IAEA-CN-85-265

NORMAL TISSUE DAMAGE IN RADIOTHERAPY DEVELOPMENT OF A CLINICAL AUDIT TOOL

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Abstract

Radiotherapy treatments are evaluated by two main outcomes, rates of cure or local tumour control and normal tissue complication rates. Many excellent schemes have been devised for recording the late effects of radiotherapy treatments including the RTOG and LENT SOMA Scales. These have proved invaluable in documenting the outcome of clinical trials, but have proved too complex and time consuming for routine daily use in busy departments. A group in Eindhoven led by Professor Lybeert undertook a pilot study of a potential way of auditing late radiation complications. Using a simplified form derived from the LENT SOMA scales, they collected data on grade 3 and 4 complications in a total of 675 patients and were able to correlate a number of particular complications with specific protocols, ICD codes and physician practice. Further review of the case records made it possible to identify specific factors which may have led to toxicity and could be taken into account to modify treatment protocols. From September 1999 clinicians in participating centres undertaking normal follow-up procedures were asked to identify patients who showed evidence of grade 3 or 4 toxicity as defined in the pro-forma. Date of radiotherapy was recorded so that a temporal correlation of complication with treatment could be made, but this study did not attempt to assess the incidence of complications, but to provide a cross-sectional study of prevalence. Centres participating in the study have been Eindhoven, Köln, Gent, Brussels, Glasgow, Mount Vernon, Madrid, Genova and Lyon. In Eindhoven 651 reports were collected between January 1995 and December 1999. 89 reports had to be discarded because complications were not validated by the reviewing radiotherapists. Dr Lybeert noticed that individual radiotherapists appeared to have different thresholds for reporting specific complications. 13 patients deaths appeared to be related to radiation problems. An overall level of detection of morbidity was approximately 9%. It was possible to link morbidity with specific protocols. Some of these employed large doses per fraction and in some cases these were given in combination with chemotherapy. In the second phase of the study, patients undergoing routine follow-up at the Beatson Oncology Centre were also studied. Forms were completed by the reviewing oncologist and checked and analysed separately by two other radiotherapists. So far a total of 7645 forms have been placed. Of these 4372 have been completed and at routine follow-up 8.9% of these have recorded grade 3 or 4 toxicity. Preliminary analysis of the data suggests again a correlation of large dose per fraction or concomitant chemotherapy with radiotherapy related problems. It is hoped that this study will be completed by December 2000. Comparison of data from different centres will be made. Data from Lyon and Mount Vernon have been extracted from existing databases. It is hoped that there may be some consistency in results which may provide a benchmark for a useful audit tool. This approach will be discussed in relation to the need to develop a simple prospective recording of late morbidity. Keywords: Radiotherapy, Morbidity, QA, Clinical audit** MORQA Project , funded by the "Europe Against Cancer Programme " of the EU

1. Introduction

Quality assurance programmes in radiotherapy are essential to ensure accuracy in treatment delivery, to optimise local tumour control and survival and to avoid as far as possible any undesirable late consequences.

The European Society of Therapeutic Radiology and Oncology with EU funding set up such programmes in 1998 with two components ;
(1) EQUAL – a European QA network
(2) MORQA – a programme designed to measure the prevalence of complications of treatment in patients who are cured of cancer.

2. Background

Radiotherapy treatments are evaluated by two main outcomes, rate of cure or local tumour control, and normal tissue complication rates. Many schemes have been used for recording late effects of radiotherapy treatments, including the RTOG and Lent-Soma scales. Although these have been used widely in documenting the outcome of clinical trials, they are complex and time consuming to record and therefore have not proved a very practical tool in busy clinical practice. There is still a need for a simple method of assessment. In particular, there would be great value from having a system which enabled the early detection of complications which were associated with a specific protocol or treatment approach, especially when new treatments are being introduced.

3. MORQA – Pilot Study

In 1995, Professor Lybeert set up a programme for registration of late morbidity in his department in Eindhoven. The existing instruments developed by major collaborative groups for measuring toxicity of treatment have proved too complex for routine daily use. He therefore used a simplified form derived from the Lent-Soma scale to collect data on Grade 3 and 4 toxicity in 675 patients over a period of 5 years. His group was able to correlate a number of particular complications with specific protocols, ICD codes and physician practice using cluster analysis techniques and the work led to changes in the patient management within the department. On the basis of his experience, this instrument was adopted as a tool for the main MORQA study.

4. MORQA – Methodology

11 centres in Europe participated in the study after initial site visits to document their structure, function and ability to collect data appropriately.

From September 1999, clinicians in participating centres undertaking routine follow-up care of patients treated with radiotherapy were asked to identify those who showed evidence of Grade 3 or 4 toxicity as defined in the pro forma. Information was sought about the date of radiotherapy (for temporal correlation of complication with treatment) and other treatments given (to assess the effect of treatment interactions). It was recognised that this study could not assess the incidence of complications but only provide a cross-sectional study of prevalence.Completed forms and patient files were assessed by two independent observers. Regular network meetings were held to monitor the progress of the study.

5. Results

A number of different follow-up practices were observed in the participating centres. It was striking that few centres had a fully comprehensive policy of following treated patients, which would be essential for obtaining data on incidence of complications. Because of this variation in practice, the data were collected in several different ways. Data were considered to be complete and representative in 4 of the 11 participating centres. From 1 centre (Mount Vernon), results from a prospectively collected database could be used to determine incidence of complications in patients with two particular types of tumours.

The majority of the effects recorded developed within the first 5 years after treatment although new complications were still recorded at 10-20 years after treatment. Other

treatments given at or near the time of radiotherapy may increase complication rates. We observed that many patients had had surgery or chemotherapy which may have contributed to the outcome. Cluster analysis for the data from Eindhoven has shown correlations with particular schedules of treatment but this could not be confirmed for the overall group of patients where clusters appeared rather to occur in association with the commonest types of tumours. Over and under reporting of side effects was noted. Clinicians unfamiliar with radiotherapy practice often ascribed effects to the treatment which were unconnected (eg. problems with dentition after radiotherapy for carcinoma of the cervix) and doctors with less experience in the specialty might fail to recognise side effects to which radiotherapy may have contributed. There was clear evidence of general lack of knowledge in this area. Review of the endpoints documented showed that some were useful and easily defined (myelitis) whereas others were rarely used (fatigue) or difficult to assess (dyspnoea). It was clear that patient and physician estimates of the severity of a problem could differ.

6. Conclusions and recommendations

1. There is no agreement on how patients who have been treated for cancer should best be followed to determine
(a) local control rates
(b) overall survival
(c) consequences of treatment
These three endpoints are essential for determining whether a new treatment represents a real improvement over an existing one (ie. shows an improvement in therapeutic ratio and not just a higher cure rate at a greater cost).
Recommendation - The development of strategies for patient surveillance is a target for future quality assurance programmes.
2. There is wide-spread ignorance about the consequences of successful treatment for cancer and the interactions of various components of the treatment. An education programme is needed to improve this situation. Collaborations should be set up with other European Cancer groups (ESSO and ESMO through FECS) to study treatment interactions.
Recommendations_- New ESTRO teaching programme on care of the cured patient and consequences of cancer treatments.
Joint initiative with FECS to study treatment outcomes.
3. The established instruments for recording outcomes of treatment are effective within clinical trials settings but too complex for routine practice. Further work is needed to develop a simple tool. This present study shows that it should contain only a small number of items (or it will not be used) and more work is needed to validate these items. Patient's views must contribute to the overall assessment of outcome.
Recommendations - Further discussion to reach a consensus at a European/International level on ways of recording outcomes of treatment.
Development of a way of recording patient's view of treatment outcome.
4. Cluster analysis (used routinely in other branches of science) does not seem to be a sensitive method for use in the study of treatment side effects probably because they are rare and affected by many factors other than radiation alone.
5. It is difficult to show a direct correlation between specific dosimetric estimates (from the EQUAL Study) with particular outcomes because the variation due to errors in radiotherapy delivery is small and co-morbidity and effects of other treatments influence radiotherapy outcomes. Nevertheless dose response curves for complications can be derived and the theoretical improvement to be expected from the QA programme calculated.

Recommendation - Continuation of both aspects of the QA programme is essential to optimise outcomes of treatment.

7. Future programme

The network meetings led to an international meeting MITRE, set up to discuss the issues of identifying, monitoring, recording, eliminating or treating undesired consequences of treatment. This meeting held in Brussels in December 2000 was attended by 160 participants from 29 countries and led to the production of a consensus statement for a strategy for future studies. Application will be made to the Commission of the European Union for funding to continue and develop the programme of quality assurance in cancer treatment

Acknowledgement

This study was made possible thanks to the support of the "Europe Against Cancer " Programme of the EU.

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