

Long term mortality after a single treatment course with X-rays in patients treated for ankylosing spondylitis

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Summary Mortality up to 1 January 1983 has been studied in 14,106 patients with ankylosing spondylitis given a single course of X-ray treatment during 1935–54. For neoplasms other than leukaemia or colon cancer, mortality was 28% greater than that of members of the general population of England and Wales, and this increase is likely to have been a direct consequence of the treatment. The proportional increase reached a maximum of 71% between 10.0 and 12.4 years after irradiation and then declined. There was only a 7% increase in mortality from these tumours more than 25.0 years after irradiation and only for cancer of the oesophagus was the relative risk significantly raised in this period. Neither the magnitude of the relative risk, nor its temporal pattern following treatment, were greatly influenced by the age of the patient at first treatment.

For leukaemia there was a threefold increase in mortality that is also likely to have been due to the radiotherapy. The relative risk was at its highest between 2.5 and 4.9 years after the treatment and then declined, but the increase did not disappear completely, and the risk was still nearly twice that of the general population more than 25.0 years after treatment. There was some evidence that the risks of acute myeloid, acute lymphatic, and chronic myeloid leukaemia were all increased, but no evidence of any increase in chronic lymphatic leukaemia. The relative risk appeared to be greatest for acute myeloid leukaemia.

For colon cancer, which is associated with spondylitis through a common association with ulcerative colitis, mortality was increased by 30%.

For non-neoplastic conditions there was a 51% increase in mortality that was likely to be associated with the disease itself rather than its treatment. The increase was apparent for a wide range of diseases and was not confined to diseases that have been associated clinically with ankylosing spondylitis.

Court Brown & Doll identified over 14,000 patients with ankylosing spondylitis who had been treated with X-irradiation at some time between 1935 and 1954 at any one of 87 radiotherapy centres in Great Britain and Northern Ireland. Initial reports analysed mortality in these patients from leukaemia (Court Brown & Doll, 1957) and other cancers (Court Brown & Doll, 1965) and related the incidence of leukaemia to the dose received. These analyses included many patients who had been treated with X-rays for their spondylitis more than once and it was not clear whether the increase that continued for many years should be attributed to the first or subsequent courses. When Smith & Doll (1978; 1982) reported on the follow-up of the patients to 1970, they avoided this difficulty by restricting the analyses to patients who had received only a single course of treatment. Their analyses showed that, when the mortality of the spondylitic patients was compared with that of the general population, the relative risk of leukaemia was at a maximum 3–5 years after treatment and subsequently declined. For other cancers of sites judged to be heavily irradiated, the relative risk was at a maximum 9–11 years after treatment and then declined to less than one after 24 years. Only a small proportion of patients had been followed beyond 20 years, however, and the decreasing trend in relative risk for these other cancers more than 11 years after treatment was not statistically significant. We have, therefore, sought to find out how long the increased mortality from leukaemia and other cancers persisted following X-ray treatment by extending the follow-up of patients who received only a single course of treatment by a further 13 years and have related the increased mortality to organ dose. We report here only the data for total and organ specific mortality and have deferred discussion of the complex relationship with dose to a later report.

Material and methods

Study population and follow-up

A total of 14,554* patients was included in the study. Four hundred and forty eight patients were excluded from further analysis because they had received radiotherapy for their spondylitis before being entered into the study (405), or they had received thorium treatment before, or simultaneously with, their first course of radiotherapy (5), or their date of birth was unknown (38) (Table I).

Follow-up information about the remaining 14,106 patients was sought from the National Health Service Central Registers. For persons who could not be found on the Registers, letters were sent to radiotherapy centres, general practitioners, or individual patients. All but 171 patients (1.2%) were traced in this way to their death, date of emigration from the United Kingdom, 1 January 1983, or 18 months after a second treatment course with radiotherapy or thorium. Re-treated patients were retained in the study for 18 months after re-treatment because some patients may have been re-treated for symptoms attributable to cancer which were misdiagnosed as a recurrence of their spondylitis. Any solid cancers induced by the re-treatment are unlikely to have appeared and caused death in this short interval. For leukaemia, however, the interval between radiation exposure and resulting death may be less than for solid cancers, and deaths from this cause occurring after a second treatment were included only if they occurred within the following 12 months (see below).

By 1 January 1983 just over half the patients had been re-treated and 346 had emigrated (Table I). A total of 2,983 patients were alive and living in the United Kingdom and

*This number is six less than reported previously (Smith & Doll, 1982). One patient was found to have been included twice, one to have received the initial radiotherapy for a disease other than spondylitis, two never to have received radiotherapy, and two computer records had serial numbers that did not appear on the original listings.