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Blood 142 (2023) 6439–6441

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Impact of Kidney Dysfunction on Overall Survival in Myeloproliferative Neoplasms: A Single-Center Retrospective Study

Eshrak Al-Shaibani[1], Taylor Young[2], Eshetu Atenafu, M.Sc, P. Stat[3], Verna Cheung[1], Safwan Alsibai[1], Vikas Gupta, MD[1], Dawn C. Maze, MD FRCPC, MSc[1], Marta Beata Davidson, MD PhD[1], Aniket Banker, MD[1], Hassan Sibai, MD[1]

[1] Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada
[2] Queen's University Department of Family Medicine, Kingston, Canada
[3] Biostatistics, University Health Network, Toronto, CAN

Introduction: Myeloproliferative neoplasms (MPN) are clonal hematopoietic stem cell disorders that can lead to the deposition of fibrous tissue, and by a propensity toward extramedullary hematopoiesis. The progression of kidney function and frequency of chronic kidney disease (CKD) in patients with MPN is unknown, although CKD is linked to increased mortality. In our study, we aimed to investigate the relationship between kidney function as measured by glomerular filtration rate (eGFR) and MPN disease and risk of thrombosis. Moreover, we analyzing the risk factors for CKD, impact of different treatment modalities and effect of CKD on survival.

Patients & Method: We haveretrospectively screened 762 patients between Jan 1989 to May 2019 with MPN at Princess Margaret Cancer Centre. Diagnosis, of Polycythemia (PV), essential thrombocytosis (ET), and myelofibrosis (MF; comprising PMF, post-ET-PMF, and post-PV-PMF) was required as defined by the WHO classification. Patients with other MPNs (CNL, CEL, HES, MDS/MPN, MPN-U, Mastocytosis accelerating phase MPN and blast phase) or missing serial creatinine measurement or their CKD attributed to other causes (diabetic nephropathy, High blood pressure, polycystic kidney disease obstructive uropathy, Glomerulonephritis before MPN diagnosis and other) were excluded, resulting in study sample of 232 patients. The total cohort was subdivided according to the calculated eGFR, (ml/min/1.73m2) into eGFR1 (≥90, n=154), eGFR2 (60-89, n=12), and eGFR3 (<60, n=66). eGFR was collected retrospectively, because of small number of patients, we combined eGFR2 and eGFR3 in one group. Overall Survival (OS) was calculated using the Kaplan-Meier and log-rank test was used to assess impact variables of interest. Cox proportional hazards model was used to assess for prognostic factors of OS as well as to assess the joint effect of potential prognostic factors.

Results: Median age for the total cohort was 58 years (range;18-88.3), 54% were male. Median follow-up duration was 86 months (range:45.5-135). Diagnosis of MPN involved ET; n=21(9%)), PV; n=32 (14%) and MF; n=179 (77%). JAK2V617F status was documented in 219 patients; 67% were positive; of 106 patients analyzed for CARL 40.6% were positive. Cardiovascular risk factors were higher in PV and MF than in ET (59.4%, 57% &38%) respectively. A higher uric acid and LDH levels were found in PV and MF. A total of 19% had a history of thrombosis and rate was higher in ET (28.6%) than PV (21.9%) or MF (16.8%). Further patient's characteristics summarized in Table1. Kidney biopsy performed in 8 patients. The most prominent histological finding included focal segmental glomerulosclerosis (n=3), Ig A nephropathy (n=3), mesangial hypercellularity and sclerosis, extramedullary haematopoiesis (n=1) and lupus nephritis (n=1).

The risk factors for CKD based on eGFR group are presented in (Table 2). MPN diagnosis is a significant risk factor for kidney function (p=0.0117). In MF a higher rate of eGFR 88.5% compared with PV and ET. JAK2V617 demonstrates a significant impact on abnormal eGFR (p=0.05);. IPSS and DIPSS score are a significant risk factor for kidney dysfunction (p=0.0014, and 0.0074 respectively). High uric acid levels and neutrophil counts were higher in high eGFR group (p=0.0014, and 0.0074 respectively). No association found between thrombosis and high eGFR.

Hydroxyurea treatment does not have an impact on CKD, however, more patients received Ruxolitinb in abnormal eGFR (p=0.001). CKD has significant impact on OS. The 5 years OS for eGFR1 was 75% (95% CI 67%-81%), and for abnormal eGFR was 63.9% (95% CI 52%-73%), p=0004 (Fig 1).

Conclusion: Higher incidence of kidney dysfunction associated in MF compared to PV and ET, there was no association between thrombosis and high eGFR as we excluded all other cause of CKD. MF with abnormal eGFR associated with high

DIPSS score. MPN patients with kidney dysfunction significantly affects OS, which indicate close monitoring and prospective study is required.

Disclosures Gupta: *GSK:* Other: Travel to EHA 2023 for invited talk at GSK sponsored MPN education session ; *BMS Celgene, Roche, AbbVie, Pfizer, Sierra Oncology, CTI Biopharma, GSK:* Other: Participation on a Data Safety Monitoring Board or Advisory Board; *Novartis, BMS Celgene, SMP Oncology, AbbVie, Constellation Biopharma, Pfizer, GSK Pharma, CTI Biopharma:* Consultancy; *Novartis, BMS Celgene, GSK:* Honoraria; *BMS, Celgene, Roche, Abb Vie, Pfizer, Sierra Oncology, CTI Biopharma:* Membership on an entity's Board of Directors or advisory committees; *Novartis, BMS Celgene, Sierra Oncology, AbbVie, Constellation Biopharma, Pfizer, GSK Pharma, CTI Biopharma:* Consultancy.

https://doi.org/10.1182/blood-2023-189318

Table 1: Patients characteristics by disease type of the total cohort and by MPN subtypes

	Total	PV	ET	MF
Median age (range)	58 (18-88.3)	50.7 (18-88.3)	45 (21-70)	60.16 (20- 85.7)
Gender, n (%)				
Male	125 (53.9)	15 (46.9)	8 (38.1)	102 (57)
Female	107 (46.1)	17 (53.1)	13 (61.9)	77 (43)
Cytogenetic, n (%)				
Normal	69 (56.6)	9 (56.3)	3 (60)	57 (56.4)
Abnormal	53 (43.4)	0	2 (40)	44 (43.6)
Missing	110	16	16	78
CARL, n (%)				
Yes	43 (40.6)	0	7 (58.3)	36 (42.9)
No	63 (59.4)	10 (100)	5 (41.7)	48 (57.1)
Missing	126	22	9	95
JAK2V617F, n (%)				
Yes	147 (63.4)	30 (93.7)	8 (38.1)	111 (62)
No	72 (31)	2 (6.3)	11 (52.4)	59 (33)
Missing	13	0	3	10
Hydroxyurea, n (%)				
Yes	91 (39.9)	15 (48.4)	10 (47.6)	66 (37.1)
No	137 (60.1)	16 (51.6)	11 (52.4)	110 (62.9)
Missing	4	1	0	3
JAK inhibitor treatments, n (%)				
Ruxolitinib	74 (32.0)	21 (65.6)	0	66 (37.1)
Others	25 (10.8)	8 (25.0)	1 (4.8)	21 (11.8)
No JAK inhibitor treatment	132 (57.1)	3 (9.4)	20 (95.2)	91 (51.1)
Missing	1	0	0	1
eGFR, n (%)				
eGFR1	154 (66.4)	26 (81.3)	18 (85.7)	110 (61.5)
eGFR2	12 (5.2)	1 (3.1)	0	11 (6.1)
eGFR3	66 (28.4)	5 (15.6)	3 (14.3)	58 (32.4)
HSCT, n (%)				
Yes	53 (22)	7 (22)	2 (9.5)	42 (23.5)
No	181(78)	25 (78)	19 (90.5)	137 (76.5)
History of diabetes, n (%)				
Yes	25 (10.8)	3 (9.4)	1 (4.8)	21 (11.7)
No	207 (89.2)	29 (90.6)	20 (95.2)	158 (88.3)
Cardiovascular risk factors, n (%)	103 (44.4)	13 (40.6)	13 (61.9)	77 (43)
Yes	129 (55.6)	19 (59.4)	8 (38.1)	102 (57)
No				
ECOG, n (%)				
0-1	220 (94.8)	30 (93.8)	21 (100)	169 (94.4)
≥2	12 (5.2)	2 (6.3)	0	10 (5.6)
Thrombosis, n (%)				
Yes	43 (18.5)	7 (21.9)	6 (28.6)	30 (16.8)
No	189 (81.5)	25 (78.1)	15 (71.4)	149 (83.2)
Median WBC (range)	9.6 (0.9- 84.9)	11.70 (1.30- 28.1)	6.15 (3.5- 13)	9.75 (0.9- 84.9)
Median platelet (range)	266.5 (0, 2538)	414 (68- 1043)	603.5 (342, 2536)	229 (0- 2254)
Median creatinine (range)	72 (10.2-289)	70 (50- 128)	69 (49- 219)	76 (10.2- 18)
Median eGFR (range)	94.4 (25.4-205)	99.3 (29.1-120)	101.6 (25.4-121.7)	92.8(29.8- 205)
Median uric acid (range)	377.5 (226- 944)	368.50 (230- 873)	285 (194- 380)	392 (226- 944)
Median LDH (range)	521.5(165- 5876)	365 (165- 1236)	306 (176- 672)	573 (165- 5876)
Median CRP (range)	4 (1-78)	4 (1-23)	1 (1-2)	5 (1-78)
IPSS score, n (%)				
0	-	-	-	37 (22)
1	-	-	-	50 (29.8)
2	-	-	-	38 (22.6)
≥3	-	-	-	43 (25.6)
Missing	-	-	-	11
DIPSS score, n (%)				
0	-	-	-	41 (24.4)
1-2	-	-	-	64 (38)
3-4	-	-	-	42 (25)
5-6	-	-	-	21 (12.5)
Missing	-	-	-	11
DIPSS plus score, n (%)				
0	-	-	-	27 (23.3)
1-2	-	-	-	30 (25.9)
3-4	-	-	-	40 (34.5)
≥4	-	-	-	19 (16.4%)
Missing	-	-	-	63

Abbreviation: CRP, C-reactive protein; DIPSS, Dynamic International Prognostic Scoring System; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate; ET, essential thrombocytosis; HSCT, hematopoietic stem cell transplantation; IPSS, International Prognostic Scoring; LDH, Lactate dehydrogenase; MF, myelofibrosis; PV, Polycythemia; WBC, white blood cell.

Table 2: Risk factors for decrease kidney function

	eGFR1 (Normal kidney) (N=154)	eGFR2/eGFR3 (abnormal Kidney) (N=78)	P value
Diagnosis, n (%)			**0.011**
PV	26 (16.9)	6 (7.7)	
ET	18 (11.7)	3 (3.8)	
MF	110 (71.4)	69 (88.5)	
Thrombosis, n (%)			0.84
Yes	28 (18.2)	15 (19.2)	
No	126 (81.8)	63 (80.8)	
Cardiovascular risk factors, n (%)			0.31
Yes	82 (53.2)	47 (60.3)	
No	72 (46.8)	31 (39.7)	
Diabetes, n (%)			0.11
Yes	13 (8.4)	12 (15.4)	
No	141 (91.6)	66 (84.6)	
WBC, median (range)	8.80 (1.3 71.7)	9.9 (0.9 84.9)	0.08
Platelets, median (range)	283 (10- 2536)	226(8- 1112)	0.04
Neutrophils, median (range)	5.9 (0.16- 41.8)	7.22 (0.15 54.85)	**0.02**
LDH, median (range)	495 (165- 5876)	546 (209 3673)	0.59
CRP, median (range)	6 (1- 56)	3.5 (1- 78)	0.36
Uric acid, median (range)	353 (168- 873)	430 (2.26- 944)	**0.001**
JAK2V617F, n (%)			**0.054**
Yes	91 (62.8)	56 (75.7)	
No	54 (37.2)	18 (24.3)	
Missing	9	4	
CARL, n (%)			0.16
Yes	34 (44.7)	9 (30)	
No	42 (55.3)	21 (70)	
Missing	78	48	
MPN duration, median (range)	92 (1.5 310.9)	75.81 (3.75 467.84)	0.34
Hydroxyurea treatment, n (%)			0.38
Yes	58 (37.9)	33 (44)	
No	95 (62.1)	42 (56)	
Missing	1	3	
Treatment (JAK inhibitor), n (%)			**0.008**
Ruxolitinib	41 (26.6)	33 (42.9)	
Other	14 (9.1)	11 (14.3)	
No JAK inhibitor treatment	99 (64.3)	33 (42.9)	
Missing	0	1	
IPSS score			**0.001**
0	31 (30.7)	6 (8.8)	
1	32 (31.7)	19 (27.9)	
2	19 (18.8)	19 (27.9)	
≥3	19 (18.8)	24 (35.3)	
Missing	9	1	
DIPSS score			**0.007**
0	33 (32.7)	8 (11.8)	
1 2	38 (37.6)	27 (39.7)	
3 4	21 (20.8)	21 (30.9)	
5 6	9 (8.9)	12 (17.6)	
Missing	9	1	
DIPSS plus score			0.27
0	20 (29.4)	7 (14.6)	
1	17 (25)	13 (27.1)	
2 3	22 (32.)	18 (37.5)	
≥4	9 (13.2)	10 (20.8)	
Missing	42	21	

Abbreviation: CRP, C-reactive protein; DIPSS, Dynamic International Prognostic Scoring System; eGFR, estimated glomerular filtration rate; ET, essential thrombocytosis; IPSS, International Prognostic Scoring; LDH, Lactate dehydrogenase; MF, myelofibrosis; PV, Polycythemia; WBC, white blood cell.

Figure 1. Overall survival according to eGFR

Figure 1