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Characteristics and Outcomes of a Cohort of 34 Patients with Testicular Germ Cell Tumors: A Single-Center Experience at Hassan II University Hospital of Fez

Samia El Hakym[1*], Ihabe Ghaffouli[2], Hafssa El Hilali[1], Chaymae Chbihi[1], Sara Nejjari[1], Diango Keita[1], Abir Oufrid[1], Imane Ouafki[1], Lamiae Amaadour[1], Karima Oualla[1], Zineb Benbrahim[1], Samia Arifi[1], Nawfel Mellas[1]

[1]Department of Medical Oncology, Hassan II University Hospital Center, Faculty of Medicine and Pharmacy of Fez, Sidi Mohamed Ben Abdellah University, Fez, Morocco
[2]Faculty of Medicine and Pharmacy of Fez, Sidi Mohamed Ben Abdellah University, Fez, Morocco
Email: *samia.elhakym@usmba.ac.ma

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Abstract

Introduction: Testicular germ cell tumors (TGCTs) are rare but account for more than 90% of testicular cancers. They mainly affect young men and have a high cure potential. This study aimed to describe the characteristics, management, and prognosis of TGCTs treated at Hassan II University Hospital of Fez. **Materials and Methods**: This monocentric retrospective study included 34 patients treated for TGCTs between May 2017 and December 2022. Epidemiological, clinical, therapeutic, and survival data were collected from medical records. **Results**: The mean age was 34 years (range: 16 - 66). Testicular enlargement was the main presenting symptom (75%). All diagnoses were confirmed by orchiectomy. According to the AJCC classification, 34% of patients were stage I, 28% stage II, and 38% stage III. Based on the IGCCCG prognostic classification, 50% of patients had a good prognosis and 50% had an intermediate prognosis. The BEP regimen was the most commonly used first-line chemotherapy. After a median follow-up of 4 years, overall survival (OS) was 90% and progression-free survival (PFS) was 85%. For seminomas, 4-year OS was 91% and PFS was 86%. For non-seminomatous tumors, OS was 85% and PFS was 80%. **Conclusion**: This series confirms the excellent prognosis of TGCTs in a Moroccan context, with survival outcomes comparable to international standards. It highlights the importance of standardized management according to stage and histological subtype.

Keywords

Testicular Germ Cell Tumor, Seminoma, Non-Seminomatous Tumor, Chemotherapy, Prognosis, Morocco

1. Introduction

Testicular cancer, although accounting for only 0.5% to 2% of all male malignancies, is the most common solid tumor in young men aged 15 to 35 years [1]. More than 90% of these cancers are testicular germ cell tumors (TGCTs), classified into two main groups: seminomas and non-seminomatous germ cell tumors (NSGCTs) [2]. TGCTs represent one of the greatest successes of modern oncology, with cure rates exceeding 95% for localized disease and remaining high even in metastatic stages, thanks to the development of effective platinum-based chemotherapy regimens [3].

This curability strongly depends on accurate risk stratification, which integrates histological subtype, tumor marker levels (alpha-fetoprotein, beta-human chorionic gonadotropin, lactate dehydrogenase), and disease stage according to the American Joint Committee on Cancer (AJCC) classification and the International Germ Cell Cancer Collaborative Group (IGCCCG) prognostic classification for metastatic disease [4]. Standard management relies on radical inguinal orchiectomy for diagnosis and local control, followed by active surveillance, adjuvant chemotherapy, or primary chemotherapy depending on stage and risk category [5].

While epidemiological and survival data from Western countries are well established, publications from North Africa, and particularly from Morocco, remain scarce. This study aimed to describe the clinicopathological profile, therapeutic strategies, and survival outcomes of a cohort of patients with TGCTs treated at the Medical Oncology Department of Hassan II University Hospital of Fez, Morocco.

2. Materials and Methods

2.1. Study Design and Population

This was an observational, descriptive, retrospective cohort study conducted at the Medical Oncology Department of Hassan II University Hospital of Fez, Morocco. All consecutive patients aged 18 years or older with histologically confirmed TGCTs treated and followed between May 1, 2017, and December 31, 2022, were included.

2.2. Data Collection and Variables

Data were extracted from electronic medical records using a standardized collection form. The following variables were collected:

- **Demographic data:** age at diagnosis.

- **Clinical data:** presenting symptoms, personal history (cryptorchidism), and family history of testicular cancer.
- **Pathological and staging data:** histological subtype (seminoma vs NSGCT), primary tumor size, lymphovascular invasion, pre-orchiectomy serum tumor markers (AFP, β-hCG, LDH), clinical stage according to the 8th AJCC edition, and IGCCCG risk group for metastatic patients.
- **Therapeutic data:** type of initial surgery, chemotherapy regimens (agents and number of cycles), use of radiotherapy, and surgery for residual masses.
- **Outcome data:** treatment response, relapse/progression events, date of last follow-up, and vital status.

2.3. Definitions and Statistical Analysis

Overall survival (OS) was defined as the time from histological diagnosis to death from any cause or last follow-up. Progression-free survival (PFS) was defined as the time from diagnosis to first evidence of disease progression, relapse, or death from any cause.

Statistical analysis was performed using SPSS software (version 26.0, IBM Corp.). Continuous variables were described using means (with ranges) or medians, and categorical variables were summarized as frequencies and percentages. Survival probabilities for OS and PFS were estimated using the Kaplan–Meier method.

2.4. Ethical Considerations

This retrospective study was conducted in accordance with local ethical standards and the principles of the Declaration of Helsinki. Patient data were anonymized to ensure confidentiality. Given the observational nature of the study using anonymized data, the requirement for individual informed consent was waived by the institutional review board.

3. Results

The cohort included 34 adult patients with testicular germ cell tumors managed between May 2017 and December 2022. The mean age at diagnosis was 34.5 ± 11.2 years, with a range from 16 to 66 years. The most represented age group was 31 - 40 years (35.3%). Baseline demographic and clinical characteristics of the patients are presented in Table 1.

Table 1. Baseline characteristics of patients (n = 34).

Characteristic	Number of patients	Percentage (%)
Age (years)		
Mean age ± SD	34.5 ± 11.2	—
11 - 20	2	5.9
21 - 30	9	26.5

Continued

31 - 40	12	35.3
41 - 50	6	17.6
>50	5	14.7
Histological subtype		
Pure seminoma	17	50.0
Non-seminomatous tumor	17	50.0
Medical history		
Cryptorchidism	4	11.8
Family history	1	2.9
Presenting symptom		
Testicular enlargement	26	76.5
Testicular pain	20	58.8

Patients with non-seminomatous germ cell tumors were significantly younger than those with pure seminomas (30.2 years versus 38.9 years; $p < 0.05$). A personal history of cryptorchidism was reported in 11.8% of patients, while a family history of testicular cancer was found in 2.9% of cases. The most frequent clinical presentation was painless enlargement of the testicle, observed in 76.5% of patients.

From a histological standpoint, pure seminomas and non-seminomatous germ cell tumors each accounted for 50% of cases. According to the AJCC 8th edition classification, 35.3% of patients were diagnosed at stage I, 26.5% at stage II, and 38.2% at stage III. The distribution of stages according to histological subtype is detailed in Table 2.

Table 2. Distribution of patients according to AJCC stage and histological subtype.

AJCC stage	Seminomas (n = 17)	NSGCTs (n = 17)
Stage I	7 (41.2%)	5 (29.4%)
Stage II	5 (29.4%)	4 (23.5%)
Stage III	5 (29.4%)	8 (47.1%)

Serum tumor markers were elevated in 70.6% of patients. Lactate dehydrogenase (LDH) was the most frequently elevated marker (58.8%), followed by β-human chorionic gonadotropin (β-hCG) in 35.3% of cases and alpha-fetoprotein (AFP) in 29.4%.

All patients underwent radical inguinal orchiectomy. Systemic chemotherapy was administered to 82.4% of patients, mainly using the BEP regimen, which was prescribed in 58.8% of cases. Carboplatin monotherapy was administered in 23.5% of patients, and salvage chemotherapy with the TIP regimen was used in

11.8%. No patient received primary radiotherapy. The different therapeutic modalities are summarized in Table 3.

Table 3. Therapeutic modalities administered.

Treatment	Number of patients	Percentage (%)
Inguinal orchiectomy	34	100
Lymph node dissection	4	11.8
Chemotherapy (all regimens)	28	82.4
BEP (1 - 3 cycles)	20	58.8
Carboplatin (AUC 7)	8	23.5
TIP (salvage therapy)	4	11.8
Radiotherapy	0	0
Sperm cryopreservation	10	29.4

Treatment-related toxicity was generally moderate. Gastrointestinal toxicity related to cisplatin was observed in 20.6% of patients, while one case of hemorrhagic cystitis associated with ifosfamide was reported, with a favorable outcome. No severe pulmonary toxicity related to bleomycin was observed (Table 4).

Table 4. Treatment-related toxicity.

Type of toxicity	Number of patients	Percentage (%)
Gastrointestinal toxicity (cisplatin)	7	20.6
Hemorrhagic cystitis (ifosfamide)	1	2.9
Severe pulmonary toxicity (bleomycin)	0	0

Among patients with metastatic disease (stages II and III), the IGCCCG prognostic classification identified 50% of patients in the good prognosis group and 50% in the intermediate prognosis group. No patients were classified in the poor prognosis group.

After a median follow-up of 48 months, survival outcomes were favorable. For the entire cohort, the 4-year overall survival rate was 90%, while the 4-year progression-free survival rate reached 85%. Survival outcomes according to histological subtype are summarized in Table 5 and Figure 1(a) & Figure 1(b).

Table 5. Four-year survival analysis in patients with testicular germ cell tumors.

Patient group	4-year Overall Survival (OS)	4-year Progression-Free Survival (PFS)
Total cohort (n = 34)	90%	85%
Pure seminomas (n = 17)	91%	86%
Non-seminomatous tumors (n = 17)	85%	80%

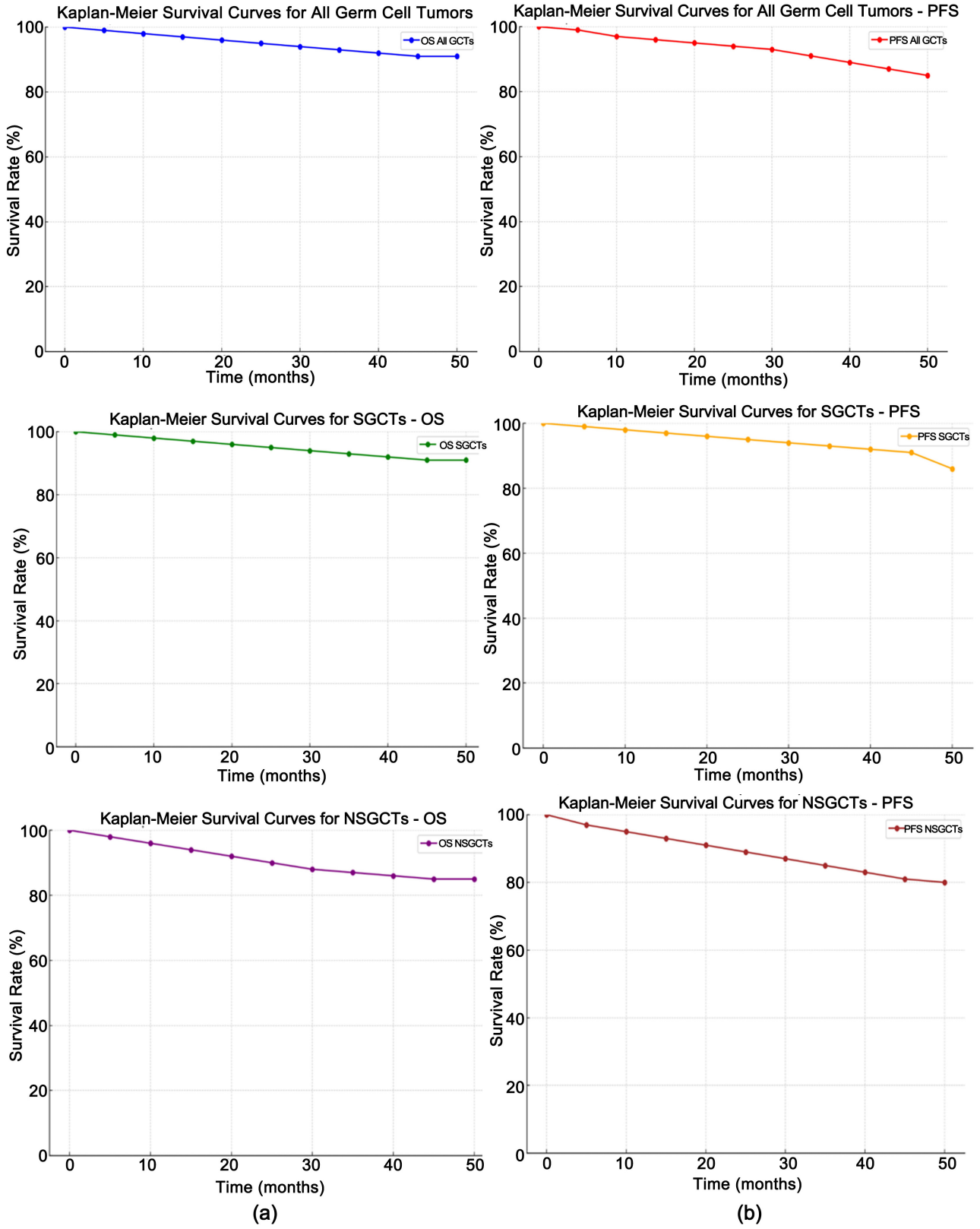

Figure 1. (a) Overall survival (OS) curve of the entire cohort according to histological subtype after a median follow-up of 48 months; (b) Progression-free survival (PFS) curves of the entire cohort according to histological subtype after a median follow-up of 48 months (n = 34).

4. Discussion

Testicular germ cell tumors (TGCTs) are the leading cause of solid cancer in young men, although they account for only 1% - 1.5% of all male cancers [6] [7]. Our retrospective study of 34 patients managed at the Hassan II University Hospital in Fez confirms the main epidemiological, clinical, and prognostic characteristics described in the literature.

The average age of our patients was 34.5 years, which aligns with international data placing the peak incidence of TGCTs between 15 and 35 years [8]. As widely reported, seminomas occur at an older age than non-seminomatous germ cell tumors (NSGCTs) [9] [10]. This age difference according to histological type reflects distinct biological mechanisms and is a consistent finding in large series.

A history of cryptorchidism was the main risk factor identified in our cohort (12.5% of cases), a rate comparable to that reported in the literature [11] [12]. Cryptorchidism is recognized as the most significant risk factor for testicular cancer, with a relative risk multiplied by 5 to 10, particularly when surgical correction is delayed [13] [14]. The finding of a family history, noted in one patient, remains rare but significant, as several studies have demonstrated an increased risk among first-degree relatives [15].

Clinically, scrotal swelling with or without testicular pain was the main presenting symptom, which is consistent with the series by Bosl *et al.* and other authors [16]. However, a significant proportion of patients were diagnosed at advanced stages, particularly among NSGCTs. This finding reflects a still-frequent diagnostic delay, often related to the trivialization of symptoms or confusion with benign conditions such as epididymitis [17] [18]. Several studies have shown that such delays are directly associated with more advanced stages at diagnosis and poorer survival [16].

The histological distribution in our series showed an equal proportion of seminomas and NSGCTs (50% each), which differs slightly from classical data reporting a predominance of non-seminomatous forms [19] [20]. This difference could be explained by the limited sample size and local epidemiological particularities. In accordance with the literature, seminomas were more frequently diagnosed at a localized stage, while NSGCTs were mostly revealed at metastatic stages [10].

Paraclinical evaluation relied on scrotal ultrasound, the reference examination with a sensitivity close to 100% for detecting testicular tumors [21], and on thoraco-abdomino-pelvic CT scan for staging [22]. Tumor markers (AFP, βHCG, and LDH) played an essential role in prognostic assessment, therapeutic monitoring, and relapse detection, in line with international recommendations [23].

Regarding treatment, all patients underwent inguinal orchiectomy, a fundamental procedure for both diagnostic and therapeutic purposes [24] [25]. Cisplatin-based chemotherapy, particularly the BEP protocol, was the main treatment for advanced forms, with results meeting international standards [26]. The absence of radiotherapy in our series reflects the current evolution of therapeutic strategies, aiming to reduce late complications, especially the risk of secondary

cancers and infertility [27].

Outcomes were generally satisfactory, with a high rate of complete remission and overall survival comparable to that reported in major international series [16] [28]. Nevertheless, patients with advanced-stage NSGCT had a more guarded prognosis, highlighting the importance of the IGCCCG prognostic classification in guiding treatment [4].

The limitations of this study lie mainly in its retrospective nature, small sample size, and lack of very long-term follow-up. However, it provides relevant local data on a rare pathology in our context and confirms the effectiveness of standard therapeutic protocols.

5. Conclusion

Testicular germ cell tumors primarily affect young men and have an excellent prognosis when diagnosed early and treated according to current guidelines. Diagnostic delay remains a major problem, particularly for non-seminomatous forms. Increased awareness among the population and healthcare professionals is essential to improve early diagnosis and prognosis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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