Surveillance as a management strategy in stage 1 testicular germ cell tumours (GCT) is increasing in popularity due to the recognition of the long-term side effects of treatment. Imaging, in particular computed tomography (CT), plays a central part in the surveillance protocols. There is a tendency towards less frequent use of imaging as supported by recent trials in non-seminomatous GCT but further studies are needed with respect to the assessment of seminoma and to evaluate the role of magnetic resonance imaging (MRI) instead of abdominal CT.

Keywords: Testis cancer; germ cell tumour; imaging; computed tomography.

Introduction

Surveillance is increasingly the preferred management strategy in stage I testicular germ cell tumours (GCT). This is due to growing awareness of the long-term complications in patients treated with radiotherapy and chemotherapy. Long-term survivors of testicular cancer have a two-fold risk of cardiovascular disease and there is a 10% excess lifetime risk of a second malignancy in patients treated with radiotherapy, chemotherapy or both after 30 years of follow up. Surveillance is designed to identify relapse at the earliest stage and therefore enable earlier treatment. Issues arise as to who, when, what and how to survey.

Most surveillance programs include clinical examination, serum markers and computed tomography (CT) scanning to follow up patients but there is great variation in the frequency of imaging between centres. The potential benefit of repeated scanning must be weighed against the consequent financial and health costs. A thoracic CT gives a radiation dose equivalent to 400 chest radiographs (8 vs 0.02 mSv); for a CT scan of the chest and abdomen the dose is increased to approximately 20 mSv (a dose equivalent to 1000 chest radiographs). This results in a 1:1000 lifetime risk of a second cancer/leukemia in a 25-year-old patient over the subsequent 40 years. In order to reduce this radiation exposure, ultrasound and magnetic resonance imaging have been suggested in surveillance programs. However, ultrasound is not as reliable as CT or MR imaging in the assessment of retroperitoneal nodes. Limited data suggest that MR imaging may be used instead of CT for abdominal disease but there are no data from larger prospective trials to support this view.

Non-seminomatous germ cell tumours

The idea of surveying patients closely and treating at the time of relapse has been popular in patients with non-seminomatous germ cell tumours (GCT). In stage I non-seminomatous GCT, approximately 30% of patients will relapse; thus treating all patients risks unnecessary toxicity in over 70% of cases. Vascular or lymphatic invasion are the most powerful predictors of relapse; the absence of yolk sac elements and the presence of undifferentiated cells are also independent prognostic variables. Relapse rates approach 50% in high risk patients compared to a relapse rate of approximately 20% in those without high risk factors. In the prospective TE04 trial, 45% of those that relapsed did not have raised markers at the time of discovery of recurrent disease.
Sixty-one percent of relapses occurred in the para-aortic nodes and 10% in the mediastinal or supraclavicular nodes. Ninety-five percent of those who did relapse were in the good prognostic group and overall survival free from GCT was 99%. As relapse is most frequent in the first year after diagnosis (up to 80%) the number of scans should be greatest during this time. Surveillance is performed rigorously with clinical follow-up, serum marker analysis and serial imaging of the thorax and abdomen.

The value of chest CT over chest radiography has been studied in a series of 168 stage I non-seminomatous GCT patients on surveillance who underwent chest X-ray rather than chest CT. Nineteen percent (42 patients) of these patients relapsed; of which 8/42 relapsed with chest disease. Seven out of eight of these latter patients had evidence of disease elsewhere which was identified on abdominal CT. The one patient in this series who had only chest disease at relapse was clearly diagnosed by chest radiography. This led the authors to conclude that chest imaging with CT would not have changed the prognosis of those who relapsed in the chest in their study.

The role of pelvic CT has also been called into question. In one series of patients with testicular GCT, pelvic lymphadenopathy was seen in 16 of 167 patients (9.6%). The presence of bulky para-aortic lymphadenopathy was the only significant predictor for pelvic disease and was present in 11 of 16 patients. In the absence of this or other risk factors for pelvic disease (previous scrotal or inguinal surgery, maldescent, tunica vaginalis invasion, retro-peritoneal lymph node dissection), routine pelvic CT for patients on surveillance for stage I disease may constitute unnecessary irradiation.

Protocols vary between centres but most will scan patients between two and six times during the first year. As yet no consensus on optimal management has been reached but it is seen that those centres that scan more frequently do not detect relapse at a significantly earlier stage than others. Indeed in one study of 46 patients, all relapses detected after the 3-month CT were picked up by clinical suspicion, raised tumour markers or chest X-ray. Furthermore results of the MRC TE08 study, a prospective randomized trial of two versus five CT scans in patients with stage I non-seminomatous GCT, showed that there was no difference in the outcome in patients in the five scan schedule compared to the two scan schedule.

Is there a role for fluorodeoxyglucose (FDG)-positron emission tomography (PET) in identifying patients for surveillance? Early studies suggested that FDG-PET may improve surveillance by predicting patients likely to relapse. A Danish pilot study on stage I non-seminomatous GCT showed that FDG-PET could identify 70% of patients who subsequently relapsed with metastatic non-seminomatous GCT. Similar results were obtained in a small German study comparing FDG-PET and retroperitoneal lymph node dissection. The negative predictive value of the Danish study was 92% which would suggest that adjuvant treatment could be avoided in most patients with stage I non-seminomatous GCT and a negative FDG-PET. This hypothesis, i.e. the use of FDG-PET to predict relapse in patients with clinical stage I non-seminomatous GCT, has been investigated by the Medical Research Council (MRC) in the UK in the TE22 study. The study showed that although FDG-PET identified a proportion of patients with disease not detected by CT, the relapse rate amongst FDG-PET negative patients remained high. The study results therefore suggest that FDG-PET scanning is not able to identify patients at sufficiently low risk of relapse to replace other treatment options in this setting.

Seminoma

In seminoma, the wide-scale adoption of surveillance was limited until recently due to the lack of a reliable tumour marker. A predominantly intra-abdominal site of relapse meant that regular cross-sectional imaging was needed. However, surveillance has recently been popularised after publication of a new predictive model for relapse in stage I seminoma. A multivariate analysis of patients from Canadian, UK and Danish centres has identified tumour size (≥4 cm) and invasion of the rete testis as significant predictors of relapse. In the absence of both these factors, patients have no more than a 12% risk of relapse, suggesting that there is a group of patients with a particularly low risk of relapse where surveillance might be an attractive option. Relapses are rare after 2 years but have been reported to occur up to 6 years after initial diagnosis. The majority of relapses are in the para-aortic nodes followed by mediastinal nodes, supraclavicular nodes and lung metastases. Only 30% of seminoma relapses are serum marker positive. No studies have addressed the optimal scanning or follow up frequency with widely differing policies. The policy at our hospital is for 6 monthly abdominal CT scans and chest X-ray for the first 2 years and the pelvis is only imaged if there has been previous pelvic surgery. Annual abdominal CT and chest X-ray are then performed until 5 years after the initial diagnosis.

Summary

Surveillance as a management strategy in stage 1 testicular GCT is gaining increasing popularity due to the recognition of the long-term side effects of treatment. The patients who are being surveyed are those likely to be at low risk of relapse, i.e. very good prognosis patients. Surveillance protocols are most intensive when the risk of relapse is highest, i.e. in the first 2 years with decreased monitoring thereafter. What these protocols survey are sites of likely relapse, i.e. the retroperitoneum...
and chest typically. How the sites of relapse are imaged is with a combination of chest radiography and abdominal CT. There is a tendency towards less frequent use of imaging as supported by recent trials in non-seminomatous GCT but further studies are needed with respect to the assessment of seminoma and to evaluate the role of MR imaging instead of abdominal CT.

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