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Quality of life after radical trachelectomy for early-stage cervical cancer: A 5-year prospective evaluation☆

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HIGHLIGHTS

- Several QOL measures decline postoperatively after radical trachelectomy.
- Most QOL scores return to baseline by 6 months after radical trachelectomy.
- A persistent decline in emotional well-being was seen up to 4 years postoperative.

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ABSTRACT

Objectives. To longitudinally assess quality of life (QOL) in women undergoing radical trachelectomy for early-stage cervical cancer.

Methods. We prospectively enrolled patients with stage IA1-IB1 cervical cancer prior to undergoing radical trachelectomy to complete validated QOL instruments. These instruments included the General Health-Related QOL (SF-12), Functional Assessment of Cancer Therapy-Cervix (FACT-Cx), MD Anderson Symptom Inventory (MDASI), Female Sexual Functioning Index (FSFI), and Satisfaction with Decision scale (SWD). Instruments were filled out at baseline, postoperatively at 6 weeks, 6 months, 1 year, and annually thereafter for 4 years.

Results. Thirty-nine patients enrolled in the study, and 32 patients were evaluable. The scores for FSFI-arousal ($p = 0.0002$), lubrication ($p < 0.0001$), orgasm ($p = 0.006$), pain ($p = 0.01$), satisfaction ($p = 0.03$) and total score ($p = 0.004$) showed a significant decline at 6 weeks then returned to baseline levels by 6 months. The scores for FACT-Cx functional well-being ($p = 0.02$) and physical well-being ($p < 0.0001$), SF-12 bodily pain ($p < 0.0001$), physical functioning ($p < 0.0001$), role physical ($p < 0.0001$), role emotional ($p = 0.03$), social functioning ($p = 0.002$), and MDASI total ($p = 0.04$) showed significantly worsened symptoms at 6 weeks then returned to baseline by 6 months. The scores for FACT-Cx emotional well-being showed significant worsening of symptoms that persisted at 6-weeks ($p = 0.004$), 6 months ($p = 0.007$), 1 year ($p = 0.001$), 2 years ($p = 0.002$), and 4 years ($p = 0.03$). There was no difference in SWD.

Conclusions. Several quality of life assessments decline immediately postoperatively after radical trachelectomy, however, return to baseline thereafter. The long-term emotional impact of this surgery highlights a need for perioperative counseling in these patients.

1. Background

Although the incidence of cervical cancer in the United States continues to decline, it continues to affect young women who desire future childbearing. Forty-six percent of cervical cancers are diagnosed in women under the age of 45 [1], thus, fertility preserving surgical options for treatment are important to discuss with appropriate patients with newly diagnosed early-stage cervical cancer. Radical trachelectomy is considered to be a safe oncologic alternative to radical hysterectomy and has been recognized by the National Comprehensive Cancer Network (NCCN) as a fertility-sparing treatment option for patients with stage IA1 with lymphovascular space invasion, stage IA2, and stage IB1 cervical cancers. [2]

Several studies have reported on quality of life (QOL) and sexual dysfunction in patients after radical hysterectomy [3–6], however, limited data is available on these measures in patients undergoing radical trachelectomy. The few prospective studies available to date have assessed short-term QOL and sexual function in radical trachelectomy

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patients undergoing vaginal or abdominal radical trachelectomy and comparing these to patients undergoing radical abdominal hysterectomy or healthy controls. These studies have shown a decrease in QOL measures in patients undergoing radical trachelectomy, which may reflect a new level of functioning in cervical cancer survivorship. [7–9] We sought to prospectively assess quality of life, sexual functioning, symptoms, and satisfaction with healthcare decisions in women undergoing radical trachelectomy for early-stage cervical cancer.

2. Methods

MD Anderson Institutional Review Board approval was obtained for this prospective study. Informed consent was obtained from eligible patients pre-operatively following surgical consent.

2.1. Patient eligibility

Women age 18–40 years diagnosed with histologically confirmed early-stage (stage IA1 with lymphovascular space invasion, stage IA2, and stage IB1) primary adenocarcinoma, squamous cell carcinoma, or adenosquamous carcinoma of the cervix who were eligible for radical trachelectomy were approached for study participation. Patients had to be suitable candidates for surgery, able to read and write in English or Spanish, and signed approved Informed Consent. Patients were excluded if they had stage IB2 or higher disease, history of a second primary malignancy within 3 years, history of pelvic or abdominal radiotherapy, pregnancy, evidence of metastatic disease by imaging, or any contraindications to surgery. Additional patients were excluded from the final analysis post-operatively if the procedure was converted to radical hysterectomy or had limited study participation for baseline or postoperative questionnaire completion.

2.2. Procedure

MD Anderson faculty trained in radical trachelectomy surgical techniques performed the procedure via abdominal, laparoscopic, or robotic method as previously described. [10–12] Pelvic lymphadenectomy with or without sentinel lymph node mapping and biopsies was performed. Method of vaginal closure, cerclage placement, and insertion of device to prevent cervical stenosis was left to the discretion of the primary surgeon. Intraoperative frozen section pathology analysis of the endocervical margin and any suspicious lymph nodes was routinely performed. If frozen section pathology revealed a positive margin < 10 mm from the endocervical resection of the specimen, either an additional margin was taken if possible, or the procedure was converted to a radical hysterectomy. If frozen section pathology revealed a positive lymph node, then the procedure in its entirety was aborted and the patient was referred for combined chemotherapy and pelvic radiation.

2.3. Study survey and data collection

After providing written consent, pre-operative demographic data and surgical outcomes were collected from the patient's electronic medical record. Patients were asked to complete 5 self-administered questionnaires pre-operative (within 2 weeks of scheduled surgery), and approximately 4–6 weeks postoperatively, 6 months after surgery, 1 year after surgery, and annually thereafter for 4 years to complete 5 years after initial surgery. For women not receiving their follow-up at MD Anderson, questionnaires were mailed to the patients at the above time points with a pre-paid return envelope marked confidential and addressed directly to the principal investigator. The 5 self-administered questionnaires included:

1) The *General Health-Related Quality of Life* (*SF-12*) instrument is a 12-item questionnaire estimating 8 health domains including physical functioning, role-physical, role-emotional, mental health, bodily pain, vitality, social functioning, and general health. Scores are given in each domain and summary scores for overall physical and mental status. [13]
2) The *Functional Assessment of Cancer Therapy* (*FACT-Cx*) is the FACT-G plus cervix subscale. The FACT-G is the generic core to measure quality of life for patients with cancer. This instrument contains 27 questions from 4 domains: physical well-being, social/family well-being, emotional well-being, and functional well-being. The cervix subscale consists of 15 questions pertaining to patients with cervix cancer. [14] Scores range from 0 to 108 for the FACT-G, and 0 to 60 on the cervix subscale. [15]
3) The *MD Anderson Symptom Inventory* (*MDASI*) is a 19-item questionnaire assessing symptoms including pain, fatigue, nausea/vomiting, anorexia, sleep disturbances, and distress. This also includes an assessment on how those symptoms have interfered with the patient's general well-being, including their general activity, mood, ability to walk and perform normal work functions, relationships with others, and enjoyment of life. The validity and reliability of the MDASI has been well-established. [16]
4) The *Female Sexual Functioning Index* (*FSFI*) is a 19-item multidimensional survey measuring 5 domains including sexual desire, arousal (both subjective and physiological), lubrication, orgasm, satisfaction, and pain. Higher scores indicate better sexual functioning. [17] The full scale score for women with sexual dysfunction was a mean of 19.2, compared with a mean of 30.5 for controls. [18]
5) The *Satisfaction with Decision* (*SWD*) scale is a 6-item survey that measures the patient's satisfaction with health care decisions. The instrument has excellent reliability (Cronbach's alpha = 0.86) and good validity. [19]

2.4. Statistics

We used descriptive statistics to summarize demographic and clinical characteristics of the patients in this study. Demographic characteristics included age, race, weight, and body mass index (BMI). Clinical characteristics included diagnosis, comorbidities, and surgical history. We used descriptive statistics to summarize the scores for the SF-12, FACT-Cx, MDASI, and FSFI instruments at baseline and at each follow-up visit (4–6 weeks -all except FSFI, 6 months, 1 year, and annually for 4 years). We estimated the mean score for each instrument at each time point with a 95% confidence interval. We illustrated the distribution of the instrument scores over time with boxplots. We summarized and analyzed the change from baseline to each follow-up visit for the SF-12, FACT-Cx, MDASI, and FSFI instruments. We used mixed effects regression to model the change from baseline in scores for the SF-12, FACT-CX, MDASI, and FSFI instruments as a function of time. As a sensitivity analysis we conducted the analysis of change scores described above with the last available instrument score replacing missing instrument scores for those patients who drop out of the study or become ineligible due to recurrence.

3. Results

3.1. Surgical outcomes

Thirty-nine patients enrolled to the study, and 32 patients were evaluable for QOL analysis after undergoing radical trachelectomy. Seven patients were excluded from final QOL analysis due to conversion to radical hysterectomy intra-operatively (n = 3) or limited study participation due to no baseline or postoperative questionnaires completed (n = 4). Clinical and demographic data is listed in Table 1. Median age was 30.7 years (range 21.4–38.7). Median BMI was 25.3 kg/m (range 16.1–44.4). Majority of patients had stage IB1 disease (n = 16, 50%), grade 2 (n = 14, 44%) or grade 3 (n = 13, 40%), and adenocarcinoma (n = 15, 47%) or squamous (n = 14, 44%) histology. Most patients underwent a robotic surgical approach (n = 21, 66%) for the radical

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