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Increased cardiovascular disease risk after exposure to low dose radiation

These risks should now be considered in radiation protection measures and policies

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In a linked BMJ article (doi:10.1136/bmj-2022-072924),[1] Little and colleagues report the results of a large meta-analysis of 93 studies evaluating associations between a range of cardiovascular diseases and exposure to radiation in various settings (mostly radiotherapy and occupational exposures, but also diagnostic radiology and environmental exposures). The authors found robust evidence for a dose dependent increase in cardiovascular risks across a broad range of radiation doses. Key findings included a higher relative risk per dose unit at lower dose ranges (<0.1 Gy), and also for lower dose rates (protracted exposures over hours to years). The studies included in the meta-analysis were published mainly during the past decade. This new meta-analysis strengthens the evidence linking low dose radiation to risk of circulatory diseases and these risks should now be carefully considered in protection against radiation in medicine and elsewhere.

Radiation induced heart disease as a result of direct damage from high dose thoracic radiotherapy (including pericardial, coronary artery, and valvular disease, as well as cardiomyopathy and conduction disorders) has been recognised for several decades.[2,3] Firm evidence for increased risks at lower doses has also been gradually accumulating since a report from the Life Span Study of atomic bomb survivors from Hiroshima and Nagasaki showed increased stroke and heart disease mortality at doses over 0.5 Gy.[4] Indications of increased risk have also been reported for specific vascular diseases in the Adult Health Study of atomic bomb survivors, but with inconsistent dose response patterns.[5]

Little and colleagues' results add novelty and importance because of the more solid and consistent evidence of cardiovascular risks at low doses than shown in previous studies. Although high doses are exceptional, low dose exposures are common and affect almost the entire population from natural and artificial sources.

The studies included in this meta-analysis cover a broad range of doses, brief and prolonged exposures, and studies evaluating incidence and mortality of various types of vascular diseases. With such diversity, considerable heterogeneity in results is to be expected. Quality of dose estimation is pivotal in studies of radiation risks, and differences in dosimetry methods might also contribute to heterogeneity of results. Despite heterogeneity in results across studies, no clear evidence of publication bias was shown. Furthermore, confounding did not appear to have a major effect where adjustment for other risk factors was possible, which increases the validity of the findings.

Inconsistencies and gaps remain in the evidence linking vascular disease to low dose radiation exposure. These include possible differences by age at exposure and effects on specific types of cardiovascular disease. Important questions also remain regarding the pathogenetic mechanisms and target tissues at low doses. Substantial evidence shows cardiovascular disease development after radiotherapy but applicability of those findings to low doses is uncertain. Oxidative stress and proinflammatory and prothrombotic responses that involve cytokines and transcription factors might have a role in radiation induced endothelial dysfunction, which results in atherosclerosis.[6] Both macrovascular and microvascular effects in cardiac and extracardiac structures are important targets, but more detailed and specific knowledge is needed.[7] Metabolic effects affecting lipids, carbohydrate metabolism, and the endocrine system might also contribute to delayed, persistent radiation effects.[8]

Medical uses of radiation are by far the most important synthetic source of radiation exposure.[9] Patients can be exposed repeatedly throughout their lifetime and receive doses from diagnostic and therapeutic procedures ranging from micrograys to tens of grays.[10]

Cancer risk is the most important health risk related to low dose radiation because the risk coefficients per dose unit are lower for cardiovascular disease than for cancer (excess relative risk per grey around 0.1-0.2 *v* 0.4-0.5).[1,11] Nevertheless, absolute cardiovascular risks attributable to radiation per dose unit are not materially lower than those for cancer risks because of the high baseline risks of cardiovascular disease.

No strict dose limits are used for radiological protection (although reference levels have been defined for various medical procedures).[12] Instead, guidance from the International Commission on Radiological Protection requires justification for use of radiation with careful assessment of the balance between benefits and risks, and avoidance of unnecessary exposure, for instance, by using alternative imaging methods that do not involve ionising radiation, such as ultrasound or magnetic resonance imaging. Any use of radiation requires optimisation, meaning exposure is limited to the lowest level that provides adequate information for clinical decision making.[13]

Evidence for cardiovascular disease will soon need to be added to the existing list of radiation induced health risks. The consequences will be extensive: concepts and standards in radiological protection

will need to be revisited by national and international professional and radiation protection organisations. More stringent standards for justification and optimisation, especially for high dose procedures, will have to be considered. Their implementation will require training to improve awareness, knowledge, and understanding of the risks associated with specific procedures and cumulative exposure. Finally, the implications extend to risk communication for patients and the public.

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