Screening for Testicular Cancer: An Evidence Review for the U.S. Preventive Services Task Force

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Background: Testicular cancer is the most common type of cancer in men aged 15 to 34 years. Because treatment produces favorable outcomes even in advanced stages, the U.S. Preventive Services Task Force (USPSTF) concluded in 2004 that screening asymptomatic men for testicular cancer is unlikely to produce additional benefits over clinical detection.

Purpose: To search for new evidence on the benefits and harms of screening for testicular cancer to assist the USPSTF in updating its 2004 recommendation.

Data Sources: English-language articles indexed in PubMed and the Cochrane Library and published between 1 January 2001 and 11 November 2009.

Study Selection: Randomized, controlled trials; meta-analyses; systematic reviews; cohort studies; and case–control studies were selected to determine the benefits of screening for testicular cancer. Randomized, controlled trials; meta-analyses; systematic reviews; cohort studies; case–control studies; and case series of large, multisite databases were selected to determine the harms of screening. Each author independently reviewed titles, abstracts, and full-text articles for possible inclusion.

Data Extraction: One author abstracted information on the benefits and harms of screening for testicular cancer.

Data Synthesis: No studies met the inclusion criteria. Three studies were considered for inclusion at the full-text stage of review. These inconclusive studies addressed testicular microlithiasis, XIST gene testing, and testis-sparing surgery.

Limitation: The focused search strategy may have missed some smaller studies or studies published in languages other than English on the benefits or harms of testicular cancer screening.

Conclusion: No new evidence was found on the benefits or harms of screening for testicular cancer that would affect the USPSTF’s previous recommendation against screening.

Primary Funding Source: Agency for Healthcare Research and Quality.

For author affiliations, see end of text.
**METHODS**

**Data Sources and Searches**

We searched the English-language literature for studies on the benefits and harms of testicular cancer screening in asymptomatic men that were published between 1 January 2001 (the last year searched by the previous USPSTF review) and 11 November 2009, using the search terms *testicular neoplasm with germinoma* and *mass screening* or *screening*. The initial search was restricted to articles indexed in the Cochrane Database of Systematic Reviews and the PubMed core clinical journal subset (previously known as the Abridged Index Medicus). When the initial search yielded few articles, searches were expanded to include noncore journals. We supplemented these searches by reviewing reference lists of recent reviews and clinical guidelines.

**Study Selection**

To determine the benefits of screening, we included randomized, controlled trials; meta-analyses; systematic reviews; cohort studies; and case–control studies. To determine the harms of screening, we included randomized, controlled trials; meta-analyses; systematic reviews; cohort studies; case–control studies; and case series of large, multisite databases. We excluded case reports, narrative reviews, editorials, and practice guidelines.

We evaluated articles at the title, abstract, and full-text stage by using predetermined exclusion criteria. Articles selected for further examination by at least 1 author advanced to the next stage of review. At the full-text article stage, differences of opinion were resolved by consensus.

**Data Extraction**

One author abstracted information on study design, sample size, entry criteria, and other outcomes of interest.

**Data Synthesis and Analysis**

Data were described and synthesized in a narrative format.

**Role of the Funding Source**

The work of the USPSTF is supported by the Agency for Healthcare Research and Quality. This review did not receive separate funding.

**RESULTS**

A total of 113 articles were retrieved and entered into a reference EndNote (Thomson Reuters, New York, New York) database. After sequential review of the titles, abstracts, and full text (Figure), we determined that none of the articles met all of the inclusion criteria. The most common reason for exclusion was that the testing or interventions were performed in symptomatic populations. Therefore, we will discuss the 3 articles that reached the full-text review stage (Table).

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**Key Question 1: What Are the Benefits of Screening Asymptomatic Men for Testicular Cancer?**

In 2004, the USPSTF identified no studies showing benefits of screening for testicular cancer. We also found no new studies that directly examined benefits of screening.

Bennett and colleagues (5) prospectively examined the association between testicular microlithiasis and testicular cancer in a cohort of men who had had ultrasonography for testicular problems or for other diagnostic purposes (for example, pain, swelling, or infertility evaluation). Of the 104 men with testicular microlithiasis, 72 had follow-up ultrasonography, with a mean follow-up of 45 months (range, 12 to 90 months). None of the men was found to have testicular tumors. The small sample size of this study, which included only symptomatic patients, makes it difficult to draw any conclusions about the short-term benefit of screening asymptomatic persons.

Kawakami and associates (6) studied the XIST gene, which deactivates the X chromosome and thus is normally methylated in men. Previous research has shown that some germ-cell tumors in men have abnormally unmethylated XIST genes. This study compared the methylation pattern of the XIST gene in patients with and without germ-cell tumors. Plasma samples from 25 patients with testicular cancer were compared with samples from 24 patients with other types of urogenital cancer and from 6 healthy patients. Of the 25 patients with testicular cancer, 16 had unmethylated XIST genes; none of the patients in the comparison populations did. Although the study suggests that the XIST gene may have promise as a marker for testicular...
cancer, the study’s small sample size and lack of clinical outcomes make drawing conclusions impossible. To establish the utility of the XIST gene in a screening test, one would first need to establish the prevalence of the methylated and unmethylated forms in a population of asymptomatic men and follow the 2 groups longitudinally to compare their risk for a diagnosis of testicular cancer.

**Key Question 2: What Are the Harms of Screening Asymptomatic Men for Testicular Cancer?**

Previous reviews found no studies showing harms from testicular cancer screening, which may include the psychological effects of false-positive results and the cost and complications of unnecessary confirmatory testing. Our review did not find any new studies on the harms of screening for testicular cancer in asymptomatic men.

A study by Carmignani and coworkers (7) compared testis-sparing surgery of testicular tumors with standard orchietomy. Patients with scrotal or testicular symptoms (for example, swelling, pain, infertility, varicocele, or erectile dysfunction) were eligible for the study. Of the 1320 patients who had had ultrasonography, 27 had tumors; 17 of these tumors were palpable. Of the 27 patients with tumors, 12 had orchietomy and 15 had testis-sparing surgery. One patient in the conservative surgery group developed a scrotal hematoma. No one in either group showed evidence of recurrent cancer after an average follow-up of 9 months (range, 1 to 19 months). Although the study was not randomized, the authors concluded that conservative surgery did not seem to pose a greater risk for recurrence of testicular cancer.

**DISCUSSION**

Although we did not identify any studies that directly discussed either the benefits or harms of testicular cancer screening, Carmignani and colleagues (7) needed to perform ultrasonography on 1320 asymptomatic men to find 27 tumors. Because symptomatic men have a higher pretest probability of cancer than asymptomatic men, one would expect the number needed to screen to detect 1 case of testicular cancer to be considerably greater, and the false-positive rate substantially higher, than those in the study by Carmignani and colleagues.

There are some established risk factors for testicular cancer, such as cryptorchidism and family history of testicular cancer, but researchers continue to look for new ones. A prospective study of 1504 healthy volunteers (8) found that 84, or approximately 5%, had testicular microlithiasis. After 5 years of follow-up, only 1 participant received a diagnosis of a testicular germ-cell tumor after discovering a palpable mass on self-examination (9).

Although these studies do not directly address the benefits of screening, they serve as a reminder for primary care clinicians to consider testicular cancer as part of their differential diagnosis in patients with testicular or scrotal symptoms. As the USPSTF stated in a previous recommendation statement (10), although the average primary care physician may see only 1 patient with testicular cancer over 20 to 25 years, 26% to 56% of patients with testicular cancer had an initially incorrect diagnosis of another testicular disorder.

In summary, we found no new studies since the 2004 USPSTF recommendation on the benefits or harms of screening for testicular cancer.

<table>
<thead>
<tr>
<th>Author, Year (Reference)</th>
<th>Study Design</th>
<th>Sample Characteristics</th>
<th>Intervention or Comparison</th>
<th>Main Results</th>
<th>Additional Information</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bennett et al, 2001 (5)</td>
<td>Prospective cohort</td>
<td>104 men with testicular microlithiasis</td>
<td>Follow-up ultrasonography</td>
<td>No new testicular tumors detected after a mean follow-up of 45 mo (range, 12 to 90 mo)</td>
<td>All patients had some urologic symptom (e.g., pain, swelling, infertility evaluation) at the time of the initial ultrasonography</td>
<td>Testicular microlithiasis in symptomatic men was not associated with subsequent development of testicular cancer</td>
</tr>
<tr>
<td>Kawakami et al, 2004 (6)</td>
<td>Diagnostic accuracy</td>
<td>25 men with testicular germ-cell tumors, 24 men with other types of urogenital cancer, and 6 healthy patients</td>
<td>Detection of unmethylated (abnormal) XIST DNA with specifically designed polymerase chain reaction primer</td>
<td>Unmethylated XIST DNA was found in 16 of 25 plasma samples in men with testicular germ-cell tumors; none of the plasma samples in the comparison groups contained unmethylated XIST DNA</td>
<td>Study was not designed to establish the utility of XIST detection as a screening test in asymptomatic men</td>
<td>Unmethylated XIST DNA may be a genetic marker for testicular cancer</td>
</tr>
<tr>
<td>Carmignani et al, 2003 (7)</td>
<td>Retrospective cohort</td>
<td>1320 patients in 1 hospital-based urology clinic, 27 of whom had testicular tumor identified by ultrasonography</td>
<td>Orchiectomy (12 men) vs. testis-sparing surgery (15 men)</td>
<td>No recurrent tumors in either group after a mean follow-up of 9 mo (range, 1 to 19 mo)</td>
<td>Assignment to type of surgery was not randomized</td>
<td>No difference in short-term tumor recurrence between men who had testis-sparing surgery vs. orchiectomy</td>
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screening for testicular cancer by testicular self-examination, physician examination, or other screening tests.

From the Agency for Healthcare Research and Quality, Rockville, Maryland.

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