Utility Scores and Treatment Preferences for Clinical Early-Stage Cervical Cancer

Elizabeth L. Jewell, MD, MHSc[1,2,3,*], Michael Smrtka, MD[1], Gloria Broadwater, MS[4], Fidel Valea, MD[1,2,3], Debra M. Davis[1,2], Kimberly C. Nolte, MHS[1,2], Renea Valea, MSW, LCSW[1,2], Evan R. Myers, MD, MPH[1,3,5,6], Gregory Samsa, PhD[6], Laura J. Havrilesky, MD, MHSc[1,2,3]

[1]Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, NC, USA; [2]Division of Gynecologic Oncology, Duke University Medical Center, Durham, NC, USA; [3]Duke Comprehensive Cancer Center, Duke University Medical Center Durham, NC, USA; [4]Cancer Center Biostatistics, Duke University Medical Center, Durham, NC, USA; [5]Division of Clinical and Epidemiological Research, Duke University Medical Center, Durham, NC, USA; [6]Duke Center for Clinical Health Policy Research, Duke University Medical Center, Durham, NC, USA

A B S T R A C T

Objectives: To determine utility scores for health states relevant to the treatment of early-stage, high-risk cervical cancer. **Methods:** Seven descriptive health states incorporating the physical and emotional aspects of medical treatment, recovery, and prognosis were developed. Forty-five female volunteers valuated each health state using the visual analogue score (VAS) and time trade off (TTO) methods. Treatment options were ranked by mean and median TTO scores. The 95% confidence intervals were calculated to determine the statistical significance of ranking preferences. The Wilcoxon rank-sum test was used to compare central tendencies related to age, race, parity, and subject history of abnormal cervical cytology. **Results:** VAS and TTO scores were highly correlated. Volunteers ranked minimally invasive radical hysterectomy with low-risk features as most preferred (mean TTO = 0.96; median TTO = 1.00) and aborted radical hysterectomy followed by chemoradiation as least preferred (mean TTO = 0.69; median TTO = 0.83). Health states that included radical surgery were ranked higher than those that included chemoradiation, either

in the adjuvant or primary setting. When survival was comparable, volunteers rated radical hysterectomy with high-risk pathology followed by adjuvant chemoradiation (mean TTO = 0.78; median TTO = 0.92; 95% CI: 0.69–0.87) similarly to chemoradiation alone (mean TTO = 0.76; median TTO 0.90; 95% CI: 0.66–0.86; p = NS). Utility scores for the majority of health states were not significantly associated with age, race, parity, or subject history of abnormal cervical cytology. **Conclusion:** Subjects consistently preferred surgical excision to treat early-stage, high-risk cervical cancer and chose a minimally invasive approach. Such utility scores can be used to incorporate quality-of-life effects into comparative-effectiveness models for cervical cancer.

Keywords: cervical cancer, cost analyses, treatment options, utility scores.

Copyright © 2011, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

Introduction

Cervical cancer is the second most common cancer among women worldwide, with approximately 493,000 new cases and 274,000 deaths in 2009. Although cervical cytology screening programs have steadily reduced the incidence of cervical cancer in developed countries, an estimated 11,270 women were diagnosed with the disease and 4070 died from their disease in the United States in 2009 [1]. Women with early-stage cervical cancer have several treatment options available, including radical hysterectomy alone, radical hysterectomy followed by adjuvant chemoradiation tailored to risk factors, chemoradiation alone, or neoadjuvant chemotherapy followed by hysterectomy.

To date, no prospective randomized clinical trial has determined the "best" treatment option for patients with high-risk, early-stage disease. Older, retrospective studies reported approximately equal rates of cure using radical hysterectomy or primary

radiotherapy [2–5]. Given similar rates of cure, treatments have traditionally been based on physician preference [6–13]. Studies over the past 10 years have demonstrated that the addition of chemotherapy to radiotherapy reduces recurrence rates and improves overall survival [10–12,14,15] and that an increasing number of patients may benefit from adjuvant chemoradiation [10]. Although many practitioners continue to favor surgery with tailored chemoradiation based on pathologic risk factors such as primary treatment for high-risk, early-stage cervical cancer, concerns regarding the cost and potential complications of multimodality therapy have led some to question the need for radical surgery [16].

In response to these issues, two groups have developed health economic models to inform the treatment of stage IB2 cervical cancer. Rocconi et al. [17] reported that radical hysterectomy was a cost-saving strategy for IB2 cervical cancer, saving $500,000 to $2.2 million dollars per additional survivor. Jewell et al. [18] designed a decision model that incorporated the costs of both treatments and

adverse events and estimated a higher cost for surgery with adjuvant treatment ($27,840 per case for radical hysterectomy with tailored adjuvant therapy) compared to primary radiotherapy ($21,403 per case for chemoradiation). Although this analysis did not find that radical hysterectomy was cost saving, sensitivity analysis showed that radical hysterectomy was potentially cost effective (i.e., the cost per life-year saved was within the range considered acceptable—approximately $50,000–75,000/life-year) [18,19]. However, neither model incorporated quality of life (QOL) measures. Cost-effectiveness models that lack consideration of QOL may under- or overestimate the value of a given treatment strategy. Utility scores are used to incorporate QOL effects into cost-effectiveness analyses. Currently, there are no utility data for treatment-related health states relevant to patients with cervical cancer.

The objective of our study was to develop, using standard methods for eliciting societal preferences, an instrument for the derivation of utility values associated with cervical cancer treatment. We estimated the perceived effect on QOL of surgical, radiotherapeutic, and chemotherapeutic treatments, with specific attention to both the usual physical and emotional effects, as well as estimated survival associated with each treatment scenario.

Methods

Health states: description

After Institutional Review Board approval was obtained, descriptions of available treatment options for women with cervical cancer were created by two gynecologic oncologists (E.J. and L.H.). These treatments included: radical hysterectomy with low-risk pathology requiring no additional treatment; minimally invasive radical hysterectomy with low-risk pathology requiring no additional treatment; radical hysterectomy with intermediate-risk pathology with subsequent observation; radical hysterectomy with intermediate-risk pathology requiring adjuvant chemoradiation; radical hysterectomy with high-risk pathology requiring chemoradiation and outpatient brachytherapy; aborted radical hysterectomy with chemoradiation and inpatient brachytherapy; and chemoradiation (including teletherapy and brachytherapy) alone. Physical and emotional aspects of each treatment were outlined and, where appropriate, details about initial postoperative recovery, outpatient whole pelvic radiation, outpatient chemotherapy, and inpatient brachytherapy were described in the health state scenario. Common side effects were incorporated into each description. Related to the phases of treatment, descriptive states were developed in which pathologic findings were known (as in the treatment with radical hysterectomy) or unknown (such as when treatment is by chemoradiation alone). Five-year survival information was included in each health scenario.

Health states: focus group

A focus group composed of two additional gynecologic oncologists, two attending radiation oncologists, two gynecologic oncology nurse clinicians, one oncology physician assistant, one clinical social worker, and two cervical cancer survivors reviewed the health state descriptions in detail and made suggestions regarding the severity or appropriateness of symptoms described as well as their emotional consequences. The cervical cancer survivors participating in the focus group were without evidence of disease and had undergone surgery and/or chemoradiation. Edits to the health state descriptions during this phase included the addition of more specific descriptions of treatments, such as external beam radiotherapy, specific physical symptoms, and physical limitations related to each treatment condition. This process resulted in a final

version of the seven descriptive health states, which can be found in Appendix A at doi:10.1016/j.jval.2010.11.017.

Health states valuation: recruitment of subjects

Forty-five members of the public were recruited using flyers in various public places at our institution. Eligible patients were English-speaking women who had no personal history of cervical cancer. Due to limited funding, we were not able to translate consents into Spanish or other languages. The decision to exclude women with cervical cancer was based upon comments from cervical cancer patients in the focus group who expressed discomfort with the presentation of prognostic information. Subjects were interviewed in an identical process in order to valuate health states related to treatment of cervical cancer. A nominal monetary incentive was offered to offset travel expenses ($25) for 60 to 90 minutes of participation. All recruited subjects completed the study.

Health states valuation: interview method

After obtaining informed consent and collecting demographic information, one of two trained research assistants interviewed volunteers using the visual analogue score (VAS) and time trade off (TTO) methods. The use of the TTO was selected over the standard gamble (SG) because the TTO is potentially less cognitively demanding for subjects. A potentially less difficult task may increase the accuracy of the response. Additionally, the TTO method requires a choice between certain health states; therefore, it measures the number of healthy years that are particular to a health state. Such information is useful to measure health-related QOL. For these reasons, the TTO method was used [19]. Each subject was asked to read a pertinent health state description and to listen while it was read aloud. Health states were scored in a random order. The subject then placed the health state on a continuum (VAS) from 0 to 100, with 100 representing perfect health and 0 representing death. Each respondent made a mark on the VAS. The scale contained no gradations other than 0 and 100. The VAS was calculated as the distance from 0 to the mark placed by the subject, divided by the measure distance from 0 to 100 on the VAS. The TTO interview was then administered as follows: the subject was asked to assume a remaining life expectancy of 30 years, and to choose between 30 years in the health state described or "X" years in a state of perfect health. The utility of the health state, a number between 0 and 1, was calculated as the minimum number
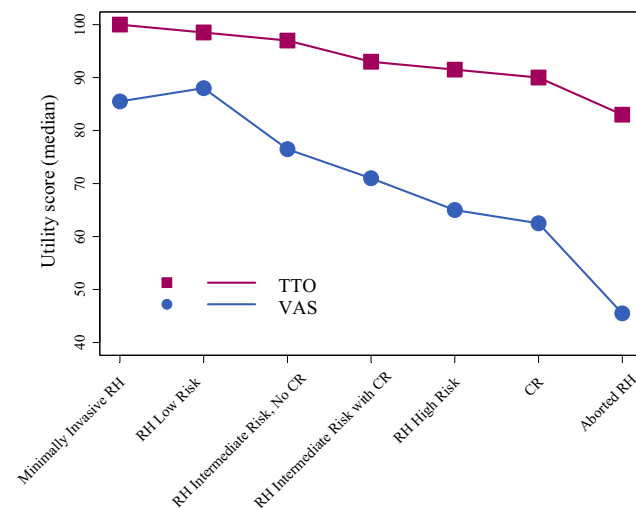

Fig. 1 – Plot of median utility scores for visual analogue score (VAS) and time trade off (TTO) for each treatment health state. CR, chemoradiation; RH, radical hysterectomy.

Table 1 – Descriptive statistics of volunteers.

Volunteer characteristics	
Age (years)	37.6 (19–61)
Race	
White	21
Asian	5
African American	19
Prior abnormal Pap	18 (40%)
Gravidity, median (range)	2 (0–17)
Parity, median (range)	2 (0–12)

of years the patient would accept divided by 30. The 30-year time horizon was chosen as a potentially meaningful life expectancy because most cervical cancer patients are diagnosed between the ages of 35 and 55. We acknowledge the limitation that the ages and health states of subjects with and without a history of cervical cancer can vary significantly [19]. Treatment health states that included prognostic information and 5-year survival information were only valuated by volunteers without a history of cervical cancer. The rationale for this methodological decision was based upon comments from cervical cancer patients in the focus group expressing discomfort with the survival information.

Statistics

SAS Version 9.2 (SAS Institute, Cary, NC) was used to perform the analysis. The mean, standard deviation, median, and range of values for each health state for all 45 subjects were calculated. In this research study, no anchor states were included to determine the comprehension of the participants. Therefore, volunteer responses with the largest average absolute difference of VAS and TTO scores were excluded from the analysis with the assumption that such individuals did not understand the utility scoring exercise. Five patients had a difference in their TTO and VAS score greater than 50 and were excluded. Health states were ranked by preference based on the mean and median. To determine the statistical difference in this scoring and ranking of health states, 95% confidence intervals (CIs) of the mean TTO scores were provided. TTO scores were used during this analysis since this choice-based method provides an accurate assessment of the utility score [19,20]. Wilcoxon rank sum tests were used to compare central tendencies for each health state for subgroups (age dichotomized at the median) and likewise for parity (grouped as none, 1–2, more than 2), race, and prior abnormal cervical cytology. The Spearman correlation coefficient and P value were used to compare scores

obtained using the two valuation methods (VAS and TTO) (Fig. 1). The Spearman Correlation evaluated the relative similarity of utility scoring using various methods of response: scaling (VAS) versus choice (TTO).

Results

All 45 recruited subjects completed the study. The mean age of the subjects was 37.6 years (range, 19-61 years old). Nineteen subjects were African American, 21 were white, and 5 were of Asian descent. Forty percent of the volunteers had a history of abnormal cervical cytology. The median parity for participants was 2 (range, 0–17). Subject characteristics are listed in Table 1.

For each health state, the mean TTO-derived utility score was greater than the mean VAS-derived utility score. The Spearman test indicated that all TTO and VAS scores were highly positively correlated with each other ($P < 0.05$). To test consistency of individual scores between VAS and TTO, the absolute difference between VAS and TTO responses for each health state was calculated. The median absolute difference per health state was 24.3, and the mean was 26.4 (range, 3.6-67.9). The responses of the five subjects (10% of the volunteers) for whom the average difference in scores was greater than 50 were removed prior to the analysis.

Utility scores for treatment of cervical cancer are listed in Table 2. The mean and median utility scores for health states requiring adjuvant chemotherapy or radiation were consistently lower than those for health states that only required surgery. The health state describing a minimally invasive radical hysterectomy with low-risk pathologic features was most preferred (TTO = 0.95), whereas an aborted radical hysterectomy with subsequent chemoradiation including brachytherapy was least preferred (TTO = 0.68). Any completed radical hysterectomy was ranked higher than chemoradiation alone, regardless of 5-year survival information and subsequent need for adjuvant chemoradiation.

Scores for the different health states (e.g., health states ranked 4–6 in Table 3) that included chemoradiation did not vary significantly regardless of whether radical hysterectomy was performed and prognosis was worse. The only statistically significant difference in utility scores was observed between the three health states not requiring chemoradiation (95% CIs for minimally invasive radical hysterectomy with low-risk pathology/no adjuvant chemoradiation, open radical hysterectomy with low-risk pathology/no adjuvant chemoradiation, and open radical hysterectomy with intermediate-risk pathology/no adjuvant chemoradiation were 0.89–0.99, 0.82–0.97, and 0.82–0.96, respectively) and the health

Table 2 – VAS and TTO scores for each treatment option.

Treatment scenario	VAS					TTO					Spearman correlation coefficient for VAS and TTO
	Mean	Median	SD	Lower CI	Upper CI	Mean	Median	SD	Lower CI	Upper CI	
Minimally invasive, low risk, no adjuvant CR	0.79	0.86	0.17	0.74	0.84	0.96	1.00	0.12	0.92	1.00	.34
RH, low risk, no adjuvant CR	0.82	0.88	0.18	0.76	0.88	0.90	0.99	0.22	0.83	0.97	.44
RH, intermediate risk, no adjuvant CR	0.72	0.77	0.20	0.66	0.78	0.90	0.97	0.21	0.83	0.97	.36
RH, intermediate risk, adjuvant CR	0.64	0.71	0.22	0.57	0.71	0.81	0.93	0.29	0.72	0.90	.56
RH, high risk, adjuvant CR	0.62	0.65	0.24	0.55	0.69	0.78	0.92	0.31	0.69	0.87	.62
CR	0.54	0.63	0.27	0.46	0.62	0.76	0.90	0.32	0.66	0.86	.69
Aborted RH, followed by CR	0.46	0.46	0.24	0.39	0.53	0.69	0.83	0.35	0.58	0.80	.61

CI, confidence interval; CR, chemoradiation; RH, radical hysterectomy; SD, standard deviation; TTO, time trade off; VAS, visual analogue score.

Table 3 – Ranking of treatment-related health states by mean TTO score with 95% CI.

Rank	Treatment	Mean	SD	Lower CI	Upper CI	Median	Min	Max
1	Minimally invasive, low risk, no adjuvant CR	0.94	17.81	0.89	0.99	1.00	0.03	1.00
2	RH, low risk, no adjuvant CR	0.89	24.99	0.82	0.97	1.00	0.03	1.00
3	RH, intermediate risk, no adjuvant CR	0.89	24.12	0.82	0.96	0.97	0.03	1.00
4	RH, intermediate risk, adjuvant CR	0.80	29.66	0.72	0.89	0.93	0.03	1.00
5	RH, high risk, adjuvant CR, HDR brachy	0.78	31.38	0.69	0.87	0.90	0.03	1.00
6	CR	0.76	32.64	0.66	0.85	0.90	0.03	1.00
7	Aborted RH, followed by CR	0.68	36.79	0.57	0.79	0.83	0.03	1.00

CI, confidence interval; CR, chemoradiation; RH, radical hysterectomy; TTO, time trade off.

state describing an aborted radical hysterectomy with subsequent chemoradiation (95% CI: 0.57–0.79; Table 3).

The results described above and their statistical significance did not change when volunteers with an average absolute difference in VAS and TTO scoring greater than 50 were included in the analysis. When analyzing the effects of age, parity, race, and history of abnormal cervical cytology on the utility scores of treatment-related health, no significant associations were observed.

Discussion

Comparative effectiveness analyses offer one way to examine options in the management of a disease. Cost-effectiveness models determine the costs and outcomes associated with different management strategies by comparing cost per year of life saved. Models that incorporate QOL assessment in the form of utility scores are called cost-utility analyses (CUAs). These models quantify improvements in survival, cost, and disease- and treatment-related morbidity [20]. QOL is an important component of decision making in health care; researchers and clinicians are becoming more aware of the need to obtain information about how the diagnosis and treatment of disease affects the physical, mental, and social well-being of patients. Studies assessing the cost and effectiveness of specific interventions should also account for the changes in QOL that are associated with each intervention and its known adverse effects. CUA studies that report results in cost per quality-adjusted life year are strongly recommended [19–21]. Our research enhances the literature about social preferences in the treatment of cervical cancer and can be used to inform future CUAs.

Our study is the first to report utility scores reflecting the female societal preference for current treatment options for early-stage cervical cancer [22–32]. We found that health states describing chemoradiation were ranked lower than health states describing surgery regardless of adjuvant chemoradiation. Even in health scenarios with similar 5-year survival, subjects ranked surgery followed by tailored adjuvant treatment as equivalent or slightly preferred over primary chemoradiation. Based on the rankings of treatment options, we hypothesize that there is a perceived benefit to the physical removal of cancer. Subjects ranked a minimally invasive approach highest, suggesting that an overnight hospitalization, smaller incision sites, and faster return to activities of daily living are preferred. Subjects also appeared to incorporate 5-year survival data into their rankings, ranking aborted radical hysterectomy, with the lowest survival estimate, as least preferred.

Other studies have examined QOL scores from the perspective of women with cervical cancer. The aim of this study was to develop utility scores assessing society's preferences for treatment options related to cervical cancer to be applied to cost-effectiveness models. Interestingly, the societal health state preferences identified in this study seem to be congruent with patient preferences reported in other studies. Frumovitz et al. [33] compared QOL and sexual functioning in cervical cancer survivors treated with either radical hysterectomy and lymph node dissection or radiotherapy. Cervical cancer survivors treated with radiotherapy had worse QOL and sexual functioning than those treated with radical hysterectomy and lymph node dissection [33]. These QOL scores are in concordance with the current study, in which subjects ranked surgery alone as preferred to chemoradiation alone. Greimel et al. [34] investigated the long-term treatment side effects on the QOL and sexual functioning of cervical cancer survivors and found that QOL scores of cervical cancer survivors who underwent surgery and adjuvant radiation were significantly lower than those of patients who had surgery alone. Similarly, Distefano et al. [35] reported a better QOL in women with locally advanced cervical cancer who received surgery alone. We similarly found subjects preferred the single-treatment modality of surgery over health states requiring adjuvant chemoradiation.

It is also interesting that subjects in this study ranked chemoradiation alone poorly; one might predict that subjects would rank this treatment as preferred over surgery, which would be followed by chemoradiation with its potential complications. In the current study, however, the health states that incorporated chemoradiation were more highly ranked if surgery was a component of the treatment even if outcomes were comparable [31–35]. It is possible that the choice of the single-treatment modality of surgery over chemoradiation may be related to the fear of radiation, anticipation of complications related to the combination of chemotherapy and radiation, or merely a preference to have the tumor surgically removed. It appeared that subjects were willing to undergo radical surgery and "risk" the need for adjuvant chemoradiation despite the expectation of the side effects and prolonged treatment detailed in the health state descriptions.

In the current study, several patients had large differences in their rating of VAS-derived scores when compared with TTO-derived scores for each health state. For example, one patient had a mean VAS score of 0.03 for all health states evaluated, but a mean TTO score of 1.0. An explanation for some of the differences between VAS and TTO scores may be the scoring method. VAS is a scaling method, whereas TTO is a choice method that requires the subject to conceptualize a tradeoff between quantity and QOL. It is possible that a health state can be considered unpleasant, and so worthy of a lower VAS score, but not so unpleasant as to compel a trade off in life expectancy. Alternatively, those patients with the largest difference between mean VAS- and TTO-derived scores may have inadequately conceptualized the TTO method. Future studies may benefit from exercises that assess whether a volunteer understands the TTO-scoring method by inclusion of graded "anchor states."

Our study had several limitations. The power of the study was limited by the small sample size and the fact that some subjects responded with a wide discrepancy of scores. As a result, the standard deviation and range of responses for each health state was broad. The study would have been strengthened by the inclusion of a more diverse population, particularly the inclusion of Latina women. Furthermore, the study focused on the acute postoperative complications related to cervical cancer treatment, including

postoperative pain, prolonged bladder catheterization, acute diarrhea related to radiation therapies, and nausea and vomiting associated with chemotherapy; assumptions were made in the health states that these symptoms resolved soon after the conclusion of treatment. The omission of late and more severe complications associated with radical surgery and chemoradiation was made in order to allow volunteers to score preferences on the average experience of treatment itself, not on all potential adverse events. Finally, our ranking of treatments was not derived using women with cervical cancer, and therefore do not necessarily represent their preferences. While QOL from the perspective of the individual patient is important and relevant, utility scores assess society's preferences, and it is therefore standard to derive these using public volunteers unaffected by the disease. This allows for utility scores to be used in health economic models that are designed from the societal perspective [19].

Conclusion

In conclusion, we have established a pilot set of societal preferences for health states related to the treatment of early-stage cervical cancer. This project expands the set of descriptive health states related to gynecologic cancers and can be used to inform cost-effectiveness models [18]. As the number of patients cured of their disease increases, treatments with equivalent survival, similar cost, but better QOL will surely be the optimal choice for patients.

Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at doi:10.1016/j.jval.2010.11.017, or if hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

REFERENCES

[1] Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2009. CA Cancer J Clin 2009;59:225–49.
[2] Hopkins MP, Morley GW. Radical hysterectomy versus radiation therapy for stage IB squamous cell cancer of the cervix. Cancer 1991;68:272–7.
[3] Landoni F, Maneo A, Colombo A, et al. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. Lancet 1997;350:535–40.
[4] Morrow CP, Bundy BN, Kurman RJ, et al. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a gynecologic oncology group study. Gynecol Oncol 1991;40:55–65.
[5] Newton M. Radical hysterectomy or radiotherapy for stage I cervical cancer. A prospective comparison with 5 and 10 years follow-up. Am J Obstet Gynecol 1975;123:535–42.
[6] Eifel PJ, Morris M, Wharton JT, Oswald MJ. The influence of tumor size and morphology on the outcome of patients with FIGO stage IB squamous cell carcinoma of the uterine cervix. Int J Radiat Oncol Biol Phys 1994;29:9–16.
[7] Havrilesky LJ, Leath CA, Huh W, et al. Radical hysterectomy and pelvic lymphadenectomy for stage IB2 cervical cancer. Gynecol Oncol 2004;93:429–34.
[8] Kamelle SA, Rutledge TL, Tillmanns TD, et al. Surgical-pathological predictors of disease-free survival and risk groupings for IB2 cervical cancer: do the traditional models still apply? Gynecol Oncol 2004;94:249–55.
[9] Keys HM, Bundy BN, Stehman FB, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant

hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med 1999;340:1154–61.
[10] Peters WA, 3rd, Liu PY, Barrett RJ 2nd, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol 2000;18:1606–13.
[11] Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med 1999;340:1144–53.
[12] Sedlis A, Bundy BN, Rotman MZ, et al. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: a gynecologic oncology group study. Gynecol Oncol 1999;73:177–83.
[13] Whitney CW, Stehman FB. The abandoned radical hysterectomy: a gynecologic oncology group study. Gynecol Oncol 2000;79:350–6.
[14] Eifel PJ, Winter K, Morris M, et al. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: an update of radiation therapy oncology group trial (RTOG) 90-01. J Clin Oncol 2004;22:872–80.
[15] Whitney CW, Sause W, Bundy BN, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB–IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol 1999;17:1339–48.
[16] Grigsby PW. Primary radiotherapy for stage IB or IIA cervical cancer. J Natl Cancer Inst Monogr 1996;21:61–4.
[17] Rocconi RP, Estes JM, Leath CA 3rd, et al. Management strategies for stage IB2 cervical cancer: a cost-effectiveness analysis. Gynecol Oncol 2005;97:387–94.
[18] Jewell EL, Kulasingam S, Myers E, et al. Primary surgery versus chemoradiation in the treatment of IB2 cervical carcinoma: a cost effectiveness analysis. Gyneco Oncol 2007;107:532–40.
[19] Gold MR, Russell L, Weinstein M. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press; 1996.
[20] Drummond M. Methods for the Economic Evaluation of Health Care Programmes. 3rd ed. Oxford Medical Publications. 2005.
[21] Brazier J, Deverill M, Green C, et al. A review of the use of health status measures in economic evaluation. Health Technol Assess 1999;3(i–iv):1–64.
[22] Calhoun EA, Bennett CL, Peeples PA, et al. Perceptions of cisplatin-related toxicities among ovarian cancer patients and gynecologic oncologists. Gynecol Oncol 1998;71:369–75.
[23] Lloyd A, Nafees B, Narweska J, et al. Health state utilities for metastatic breast cancer. Br J Cancer 2006;95:683–90.
[24] Ortega A, Dranitsaris G, Sturgeon J, et al. Cost-utility analysis of paclitaxel in combination with cisplatin for patients with advanced ovarian cancer. Gynecol Oncol 1997;66:4454–63.
[25] Ramsey SD, Andersen MR, Etzioni R, et al. Quality of life in survivors of colorectal carcinoma. Cancer 2000;88:1294–303.
[26] Stein K, Sugar C, Velikova G, Stark D. Putting the 'Q' in quality adjusted life years (QALYs) for advanced ovarian cancer—an approach using data clustering methods and the internet. Eur J Cancer 2007;43,104–13.
[27] Sun CC, Bodurka DC, Donato ML, et al. Patient preferences regarding side effects of chemotherapy for ovarian cancer: do they change over time? Gynecol Oncol 2002;87:118–28.
[28] Havrilesky LJ, Broadwater G, Davis DM, et al. Determination of quality of life-related utilities for health states relevant to ovarian cancer diagnosis and treatment. Gynecol Oncol 2009;113:216–20.
[29] Bruner DW, Hanlon A, Mazzoni S, et al. Predictors or preferences and utilities in men treated with 3D-CRT for prostate cancer. Int J Radiat Oncol Biol Phys 2004;58:34–42.
[30] EuroQol—a new facility for the measurement of health related quality of life. The EuroQol Group. Health Policy 1990;16:199–208.
[31] Frank SJ, Pisters LL, Davis J, et al. An assessment of quality of life following radical prostatectomy, high dose external beam radiation therapy and brachytherapy iodine implantation as monotherapies for localized prostate cancer. J Urol 2007;177:2151–6.
[32] Shrader-Bogen CL, Kjellberg JL, McPherson CP, et al. Quality of life and treatment outcomes: prostate carcinoma patients' perspective after prostatectomy or radiation therapy. Cancer 1997;79:1977–86.
[33] Frumovitz M, Sun CC, Schover LR, et al. Quality of life and sexual functioning in cervical cancer survivors. J Clin Oncol 2005;23:7428–36.
[34] Greimel ER, Winter R, Kapp KS, et al. Quality of life and sexual functioning after cervical cancer treatment: a long-term follow-up study. Psychooncology 2009;18:476–82.
[35] Distefano M, Riccardi S, Capelli G, et al. Quality of life and psychological distress in locally advanced cervical cancer patients administered pre-operative chemoradiotherapy. Gynecol Oncol 2008;111:144–50.