Surveilling Middle-Risk Prostate Cancer: Cautionary Data
January 10, 2017

While increasing numbers of low-risk prostate cancers are now managed with active surveillance (AS), the role of this conservative approach is less clear in men with intermediate-risk disease. Now one of the world's leading prostate cancer research groups says that AS should not be used in routine clinic settings among men with Gleason 7 scores. "Active surveillance for patients with Gleason 7 disease should be offered only in the setting of a clinical study," write Hima Bindu Musunuru, MD, from the Sunnybrooke Health Sciences Centre and University of Toronto, Ontario, Canada, and colleagues, who include urologist Laurence Klotz, MD. Their study was published in the December 2016 issue of the Journal of Urology.

Since the mid-1990s, the group has had a protocol that offers AS to all patients with low risk (cT1-T2b, Gleason score of 6, and prostate-specific antigen [PSA] 10 ng/mL or less) and selects intermediate-risk disease (age older than 70 years with cT2c or PSA of 15 ng/mL or less, or Gleason score of 3+4 or less). In 2000, the protocol was restricted to low-risk patients and those with "favorable" intermediate risk (Gleason score of 3+4) and life expectancies of less than 10 years. Thus, the group's definition of intermediate risk has included some men with Gleason 6 and some with Gleason 7 scores.

In a new study of 213 intermediate-risk and 732 low-risk cases, the Canadian group found that the intermediate-risk group had a substantially inferior 15-year metastasis-free survival (MFS) rate, which was the primary outcome. Specifically, the 15-year MFS rates were 82% for intermediate risk vs 95% for low risk (hazard ratio [HR], 3.14; 95% confidence interval [CI], 1.51 - 6.53; P < .001).
When the researchers took a closer look at the risk groups, they found that some intermediate-risk patients had the acceptable outcome of an MFS greater than 90%, but this occurred only in those who had Gleason 6 scores.

Table. Estimated 15-Year MFS Rates

Risk Group	MFS Rate (%)
Low risk	
Gleason score ≤ 6 with PSA < 10 ng/mL	94
Intermediate risk	
Gleason score ≤ 6 with PSA 10-20 ng/mL	94
Gleason score 3+4 with PSA ≤ 20 ng/mL	84
Gleason score 4+3 with PSA ≤ 20 ng/mL	63

Median age was 72 years in the intermediate-risk cohort and 67 years in the low-risk group. Median follow-up was 6.7 years for intermediate risk vs 6.5 years for low risk.

Overall, 29% of the patients in the intermediate-risk cohort and 19.4% in the low-risk cohort have been followed for more than 10 years. For the secondary endpoint of overall survival (OS), the estimated 10- and 15-year OS for intermediate risk cases was 67% and 51%, and for low risk, 84% and 67%. For the secondary endpoint of cause-specific survival (CSS), the estimated 10- and 15-year CSS for intermediate-risk cases was 97% and 89%, and for low-risk cases, the estimates were 98% and 97%, respectively. This translated into a significantly increased risk for cancer-specific mortality (HR, 3.74; 95% CI, 1.32 - 10.61; P < .008) in the intermediate-risk population.

The new study is important because earlier research found no significant difference in progression-free survival in low- and intermediate-risk populations (J Clin Oncol. 2011;29:228), say a trio of urologists from Johns Hopkins University, Baltimore, Maryland, in an accompanying editorial. However, that earlier study did not consider "more clinically meaningful oncologic outcomes," and only 6% of the patients had a Gleason score greater than 6, observe Jeffrey Tosoian, MD, Ridwan Alam,

MD, and H. Ballentine Carter, MD. "It is prudent to proceed with caution when considering AS in men with Gleason score 7 cancer," write the editorialists.

At Johns Hopkins, men with Gleason scores of 7 or greater are typically candidates for prostatectomy, radiation therapy, and other curative treatments if they do not have prohibitive comorbidities, said Dr Tosoian in an email to Medscape Medical News. "It is our approach to exclude men that are otherwise fit for curative intervention from AS if they have Gleason score ≤ 7 cancer, based on the lack of data supporting the relative safety of the practice," he commented. "Men with a limited life expectancy could reasonably consider an observational (i.e. conservative) approach — but it is worth noting that the term 'active surveillance' refers specifically to the management of men who are candidates for active treatment," Dr Tosoian added.

Dr Tosoian also explained that using AS in intermediate-risk disease is not bound by strict rules. "Navigating active surveillance is not a straightforward endeavor, particularly as we seek to expand the population of eligible patients," he observed. "In the absence of definitive evidence, it is not unreasonable to consider AS in men with intermediate-risk disease whose preferences are consistent with avoiding curative intervention, so long as those men understand the limitations of existing data and are willing to accept the risk associated with the approach." But he was also clear: "The data from Toronto suggest that the use of AS poses a significantly greater risk of adverse outcomes to intermediate-risk men than low-risk men."

The study authors and editorialists have disclosed no relevant financial relationships.

J Urol. 2016;196:1651-1658. Study abstract, Editorial extract