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Is radioiodine good for hyperthyroidism?

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When attending endocrine meetings, I am always surprised by the lack of consensus regarding the best treatment for hyperthyroidism. National surveys (reviewed in Vaidya *et al*.[1]) show that although most members of specialist thyroid societies around the world prefer antithyroid drugs as first line treatment (for a typical first episode of Graves' hyperthyroidism in a young woman), there is considerably more use of radioiodine as first line treatment in the US, at least when reported in 1990.[1]

If radioiodine is chosen to treat hyperthyroidism, there is also a surprising lack of consensus about issues such as size of dose, timing of second dose, and role of antithyroid drugs before and after radioiodine.[1] Although formal dose titration based on time-consuming and costly investigations of thyroid size or of isotope uptake or turnover is clearly not helpful in 'selecting' the radioiodine dose, certain factors (e.g. greater biochemical severity of hyperthyroidism, larger goiter size and perhaps male gender and use of thionamides before radioiodine therapy) impact negatively on the likelihood of cure with a single dose and the likelihood of hypothyroidism, just as these factors impact on the likelihood of remission with antithyroid drugs.

Proponents of radioiodine point to the well-documented vascular morbidity,[2,3] especially risk of atrial fibrillation, and vascular mortality (both cardiovascular and cerebrovascular) associated with hyperthyroidism, along with the poor long-term remission rate for medical treatment alone, and a consequent need for definitive treatment. 'Cure' would logically be associated with the best chance of ameliorating the impact of hyperthyroidism on cardiovascular risk, but does the mode of inducing cure alter prognosis? Several large cohort studies, including our own in the UK[4,5] and a recent one from Finland,[6] reported increased mortality from vascular causes (including cardiovascular and cerebrovascular deaths) in radioiodine-treated patients compared with the background population. These studies indicated higher cumulative doses of radioiodine to be associated with increased mortality (although the dose was an independent factor only in the 1998 UK study[4]). This raises the question: is the treatment itself a causative factor or does this 'dose response' reflect bias due to the severity of hyperthyroidism or other confounding risk factors?

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Few studies have compared the outcome of different treatment modalities, probably because of difficulty in following those receiving thionamides, the fact that most eventually require radioiodine, and the limited use of surgery. Overall, the available data suggest that the underlying hyperthyroidism, rather than radioiodine itself, causes the vascular mortality. A potentially important observation in both the UK and Finnish cohorts is that development of hypothyroidism after radioiodine therapy abolishes this excess vascular mortality. Speculatively, this is because hypothyroidism is the best marker of 'cure' of hyperthyroidism and provides the best chance to reverse the effects of thyroid hormone excess, although other explanations may exist. The findings from these large cohort studies support a policy of inducing hypothyroidism with large administered doses of radioiodine. Our own policy is to administer a fixed dose (600 MBq), which results in cure in 85% of patients (with similar efficacy in Graves' disease and toxic nodular hyperthyroidism) and hypothyroidism requiring levothyroxine treatment in 60% by 12 months. Long-term follow-up is still important to define cancer risk, especially in younger age groups, because of the generally very reassuring but still inconsistent data regarding cancer incidence and mortality following radioiodine treatment.

Supplementary information, in the form of a list of references cited in this article, is available on the *Nature Clinical Practice Endocrinology & Metabolism* website.

JA Franklyn is an Advisory Board member of Nature Clinical Practice Endocrinology & Metabolism.

Competing interests
The author declared no competing interests.

www.nature.com/clinicalpractice
doi:10.1038/ncpendmet0728