

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

Verkooijen RB, Verburg FA, Van Isselt JW, Lips CJ, Smit JW, Stokkel MP. The success rate of I-131 ablation in differentiated thyroid cancer: comparison of uptake-related and fixed-dose strategies. *Eur J Endocrinol* 2008;159:301-7.

SUMMARY

BACKGROUND Remnant ablation with ¹³¹I 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 ¹³¹I based upon tumor stage compared with an ¹³¹I 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 ¹³¹I 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 ¹³¹I-uptake protocol and 206 others (57%) were treated at the University Medical Center Utrecht according to a fixed-dose protocol.

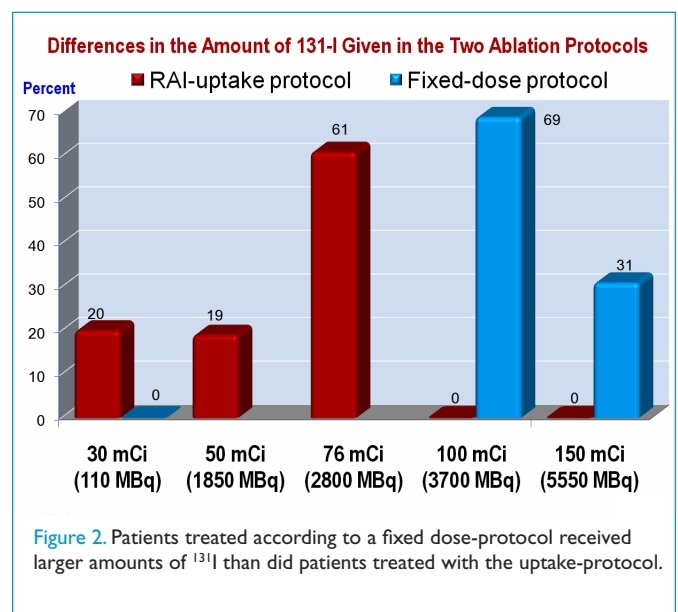
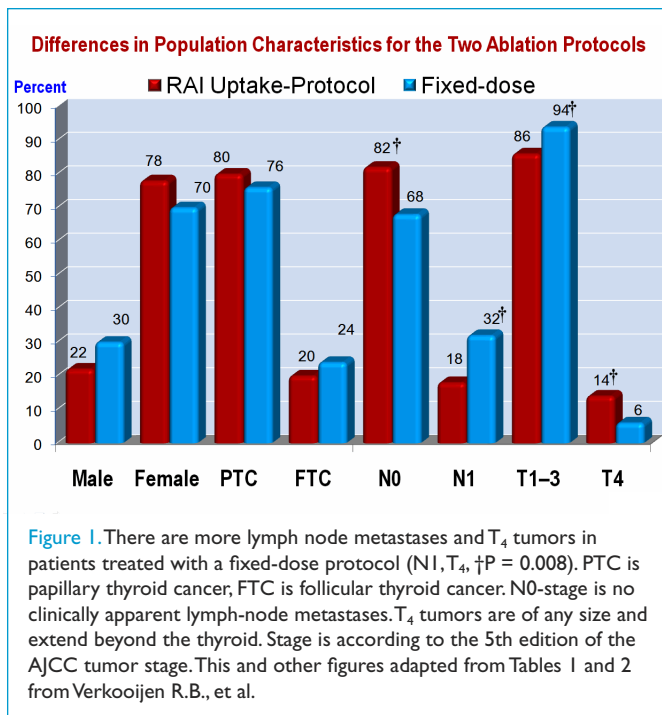
For the uptake protocol, the 24-hour neck uptake of 1 mCi of ¹³¹I (40 MBq) was stratified into 3 levels: >10, 5 to 10, or <5%, which was followed by 30, 50, or 75 mCi of ¹³¹I (2800, 1850, or 1110 MBq), respectively.

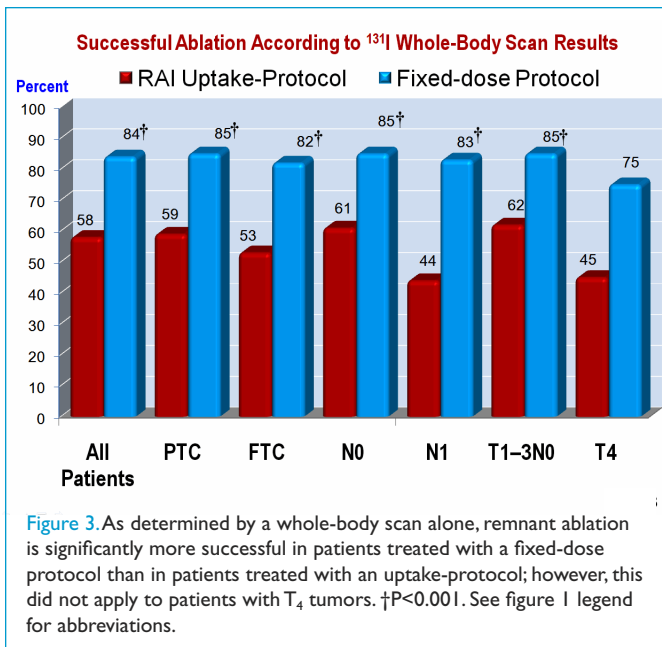
For the fixed-dose protocol, 100 or 150 mCi of ¹³¹I (3700 to 5550 MBq) was administered depending upon the tumor stage.* Using this protocol, most patients were treated with 100 mCi for T1 to T3 tumors, which are 1 to 4 cm and limited to the thyroid gland without lymph-node metastases. Those treated with 150 mCi had T4 tumors, which are tumors of any size extending beyond the thyroid capsule with or without lymph-node metastases.

Follow-up was performed 6 and 12 months after ¹³¹I ablation when patients were evaluated by serum thyroglobulin (Tg) after levothyroxine withdrawal and ¹³¹I 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.

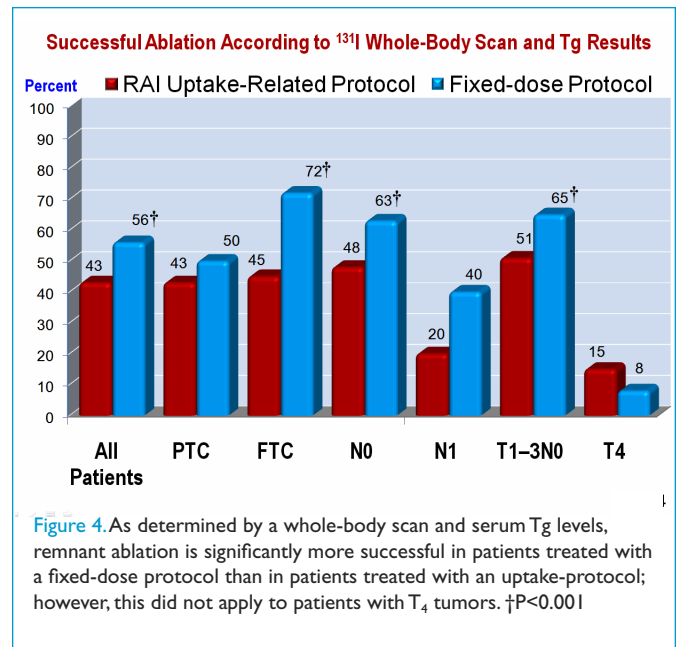
* Tumor stage (T=tumor stage, N=lymph-node stage and M=distant metastasis) was determined according to the 5th edition of the American Joint Committee on Cancer (AJCC), www.cancerstaging.org.

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





no statistically significant differences in the gender ratio or tumor histology among the two groups ($P = 0.07$, Figure 1). However, lymph-node metastases were found in 27 patients (18%) in the uptake-protocol group and 66 patients (32%) in the fixed-dose group ($P = 0.008$, Figure 1). Larger ¹³¹I activities were given to patients treated with the fixed-dose protocol than those given to the uptake protocol group (Figure 2). With the uptake protocol, 60 of 139 patients (43%) had successful ¹³¹I ablation 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 T₄ 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 ¹³¹I than is treatment based upon a 24-hr ¹³¹I uptake in patients with non-metastatic tumors measuring 1 to 4 cm confined to the thyroid gland.

COMMENTARY

The main conclusion of this study by Verkooijen et al. is that empirically selecting ¹³¹I activity based upon tumor stage is more effective than is uptake-selected ¹³¹I activity. In effect, this conclusion compares the efficacy of low and high ¹³¹I 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 ¹³¹I are therapeutically more effective than are the smaller ¹³¹I 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 ¹³¹I 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 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 ¹³¹I. (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 T₄ 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 T₄ tumors. The authors also found a low sensitivity of ¹³¹I 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