Introduction

Female sexual dysfunction (FSD) is common in gynaecological cancer survivors after chemotherapy, radiotherapy and drug therapy\(^1\). All cancers have the potential to affect sexual function; however, gynaecological cancer represents greater risks for sexual dysfunction\(^2\) and is the second most common cancer in the world\(^3\). Nevertheless, cervical cancer remains the most frequent among women, with estimates for Brazil of 260,640 new cases among females. There was a twofold increase in the incidence of gynecological cancer in developing countries already in 2013\(^4\).

Most changes due from treatment affect sexuality negatively such as vaginal dryness and stenosis\(^5^-^7\), dyspareunia and vaginal shortening\(^2^,^3^,^8\), arousal disorders, among others\(^9^,^10\). The Female Sexual Function Index (FSFI) was developed by Rosen and colleagues\(^5\) to assess female sexual function, which has been used for different populations: women with chronic pelvic pain\(^9\), pregnancy\(^7\), postmenopausal\(^8\) and those with vulvovaginal candidiasis\(^6\). This is a brief scale that assesses female sexual function, consisting on a self-report of six major areas: orgasm, desire, arousal, satisfaction, lubrication and pain, arranged into 19 questions.
The questionnaire should be answered based on the sexual activity of the last four weeks. The final score indicates the presence or absence of FSD and allows comparisons between populations or individuals at different stages of life and treatment.

Recently, Baser and colleagues (1) conducted a psychometric validation of FSFI in female cancer survivors, obtaining a satisfactory result in the administration of this instrument, encouraging its wide use in this population.

Sexual dysfunction is an important component in measuring the quality of life of the individual. In the population of this study, the knowledge of this variable can determine preventive actions and/or health promotion, minimizing the effects of treatment or disease. The scarcity of studies on the subject can explain the need for information on the diagnosis of FSD in gynecologic cancer. Given the above, the present study aims to review all studies using the FSFI as a tool to assess sexual function in women after gynecologic cancer treatment, including studies based on scientific evidence in order to extend the results to clinical practice. The questions to be answered are:

1. What is the level of evidence of studies?
2. What is the frequency and methodological quality of studies that used FSFI?
3. What are the main results of sexual dysfunction in women with gynecologic cancer indicated by FSFI?

Methods

The initial design for this review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA guidelines). The survey of studies was held between May 15 and June 15, 2013, considering the inclusion of all models from 2000 when the FSFI instrument was developed.

The keywords used in accordance with the description of Mesh terms, were: “gynaecologic cancer”, “endometrial cancer”, “cervical cancer”, “vaginal cancer”, “vulvar cancer”, “uterine cancer”. These were combined with the “OR” Boolean operator. Additionally, the following terms were used: “chemotherapy”, “radiotherapy”, “surgery”, also combined with the “OR” Boolean operator, and finally, the crossing with the “AND” Boolean operator was performed, adding the last term “sexual function”. The research strategies in databases were used for the first time regardless of language, being subsequently selected studies in English, Portuguese and Spanish, as shown in Table 1. The survey was conducted in the following indexed databases: OvidSP, PubMed and Scopus (figure 1).

Table 1: Evidence hierarchy used in the qualitative analysis of the methodology used in the studies included (Johnson et al., 2010).

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I (strong evidence) Randomized, randomized clinical trial or review of controlled trials</td>
<td>IA: Sample size calculation, precise definition and standard of outcome variables</td>
</tr>
<tr>
<td></td>
<td>IB: None of the above</td>
</tr>
<tr>
<td>Level II (fairly strong evidence) Randomized study with comparison between groups (non-randomized controlled study or good observational study)</td>
<td>IIA: Sample size calculation, precise definition and standard of outcome variables</td>
</tr>
<tr>
<td></td>
<td>IB: One of the above</td>
</tr>
<tr>
<td></td>
<td>IC: None of the above</td>
</tr>
<tr>
<td>Level III (weak evidence) Retrospective</td>
<td>IIA: Comparison group, sample size calculation, precise definition and standard of outcome variables</td>
</tr>
<tr>
<td></td>
<td>IIB: Two of the above</td>
</tr>
<tr>
<td></td>
<td>IIC: None of the above</td>
</tr>
<tr>
<td>Level IV (weak evidence)</td>
<td>Cross-sectional studies</td>
</tr>
</tbody>
</table>

Figure 1: Research Strategies in chosen databases: OvidSP, PubMed and Scopus.

All titles and abstracts retrieved by electronic search were printed and manually reviewed by three independent reviewers. The following inclusion criteria were adopted: original articles such as randomized controlled trials, quasi-randomized, cross-sectional studies, cohort studies, case-control studies, and studies that used FSFI as a tool to assess sexual function in women undergoing gynecologic cancer treatment published between 2000 and 2013. Excluded studies were: pilot studies, reviews, case reports, conference and studies related to other types of cancers, articles unavailable in full version and duplicates.
Due to the heterogeneity of drawings and samples of selected studies, it was not possible to perform quantitative analysis of results, but rather a qualitative assessment. This tool has a checklist of 22 items that should be included and classified into three categories: Good (studies fulfilling ≥ 80% the inclusion criteria), moderate (studies fulfilling 50% to 80% the inclusion criteria) and poor (studies fulfilling <50% the inclusion criteria).

Although the STROBE guidelines have not been developed for the methodological analysis of published articles, it has recently been used as a tool for qualitative analysis of observational studies by several authors\(^{(11-15)}\). Another tool to assess the quality of articles was the hierarchical system of evidence, described by Sackett et al.,\(^{(16)}\) used to determine the level of evidence of studies selected and included in this study (Table 1).

**Results**

As seen in Figure 2, from the 528 articles selected by searching databases, 49 articles fulfilled the inclusion criteria, and of these, 35 were excluded because they were not available in full even after contact with the author; were doubled in databases, and/or because the language was other than English, Portuguese or Spanish. Thus, 16 articles were included for qualitative synthesis described in Table 2.

FSFI was administered in eight different countries (Figure 3): United States (USA)\(^{(1,17-22)}\), Germany\(^{(23, 24)}\), Italy\(^{(25, 26)}\), Turkey\(^{(27)}\), Portugal\(^{(28)}\), Netherlands\(^{(29)}\), Brazil\(^{(30)}\) and Taiwan\(^{(31)}\), with the following frequency: USA (43.75%), Germany (12.5%), Italy (12.5%), Turkey (6.25%), Portugal (6.25%), Netherlands (6.25%), Brazil (6.25%) and Taiwan (6.25%).

Methodological quality was assessed by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE), classified as moderate to good studies as described in Table 3. In general, the methodological flaws were not adopting specifications to describe any efforts to address potential sources of bias (100% of articles), study design unexplained in methods (18.75%) and lack of financing sources (87.5%). Thus, the hierarchical analysis of evidence found that the present studies showed fairly strong (68.75%) and low evidence (31.25%), as shown in Table 2, since the analysis of the type of study showed a predominance of observational analytical studies without sample calculation.

**Figure 2:** Flow diagram of inclusion and exclusion of studies published in OvidSP, PubMed and Scopus databases.
FSFI was used in studies (Table 2) with the main purpose of verifying the presence of FSD or any discomfort during sexual intercourse combined with post gynaecological cancer treatment. The study participants had cervical cancer (17, 18, 31), cervix cancer (1, 17, 26), myoma (27), cervical intraepithelial neoplasia (25), vulvar cancer (20, 21, 29, 30), endometrial cancer (17, 19, 22, 23) and ovarian cancer (29), and some of them were submitted to radical hysterectomy (1, 17, 19, 26), myomectomy (27), vulvar excision (20, 21, 28), vulvectomy (29, 30), brachytherapy (23) and radiotherapy (28).

Study results showed that radical hysterectomy significantly worsens sexual function, regardless of the type of surgical approach, as well as radiotherapy and brachytherapy. However, when women remain sexually active after gynaecological cancer treatment, no dysfunction such as discomfort was reported, and sexual intercourse was possible.

Table 2: Description of the main results of eligible studies regarding the use of FSFI in women with gynaecological cancer.

<table>
<thead>
<tr>
<th>Ref</th>
<th>Author</th>
<th>Method</th>
<th>Participant</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Country</th>
<th>Evaluation (Chart 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>Bauer et al., 2012</td>
<td>The data were obtained from three review studies of psychosexual adjustment of women who survived cancer treated at the Memorial Sloan-Kettering Cancer Center</td>
<td>219 women who survived gynaecological cancer</td>
<td>Radical hysterectomy or surgical removal of the cervix</td>
<td>The results support the continued use of FSFI to assess the sexual function and dysfunction related to cancer and female cancer survivors</td>
<td>USA</td>
<td>IV</td>
</tr>
<tr>
<td>(2)</td>
<td>Becker et al., 2010</td>
<td>Application of FSFI and EORTC-QLQ-C30/C24 in women with 5 years after the initial endometrial cancer treatment</td>
<td>60 patients; 55 eligible, of those, 29 with vaginal brachytherapy and 26 without</td>
<td>Surgery and brachytherapy</td>
<td>Adjunct brachytherapy after surgery does not seem to have significant impact on quality of life after 5 years and sexual function in endometrial cancer survivors</td>
<td>Germany</td>
<td>III</td>
</tr>
<tr>
<td>(3)</td>
<td>Catrè et al., 2010</td>
<td>Application of FSFI in women after cancer treatment that resulted in infertility</td>
<td>75 women after cervical cancer surgery</td>
<td>Radical removal of the cervix or radical hysterectomy</td>
<td>FSFI scores for the total sample were below cut-off (26.53), suggestive of Female sexual dysfunction (FSD), however, it increased from 16.79 (preoperatively) to 23.78 at 12 months and 22.20 at 24 months postoperatively.</td>
<td>USA</td>
<td>III</td>
</tr>
<tr>
<td>(4)</td>
<td>Catrè et al., 2010</td>
<td>Application of FSFI in a time interval between hysterectomy</td>
<td>88 women treated for cervical cancer, endometrial cancer, uterus cancer, and ovarian cancer in hospitalization</td>
<td>Radical hysterectomy or surgical removal of the cervix</td>
<td>Seventy-seven percent of women reported being sexually active. About 62% were satisfied with the emotional discussion in their relationship, more than half (50%) indicated satisfaction with their overall sex life.</td>
<td>USA</td>
<td>III</td>
</tr>
<tr>
<td>(5)</td>
<td>Dauri et al., 2011</td>
<td>Application of FSFI in a time interval between hysterectomy</td>
<td>473 patients; 209 eligible, 104 were followed</td>
<td>Hysterectomy from 6 months to 5 years</td>
<td>Prevalence of FSD in the sample. Premenopausal endometrium cancer was associated as a risk factor.</td>
<td>USA</td>
<td>III</td>
</tr>
<tr>
<td>(6)</td>
<td>Finkau et al., 2009</td>
<td>Application of FSFI before and after myomectomy</td>
<td>84 women with myoma and 75 control</td>
<td>Myomectomy</td>
<td>Myomectomy decreases pain during sexual intercourse, improving sexual function.</td>
<td>Turkey</td>
<td>III</td>
</tr>
<tr>
<td>(7)</td>
<td>Femuri et al., 2012</td>
<td>Application of FSFI with women undergoing inguinal and vulvar vulvectomy</td>
<td>56 patients; 28 healthy women and 28 women with vulvar cancer</td>
<td>Vulvectomy</td>
<td>Vulvectomy with lymphadenectomy favors the development of lymphedema of the lower limbs, with a negative effect on QL and no effect on sexual function.</td>
<td>Brazil</td>
<td>III</td>
</tr>
<tr>
<td>(8)</td>
<td>Fotopoulou et al., 2008</td>
<td>Application of FSFI in women after gynaecological surgery</td>
<td>7 women with sigmoïdectomy</td>
<td>Partial or complete coital potency.</td>
<td>Sexually active women have no graft stenosis and vaginal intercourse seems to be possible without discomfort.</td>
<td>Germany</td>
<td>III</td>
</tr>
<tr>
<td>(9)</td>
<td>Kuusinenvaara et al., 2012</td>
<td>Application of FSFI in women after gynaecological cancer survivors</td>
<td>309 women with vulvar cancer, 120 eligible</td>
<td>Vulvectomy, radical excision and/or inguinal lymph node dissection.</td>
<td>45% of women who survived vulvar cancer and who had a male partner were sexually active. Having a partner has a positive effect on sexual function.</td>
<td>Netherland</td>
<td>IV</td>
</tr>
<tr>
<td>(10)</td>
<td>Lee et al., 2006</td>
<td>The research questions addressed were: 1) Is there internal consistency in the FSFI score? 2) Is there discriminant validity of FSFI validity comparing women after vulvar surgery? 3) Is there a diverging validity of FSFI and EORTC-QLQ-C30?</td>
<td>86 participants; convenience group (n=45) submitted to an urban centre for vulvar cancer intraepithelial neoplasia (VIN) and control group (n=45).</td>
<td>Vulvar excision for treating vulvar intraepithelial neoplasia</td>
<td>Study demonstrates the reliability and the validity of FSFI in assess sexual function in women after vulvar excision for VIN</td>
<td>USA</td>
<td>III</td>
</tr>
</tbody>
</table>
Discussion

The FSFI is a multidimensional instrument to measure female sexual function\(^5\). FSD is present in 30 to 100% of gynaecological cancer survivors\(^{12-34}\).

Regarding the frequency of FSFI use by type of study, there was a higher prevalence of case-control studies, followed by cross-sectional studies, prospective studies and cohorts. The levels of evidence found were IIB for all case control, prospective cohort studies, since they did not report the use of sample size calculation, and IV for cross-sectional studies, which according to the hierarchy of evidence have less scientific relevance and limited results.

Most studies founded were conducted in USA, probably because the FSFI was developed and validated in this country\(^5\), such as the validity of the psychometric properties of FSFI for cancer survivors\(^1\). In other countries, the low incidence of studies is due to the recent validation in the following languages: German\(^{35}\), Turkish\(^{36}\), Dutch\(^{37}\), Portuguese\(^{38}\), Italian\(^{39}\) and Thai\(^7\).

Based on 16 studies selected, the methodological quality found varied from Good\(^{11, 17-19, 23, 25, 26, 29, 30}\) to moderate\(^{20-22, 24, 27, 28, 31}\). Articles did not pointed the control of biases, which may have compromised the methodology, since FSD is multifactorial and involves, for example, psychological, hormonal and even physical factors, this shows that FSD is not only caused by changes from gynaecological cancer and its treatment.

Among studies with better methodological quality, Serati et al.,\(^{26}\) used FSFI to assess sexual function in women who underwent radical hysterectomy via laparotomy or laparoscopy in the treatment of cervix cancer. They compared the group of surgical intervention with healthy women.
after 6 months. Of the 20 women who underwent laparoscopy 75% of them reported worst sexual function, while in the laparotomy group this value changed to 55%. The FSFI scores were significantly higher in all domains on control group, concluding that radical hysterectomy compromises female sexual function, regardless of the surgery type. The lack of control of sexual function pre-intervention prevented the monitoring of the outcome after surgery.

The following year, Serati et al.,(23) investigated sexual function with FSFI in 58 women with cervix intraepithelial neoplasia before and after 6 months of intervention with the Loop Electro surgical Excisional Procedure. No significant changes in sexual function of these women were observed, with only a small decline in the domain “desire” (p = 0.02).

Becker et al.,(20) interviewed 40 women treated for at least 5 years for endometrial cancer of early-stage and divided them into two treatment groups: surgery and adjuvant brachytherapy. The FSFI results showed no significant differences in sexual function between two treatments. This study has important limitations such as sample size and the lack of diagnostic features, which may have influenced the results.

Prospectively, Carter et al.,(18) described the sexual dysfunction of 52 women who underwent radical surgery for cervix cancer over two years. Although the sample size was considered small, the study indicated that unexpectedly, FSFI was < 26.55, regardless of the proposed surgery. Unlike the results of Backer et al.,(26), women who did not receive chemotherapy and/or radiotherapy stood out (p = 0.01) for obtaining the highest FSFI scores. The study concluded that 68% of survivors had FSFI score lower than 26.55, indicating FSD, although it criticizes the cut-off as insensitive for women with gynaecological cancer.

Damast et al.,(19) conducted a study in the USA with 104 patients at early-stage of endometrial cancer that underwent hysterectomy and adjuvant brachytherapy in an interval from 6 months to 5 years. Similarly to the study of Carter et al., 18 all FSFI domains obtained scores were below the cutoff point < 26.55, with emphasis for lubrication and pain domains. Moreover, the study emphasized that the factors associated to the treatment such as the use of lubricant and type and duration of surgery could be associated with worse sexual function.

The only Brazilian study that used FSFI to assess sexual function in cancer survivors was conducted by Ferreira et al.,(30). In order to verify the occurrence and severity of FSD, the study addressed women with vulvar cancer undergoing surgical treatment. Twenty-eight underwent vulvectomy for at least 6 months and were prospectively assessed with the healthy control group, on cancer group 21.4% sexually active after disease against 32.1% in the control group.

Hazewinkel et al.,(29) studied the sexual function of 76 women with vulvar cancer who received greater or lesser level of treatment. Unlike the study by Ferreira et al.,(30) 50% of women reported similar sexual function and 49% reported that sexual function was worse than before surgery. FSD was attributed to age and adjuvant radiotherapy. One of these limitations refers to the influence of the current partner in sexual function, and the fact that they were unable to calculate the total FSFI score due to lack of information, reporting that the use of this instrument can be little useful in this population. Dissimilarly, in the study by Baser et al.,(26) the results supported the use of FSFI in the population affected by cancer and specifically female cancer, by evaluating the reliability and validity of the FSFI construct in this population. This study also had good methodological quality.

On the other hand, studies with worse methodological quality also showed relevant data. Likes et al.,(20) also showed reliability and validity of FSFI to measure sexual function in women after vulvar excision for vulgar intraepithelial neoplasia. In their next study, Likes et al.,(31) evaluated women after surgical treatment for vulvar intraepithelial neoplasia using FSFI validation and concluded that age and most advanced vulvar excision were associated with lower FSFI scores in this population, corroborating Hazewinkel et al.,(29) considering predisposing factors for FSD after surgery as treatment for gynaecological cancer.

Onujiogu et al.,(22) evaluated the sexual function of women after surgery for endometrial cancer and Rodrigues et al.,(20) women treated for cervical, rectal or anal cancer treated with radiotherapy and both concluded that these women showed higher risk of FSD, regardless of treatment. Tsai et al.,(33) confirmed this trend in their study, showing 66.7% of prevalence of this FSD in treatment for cervical cancer.

On the other hand, studies have found satisfactory results indicating maintenance of sexual activity without discomfort with sexual intercourse(24) or
improved sexual function\(^{(7)}\) after elective treatment. Specifically, improvement was identified in women post myomectomy, as it decreased pain during intercourse compared with preoperative results.

**Conclusion**

The studies included in this review showed low levels of scientific evidence, despite the moderate and good methodological quality. Thus, it is needed to conduct randomized clinical trials in order to define the prevalence and risks of FSD in the different treatments and types of gynaecological cancers. It is noteworthy that American studies were predominant, and there are ethnic specificities suggesting studies with other populations, especially the Brazilian. Further studies on the oncology area with emphasis on female sexual function should be carried out in view of the variability of results found in this study.

**References**


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Corresponding author
Dr. FABIANA FLORES SPERANDIO
Centro de Ciências da Saúde e do Esporte (CEFID) - Laboratório de Saúde da Mulher
Paschoal Simone, 358, Coqueiros, 88080-350 Florianópolis (SC) (Brazil)