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POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Cardiovascular Outcomes Among Myeloproliferative Neoplasm Patients with or without Agent Orange Exposure Using a Large Veteran Database

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Cardiovascular Disease (CVD) and its complications contribute significantly to the morbidity and mortality of individuals with Myeloproliferative Neoplasms (MPNs), apart from the increased incidence of untoward thrombosis and bleeding. The prevalence of CVD, such as Heart Failure (HF) and Pulmonary Hypertension (PH) in individuals with MPNs and its association with exposure to Agent Orange (AO), a dioxin-containing carcinogen, remain undefined. These findings will be essential in risk stratification and multidisciplinary management of MPNs to prevent progression of CVD.

Utilizing the Veterans Affairs Informatics and Computing Infrastructure (VINCI) database, a case-control study was performed from January 1, 2006 - January 26, 2023 to characterize the association of CVD in Veterans with MPNs, arterial thrombosis (AT), venous thrombosis (VT), bleeding, and AO exposure. ICD-9 and -10 codes identified Veterans with MPN, AT, VT, bleeding, CV risk factors, such as hypertension (HTN), hyperlipidemia (HLD), diabetes (DM), smoking, and CVD sequelae, such as HF and PH. Age-, sex-, and race-matched controls (1:1) were selected from VINCI, who are Veterans without MPNs from Illinois, the state most representative of the U.S. population. Composite CVD outcome includes any Veteran with either HTN, HLD, DM, HF, or PH. Exposure to AO was self-reported and verified through Veterans' duration and location of service. Qualitative data were compared by chi-square tests.

Among 93,269 Veterans with MPN, there were higher rates of composite CVD, CV risk factors, HF, PH, AT, VT, and bleeding (Figure 1) compared to matched controls. All MPN subtypes, Essential Thrombocythemia (ET), Polycythemia Vera (PV), and Primary Myelofibrosis (PMF) were each associated with increased prevalence of HTN, HLD, DM, HF, and PH ($p<0.0001$). Among Veterans with MPNs with AT, VT, or bleeding, there was a significant association with each CV risk factors, HF, and PH ($p<.001$). Among Veterans with MPN with AO exposure, there were higher rates of composite CVD, CV risk factors, HF, PH, AT, and bleeding (Figure 1) when compared to those without AO exposure. Among matched controls with AO, there were higher rates of HLD and AT compared to matched controls without AO. Veterans born before 1960 with AO exposure had younger mean age at MPN diagnosis compared to those without AO, 66 ± 7 (SD) years vs. 69 ± 10 (SD) years, $p<0.0001$, respectively. Among the 24,385 (26.1%) Veterans with MPNs with HF vs. 1,749 (1.9%) Veterans with MPNs with PH: 46.1% vs. 38.9% had ET; 48.8% vs. 56% had PV; and 5.1% vs. 5.1% had PMF; 92.7% vs. 91.2% were born before 1960; 96.8% vs. 95.3% were male; 75.8% vs. 72.1% White; 14.7% vs. 19.3% Black; 7.5% vs. 6.9% unknown race, respectively. Among MPNs with PH, there is a higher rate of pulmonary embolism (4.87% vs. 1.1%, $p<0.0001$) when compared to matched controls.

There is decreased overall survival among Veterans with MPNs with HF and PH (Figure 2) and Veterans with MPNs compared to matched controls.

In summary, the CV risk factors, HF and PH, are increased in Veterans with MPNs and are associated with increased risk for AT, VT, and bleeding complications. Not only is AO exposure associated with development of MPN, as previously reported

(J Clin Oncology 2023 41:16_suppl, 7011), but AO exposure appears to increase CVD complications among Veterans with MPNs. Further studies evaluating contributions of driver mutation and CHIPs to cardiac and vascular remodeling are needed and will elucidate the implications of AO and its imputed toxic effects on DNA to the accelerated development of MPNs and its CVD complications. Future targeted therapies and strategies should be developed to mitigate the consequences of progressive CVD, and prevention of AT, VT, and bleeding complications in individuals with MPNs.

Disclosures Kessler: *CSL Behring:* Other: Scientific advisory board; *Genentech:* Other: Scientific advisory board; *Novo Nordisk:* Other: Scientific advisory board; *Octapharma:* Other: Scientific advisory board, Research Funding; *Bayer:* Consultancy, Other: Chair, DSMB, scientific advisory board, Research Funding.

Figure 1. Prevalence of Cardiovascular Disease, Thrombosis, and Bleeding Among Veterans with Myeloproliferative Neoplasms (MPN) with or without Agent Orange (AO) Exposure

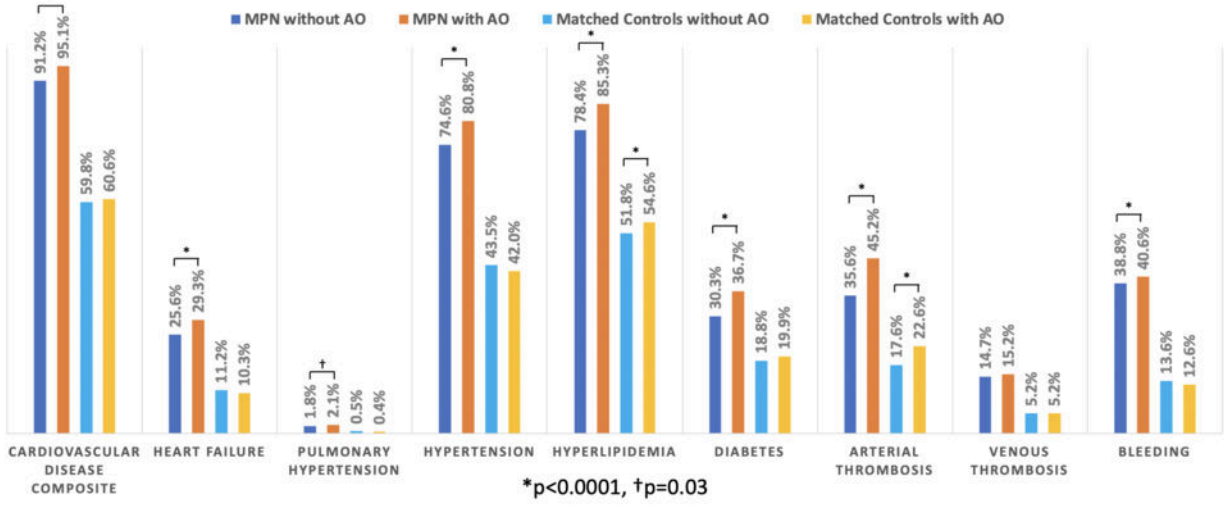

Figure 2. Overall Survival of Veterans with Myeloproliferative Neoplasms with Heart Failure and Pulmonary Hypertension

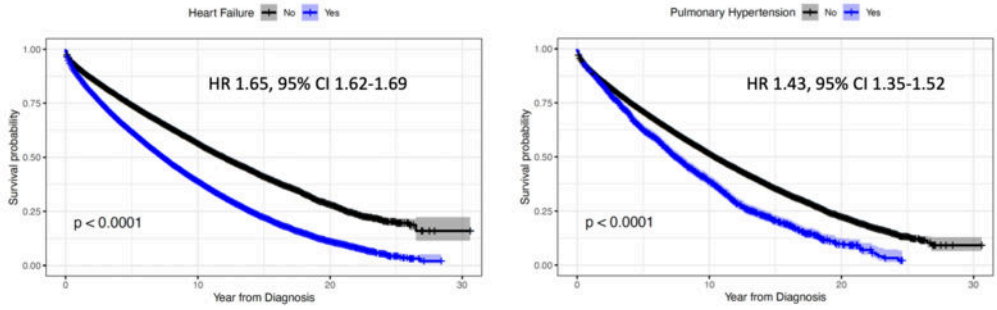

Figure 1

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