Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part II: Recommended Approaches and Details of Specific Care Options

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Abbreviations and Acronyms

ADT = androgen deprivation therapy
DRE = digital rectal examination
EBRT = external beam radiotherapy
HIFU = high intensity focused ultrasound
MRI = magnetic resonance imaging
PIVOT = Prostate Cancer Intervention Versus Observation Trial
PLND = pelvic lymphadenectomy
ProtecT = Prostate Testing for Cancer Treatment Trial
PSA = prostate specific antigen
QoL = quality of life
RCT = randomized clinical trial
SDM = shared decision making
SPCG-4 = Scandinavian Prostate Cancer Group Study Number 4

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Purpose: This guideline is structured to provide a clinical framework stratified by cancer severity to facilitate care decisions and guide the specifics of implementing the selected management options. The summary presented herein represents Part II of the two-part series dedicated to Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline discussing risk stratification and care options by cancer severity. Please refer to Part I for discussion of specific care options and outcome expectations and management.

Materials and Methods: The systematic review utilized in the creation of this guideline was completed by the Agency for Healthcare Research and Quality and through additional supplementation by ECRI Institute. This review included articles published between January 2007 and March 2014 with an update search conducted through August 2016. When sufficient evidence existed, the body of evidence for a particular treatment was assigned a strength rating of A (high), B (moderate), or C (low) for support of Strong, Moderate, or Conditional Recommendations. Additional information is provided as Clinical Principles and Expert Opinions (table 2 in supplementary unabridged guideline, http://jurology.com/).

Results: The AUA (American Urological Association), ASTRO, and SUO (Society of Urologic Oncology) formulated an evidence-based guideline based on a risk stratified clinical framework for the management of localized prostate cancer.

Conclusions: This guideline attempts to improve a clinician's ability to treat patients diagnosed with localized prostate cancer, but higher quality evidence in future trials will be essential to improve the level of care for these patients. In all cases, patient preferences should be considered when choosing a management strategy.

Key Words: prostate, prostatic neoplasms, guideline

RECOMMENDED APPROACHES AND DETAILS OF SPECIFIC CARE OPTIONS

Active Surveillance

For patients who elect active surveillance as a management approach, surveillance should include at least annual prostate specific antigen testing and digital rectal exam as part of the surveillance strategy to help guide considering definitive treatment if the severity of cancer progresses. Periodic re-biopsy to

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monitor cancer grade, and MRI to monitor tumor size or invasiveness, can further inform the surveillance process.

In the Prostate Testing for Cancer Treatment Trial, which showed similar survival with active surveillance versus radiotherapy or radical prostatectomy, trial subjects on active surveillance had only regular PSA testing and DREs performed. While the optimal frequency of PSA and DRE has not been established, ProtecT prescribed PSA testing every 3 months in the first year, then every 6 to 12 months thereafter with DRE performed during urology follow-up visits.[1]

For patients who elect active surveillance as a management approach (versus watchful waiting) there is an assumption that active treatment should be initiated upon the detection of adverse features that may change the patient's risk category. This may be due either to an incorrect original classification or to true progression from a lower risk to a higher risk category.[2,3] Thus, if there is adverse reclassification due to the detection of a higher Gleason score than was present at the initiation of surveillance, definitive treatment should be considered. Other factors that may lead to adverse reclassification include growth or invasion on multiparametric MRI and suspicious rises in PSA that may change PSA density.[4] In the Prostate Cancer Intervention Versus Observation Trial and ProtecT studies, approximately 20% and 50%, respectively, of patients who started on active surveillance received treatment within 10 years.[1,5]

28. **Localized prostate cancer patients who elect active surveillance should have accurate disease staging including systematic biopsy with ultrasound or MRI guided imaging. (Clinical Principle)**

29. **Localized prostate cancer patients undergoing active surveillance should have routine surveillance PSA testing and DRE. (Strong Recommendation; Evidence Level: Grade B)**

30. **Localized prostate cancer patients undergoing active surveillance should be encouraged to have a confirmatory biopsy within the initial two years and surveillance biopsies thereafter. (Clinical Principle)**

31. **Clinicians may consider multiparametric prostate MRI as a component of active surveillance for localized prostate cancer patients. (Expert Opinion)**

32. **Tissue based genomic biomarkers have not shown a clear role in active surveillance for localized prostate cancer and are not necessary for follow-up. (Expert Opinion)**

33. **Clinicians should offer definitive treatment to localized prostate cancer patients undergoing active surveillance who develop adverse reclassification. (Moderate Recommendation; Evidence Level: Grade B)**

Prostatectomy

Prostate cancer is typically a slowly evolving disease. Numerous studies exploring its natural history have suggested that, even if high grade and left untreated, disease specific survival is a median of 8-10 years after diagnosis.[6-12] It is, therefore, unlikely that men with short life expectancy will benefit from prostatectomy or other treatment. It is also unlikely that clinical trials following patients for a shorter interval than 8-10 years will be able to demonstrate a survival advantage attributable to the intervention being studied.

In comparison to watchful waiting, the survival benefit from radical prostatectomy was observed predominantly in the <65 year old men in the Scandinavian SPCG-4 trial,[13] Even though men > 65 years of age did not experience a significant decrease in mortality in SPCG-4, these older men demonstrated a trend towards longer life and decrease in metastases. In the American PIVOT, prostatectomy was associated with survival advantage over watchful waiting among men having PSA over 10 ng/ml and among those having cancer severity with intermediate or worse risk by clinical criteria.

Population-based observational studies and limited prospective trials have shown that blood loss and transfusion rates are lower when radical prostatectomy is performed using robot-assisted laparoscopic technique as compared to an open retropubic technique. Other outcomes, including cancer control, urinary incontinence, and erectile dysfunction, were found not to be different between robot-assisted laparoscopic and open retropubic approaches in these studies.

Pelvic lymphadenectomy is the most effective means of detecting regional nodal metastases.[14] However, evidence is lacking as to whether or not the removal of lymph nodes containing metastatic prostate cancer has therapeutic benefit. This, coupled with knowledge that PLND carries specific risks, such as lymphocele, has tempered enthusiasm for routine pelvic lymphadenectomy, and supports the option of recommending PLND based on cancer severity.[15-21]

34. **Clinicians should inform localized prostate cancer patients that younger or healthier men (e.g., <65 years of age or >10 year life expectancy) are more likely to experience cancer control benefits from prostatectomy than older men. (Strong Recommendation; Evidence Level: Grade B)**

35. **Clinicians should inform localized prostate cancer patients that open and**