Quality of Life Is Better After Modern Radiotherapy Compared With Surgery

For decades, organ preservation has been an abiding principle of radiotherapy, with the underlying belief being that a person with preserved native anatomy has better physical functioning (and consequently a better quality of life) than one who has undergone surgical removal of organs followed by reconstruction. Comparing modern radiotherapy vs surgery for prostate cancer, we argue the following points:

• Head-to-head comparisons have shown modern radiotherapy to be much better than surgery in terms of urinary and sexual function.

• While bowel toxicity has historically been moderately worse after radiotherapy, this decline in function can now be mitigated largely by using modern radiotherapy techniques, such as image guidance and possible additional rectal spacing.

• Quality of life following radiotherapy has continued to improve as advances have been made in radiotherapeutic techniques, whereas prostate surgery—despite the availability of newer, once-promising techniques such as laparoscopic or robot-assisted radical prostatectomy—remains largely unchanged in regard to long-term...
impacts on quality of life. Thus, radiotherapy is the better choice for treatment of prostate cancer.

Typically, quality-of-life evaluation after prostate cancer treatment involves three major domains: urinary function, sexual function, and bowel function. Older studies comparing quality of life after surgery vs radiotherapy have been difficult to interpret given the differences in patient populations, which likely bias in favor of radical prostatectomy, and the fact that older radiation techniques were used. Patients who undergo radical prostatectomy are typically younger and have fewer comorbidities, with better baseline sexual function and physical function overall. Furthermore, the rapid changes occurring in radiation technology make it difficult, if not misleading, to evaluate radiotherapy for prostate cancer that was administered prior to 2010.

Several large, modern, prospective cohort studies have assessed quality of life after prostate cancer-directed therapy. The CEASAR study, which investigated 2,550 men diagnosed with prostate cancer in 2011 and 2012, found that men who underwent radical prostatectomy had greater declines in patient-reported urinary and sexual functioning than those treated with external beam radiotherapy.[1] Notably, 77% of the surgically treated men in this study underwent robotic surgery, largely reflecting the contemporary standard of care. The study found that patients who underwent radical prostatectomy had an almost threefold increase in moderate or severe problems with urinary leakage compared with those who received radiotherapy (14% vs 5%, respectively; odds ratio [OR], 4.5; 95% CI, 2.7–7.3). Despite better baseline function, more men who underwent radical prostatectomy were bothered by sexual dysfunction compared with those treated with external beam radiotherapy (44% vs 28%; \( P < .001 \)).

For the men in the CEASAR study who had erections sufficient for intercourse prior to treatment, the outcomes achieved with radiotherapy were superior to those with surgery. At 3-year follow-up, 43% of men who underwent radical prostatectomy and 53% of men treated with radiotherapy maintained functional erections, even though the men who had surgery were on average 6 years younger (62 years vs 68 years) than those who had received radiotherapy and would intrinsically be assumed to have better maintenance of sexual function over time.[1] Regarding bowel function, there were similar frequencies of bowel bother, bloody stools, and bowel urgency between the groups treated with prostatectomy vs external beam radiotherapy, although the odds of bowel urgency were lower at 3 years for men treated with radical prostatectomy compared with external beam radiotherapy (3% vs 7%; OR, 0.3; 95% CI, 0.2–0.6) and active surveillance (3% vs 5%; OR, 0.5; 95% CI, 0.3–0.9).[1]

Chen et al.[2] also recently examined a prospective cohort of patients in North Carolina who were treated from 2011 to 2013 in the North Carolina Prostate Cancer Comparative Effectiveness & Survivorship Study (NC ProCESS), which enrolled 1,141 men. They found that sexual function was poor at 24 months post-treatment after prostatectomy for 57.1% of men who reported normal baseline sexual function compared with 27.2% of men who received external beam radiotherapy. Among men
with normal urinary control at baseline, only 34.3% reported normal control 24 months after prostatectomy compared with 73% after external beam radiotherapy. Regarding bowel function, 57.4% of men with normal baseline function had normal function after prostatectomy compared with 42.7% after external beam radiotherapy. The CEASAR[1] and Chen et al[2] studies were published simultaneously in *JAMA*, and the editorialists noted that the findings support that “urinary incontinence and sexual dysfunction [is] worse after surgery, followed by recovery but persistent difficulty for some men.”

Given the age- and health-related bias favoring men selected for prostatectomy, perhaps the most powerful argument regarding urinary and sexual function comes from the landmark UK ProtecT study, which randomized patients between 1999 and 2009 to active surveillance, radical prostatectomy, or three-dimensional (3D) conformal radiotherapy.[3] Despite the older radiation technology used in the study, effects on urinary function and sexual function with radiotherapy were modest compared with surgery. Men who underwent prostatectomy were more likely to be wearing incontinence pads (17%) compared with those treated with radiotherapy (4%). Interestingly, men who received radiotherapy had a lower likelihood of wearing pads compared with men in the active surveillance group (8%). Improvements in urinary irritative/obstructive symptoms were also seen previously with radiotherapy.[4] Furthermore, men who underwent radiotherapy (despite 6 months of androgen deprivation therapy) had better long-term sexual functioning compared with men who underwent surgery.[3] Specifically, 30% of men treated with radiation could have erections firm enough for intercourse 6 years after treatment compared with 17% of the men who underwent prostatectomy. Bowel function was worse for the radiotherapy group in the ProtecT study, with a greater frequency of bloody stools reported among men treated with 3D conformal radiotherapy (5.6%) compared with patients who underwent prostatectomy (1.1%).[3]

As these studies show, the bowel bother domain is usually the most problematic quality-of-life domain for radiotherapy. However, recent innovations have improved bowel outcomes after radiotherapy. Modern image-guided radiotherapy has been shown to have relatively minimal impact on bowel symptoms and compares favorably with older data.[5] In addition to image guidance, other technologies, such as radiofrequency prostate tracking, have also been shown to reduce declines in bowel function.[6] Displacing the rectum using an injected bioabsorbable hydrogel spacer can further reduce bowel toxicity: a recent blinded, prospective, randomized, phase III trial demonstrated that at 3-year follow-up, 41% of men who did not have a hydrogel spacer placed experienced a decline in bowel-related quality of life compared with 14% of men in whom a spacer was used.[7] Thus, modern radiotherapy of the sort practiced in 2017 is associated with lower levels of bowel toxicity and changes in quality of life compared with treatments delivered a decade ago.

Another complaint often levied against radiotherapy is treatment duration, which historically has often been 8 weeks or longer. However, several phase III trials have demonstrated noninferiority for both disease control and major toxicity (as well as meaningful improvements in quality of life) with the use of regimens involving as few as 7 to 28 radiotherapy sessions, which can be completed in a fraction of the time typically utilized for prostate radiotherapy.[8-10] Notably, these three large randomized trials...
(each with between 1,000 and 3,000 patients enrolled) demonstrated no difference in severe early or late toxicity by treatment arm (although in some of these trials, small increases in more mild urinary or bowel toxicity were observed).

In contrast, new surgical technology has not improved quality-of-life outcomes. Comparing laparoscopic radical prostatectomy (LRP), robot-assisted radical prostatectomy (RARP), and open radical prostatectomy (ORP), a recent Cochrane Database systematic review concluded, “There is no high-quality evidence to inform the comparative effectiveness of LRP or RARP compared to ORP for oncological outcomes. Urinary and sexual quality-of-life–related outcomes appear similar. Overall and serious postoperative complication rates appear similar. The difference in postoperative pain may be minimal.”[11] A nonrandomized but prospective comparison of (laparoscopic) RARP vs ORP in Sweden found no difference in urinary symptoms, but the authors noted a small improvement in erectile dysfunction with RARP.[12] However, an analysis of the Surveillance, Epidemiology, and End Results–Medicare dataset identified higher rates of erectile dysfunction and voiding dysfunction with minimally invasive radical prostatectomy compared with ORP,[13] perhaps indicating that the small potential benefit seen in prospective studies may not translate when applied across all communities.

In conclusion, modern radiotherapy is superior to prostatectomy in terms of a patient’s post-treatment quality of life. Obsolete comparisons of older forms of radiotherapy and prostatectomy do not reflect current knowledge. The most recent prospective comparisons of radiotherapy and prostatectomy report better urinary and sexual function following radiotherapy. Modern innovations such as hydrogel spacers, image guidance, radiofrequency tracking, and hypofractionated[14] and stereotactic[15] delivery of radiation have reduced the bowel bother that occurs after radiotherapy treatment, to the point where the risk of bowel effects with radiotherapy is greatly outweighed by the serious urinary incontinence and declines in sexual function brought about by prostatectomy. Innovations in prostate surgery have not significantly improved patients’ quality of life. Therefore, in 2017, the preferred option for prostate cancer treatment is undoubtedly modern radiotherapy.

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References:


