Review

Surveillance or Adjuvant Treatment With Chemotherapy or Radiotherapy in Stage I Seminoma: A Systematic Review and Meta-Analysis of 13 Studies

Fausto Petrelli,[1] Andrea Coinu,[1] Mary Cabiddu,[1] Mara Ghilardi,[1] Karen Borgonovo,[1] Veronica Lonati,[2] Sandro Barni[1]

Abstract

Objective: Testicular stage I seminoma has a remarkable cure rate with orchiectomy alone. The benefit of adjuvant therapy is questionable, and a direct comparison with active surveillance is lacking. We performed a meta-analysis to evaluate the benefit of adjuvant radiotherapy (RT) or chemotherapy (CT) compared with surveillance alone on relapse-free survival (RFS), overall survival (OS), and noncancer-related mortality in patients with stage I seminoma. **Methods:** We performed a systematic search of PubMed, EMBASE, Web of Science, SCOPUS, and the Cochrane Register of Controlled Trials. Meta-analysis was performed using the fixed- or random-effects models. The primary endpoint was 5-year RFS, and secondary endpoints were 5-year OS and 5-year noncancer-related mortality, reported as odds ratios (ORs) and 95% confidence intervals (CIs). **Results:** A total of 13 trials (11 retrospective and 2 prospective cohort series), including 12,075 patients with stage I seminoma, were analyzed. The relapse rates were 3.9% versus 14.8% in the adjuvant therapy and surveillance arms, respectively. Overall, adjuvant therapy significantly improved 5-year RFS (OR, 0.17; 95% CI, 0.1-0.29; $P < .00001$), but not 5-year OS (OR, 1.03; 95% CI, 0.46-2.28; $P = .94$). Mortality due to other causes was not significantly increased with CT or RT. **Conclusions:** Adjuvant RT and CT reduce recurrence risk by 80% of stage I seminoma. However, they do not increase OS or noncancer-related mortality. Both treatment options can be offered to patients with stage I seminoma, taking into consideration the side effects and high cure rate of testicular cancer at relapse.

Clinical Genitourinary Cancer, Vol. 13, No. 5, 428-34 © 2015 Elsevier Inc. All rights reserved.
Keywords: Adjuvant therapy, Meta-analysis, Seminoma, Stage I, Surveillance

Introduction

Testicular germ-cell tumors are highly curable neoplasms even in advanced stages. In particular, men with stage I pure seminoma have an excellent prognosis after orchiectomy. In particular, active surveillance is the preferred option because the prognosis after surgery is excellent. In fact, if relapse occurs, treatment in the setting of recurrent disease can be administered with curative intent in almost all cases. Men who are choosing active surveillance should be informed that their chance of survival with this approach is excellent with or without the administration of adjuvant therapy. A systematic review of active surveillance (n = 14 studies) showed that the relapse rate was 17%.[1] Of these, late relapses (variably defined, but at least 2 years) were reported in 2% of all men in these studies and 9% of those who relapsed. Finally, mortality due to stage I seminoma was exceedingly rare (0.3% died of testicular cancer).

For men who are willing to accept the risks of adjuvant therapies, treatment options after orchiectomy include single-agent carboplatin or radiotherapy (RT). In general, carboplatin is associated with less long-term toxicity risks than adjuvant RT. In addition, given their excellent prognosis, single-agent carboplatin is used rather than a multi-agent cisplatin-based regimen. The efficacy of adjuvant carboplatin was demonstrated in a phase III trial conducted by the

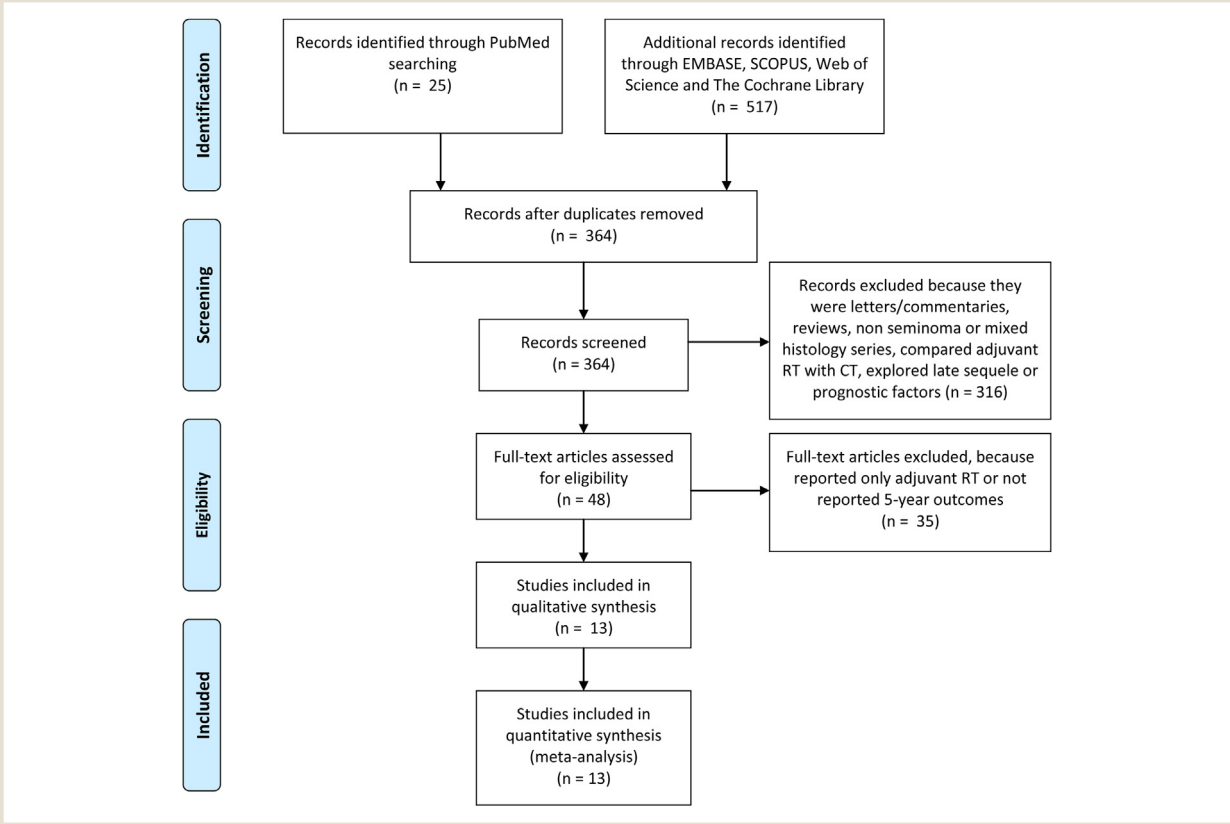
[1]Oncology Department, Medical Oncology Unit, Azienda Ospedaliera Treviglio, Treviglio (BG), Italy
[2]Oncology Department, Radiotherapy Unit, Azienda Ospedaliera Treviglio, Treviglio (BG), Italy

Submitted: Feb 13, 2015; Revised: Apr 10, 2015; Accepted: Apr 12, 2015; Epub: Apr 20, 2015

Address for correspondence: Fausto Petrelli, MD, Department of Oncology, Medical Oncology Unit, Azienda Ospedaliera Treviglio, Piazzale Ospedale 1, 24047 Treviglio (BG), Italy
E-mail contact: faupe@libero.it

1558-7673/$ - see frontmatter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.clgc.2015.04.005

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flow Diagram of Included Studies



Abbreviations: CT = chemotherapy; RT = radiotherapy.

European Organization for Research and Treatment of Cancer.[2,3] In this trial, 1477 men with stage I seminoma were randomly assigned to adjuvant RT or a single course of carboplatin (dosed at an area under the concentration × time curve of 7). At a median follow-up of 6.5 years, relapse-free rates were similar to those with carboplatin and RT (94.7% and 96.0%, respectively). There were no deaths due to stage I seminoma.

RT prevents relapse in 96% of patients with clinical stage I seminoma.[4,5] Although adjuvant RT is associated with an increased risk of long-term toxicities (eg, an increased risk for second malignancies), contemporary clinical trials have identified meaningful reductions in the size of the treatment field and the dose delivered, which could lead to a reduction in long-term risks of second malignant neoplasms compared with historical series.[6] The favorable outcome in patients with clinical stage I seminoma who received adjuvant RT was illustrated by a combined analysis of 3 randomized phase III trials.[5] Recurrences were observed in 4% of patients, but there were only 4 cancer-related deaths, with the remaining subjects successfully treated with chemotherapy (CT) at the time of relapse.

In regard to the best choice of treatment in reducing relapses and improving overall survival (OS), there have been no randomized trials comparing adjuvant therapy with active surveillance for stage I testicular cancer. Regardless of treatment strategy, however, the long-term cancer-specific survival approaches 100% regardless of primary treatment, and an appropriate randomized trial would require thousands of patients to answer the question. Therefore, treatment must be tailored to individual patient preferences, side effects of adjuvant treatments, and clinicopathologic risk factors, in particular size.

In light of the lack of randomized data comparing adjuvant RT or CT with observation alone for this highly curable disease, we carried out a systematic review and meta-analysis of currently available evidence to better evaluate the absolute benefit of adjuvant therapy compared with no adjuvant therapy in terms of 5-year relapse-free survival (RFS) and OS.

Materials and Methods

Search Strategy and Study Eligibility

We carried out this systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[7] Eligible studies were searched in PubMed, Embase, SCOPUS, Web of Science, and The Cochrane Register of Controlled Trials until December 2014.

The following inclusion criteria have been adopted: English language, retrospective and prospective trials/studies reporting data on any CT regimen or RT modality compared with surveillance strategy alone for patients with stage I seminoma, and availability of 5-year event/rate or number of relapses and/or deaths. Principal exclusion criteria were overlapping publications, lack of 5-year

Download English Version:

https://daneshyari.com/en/article/2752169

Download Persian Version:

https://daneshyari.com/article/2752169

Daneshyari.com