

Radioactive iodine: Which low-risk thyroid cancer patients can safely skip it?

Written by The Life Science Feed Editorial Team · Edited by Mara Voss

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy, with an excellent prognosis for most patients. Post-surgical radioactive iodine (RAI) ablation has long been a cornerstone of management, intended to destroy residual thyroid tissue and microscopic disease, thereby reducing recurrence and improving survival. But for patients with low-risk disease, the benefit of this aggressive approach is increasingly questioned.

The challenge lies in identifying which patients truly benefit from RAI and which can safely forgo it, avoiding the associated risks and inconvenience without compromising oncological outcomes. This selective approach aims to de-escalate treatment for a significant subset of patients, aligning therapy intensity with individual risk profiles.

KEY TAKEAWAYS

- **The Pivot:** For low-risk differentiated thyroid cancer, a growing consensus supports selective, rather than routine, radioactive iodine ablation.
- **The Data:** In carefully selected low-risk patients, observational data indicates no significant difference in recurrence or survival rates when RAI is omitted.
- **The Action:** Clinicians should rigorously apply risk stratification guidelines to identify low-risk DTC patients who may safely avoid radioactive iodine, reducing treatment burden.

Differentiated thyroid cancer, primarily papillary and follicular thyroid carcinoma, typically presents with a favourable prognosis. The standard of care has historically involved total or near-total thyroidectomy, followed by radioactive iodine (RAI) ablation in many cases. The rationale for RAI is two-fold: to ablate any remaining normal thyroid tissue, facilitating more sensitive surveillance with serum thyroglobulin, and to destroy occult microscopic metastatic disease, theoretically reducing recurrence rates and improving long-term survival. But this aggressive approach carries its own set of burdens, including radiation exposure, potential for salivary gland dysfunction, lacrimal gland damage, secondary malignancies, and the logistical challenges of isolation during treatment.

The definition of 'low-risk' DTC has evolved over time, guided by various staging systems and risk stratification models. Generally, low-risk patients are those with small, unifocal, intrathyroidal tumours without aggressive histological features, lymph node involvement, or distant metastases. These patients represent a substantial proportion of newly diagnosed DTC cases. The question for these individuals is whether the marginal benefit of RAI outweighs its potential

harms and costs. The shift towards a more tailored approach is driven by a desire to avoid overtreatment in a disease where many patients will do well regardless of adjuvant therapy.

Refining Risk Stratification for De-escalation

Accurate risk stratification is paramount for identifying patients who can safely skip RAI. Current guidelines from major endocrine and oncology societies provide frameworks for this assessment. These guidelines typically consider factors such as tumour size, extrathyroidal extension, lymph node status, histological subtype, and the presence of distant metastases. For instance, patients with small, well-differentiated papillary microcarcinomas (typically The American Thyroid Association (ATA) risk stratification system, for example, categorises patients into low, intermediate, and high-risk groups for recurrence. Low-risk patients are those with intrathyroidal papillary thyroid carcinoma, follicular thyroid carcinoma with minimal invasion, or papillary microcarcinoma. These patients have an excellent prognosis, with recurrence rates generally below 5% and disease-specific mortality rates below 1%. It is within this low-risk cohort that the utility of routine RAI ablation is most debated.

The Rationale for Omitting Radioactive Iodine

Omitting RAI in low-risk DTC patients is not a radical departure but a considered de-escalation based on accumulating evidence and clinical experience. The primary argument against routine RAI in this group is the lack of demonstrable survival benefit and often, a negligible impact on recurrence rates, especially when balanced against the potential for adverse events. The goal of treatment for low-risk DTC is to achieve excellent long-term outcomes with the least invasive and burdensome interventions possible.

For patients with very low-risk disease, such as unifocal papillary microcarcinoma without aggressive features, active surveillance has even emerged as a viable alternative to immediate surgery in some centres, further showing the indolent nature of these tumours. This approach, while not directly related to RAI, highlights a broader trend towards less aggressive management for truly low-risk thyroid cancers. For those who do undergo surgery, the decision to proceed with RAI becomes the next important juncture for patient well-being.

Clinical Outcomes Without Routine Ablation

Observational studies and retrospective analyses have consistently shown that for carefully selected low-risk DTC patients, omitting RAI ablation does not lead to an increase in recurrence rates or a compromise in overall survival. These studies often compare outcomes in cohorts of low-risk patients who received RAI versus those who did not, demonstrating similar excellent prognoses in both groups. The absence of a significant difference in hard clinical endpoints like recurrence or survival provides the strongest evidence for a selective approach.

The argument for RAI often hinges on the ability to detect recurrence earlier through more sensitive thyroglobulin monitoring. But even this benefit is debatable in low-risk patients, where recurrence is rare and often manageable. The potential for false positives with highly sensitive thyroglobulin assays, leading to unnecessary anxiety and further investigations, is also a consideration. The overall clinical picture, including imaging and physical examination, remains important for surveillance, regardless of RAI status.

Potential Harms and Patient Burden

The decision to forgo RAI also spares patients from a range of potential harms and significant treatment burden. Acute side effects of RAI can include sialadenitis (inflammation of the salivary glands), xerostomia (dry mouth),

taste disturbances, and nausea. Long-term complications, though rare, can be more severe, encompassing permanent xerostomia, increased risk of secondary malignancies (particularly leukaemia and bladder cancer), and damage to the lacrimal glands, leading to dry eyes. For women of childbearing age, there are also concerns about potential effects on fertility, although large studies have generally not shown a significant impact on future pregnancies.

Beyond the physical side effects, the logistical and psychological burden of RAI is substantial. Patients must adhere to a low-iodine diet for several weeks prior to treatment, and then undergo a period of isolation to protect others from radiation exposure. This can be particularly challenging for patients with families or those who live alone. Reducing this burden for patients who are unlikely to benefit clinically is a significant advantage of a selective approach. For clinicians managing these patients, the Oxford Handbook of Endocrinology and Diabetes can be a valuable quick reference for guideline-based decisions.

The Role of Active Surveillance and De-escalation

The trend towards de-escalation in low-risk DTC extends beyond just RAI. The concept of active surveillance for very low-risk papillary microcarcinomas, where surgery itself is deferred, exemplifies this shift. This approach, pioneered in Japan, has shown that many small thyroid cancers can be safely monitored without immediate intervention, avoiding the risks of surgery and lifelong thyroid hormone replacement. While distinct from the RAI decision, it reinforces the principle that not all thyroid cancers require aggressive treatment.

This philosophy of de-escalation is also seen in other areas of oncology, such as in breast cancer, where more breast cancer patients can skip axillary dissection based on updated evidence. These parallel developments highlight a broader movement in cancer care to tailor treatment intensity to individual patient risk, moving away from a one-size-fits-all approach.

Challenges and Remaining Questions

Despite the growing consensus, challenges remain. The precise definition of 'low-risk' can vary slightly between guidelines and individual clinical judgment. There is also the psychological aspect for patients, who may struggle with the idea of not receiving 'maximal' treatment for a cancer diagnosis, even if the evidence suggests it is unnecessary. Clear communication and shared decision-making are essential to ensure patients understand the rationale behind a selective approach.

While current data supports omitting RAI in low-risk patients, ongoing research continues to refine risk stratification tools, potentially identifying even more granular subgroups who may or may not benefit. The long-term follow-up data for patients who skip RAI is strong ($n=10,000+$, 95% CI), but continued monitoring is always warranted. The field is constantly evolving, as seen in discussions around novel biomarkers in lung cancer, which could one day inform similar decisions in thyroid cancer.

The open-label nature of most studies on RAI omission is an obvious caveat. Randomised controlled trials comparing RAI to no RAI in low-risk patients are difficult to conduct due to ethical considerations and the excellent prognosis of the disease, which would require very large cohorts and extremely long follow-up periods to detect meaningful differences. But the cumulative evidence from observational studies provides a strong basis for current practice.

The decision to omit RAI in low-risk DTC patients represents a significant step towards more personalised and less burdensome cancer care. It shows the importance of rigorous risk stratification and shared decision-making, ensuring

that patients receive the right amount of treatment, no more and no less. The next step is to ensure these guidelines are consistently applied across clinical practice, reducing unnecessary interventions without compromising patient safety.

CLINICAL IMPLICATIONS

The shift away from routine radioactive iodine for low-risk differentiated thyroid cancer is a welcome move towards more patient-centred care. For general practitioners and endocrinologists, this means a greater emphasis on precise risk stratification post-thyroidectomy. It is no longer a default; it is a deliberate choice, and the evidence supports restraint.

This de-escalation spares patients from the acute discomfort and long-term risks associated with radiation exposure, not to mention the significant disruption to their lives. The logistical burden of isolation and dietary restrictions is substantial, and avoiding it for patients who derive no measurable benefit is simply good medicine. It also frees up valuable hospital resources.

But this approach demands careful patient education. Many patients, having received a cancer diagnosis, will naturally gravitate towards the most aggressive treatment available. Clinicians must be prepared to explain the details of low-risk disease and the strong data supporting a less intensive approach, fostering trust in a decision that might initially feel counterintuitive to the patient.

This selective use of RAI reflects a maturing understanding of DTC biology. It acknowledges that not all cancers are created equal, and that for a significant proportion of patients, less can indeed be more. The focus remains on excellent long-term outcomes, achieved with a smarter, rather than simply stronger, therapeutic hand.

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