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ASSOCIATIONS OF JAK2 MUTANT ALLELE BURDEN WITH OCCURRENCE OF CKD (CHRONIC KIDNEY DISEASE) AND DYNAMICS OF KIDNEY FUNCTION OVER TIME IN PATIENTS WITH CHRONIC MYELOPROLIFERATIVE NEOPLASMS

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INTRODUCTION

Chronic-kidney-disease (CKD) is common in patients with chronic-myeloproliferative-neoplasms (MPNs) and two diseases may be causally related through development of MPN-related glomerulopathy [1]. CKD substantially increases thrombotic risk for both arterial and venous thrombotic events in MPN patients [2, 3].

AIM

To evaluate associations of JAK2-V617F mutant-allele-burden (MAB) with occurrence of CKD and dynamics of kidney function over time.

METHOD

DESIGN: Retrospective cohort study

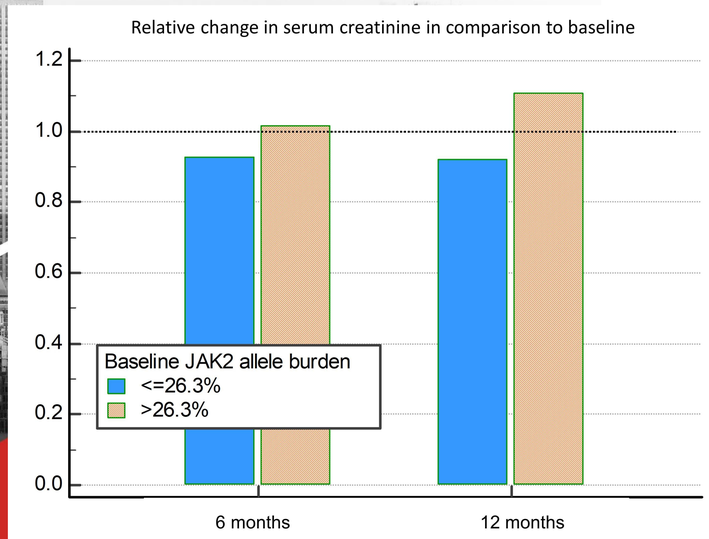
SETTING: Tertiary hematology referral centre.

PATIENTS OR OTHER PARTICIPANTS: A total of 230 consecutive evaluated JAK2-V617F-mutated MPN patients (98 polycythemia-vera, 94 essential-thrombocythemia, 20 primary-myelofibrosis, 18 other) evaluated in period 2006-2022.

INTERVENTIONS: MAB was determined using the quantitative real-time PCR (7300 RealTime-PCR-System (Applied-Biosystems,Foster-City,California,USA).

MAIN OUTCOMES MEASURES: Occurrence of CKD defined by CKD-EPI formula as estimated-glomerular-filtration rate <60 ml/min/1.73 m2 present for >3 months. Increase or decrease in serum-creatinine values at 6- and 12-months in comparison to baseline.

Dynamics of serum creatinine were evaluated as ratios of 6 or 12 month measurements in relation to baseline, values over 1 representing unfavorable and below 1 favorable dynamics of kidney function for the given time period.



RESULTS

Median age was 67 years. There were 50.2% females. Median MAB was 26.3%. A total of 24.9% patients had CKD which did not significantly differ between MPN subsets (P=0.140). Patients presenting with higher MAB stratified at the median had a higher frequency of CKD at baseline (32.6% vs 16.7%, P=0.012). In the multivariate-logistic-regression-model adjusted for clinically meaningful variables higher MAB stratified at the median remained significantly associated with CKD (OR 2.81, P=0.024) independently of older age (OR 1.11, P<0.001) and arterial-hypertension (OR 2.96, P=0.015).

Patients with higher in comparison to lower MAB stratified at median value significantly differed regarding the dynamics-of-kidney-function at 6-months (mean 2% worsening vs 7% improvement, P=0.032) and 12-months (mean 11% worsening vs 8% improvement, P=0.007). In the multivariate-logistic-regression-model adjusted for clinically meaningful variables higher MAB remained significantly associated with worsening of kidney-function at 6-months (OR 3.37, P=0.038) independently of older age (OR 1.05, P=0.024) and ACE-inhibitor-use (OR 0.21, P=0.024). In the similar model evaluating kidney-function dynamics at 12 months higher MAB remained the only significantly associated factor (OR 9.79, P=0.026).

CONCLUSIONS

MPN patients presenting with higher MAB seem to have a higher occurrence of concomitant CKD and demonstrate unfavorable dynamics of kidney-function over time. Although causal relationship cannot be inferred due to limitations of the study design, our observations support the view that biology of MPN and CKD might be intertwined.

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