

# Long term efficacy and toxicity outcome of adjuvant external beam radiotherapy for medullary thyroid cancer

## A single institution cohort study

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### Background

Medullary thyroid cancer (MTC) is a relatively aggressive entity with high risk of locoregional recurrence and distant metastases.

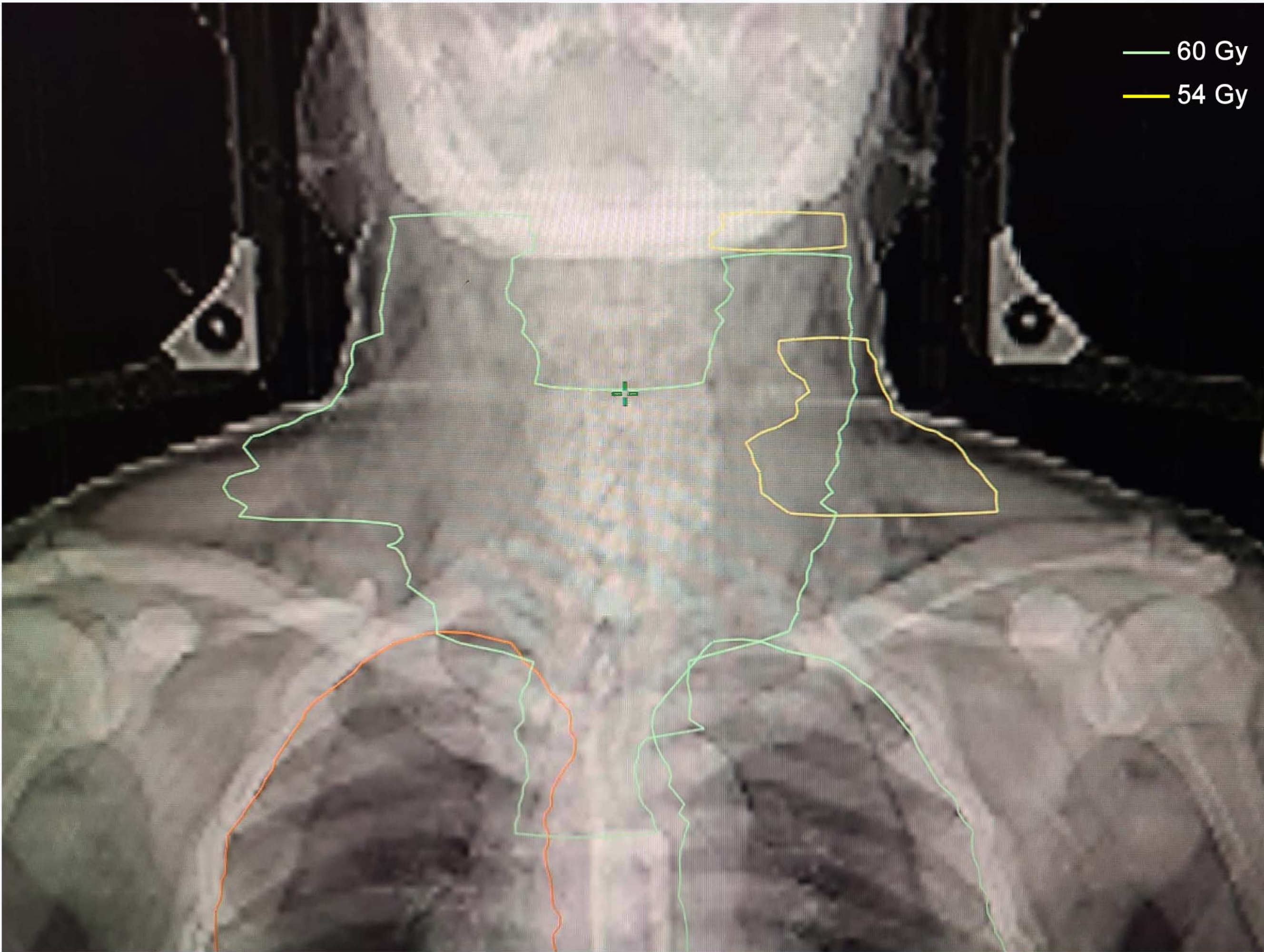
There is no role for adjuvant radioactive iodine and TSH suppression, while adjuvant external beam radiotherapy (EBRT) remains controversial. Guidelines and a recent systematic review suggested EBRT for extensive disease, which includes nodal involvement, extrathyroidal extension and residual disease, but data remained scarce.<sup>1,2</sup> Toxicity of EBRT was inconsistently reported.

### Methods

All consecutive patients diagnosed with MTC who received curative intent treatment from 2000 to 2018 in a tertiary institution were included. All patients received total thyroidectomy, prophylactic central compartment dissection and as-required therapeutic lateral compartments dissection.

Patients at high risk of relapse (R1-2 resection, multiple cervical lymph node metastases, extrathyroidal extension) were offered adjuvant EBRT. Radiotherapy volume covered thyroid bed and level II - VI. The thyroid bed, central compartment, level II-V on affected side and lower level II – IV on unaffected side was covered by 60Gy in 30 daily fractions with additional boost to gross residual up to 66Gy. Level V and upper level II on the unaffected side were treated to 54Gy in 30 daily fractions.

Relapse, survival and toxicity outcomes were reported.



### Results

#### Patient demographics

	Adj EBRT (n=19)	No adj EBRT (n=22)	P value
Age (median (range))	53.7 (33-72)	44.3 (17-87)	0.143
Sex (M)	8 (42.1%)	8 (36.4%)	0.707
T stage			
1	4	10	0.007
2	5	11	
3	8	1	
4	2	0	
N stage			
N0	3	16	<0.01
N1	16	6	
Margin			
R0	13	22	<0.001
R1	4	0	
R2	2	0	

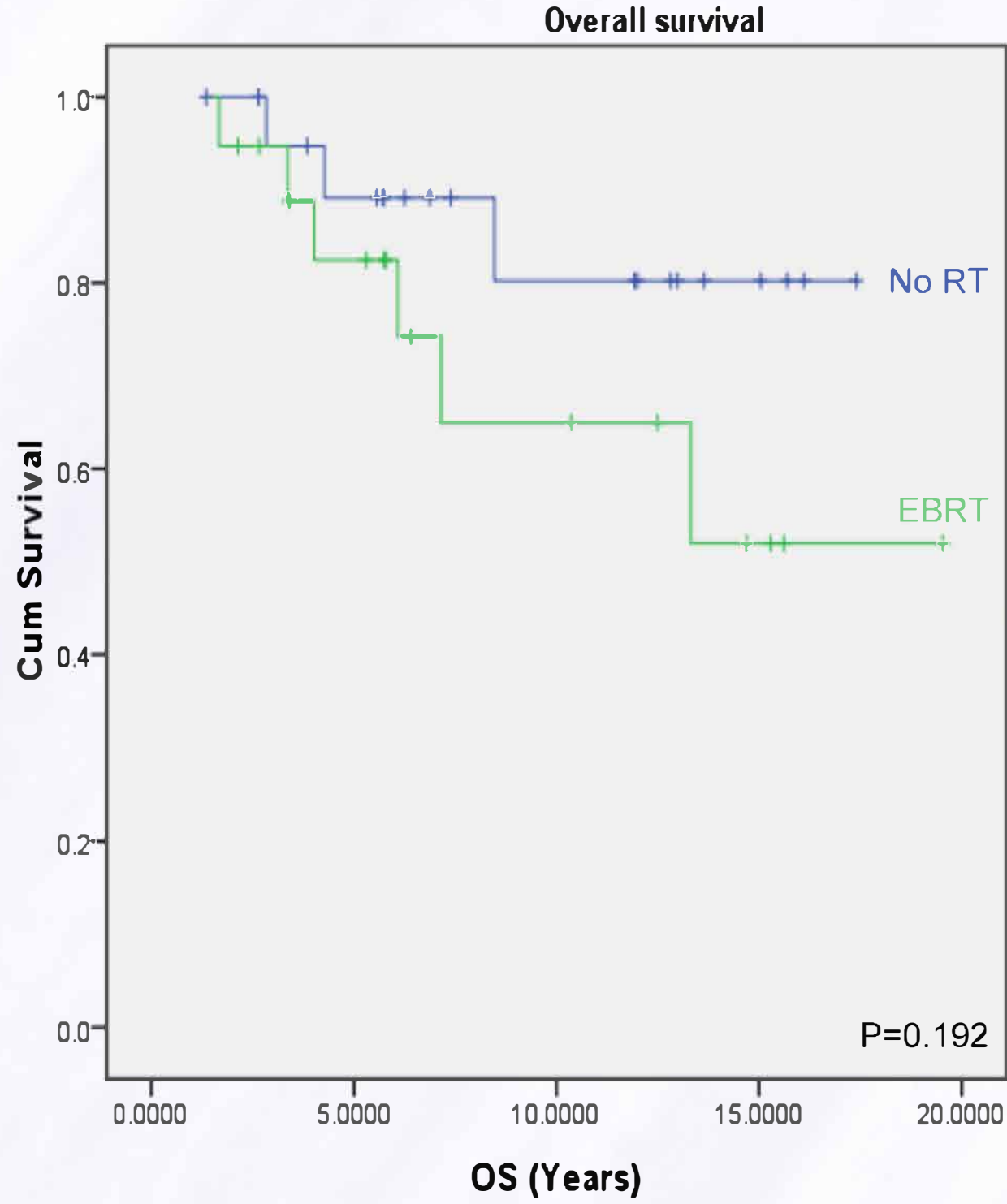
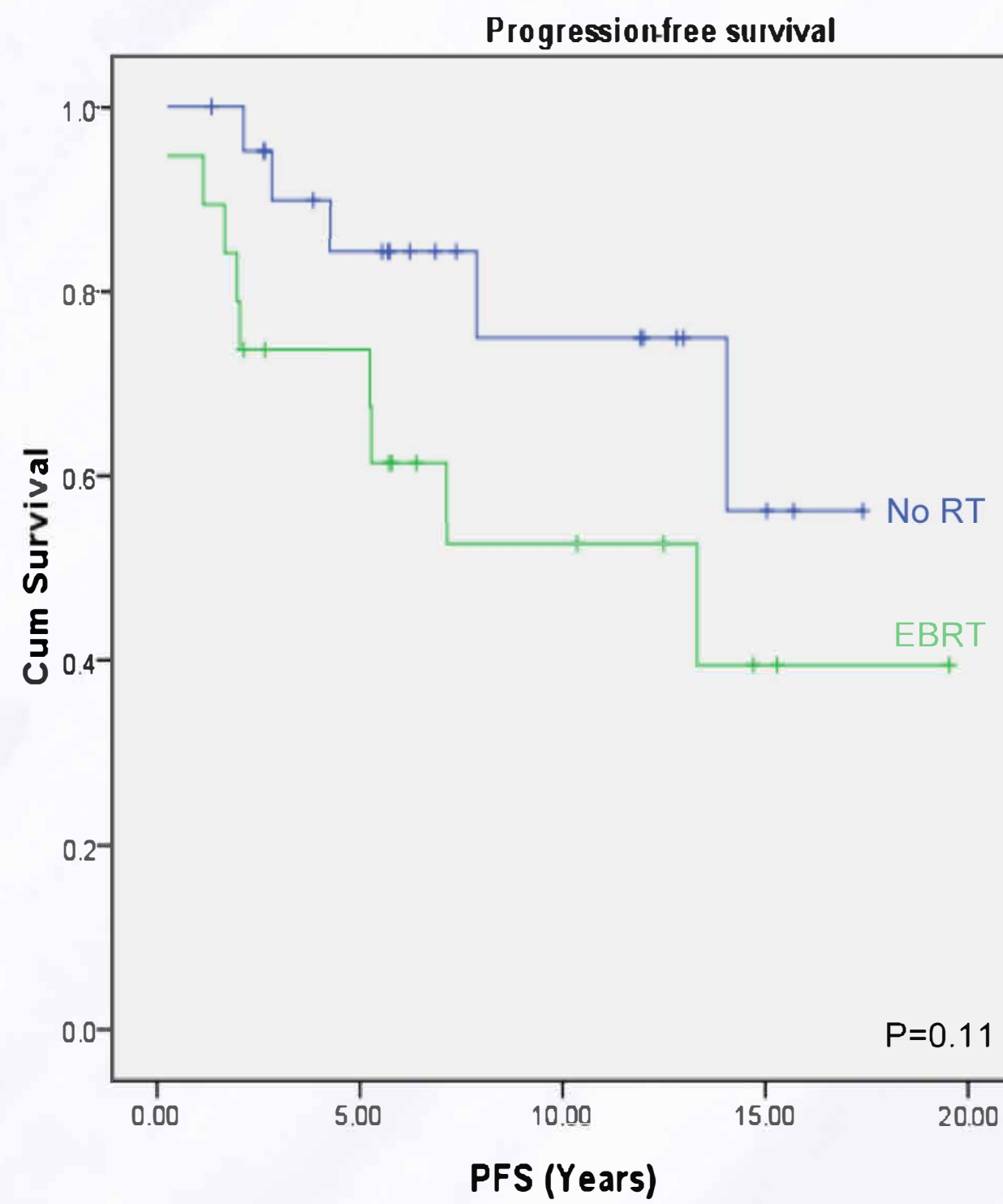
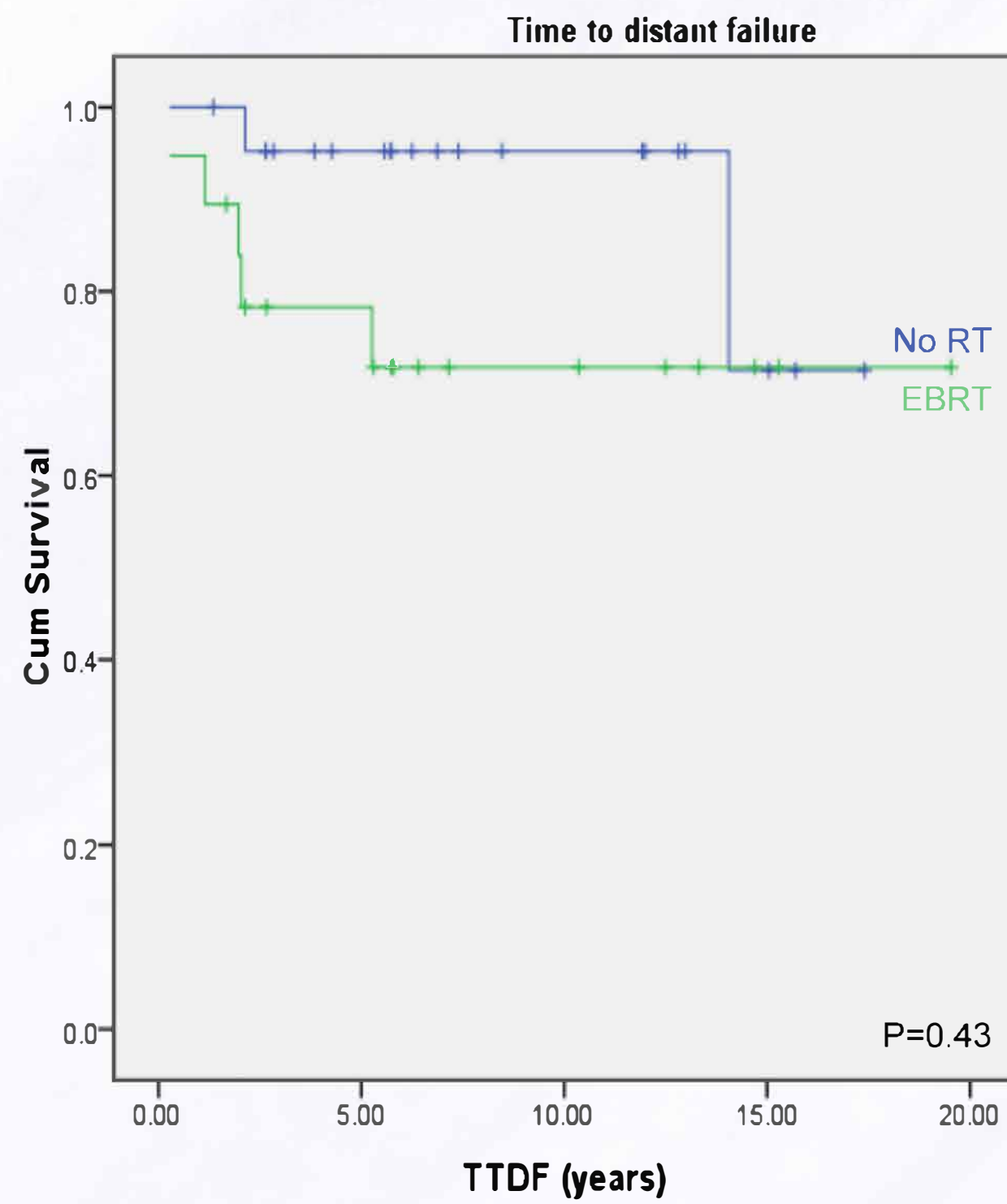
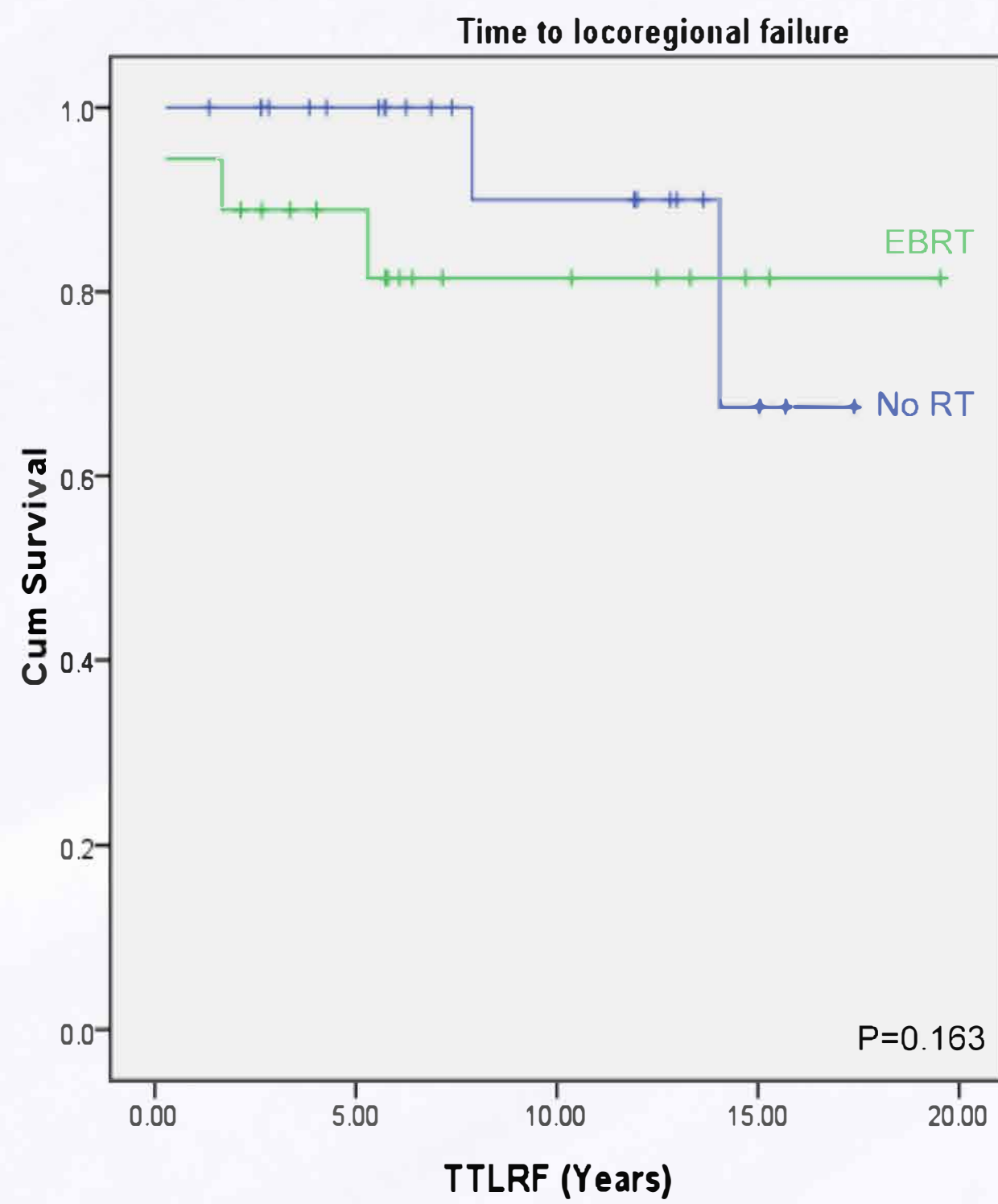
Median FU = 12 years

Patients in EBRT group suffers from significantly more advanced disease in terms of higher T and N stage and significantly more microscopic and gross residual disease.

#### Outcomes

10-yr locoregional control rate in EBRT group was 80% (vs 90% in no EBRT group, p=0.163). 10-yr distant relapse-free rate in EBRT group was 70% (vs 95%, p=0.430). 10-yr overall survival in EBRT group was 65% (vs 80%, p=0.192)

Despite at high risk, only 2 (2/19) had locoregional relapse after EBRT compared to also 2 (2/21) relapses in no-EBRT group. Higher incidence of distant metastases in EBRT group (5/19 vs 2/21) may reflect more advanced underlying disease. Locoregional relapse free rate (LRFR), distant relapse free rate (DRFR), progression free survival (PFS) and overall survival was not significantly different.



#### Adverse events

Acute side effects of EBRT were well tolerated, with all patients experiencing only G1/2 mucositis, esophagitis and dermatitis. None required hospitalization due to side-effects nor artificial nutrition.

No G3/4 long term side-effects were observed.

### Discussion

Our data show that EBRT can strengthen locoregional control in patient at high risk of relapse and decrease the risk to close to that of lower risk group. Numerical comparison between our cohort and historic cohort revealed improved locoregional control rates (historic 5-yr LRC 29% in N1 disease)<sup>3</sup>, reflecting EBRT might be helpful in high-risk group. While there is no concrete international consensus on the definition of high risk which mandates adjuvant EBRT, patients with extrathyroidal extension, multiple cervical LN metastases and microscopic or gross residual disease are common indications in literature.<sup>2</sup> Good locoregional control can prevent development of difficult-to-manage head and neck symptoms, but risk of distant metastases for such advanced disease remained high. Role of adjuvant treatment including EBRT in patients with persistently elevated calcitonin levels remained uncertain. Our observed 10-yr survival rate compares to existing series in literature.<sup>2</sup>

Most of the patients in our series were treated using IMRT technique, which effectively limited radiation dose in various organ-at-risks. This might have help contributed to the low incidence of G3/4 short- and long-term adverse events.

### Conclusions

Adjuvant EBRT in advanced MTC results in encouraging locoregional control and low incidence of significant short and long-term side-effects. Further work should focus on more precise definition of high-risk group which will yield benefit from EBRT.

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