully documented [18]. There were a total of 36,747 cases of TC in the Scandinavian countries from 1960 to 2014 [19]. 9.4 affected individuals per 100,000 males in Denmark had the highest incidence of TC for decades, but while the incidence rate stabilized in Denmark, the rate is now highest, 9.9 affected individuals per 100,000 males in Norway [20, 21]. In the United States, TC is more common in white individuals (6.9 affected individuals per 100,000 males) than in African Americans (1.2 affected individuals per 100,000 males) [18]. TC took first place with 24.8 percent of men in the 15-24 age group in Turkey [22]. An analysis from the International Agency for Research on Cancer indicates age-standardized rates of TC varied from less than 1/100,000 person 14-35 years in Africa and Asia [23]. Worldwide, there are approximately 72,000 cases and 9000 deaths per year attributable to TC [24]. TC death in the United States accounts for approximately 4% of the annual incidence [25]. There is a significant global variability in mortality rates that are largely inverse in incidence rates. TC mortality is highest in low-income countries compared with higher-income countries [20]. Also, in spite of the highest incidences of this disease in Europe, North America and New Zealand account for only one-fifth of mortalities caused by TC [26]. About 50% of patients worldwide with TC are diagnosed with seminoma and the median ages at diagnosis 37 years [27].

2.1 Risk factors

The majority of TC (98%) had germ cell tumors; therefore, the terms testicular germ cell tumor and TC are often used interchangeably [28]. While most cancers occur in adulthood, the incidence of TC does not increase with age. The peak ages of occurrence are 25–29 years for non-seminomas and 35–39 years for seminomas [29]. The risk factors for TC are not well understood, but the risk factors most consistently associated with cryptorchidism, contralateral testicular tumor, a family history of TC, male factor infertility, and testicular microlithiasis [30–32].

Cryptorchidism, also referred to as maldescended testis, is the failure of descent of one or both of the testes into the scrotum and is a common clinical diagnosis in newborn boys and one of the strongest risk factors for infertility and testicular cancer [33–35]. Approximately 10% of all cases of testicular tumors occur in boys with a history of cryptorchidism [36]. In a study of patients with bilateral germ cell tumor, while 9.5% had cryptorchidism history, cryptorchidism was found in 2.2% of patients with unilateral tumors [37]. In addition, in a cohort study, cryptorchidism repair prior to puberty was associated with a doubling in risk of testicular cancer; postponement of the repair after the age of 12 showed that the risk increased fivefold [38].

TC is associated with a family history link as well [33–35]. Men, who have a first-degree relative with testicular cancer, have a reasonably increased risk [39]. Patients

with a history of personal testicular cancer have a 12-fold higher risk of developing TC than the general population [40]. Family cancer studies have shown that sons whose fathers have TC have four times the risk of testicular cancer and brothers of patients with TC have eight times the risk of having testicular cancer [41]. Family history of this relationship is white men are more likely than black men to develop TC [15]. In a study with a large population, contralateral testicular cancer explained that a man younger than age of 30 with testicular seminoma has a 3.1% risk of developing a TC [42].

TC has increased in the last 30 years, while in Western countries there has been a decrease in semen quality and fertility [41]. Men with infertility have an increased risk of TC, with an incidence ratio of 1.6–2.8 [43]. The cohort study, based on more than 22,000 men undergoing evaluation for infertility, examined an association between infertility and the development of testicular cancer [44]. Other risk factors in TC are vasectomy, scrotal trauma, inguinal hernia, diet, smoking, the gene, environment (such as heavy metals exposure and endocrine disruptors), and hormones [45–50].

3. Diagnosing testicular cancer

TC is often seen as a painless mass in the testis, but in many patients there is a widespread pain, swelling, or stiffness in the scrotum [51]. Testicular masses appear more often on the right side [8]. Acute testicular pain is less widespread and is reasoned by swift expansion of the testis owing to intratumor hemorrhage or infarction caused by swift tumor growth [39]. Men often notice a history of testicular trauma, though accidental trauma is probably liable for leading the testicular mass to the men's attention, firstly. Men may complain of unclear scrotal pain or heaviness [39]. Testicular masses can be urgently evaluated by physical exam and bilateral testicular ultrasound [6]. Physical examination may be determinative but is sometimes vague in differentiating a malignancy from nonmalignant testicular masses [52].

The physician should carefully examine the testes, noting their notional size and density and palpating for any testicular masses [39]. Any doubtful symptoms should give rise to adjuvant studies [53]. **Table 1** shows the signs and symptoms of TC [15].

Discomfort	Metastases*
Dull ache in the scrotum or abdomen	Gastrointestinal symptoms
Acute pain in the testicle or scrotum	Gynecomastia
Scrotal heaviness	Lumbar back pain
Mass effect	Neck mass
Firmness of the testicle	Respiratory symptoms (e.g., cough, hemoptysis, dyspnea)
Infertility	
Intratesticular mass	
Painless swelling and redness	

*About 5% of patients with testicular cancer have symptoms of metastases.
 Information from Ref. [15].

Table 1.
Signs and symptoms of testicular cancer.

In men showing with testicular mass, unexplained scrotal pain or signs, ultrasonography should be regarded an appendage of the physical examination due to being broadly existing, cheap, and noninvasive [54]. After Physical examination, for revealing a mass in the testicle and the first radiological evaluation was Ultrasonography [55]. First of all intratesticular mass or the extratesticular location is examined. The intratesticular masses tend to be malignant, and the extratesticular masses tend to be benign. The nature of the detected masses (solid or cystic) is determined by Ultrasonografi (US). Solid masses suggest more malignancy, whereas cystic masses are often benign, such as rete testis ectasia, simple cyst, and tunica albuginea cyst [55].

Tumor markers are also an important part of the diagnostic workup. Beta-human chorionic gonadotropin (Bhcg), alpha-fetoprotein (AFP), and lactate dehydrogenase (LDH) levels are checked for the diagnosis of testicular tumors [56]. At the same time, these marker levels should be acquired after orchiectomy and to monitor chemotherapy treatment [39]. At the beginning of cancer, levels of these markers tend to be in the normal level. LDH levels are often elevated metastatic testicular cancer [15].

A biopsy can damage the testicles and spread the cancer into scrotum, so biopsy is not recommended [57]. But if suspected of having testicular tumor, one should undergo a radical inguinal orchiectomy for pathologic evaluation [39].

4. The stages of testicular cancer

Testicular cancers are classified as seminomas or non-seminomas. The seminomas are most common tumor with 40%. Three histological subtypes are defined. The most common type is classical type seminoma with 85%. Firstly, it makes lenfoj metastasis. It responds to radiotherapy and chemotherapy very well [58]. Non-seminoma tumors account for 4% of all testicular tumors. Leydig cell tumors are the most common and this tumor constitutes 1–2% of all testicular tumors. It has a benign character in children but it is 10% malignant in adults [59].

Staging in TC is useful for determining prognosis and treatment. Patients are classified as Stage I (limited to the testis), Stage II (lymph node involvement), and Stage III (metastasis to visceral organs) [60] (**Table 2**). Among the important factors to be considered when staging are the degree of metastasis, elevation of tumor markers, and histology (seminoma or nonseminoma).

Stage I	The tumor is in the testis. No evidence of metastasis was found in any of the testis
Stage IM	After orchiectomy tumor markers in height is observed
Stage II	Retroperitoneal lymphadenopathy is present
IIA	Lymphadenopathy <2 cm across
IIB	= 2–5 cm across
IIC	>5 cm across
Stage III	Supradiaphragmatic lymphadenopathies are present
Stage IV	Organ metastasis/hematogenous spread

Information from Refs. [61, 62].

Table 2.
Classifications of testicular cancer staging.

5. Treating testicular cancer

The primary treatment for testicular tumors is radical inguinal orchiectomy involving the removal of the testis and spermatic cord. After orchiectomy, the type of tumor (seminoma or nonseminoma tumor) and its stage are determined by microscopic diagnosis for further treatment [63]. Treatment options include observation, dissection of the retroperitoneal lymph node, radiation, and chemotherapy [15]. Treatment options for specific stages of disease are summarized in **Table 3**. To determine the success and continuity of treatment, evaluation is made by looking at the changes in serum tumor markers [15].

Stage	Seminoma	Nonseminoma
I	Usually low-dose radiotherapy as a preservative	Retroperitoneal lymph node dissection or monthly follow-up observations IB: Take into two courses of chemotherapy IS: The whole-dose chemotherapy if serum tumor marker levels do not drop swiftly after surgery
II	IIA: Radiation therapy of the local lymph nodes IIB or IIC: Three courses of three-drug chemotherapy	IIA: Retroperitoneal lymph node dissection, followed by monthly monitoring and frequent lab tests or observation, was made by two courses of chemotherapy, two drugs IIB or IIC: If computed tomography still indicates lymph nodes, three or four courses of three-drug chemotherapy followed by retroperitoneal lymph node dissection
III	Three-drug chemotherapy: If there is no answer, think of the clinical tests of other chemotherapy drugs in combination Have brain metastasis: Treat with brain radiation or operating disposal	Three-drug chemotherapy: operating disposal of permanent tumors High serum tumor marker levels: These patients often do not respond to usual chemotherapy; therefore, more aggressive clinical trials may be considered High serum tumor marker levels: These patients frequently do not answer to normal chemotherapy; hence, more aggressive clinical trials can be thought

Information from Ref. [15].

Table 3.
Treatment types for the stages of testicular cancer.

6. Fertility issue

Studies have shown that fertility decreased after treatment in TC patients. In addition, treatment with chemotherapy and radiotherapy was reported to cause significant gonadal damage in men [64, 65].

In one study, half of the patients wanted to have children after TC treatment. However, according to the results of the study, fertility rate was lower after treatment than before treatment [66]. In the other study after treating for TC, 13 percent of patients developed hypogonadism [67]. Therefore, since the treatments to be applied to TC patients have a negative effect on fertility, solutions such as sperm banking, testicular tissue freezing, or removal of testicular sperm should be discussed with the patient before starting the treatment [68, 69].

7. The importance of early detection of TC and TSE

The aim of any cancer screening program is to diagnose the disease at an earlier and more easily treatable stage by improving disease-specific survival and minimizing treatment morbidity [70].

As with all cancer cases, when testicular cancer is diagnosed in early stages, the rate of treatment for TC is approximately 96%, significantly affecting survival [71]. Unfortunately, more than 50% of cases are diagnosed after the disease has spread to the primary site, and men must be persuaded to avoid medical treatment as soon as a mass is detected [72]. Once the cancer has expanded over the local nodes (Stage III), the survival rate decreases extremely. This is because approximately every 10–30 days, the tumor doubling times were fast. Therefore, early diagnosis equates with a better long-term overall prognosis [6]. Obviously, for testicular cancer, a potentially lethal disease, early detection and early treatment are very important [6]. Rapid diagnosis of these neoplasms provides the opportunity to treat these patients at the earliest stage of the disease and thus minimize long-term morbidity [70].

Despite the importance of early diagnosis, invisible dangers are common in early and definitive diagnosis of testicular tumors. There are many studies based on delay in the diagnosis of testicular cancer [73–75]. In a comprehensive study on delayed diagnosis (DD) in testicular cancer, DD confirmed that it had a significant effect on survival in TC patients receiving modern treatments, including chemotherapy [76]. On the other hand, Nikzas et al. found no effect on survival in delay between 1980 and 1987 in 232 patients studied in Great Britain [77].

Both patients and health professionals can contribute to delay in diagnosis. Patient-induced delays due to unawareness, embarrassment, fear of cancer, or fear of emasculation are accepted [75, 78–80]. The results of literature reviews suggest that approximately 20–30% of cancer patients delay seeking help for more than 3 months after having experienced possible symptoms of cancer [81].

TC affects young and generally healthy males who do not accept the threat of deadly disease. Moreover, that testicular cancer requires loss of external genitals during a time in the man's life when sexuality is very important is additionally stressful [70]. The physician-mediated delay is most often the misdiagnosis of a testicular tumor as an infection. Unluckily for clinicians, classic painless testicular mass of patients ultimately diagnosed with TC is only half the resulting symptoms [82].

For early diagnosis several organizations, including the American Cancer Society and American Urological Association, recommend that physicians include testicular examination as part of routine control [83]. It is also recommended that primary healthcare professionals teach and encourage TSE to males between the ages of 15 and 35 years [84]. At the same time, the American Cancer Society recommends to men, especially who at high risk for TC, TSE as an effective and cost-free method [71]. Studies have shown that men at risk for TC are not educated and do not know how to perform TSE [6]. Moreover, many studies reported that close to all men of the risk group (adult men below age 35) had never performed TSE and very few knew that men who were in the 18- to 50-year-old age group should perform TSE every month [16, 85].

TSE is the cheapest and easiest method for screening firstly taught by the nurses or physicians to the man. The man is taught to perform the TSE when the scrotum is soft and relaxed, usually after a shower. In addition, TSE is recommended to be done at least once a month starting at the onset of puberty [17]. TSE teaching begins when the man becomes familiar with the major structures of the testis, scrotum, testicle, and epididymis [86]. After being familiar with the normal tissue and structures of the testes, the man is better readied to identify normal physiological structures. Any suspicious masses are notified to a healthcare professional as soon

as possible [86]. However, the role of TSE in screening of testicular cancer is still a matter of debate. In testicular cancer, regular TSE to prove the relationship between life and life US Preventive Services Task Force Some organizations such as the Canadian Task Force are out of the ordinary they do not recommend regular TSE because they can cause anxiety and unnecessary doctor visits [87, 88]. However, self-testis may be useful in increasing the incidence of testicular cancer and in early diagnosis because of the very low number of men participating in preventive healthcare [89]. TSE is a convenient method to detect testicular cancer and contribute to healthier lifestyles for men at risk [71]. Furthermore, TSE, potentially positive, can produce sustainable health behavior choices [90].

8. Conclusions

In conclusion, studies have shown that the incidence of TC is increasing, especially in developed countries, where it is the most commonly diagnosed malignancy in young men. For this reason, young men should be encouraged to be aware of early detection of TC, to raise awareness and to apply to the health institution. In general, with rates of treatment above 95% (80% for metastatic disease), TC is considered to be a curable cancer when diagnosed early. At the same time, contrary to the supposition of men, treatment of TC is generally a type of cancer that does not cause sexual problems and does not affect fertility, and men's masculinity is maintained unless both testicles are affected for a long time. The men that will be given TSE training may need to be present as educators because some men find the discussion of their testicles embarrassing. Furthermore, teaching young men to conduct TSE may result in these men taking increased responsibility for their own healthcare. When men are aware of what is normal for themselves, they are more likely to consult in the absence of false assurances from the absence of a lack of precariousness when they detect any abnormal condition. It is equally important to tell men that the diagnosis of testicular cancer is not death and the rate of treatment is excellent. Efforts should be made to make men aware that there may be a disease in their testicles even when there is no pain.

Conflict of interest

The author declared no potential conflicts of interest with respect to the publication of this chapter.

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