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Dynamic Risk Stratification in Differentiated Thyroid Cancer

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Background

Differentiated Thyroid Cancer (DTC) is characterized by excellent prognosis when appropriate treatment is given. However, a significant degree of overtreatment still exists because of the inability to accurately identify small patient cohorts who experience a more aggressive form of the disease, often associated with certain poor prognostic factors. Identifying these cohorts at an early stage would allow patients at high risk to receive more aggressive treatment while avoiding unnecessary and invasive treatments in those at low risk.

Methods

Demographic, clinical, pathological, diagnostic, treatment, and follow up data were recorded retrospectively for 549 DTC patients who had been consecutively recruited. Each cohort patient was classified in one out of four treatment response categories (according to the latest ATA GLs). Chi-square test and one-way ANOVA were used to evaluate the association of the prognostic factors with the categories of treatment response.

Methods: Remnant score

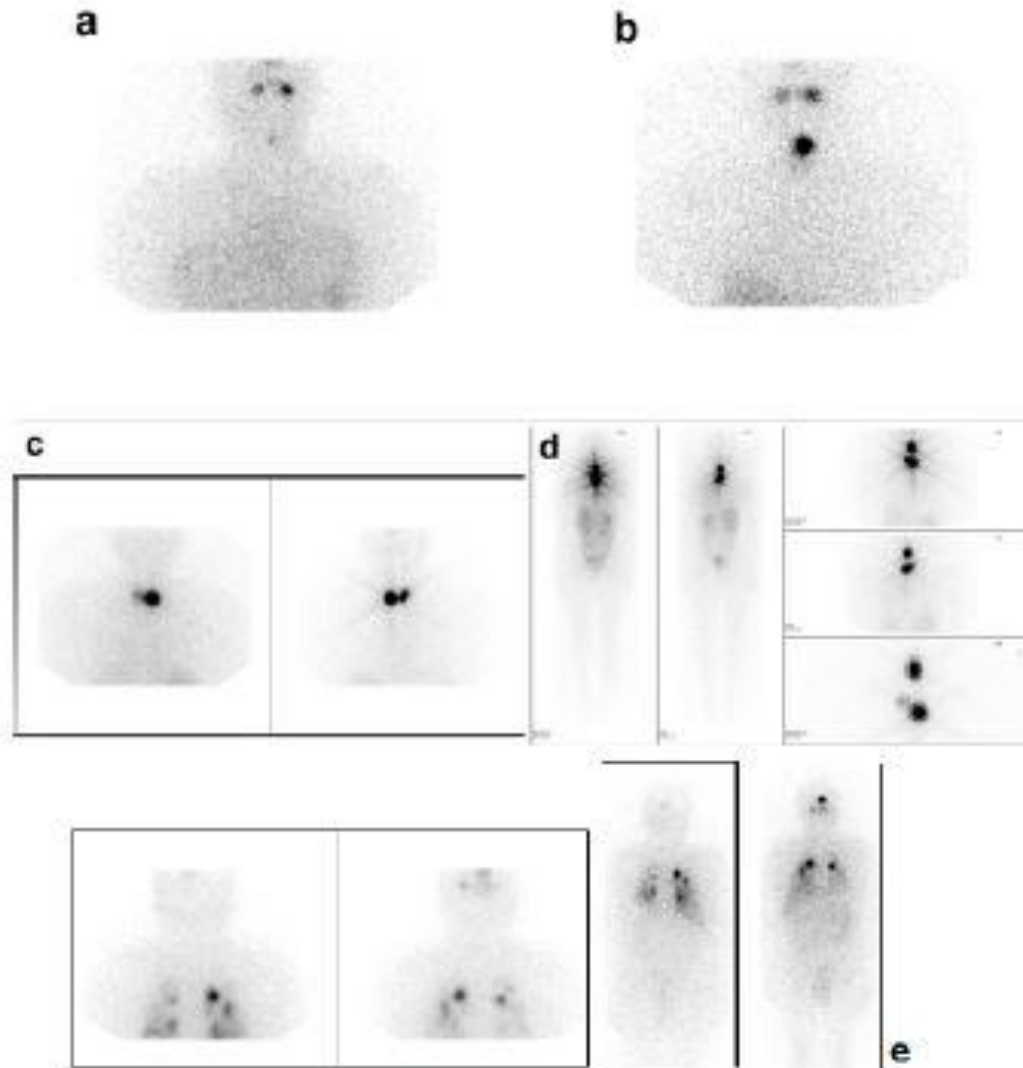
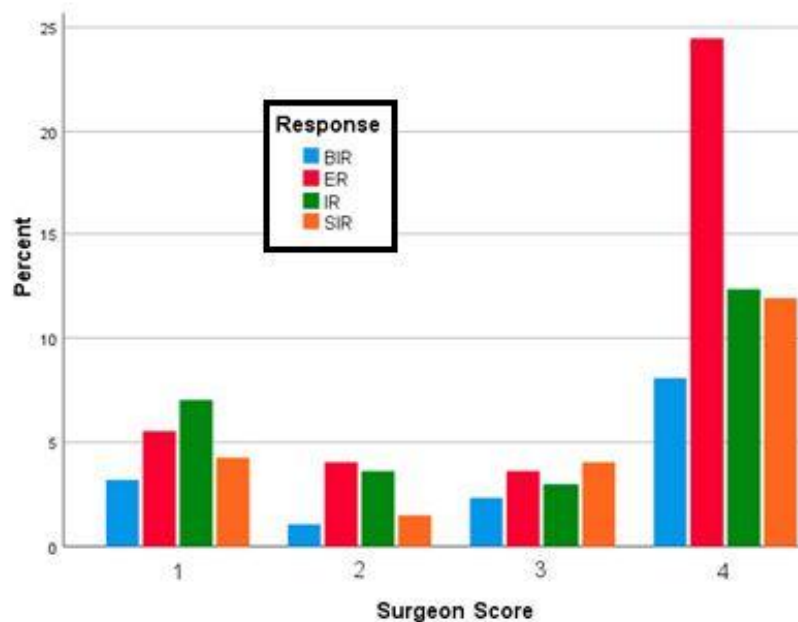


Figure 1. Representative post-ablation whole body scan (WBS) images illustrating scores for intensity of uptake and maximum remnant scores: (a) score 1 (low uptake), (b) score 2 (intermediate uptake), (c) score 3 (high uptake), (d) score 4 (star effect), (e) score 5 (distant metastases).

Results

- Patients with follicular malignant neoplasms had significantly higher evidence of a structural incomplete response (SIR) compared with other response categories (chi-square test, $p = 0.001$),
- Patients with T1 stage were significantly more likely to show an excellent response (ER) than any other response category (chi-square test, $p = 0.039$),
- None of the patients with distant metastases showed an ER. Patients without distant metastases were more likely to have an excellent RTT (chi-square test, $p < 0.001$).
- ER results were more prevalent in patients referred by a surgeon having a score of 4 than referred by less experienced surgeons (chi-square test, $p = 0.037$)



Treatment Response Category	% (n)
ER (Excellent Response)	37.7% (177)
BIR (Biochemical Incomplete Response)	14.7% (69)
SIR (Structural Incomplete Response)	21.7% (102)
IR (Indeterminate Response)	26% (122)

Referrals	Median (IQR): 2.0 (1, 4)
Surgeons' score (among 95 surgeons)	
1	76.84% (73)
2	8.42% (8)
3	6.32% (6)
4	8.42% (8)

Results Cont.

- During RAI the mean remnant score of ER is significantly lower than the incomplete response (IR) ($p = 0.003$) and SIR ($p < 0.001$), the mean remnant score of biochemical incomplete response (BIR) is significantly lower than SIR ($p < 0.001$), and the mean remnant score of IR is significantly lower than SIR ($p < 0.001$)
- During RAI the mean Tg value in ER, BIR and IR is significantly lower than SIR ($p=0.001$ for all)
- During follow-up WBS the mean Tg value in SIR is significantly higher than in ER, in IR and in BIR ($p < 0.001$ for all).
- During follow-up WBS the mean Tg-Ab value in SIR is significantly higher than in ER ($p < 0.001$), in BIR ($p = 0.028$) and in IR ($p = 0.042$)

Discussion

Most risk stratification systems include the same core parameters of age, tumor size, grade, presence of local invasion, and regional or distant metastases. Here we discuss these common factors as well as their association with treatment response, but also other upcoming markers including histology and multifocality of primary tumor, dose administered and preparation method for Radioiodine Therapy (RAI), Thyroglobulin (Tg), Anti-thyroglobulin Antibodies (Tg-Ab) levels both at initial management and during follow-up, and the presence of previously existing benign thyroid disease. A lack of definitive evidence continues to create confusion when conveying accurate prognostic information to the DTC patient population and when determining treatment regimen. In all cases a combined multidisciplinary approach, with consideration of the available guidelines and stratification systems, should be utilized when planning an individualized treatment program including follow up strategy, to offer the best care.