Radiotherapy more effective than chemotherapy for early stage II testicular cancer

May 2 2016

A large study of testicular cancer patients has shown that radiation therapy is a better treatment than chemotherapy for patients with stage IIa disease (where one or more regional lymph nodes contain cancer cells but they are less than 2cms in diameter).

These findings, presented at the ESTRO 35 conference today (Monday) and published simultaneously in *Clinical Oncology*, are important because, until now, there has been little evidence about which treatment for testicular seminoma is more effective, and there has been a tendency to move away from radiation therapy towards chemotherapy for treating stage IIa-b patients. Guidelines from the US National Cancer Comprehensive Network recommend radiotherapy for stage IIa, while those from the European Association of Urology allow for either radiation therapy or chemotherapy; both sets of guidelines are equivocal for stage IIb.

The study of 2,437 patients presented today is the largest group of patients with stage II testicular seminoma evaluated so far, and researchers found that 99% of patients with IIa disease were alive after five years if they had been treated with radiation therapy, versus 93% of patients treated with chemotherapy. For patients with IIb disease, the five-year overall survival was 95% for those treated with radiation therapy and 92% for those treated with chemotherapy.

Dr Scott Glaser, resident physician at the University of Pittsburgh Cancer Institute, USA, told the conference: "For patients with IIa testicular seminoma, this improvement in outcome with radiation over chemotherapy persisted after adjustments for all available factors that could introduce a bias. For patients with stage IIb disease, similar rates of overall survival were seen regardless of treatment with multi-agent chemotherapy or radiation therapy. This suggests that an individualised approach is necessary for such patients."

He continued: "Testicular seminoma is a rare disease, there is a lack of randomised data to guide treatment and many prior studies have been limited by small sample sizes. It has, therefore, been difficult to tease out small differences in efficacy of radiation therapy versus chemotherapy. The trend away from radiation therapy may be due to a misperception that it is more toxic than three or four cycles of multi-agent chemotherapy. Across this large, national dataset, radiation therapy was associated with a better outcome for stage IIa patients and equivalent outcomes for stage IIb patients. However, potential explanations for these improved outcomes are less clear."

The study, led by Dr Sushil Beriwal, an associate professor of radiation oncology at the University of Pittsburgh, analysed data from 2,437 patients with stage II testicular seminoma diagnosed between 1998-2012 and treated with radiation therapy or multi-agent chemotherapy after removal of the cancerous testicle. Of the total number, 960 patients had IIa disease, of whom 78% received radiation therapy and 22% received chemotherapy; 812 had IIb disease, with 54% and 46% receiving radiation therapy and chemotherapy respectively; and 665 had IIc disease, with 4% and 96% receiving radiation therapy and chemotherapy respectively.

"For stage IIc patients, there is clear consensus that multi-agent chemotherapy is the preferred treatment as the risk of distant

progression is high, whereas for stage IIa-b there is no such consensus as to the optimal treatment and practice patterns vary significantly. In our series, 96% of stage IIc patients received multi-agent chemotherapy, which also severely limits meaningful comparison to other treatments," explained Dr Glaser.

He said the results support the recommendation that radiation therapy should be the preferred option for treating patients with stage IIa. "We view stage IIb disease as a spectrum where smaller volume disease patients (i.e. those with a 2-3 cm tumour in a single lymph node) may act more like IIa disease and attain the greatest benefit from radiation therapy, whereas patients with a larger volume of disease (i.e. 4-5 cm tumour or that has spread to multiple lymph nodes) may act more like IIc disease and attain the greatest benefit from chemotherapy."

Dr Glaser concluded: "Our results demonstrate the need for a collaborative group effort to open a randomised trial for stage IIa-b testicular seminoma patients examining the role of radiation therapy and chemotherapy."

Limitations of the study include its retrospective nature as it used a national data registry (the US National Cancer Data Base), a relatively short follow-up period (an average of 65 months) as certain toxic effects of treatment may only become apparent after longer follow-up, and the fact that the researchers were unable to describe how well the disease was controlled and deaths that were specifically from the cancer.

Testicular cancer is divided into two main types: seminoma and non-seminoma. Both develop from the germ cells in the testes. Testicular seminoma is one of the most treatable and curable cancers with a survival rate of over 95% if it is discovered in the early stages.

President of ESTRO, Professor Philip Poortmans, who was not involved

in the research, commented: "In cases where there is an absence of prospective randomised trials, such as in rare tumours like stage II testicular seminoma, the analysis of 'real-life' data can help us to verify whether assumptions that are used to guide our treatment recommendations are valid or not. The movement away from radiation therapy in favour of chemotherapy, induced by the fear of a higher rate of late toxicity, is now suggested to be probably not the right one for patients with stage IIa testicular seminoma, with an overall survival benefit in favour of radiation therapy up to at least ten years after treatment. Ideally, these results should be confirmed in a prospective trial with a very long-term follow-up, including a thorough analysis of side effects. However, this might be difficult to achieve."

More information: *Clinical Oncology*, DOI: 10.1016/j.clon.2016.02.008

Provided by European Society for Radiotherapy and Oncology