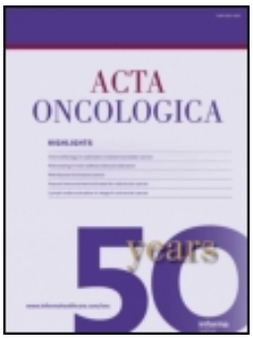

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Dr Marcus Hentrich, Norbert Weber, Thorsten Bergsdorf, Bernhard Liedl, Reiner Hartenstein & Arthur Gerl

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ORIGINAL ARTICLE

Management and outcome of bilateral testicular germ cell tumors: Twenty-five year experience in Munich

MARCUS HENTRICH[1], NORBERT WEBER[2], THORSTEN BERGSDORF[3], BERNHARD LIEDL[4], REINER HARTENSTEIN[1] & ARTHUR GERL[2,5]

[1]*Department of Medical Oncology, Munich Harlaching Hospital, Sanatoriumsplatz 2, 81545 Munich,* [2]*Oncology Practice, Sendlinger Straße 37, 80331 Munich,* [3]*Department of Urology, Munich Harlaching Hospital, Sanatoriumsplatz 2, 81545 Munich,* [4]*Department of Urology, University Hospital Großhadern, Marchioninistraße 15, 81377 Munich,* [5]*Department of Internal Medicine III, University Hospital Großhadern, Marchioninistraße 15, 81377 Munich, Germany*

Abstract
We analyzed characteristics, therapy and outcome of patients with bilateral testicular germ cell tumor (TGCT) at our institutions. Among 1 180 TGCT patients diagnosed and/or treated between 1979 and 2003, 47 (4.0%) developed a second TGCT. Nine of 14 patients (64%) with synchronous TGCT are alive with no evidence of disease (NED) at a median follow-up of 37 months. Thirty-three patients had a metachronous bilateral TGCT. Median time to the 2nd TGCT was 71 months. At diagnosis of 2nd TGCT 30 patients had stage I, 1 had stage II and 2 had stage III disease. Thirty-two of 33 patients are alive with NED at a median follow up of 41 months. No patient died from second TGCT. As a review of the literature confirms our data we do not recommend a routine biopsy of the contralateral testicle for early detection of testicular intraepithelial neoplasia (TIN).

Patients with a history of testicular cancer are at significantly higher risk for developing a secondary testicular germ cell tumor (TGCT) in the remaining testis. The incidence of bilateral TGCT varies between 1.0–5.0% depending on the series analyzed [1–6]. Whether cisplatin containing chemotherapy in fact does reduce the risk for developing a secondary TGCT remains a matter of debate [7–10]. Contralateral carcinoma in situ (CIS), also known as testicular intraepithelial neoplasia (TIN), occurs in approximately 5% of patients and has been shown to be a risk factor for another TGCT as 50% of patients develop testicular cancer within 5 years [11,12]. Though recommended in some European countries [4,13], contralateral biopsy for early detection of TIN remains controversial, mainly because the majority of patients do not demonstrate carcinoma in situ, and treatment of TIN may be associated with undesirable physical and emotional consequences [14].

The objectives of this study were first, to determine whether characteristics, clinical course and outcome of a secondary metachronous TGCT justifies a contralateral testicular biopsy and second, to analyze characteristics, therapy and outcome of patients with bilateral synchronous TGCT in patients at our institutions over a 25 year time period.

Patients and methods

The medical records of patients with a second TGCT at our institutions between January 1979 and December 2003 were reviewed with regard to histology, stage, treatment and outcome. In addition, phone calls to patients or to their physicians were performed. All of our institutions serve as oncology referral centers for the greater Munich area.

A seminoma (S) was regarded as a tumor only containing seminomatous tissue, whereas a nonseminoma (NS) may have included both, nonseminomatous and seminomatous elements. Management of all patients included an inguinal orchiectomy

Correspondence: Dr M. Hentrich, Department of Medical Oncology, Munich Harlaching Hospital, Academic Teaching Hospital of the University of Munich, Sanatoriumsplatz 2, 81545 München, Germany. Tel: +49 89 6210 3363. Fax: +49 89 6210 3320. E-mail: tumorzentrum.hentrich@khmh.de

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(with the exception of one patient with bilateral testicular masses whose TGCT was diagnosed by excision of a skin metastasis). Biopsies of the contralateral testicle were not routinely performed. In selected cases of synchronous or metachronous bilateral TGCT a testis-conserving surgery was chosen for the second TGCT followed by testis irradiation (20 Gy). Subsequent management varied over the period of study usually following standard treatment strategies. Retroperitoneal lymph node dissection (RPLND) was performed in the majority of patients with stage I nonseminoma. Cisplatin based adjuvant or inductive chemotherapy was introduced at our institutions in 1979. After chemotherapy for NS, patients had follow-up examinations at 3-month intervals during the first 2 years, at 6-month intervals between the third and fifth year and thereafter annually. Follow-up included clinical examination, laboratory testing with serum tumor markers, chest X-ray, abdominal CT scans and/or ultrasound as well as further CT scans depending on the sites of primary involvement. Ultrasound examination of the testis was frequently but not consistently done.

Studies on bilateral testicular cancer, published from 1983 through December 2003, were identified through a MEDLINE search by referencing the keywords "Bilateral testicular cancer" and "Bilateral testicular germ cell tumor". Additional studies were identified by reviewing the bibliographies of the original articles, review articles, and textbook chapters.

Results

Of 1 180 patients who were treated and/or diagnosed at our institutions, 33 patients were found to have a metachronous and 14 a synchronous bilateral TGCT. Patients' characteristics, treatments and outcome are outlined in Tables I and II.

Metachronous TGCT

In patients with metachronous tumors the median age at diagnosis of the first and second TGCT was 26 and 34 years, respectively. Median time to the second TGCT was 71 months (range 19–216 months) in all patients studied with no difference observed between patients, who were pretreated by chemotherapy (n = 14) and those who had not received prior chemotherapy (n = 19). Eighteen of 33 patients presented with concordant germ cell tumor histology, which was nonseminomatous in 12 patients and seminomatous in six. A discordant histology was found in 15 patients with the first TGCT to be of nonseminomatous and seminomatous origin in 12 and 3 cases, respectively.

At diagnosis of the first TGCT 23 of 33 patients (70%) had stage I disease, 9 (27%) stage II and 1 stage III disease. At diagnosis of the second testicular germ cell tumor 30 patients (91%) had stage I, 1 had stage II and 2 had stage III disease.

Treatment of 1st TGCT

Fourteen of 33 patients (42.4%) received chemotherapy at some time after orchiectomy for the first TGCT: adjuvant chemotherapy with or without RPLND was administered in 9 patients with stage I or resected stage II nonseminoma and 5 patients received chemotherapy for metastatic disease (3 of them for relapse following stage I nonseminoma). Nine patients received radiotherapy for early stage seminoma (n = 8) or stage I nonseminoma (n = 1). Two patients with stage I nonseminoma were followed by observation only and 8 patients were treated by RPLND without further therapy for their first TGCT.

Treatment of 2nd TGCT

Twelve of 33 patients were treated by chemotherapy after diagnosis of the 2nd TGCT. Two patients (stage I nonseminoma) went through a period of observation for their 2nd tumor and received 4 courses platinum based chemotherapy after detection of a retroperitoneal relapse. Five patients received 2 cycles of carboplatin for stage I seminoma and 2 patients with stage I nonseminoma received 2 and 3 courses of adjuvant chemotherapy according to the PEB regimen, respectively. Two patients with stage III nonseminoma underwent 3 and 4 courses of standard chemotherapy, respectively. Furthermore, one patient who had suffered a late relapse of his 1st TGCT (stage III nonseminoma) had already been treated by different chemotherapy regimens for further relapses when the second TGCT was diagnosed. Chemotherapy continued after diagnosis of the 2nd TGCT. Two patients previously not irradiated received adjuvant radiation therapy for a stage I seminoma and one patient with stage II nonseminoma underwent RPLND. Eighteen patients with stage I disease (10 seminoma, 8 nonseminoma) were followed by observation only.

Outcome of patients with metachronous TGCT

Thirty-two of 33 patients are alive with NED at a median follow up of 41 months (range 1–184) after diagnosis of the second TGCT. One patient died of a late relapse of his first TGCT.

Table I. Characteristics, therapy and outcome of 33 patients with metachronous bilateral TGCT.

Pat.	Age	Histology 1st TGCT	TNM stage	Treatment* 1st GCT	Interval to 2nd TGCT	Histology 2nd GCT (months)	TNM stage	Treatment 2nd GCT[a]	Follow-Up 2nd GCT (months)	Outcome
1	33	L-seminoma	I	radiotherapy	14	seminoma	I	testis-preserving surgery+ irradiation R-testis/wait & see	73	NED
2	26	R-seminoma	I	radiotherapy	55	seminoma	I	wait & see	61	NED
3	25	R-seminoma	I	2x PEB	76	seminoma	I	2x Carbo	41	NED
4	33	R-seminoma	I	radiotherapy	100	seminoma	I	2x Carbo	9	NED
5	32	L-seminoma	I	radiotherapy	27	seminoma	I	wait & see	164	NED
6	34	R-seminoma	I	radiotherapy	45	seminoma	I	2x Carbo	5	NED
7	22	R-seminoma	I	radiotherapy	58	nonseminoma	II	RLA	32	NED
8	33	R-seminoma	II	radiotherapy	19	nonseminoma	III	4x PVB	184	NED
9	35	L-seminoma	I	radiotherapy	216	nonseminoma	I	wait & see	120	NED
10	21	R-nonseminoma	I	RLA	160	seminoma	I	2x Carbo/3x PEB, 4x PEI (relapse)	28	NED
11	22	R-nonseminoma	I	radiotherapy	180	seminoma	I	wait & see	8	NED
12	24	R-nonseminoma	I	2x PEB	31	seminoma	I	wait & see	102	NED
13	33	R-nonseminoma	I	RLA	71	seminoma	I	2x Carbo	72	NED
14	31	R-nonseminoma	II	RLA/2x PEB	28	seminoma	I	testis-preserving surgery+irradiat. L-testis/wait & see	66	NED
15	18	L-nonseminoma	I	RLA	133	seminoma	I	Radioth	133	NED
16	26	L-nonesminoma	I	RLA/CT **	101	seminoma	I	Radioth	31	NED
17	20	R-nonseminoma	III	CT, RLA ***	97	seminoma	I	CT for 1st GCT	27	DOD
18	22	L-nonseminoma	I	RLA/2x PEB	135	seminoma	I	wait & see	124	NED
19	20	L-nonseminoma	II	RLA/2x PEB	76	seminoma	I	wait & see	60	NED
20	15	R-nonseminoma	II	CT †	102	seminoma	I	wait & see	52	NED
21	20	L-nonseminoma	II	RLA	186	seminoma	I	wait & see	7	NED
22	25	R-nonseminoma	I	RLA	186	nonseminoma	I	wait & see	90	NED
23	32	R-noneminoma	I	wait & see	32	nonseminoma	III	3x PEB	52	NED
24	23	L-nonseminoma	I	RLA	86	nonseminoma	I	2x PEB	10	NED
25	23	L-nonseminoma	II	RLA/4x IBV	161	nonseminoma	I	wait & see	6	NED
26	39	R-nonseminoma	I	RLA/4x PEB (relapse)	66	nonseminoma	I	wait & see	42	NED
27	26	R-nonseminoma	I	RLA	95	nonseminoma	I	wait & see	32	NED
28	27	L-nonseminoma	I	RLA	51	nonseminoma	I	3x PEB	121	NED
29	30	L-nonseminoma	II	4x PEB	35	nonseminoma	I	wait & see	23	NED
30	38	R-nonseminoma	I	3x PEB (relapse)	30	nonseminoma	I	wait & see/4x PEI (retrop. relapse)	13	NED
31	23	R-nonseminoma	I	wait & see‡	55	nonseminoma	I	wait & see	8	NED
32	28	R-nonseminoma	II	2x PEB	36	nonesminoma	I	wait & see/2x PEB, 2x CE (retrop. relapse)	12	AWD
33	33	R-nonseminoma	II	RLA/2x CEB (renal insuff.)	38	nonseminoma	I	wait & see	1	NED

RLA, retroperitoneal lymphadenectomy; PEB, cisplatin, etoposide, bleomycin; CEB, carboplatin, etoposide, bleomycin; PEI, cisplatin, etoposide, ifosfomide; IBV, ifosfamide, bleomycin, vinblastine; CT, chemotherapy; NED, no evidence of disease; DOD, dead of disease; AWD, alive with disease; CT, chemotherapy; *after orchiectomy; **7 mo after diagnosis of the 1st TGCT lung metastases treated by chemotherapy+surgery (NED), 11 mo later solitary brain metastasis treated by surgery+ radiotherapy (NED); ***multiple relapses treated by different chemo-regimens; †non-cisplatin containing adjuvant chemo; 21 mo after diagnosis of the 1st TGCT pulm. metast. treated by chemo (PVB) resulting in CR; ‡contralateral biopsy done with no evidence of testicular intraepithelial neoplasia.

Table II. Characteristics, therapy and outcome of 14 patients with synchronous bilateral TGCT.

Pat.	Age	R-Histology	L-Histology	TNM stage	Bilateral Orchiectomy	Additional Treatment	Follow-up (months)	Outcome
1	27	nonseminoma	seminoma	I	Yes	2x PE	22	NED
2	27	nonseminoma	seminoma	II	Yes	4x PEB	67	NED
3	25	nonseminoma	seminoma	II	L-testis-preserving surgery	3x PEB	4	NED
4	31	nonseminoma	seminoma	II	L-testis-preserving surgery	4x PVB	31	NED
5	36	nonseminoma	seminoma	I	Yes	RLA	76	NED
6	36	nonseminoma	seminoma	III	Yes	4x PEB; TaxHD-PEI; Tax/Gem; VP-16	40	DOD
7	21	nonseminoma	seminoma	I	Yes	2x PEB	7	NED
8	39	seminoma	seminoma	I	Yes	2x Carbo	46	NED
9	33	seminoma	seminoma	I	Yes	Radiotherapy	6	NED
10	19	seminoma	seminoma	II	Yes	Radiotherapy	47	NED
11	30	seminoma	seminoma	II	Yes	Radiotherapy; relapse after 28 mo;1x PEI	29	DOD*
12	23	nonseminoma	nonseminoma	III	Yes	1x PVB	0.5	DOD/MOF
13	26	nonseminoma	nonseminoma	III	Yes	RLA; Radioth (bone met.) multiple regimens**	24	DOD
14	40	unclassifiable†	unclassifiable†	III	No†	4x ECBC; TIP-CET	32	DOD

RLA, retroperitoneal lymphadenectomy; NED, no evidence of disease; DOD, dead of disease; MOF, multiorgan failure; PE, cisplatin, etoposide; PEB, cisplatin, etoposide, bleomycin; TaxHD-PEI, paclitaxel/high-dose cisplatin/etoposide/ifosfamide; TIP-CET, paclitaxel/ifosfamide/cisplatin-high dose carboplatin/etoposide/thiotepa; ECBC, cisplatin, etoposide, bleomycin, cyclophosphamide; *dead in neutropenic sepsis; **for multiple relapses; † bilateral testicular masses-nonseminoma diagnosed by skin biopsy.

Synchronous TGCT

The median age of 14 patients with synchronous TGCT was 30 years. Seven of 13 evaluable patients (54%) presented with discordant and 6 (46%) with concordant histology (4 seminoma, 2 nonseminoma). In addition, a nonseminomatous TGCT was diagnosed by skin biopsy in one patient with bilateral testicular masses. Orchiectomy was not performed in this case of advanced disease, because therapy had urgently to be initiated. Five patients had stage I disease, 5 stage II and 4 stage III disease.

Five of 14 patients died of disease (n = 3) or toxicity (n = 2) after chemotherapy. Of 4 patients with NS carrying International Germ Cell Cancer Collaborative Group (IGCCCG) poor-risk features three died of refractory disease and one of toxicity. Another patient with stage II seminoma died from neutropenic sepsis after initiation of chemotherapy for recurrent disease. Nine of 14 patients (64%) are alive with no evidence of disease (NED) at a median follow-up of 37 months (range 3–76).

Testis Preserving Surgery

Two patients with metachronous tumors underwent testis-sparing surgery for their second germ cell tumor followed by irradiation of the remaining testis with 20 Gy. Both patients developed Leydig cell dysfunction and therefore receive testosterone replacement.

One patient with stage II synchronous tumors underwent organ sparing excision of the smaller tumor prior to chemotherapy (4x PVB); he had been treated in 1985 and had not undergone consecutive testis radiotherapy. Another patient with stage II bilateral disease underwent excision of the smaller tumor in 2001; radiation of the remaining testicle was planned after 3 cycles of PEB but the patient was lost for follow-up.

All tumors enucleated were pT1 seminomas. Both patients with metachronous bilateral GCT and the evaluable patient with synchronous bilateral tumors were free of disease at 66, 73 and 31 months, respectively.

Discussion

In this study, 47 of 1 180 patients with testicular cancer (4.0%) developed bilateral germ cell tumors. However, the true incidence is difficult to determine since a significant proportion of patients were referred to our institutions and represent a selected group of patients. Several risk factors for development of a second TGCT have been established, such as cryptorchism, infertility, microcalcification,

genetic predisposition and, in particular, presence of TIN [12].

A surgical testicular biopsy to detect TIN provides a diagnostic sensitivity of 85–100%. Once diagnosed, radiotherapy at doses of 18–20 Gy is considered treatment of choice. However, infertility is an inevitable consequence of low-dose radiotherapy to the testis with Leydig cell function being affected at doses of 14–20 Gy [15]. Recent data indicate that a dose of 16 Gy is probably insufficient in eradicating all malignant cells [16]. Furthermore, there are reports on the development of TGCT despite previous local radiotherapy to the testis [17,18].

The question whether the contralateral testis should be biopsied routinely after diagnosis of a first TGCT remains a matter of debate. Testis biopsy is unnecessary in the majority of patients and minor complications, such as superficial serous exsudate or postoperative pain may occur. Most important, the clinical value of contralateral biopsy remains unclear. Follow-up examinations are mandatory independent of having detected TIN or not.

Early stage metachronous TGCT was diagnosed in the majority of patients as outlined in Table III, which summarizes results of 30 studies on bilateral TGCT published after 1980.

A total of 589 of 28689 (2.1%) developed a metachronous TGCT, a proportion significantly lower than the 5% incidence rate of TIN (Table III). However, these data are not prospective in nature and should be regarded with caution. Because migration of patients between different institutions is usually not regarded a selection bias might have occurred. One study from New Zealand calculated the cumulative risk of developing a second TGCT to be 5.2% [8].

Our data as well as previous studies [2,8,10,38] demonstrate that chemotherapy for a first TGCT does not prevent development of a second germ cell tumor. Fourteen of 33 patients in this series had received chemotherapy for their first TGCT. Likewise, failure of chemotherapy to eradicate TIN has also been observed [39,40].

There were no second germ cell cancer associated deaths in our series. One patient died of multiple recurrences of his first TGCT. Survival data are available in 24 524 of 28 689 reported patients analyzed for prevalence of metachronous testicular germ cell cancer (Table III). Four hundred and eighty-nine of 24 524 patients (2.0%) developed a metachronous TGCT and 33 of 489 patients (6.8%) were dead of disease at time of publication. However, looking at these patients in detail, only some died of the second TGCT provided that appropriate treatment was applied: 13 died before introduction of cisplatin [25,29,37], 1 patient refused chemotherapy [27], 4 died of their first TGCT [1,25,28, this series], and in one patient non germ cell tumor histology (primitive neuroectodermal tumor) was found at post-chemotherapy retroperitoneal lymph node dissection [5]. It is therefore assumed that only 14 of 24 524 patients (0.06%) retrospectively investigated died of the second TGCT while on appropriate treatment. Furthermore, the cause of death was not stated in 2 patients [33] leaving a number of 13 patients who died of testicular cancer.

As bilateral TGCT is rare, a prospective study which compares patients in which a testicular biopsy is to be performed with those on observation only, will hardly be successful. Though quality-of-live data after having made a contralateral biopsy are not available to date it may be assumed that the knowledge of TIN may cause emotional problems at least in patients who want to father children since bilateral testicular cancer and/or CIS do not preclude paternity [41–43]. Based on the favorable outcome of patients with a secondary metachronous TGCT reported so far, we do not recommend routine biopsy of the contralateral testicle. However, a contralateral biopsy might be discussed with patients at high risk of TIN [44,45].

Treatment of a second testis cancer should in principle not differ from therapy of a first TGCT. However, if radiotherapy or RPLND had already been performed, observation or chemotherapy should be chosen depending on the stage of the second tumor. The value of an adjuvant radiotherapy after having performed a RPLND has to be questioned because of the altered lymphatic drainage. RPLND may be difficult when radiotherapy had previously been applied due to an alteration of the tissue in the irradiated field.

Only a minority of bilateral testicular germ cell cancer are synchronous. Simultaneous development occurred in 111 of 689 cases of bilateral TGCT (16.1%) reported in 29 studies published since the early eighties (Table III). Dieckmann et al. [46], in their review of the world literature through 1988, reported a total of 151 cases of bilateral synchronous cancer and 114 of these (75.5%) demonstrated seminoma in both testicles. Only 19 patients (12.6%) had different histologic findings. By contrast, 8 of 21 additional cases (38%) recently reviewed [47] and 7 of 13 evaluable patients (54%) in this study presented with discordant histology. The overall prognosis of patients with synchronous bilateral TGCT is good, mainly because most patients present with early stage disease. The outcome of patients with advanced nonseminomatous synchronous bilateral TGCT is dependent on IGCCCG prognostic categories.

Table III. Reported cases of bilateral TGCT.

Period (yrs)	Patients (n)	Bilateral TGCT No (%)	Synchr. only No (%)	Metachr. only No (%)	Metachronous TGCT						
					Interval^{+} (mo)	Age^{+} at 1st TGCT	% Stage I of 2nd metachr. TGCT	NED (%)	DOD (n)	Follow-up) (yrs)	Year of Pub. [Reference]
1966–80	396^{++}	11 (–)	1 (–)	10 (–)	36	28	–	90.1	0	3	1983 [19]
1956–80	1300	26 (1.9)	2 (0.2)	24 (1.9)	41	33.5	87.5	88.5	3*	–	1986 [20]
1972–85	500	7 (1.4)	1 (0.2)	6 (1.2)	20.8	–	100	100	0	3.4	1986 [11]
1969–85	412	20 (4.8)	1 (0.2)	19 (4.6)	73	29	73.7	89.5	2**	5.7	1987 [1]
1978–86	120	9 (7.5)$^{+++}$	1 (0.8)	8 (6.7)$^{+++}$	54.6	26	75	87.5	1	1.9	1988 [21]
1950–85	730	14 (1.9)	4 (0.6)	10 (1.4)	60	26.9	80	100	0	5	1988 [22]
1979–87	784	17 (2.2)	3 (0.4)	14 (1.8)	36.5	26	71.4	–	–	–	1989 [2]
1977–86	500	16 (3.2)	4 (0.8)	12 (2.4)	36	25	–	100	0	3.5	1990 [23]
1974–88	210	6 (2.9)	0	6 (2.9)	48	–	100	83.3	1	1.9	1990 [24]
1962–84	1219	38 (3.1%)	0	38 (3.1%)	56.4	–	81.6	78.9	8***	7	1990 [25]
1960–79	2850	73 (2.6)	5 (0.2)	68 (2.4)	5.4 (S) 5.0 (NS)	35	71	–	–	–	1991 [3]
1980–88	502	23 (4.6)	4 (0.8)	19 (3.8)	80.3	30	47.4	94.4	1	5.8	1991 [26]
1969–90	531	21 (4.0)	3 (0.6)	18 (3.4)	–	29	–	–	–	–	1993 [4]
1972–85	773	27 (3.5)	3 (0.4)	24 (3.1)	60	–	75	96.3	1†	9	1993 [27]
1968–91	210	6 (2.9)	0	6 (2.9)	59	29	–	100	0	2.5	1995 [7]
1974–91	368	13 (3.5%)	5 (1.4)	8 (2.2)	49	–	100	87.5	1**	7.1	1995 [28]
1978–94	741	16 (2.2)	5 (0.7)	11 (1.5)	54	28	100	100	0	–	1996 [8]
1980–95	365	11 (3.0)	–	11 (3.0)	86‡ 74	30	100	100	0	–	1997 [9]
–	2088	21 (1.0)	5 (0.2)	16 (0.8)	65.1	28.4	43.8	81.3	1$^{\#}$	3.7	1998 [5]
1967–97	445 (St I)	16 (3.6)	0	16 (3.6)	56.4	32.8	87.5	87.5	2$^{\#\#}$	6.1	1998 [29]
1975–97	820	30 (3.7)	6 (0.7)	24 (2.9)	67.2	28.7	83	100	0	2.5	1999 [30]
1980–98	552	11 (2.0)	4 (0.7)	7 (1.3)	87	26.6	100	100	0	4.4	2000 [31]
1982–98	488	12 (2.46)	0	12 (2.5)	63.8	36	83.3	83.3	0	–	2000 [32]
1977–01	960	27 (2.8)	3 (0.3)	24 (2.5)	66	–	62.9	92.6	2$^{\#\#\#}$	5.7	2001 [33]
1980–99	274	9 (3.3%)	3 (1.1)	6 (2.2)	96	29	83.3	100	0	7.2	2002 [34]
1978–99	2431	24 (1.0)	4 (0.2)	20 (0.8)	64.3	27	75	100	0	3.6	2002 [6]
1988–98	2386	72 (3.0)	19 (0.8)	53 (2.2)	76	28	79.3	96.2	2¶	3.5	2003 [35]
1989–98	570	19 (3.3)	1 (0.2)	18 (3.2)	76	35.5	–	94.4	1	4.3	2003 [36]
1950–01	3984	58 (1.5)	10 (0.3)	48 (1.2)	50.5	28.1	62.5	90	6$^{\#\#}$	5	2003 [37]
1979–03	1180	47 (4.0)	14 (1.2)	33 (2.8)	71	26	91	97	1**	3.4	current series
	28689	700 (2.44)	111 (0.39)	589 (2.05)					33		

NED, no evidence of disease; DOD, dead of disease; –, not reported; +mean or median; $^{++}$patients with testicular lymphoma also included; $^{+++}$3 pts referred to the department with 2nd TGCT; *1 pt possibly died of 1st TGCT; **1 pt died of recurrent primary TGCT; ***1 pt died of primary TGCT, 5 of 7 died before introduction of cisplatin; † died after refusing chemotherapy; ‡pts pretreated by chemotherapy, pts on surveillance; $^{\#}$primitive neuroectodermal tumor at post-chemotherapy retroperitoneal lymph node dissection; $^{\#\#}$pts died before introduction of cisplatin; $^{\#\#\#}$not stated whether dead of disease or dead of other cause; ¶1 pt died of radiotherapy-related pancreatic cancer.

Organ sparing surgery in patients with bilateral TGCT has been reported to be successful in selected cases providing endocrinological and psychological advantages [48,49]. This procedure can be considered in reliable patients with stage T1 tumor without infiltration of the rete testis and normal preoperative plasma testosterone level. Patients should receive postoperative local irradiation and must be followed meticulously for tumor recurrence and serum testosterone concentration.

In conclusion, the prognosis of patients with bilateral metachronous testicular germ cell tumors is excellent. The majority of patients do present with early stage disease, and death from a second TGCT is an extremely rare event. A routine biopsy of the contralateral testicle can therefore not be recommended. Due to early detection of second TGCT an increasing proportion of patients may benefit from organ preserving surgery.

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