BRAF V600E positive papillary thyroid carcinoma is associated with suspicious ultrasound features

J. Sastre-Marcos [1], F. Del Val-Zaballos [1], CM. Cortés-Muñoz [1], Y. Campos-Martín [2], S. Aso-Manso [2], I. Jaen-Díaz [3] A. Vicente-Delgado [1], J. López-López [1]

1.- Endocrinology. 2.- Pathology. Complejo Hospitalario de Toledo. 3.- CS Buenavista. Sonographer. Toledo. Spain

Background and Aims:

Papillary thyroid carcinoma with BRAF V600E mutation is associated with more aggressive behavior; detection of the mutation on fine-needle aspiration (FNA) preoperatively can alter the initial operative approach. In this study we studied if BRAF V600E mutation is associated with specific ultrasound (US) characteristics.

Patients and Methods:

- From 2010 to 2014 we reviewed patients with thyroid nodules with the following inclusion criteria: **1**) US guided FNA of the nodule and **2**) molecular testing for BRAF V600E on the FNA
- BRAF V600E mutation was detected using fluorescence melting curve and secuencing (PCR).
- An expert on US, blinded to the BRAF status reviewed US examinations and recorded the sonographic characteristics for each nodule. Six US characteristics were collected: margins (well vs poorly defined), echogenicity (iso or hyperecoic vs hypoecoic), halo (present vs absent), nodular vascularization (peripheral vs intranodular), calcifications (absent vs present) and structure (cystic or spongiform vs solid).
- US findings were classified into three categories: 1) Probably benign: without any suspicious characteristics.
  2) Suspicious: with one or more high risk characteristics.
  3) Indeterminate: nodules that cannot be classified as benign or suspicious.
- Demographic and clinical characteristics were also analysed. Univariate (χ^2 and Student´s t test) and multivariate analysis were carried out.

Results:

Table 1. Clinical and demographic characteristics .

	N:271
Sex women (%)	232 (85,6)
Age (years, m±sd)	52,2 ± 16,2
BRAF mutation on FNA (%)	79 (29,2)
Autoimmune thyroid disease (%)	62 (23)
With US suspicious characteristics* (%)	166 (61,3)

* At least one suspicious characteristics

Table 2. Correlation between clinical and sonographic characteristics

	BRAF positive (79)	BRAF negative (172)	p
Sex men (%)	21,5	11,5	<0,05
Age (years, m±sd)	48,6 ± 16,1	53,6 ± 16,1	<0,05
With US suspicious characteristics* (%)	89,9	49,5	<0,001
Hypoechogenicity (%)	74,6	62,1	0,088
Calcifications (%)	67,6	38,9	<0,001
Ill defined margins (%)	21,1	15,8	0,377

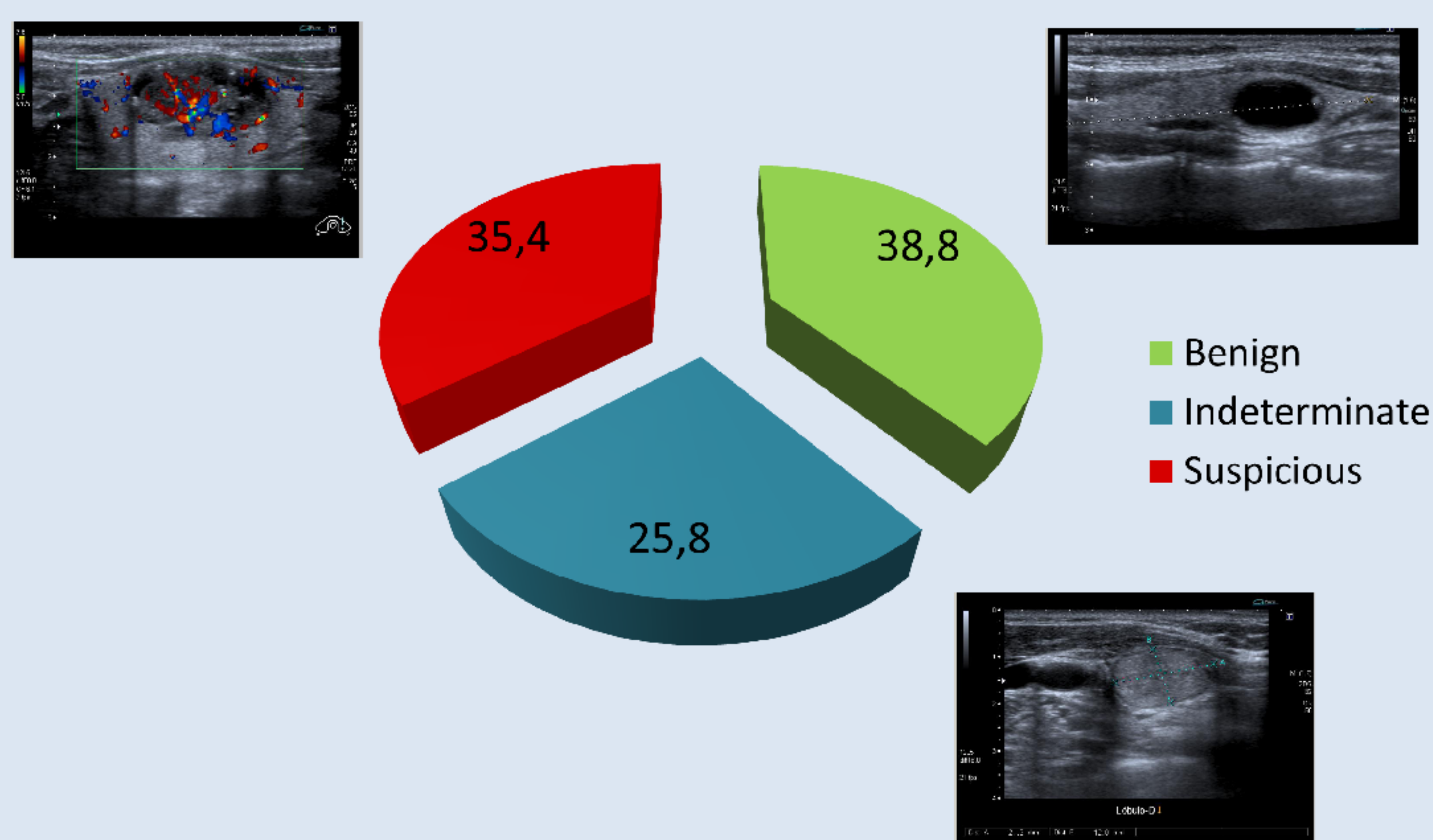Figure 1. Classification of nodules using US characteristics (%)

- Benign 38,8
- Indeterminate 25,8
- Suspicious 35,4

Figure 2. Ultrasound features using BRAF V600E status

p< 0,001

BRAF positive: Benign 10,1 / Indeterminate 26,6 / Suspicious 63,3
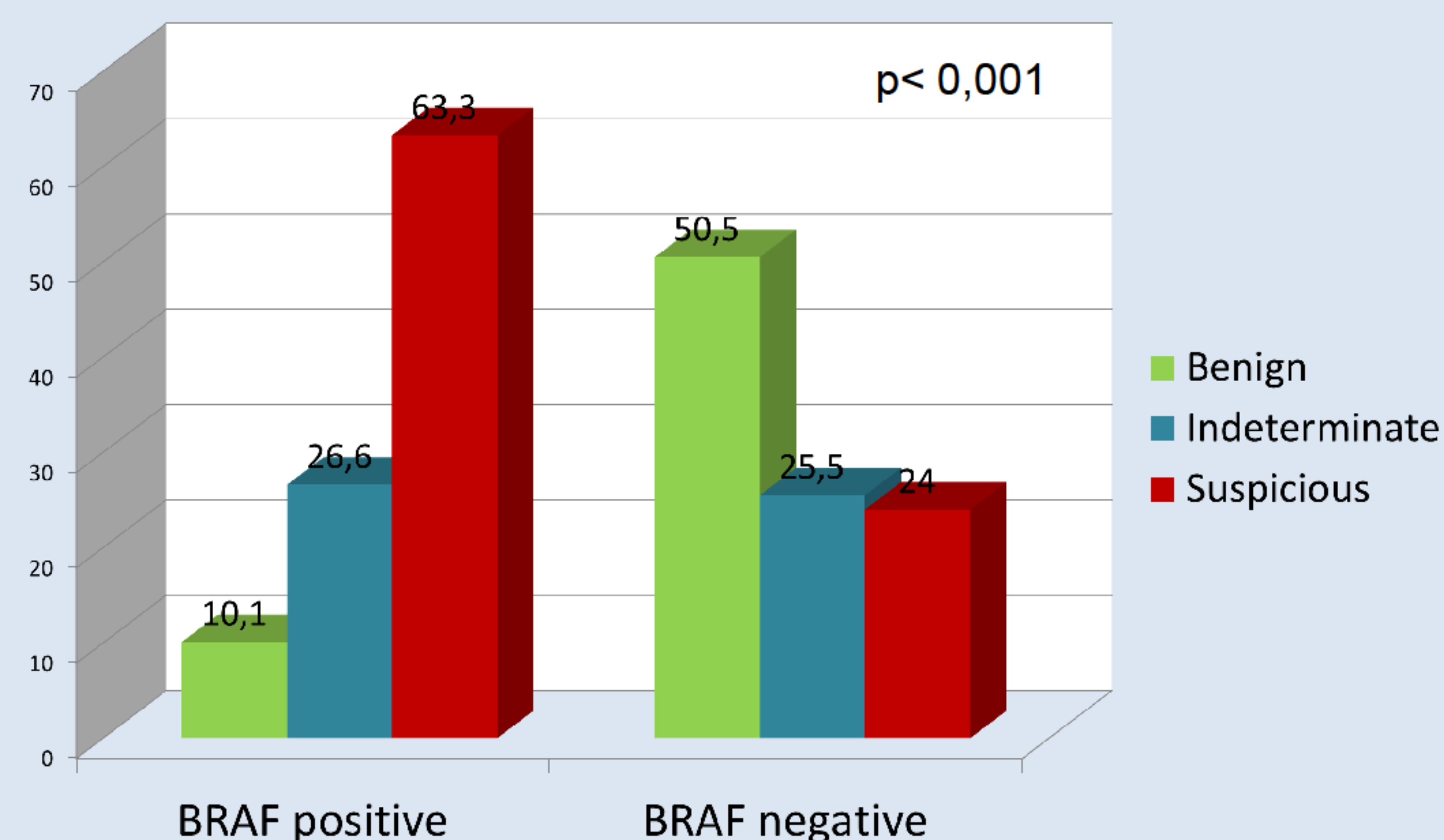BRAF negative: Benign 50,5 / Indeterminate 25,5 / Suspicious 24

Table 3. Multivariable analysis for characteristics independently associated with BRAF V600E mutation

Factor	OR	95% CI	p
US calcifications	3,8	1,8-8,0	<0,001
US Hypoechogenicity	2,7	1,2-6,2	<0,05

- 154 nodules were operated (54,2%): 91 papillary thyroid carcinomas, 2 follicular and 2 medullary carcinomas.
- In operated papillary carcinoma BRAF V600E mutation was present in 67 of 91 (74%).
- There were no differences in extrathyroidal nor ganglionar metastases between BRAF positive and negative papillary carcinoma.

Conclusion:

Suspicious US characteristics are highly associated with BRAF positive FNA. Routine cervical US and molecular testing can contribute to improve preoperative risk classification of papillary thyroid cancer.