Management of stage I seminomatous testicular cancer: a systematic review
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CRD summary
The review concluded that five-year survival in stage I seminomatous testicular cancer post-orchidectomy patients was more than 95% regardless of management strategy. Optimal management was not defined and surveillance was the preferable option as it minimised possible toxic effects of other strategies. The authors' cautious conclusions appear to reflect the evidence presented and are likely to be reliable.

Authors’ objectives
To evaluate the safety and effectiveness of different management and treatment options for patients with stage I seminomatous testicular cancer post-orchidectomy.

This abstract will focus on only the primary studies.

Searching
MEDLINE and EMBASE were searched from 1981 to May 2007 for publications in English; search terms were reported. American Society of Clinical Oncology meeting proceedings were searched over the same time period. An update search on clinical management data alone was performed to June 2009.

Study selection
Randomised (any number of patients) or non-randomised (at least 100 patients) studies of patients with stage I seminoma post-orchidectomy were eligible for inclusion. Studies needed to report at least one of the outcomes: survival, recurrence, long-term toxicity (including second malignancy) and quality of life. Studies that examined long-term toxicity or quality of life had to include at least 400 patients. Studies conducted in narrow patient groups (such as HIV-positive patients) and studies where staging was carried out by lymphangiogram were excluded.

Interventions in the included studies were: radiation therapy (range 20 to 30Gy), para-aortic or extended field (dogleg) radiation therapy; chemotherapy (one or two cycles of carboplatin); and surveillance, where comparisons were made only in the non-randomised studies. Survival was reported mostly at five years (range two to 20 years).

Two independent reviewers performed the selection. Disagreements were resolved by consensus.

Assessment of study quality
Methodological quality of the randomised controlled trials (RCTs) was assessed using Cochrane Library criteria that included: randomisation method; description of withdrawals and drop-outs; intention-to-treat analysis; power; and study design. Each criterion was rated as met, unmet or unclear.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
The number of events for each outcome was extracted in order to calculate percentages with 95% confidence intervals (CI) where possible.

One reviewer performed the extraction, which was checked by a second reviewer.

Methods of synthesis
Results were summarised in separate tables for RCTs and non-randomised studies and a narrative synthesis provided due to the clinical heterogeneity of the evidence.
Results of the review
Forty-two studies were identified (n at least 57,870): three RCTs (n=2,639, range 478 to 1,477) and 39 non-randomised studies (n at least 55,231). The non-randomised studies included 24 treatment studies (n at least 6,401, range 103 to 721) and 15 long-term toxicity studies (n at least 48,830, range 230 to 40,576). All three RCTs had a non-inferiority design, 90% power and unclear details of loss to follow-up. Two RCTs performed intention-to-treat and per protocol analysis. One RCT described the method of randomisation clearly.

Survival: All three RCTs found no significant differences between treatment groups in relapse-free survival after five years.

Non-randomised studies found that five-year overall survival did not differ greatly for different management strategies: surveillance, range 97 to 100% (four studies); radiation therapy, range 95 to 100% (six studies); and carboplatin, range 94 to 100% (five studies). Relapse patterns varied for the different strategies. Most patients under surveillance and treated with adjuvant carboplatin had para-aortic nodal relapse; 2% to 3% of patients treated with para-aortic radiotherapy were noted to have pelvic nodal relapse.

Toxicity: Results were reported for acute toxicity in two RCTs. Results for long-term toxicity were reported for the non-randomised studies including second malignancy (12 studies), cardiac toxicity (two studies) and quality of life (one study).

Authors’ conclusions
The optimal management of stage I seminoma remains to be defined. Surveillance appears to be the preferable option as it minimises the toxic effects that might be associated with other strategies.

CRD commentary
The review addressed a well-defined question in terms of participants, interventions, study design and relevant outcomes. Relevant databases were searched. Only for studies published in English were searched for and a limited search was made for unpublished studies; therefore, some relevant studies may have been missed. Publication bias was not assessed. Study quality was assessed using suitable criteria for the RCTs. This was not the case for the non-randomised studies, for which no relevant information was provided to enable assessment of study quality. Efforts were made to reduce error and bias during most of the review process. Some relevant study details were reported, but few details of study participants were reported. Numbers of participants were not reported for 11 non-randomised studies (mostly toxicity). The authors commented that patients were duplicated in some studies. A narrative synthesis was provided due to the clinical heterogeneity of the evidence.

The review was not well reported and some studies may have been missed during the searches, but the authors’ cautious conclusions appear to reflect the evidence presented and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that surveillance required a commitment to more intense and prolonged follow-up from both patients and clinicians in order to detect relapse at an early stage and should include more frequent computerised tomography monitoring. The authors recommended more intense and prolonged follow-up with treatment with adjuvant carboplatin. Current available evidence should be presented to patients in order to select the most appropriate option for each patient. The authors provided a suitable table of benefits and risks.

Research: The authors commented that further prospective studies of toxicity outcomes would require monitoring large numbers of patients for long periods of time.

Funding
Not stated.

Bibliographic details

PubMedID
19775876

DOI
10.1016/j.clon.2009.08.006

Original Paper URL
http://dx.doi.org/10.1016/j.clon.2009.08.006

Indexing Status
Subject indexing assigned by NLM

MeSH
Humans; Male; Seminoma /therapy; Testicular Neoplasms /therapy

AccessionNumber
12010001279

Date bibliographic record published
23/06/2010

Date abstract record published
22/12/2010

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.