The success rate of thyroid remnant ablation in low risk patients is greater using a fixed amount of $^{131}$I determined by tumor stage than selecting it according to a 24-hr $^{131}$I uptake.


**BACKGROUND** Remnant ablation with $^{131}$I has for decades been an integral part of the management of differentiated thyroid cancer, yet the optimal protocol remains uncertain. The aim of this retrospective study was to compare the success rate of remnant ablation performed according to a fixed amount of $^{131}$I based upon tumor stage compared with an $^{131}$I activity determined by an uptake-based protocol.

**METHODS** The study subjects are 359 patients treated with total or near-total thyroidectomy for differentiated thyroid carcinoma without distant metastases that subsequently had $^{131}$I remnant ablation in one of two academic hospitals in the Netherlands. A total of 153 patients (43%) were treated at the Leiden University Medical Center according to a $^{131}$I-uptake protocol and 206 others (57%) were treated at the University Medical Center Utrecht according to a fixed-dose protocol.

For the uptake protocol, the 24-hour neck uptake of 1 mCi of $^{131}$I (40 MBq) was stratified into 3 levels: >10, 5 to 10, or <5%, which was followed by 30, 50, or 75 mCi of $^{131}$I (2800, 1850, or 1110 MBq), respectively.

Follow-up was performed 6 and 12 months after $^{131}$I ablation when patients were evaluated by serum thyroglobulin (Tg) after levothyroxine withdrawal and $^{131}$I whole body diagnostic scans performed 24 hours after 1 mCi (40 MBq), although a few were performed with recombinant human thyrotropin (rhTSH). Successful ablation was defined as a Tg-off below the functional sensitivity of the assay and negative diagnostic whole body scans.

* Tumor stage (T=tumor stage, N=lymph-node stage and M=distant metastasis) was determined according to the 5th edition of the American Joint Committee on Cancer (AJCC), www.cancerstaging.org.

**RESULTS** The mean patient ages in the uptake and fixed-dose protocol groups were, respectively, 42.6 (range 15 to 87) and 43.1 years (range 19 to 82, P = 0.68). There were more lymph node metastases and T4 tumors in patients treated with a fixed-dose protocol (N1, T4, †P = 0.008). PTC is papillary thyroid cancer, FTC is follicular thyroid cancer. N0-stage is no clinically apparent lymph-node metastases. T4 tumors are of any size and extend beyond the thyroid. Stage is according to the 5th edition of the AJCC tumor stage. This and other figures adapted from Tables 1 and 2 from Verkooijen R.B., et al.
The main conclusion of this study by Verkooijen et al. is that empirically selecting $^{131}$I activity based upon tumor stage is more effective than is uptake-selected $^{131}$I activity. In effect, this conclusion compares the efficacy of low and high $^{131}$I activities in the range of 30 to 75 mCi with amounts in the range of 100 to 150 mCi. Thus the essential conclusion is that larger fixed amounts of $^{131}$I are therapeutically more effective than are the smaller $^{131}$I activities that usually result from an uptake-determined protocol. Still, successful remnant ablation was achieved in only 56% of those treated with the fixed-dose protocol compared with 111 of 199 (56%) patients who were treated with a fixed-dose protocol ($P = 0.022$); however, successful ablation depended upon whether it was defined by whole body scans alone or with serum Tg measurements. Moreover, patients with $T_4$ tumors had similar ablation rates with the two protocols (Figures 3 and 4).

**CONCLUSION** The success rate of thyroid remnant ablation is greater following a fixed amount of $^{131}$I than is treatment based upon a 24-hr $^{131}$I uptake in patients with non-metastatic tumors measuring 1 to 4 cm confined to the thyroid gland.

Figure 3. As determined by a whole-body scan alone, remnant ablation is significantly more successful in patients treated with a fixed-dose protocol than in patients treated with an uptake-protocol; however, this did not apply to patients with $T_4$ tumors. †$P < 0.001$. See figure 1 legend for abbreviations.

Figure 4. As determined by a whole-body scan and serum Tg levels, remnant ablation is significantly more successful in patients treated with a fixed-dose protocol than in patients treated with an uptake-protocol; however, this did not apply to patients with $T_4$ tumors. †$P < 0.001$.

**COMMENTARY**

The main conclusion of this study by Verkooijen et al. is that empirically selecting $^{131}$I activity based upon tumor stage is more effective than is uptake-selected $^{131}$I activity. In effect, this conclusion compares the efficacy of low and high $^{131}$I activities in the range of 30 to 75 mCi with amounts in the range of 100 to 150 mCi. Thus the essential conclusion is that larger fixed amounts of $^{131}$I are therapeutically more effective than are the smaller $^{131}$I activities that usually result from an uptake-determined protocol. Still, successful remnant ablation was achieved in only 56% of those treated with the fixed-dose protocol and was a mere 43% in those treated according to the uptake-related protocol—both very low ablation rates.

For example, the large randomized study by Pacini et al. (1) found that successful ablation was achieved at 8 months in 100% of the patients prepared by either thyroid hormone withdrawal or rhTSH-stimulation. Successful ablation was rigorously defined by no visible $^{131}$I uptake 48 hours after a 4 mCi diagnostic whole body scan or, if visible uptake was found, an uptake of <0.1%. Moreover, an rhTSH-stimulated Tg$<1$ ng/ml as the criterion for successful ablation found a that 96% had a successful outcome. Other prospective randomized studies also report successful remnant ablation in about 80% of patients treated with 30 to 50 mCi of $^{131}$I.(2;3)

Why is there a discrepancy among these studies? The most obvious answer is that almost 10% of the patients in the Verkooijen study had $T_4$ tumors, which are tumors of any size extending beyond the thyroid capsule, some of which had lymph-node metastases. The authors point out that neither protocol failed to show a significant advantage in patients with $T_4$ tumors. The authors also found a low sensitivity of $^{131}$I diagnostic whole body scans, an observation also reported by others (4), which means that tumor was missed by this test. There are other important features of this study that bear mention. First, different Tg assays were used in the two hospitals and long-term recurrence rates are not available. I agree with the authors’ conclusion that follow-up studies are necessary to judge whether the difference between the
two methods of selecting $^{131}$I activity results in long term differences in outcome.

For now, the weight of evidence suggests that remnant ablation can be successfully performed in patients treated with 30 to 50 mCi (1110 to 1850 MBq) provided the patient has low-risk tumors confined to the thyroid gland, which is the majority of patients with papillary thyroid cancer.

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References


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