Introduction

Gynecological malignancies are a leading cause of morbidity in women in the United States and the European Union [1, 2]. According to the most current cancer statistics, the standardized incidence rate for combined malignant ovarian and endome-trial tumors was ~34/100,000 in Europe and ~24/100,000 worldwide, with the US figures on a par with the worldwide data [3, 4].

With the introduction of effective radical surgery and adjuvant chemotherapy and/or radiotherapy, the survival of patients with gynecological cancer has improved substantially [5–7]. Exact figures...
about the respective percentage of primary diagnoses in cancer survivors are difficult to obtain, but malignancies of the female genitalia appear to be the most common underlying disease in long-term survivors [8].

Longer survival times and potential treatment-related morbidity have led to a greater emphasis being placed on other criteria in addition to survival, such as health-related quality of life (HRQL) including sexuality. Such endpoints are also increasingly used in intervention studies in oncology [9–11]. While certain basic criteria for HRQL are universally applicable, there are a growing number of multidimensional instruments used to measure quality of life. The selection of reliable and validated instruments (such as the EORTC QLQ-C30) is therefore important and caution is mandated when comparing results between studies [12]. All treatment modalities for gynecologic malignancies, i.e., pelvic surgery, radiation and drug therapy, have the potential to impair sexual function through a variety of anatomical, physiological and psychological pathways, and sexual dysfunction is indeed frequently mentioned in the literature [13–19]. However, controlled studies are relatively rare, and their results conflicting. While some report significant and substantial differences between women with cancer and healthy controls [13,14,18,19], others deny such a disparity [20], and the impact of sexual dysfunction on quality of life is a matter of controversy [14,15].

Valid empirical data on the prevalence of sexual dysfunction in patients with gynecological malignancies based on comparisons with age-matched cancer-free controls is relatively rare; a higher prevalence, if present, may be an expression of the underlying disease itself, the patient’s success in coping or other important confounding factors rather than the treatment itself [21,22]. According to the literature, the significance of manifest sexual dysfunction in survivors of a life-threatening disease may be very different from that in a healthy population [23]. Evidence-based decisions on the relevance of sexual dysfunction in gynecological cancer survivors are currently not possible, and hence no recommendations can be made with regard to possible remedies. Not only is the evidence for a higher incidence of impaired sexual desire, functioning and pleasure and relevance of this for the quality of life of women with gynecological cancer relatively weak and controversial, but it is also unclear if and to which extent the dysfunction is attributable to the treatment, the disease itself or to psychological aspects of the patient’s coping strategy [20]. We therefore conducted a cross-sectional study to investigate sexual functioning in patients with ovarian and endometrical cancer and compared the results with those of healthy controls.

Methods

This study was approved by the ethics committee of the Medical Association of the German Federal State of Hesse. Since 2001, all consecutive patients with gynecologic cancer treated at our hospital are prospectively recorded in a clinical tumor registry. All patients’ records are updated annually. In order to be eligible for the study, patients had to fulfill the following criteria: malignancy of the ovary or endometrium, and primary therapy at our institution completed ≥ 12 months before enrolment without any evidence of relapse. A total of 335 patients who met these criteria were identified and a control sample without oncological disease consisting of 392 age-matched women was recruited in the Department of Prosthodontics, University Hospital Mainz. The questionnaire was sent out by mail between December 2009 and May 2010.

When designing the questionnaire, we attempted to strike a balance between a thorough and comprehensive assessment and a level of complexity which would not deter compliance; in view of this consideration, the decision was taken not to do a full HRQL evaluation. The questionnaire comprised three pages of validated German versions of the following items:

1. The “Sexual Activity Questionnaire” (SAQ): The SAQ comprises three sections covering sexual activity, perception of desire and possible complaints during sexual intercourse. The first section contains questions on the presence of a partner, change(s) of partner(s) in the past 6 months and current sexual activity. Depending on the answer to the latter question, respondents are requested to either answer questions on sexual function and experience or on the reasons for sexual inactivity.

2. An excerpt of the “Female Sexual Function Index” (FSFI-d) on frequency, difficulties and satisfaction with attained orgasms is assessed using a 5-point verbal rating scale.

3. An excerpt of the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) which investigates patient self-assessment of general health and quality of life (both of which are not sufficiently covered in 1, and 2.) on a numerical rating scale from 1 (“very bad”) to 7 (“excellent”).

All questionnaires are validated in terms of their psychometric properties (using Cronbach’s α-values of ≥ 0.8 [24,25]) and are used extensively in pertinent investigations [16,17,26–30].

Three scores were calculated based on the SAQ: a pleasure score (sum of points for questions 1, 2, 4, 7, 8 and 10 in section 3; more points equal more pleasure), a discomfort score (sum of points for questions 5 [“perceived dryness during intercourse during the past 4 weeks”] and 6 [“pain or other complaints during intercourse during the past 4 weeks”]; more points equal more discomfort) and a habit score (points for question 9 [comparison of the frequency during the past 4 weeks with usual habits]; more points equal a higher frequency); an orgasm score was calculated as the sum of points in the three FSFI-d questions (more points equal more frequent and/or more satisfactory orgasms). The point score for health and quality of life was calculated based on the EORTC manual [31]. All statistical analyses were done with SPSS 16.0 (Chicago, IL, USA). Patients with incomplete datasets were only excluded in the analyses where variables were missing but were included in all other evaluations. Comparisons of two or more groups of discrete variables were done with Fisher’s exact test or χ² test. Median, mean, standard deviation and 95% confidence interval were calculated for metric variables, and group differences were evaluated with the Mann-Whitney U test. All p-values were two-sided, and p < 0.05 was considered significant.

Results

Seventy-nine patients (23.6%) and 87 control subjects (22.2%) returned a completed questionnaire and were eligible for evaluation. Forty-nine patients (62.0%) had undergone treatment for ovarian cancer and 30 patients (38.0%) for endometrial cancer. Forty-four patients (55.7%) received adjuvant or primary chemotherapy and 19 patients (24.1%) were treated with radiotherapy. The median interval after the first diagnosis was 4.1 years (range:
The mean age of the 79 patients who completed the questionnaire was 62 years (range: 18–86 years). Control subjects were on average 5 years younger (mean: 57 years; range: 36–80 years), but age and menopausal status did not differ significantly between groups. Most subjects in both groups (74.7% of controls and 80.6% of patients) lived together with a partner. Changes of sexual partners in the 6 months preceding the questionnaire were rare (4.0% of controls, none of the patients). Forty-three control subjects (49.5%) and 32 patients (40.5%) described themselves as sexually inactive. This differs from the general well-being of 31.9% in control subjects (44.7 vs. 4.5%, p < 0.05) or her partner (14 (17.7) vs. 14 (19.4), 0.326). The lack of interest in sex was the single most important reason for sexual inactivity in the control group (given by 17 subjects (38.6%) who described themselves as sexually inactive). In contrast, patients most frequently cited lack of interest as the reason for sexual inactivity (n = 19, 40.4%). The lack of a sexual partner was the single most important reason for sexual inactivity (n = 19, 40.4%). The only point score with a significant difference between groups was the discomfort score with 2.62 ± 2.3 (95% CI: 2.2–3.0) points in patients vs. 1.34 ± 1.7 (95% CI: 1.1–1.3) points in controls (p < 0.05). There was a nonsignificant tendency towards reduced pleasure (9.4 ± 4.3 vs. 10.7 ± 3.8 points, p = 0.139) and lower orgasm scores (10.7 ± 3.6 vs. 12.0 ± 3.0 points, p = 0.094) in patients compared with controls. Self-rated health status and quality of life showed no appreciable difference between groups with 67 (C) versus 69 (GC) out of 100 possible points (Fig. 1).

## Discussion

The results of the present study confirm a high incidence of sexual inactivity and discomfort during sexual intercourse in gynecological cancer survivors. In accordance with the mental and physical aspects of cancer survivorship and treatment sequelae, patients reported a lack of interest and physical problems as the most frequent reasons for sexual inactivity (59.5%), and the SAQ discomfort score for GC women was significantly higher than in control subjects. However, a comparison between groups of other aspects of sexual function (pleasure, habit, and orgasm score) and of quality-of-life indicators did not yield an appreciable difference. Due to the lack of a thorough evaluation of possible confounding variables, this does not directly rule out the impact of doubtlessly increased – discomfort during sexual intercourse on quality of life. However, the patients’ general well-being was on a par with that of the control subjects, and it is unlikely – albeit not impossible – that this is due to compensating factors outside the scope of this investigation. Therefore, the impact of sexual impairment on quality of life in our patient sample appears to be limited.

However, certain methodological aspects of the study mean that these results should be interpreted with caution. First of all, the response rates were rather low, with only around 1 in 4 questionnaires returned in both groups. However, the participation rate in published postal surveys of sexual issues is often only between 15 and 50% [32–36], and a comparison between responders and non-responders published by Dunne et al. [37] showed only marginal differences on re-investigation. In our series, we did not analyze the non-responders. Some patients responded with a num-

## Table 1

Baseline data, relationship status and sexual activity in patients and controls.

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (% of valid answers)</th>
<th>p-value (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controls (n = 87)</td>
<td>Patients (n = 79)</td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>57 (62)</td>
<td>36–80</td>
</tr>
<tr>
<td>Age groups (menopausal status)</td>
<td>≤ 49 yrs</td>
<td>19 (25.3)</td>
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<tr>
<td></td>
<td>≥ 50 yrs</td>
<td>56 (74.7)</td>
</tr>
<tr>
<td>n/a</td>
<td>12</td>
<td>–</td>
</tr>
<tr>
<td>SAQ, 1st section</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steady relationship</td>
<td>yes</td>
<td>59 (74.7)</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>19 (25.3)</td>
</tr>
<tr>
<td></td>
<td>n/a</td>
<td>8</td>
</tr>
<tr>
<td>Change of sexual partner</td>
<td></td>
<td></td>
</tr>
<tr>
<td>during the past 6 months</td>
<td>yes</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>72 (96.0)</td>
</tr>
<tr>
<td></td>
<td>n/a</td>
<td>12</td>
</tr>
<tr>
<td>Sexual activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>43 (49.4)</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>44 (50.6)</td>
</tr>
</tbody>
</table>

## Table 2

Reasons for sexual inactivity cited by eligible subjects (multiple answers permitted).

<table>
<thead>
<tr>
<th>Reasons for sexual inactivity</th>
<th>n (% of valid answers)</th>
<th>p-value (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controls (n = 44)</td>
<td>Patients (n = 47)</td>
</tr>
<tr>
<td>SAQ, 2nd section</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No partner</td>
<td>17 (38.6)</td>
<td>11 (23.4)</td>
</tr>
<tr>
<td>General well-being (fatigue), patient</td>
<td>4 (9.1)</td>
<td>3 (6.4)</td>
</tr>
<tr>
<td>General well-being (fatigue), partner</td>
<td>4 (9.1)</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>No interest in sex, patient</td>
<td>9 (20.5)</td>
<td>19 (40.4)</td>
</tr>
<tr>
<td>No interest in sex, partner</td>
<td>4 (9.1)</td>
<td>7 (14.9)</td>
</tr>
<tr>
<td>Physical problem, patient</td>
<td>4 (9.1)</td>
<td>13 (27.7)</td>
</tr>
<tr>
<td>Physical problem, partner</td>
<td>2 (4.5)</td>
<td>10 (21.3)</td>
</tr>
<tr>
<td>Other reasons</td>
<td>19 (43.2)</td>
<td>18 (37.0)</td>
</tr>
</tbody>
</table>
number of major concerns regarding such a questionnaire so that we abandoned our intention of reminding non-responding patients. The fact that rates in both groups of the present study were approximately equivalent also rather contradicts systematic bias. Of course, the limited number of participating patients and controls is in itself a limiting factor with regard to the general applicability of our results. The same applies to the chosen entities “ovarian cancer” and “endometrial cancer”. Our results cannot be generalized for other gynecologic cancers such as vulvar or cervical cancer. There could be significant differences due to the different surgical procedures and types of adjuvant treatment involved, which could include higher rates of radiotherapy compared to the investigated cohorts. Unfortunately, our sample size is too small to perform a meaningful subgroup analysis with regard to age, time elapsed since therapy, type of surgery, type of adjuvant therapy, etc.

Even though the data was obtained from participants in a prospective study, the results are based on a single cross-sectional questionnaire, and thus it is impossible to determine changes in sexual function over time in either group. Moreover, the decision to keep the questionnaire short inherently limited the scope of the results, especially with regard to quality of life and its possible connection to sexual function.

Other methodological aspects strengthen the study’s results and provide information beyond the scope of most existing cross-sectional studies; they include the case-control study design, the meticulous documentation of all relevant clinical data and, in particular, the control group with its excellent age match and probable absence of any of the physical and mental difficulties implicated in sexual dysfunction in gynecological cancer survivors. The difference in sexual activity between patients and controls in the present study – 40 vs. 50% – was lower than expected. However, sexual activity in the general female population of the same age bracket is not necessarily much higher. In a study published by Lindau et al., the self-reported rate of sexual activity declined from 73% in subjects aged between 57 and 64 years to 53% for women between the age of 65 and 74 years, and to 26% for women between 75 and 85 years of age. Other results of the study in 3005 adults (1550 females) were also remarkably similar to our findings: half of the women who were sexually active reported at least one troublesome sexual problem, and the most common reason cited for lack of activity was low desire (reported in 43%), a figure almost precisely similar to the finding in our study [38].

While an appreciable, albeit moderate, impairment of sexual function and – especially – of desire in gynecological cancer survivors is clear in the present sample, its biological and psychological background is much less straightforward. First of all, the physical problems of the patients’ partners are significantly more common than reported for the partners of controls, indicating the complex nature of possible causes; the complete absence of repercussions on quality of life and self-rated health status indicate a similar complexity of consequences. However, we have to be cautious about generalizing our results on quality of life because only 2 questions from the quality-of-life questionnaire were studied and some effects may have been overlooked due to this limited approach.

Our study raises some doubt about the equation of “sexual functioning” with “quality of life” in female cancer survivors sometimes found, implicitly or explicitly, in the literature [39]. In the present study, women who had survived ovarian or endometrial cancer generally assessed their own health status and quality of life as satisfactory (approximately in the middle between “very bad” and “excellent”) according to the well-validated EORTC QLQ-C30 assessment, notwithstanding certain physical impairments in sexual activity. This is in accordance with other published studies [13,20,23] and possibly indicates a significant shift in priorities experienced by cancer survivors. In keeping with our personal experience, the first and foremost concern of survivors of ovarian and endometrial cancer is tumor recurrence [28]; according to the present study, this would seem to put other difficulties in life – including a possible impairment of sexual desire and fulfillment – into perspective [23]. It is difficult to draw definitive conclusions from our findings which can be used for patient counseling. The following conclusion could serve as a summary of our clinical experience and of the limited results of our study. The problem of sexual function might be overestimated by us in some patients but could be a major factor influencing quality of life in others. Patients and their partners need all the support we can offer.
Conflict of Interest

The study was funded by “Let’s GO”, an independent association which supports women with gynecologic cancer affiliated to the Dr. Horst Schmidt Klinik, Wiesbaden, Germany (http://www.lets-go-ev.org/startseite/). “Let’s GO” was not involved in any aspects of the study apart from the grant.

All authors declare they have no relevant conflicts of interest.

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