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POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Sex-Specific Impact on Disease Outcome and Mutational Landscape in Essential Thrombocythemia

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Background:Male sex has been confirmed as an independent risk factor on survival effect in patients withessential thrombocythemia by mutation-enhanced international prognostic scoring system for essential thrombocythemia (MIPSS-ET) (Tefferi A, et al., Br J Haematol. 2020). Females are more common in ET patients (Grinfeld, et al., N Engl J Med. 2018). Epigenetic alterations (EAs) are found in approximately 20% inET. However, the prognostic role of epigenetic alterations is still not established in this patient population. Sexual dimorphism significantly contributes to patient heterogeneity, and adopting a sex-informed perspective has emerged as a pioneering paradigm in the field of precision medicine. The objective of our study was to comprehensively elucidate the impact of sex diversity on essential thrombocythemia, encompassing disease genotype, phenotype, and clinical outcomes.
Methods:In this study, we performed retrospective chart review of 556 consecutive patients aged 18 years or older with a diagnosis of essential thrombocythemia according to the 5 th World Health Organization classification of myeloid neoplasms (Khoury JD, et al., Leukemia. 2022). Recruitment periods for these patients were between January 2008 to June 2022. Overall survival (OS) from the time of diagnosis was estimated by Kaplan-Meier method with log-rank test. The effect of sex on clinical outcome, with OS, myelofibrosis-free survival, and thrombosis-free survival as the main endpoint, was analyzed in our cohort.
Results:This study included 245 (44.1%) men and 311 (55.9%) women. The percentages of age>60 years at diagnosis were 26.1% for men and 21.2% for women (p=0.176). Patients in the women cohort had lower red blood cell levels (4.54 vs. 4.81, p<0.001), lower hemoglobin levels (135 g/L vs. 146 g/L, p<0.001), lower percentage of cardiovascular risk factor (21.8% vs. 39.3%, p<0.001), and lower percentage of abnormal karyotype (37.3% vs. 50.6%, p=0.009). The treatment distributions between men and women cohorts were comparable (p>0.05). Sex biases were observed at the single-gene level with mutation in two genes enriched in males (SF3B1 p=0.008, ZRSR2 p=0.024). The ASXL1 gene mutation exhibited a discernible inclination towards a higher prevalence in males (p=0.098). Additionally, sex biases were observed in co-mutational pathways of founding genomic lesions (genes related to spliceosome mutation (SM), predominantly in men, p<0.001). Patients with SM had inferior OS and myelofibrosis-free survival than those without SM (p=2e-04, p=0.0078). Sex disparity was observed in the transcriptome signature of bone marrow CD34+ cells from ET patients. From results of GO analysis, we observed that up-regulated differentially expressed genes in male patients were significantly associated with the unfolded protein signaling pathway, as well as dysregulation of hematopoietic differentiation. Moreover, we found that lipid and atherosclerosis, and platelet activation pathways were enriched in male patients by KEGG analysis. Based on our analysis, we hypothesize that male ET patients exhibit enhanced bone marrow megakaryocyte production and platelet activation compared to female patients. Overall, Men had worse OS and thrombosis-free survival than women (both of median survival not reached; p=0.0081, p=0.019, respectively), but the myelofibrosis-free survival was not significantly different between men and women (p=0.52).
Conclusions: The findings from our study indicate that the implementation of a sex-informed approach has the potential to enhance the precision of personalized decision making in individuals diagnosed with essential thrombocythemia. Therefore, it is imperative to incorporate this approach in the planning and execution of clinical trials in the future.

Disclosures No relevant conflicts of interest to declare.

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