

# Clinical evaluation and outcome of indeterminate (Thy 3) thyroid nodules

Massimo Giusti (1), Barbara Massa (2), Margherita Balestra (1), Paola Calamaro (2), Stefano Gay (1), Simone Schiaffino (3), Giovanni Turtulici (3), Simonetta Zupo (4), Eleonora Monti (1), Gianluca Ansaldo (5).

Endocrine Unit (1), Cytopathology and Pathology Unit (2), Molecular Diagnostic Unit (4), Endocrinology Surgery Unit (5), San Martino University Hospital, Genoa, Italy Radiology Unit (3) Evangelico Hospital, Genoa, Italy.

## BACKGROUND

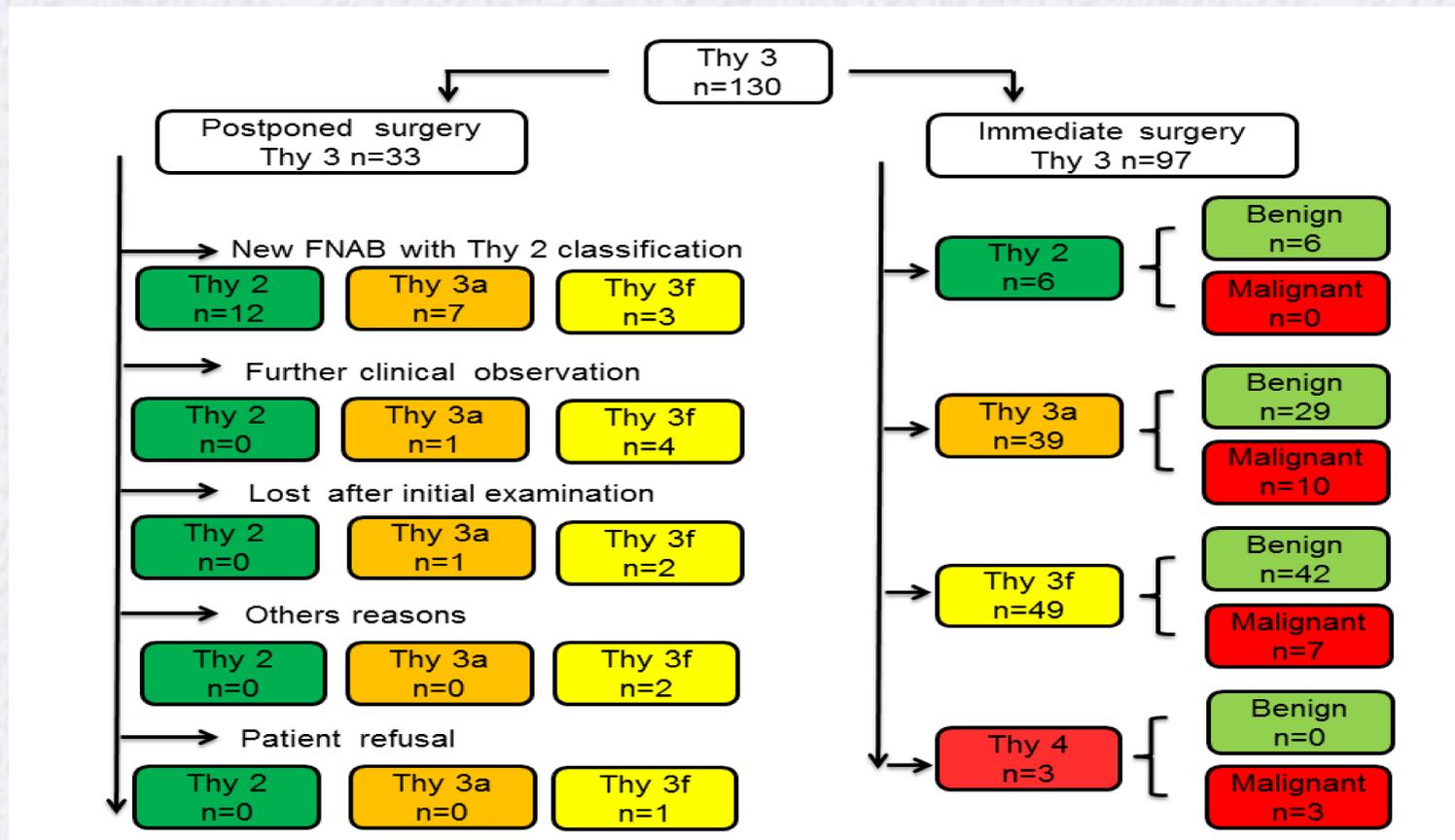
In thyroid nodules with indeterminate cytology, presurgical evaluations for risk management comprise biochemical tests, ultrasonography (US), elastography-US (USE), contrast-enhanced US (CEUS) and mutation analysis.

## AIM

The cytology of 130 Thy 3 nodules was reviewed according to the BTA 2014 classification

## RESULTS

Nodules were divided into Thy 3a and Thy 3f categories. Histology was available in 97 nodules. Malignancy was the final diagnosis in 19% of surgically treated nodules. No significant difference in the risk of malignancy was found between Thy 3a (26%) and Thy 3f (14%) nodules. Post-surgical histologic examination of the Thy 3a and Thy 3f nodules showed a higher incidence of Hurtle cell adenomas in Thy 3f (29%) than in Thy 3a (3%) nodules ( $p=0.01$ ). BRAF V600E mutation was positive in some Thy 3a but not in any Thy 3f nodules ( $p=0.04$ ). Cut-off values by ROC analysis from US (score), USE (ELX 2/1 strain index) and CEUS (time-to-peak index and peak index) were similar in Thy 3a and Thy 3f nodules. Data showed that malignancy can be suspected if the US score is  $\geq 2$ , ELX 1/2 strain index  $\geq 1$ , time-to-peak index  $\geq 1$  and peak index  $\leq 1$ . In a group of 24 revised nodules (12 Thy 3a and 12 Thy 3f) the diagnostic power of cumulative pre-surgical analysis by means of US, USE and CEUS showed high positive and negative predictive values (83% and 100%, respectively) for the presence of malignancy in Thy 3a and Thy 3f nodules. In our series of revised Thy 3 nodules, malignancy was low and displayed no significant differences between Thy 3a and Thy 3f categories.



Flow schematic of Thy 3 nodules managed between 2011-2014 and re-evaluated according to BTA 2014 classification. Malignancy is specific to the targeted nodule; other nodules were not considered. In 6 cases, no further clinical data were available owing to patient loss, death due to causes unrelated to thyroid disease, other severe comorbidity and patient refusal.

## CONCLUSIONS

The use of cut-offs based on histology as a reference, in both Thy 3a and Thy 3f nodules, could reduce surgery. In mutation-negative Thy 3 nodules, observation should be the first choice when not all instrumental results are suspect.