Adjuvant and Salvage Radiotherapy after Prostatectomy: American Society of Clinical Oncology Clinical Practice Guideline Endorsement
Introduction

The purpose of this endorsement is to endorse the AUA/ASTRO guideline on Adjuvant and Salvage Radiotherapy after Prostatectomy in accordance with ASCO’s policy and set of procedures for endorsing clinical practice guidelines developed by other professional organizations.
Methods

An ASCO Endorsement Panel was convened to consider endorsing the Adjuvant and Salvage Radiotherapy After Prostatectomy: AUA/ASTRO Clinical Practice Guideline recommendations that were based on a systematic review of the medical literature. The panel evaluated the methodology employed in the AUA/ASTRO guideline using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) review instrument and carefully reviewed the guideline content to determine appropriateness for ASCO endorsement.
Clinical Questions

The four research question domains were:
(1) patient counseling
(2) the use of radiotherapy in the adjuvant and salvage contexts
(3) defining biochemical recurrence
(4) conducting a re-staging evaluation.

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Recommendations

ASCO Qualifying Statements (in **bold italics**)

**AUA/ASTRO Guideline 1:** Patients who are being considered for management of localized prostate cancer with radical prostatectomy should be informed of the potential for adverse pathologic findings that portend a higher risk of cancer recurrence and that these findings may suggest a potential benefit of additional therapy after surgery.

**AUA/ASTRO Guideline 2:** Patients with adverse pathologic findings including seminal vesicle invasion, positive surgical margins, and extraprostatic extension should be informed that adjuvant radiotherapy, compared to radical prostatectomy only, reduces the risk of biochemical (PSA recurrence, local recurrence, and clinical progression of cancer. They should also be informed that the impact of adjuvant radiotherapy on subsequent metastases and overall survival is less clear; one of two randomized controlled trials that addressed these outcomes indicated a benefit but the other trial did not demonstrate a benefit (*reduced risk of metastasis and death*).
Recommendations

AUA/ASTRO Guideline 3: Physicians should offer adjuvant radiotherapy to patients with adverse pathologic findings at prostatectomy including seminal vesicle invasion, positive surgical margins, or extraprostatic extension because of demonstrated reductions in biochemical recurrence, local recurrence, and clinical progression.

ASCO Endorsement Qualifying statement:

In the first sentence, the word “offer” should be interpreted as having a detailed discussion with the patient about the risks and benefits of adjuvant radiation. This discussion should be heavily influenced by our final qualifying statement and include a thorough discussion of the absolute risk of recurrence in light of exact pathological findings and post-operative PSA levels. As such, though adjuvant radiation appears to be equally effective for all stages and post-operative PSA levels in terms of reducing the relative risk of recurrence, the absolute benefit is highly influenced by the absolute risk of recurrence. For men at low risk of recurrence, the benefits are modest. Moreover, all potential benefits must be weighed against the known risks.

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Recommendations

AUA/ASTRO Guideline 4: Patients should be informed that the development of a PSA recurrence after surgery is associated with a higher risk of development of metastatic prostate cancer or death from the disease. Congruent with this clinical principle, physicians should regularly monitor PSA after radical prostatectomy to enable early administration of salvage therapies if appropriate.

ASCO Endorsement Qualifying statement:
While this Endorsement Panel concurs, as noted in the discussion for guideline statement #3 and in our final qualifying statement, not all men are at equal risk of recurrence. At this time, there are insufficient data to recommend different follow-up strategies based differing risk of recurrence though, and thus all men should be followed after surgery.

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AUA/ASTRO Guideline 5: Clinicians should define biochemical recurrence as a detectable or rising PSA value after surgery that is >0.2 ng/ml with a second confirmatory level >0.2 ng/ml.

ASCO Endorsement Qualifying statement:
**Defining an exact cut-point for PSA recurrence is challenging.** We acknowledge this difficulty and while we agree that 0.2 ng/ml is a reasonable cut-off and is widely used in research publications and in clinical practice, the benefits of using this cut-point versus others are unclear. As such, we felt the evidence to support this recommendation was clinical practice rather than clinical evidence.

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AUA/ASTRO Guideline 6: A re-staging evaluation in the patient with a PSA recurrence may be considered.

ASCO Endorsement Qualifying statement:
While the Endorsement Panel agrees with this statement, the discussion centered about which imaging modalities to use. At this time, there is no clear consensus and unfortunately all imaging modalities have limited sensitivity and specificity in the very low PSA range where salvage radiation is most effective (i.e. PSA <1 ng/ml). We note that this is a rapidly evolving field with much research and it is hoped that in the future there will be more clarity on this point.
Recommendations

AUA/ASTRO Guideline 7: Physicians should offer salvage radiotherapy to patients with PSA or local recurrence after radical prostatectomy in whom there is no evidence of distant metastatic disease.

ASCO Endorsement Qualifying statement:
Again, “offer” should be interpreted as having a detailed discussion with the patient about the risks and benefits of adjuvant radiation. This discussion should be heavily influenced by our final qualifying statement and include a thorough discussion of the absolute risk of recurrence in light of exact pathological findings and post-operative PSA levels. As such, though adjuvant radiation appears to be equally effective for all stages and post-operative PSA levels in terms of reducing the relative risk of recurrence, the absolute benefit is highly influenced by the absolute risk of recurrence. For men at low risk of recurrence, the benefits are modest. Moreover, all potential benefits must be weighed against the known risks.

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Recommendations

AUA/ASTRO Guideline 8: Patients should be informed that the effectiveness of radiotherapy for PSA recurrence is greatest when given at lower levels of PSA.

ASCO Endorsement Qualifying statement:
While PSA control rates are best when salvage radiation is given when the PSA is <1 ng/ml, there is no guarantee of cure as salvage radiation is not curative for all men. While there are many technical issues related to measuring the rate of PSA rise typically measured as PSA doubling time (PSADT; i.e. when to start counting, how many values, over what time period, etc.) data suggest a short PSADT predicts a poor response to salvage radiation in terms of PSA control. However, as these men are at the highest risk of clinically meaningful progression, they stand the most to gain from salvage radiation and indeed, retrospective data suggest that salvage radiation therapy improves overall survival, but only in those with a short PSADT.
Recommendations

AUA/ASTRO Guideline 9: Patients should be informed of the possible short-term and long-term urinary, bowel and sexual side effects of radiotherapy as well as of the potential benefits of controlling disease recurrence.

ASCO Endorsement Qualifying statement:

Not all men who are candidates for adjuvant RT have the same risk of recurrence and though RT is equally effective in terms of relative risk reduction not all men will derive the same benefit. Items such as Gleason score (especially Gleason 8-10), pathological findings (especially seminal vesicle invasion or extensive positive margins), and an elevated post-operative PSA place men at particularly high risk of recurrence or clinical progression and these men likely derive the greatest benefit in terms of absolute risk reduction from adjuvant RT. For other men, the absolute risk benefit is likely lower resulting in a less favorable risk-benefit ratio. Similarly, not all men who develop a PSA recurrence have the same risk of clinically-meaningful disease progression and therefore the risk-benefit ratio for salvage radiation is likewise different for each patient.

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Endorsement Recommendation


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Additional Resources

More information, including a Methodology Supplement, and clinical tools and resources, is available at:
www.asco.org/endorsements/adjuvantRTprostatectomy

Patient information is available at www.cancer.net
Acknowledgements

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