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## Testis Cancer

# Burden or Relief: Do Second-Opinion Centers Influence the Quality of Care Delivered to Patients with Testicular Germ Cell Cancer?

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### Abstract

**Background:** To improve the quality of care, the German Testicular Cancer Study Group (GTCSG) has been publishing a series of testicular germ cell cancer guidelines since 1996. These guidelines were updated in the 2008 publication, "European Consensus on Diagnosis and Treatment of Germ Cell Cancer." Several studies have shown that published guidelines have a limited effect on clinical practice. For this reason, the GTCSG made a further effort in 2006 to improve the quality of care by establishing a national second-opinion system for therapy planning for patients who underwent orchiectomy and staging evaluations.

**Objective:** The primary aim was to analyze the influence of the second-opinion system on guideline implementation with a view to improving the quality of care.

**Design, setting, and participants:** An Internet data exchange was established between the urologist seeking advice and the second-opinion centers. Second-opinion centers were 18 clinics that had contributed toward developing treatment guidelines.

**Measurements:** Data sets included the primary clinical, radiologic, and pathohistologic data; the planned therapy; the therapy recommended by the second-opinion center; and the follow-up.

**Results and limitations:** From February 2006 to September 2008, 642 second opinions were requested. The therapy planned by the urologist seeking advice differed from that recommended by the second-opinion center in 32.3% of the cases. The discrepancy was significantly higher for nonseminomas than for seminomas ( $p = 0.045$ ) and showed a tendency to increase with advancing tumor stage ( $p = 0.067$ ). In cases of discrepancy, the applied therapy coincided with the second opinion in 71.8% of the cases. A discrepant second opinion prevented overtreatment in 40.3% and undertreatment in 26.5%.

**Conclusions:** Approximately every sixth second opinion resulted in a relevant change in the scope of therapy. Published guidelines for germ cell cancer are applied only sporadically and should be supported by second-opinion systems.

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## 1. Introduction

The diagnosis and therapy of testicular germ cell cancer are subject to constant change. Quality-of-care indicators for germ cell cancer are subject to change as well. Measuring points include the quality of life, the recurrence-free survival, and the survival time. Fortunately, their significance is limited by the low recurrence rate and mortality of germ cell tumors owing to their high cure rate of nearly 95% [1]. Accordingly, the quality of care can only be conclusively determined after a long latency because it is strongly influenced by factors such as late treatment toxicity.

Another quality-of-care indicator is treatment according to evidence-based guidelines. Guidelines for the diagnosis and therapy of germ cell cancer were first published in Germany in 1996 with the aim of preventing inadequate care. They have undergone several evidence-based updates since then. The latest one was the "European Consensus on Diagnosis and Treatment of Germ Cell Cancer," formulated in 2008. The aim of developing the guidelines was to achieve high-quality care based on the latest research evidence.

Only limited data are available on the quality of care for germ cell cancer. Little information has been collected on the guideline conformity of treatment [2]. Epidemiologic data on mortality suggest a need to improve the quality of care in Europe [3]. Past approaches for improving the quality of care are outlined in the following sections.

### 1.1. Clinical trials

We believe clinical trials improved the treatment results but had only a limited direct effect on the quality of care. This may be partly due to the fact that <5% of the germ cell cancer patients in Germany were treated in therapy studies [4] and that it takes time to achieve clinical implementation of study results.

### 1.2. Evidence-based treatment guidelines

Evidence-based treatment guidelines probably offer the best opportunity to disseminate the latest results of clinical trials and research efforts and to give treatment recommendations to the broad community of physicians. However, it remains open to discussion whether these guidelines are broadly implemented simply because they were published or whether they are only implemented at centers with a special interest in the management of testis cancer patients [2].

### 1.3. Second-opinion centers

In view of the potentially limited effectiveness of the two strategies just discussed, the German Testicular Cancer Study Group (GTCSG) took another step to improve the quality of care. The central objective of this project was to establish a nationwide network of second-opinion centers for consultations before initiating therapy in patients who had undergone orchiectomy and evaluation for metastasis.

The dialogue between primary caregivers and second-opinion centers should enable better implementation of the guidelines.

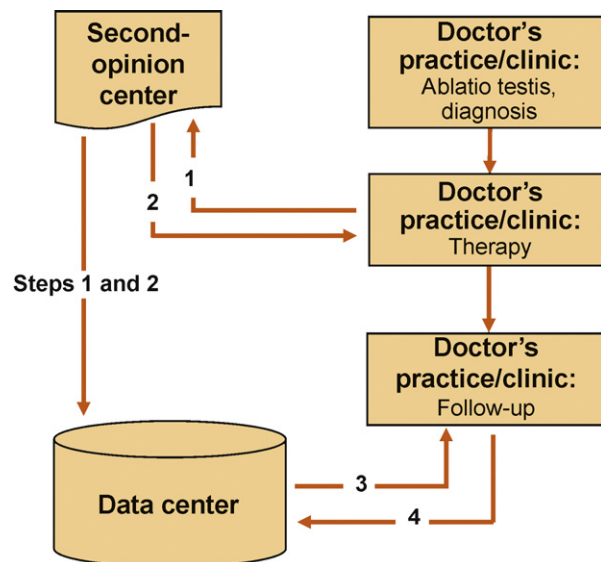
The main hypothesis of the project was that consultation services were required in Germany for planning the initial therapy after orchiectomy and evaluation for metastasis. Initial objections were based on the view that urologists in Germany were already treating germ cell cancer in accordance with guidelines, as indicated by the high survival rate [5,6]. This paper summarizes the aims and preliminary results of the project. It also advocates the establishment of second-opinion networks because they can improve the quality of care more inexpensively and effectively than other approaches.

## 2. Material and methods

In 2006, the GTCSG cooperated with the DOCxcellence Co, Berlin, Germany, in developing a modular Internet-based interactive database program. The system was checked by the data protection commissioner of the State of Berlin and found to be in accordance with the law. It also received security clearance for nationwide application. Patients must give their informed consent to the registration and utilization of their personal data by the system.

The system is available at no cost to all urologists in Germany, regardless of whether they work in clinics or private practices. It provides a second opinion for therapy planning after the primary diagnosis of germ cell cancer and tumor staging.

The system functions as follows (Fig. 1): After one-time-only user registration by any urologist without delay or restriction, the patient



**Fig. 1** – Data flow of second-opinion centers for patients with testicular germ cell tumors. After one-time-only user registration by any urologist without delay or restriction, the patient data are anonymized. The primary clinical data set of the respective patient can then be put in a data mask online. This data set is minimized to 21 data fields relevant to the treatment decision. To avoid misinformation, data input is checked by a system-immanent algorithm. The user can then select one of the 18 previously existing second-opinion centers and send the request by e-mail or fax (step 1). Physicians at the respective second-opinion center then recommend a therapy (step 2). In complex cases, they enter into a dialogue with the urologist making the inquiry. The project is supported by a data center that registers the applied therapy 3 mo after the request for a second opinion (steps 3 and 4) and carries out a follow-up 2 yr later.

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During the study period, 18 clinics functioned as second-opinion centers in Germany and Austria [7]. The criteria for selecting second-opinion centers were multidimensional. The main criterion was the center's contribution toward developing the treatment guidelines for germ cell cancer [8,9]. Centers also had to present evidence of clinical and research activities in the field of germ cell cancer. A yearly audit checks the guideline conformity of second-opinion recommendations that differed from the first opinion.

The following items were determined to be project impact and care quality indicators: (1) Therapy planned by the urologist making the request ("first opinion") versus therapy recommended by the second-opinion center ("second opinion"), and (2) guideline conformity of the applied and recommended therapy, and (3) relapse-free follow-up.

### 2.1. Statistics

For this interim analysis, the anonymized patient data were evaluated with SPSS v.11.0 by the Dross Institute of Statistics at the Free University of Berlin. The urologists requesting a second opinion could choose 1 of 15 different treatment options as their first opinion, including "Findings do not enable a definite recommendation" and "Others: free text."

The second opinions were multiple-choice answers relating to the same 15 categories. Second-opinion centers could then recommend up to four alternative treatment options and make free-text comments.

The initially planned treatment was considered to be congruent with the second opinion if it coincided with at least one recommendation made by the second-opinion center. Incongruent cases were differentiated as follows:

- First opinion favors more extensive treatment, that is, "overtreatment" according to guidelines.
- First opinion favors less extensive treatment, that is, "undertreatment" according to guidelines.
- Incongruence without a clearly distinguishable difference in the scope of therapy.

In these cases, the treatment scope of alternative options was assessed in relation to the clinical tumor stage for which it was recommended by the guidelines [8,9].

Significance was determined by Pearson  $\chi^2$  test (two-sided). Standardized residues of cells of the cross-classified table were used for content-related interpretation of a significant result. Significance was also determined using a Monte Carlo simulation with 10 000 trials and a 99% confidence interval.

## 3. Results

From June 2006 to August 2008, 642 requests for second opinions were addressed to 18 German second-opinion centers by 162 urologists working in clinics or private practices in Germany. Thirty-eight percent of the advice seekers worked in clinics, 31% worked in private practice, and 21% had an unclear status. The clinics were university

**Table 1 – Patient characteristics**

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Total second-opinion requests	642 <sup>*</sup>
Average patient age, yr	39.1
Histologic finding at time of diagnosis of germ cell tumor seminoma	275 (53.5%)
Average age, yr	42.5
Nonseminoma	235 (45.7%)
Average age, yr	35.0
Unclear whether seminoma or nonseminoma	4 (0.8%)
Evidence of contralateral TIN at time of second-opinion request	37 (6.3%)
Patient age $\geq 40$ yr	15 (40.5%)
Patient age $< 40$ yr	22 (59.5%)

TIN = testicular intraepithelial neoplasia.  
<sup>\*</sup> In 128 patients, the initially planned therapy and the second-opinion recommendation have not yet been compared with the applied therapy.

facilities in 4% of the cases, regional care centers in 42%, and local hospitals in the remaining cases. Practice inquiries came from single practices in 28% of the cases, from group practices in 46%, and from practices with an unclear legal status in 26%. Table 1 summarizes patient characteristics.

At the time of this interim report, 514 data sets for 642 inquiries were complete except for the 2-yr follow-up. A discrepancy was found between the initial treatment plan of the inquiring urologist, referred to as the first opinion, and the treatment recommended by the second-opinion centers ("second opinion") in approximately one-third of the cases. The initial treatment plan coincided with the second opinion in 68% (Tables 2 and 3). The percentage of discrepant recommendations tended to increase with increasing tumor stage (Pearson  $\chi^2$  test,  $p = 0.061$ ) (Table 2). The percentage of discrepant first and second opinions was lower for low tumor stage than for advanced tumor stages.

Comparison of first and second opinions in relation to the tumor type showed a significantly higher discrepancy between the first and second opinion for nonseminomas than for classical seminomas (Pearson  $\chi^2$  test,  $p = 0.045$ ) (Table 3).

In the case of a discrepant second opinion, the treatment scope of the first opinion was compared with that of the second opinion and the guidelines to determine whether the first opinion favored under- or overtreatment [8,9]. The discrepant second opinion favored a less intensive therapy in 40.3% of the cases and a more intensive one in 26.5%. No clear distinction could be made with regard to the extent and intensity of treatment in 33.1%.

In the case of a discrepant second opinion, urologists followed the recommendations in 71.8% and favored their own initial plan of treatment in 15.6%. In 7.1%, the applied therapy differed from both the first and second opinion. In 5.5% of the cases, the therapy could not be evaluated by the time of the interim report. Only a small percentage answered the question regarding the reasons for a deviation from guideline recommendations. The most common answer was that the patient expressed a therapy preference that corresponded to the initial treatment plan and not to

**Table 2 – Comparison of first and second opinions in relation to the clinical tumor stage<sup>\*</sup>**

			First and second opinions				Total
			Coinciding	Discrepant: Second opinion favored more extensive therapy	Discrepant: No clear difference in scope of therapy	Discrepant: First opinion favored more extensive therapy	
Clinical tumor stage (categorized)	Ia, Ib, Is	No.	243	31	27	46	347
		%	70.0	8.9	7.8	13.3	100
	IIa, IIb	No.	54	5	11	9	79
		%	68.4	6.3	13.9	11.4	100
	IIc, IIIa, IIIb, IIIc	No.	51	8	17	12	88
		%	58.0	9.1	19.3	13.6	100
Total	No.	348	44	55	67	514	
	%	67.7	8.6	10.7	13.0	100	

<sup>\*</sup> The extent of therapy was evaluated according to the guideline recommendations for the respective tumor stage [8,9]. Pearson  $\chi^2$  test (two-sided) showed that the percentage of discrepant recommendations tended to increase with increasing tumor stage ( $p = 0.065$ ).

**Table 3 – Comparison of first and second opinions on seminoma versus nonseminoma<sup>\*</sup>**

			First and second opinions				Total
			Coinciding	Discrepant: Second opinion favored more extensive therapy	Discrepant: No clear difference in scope of therapy	Discrepant: First opinion favored more extensive therapy	
Tumor type (histology)	Seminoma (classical seminoma)	No.	194	21	20	40	275
		%	70.5	7.6	7.3	14.5	100
	Nonseminoma	No.	151	22	34	28	235
		%	64.3	9.4	14.5	11.9	100
Total	No.	345	43	54	68	510	
	%	67.6	8.4	10.6	13.3	100	

<sup>\*</sup> Four of 514 cases were excluded from analysis because the germ cell tumors in these patients could not be classified for specific histology at the time of assessment. The extent of therapy was evaluated according to guideline recommendations for the respective tumor stage [8,9]. Pearson  $\chi^2$  test (two-sided) showed a significantly higher discrepancy ( $p = 0.045$ ) between first and second opinions in nonseminoma patients than in seminoma patients.

the second opinion. A less frequent answer was that the initial treatment was performed because of a misunderstanding. However, most urologists did not respond to our telephone inquiry.

Considering the discrepant second opinions in a third of the cases, their treatment scope related to that of the first opinion, and their degree of implementation, it appears that second opinions prevented overtreatment in 10.7 cases and undertreatment in 16. Approximately every sixth second opinion led to a relevant change in the treatment scope.

#### 4. Discussion

The advantages of therapy according to evidence-based guidelines are undisputed and have provided the motivation for developing guidelines for various diseases in the past [10]. The purpose was to disseminate the most recent evidence-based study results (ie, expert knowledge) with the aim of improving the quality of care in an existing care delivery system. The question arises whether developing guidelines can really achieve sustained improvement of care results if the delivery system remains unchanged or whether the guidelines should also include implementation strategies. This question is highly relevant because only the

proof of improved quality justifies the guideline approach, which may require additional or supplementary measures. The data obtained thus far from the second-opinion project partly answer these questions.

The 32.3% discrepancy between the therapy planned by the requesting urologist and the guideline-based treatment recommended by the second-opinion center shows that penetration of the guidelines is limited despite their universal availability. It still remains a matter of speculation whether this is due to clinically necessary deviations from the guidelines, ignorance of the guidelines, misinterpretation of the guidelines, or misinterpretation of the patient data.

In any case, the high discrepancy rate underlines the fact that simply publishing guidelines can only lead to partial achievement of their aim: to disseminate expert knowledge with the aim of improving the quality of care for germ cell tumor patients.

The effectiveness of publishing guidelines without offering supporting measures is also questioned by other studies [11,12]. A publication by Ryan et al, for example, demonstrated that two National Institute for Health and Clinical Excellence guidelines had an only marginal effect because the applicable scale of fees counteracted their implementation [13].

One can only speculate about effective strategies for guideline implementation. One promising approach is “active” dissemination by repeatedly sending new guidelines to users instead of “passively” ensuring Internet access. Moreover, the health care and insurance systems should create incentives for guideline-based therapy.

Long-term data on the clinical course of the patients are still pending. Assuming that patients usually profit from guideline-based treatment, the results of the study suggest (1) that initial therapy planning requires improvement, (2) that second-opinion centers can contribute toward improving implementation of the guidelines, and (3) that the quality of care is regionally improved by second-opinion centers.

The results of this second-opinion project are supported by comparable projects for other tumor entities. Two studies on second opinions requested for breast cancer and colon cancer showed decisive modifications of the initially planned therapy in a number of patients [14,15].

#### 4.1. How do urologists handle the requested second opinion?

The interim results of our study show a high degree of readiness to accept expert advice. A discrepant expert opinion was adopted in 71.8% of the cases. Only a few urologists had reservations about questioning their own therapy plan. This raises the question about the reasons for their willingness to alter the planned treatment as well as for their reservations about following the expert advice. The motivation in either case is still open to speculation.

#### 4.2. What is the clinical impact of a second-opinion request?

The discrepant second opinion called for less intensive therapy than initially intended in 40.3% and for more intensive therapy in 26.5%. This fact is important, considering that inadequate therapy can severely reduce the quality of life and may even lead to life-threatening complications and delayed side effects that are not fully assessable at present [16–18].

## 5. Conclusions

The interim results of the second-opinion project for germ cell cancer show that therapy planning by urologists cooperating with second-opinion centers helps to improve the implementation of guideline recommendations. Approximately every sixth second opinion led to a relevant change in the treatment scope. In view of these results, we advocate the development and utilization of second-opinion networks.

**Author contributions:** Mark Schrader had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Weissbach, Hartmann, Heidenreich, Krege, Miller, Schrader.

**Acquisition of data:** Weissbach, Hartmann, Heidenreich, Krege, Miller, Albers, Schrader.

**Analysis and interpretation of data:** Schrader, Weissbach, Heidenreich.

**Drafting of the manuscript:** Schrader, Weissbach, Miller, Heidenreich.

**Critical revision of the manuscript for important intellectual content:** Weissbach, Hartmann, Heidenreich, Krege, Miller, Schrader.

**Statistical analysis:** Schrader, Miller.

**Obtaining funding:** Schrader, Miller, Weissbach.

**Administrative, technical, or material support:** Miller.

**Supervision:** Schrader, Weissbach, Hartmann, Krege, Albers, Miller, Heidenreich.

**Other (specify):** None.

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