Surveillance programs for early stage non-seminomatous testicular cancer: a practice guideline

Segal R, Lukka H, Klotz L H, Eady A, Bestic N, Johnston M, Cancer Care Ontario Practice Guidelines Initiative Genitourinary Cancer Disease Site Group

Authors' objectives
To identify a surveillance programme appropriate for men with clinical stage I non-seminomatous testicular cancer.

Searching
MEDLINE was searched from 1988 to December 2000, and Cancerlit from 1988 to November 2000. The search strategy used the MeSH 'testicular neoplasms', 'neoplasms', 'germ cell and embryonal', 'neoplasm recurrence', 'local', 'recurrence' and 'follow up studies', and the textwords 'nonsemin:; 'non semin:', 'foll:' and 'recur:'. The principal authors were contacted for confirmation of the surveillance schedule and outcome data. In addition, the authors searched personal files, meeting proceedings (including ASCO to 2000), the citations in identified studies and other bibliographies. Experts in the field were asked for other material. It is unclear whether only published material was eligible.

Study selection
Study designs of evaluations included in the review
Full reports of any prospective design were eligible if they: (1) had clearly defined entry criteria; (2) provided a detailed description of the surveillance programme; (3) provided primary data on survival, relapse rate and/or salvage rate for relapsed patients; and (4) were published in English.

The review included one randomised trial and 12 case series. There were no randomised trials comparing surveillance schedules. The authors included one randomised trial comparing surveillance alone with radiotherapy after orchiectomy. Another randomised trial compared surveillance with adjuvant post-operative radiotherapy; however, the post-operative radiotherapy data were disregarded as this is not a standard treatment. It is unclear how the authors used the data from this study. Twelve case series were included where men received surveillance following orchiectomy. The surveillance periods ranged between 2 and 5 years (median follow-up: 21 to 136 months).

Specific interventions included in the review
All surveillance regimens for men with clinical stage I testicular cancer who received no adjuvant treatment were eligible for inclusion. The studies had to provide detailed descriptions of the surveillance programme.

The review assessed surveillance programmes for men with clinical stage I non-seminomatous germ cell tumours of the testis. One study compared surveillance alone with radiotherapy after orchiectomy. The other (non-comparative) studies followed men receiving a specific surveillance intervention after orchiectomy.

Each surveillance programme used a slightly different schedule of blood tests, chest X-rays, computed tomography (CT) scans and follow-up visits. Detailed tables of the different schedules were presented in the review.

Reference standard test against which the new test was compared
The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis.

Participants included in the review
Men with clinical stage I testicular cancer were eligible if they met the following criteria: (1) no prior therapy (radiotherapy or retroperitoneal lymph node dissection were prohibited); (2) normal beta-subunit of human chorionic gonadotropin and alpha-fetoprotein levels; (3) normal complete blood count and serum biochemistry; and (4) normal chest X-ray and CT scans of the abdomen, pelvis and lymphangiogram.

A total of 1,174 male outpatients with clinical stage I testicular cancer were included. The authors did not provide
details about the participants' age or other characteristics.

Outcomes assessed in the review
The primary outcome measures were survival, relapse rate and salvage rate for men who relapsed. The median time to relapse was a secondary outcome. Studies that did not include one of the primary outcomes were excluded from the review.

How were decisions on the relevance of primary studies made?
The studies were selected and reviewed by one member of the Cancer Care Ontario Practice Guideline Initiative Genitourinary Cancer Disease Site Group and methodologists. Apart from describing the general inclusion criteria and the search strategy, the authors do not state how the papers were selected for the review.

Assessment of study quality
The authors do not report the method used to assess validity, or how the validity assessment was performed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
Data for relapse rate, salvage rate and survival were statistically pooled by summing the number of events and dividing by the total number of men at risk (evaluable). The pooled values for median follow-up time and median time to relapse were calculated by summing the median from each study multiplied by the number of evaluable men, and dividing this total by the sum of participants in all trials.

The authors did not outline any methods for assessing publication bias.

How were differences between studies investigated?
The authors do not report a method for assessing heterogeneity between the studies.

Results of the review
One randomised trial and 12 case series were included with a total of 1,174 participants (1,133 evaluable). There were 79 men (77 evaluable) in the randomised trial and 1,095 men (1,056 evaluable) in the case series.

The pooled survival rate was 98% (95% confidence interval, CI: 97, 99). The pooled relapse rate was 29% (95% CI: 26, 32), with a median time to relapse of 6 months. The pooled salvage rate was 94% (95% CI: 91, 97).

The surveillance protocols described in the studies were similar in format, with only slight differences in the scheduling of visits and the radiological investigations used. Variations in surveillance schedules (frequency of CT scans, blood tests, etc.) were not associated with differences in survival, relapse or salvage rates, especially after 2 years (P-values were not provided).

No information was presented about heterogeneity analyses, subgroup or sensitivity analyses, publication bias or inter-rater agreement.

Authors’ conclusions
Men with clinical stage I testicular cancer who have a normal physical examination, radiological scans and serum markers (or serum markers that fall within normal limits during their expected half-lives) can safely be put on surveillance instead of receiving ongoing treatment.
There was no evidence that one surveillance schedule was superior to another. The authors recommended the following surveillance schedule, based on cost and patients’ convenience.

1. Physical examination, blood serum marker tests and chest X-rays every month during the first year; every 2 months during the second year; every 3 months in the third year; and every 6 months during the fourth and fifth years.

2. CT scans of the abdomen and pelvis every 3 months in the first year; every 4 to 6 months in the second year; every 6 months in the third year; and once in the fourth and fifth years.

**CRD commentary**

This review had a clearly defined research question and inclusion criteria. The topic was relevant given the need for appropriate surveillance regimens and the paucity of evidence in this area. The review used standard search strategies, but was limited by the quality of the available studies and by omissions in the published report: Two major databases were searched using standard terms. The review may have benefited from searches of other databases such as CINAHL, Current Contents, Dissertation Abstracts, EMBASE and the Conference Papers Index. The authors justified their use of particular search terms, but made little attempt to include unpublished studies. Experts were contacted and conference proceedings searched, but it is unclear whether the authors aimed to exclude all unpublished work.

The report was limited by a lack of information about how the studies were selected for the review, and how many of the reviewers were involved in decisions about relevance and validity. No information was provided about the number of studies that may have been identified but excluded for various reasons. In addition, no validity assessment tools were described. The quality of the included studies was also poor, given that the authors aimed to compare different surveillance regimens.

The report omitted details about the data extraction process and inter-rater reliability. The statistical pooling methods were clearly described, but there was no assessment of heterogeneity, publication bias or other biases. The authors mentioned that only partial data from one randomised trial was used, but it is unclear whether the authors have labelled this as case series data throughout the report. There was no attempt to weight the studies.

Overall, the review addressed a relevant topic with little established evidence. One of the main findings was that there is little strong evidence to recommend one surveillance regimen over another. The authors recommended a regimen based on cost and convenience factors, but given that no cost-benefit analysis was presented it is arguable whether these recommendations are totally evidence-based.

**Implications of the review for practice and research**

Practice: The authors state several implications for practice.

1. Men with clinical grade I testicular cancer who meet certain criteria are eligible for surveillance rather than treatment. Men who have abnormal physical examination, radiological scans or serum markers should not be offered surveillance alone.

2. Physicians should discuss whether a man is willing to attend regular visits and screening to assess whether surveillance is a suitable option for him.

3. A recommended surveillance schedule is: (a) physical examination, blood serum marker tests and chest X-rays every month during the first year; every 2 months during the second year; every 3 months in the third year, and every 6 months during the fourth and fifth years; plus (b) CT scans of the abdomen and pelvis every 3 months in the first year; every 4 to 6 months in the second year; every 6 months in the third year, and once in the fourth and fifth years.

Research: The authors did not state any implications for further research.

Reviewer’s statement: This review cannot tell us whether surveillance is more or less effective than ongoing treatment, as only one trial directly compared surveillance with treatment. The findings of this review suggest that there is no strong evidence to recommend one surveillance regimen over another since no randomised trial compared different
schedules. There is a need for randomised trials comparing varying surveillance options, including the schedule recommended by the reviewers. Cost-benefit analyses (including financial and social costs) may also help practitioners decide between different surveillance options.

**Funding**
Cancer Care Ontario and the Ministry of Health and Long-Term Care.

**Bibliographic details**

**PubMedID**
11268306

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Germinoma /diagnosis; Humans; Male; Neoplasm Staging; Ontario; Population Surveillance; Testicular Neoplasms /diagnosis

**AccessionNumber**
12001004134

**Date bibliographic record published**
31/01/2003

**Date abstract record published**
31/01/2003

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.