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Abstract #71

Introduction

- Venous thromboembolism (VTE) is a common complication in patients with metastatic renal cell carcinoma (mRCC).
- It can be caused by inherited and/or acquired risk factors such as hypercoagulation, and treatment-related factors.
- Anti-cancer therapies such as tyrosine kinase inhibitors (TKIs) and immunotherapies (IOs) have also been reported to be associated with higher VTE events¹. Identifying patients with mRCC at the highest risk of developing VTE may provide the rationale for initiating prophylactic anticoagulation.

Methods

- In this IRB-approved retrospective study, patients who were diagnosed with mRCC between July 1st, 2012, and June 30th, 2022 were included.
- Variables included were patients' clinical characteristics, treatment, and anticoagulation therapy.
- Patients with mRCC who were diagnosed during the same period were used as the control arm.
- Pearson's Chi-square test was used for comparison between categorical variables.
- A multivariable logistic model was used to assess predictors of VTE.
- CGP was performed using the Tempus and Foundation Medicine platforms.
- Primary metastatic biopsy were collected before or within 90 days of treatment start.
- Variants of unknown significance were excluded from the analysis.
- Gene prevalence was compared using a chi square test.

Results

Table 1. Baseline characteristics and association with VTE rates.

Characteristics, No (%)	VTE (Total=44)	No VTE (Total=302)	P-value
Age, mean (95%CI), y	63.7 (60.8-66.7)	61 (60.4-62.9)	0.29
Male	34 (79.1)	207 (68.7)	0.23
BMI, mean (95%CI)	31.7 (29.2-34.1)	29.1 (28.3-29.8)	0.03
Race			0.89
White	39 (92.9)	260 (89)	
Black/African American	0 (0)	1 (0.3)	
Hispanic/Latino	2 (4.8)	16 (5.4)	
Asian/Pacific Islander	1 (2.4)	8 (2.7)	
Native American	0 (0)	1 (0.3)	
Nephrectomy	34 (79.1)	251 (83.7)	0.51
clear cell RCC	39 (90.7)	233 (82.3)	0.19
Fuhrman Grade			0.34
< 2	7 (21.2)	53 (23.9)	
> 2	26 (78.8)	169 (76.1)	
Chronic kidney disease	9 (20.5)	78 (25.8)	0.44
ECOG > 1	3 (6.8)	50 (16.6)	0.09
Anemia	25 (65.8)	177 (62.5)	0.83
Neutrophilia	6 (13.6)	61 (20.2)	0.30
Hypercalcemia	5 (14.3)	16 (5.7)	0.07
Thrombocytosis	4 (9.1)	41 (13.6)	0.41
Treatment			0.008
IO only	6 (14.3)	21 (7.2)	
TKI only	25 (59.5)	219 (75.0)	
TKI/IO	8 (19.1)	17 (5.8)	
Other	3 (7.1)	35 (12.0)	

Results

- Among 346 patients who were diagnosed with mRCC, 44 patients developed venous thrombotic events within 12 months after their cancer diagnosis (incidence rate: 12.7%).

Table 2. Baseline characteristics and association with VTE rates.

Tumor somatic mutation	VTE (N=25)	No VTE (N=119)	p-value
VHL	20 (76.9)	69 (58.0)	0.12
PBRM1	14 (53.9)	50 (42.4)	0.40
SETD2	4 (16.0)	19 (16.2)	0.99
BAP1	3 (12.0)	10 (8.6)	0.70
TP53	6 (24.0)	28 (23.9)	0.99
TERT	1 (4.0)	12 (10.2)	0.47
CDKN2A	3 (12.0)	12 (10.3)	0.73
KDM5C	2 (8.0)	13 (11.0)	0.99
PTEN	1 (4.0)	12 (10.3)	0.47
ARID1A	3 (12.0)	14 (12.0)	0.99
MTOR	5 (20.0)	13 (11.0)	0.32

Results

- Patients who developed VTE had higher BMI on diagnosis (31.7 vs. 29.1, p=0.03). Immunotherapy was significantly associated with VTE development (31.8% vs. 12.3%, p<0.001), while there was no significant association between TKI use and VTE events (63.6% vs. 88.1%, p=0.45) (Table 1).
- In multivariate analysis, only BMI (OR=1.06, [1.01-1.12], p= 0.028) was associated with higher rates of VTE.
- CGP was available in 144 patients. There was no significant differences in mutation rates between both groups (Table 2).

Conclusions

- In this real-world setting, VTE is more commonly associated with mRCC than what was reported in previous clinical trials.
- Higher BMI at diagnosis was associated with a significantly increased risk of VTE development.
- Further tumoral transcriptomic analyses are needed to identify molecular markers associated with VTE in this patient population.

Limitations

- Retrospective nature of the study
- Restricted sample size
- Single-institution cohort

References

1-Wu MD, Moslehi JJ, and Lindner J. Arterial Thrombotic Complications of Tyrosine Kinase Inhibitors. *Arterioscler Thromb Vasc Biol* 2021 Jan;41(1):3-10.