

# Characterization and prognostic implication of pulmonary hypertension among patients with myeloproliferative neoplasms

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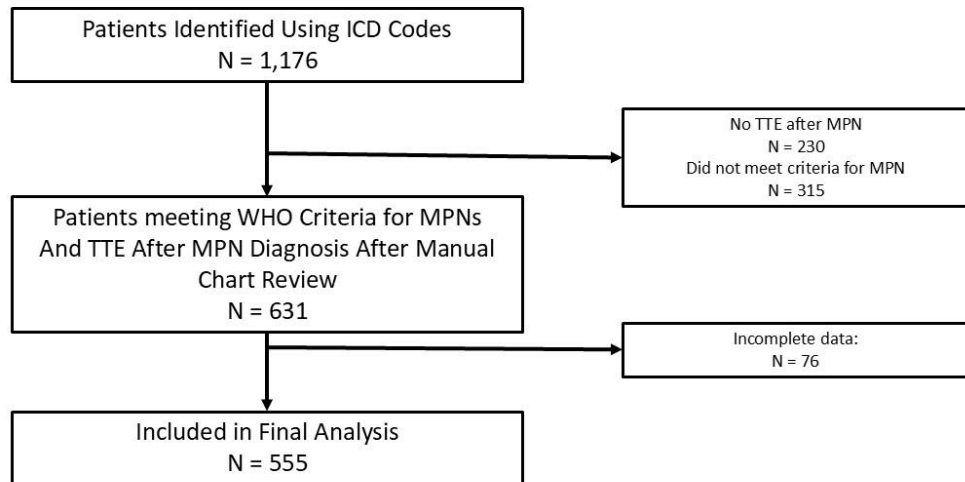
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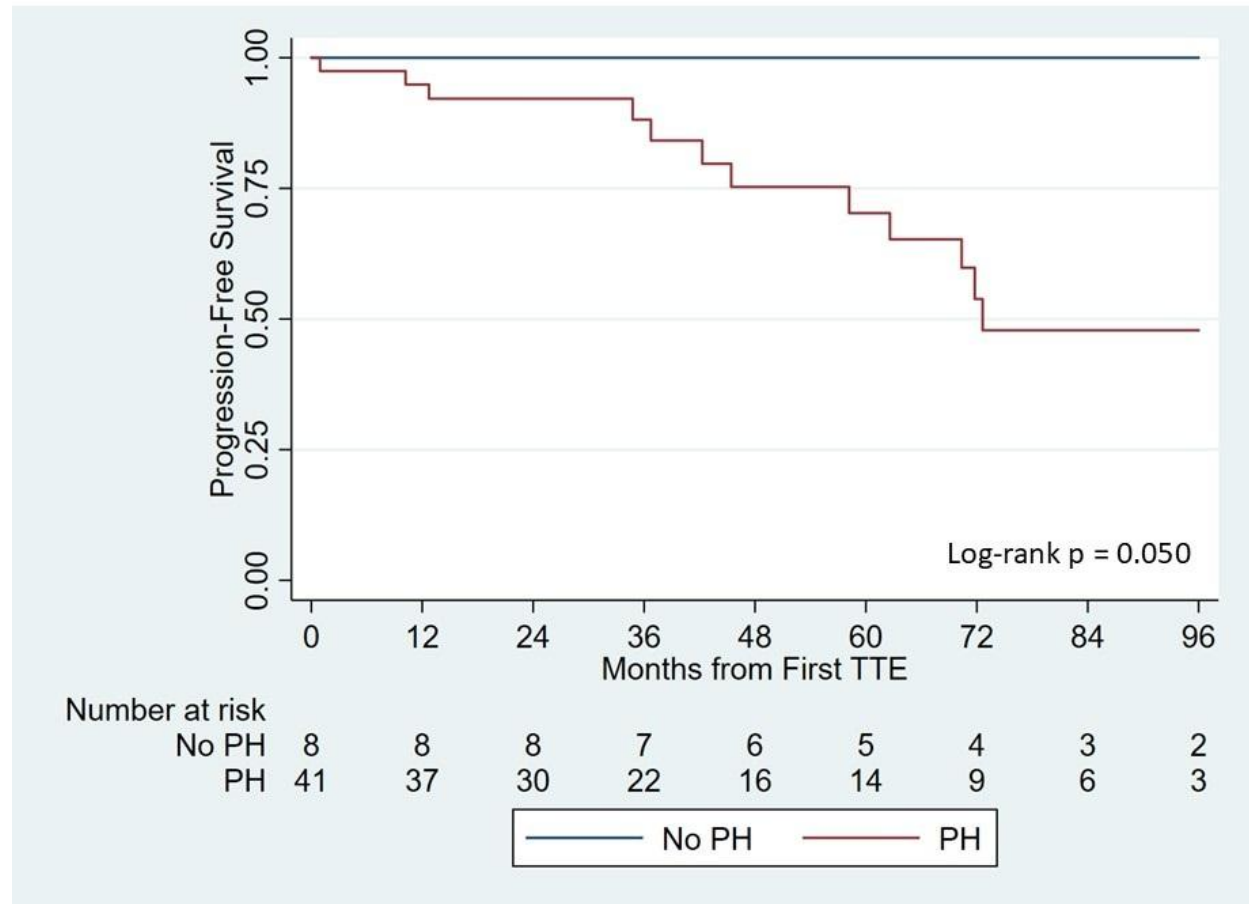
**Supplemental Figure 1: Flowchart of patients included in our study.**

**Supplemental Figure 1**



**Supplemental Figure 2: Kaplan-Meier Curve of Disease Progression-Free Survival of Patients with versus without PH on RHC**

## Supplemental Figure 2



**Supplemental Table 1: Echocardiographic Characteristics by Pulmonary Hypertension**

|                                          | <b>All Patients<br/>N = 555</b> | <b>PASP &lt; 40 mmHg<br/>N = 360</b> | <b>PASP ≥ 40 mmHg<br/>N = 195</b> | <b>P value</b> |
|------------------------------------------|---------------------------------|--------------------------------------|-----------------------------------|----------------|
| Age at TTE, median (IQR)                 | 74 (65, 81)                     | 71 (61, 78)                          | 79 (70, 85)                       | < 0.001        |
| Outpatient TTE, N (%)                    | 415 (74.8)                      | 292 (81.1)                           | 123 (63.1)                        | < 0.001        |
| HF or Dyspnea Indication for TTE, N (%)  | 187 (33.7)                      | 87 (24.2)                            | 100 (51.3)                        | < 0.001        |
| Indications for TTE, N (%)               |                                 |                                      |                                   |                |
| HF                                       | 66 (11.9)                       | 18 (5.0)                             | 48 (24.6)                         | < 0.001        |
| Dyspnea                                  | 125 (22.5)                      | 71 (19.7)                            | 54 (27.7)                         | 0.034          |
| Chest Pain                               | 33 (5.9)                        | 26 (7.2)                             | 7 (3.6)                           | 0.093          |
| Arrhythmia                               | 99 (17.8)                       | 67 (18.6)                            | 32 (16.4)                         | 0.56           |
| Murmur                                   | 86 (15.5)                       | 58 (16.1)                            | 28 (14.4)                         | 0.62           |
| Screening                                | 107 (19.3)                      | 88 (24.4)                            | 19 (9.7)                          | < 0.001        |
| Other Indication                         | 65 (11.7)                       | 42 (11.7)                            | 23 (11.8)                         | 0.96           |
|                                          |                                 |                                      |                                   |                |
| H2FPEF Score, median (IQR)               | 3 (2, 4)                        | 2 (1, 4)                             | 4 (3, 6)                          | < 0.001        |
|                                          |                                 |                                      |                                   |                |
| Chamber Characteristics                  |                                 |                                      |                                   |                |
| LVEF, median % (IQR)                     | 64 (60, 68)                     | 65 (60, 69)                          | 61 (55, 66)                       | < 0.001        |
| LVEF < 50%, N (%)                        | 34 (6.1)                        | 14 (3.9)                             | 20 (10.3)                         | 0.005          |
| LVEDD, median cm (IQR)                   | 4.5 (4.1, 4.9)                  | 4.4 (4.0, 4.9)                       | 4.6 (4.2, 5.1)                    | < 0.001        |
| LVH Present, N (%)                       | 109 (19.6)                      | 60 (16.7)                            | 49 (25.1)                         | 0.019          |
| LA Diameter, median cm (IQR)             | 3.9 (3.5, 4.3)                  | 3.8 (3.4, 4.2)                       | 4.2 (3.8, 4.6)                    | < 0.001        |
| Moderate or Severe LA Enlargement, N (%) | 114 (20.5)                      | 40 (11.1)                            | 74 (37.9)                         | < 0.001        |
| Moderate or Severe RA Enlargement, N (%) | 51 (9.2)                        | 6 (1.7)                              | 45 (23.1)                         | < 0.001        |
|                                          |                                 |                                      |                                   |                |
| Right Ventricular Characteristics        |                                 |                                      |                                   |                |
| Reduced RV Systolic Function, N (%)      | 31 (5.6)                        | 3 (0.8)                              | 28 (14.4)                         | < 0.001        |
| RV Dilation, N (%)                       | 71 (12.8)                       | 22 (6.1)                             | 49 (25.1)                         | < 0.001        |

|                                                              |                   |                 |                   |         |
|--------------------------------------------------------------|-------------------|-----------------|-------------------|---------|
| RV Basal Diameter, median cm (IQR)                           | 3.8 (3.3, 4.2)    | 3.7 (3.2, 4.1)  | 4.1 (3.6, 4.6)    | < 0.001 |
| TAPSE, median cm (IQR)                                       | 2.3 (2.0, 2.6)    | 2.3 (2.0, 2.6)  | 2.3 (1.9, 2.9)    | 0.92    |
| RVOT AT, median m/s (IQR)                                    | 107 (90, 122)     | 116 (101, 130)  | 86 (73, 97)       | < 0.001 |
| Moderate or Severe TR, N (%)                                 | 85 (15.3)         | 16 (4.4)        | 69 (35.4)         | < 0.001 |
| TR Peak Velocity, median m/s (IQR)                           | 2.7 (2.3, 3.0)    | 2.4 (2.2, 2.7)  | 3.2 (3.0, 3.5)    | < 0.001 |
| PASP, median mmHg (IQR)                                      | 34 (26, 44)       | 28 (23, 33)     | 49 (43, 58)       | < 0.001 |
|                                                              |                   |                 |                   |         |
| Other Valvular Characteristic                                |                   |                 |                   |         |
| Moderate or Severe MR, N (%)                                 | 72 (13.0)         | 22 (6.1)        | 50 (25.6)         | < 0.001 |
| Moderate or Severe AR, N (%)                                 | 17 (3.1)          | 11 (3.1)        | 6 (3.1)           | 1.00    |
| Any Prosthetic Valve, N (%)                                  | 13 (2.3)          | 7 (1.9)         | 6 (3.1)           | 0.39    |
| Peak AV Velocity, median m/s (IQR)                           | 1.5 (1.3, 1.9)    | 1.5 (1.2, 1.7)  | 1.7 (1.4, 2.1)    | < 0.001 |
| Peak LVOT velocity, median m/s (IQR)                         | 1.0 (0.9, 1.2)    | 1.0 (0.9, 1.2)  | 1.0 (0.9, 1.2)    | 0.15    |
| Estimated Cardiac Output, median ml/min/m <sup>2</sup> (IQR) | 5.1 (4.2, 6.1)    | 5.1 (4.3, 6.0)  | 5.1 (4.1, 6.5)    | 0.61    |
|                                                              |                   |                 |                   |         |
| Diastology                                                   |                   |                 |                   |         |
| Mitral Early (E) Inflow Velocity, median cm/s (IQR)          | 80 (67, 101)      | 76 (62, 92)     | 100 (80, 119)     | < 0.001 |
| Mitral A (A) Wave Velocity, median cm/s (IQR)                | 80 (60, 98)       | 79 (64, 97)     | 80 (50, 104)      | 0.96    |
| Mean E/E', median (IQR)                                      | 10.3 (8.0, 13.5)  | 9.1 (7.5, 12.2) | 12.8 (10.0, 16.8) | < 0.001 |
| E/A, median (IQR)                                            | 1.00 (0.79, 1.39) | 0.9 (0.8, 1.2)  | 1.2 (0.9, 2.0)    | < 0.001 |

AV, aortic valve; AR, aortic regurgitation; HF, heart failure; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; LVOT, left ventricular outflow tract; MR, mitral regurgitation; PASP, pulmonary artery systolic pressure; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract; TAPSE, tricuspid annular plane systolic excursion; TTE, transthoracic echocardiogram; TR, tricuspid regurgitation

**Supplemental Table 2: Characteristics and Outcomes of Patients with versus without PH on RHC**

|                                                 | <b>All Patients<br/>N = 49</b> | <b>No PH<br/>N = 8</b> | <b>PH<br/>N = 41</b> | <b>P value</b> |
|-------------------------------------------------|--------------------------------|------------------------|----------------------|----------------|
| Age at MPN<br>Diagnosis, median<br>(IQR)        | 67 (62, 73)                    | 64 (60, 70)            | 68 (62, 77)          | 0.44           |
| Female Sex                                      | 24 (49.0)                      | 3 (37.5)               | 21 (51.2)            | 0.37           |
| Non-White Race, N<br>(%)                        | 6 (12.2)                       | 0                      | 6 (14.6)             | 0.57           |
| Time from MPN to<br>RHC, median<br>months (IQR) | 76 (52, 111)                   | 73 (37, 129)           | 76 (59, 106)         | 0.63           |
| Follow-up Since<br>RHC, median<br>months (IQR)  | 28 (10, 53)                    | 49 (3, 90)             | 27 (12, 52)          | 0.65           |
| PASP > 40 mmHg on<br>First TTE                  | 31 (63.3)                      | 1 (12.5)               | 30 (73.2)            | 0.002          |
| LHD on First TTE                                | 33 (67.3)                      | 5 (62.5)               | 28 (68.3)            | 1.00           |
|                                                 |                                |                        |                      |                |
| MPN<br>Characteristics, N<br>(%)                |                                |                        |                      |                |
| MPN Type                                        |                                |                        |                      | 0.19           |
| PV                                              | 24 (49.0)                      | 3 (37.5)               | 21 (51.2)            |                |
| ET                                              | 18 (36.7)                      | 5 (62.5)               | 13 (31.7)            |                |
| MF                                              | 7 (14.3)                       | 0                      | 7 (17.1)             |                |
| Driver Mutation                                 |                                |                        |                      | 0.84           |
| JAK2                                            | 39 (79.6)                      | 6 (75.0)               | 33 (80.5)            |                |
| CALR                                            | 3 (6.1)                        | 1 (12.5)               | 2 (4.9)              |                |
| MPL                                             | 1 (2.0)                        | 0                      | 1 (2.4)              |                |
| Triple Negative                                 | 6 (12.2)                       | 1 (12.5)               | 5 (12.2)             |                |
| Secondary<br>Mutation, N (%)                    | 17 (34.7)                      | 0                      | 17 (41.5)            | 0.038          |
| Treatment for MPN                               |                                |                        |                      |                |
| Any                                             | 38 (77.5)                      | 6 (75.0)               | 32 (78.0)            | 0.85           |
| Hydroxyurea                                     | 26 (53.1)                      | 4 (50.0)               | 22 (53.7)            | 0.85           |
| Ruxolitinib                                     | 5 (10.2)                       | 1 (12.5)               | 4 (9.8)              | 0.81           |
| Phlebotomy                                      | 13 (26.5)                      | 1 (12.5)               | 12 (29.3)            | 0.33           |
| Spleen Size, median<br>cm (IQR)                 | 14.2 (11.0, 17.7)              | 14.1 (10.4, 16.3)      | 14.2 (11.5, 18.0)    | 0.70           |
|                                                 |                                |                        |                      |                |
| Co-Morbidities                                  |                                |                        |                      |                |
| Prior HF<br>Hospitalization                     | 7 (14.3)                       | 0                      | 7 (17.1)             | 0.21           |
| Prior ASCVD c                                   | 25 (51.0)                      | 7 (87.5)               | 18 (43.9)            | 0.028          |
| HTN                                             | 30 (61.2)                      | 3 (37.5)               | 27 (65.8)            | 0.13           |

|                                        |                   |                   |                  |         |
|----------------------------------------|-------------------|-------------------|------------------|---------|
| AF                                     | 8 (16.3)          | 1 (12.5)          | 7 (17.1)         | 0.75    |
| Prior VTE                              | 12 (24.5)         | 2 (25.0)          | 10 (24.4)        | 0.97    |
| Diabetes                               | 8 (16.3)          | 1 (12.5)          | 7 (17.1)         | 0.75    |
|                                        |                   |                   |                  |         |
| Laboratory Values,<br>median (IQR)     |                   |                   |                  |         |
| WBC, K/ $\mu$ L                        | 11.8 (7.2, 17.6)  | 11.4 (7.0, 18.3)  | 11.9 (7.3, 17.6) | 0.98    |
| Hemoglobin, g/dL                       | 12.3 (10.3, 14.3) | 13.1 (11.4, 14.4) | 12.3 (9.6, 14.1) | 0.34    |
| Platelet Count, K/ $\mu$ L             | 394 (247, 489)    | 587 (388, 762)    | 373 (244, 460)   | 0.023   |
| Creatinine, mg/dL                      | 1.1 (0.8, 1.4)    | 1.2 (0.8, 1.3)    | 1.1 (0.8, 1.5)   | 0.93    |
| LDH, U/L                               | 460 (273, 695)    | 674 (238, 860)    | 444 (279, 599)   | 0.57    |
|                                        |                   |                   |                  |         |
| Pressures, median<br>mmHg (IQR)        |                   |                   |                  |         |
| Right Atrial<br>Pressure               | 8 (5, 11)         | 5 (3, 8)          | 8 (6, 12)        | 0.043   |
| Mean PAP                               | 32 (23, 38)       | 18 (15, 19)       | 34 (28, 40)      | < 0.001 |
| Systolic PAP                           | 51 (37, 58)       | 28 (24, 30)       | 55 (42, 60)      | < 0.001 |
| Diastolic PAP                          | 20 (14, 25)       | 10 (9, 11)        | 20 (17, 25)      | < 0.001 |
| PCWP                                   | 15 (12, 18)       | 12 (6, 14)        | 15 (13, 19)      | 0.017   |
| PVR                                    | 3.1 (1.7, 4.0)    | 1.3 (0.9, 1.4)    | 3.2 (2.0, 4.4)   | < 0.001 |
| Cardiac Output,<br>L/min               | 5.1 (4.3, 6.2)    | 5.0 (3.3, 6.1)    | 5.1 (4.3, 6.2)   | 0.58    |
| Cardiac Index,<br>L/min/m <sup>2</sup> | 2.9 (2.4, 3.2)    | 2.6 (1.9, 3.0)    | 3.0 (2.5, 3.4)   | 0.18    |
|                                        |                   |                   |                  |         |
| Type of PH, N (%)                      |                   |                   |                  | N/A     |
| Pre-Capillary                          | 18 (36.7)         | 0                 | 18 (43.9)        |         |
| Isolated Post-<br>Capillary            | 6 (12.2)          | 0                 | 6 (14.6)         |         |
| Combined Pre- and<br>Post-Capillary    | 13 (26.5)         | 0                 | 13 (31.7)        |         |
| NOS                                    | 4 (8.2)           | 0                 | 4 (9.8)          |         |
|                                        |                   |                   |                  |         |
| Outcomes, N (%)                        |                   |                   |                  |         |
| MPN Disease<br>Progression             | 12 (24.5)         | 0                 | 12 (29.3)        | 0.17    |
| All-Cause Death                        | 27 (55.1)         | 5 (62.5)          | 22 (53.7)        | 0.71    |



**Supplemental Table 3: Characteristics of Patients with PH on Any TTE Who With Versus Without Left Heart Disease At Time of PH Diagnosis**

|                                                         | All Patients<br>N = 266 | No Left Heart<br>Disease<br>N = 94 | Left Heart Disease<br>N = 172 | P value |
|---------------------------------------------------------|-------------------------|------------------------------------|-------------------------------|---------|
| Age at MPN<br>Diagnosis, median<br>(IQR)                | 72 (65, 81)             | 69 (61, 79)                        | 74 (68, 81)                   | 0.015   |
| Age at PH Diagnosis,<br>median (IQR)                    | 80 (72, 85)             | 77 (68, 84)                        | 81 (75, 86)                   | < 0.001 |
| Female Sex                                              | 138 (51.9)              | 44 (46.8)                          | 94 (54.7)                     | 0.25    |
| Non-White Race, N<br>(%)                                | 30 (11.3)               | 14 (14.9)                          | 16 (9.3)                      | 0.22    |
| Follow-up Since PH<br>Diagnosis, median<br>months (IQR) | 33.2 (13.8, 62.7)       | 39.7 (18.9, 72.5)                  | 30.3 (11.7, 55.8)             | 0.020   |
| MPN Characteristics,<br>N (%)                           |                         |                                    |                               |         |
| MPN Type at First TTE                                   |                         |                                    |                               | 0.16    |
| PV                                                      | 104 (39.1)              | 44 (46.8)                          | 60 (34.9)                     |         |
| ET                                                      | 100 (37.6)              | 31 (33.0)                          | 69 (40.1)                     |         |
| MF                                                      | 62 (23.3)               | 19 (20.2)                          | 43 (25.0)                     |         |
| Driver Mutation                                         |                         |                                    |                               | 0.87    |
| JAK2                                                    | 208 (78.2)              | 76 (80.9)                          | 132 (76.7)                    |         |
| CALR                                                    | 18 (6.8)                | 5 (5.3)                            | 13 (7.6)                      |         |
| MPL                                                     | 12 (4.5)                | 4 (4.3)                            | 8 (4.7)                       |         |
| Triple Negative                                         | 28 (10.5)               | 9 (9.6)                            | 19 (11.0)                     |         |
| Driver Mutation VAF,<br>median % (IQR)                  | 54.3 (32.8, 84.7)       | 55.4 (28.8, 89.0)                  | 52.4 (36.6, 79.0)             | 0.55    |
| Non-Phenotypic<br>Driver Mutations, N<br>(%)            |                         |                                    |                               |         |
| Any                                                     | 78 (29.3)               | 26 (27.7)                          | 52 (30.2)                     | 0.68    |
| HMR <sup>a</sup>                                        | 31 (11.7)               | 6 (6.4)                            | 25 (14.5)                     | 0.070   |
| DTA <sup>b</sup>                                        | 44 (16.5)               | 11 (11.7)                          | 33 (19.2)                     | 0.12    |
| Treatment for MPN                                       |                         |                                    |                               |         |
| Any                                                     | 216 (81.2)              | 77 (81.9)                          | 139 (80.8)                    | 0.87    |
| Hydroxyurea                                             | 142 (53.4)              | 46 (48.9)                          | 96 (55.8)                     | 0.30    |
| Ruxolitinib                                             | 30 (11.3)               | 11 (11.7)                          | 19 (11.0)                     | 0.84    |
| Phlebotomy                                              | 47 (17.7)               | 24 (25.5)                          | 23 (13.4)                     | 0.013   |
| Spleen Size, median<br>cm (IQR)                         | 13.3 (11.3, 16.8)       | 13.1 (11.2, 16.9)                  | 13.3 (11.3, 16.8)             | 0.99    |
| Co-Morbidities                                          |                         |                                    |                               |         |
| Prior ASCVD <sup>c</sup>                                | 116 (43.6)              | 35 (37.2)                          | 81 (47.1)                     | 0.15    |
| Hypertension                                            | 188 (70.7)              | 62 (66.0)                          | 126 (73.3)                    | 0.26    |
| Atrial Fibrillation                                     | 74 (27.8)               | 4 (4.3)                            | 70 (40.7)                     | < 0.001 |
| CKD                                                     | 43 (16.2)               | 8 (8.5)                            | 35 (20.3)                     | 0.014   |
| Prior VTE                                               | 46 (17.3)               | 21 (22.3)                          | 25 (14.5)                     | 0.1     |

|                                        |                  |                  |                  |         |
|----------------------------------------|------------------|------------------|------------------|---------|
| Diabetes                               | 38 (14.3)        | 15 (16.0)        | 23 (13.4)        | 0.59    |
| Current or Former Smoking              | 130 (48.9)       | 43 (45.7)        | 87 (50.6)        | 0.52    |
| OSA                                    | 14 (5.3)         | 3 (3.2)          | 11 (6.4)         | 0.39    |
| Chronic Lung Disease                   | 36 (13.5)        | 10 (10.6)        | 26 (15.1)        | 0.35    |
| H2FPEF Score, median (IQR)             | 4 (3, 6)         | 3 (3, 4)         | 5 (4, 7)         | < 0.001 |
| Medications at time of TTE, N (%)      |                  |                  |                  |         |
| Aspirin                                | 182 (68.4)       | 66 (70.2)        | 116 (67.4)       | 0.68    |
| Anticoagulation                        | 92 (34.6)        | 21 (22.3)        | 71 (41.3)        | 0.002   |
| Statin                                 | 133 (50.0)       | 42 (44.7)        | 91 (52.9)        | 0.25    |
| Anti-Hypertensive                      | 222 (83.5)       | 70 (74.5)        | 152 (88.4)       | 0.004   |
| Laboratory Values at TTE, median (IQR) |                  |                  |                  |         |
| WBC, K/ $\mu$ L                        | 11.8 (7.8, 17.1) | 11.4 (7.0, 16.1) | 11.9 (8.5, 17.6) | 0.26    |
| Hemoglobin, g/dL                       | 11.8 (9.9, 13.6) | 12.0 (9.8, 13.8) | 11.7 (9.9, 13.3) | 0.52    |
| Platelet Count, K/ $\mu$ L             | 409 (242, 607)   | 401 (231, 598)   | 412 (253, 614)   | 0.53    |
| Creatinine, mg/dL                      | 1.1 (0.8, 1.4)   | 1.0 (0.8, 1.3)   | 1.2 (0.8, 1.4)   | 0.28    |
| BNP, pg/mL                             | 516 (197, 1629)  | 158 (56, 558)    | 584 (271, 1815)  | < 0.001 |

ASCVD, atherosclerotic cardiovascular disease; CALR, calreticulin; CKD, chronic kidney disease; DTA, *DNMT3A*, *TET2* or *ASXL1* mutations; HF, heart failure; HMR, high molecular risk; IQR, interquartile range; LDH, lactate dehydrogenase; MPN, myeloproliferative neoplasm; OSA, obstructive sleep apnea; TTE, transthoracic echocardiogram; VAF, variant allele fraction; VTE, venous thromboembolism; WBC, white blood cell count

<sup>a</sup> Presence of either *ASXL1*, *SRSF2*, *EZH2*, *LDH1/2*, or *U2AF1Q157*

<sup>b</sup> Presence of either *DNMT3A*, *TET2* or *ASXL1* mutations

<sup>c</sup> Prior coronary artery disease, peripheral vascular disease, or ischemic stroke

**Supplemental Table 4: Characteristics of Patients with PH Who Developed MPN Progression Versus Those Who Did Not**

|                                       | <b>No MPN Progression<br/>N = 207</b> | <b>MPN progression<br/>N = 59</b> | <b>P value</b> |
|---------------------------------------|---------------------------------------|-----------------------------------|----------------|
| Age at MPN Diagnosis, median (IQR)    | 74 (66, 81)                           | 69 (63, 76)                       | 0.007          |
| Age at PH TTE, median (IQR)           | 81 (73, 86)                           | 76 (70, 83)                       | 0.005          |
| Female Sex                            | 114 (55.1)                            | 24 (40.7)                         | 0.056          |
| Non-White Race, N (%)                 | 24 (11.6)                             | 6 (10.2)                          | 1.00           |
| MPN Characteristics, N (%)            |                                       |                                   |                |
| MPN Type at First TTE                 |                                       |                                   | 0.69           |
| PV                                    | 83 (40.1)                             | 21 (35.6)                         |                |
| ET                                    | 75 (36.2)                             | 25 (42.4)                         |                |
| MF                                    | 49 (23.7)                             | 13 (22.0)                         |                |
| Driver Mutation                       |                                       |                                   | 0.12           |
| JAK2                                  | 164 (79.2)                            | 44 (74.6)                         |                |
| CALR                                  | 14 (6.8)                              | 4 (6.8)                           |                |
| MPL                                   | 6 (2.9)                               | 6 (10.2)                          |                |
| Other/Unknown                         | 23 (11.1)                             | 5 (8.5)                           |                |
| Driver Mutation VAF, median % (IQR)   | 45.2 (25.7, 74.2)                     | 83.4 (54.4, 92.5)                 | < 0.001        |
| Secondary Mutation, N (%)             |                                       |                                   |                |
| Any                                   | 40 (19.3)                             | 38 (64.4)                         | < 0.001        |
| DTA <sup>a</sup>                      | 29 (14.0)                             | 15 (25.4)                         | 0.047          |
| HMR <sup>b</sup>                      | 16 (7.7)                              | 15 (25.4)                         | < 0.001        |
| RUNX1                                 | 3 (1.4)                               | 5 (8.5)                           | 0.015          |
| TP53                                  | 1 (0.5)                               | 8 (13.6)                          | < 0.001        |
| Other                                 | 18 (8.7)                              | 18 (30.5)                         | < 0.001        |
| Treatment for MPN                     |                                       |                                   |                |
| Any                                   | 164 (79.2)                            | 52 (88.1)                         | 0.13           |
| Hydroxyurea                           | 109 (52.7)                            | 33 (55.9)                         | 0.77           |
| Ruxolitinib                           | 24 (11.6)                             | 6 (10.2)                          | 1.00           |
| Phlebotomy                            | 40 (19.3)                             | 7 (11.9)                          | 0.25           |
| Spleen Size, median cm (IQR)          | 13.0 (10.5, 15.4)                     | 15.4 (13.1, 19.7)                 | < 0.001        |
| Co-Morbidities at time of TTE with PH |                                       |                                   |                |
| Prior Heart Failure                   | 34 (16.4)                             | 5 (8.5)                           | 0.15           |
| Prior ASCVD <sup>c</sup>              | 91 (44.0)                             | 25 (42.4)                         | 0.88           |
| HTN                                   | 146 (70.5)                            | 42 (71.2)                         | 1.00           |
| AF                                    | 73 (35.3)                             | 13 (22.0)                         | 0.060          |

|                                          |                   |                   |         |
|------------------------------------------|-------------------|-------------------|---------|
| CKD                                      | 34 (16.4)         | 9 (15.3)          | 1.00    |
| Prior VTE                                | 37 (17.9)         | 14 (23.7)         | 0.35    |
| Diabetes                                 | 27 (13.0)         | 11 (18.6)         | 0.29    |
| Hyperlipidemia                           | 98 (47.3)         | 27 (45.8)         | 0.88    |
| Current or Former Smoking                | 105 (50.7)        | 25 (42.4)         | 0.30    |
| Chronic Lung Disease                     | 31 (15.0)         | 5 (8.5)           | 0.28    |
|                                          |                   |                   |         |
| Laboratory Values at TTE, median (IQR)   |                   |                   |         |
| WBC                                      | 11.7 (7.6, 17.5)  | 12.3 (8.2, 16.8)  | 0.81    |
| Hemoglobin                               | 12.2 (10.1, 13.7) | 10.3 (8.9, 12.5)  | < 0.001 |
| Platelet Count                           | 437 (271, 631)    | 332 (193, 601)    | 0.060   |
|                                          |                   |                   |         |
| Outpatient TTE                           | 125 (60.4)        | 46 (78.0)         | 0.042   |
| HF or Dyspnea Indication for TTE, N (%)  | 101 (48.8)        | 23 (39.0)         | 0.24    |
|                                          |                   |                   |         |
| Chamber Characteristics                  |                   |                   |         |
| LVEF, median % (IQR)                     | 62 (55, 67)       | 61 (56, 65)       | 0.22    |
| LVEF < 50%, N (%)                        | 29 (14.0)         | 1 (1.7)           | 0.044   |
| LVEDD, median cm (IQR)                   | 4.5 (4.1, 5.1)    | 4.7 (4.3, 5.1)    | 0.51    |
| LVH Present, N (%)                       | 53 (25.6)         | 16 (27.1)         | 0.69    |
| LA Diameter, median cm (IQR)             | 4.2 (3.8, 4.6)    | 4.3 (4.0, 4.8)    | 0.28    |
| Moderate or Severe LA Enlargement, N (%) | 94 (45.6)         | 17 (28.8)         | 0.034   |
| Moderate or Severe RA Enlargement, N (%) | 56 (27.2)         | 8 (13.6)          | 0.033   |
|                                          |                   |                   |         |
| Right Ventricular Characteristics        |                   |                   |         |
| Reduced RV Systolic Function, N (%)      | 31 (15.0)         | 3 (5.1)           | 0.064   |
| RV Dilation, N (%)                       | 56 (27.1)         | 9 (15.3)          | 0.088   |
| TAPSE, median cm (IQR)                   | 2.1 (1.7, 2.5)    | 2.3 (2.0, 3.0)    | 0.016   |
| RVOT AT, median ms (IQR)                 | 87 (75, 98)       | 77 (68, 95)       | 0.65    |
| Moderate or Severe TR, N (%)             | 83 (40.1)         | 16 (27.1)         | 0.066   |
| TR Peak Velocity, median m/s (IQR)       | 3.2 (3.0, 3.5)    | 3.2 (3.0, 3.4)    | 0.13    |
| PASP, median mmHg (IQR)                  | 50 (44, 59)       | 47 (42, 55)       | 0.13    |
| TAPSE/PASP ratio, median mm/mmHg (IQR)   | 0.42 (0.32, 0.52) | 0.50 (0.35, 0.66) | 0.058   |

|                                                          |                   |                   |       |
|----------------------------------------------------------|-------------------|-------------------|-------|
|                                                          |                   |                   |       |
| Other Valvular Characteristic                            |                   |                   |       |
| Moderate or Severe MR, N (%)                             | 63 (30.4)         | 9 (15.3)          | 0.022 |
| Moderate or Severe AR, N (%)                             | 13 (6.3)          | 1 (1.7)           | 0.31  |
| Peak AV Velocity, median m/s (IQR)                       | 1.65 (1.35, 2.13) | 1.74 (1.48, 2.07) | 0.39  |
| Peak LVOT velocity, median m/s (IQR)                     | 1.00 (0.85, 1.18) | 1.04 (0.95, 1.20) | 0.12  |
| LVOT VTI, median cm (IQR)                                | 22.0 (17.5, 27.0) | 24.6 (22.0, 29.4) | 0.096 |
| Cardiac Output Estimated by LVOT VTI, median L/min (IQR) | 4.90 (3.91, 6.06) | 5.39 (4.93, 7.37) | 0.017 |
| Cardiac Output Estimated by LVOT > 7 mL/min, n (%)       | 11 (5.3)          | 8 (13.6)          | 0.021 |
|                                                          |                   |                   |       |
| Diastology                                               |                   |                   |       |
| Mitral Early (E) Inflow Velocity, median cm/s (IQR)      | 100 (80, 120)     | 96 (77, 110)      | 0.37  |
| Mitral A (A) Wave Velocity, median cm/s (IQR)            | 80 (45, 104)      | 70 (50, 97)       | 0.91  |
| Mean E/E', median (IQR)                                  | 12.9 (10.6, 16.4) | 12.8 (9.2, 16.8)  | 0.78  |
| Mean E/E' > 14, N (%)                                    | 77 (37.2)         | 16 (27.1)         | 0.17  |
| H2PEF Score, median (IQR)                                | 4 (3, 6)          | 4 (3, 5)          | 0.10  |

Abbreviations defined in Table 1

<sup>a</sup> Presence of either *DNMT3A*, *TET2* or *ASXL1* mutations

<sup>b</sup> Presence of either *ASXL1*, *SRSF2*, *EZH2*, *LDH1/2*, or *U2AF1Q157*

<sup>c</sup> Prior coronary artery disease, peripheral vascular disease, or ischemic stroke