Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part I: Risk Stratification, Shared Decision Making, and Care Options

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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 represents Part I of the two-part series dedicated to Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline discussing risk stratification and care options by cancer severity.

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

Abbreviations and Acronyms

ADT = androgen deprivation therapy

CT = computerized tomography

EBRT = external beam radiotherapy

HIFU = high intensity focused ultrasound

MRI = magnetic resonance imaging

PIVOT = Prostate Cancer Intervention Versus Observation Trial

ProtecT = Prostate Testing for Cancer Treatment Trial

PSA = prostate specific antigen

SDM = shared decision making

SPCG-4 = Scandinavian Prostate Cancer Group Study Number 4

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RISK STRATIFICATION

After diagnostic biopsy and appropriate initial staging has demonstrated localized prostate cancer, risk stratification of prostate cancer severity or aggressiveness should include prostate specific antigen, clinical stage digital rectal exam, Grade Group, amount of cancer on biopsy, PSA density, and imaging. The Panel agreed that segregating patients into a limited number of risk groups based upon these factors simplifies decision making and has both

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clinical and practical value. The core of the Panel's risk grouping is the original low, intermediate, and high risk grouping proposed by D'Amico et al.[1]

The Panel further subcategorized low risk to distinguish men with very low risk disease based upon the initial identification by Epstein et al that men at the lowest risk of having significant cancer (defined as 0.2 cm^3 or larger) were those with 2 or fewer cores positive, no core with >50% involved, Gleason 3+3/Grade Group 1, and a PSA density <0.15 ng/ml/cc.[2] Multiple studies have since used this definition showing that these men have a very favorable outcome with a low probability of adverse pathology at surgery and low rate of metastatic disease when managed with active surveillance.[3,4]

The intermediate risk group is defined by the well-established D'Amico criteria for grade and PSA, with updating of digital rectal exam wherein, consistent with National Comprehensive Cancer Network® recommendations, cT2c is categorized as intermediate risk not high risk (unless high risk Gleason score is present or PSA is over 20).[5]

The Panel determined that to facilitate care decisions, it would be prudent to subcategorize the intermediate risk group into "favorable" and "unfavorable" categories of cancer severity, based largely on contemporary "Grade Group" designations of histopathologic Gleason score (wherein Gleason score 3+3 or less corresponds to Grade Group 1; Gleason score 3+4 corresponds to Grade Group 2; Gleason score 4+3 corresponds to Grade Group 3; Gleason score 8 corresponds to Grade group 4; and Gleason score 9-10 corresponds to Grade Group 5).[6-8]

The panel determined that patients having histopathology Grade Group 2 should be classified as "favorable" intermediate risk when their PSA is less than 10, whereas Grade Group 2 with PSA from 10-20, as well as all Grade Group 3 with PSA <20, should be classified as "unfavorable" intermediate risk (table 1). The need to sub-classify the intermediate risk category into "favorable" and "unfavorable" categories was prompted by clinically significant differences in recommendations pertaining to a breadth of clinical decisions, ranging from advisability of imaging studies for staging, to advisability of pelvic lymph node dissection during prostatectomy, to advisability of using androgen suppressive therapy in conjunction with radiation.

The Panel did not substratify high risk patients into high risk and very high risk. The rationale is not based upon differences in outcome, but rather the similarity in treatment options and lack of clinical utility for substratifying high and very high risk men. The risk stratification system used in this guideline can be found in table 1.

Management options for localized prostate cancer stratified by cancer severity risk group are summarized in table 2 based on level of evidence and strength of recommendation and discussed below.

SHARED DECISION MAKING

SDM is a collaborative decision making process between patients and their clinicians. SDM is especially relevant in discussion of prostate cancer treatment because such decisions involve multiple clinically accepted options, and the ratio of benefits to harms is uncertain, equivalent, or "preference sensitive."[9,10] SDM aims to improve the quality of medical decisions by helping patients choose options consistent with their own values and in accordance with the best available scientific evidence.[11-14]

In most cases, there is not a single best treatment choice with regard to oncologic outcomes or side effects. Treatment selection should consider patient, tumor, and treatment-related factors. Clinicians should fully engage in SDM, allowing patient values to drive this decision.

1. **Counseling of patients to select a management strategy for localized prostate cancer should incorporate SDM and explicitly consider cancer severity (risk category), patient values and preferences, life expectancy, pre-treatment general functional and genitourinary symptoms, expected post-treatment functional status, and potential for salvage treatment. (Strong Recommendation; Evidence Level: Grade A)**

2. **Prostate cancer patients should be counseled regarding the importance of modifiable health-related behaviors or risk factors, such as smoking and obesity. (Expert Opinion)**

Table 1. *Risk Stratification for Localized Prostate Cancer (table 3 in unabridged guideline, http://jurology.com/)*

Very Low Risk	PSA <10 ng/ml AND Grade Group 1 AND clinical stage T1-T2a AND <34% of biopsy cores positive AND no core with >50% involved, AND PSA density <0.15 ng/ml/cc
Low Risk	PSA <10 ng/ml AND Grade Group 1 AND clinical stage T1-T2a
Intermediate Risk	PSA 10-<20 ng/ml OR Grade Group 2-3 OR clinical stage T2b-c • Favorable: Grade Group 1 (with PSA 10-<20) OR Grade Group 2 (with PSA<10) • Unfavorable: Grade Group 2 (with either PSA 10-<20 or clinical stage T2b-c) OR Grade Group 3 (with PSA < 20)
High Risk	PSA ≥20 ng/ml OR Grade Group 4-5 OR clinical stage ≥T3*

* Clinical stage T3 cancer is considered locally advanced and, therefore, outside the scope of this guideline.