Postoperative radiotherapy following breast-conserving surgery in a minimum-risk older population

A randomised controlled trial of postoperative radiotherapy following breast-conserving surgery in a minimum-risk older population. The PRIME trial

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Executive summary

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Executive summary

Background

Postoperative breast irradiation is the standard treatment following breast-conserving surgery and adjuvant endocrine therapy, irrespective of age. However, the differences between older and younger patients in response to treatment are poorly defined, since patients aged over 70 years are frequently excluded from trials.

The use of breast irradiation declines substantially with age, although just over half of the cases of breast cancer occur in women aged 65 years and older. Current data suggest that the risk of local recurrence after conservation surgery and endocrine therapy may decline with age. At the same time, there are competing risks of death, particularly vascular, in older patients.

Objectives

The objectives of this study were to assess whether omission of postoperative radiotherapy in women with 'low-risk' axillary node negative breast cancer (T0–2) treated by breast-conserving surgery and endocrine therapy improves quality of life and is more cost-effective.

Methods

Design

A randomised controlled clinical trial, using a method of minimisation balanced by centre, grade of cancer, age, lymphatic/vascular invasion and preoperative endocrine therapy, was performed. A non-randomised cohort was also recruited, in order to complete a comprehensive cohort study.

Setting

The setting was breast cancer clinics in cancer centres in the UK.

Participants

Patients aged 65 years or more were eligible provided that their cancers were considered to be at low risk of local recurrence, were suitable for breast-conservation surgery, were receiving endocrine therapy and were able and willing to give informed consent.

Interventions

Interventions were the standard treatment of postoperative breast irradiation or the omission of radiotherapy.

Main outcome measures

Quality of life was the primary outcome measure, together with anxiety and depression and cost-effectiveness. Secondary outcome measures were recurrence rates, functional status, treatment-related morbidity and cosmesis. The principal method of data collection was by questionnaire, completed at home with a research nurse four times over 15 months.

Results

The hypothesised improvement overall in quality of life with the omission of radiotherapy was not seen in the EuroQol assessment or in the functionality and symptoms summary domains of the European Organisation for Research in the Treatment of Cancer (EORTC) scales. Some differences were apparent within subscales of the EORTC questionnaires, and insights into the impact of treatment were also provided by the qualitative data obtained by open-ended questions. Differences were most apparent shortly after the time of completion of radiotherapy. Radiotherapy was then associated with increased breast symptoms and with greater fatigue but with less insomnia and endocrine side-effects. Patients had significant concerns about the delivery of radiotherapy services, such as transport, accommodation and travel costs associated with receiving radiotherapy. By the end of follow-up, patients receiving radiotherapy were expressing less anxiety about recurrence than those who had not received radiotherapy.

Functionality was not greatly affected by treatment. Within the randomised controlled trial, the Barthel Index demonstrated a small but significant fall in functionality with radiotherapy compared with the no radiotherapy arm of the trial. Results from the non-randomised patients did not confirm this effect, however. Cosmetic results were better in those not receiving radiotherapy but this did not appear to be an

important issue to the patients. The use of home-based assessments by a research nurse proved to be an effective way of obtaining high-quality data.

Costs to the NHS associated with postoperative radiotherapy were calculated to be of the order of £2000 per patient. In the follow-up in this study, there were no recurrences, and the quality of life utilities from EuroQol were almost identical. Within this time frame, no radiotherapy is therefore the cost-effective choice. In the longer term, cost-effectiveness will depend on the extent of any greater recurrence rates in patients not receiving radiotherapy and the effect of the recurrence on their quality-adjusted life-years.

Conclusions

Although there are no differences in overall quality of life scores between the patients treated with and without radiotherapy, there are several dimensions that exhibit significant advantage to the omission of irradiation.

Over the first 15 months, radiotherapy for this population is not a cost-effective treatment. However, the early postoperative outcome does not give a complete answer and the eventual cost-effectiveness will only become clear after long-term follow-up. Extrapolations from these data suggest that radiotherapy may not be a cost-effective treatment unless it results in a recurrence rate that is at least 5% lower in absolute terms than those treated without radiotherapy.

Implications for healthcare

The results of this trial have the following implications for healthcare:

- The evidence suggests that there are significant differences in some dimensions of quality of life, although there is no significant overall quality-of-life advantage in the omission of adjuvant radiotherapy.
- Although there is a short-term economic benefit from the omission of radiotherapy in this group of patients, the longer-term benefit has yet to be determined.
- Comprehensive capture of quality of life and co-morbidity data may be facilitated by nurse-led home assessment.
- Cosmesis, although impaired by radiotherapy, appears to be of limited importance to the majority of patients within the first 15 months following surgery.
- More needs to be done to improve access to hospitals for older patients.
- Older low-risk patients have significant concerns about recurrence of breast cancer, even following radiotherapy.

Recommendations for further research

The following are recommended for further research.

1. Long-term data on quality of life and clinical outcomes in PRIME or similar trials should be obtained.
2. Further economic modelling on the longer term costs and consequences of omitting radiotherapy is needed.
3. The application of novel methodologies (such as touch screen technology) for capturing and grading co-morbidity and quality of life at baseline and at clinical follow-up should be investigated.
4. The influence of specific types and degrees of co-morbid disease on quality of life requires study.
5. Methodologies to integrate the prediction of recurrence rates from breast cancer with the competing effects of mortality from other diseases need to be refined to improve clinical decision-making.
6. A validated questionnaire/scale to assess the impact of access to healthcare services should be developed.

Publication

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The research reported in this monograph was commissioned by the HTA Programme as project number 96/03/01. The contractual start date was in January 1999. The draft report began editorial review in March 2006 and was accepted for publication in January 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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