A Roadmap for Improving the Management of Favorable Risk Prostate Cancer

A proposed solution to concerns about overtreatment of men with favorable risk, early stage prostate cancer is the unlinking of diagnosis from treatment through expanded use of active surveillance and selective delayed intervention. At a population level the safety and impact of surveillance as a strategy for reducing overtreatment depend on accurate initial identification of men with indolent tumors, followed by periodic monitoring for changes in either cancer severity or patient preferences which may prompt transition to definitive therapy while the cancer is still curable.

Although recent reports indicate that a growing proportion of men with favorable risk prostate cancer are undergoing surveillance,[1] rates of adoption in the United States often lag behind those reported internationally,[2] and challenges to safe and successful implementation across large populations remain. The documented wide variation in adoption across physicians[3] may indicate residual uncertainty regarding patient selection for surveillance. Furthermore, many men are entering surveillance after a single diagnostic biopsy and without an early reassessment aimed at confirming tumor severity (eg repeat biopsy or other testing).[4] Finally, the surveillance process is predicated on adherence to a regular cadence of repeat clinical evaluations, prostate specific antigen (PSA) blood tests and prostate biopsy but, in reality, many men receive less frequent followup than recommended by current guidelines.[4,5]

This less active surveillance is concerning in light of recent data indicating that men infrequently monitored have an increased risk of cancer progression relative to those receiving definitive treatment with surgery or radiation.[6] Accordingly, coordinated efforts aimed at refining patient selection, expanding the use of confirmatory tests of cancer severity and ensuring reliable followup are essential to increase the safety, sustainability and ultimate impact of surveillance as a strategy for reducing overtreatment.

MUSIC (Michigan Urological Surgery Improvement Collaborative) is pursuing each of these priorities. MUSIC is a consortium of more than 250 urologists from 44 diverse academic and community practices in Michigan. Using data from a large clinical registry, the collaborative has detailed the contemporary state of surveillance in Michigan.[4,7] Recent data indicate that rates of surveillance approach 44% among all men diagnosed with Gleason score 3+3=6 or low volume Gleason Score 3+4=7 prostate cancer (ie no more than 3 cores containing cancer and no core more than 50% involved with tumor), with surveillance being substantially more common among men with Gleason 6 (1,806/3,475, 52.0% receive surveillance) vs 3+4 disease (203/1,139, 17.8% receive surveillance). Importantly, across MUSIC practices there is nearly a sixfold variation in the use of surveillance (fig. 1). Likewise, we have documented wide practice level variation in the receipt of confirmatory tests (ie repeat biopsy or multiparametric prostate magnetic resonance imaging (MRI) with or without targeted biopsy) to ensure appropriate staging before surveillance, and in rates of recommended followup testing among patients followed for at least 30 months (fig. 1).

In an effort to address this variation, and improve the safety and sustainability of surveillance for men in Michigan, we leveraged MUSIC's data and infrastructure to develop a multidimensional improvement strategy built around the "MUSIC roadmap for the management of men with favorable-risk prostate cancer" (available at www.musicurology.com/active-surveillance). The roadmap provides guidance for managing favorable risk prostate cancer (localized disease and Gleason score 3+3 or low volume 3+4 with no more than 3 cores containing cancer and no core greater than 50% involved with cancer) and includes a conceptual framework that defines the consideration phase and the surveillance phase. The consideration phase focuses on identifying patients most appropriate for surveillance, whereas the surveillance phase addresses how to safely and consistently implement this management strategy (fig. 2). To achieve greater consistency in care, both phases of the

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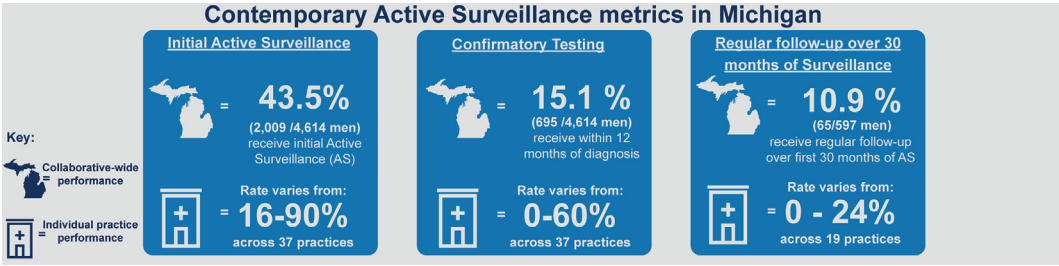

Figure 1. Contemporary active surveillance metrics in Michigan. Metrics reported for all eligible men diagnosed with favorable risk prostate cancer in MUSIC registry between January 2012 and October 2015. Practices were included in practice level variation reports only when 10 or more eligible men with sufficient followup were managed at that practice site. Confirmatory testing defined as receipt of either repeat prostate biopsy or multiparametric prostate MRI within 12 months of diagnosis, rates do not account for whether genomic test was used to confirm cancer risk. Regular followup defined as receipt of at least 4 repeat PSA tests and 2 tumor burden re-assessments (ie either prostate biopsy or prostate MRI) within 30 months of diagnosis.

roadmap provide clinicians with pragmatic tools for counseling patients and making management decisions at each step in the process (fig. 2).

In the consideration phase the roadmap outlines 4 evidence-based steps for identifying the best candidates for surveillance. At step 1 tailored tools are provided which allow for formal estimates of life expectancy.[8] For men with life expectancy less than 10 years, a conservative approach (watchful waiting) is indicated. For men with life expectancy that exceeds 10 years, step 2 is introduced to leverage readily available clinical information (ie life expectancy, race, erectile function/importance of sexual activity, prostate specific antigen (PSA) density and biopsy tumor burden) to determine the suitability of surveillance based on formal appropriateness criteria developed and published by a MUSIC consensus panel.[7] These criteria and accompanying paradigmatic counseling statements are recommended for use during shared decision making. For men who elect to consider surveillance, the roadmap then calls for performance of 1 or more confirmatory test(s) to refine risk stratification (step 3). In this step the roadmap specifies repeat

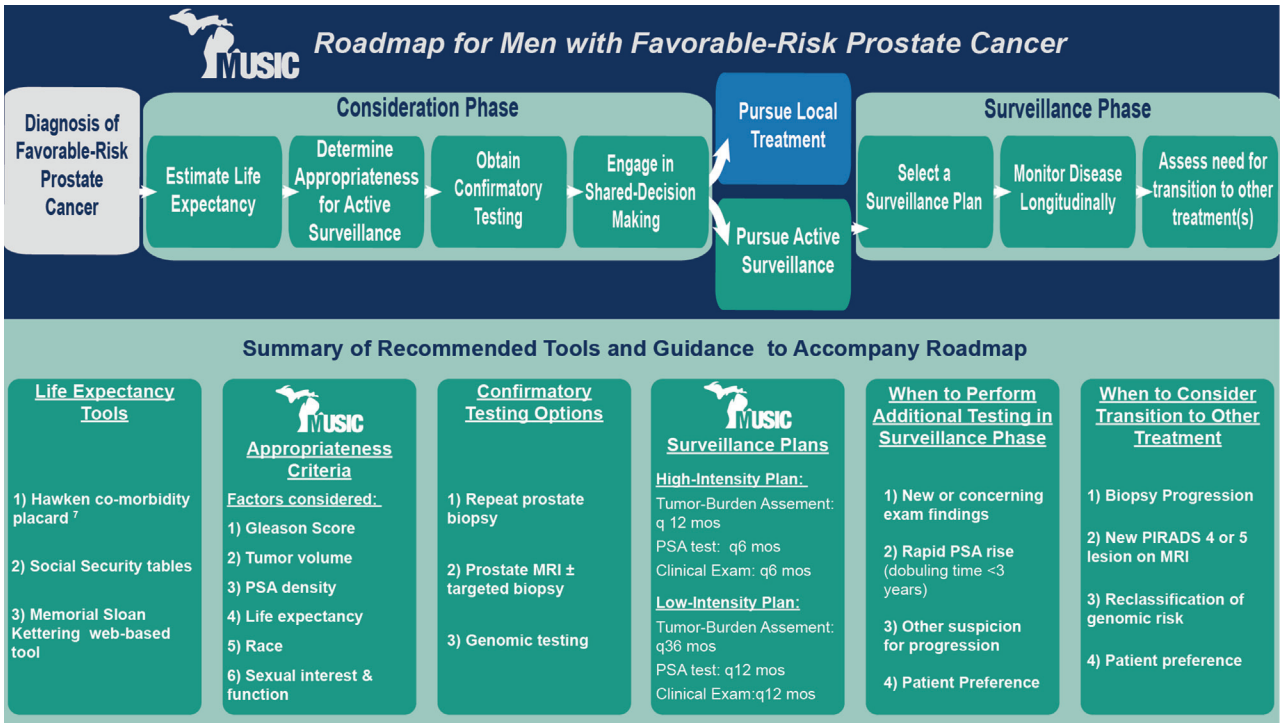

Figure 2. MUSIC roadmap for management of favorable risk prostate cancer (www.musicurology.com/active-surveillance). Recognizing importance of patient preferences while considering and ultimately implementing active surveillance, we recommend assessment of patient values and preferences throughout all steps in addition to shared decision making recommended as step 4 in consideration phase. *PIRADS*, prostate imaging reporting and data system.

prostate biopsy, prostate MRI with or without targeted biopsy and/or genomic testing as confirmatory options with the recommendation that at least 1 is performed within 6 months of diagnosis. The roadmap also provides guidance for interpreting results. After confirmatory testing, shared decision making represents step 4 of the consideration phase.

Men choosing active surveillance then enter the surveillance phase. The roadmap provides specific recommendations for long-term monitoring designed to identify changes in cancer severity. Addressing the absence of uniform guidelines around the best schedule and type of followup tests, the roadmap provides patients and clinicians with 2 explicit surveillance pathways and clinical criteria that should prompt consideration of a transition to definitive therapy. Two specific surveillance plans (low and high intensity) adapted from previously published protocols and clinical experience in Michigan are recommended. After choosing the plan that best balances risk of progression with the burden of followup for an individual patient, the surveillance process is implemented and will vary in duration based on clinical circumstances. If followup evaluations indicate changes in tumor behavior (ie higher grade or higher volume cancer), the roadmap provides guidelines for when to obtain further testing and/or transition to treatment (eg surgery or radiation) or to watchful waiting.

To assess the impact of the roadmap MUSIC developed several accompanying quality measures (detail at www.musicurology.com/active-surveillance/measures). The measures will provide performance feedback to individual urologists via a web based dashboard that allows comparison of practice patterns with other surgeons across the state. These will be continually updated and examined at a practice and statewide level to understand the impact of the roadmap on the quality of prostate cancer care in Michigan.

As with other conditions, widespread variation in the adoption and implementation of active surveillance stems, in part, from clinical uncertainty surrounding best practices for this relatively new management strategy. In Michigan the "MUSIC roadmap for men with favorable-risk prostate cancer" represents an attempt to address this challenge across a statewide urology collaborative. By providing structured steps, and electronic and hard copy clinical tools for identifying who is a candidate for surveillance and how to implement this strategy, we believe the roadmap provides useful direction for reducing overtreatment of men with favorable risk prostate cancer.

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Gregory B. Auffenberg,* Brian R. Lane, Susan Linsell, Andrew Brachulis, Zaojun Ye, Nikola Rakic, James Montie,† David C. Miller† and Michael L. Cher

From the Department of Urology, University of Michigan, Ann Arbor, Division of Urology, Spectrum Health (BRL), Grand Rapids and Department of Urology, Wayne State University (MLC), Detroit, Michigan

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*Correspondence: Department of Urology, University of Michigan, 2800 Plymouth Rd. NCRC Building16, Ann Arbor, Michigan 48109 (telephone: 734-647-9188; Fax: 734-232-2400; e-mail: gauffen@umich.edu).

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