Clinicopathological features and outcome of thyroglobulin elevation and negative iodine scintigraphy (TENIS) patients with negative neck ultrasound: Experience from a thyroid carcinoma clinic in India

ABSTRACT
Management of differentiated thyroid carcinoma (DTC) patients with thyroglobulin (Tg) elevation and negative iodine scintigraphy (TENIS) and negative neck ultrasound scan causes considerable diagnostic and therapeutic dilemma, especially in resource-poor settings. The aim of this study was to evaluate clinicopathological features and outcome of TENIS patients with negative neck US attending a thyroid cancer clinic in India. From a DTC database of 722 containing 193 TENIS patients, subjects with negative neck US and negative Tg antibody (TgAb) were selected retrospectively and analyzed using appropriate statistical methods. The study group included 64 patients (male – 17, female – 47, mean age – 44.7 ± 12.8 years) with 54 papillary and 10 follicular thyroid carcinomas, American Thyroid Association (ATA) recurrence risk categorization (2009) – low – 16, intermediate – 28, and high – 20. Most of the patients became TENIS within 1 year of diagnosis with median Tg level of 6.5 ng/mL (1.2–996 ng/mL) and mean follow-up of 7.8 years. On follow-up, Tg dropped spontaneously in 27 patients, more among the low and intermediate-risk categories. For those with high or increasing Tg level, further imaging (fluorodeoxyglucose positron emission tomography/computed tomography) was done and 14 out of 18 were positive. Treatment included empiric radioactive iodine therapy-16, external beam radiation therapy (EBRT)-7, and lymph node dissection (LND)-10. A favorable outcome was seen in 36 patients and unfavorable in 28. Distant metastases were associated with unfavorable outcome and poor survival. Progression-free survival was significantly better in the Tg group of <10 at the time of TENIS (111 months) compared to the Tg group >10 (72 months). Tg level dropped spontaneously in nearly half the patients, especially if levels were <10 and more so among the low-risk category. Distant metastasis was predictive of unfavorable outcomes. Along with Tg level, the ATA risk category might help to predict clinical course and reduce unnecessary expensive imaging in resource-poor settings.

Keywords: TENIS, negative Thyroglobulin antibody, differentiated thyroid carcinoma, outcome, progression-free survival.

INTRODUCTION
During the management of differentiated thyroid carcinoma (DTC), it is not uncommon to come across cases with detectable or elevated thyroglobulin (Tg) and a negative diagnostic whole-body iodine-131 scan (DxWBS I). This is referred to as Tg elevation and negative iodine scintigraphy (TENIS) syndrome and is seen in 10%–27%. This causes considerable diagnostic and therapeutic dilemma. In such patients, ultrasound (US) neck helps in identifying local disease which can be managed appropriately and may sometimes even eliminate the need for empiric radioactive

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How to cite this article: Vijayan R, Palaniswamy SS, Vadayath UM, Nair V, Kumar H. Clinicopathological features and outcome of thyroglobulin elevation and negative iodine scintigraphy (TENIS) patients with negative neck ultrasound: Experience from a thyroid carcinoma clinic in India. World J Nucl Med 2021;20:361-8.
Vijayan, et al.: TENIS with negative neck ultrasound

iodine therapy (eRAI). However, when the neck US is negative, these patients might need further studies such as computed tomography (CT) of the chest, and fluorodeoxyglucose positron emission tomography/CT (FDG PET/CT) to localize iodine nonavid disease and to decide on further treatment plans. These expensive imaging modalities may not be affordable to many.

Many such patients may undergo eRAI with high dose I131. The posttherapy scan (RxWBS I) after eRAI may show iodine avid disease or may be negative. The use of eRAI is controversial and all experts do not share the same view.[3–6] Moreover, this may add to the cost of treatment and may not be a feasible option in a resource‑poor setting like ours. Hence, the management of TENIS patients, especially those with negative US neck, poses a challenge. We aimed at evaluating this group of TENIS patients (henceforth referred to as the TENIS subgroup) to see if factors contributing to the outcome could be predicted. The objective of the present study was to evaluate the prevalence of this TENIS subgroup in our population of DTC, their clinicopathological, treatment characteristics, and outcome.

SUBJECTS AND METHODS

This was a retrospective study conducted for which the institutional ethical committee approval (dated November 9, 2020; IEC-AIMS-2020-ENDO-188) was given. The patients were taken from the thyroid carcinoma database after taking their informed consent for data collection and its usage for research purposes. Consecutive patients were selected who fulfilled the following inclusion criteria and formed the study cohort (TENIS subgroup).

Patients with DTC who at first or any subsequent evaluation had

- A negative DxWBS I but had detectable stimulated Tg > 1.0 ng/mL (when thyroid‑stimulating hormone (TSH) after thyroxine withdrawal was >30 micro IU/mL) on the day of the scan, after having been on a low iodine diet for 3 weeks
- Negative Tg antibody (TgAb) defined as any value below the upper limit of the reference range of the assay used and
- Negative neck US.

Excluded were patients <18 years of age, those who had not received RAI ablation after total thyroidectomy, other thyroid cancers, and those with insufficient data for analysis. Out of this group, those who had at least three stimulated Tg on follow‑up formed the study cohort.
Statistical analysis
Statistical analysis was performed using IBM SPSS version 20.0 software (IBM Corporation, Armonk, NY, USA). Categorical variables were expressed as frequency and percentage. Numerical variables were presented as median as well as mean and standard deviation. Chi-square test was used for the comparison of quantitative data between the two groups. Logistics analysis was used for univariate and multivariate analysis. Kaplan–Meier method was used to calculate progression-free survival (PFS) and a log-rank test was applied for calculating significance. Receiver operating characteristic (ROC) curve analysis was used to mark the Tg cutoff values above which, both the sensitivity and specificity for the unfavorable outcome reached an optimal value. The values of \( P < 0.05 \) were considered statistically significant with 95% of confidence interval.

RESULTS
From a DTC database of 722 patients, 193 (26.7%) with TENIS were identified. Among these, 101 patients had negative neck US and negative Tg antibody. From these, 64 patients with at least 3 subsequent Tg values and 2-year follow-up were included in the present study (TENIS subgroup). Baseline characteristics of the study cohort are described in Table 1.

More than 80% of the patients became TENIS by 1 year and almost half had Tg level < 10 at that time. Majority of the tumor types (84.4%) were papillary thyroid carcinoma (PTC) and its variants and 43.8% belonged to the intermediate risk for recurrence (ATA 2009). The mean duration of follow-up was 7.8 ± 2.5 years and 75% had 5–10 years follow-up [Table 2].

Since half the cohort had Tg level below 10 ng/mL, these patients were divided into two groups, Tg < 10 and Tg > 10 for comparison [Figure 1]. The distribution of variables in the two Tg categories showed that basic variables were comparable except that the low-risk ATA category was more common in Tg < 10 group.

Follow-up
During follow-up, spontaneous drop in Tg level was seen in 27/64 patients (42.2%). In the rest, distant metastases (DM) were detected in nine patients and lymph node (LN) metastases appeared in 20 patients [Table 2]. LN metastases were detected by US in 12 patients, FDG-PET/CT in five patients, posttherapy scan in one patient, and by both US and FDG-PET/CT in two patients. Further evaluation including FDG-PET/CT scan was done for 18 subjects with high or increasing Tg levels, out of which 14 were positive: LN metastasis in 7 and DM in 10 [Table 2]. Treatment constituted of LN dissection (LND-10), eRAI therapy (16), and external beam radiation therapy (EBRT-7).

Table 1: Baseline characteristics of thyroglobulin elevation and negative iodine scintigraphy subgroup (n=64)

| Variable | n (%) |
|----------|-------|
| Gender   |       |
| Male     | 17 (26.6) |
| Female   | 47 (73.4) |
| Mean age at presentation (years) | 44.7±12.8 |
| Age category |       |
| <30      | 7 (10.9) |
| 30-50    | 35 (54.7) |
| >50      | 22 (34.4) |
| Type of tumor |       |
| Classical PTC | 30 (46.9) |
| Other variants of PTC | 24 (37.5) |
| FTC      | 10 (15.6) |
| ATA 2009 risk stratification |       |
| Low      | 16 (25) |
| Intermediate | 28 (43.8) |
| High     | 20 (31.3) |
| Presence of distant metastasis prior to becoming TENIS | 12 (18.8) |
| Bone     | 6 |
| Lung     | 2 |
| Bone and lung | 3 |
| Bone, lung, and liver | 1 |
| Median dose of RAI ablation (MBq) (range) | 3330 (1850-7030) |
| Tg level at time of TENIS (ng/mL) |       |
| Median   | 6.5 (1.2-996) |
| <10      | 35 (54.7) |
| >10      | 29 (45.3) |
| Distribution of Tg level (ng/mL) |       |
| <2       | 11 (17.2) |
| 2-10     | 24 (37.5) |
| 10-20    | 8 (12.5) |
| 20-50    | 8 (12.5) |
| 50-100   | 6 (9.4) |
| >100     | 7 (10.9) |
| Time of becoming TENIS from diagnosis |       |
| 6 months | 40 (62.5) |
| 1 year   | 13 (20.3) |
| 1.5 years | 8 (12.5) |
| 2 years  | 3 (4.7) |
| Time of becoming TENIS from the last dose of RAI therapy |       |
| 6 months | 46 (71.9) |
| 1 year   | 10 (15.6) |
| 1.5 years | 5 (7.8) |
| 2 years  | 3 (4.7) |

PTC: Papillary thyroid carcinoma, FTC: Follicular thyroid carcinoma, RAI: Radioactive iodine, TENIS: Thyroglobulin elevation and negative iodine scintigraphy, ATA: American Thyroid Association, Tg: Thyroglobulin

Empiric radioactive iodine therapy
In the TENIS subgroup of 64 patients, 16 (11 females and 5 males) were given eRAI therapy [Table 4]. Tg at the time of TENIS ranged from 1.2 to 996 ng/mL. Among these, 12 had FDG PET/CT Scan before eRAI therapy, of which 11 were
positive and showed lesions in thyroid bed and metastatic lesions in the neck nodes, lung, skeleton, and liver. Post eRAI therapy, 1 131 scan was positive in four patients, two showing neck uptake only, one showing bone and other liver metastasis. Among the 12 who had single-dose eRAI only, six showed positive response, one had partial response, while the negative response was seen in five patients. Of the four patients who received two doses of eRIA, one showed partial response, while the remaining three had excellent response, however, with persistent high Tg.

**Outcome at last follow-up**

When the outcome of these patients was assessed at the last follow-up, 33 (51.6%) had become NED. Spontaneous normalization of Tg was seen in 27 patients, whereas three became NED after further RAI therapy and three after LN excision. The mean time to become NED was 4.07 ± 1.99 years. Patients who had spontaneous drop in Tg were comparable to the rest in terms of age, gender, time

**Table 2: Follow-up and treatment modalities of thyroglobulin elevation and negative iodine scintigraphy subgroup (n=64)**

| Variables | n (%) |
|-----------|-------|
| Mean follow-up (years) | 7.6±2.5 (4-14) |
| Follow-up duration (years) | |
| <5 | 7 (10.9) |
| 5-10 | 48 (75) |
| >10 | 9 (14.1) |
| PET CT scan done | |
| Positive | 14 (17.8) |
| Negative | 4 (22.2) |
| Metastasis detected | |
| Lymph node metastasis | 20 (31.3) (USG-12, FDGPET-5, both-2 and one by posttherapy scan) |
| Distant metastasis | |
| Lung | 6 |
| Bone and lung | 2 |
| Bone, lung, and liver | 1 |
| Further treatment | |
| eRAI therapy | 16 (25) |
| Salvage surgeries (LND) | 10 (15.6) |
| EBRT | 7 (10.9) (for distant mets-4 for thyroid bed-3) |
| Course of the disease | |
| Remaining TENIS | 3 (4.7) |
| Tg dropping spontaneously | 27 (42.1) |
| Tg dropped by treatment | 6 (9.4) (3 LND and 3 RAI) |
| Tg increasing | 28 (43.8) |

**Table 3: Details of thyroglobulin elevation and negative iodine scintigraphy patients with positive fluorodeoxyglucose-positron emission tomography/computed tomography scan (n=14)**

| Patient | Age (years) | Gender | FDG PET/CT findings | Interventions | Follow-up |
|---------|-------------|--------|---------------------|---------------|-----------|
| 1       | 68          | Male   | LN                  | None          | Developed adrenal mass, sepsis, acute renal failure, and died |
| 2       | 37          | Male   | LN                  | eRAI          | Ultrasound positive |
| 3       | 52          | Female | Thyroid bed + LN   | eRAI          | Tg dropped |
| 4       | 56          | Female | LN                  | Palliative EBRT and sorafenib | No significant change |
| 5       | 78          | Male   | LN + bone           | eRAI          | Tg after 6 months not available |
| 6       | 19          | Female | LN + lung           | eRAI          | RxWBS showed right cervical node uptake |
| 7       | 60          | Female | LN + lung           | none          | RxWBS negative, no Tg available |
| 8       | 45          | Male   | Lung                | eRAI          | RxWBS right thyroid bed and neck node uptake |
| 9       | 55          | Female | Lung                | eRAI          | RxWBS negative, no drop in Tg |
| 10      | 44          | Female | Nonavid lesions     | None          | RxWBS negative, no drop in Tg |
| 11      | 61          | Male   | Bone                | None          | |
| 12      | 69          | Female | Pleural nodule      | eRAI          | |
| 13      | 54          | Female | Nonavid lesions     | None          | |
| 14      | 30          | Female | Nonavid lesions     | None          | |

**Figure 1: Comparison of the distribution of variables among Tg TENIS groups. Tg: Thyroglobulin, TENIS: Thyroglobulin elevation and negative iodine scintigraphy**
of becoming TENIS, time from last RAI therapy, dose of RAI, and type of tumor. However, ATA high-risk category (4/27 vs. 16/37; \(P = 0.004\)), Tg level >10 (4/27 vs. 25/37; \(P < 0.01\)), presence of distant metastasis (2/27 vs. 19/37; \(P < 0.01\)), and lymph node metastasis (9/27 vs. 25/37; \(P = 0.007\)) were significantly lower in this group.

Of the 20 PSD patients, 16 showed DM and four had persistent LN metastasis. Among those with DM, 11 had progressive disease with increasing Tg and worsening structural disease. Among the eight PBD patients, one had bone metastasis but on follow-up, all showed a falling trend in Tg except one who showed a rise. The three ID patients showed a falling trend in Tg.

**Empiric radioactive iodine therapy and outcome**

Although the short-term response to eRAI was encouraging (of the 20 treatments, 12 showing some form of response with falling Tg level), only two became NED/ID on the last evaluation. Eleven continued to have PSD (two lymph nodal metastasis, two thyroid bed lesions, and seven lung/bone metastases) and three died from progressive disease. However, of these 16 patients, nine had undergone LN exploration and five had EBRT as well later in the course. All these additional treatments could have influenced the final outcome of these patients and hence, the independent impact of eRAI therapy on outcome could not be assessed.

**Thyroglobulin level and outcome**

When Tg level at TENIS was <10 ng/mL, almost 70% became NED, but only 40% did so when Tg was >10 ng/mL and this difference was statistically significant (\(P = 0.007\)). Among NED, spontaneous Tg drop was seen in 22/24 in Tg <10 compared to 5/9 patients in Tg >10, the difference being significant (\(P = 0.017\)). Moreover, DM was more common (41.4%) in Tg >10 compared to 17.1% in Tg <10 group and this difference was also statistically significant (\(P = 0.03\)). When Tg level was <2 ng/mL, all 11 patients became NED (10 patients Tg dropped spontaneously, while one patient had bone metastasis and Tg dropped after RAI treatment). On the contrary, all seven patients with Tg level >100 ng/mL had persistent disease, five with DM, and two with LN metastasis [Figure 2].

Univariate analysis showed all factors except gender, time of TENIS, and type of tumor associated significantly with unfavorable outcome [Table 5], but multivariate analysis showed that only DM was significantly associated with unfavorable outcome (\(P = 0.002\)).

**Thyroglobulin level cutoff for predicting outcome**

ROC curve analyses showed that the highest area under the curve in terms of best compromise between sensitivity and specificity for unfavorable outcome (sensitivity – 68.8%; specificity – 72.3%) was achieved at a stimulated Tg level >10.42 ng/mL [Figure 3]. Overall median survival was 112 months for this cohort. When PFS was calculated using Kaplan–Meier method [Figure 4], a significant difference was noted (\(P = 0.03\)), with better PFS in those with Tg <10 ng/mL group (111 months) compared to 72 months for Tg >10 [Figure 4].

**American Thyroid Association risk category and outcome**

ATA risk levels and Tg TENIS were used in combination for predicting the outcome on the last follow-up [Figure 5]. Best results were seen when initial risk was low and Tg at TENIS <10 ng/mL, ten out of 11 such patients having had spontaneous conversion to NED. One patient had PBD, but the Tg level showed falling trend. On the other hand, when patients initially fell into the high risk (20/64), the outcome was unfavorable even with a Tg of <10 ng/mL. Although NED

### Table 4: Characteristics and response of patients who received empiric radioactive iodine therapy (n=16)

| Variables                                              | n (%)          |
|--------------------------------------------------------|----------------|
| Gender                                                 | n (%)          |
| Male                                                   | 5 (31.2)       |
| Female                                                 | 11 (68.8)      |
| Age (years)                                            | 8 (50)         |
| <55                                                     | 8 (50)         |
| >55                                                     |                |
| Type of tumor                                           | n (%)          |
| PTC                                                    | 11 (68.8)      |
| FTC                                                    | 5 (31.2)       |
| ATA risk category                                      | n (%)          |
| Low                                                    | 1 (6.2)        |
| Intermediate                                           | 7 (43.8)       |
| High                                                   | 8 (50)         |
| Initial Tg at the time of TENIS (ng/mL)                |                |
| 5-10                                                   | 2 (10)         |
| 10-50                                                  | 5 (25)         |
| 50-100                                                 | 5 (25)         |
| 100-500                                                | 6 (30)         |
| >500                                                   | 2 (10)         |
| DM±lymph node metastasis                               | 10 (62.5)      |
| Lymph node metastasis alone                            | 5 (31.2)       |
| Thyroid bed lesions                                    | 1 (6.3)        |
| Number of eRAI therapy                                 |                |
| Once                                                   | 12 (75)        |
| More than once                                         | 4 (25)         |
| Response (20 treatments)                               |                |
| Positive                                               | 7 (35)         |
| Partial                                                | 5 (25)         |
| Negative                                               | 8 (40)         |

ATA: American Thyroid Association, DM: Distant metastasis, eRAI: Empiric radioactive iodine, Tg: Thyroglobulin, PTC: Papillary thyroid carcinoma, FTC: Follicular thyroid carcinoma, TENIS: Thyroglobulin elevation and negative iodine scintigraphy.
occurred spontaneously in one patient, four others required additional therapy. With high risk and Tg > 10 ng/mL, only one patient became NED and the rest had persistent and progressive disease. This kind of difference in outcome was not very obvious in the intermediate-risk category.

**DISCUSSION**

The present study evaluated a subgroup of 64 patients with DTC and negative neck US, who had become TENIS at different periods of follow-up. The prevalence of this TENIS subgroup in this DTC cohort was comparable with that of TENIS from other publications. This study population, however, was different from conventional TENIS since, by a negative US, we largely eliminated local disease which could be managed differently. Patients showed similar age and gender distribution compared to our general DTC patients.[9] The distribution of tumor types was not different either. However, when ATA risk categories were compared with our general DTC cohort, more TENIS patients had high risk (29.5% vs. 8.9%) and less, low risk (24.5% vs. 41%).[9]

One important finding of this study is that normalization of Tg level is possible in nearly 50% of US neck negative TENIS patients and majority did so spontaneously. Although not from a similar TENIS subgroup, Pacini et al. found that 67.9% of untreated TENIS patients normalized Tg and no structural disease ever appeared in these patients on follow-up.[5]

In addition, the present study showed that a Tg cutoff at TENIS of 10.4 ng/mL can be helpful in predicting the long-term outcome in this subgroup. A value above this cutoff predicted the possibility of PSD and disease progression. The cutoff for Tg level of 10.4 ng/mL in the present study validates the ATA recommendation that one dose of eRAI can be given when Tg is > 10 ng/mL and rising.[10] PFS in our patients is also significantly better with a Tg < 10. However, the best prediction of outcome in our cohort was on combining...
Table 5: Univariate analysis of factors associated with unfavorable outcome in thyroglobulin elevation and negative iodine scintigraphy subgroup

| Variable category | n   | Outcome | P     |
|-------------------|-----|---------|-------|
|                   |     | Favorable NED/ID (n=36), n (%) | Unfavorable PSD/PBD (n=28), n (%) |
| Age category      |     |         |       |
| <55               | 48  | 32 (66.7) | 16 (33.3) | 0.004 |
| >55               | 16  | 4 (25)   | 2 (75)   |       |
| Gender            |     |         |       |
| Male              | 17  | 7 (48.1)  | 10 (52.7) | >0.05 |
| Female            | 47  | 29 (61.7) | 18 (31.3) |       |
| Risk stratification |     |         |       |
| Low               | 16  | 14 (87.5) | 2 (12.5)  | 0.003 |
| Intermediate      | 28  | 16 (57.1) | 12 (42.9) |       |
| High              | 20  | 6 (30)    | 14 (70)   |       |
| Tg level          |     |         |       |
| <10               | 35  | 24 (68.6) | 11 (31.4) | 0.023 |
| >10               | 29  | 12 (41.4) | 17 (59.6) |       |
| Time to TENIS (months) |     |         |       |
| 6                 | 40  | 25 (62.5) | 15 (37.5) | >0.05 |
| >6                | 24  | 11 (45.8) | 13 (54.2) |       |
| Distant metastasis (12 preexisting + 9 newly detected) |     |         |       |
| Yes               | 21  | 4 (19)    | 17 (81)   | <0.01 |
| No                | 43  | 32 (74.4) | 11 (24.6) |       |
| LN metastasis (total) |     |         |       |
| Yes               | 34  | 15 (44.1) | 19 (55.9) | 0.037 |
| No                | 30  | 21 (70)   | 9 (30)    |       |
| Salvage surgeries (total) |     |         |       |
| Yes               | 17  | 5 (29.4)  | 12 (70.6) | <0.01 |
| No                | 47  | 31 (65.9) | 16 (34.1) |       |
| Tumor type        |     |         |       |
| PTC               | 54  | 33 (61.1) | 21 (38.9) | >0.05 |
| FTC               | 10  | 3 (30)    | 7 (70)    |       |
| eRAI therapy      |     |         |       |
| Yes               | 16  | 2 (12.5)  | 14 (87.5) | <0.01 |
| No                | 48  | 34 (70.8) | 14 (29.2) |       |
| FDG PET/CT positive |     |         |       |
| Yes               | 18  | 3 (16.6)  | 15 (83.3) | <0.01 |
| No                | 4   | 1         | 3        |       |

LN: Lymph node, Tg: Thyroglobulin, PTC: Papillary thyroid carcinoma, FTC: Follicular thyroid carcinoma, TENIS: Thyroglobulin elevation and negative iodine scintigraphy, FDG PET CT: Fluorodeoxyglucose positron emission tomography computed tomography, eRAI: Empiric radioactive iodine, NED/ID: No evidence of disease/indeterminate disease, PSD/PBD: Persistent structural disease/persistent biochemical disease

ATA risk category and Tg level [Figure 4]. This shows the importance of considering the initial risk category along with Tg level in determining the follow-up of this TENIS subgroup.

Compared to the general DTC cohort, where no patients died (236 patients with DTC with median follow-up 53 months), three disease-specific deaths occurred in this small cohort (4.6%) suggesting that our TENIS subgroup represents a form of aggressive DTC requiring meticulous follow-up and aggressive management. Although eRAI therapy was associated with poor outcome in this cohort, it may be due to the fact that most of these patients fell in the high-risk category and had DM. We were unable to assess the independent effect of eRAI on the outcome as some of these patients underwent EBRT or further surgeries which could have influenced the outcome. This study, however, is not powered enough to make any strong conclusion because of the small sample size. Tyrosine kinase inhibitors (TKI) could not be used in many because of socioeconomic reasons.

**Strengths and limitations**

The strength of this study is the uniqueness of dealing with a rare clinical entity, with reasonable follow-up period without much dropouts. The addition of neck US before considering eRAI which was not done in many such studies helps to make management cost-effective in our resource-limited setting. The study findings have improved our understanding of the course and outcome of TENIS patients in this part of the
world. The added strength of this study is the use of ATA recurrence risk stratification along with Tg level in deciding the management strategy. Larger studies will be needed for confirmation.

Limitations include the retrospective nature and small sample size, especially those given eRAI which precluded subgroup analysis. Moreover, FDG PET/CT scans could not be performed for all patients due to socioeconomical reasons and hence, the PET positivity of TENIS and its influence on outcome could not be fully assessed.

CONCLUSION

The present study showed that patients with TENIS and a negative neck US who have Tg at TENIS < 10 ng/mL should do well and can be maintained on follow-up, especially if they fall into the ATA 2009 low-risk category. On the other hand, when these patients belong to the high-risk category and with Tg > 10 ng/mL, they need to be closely followed and periodically imaged for disease progression. DM portends unfavorable outcomes. eRAI given to such high-risk patients did not benefit the outcome. Other than the Tg cutoff of 10 ng/mL, the ATA risk category can possibly help to predict the outcome, but larger studies are needed for confirmation. In those who show poor response to eRAI, early consideration should be given for other modes of therapy such as TKIs, EBRT, and metastases resection.

Acknowledgment

The authors acknowledge the Thyroid Cancer Care Team and the Department of Biostatistics at Amrita Institute of Medical Sciences and Research Centre, Amrita Vishwa Vidyapeetham, Kochi-682041, Kerala, India for their valuable assistance.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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