





# Mitigation of atrial fibrillation-related complications with antithrombotic and cyto-reductive therapy in patients with Myeloproliferative Neoplasms: Implications from the GSG-MPN bioregistry

Hyunyeon Rosa Cho<sup>1</sup>  | Susanne Isfort<sup>1,2</sup> | Kim Kricheldorf<sup>1</sup> | Frank Stegelmann<sup>3</sup> | Martine Klausmann<sup>4</sup> | Florian H. Heide<sup>2,5</sup> | Martin Griesshammer<sup>6</sup> | Holger Schulz<sup>7</sup> | Andreas Hochhaus<sup>8</sup> | Joachim Göthert<sup>9</sup> | Rudolf Schlag<sup>10</sup> | Wiebke Hollburg<sup>11</sup> | Lino Teichmann<sup>12</sup>  | Katja Sockel<sup>13</sup> | Stefan Wilop<sup>14</sup> | Deniz Gezer<sup>1</sup> | Martin Kirschner<sup>1</sup> | Konstanze Döhner<sup>3</sup>  | Tim H. Brümmendorf<sup>1</sup> | Steffen Koschmieder<sup>1</sup>  | for the German Study Group for Myeloproliferative Neoplasms (GSG-MPN)

Correspondence: Steffen Koschmieder ([skoschmieder@ukaachen.de](mailto:skoschmieder@ukaachen.de))

Vascular complications such as thromboembolic events (TEs) and severe bleeding events (BEs) are the major causes of morbidity and mortality in patients (pts) with Myeloproliferative Neoplasms (MPNs).<sup>1</sup> TEs are promoted by the hypercoagulable state in MPN, caused by elevated blood counts, activation of platelets, leukocytes, and endothelial cells, the presence of the JAK2V617F mutation, and increased circulating procoagulant microparticles and the occurrence of acquired activated protein C resistance. Disease-associated bleeding may occur via acquired von Willebrand syndrome, platelet dysfunction, antiplatelet agents (APAs), and thrombocytopenia.<sup>2</sup> In addition, hemostasis can be disturbed by anticoagulation therapy, acquired hemophilia,<sup>3</sup> or complications such as liver dysfunction or disseminated intravascular coagulopathies due to infection.<sup>2</sup>

Atrial fibrillation (AF) is the most common sustained arrhythmia, with increasing prevalence with age.<sup>4,5</sup> The incidence of AF has rarely been

studied in MPN, but was suggested to be higher compared to the general population.<sup>6</sup> The same study found that MPN pts with AF had a higher frequency of cardiovascular risk factors (CVRFs) and thrombotic complications and a shorter thrombosis-free survival than MPN pts without AF.<sup>6</sup> However, in a separate study comparing 63 pts with polycythemia vera (PV) and AF to 124 control pts with AF only, no increased incidence of thrombosis was found.<sup>7</sup> Both studies found no increase in major BE. However, none of the two studies reported the use and effects of cyto-reductive therapy (CRT) in their cohorts, a critical means to decrease the risk of both initial and recurrent thrombosis in high-risk MPN pts.

Therefore, we conducted this retrospective analysis of 2,780 MPN pts enrolled in the GSG-MPN bioregistry, in order to identify the characteristics of AF in MPN pts and to assess the benefit-risk profile of antithrombotic therapies (ATTs) alone or in combination with MPN-specific CRT. The German Study Group MPN bioregistry

<sup>1</sup>Department of Hematology, Oncology, Hemostaseology, and Stem Cell Transplantation, Faculty of Medicine, RWTH Aachen University, and Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf (CIO ABCD), Aachen, Germany

<sup>2</sup>Hematology, Hemostasis, Oncology and Stem Cell Transplantation, Hannover Medical School (MHH), Hannover, Germany

<sup>3</sup>Department of Internal Medicine III, University Hospital Ulm, Ulm, Germany

<sup>4</sup>Gemeinschaftspraxis, Aschaffenburg, Aschaffenburg, Germany

<sup>5</sup>Internal Medicine C, University Medicine Greifswald, Greifswald, Germany

<sup>6</sup>University Clinic for Hematology, Oncology, Haemostaseology and Palliative Care, Johannes Wesling Medical Center Minden, University of Bochum, Bochum, Germany

<sup>7</sup>Practice for Clinical Hematology and Oncology, Frechen, Germany

<sup>8</sup>Department of Hematology and Oncology, Jena University Hospital, Jena, Germany

<sup>9</sup>Department of Hematology, West German Cancer Center (WTZ), University Hospital Essen, Essen, Germany

<sup>10</sup>Hämatologisch-Onkologische Schwerpunktpraxis Würzburg, Würzburg, Germany

<sup>11</sup>HOPA-Hämatologisch-Onkologische Praxis Altona, Hamburg, Germany

<sup>12</sup>Department of Medicine III, University Hospital Bonn, and Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf (CIO ABCD), Bonn, Germany

<sup>13</sup>Medical Clinic and Polyclinic I, University Hospital Dresden, TU Dresden, Dresden, Germany

<sup>14</sup>MVZ West GmbH Würselen, Hämatologie-Onkologie, Würselen, Germany

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2025 The Author(s). *HemaSphere* published by John Wiley & Sons Ltd on behalf of European Hematology Association.

**TABLE 1** Comparisons of pts with versus without atrial fibrillation with age-matched data. (continued on next page)

Variables	With AF <sup>a</sup> (n = 134)			Without AF <sup>a</sup> (n = 134)			P
	N	% column	Median (IQR)	N	% column	Median (IQR)	
Age (n = 268)							
<65	18	13.4	76.0 (70–81)	18	13.4	75.9 (70–81)	0.987
65–74	36	26.9		37	27.6		>0.999
>74	80	59.7		79	59.0		
Sex (n = 268)							
Men	74	55.2		59	44.0		0.087
Women	60	44.8		75	55.6		
MPN subtype <sup>c</sup> (n = 265)							
PV	42	31.3		42	32.1		0.136
ET	41	30.6		44	33.6		
PMF	27	20.1		33	25.2		
PostPV-MF	6	4.5		2	1.5		
PostET-MF	2	1.5		4	3.1		
MPN- U	11	8.2		6	4.6		
Others	5	3.7		0	0.0		
Leukocyte count (n = 265)							
<3.5/nL	2	1.5	9.4 (8–14)	4	3.1	9.67 (7–13)	0.373
3.5–10/nL	74	55.2		66	50.4		0.547
>10/nL	58	43.3		61	46.6		
Hematocrit (n = 261)							
≤45/nL	80	60.6	42.5 (36–48)	88	68.2	42.8 (34–47)	0.434
>5/nL	52	39.4		41	31.8		0.245
Platelet count (n = 264)							
<150/nL	11	8.2	451.0 (296–697)	16	12.3	501.5 (331–677)	0.791
150–450/nL	55	41.0		42	32.3		0.261
>450/nL	68	50.7		72	55.4		
LDH (n = 235)							
≤250 U/L	43	35.0	311.0 (232–407)	29	25.9	328.9 (245–455)	0.198
>250 U/L	80	65.0		83	74.1		0.157
Myocardial infarction (n = 242)							
Yes	10	7.9		11	9.6		0.655
No <sup>e</sup>	117	92.1		104	90.4		
Congestive heart failure (n = 244)							
Yes	28	21.9		9	7.8		0.002
No <sup>e</sup>	100	78.1		107	92.2		
Diabetes mellitus (n = 268)							
Yes	28	20.9		12	9.0		0.009
No <sup>e</sup>	106	79.1		122	91.0		
Hypertension (n = 238)							
Yes	90	72.6		69	60.5		0.054
No <sup>d</sup>	34	27.4		45	39.5		
Splenomegaly (n = 237)							
Yes	63	52.5		69	59.0		0.360

TABLE 1 (Continued)

Variables	With AF <sup>a</sup> (n = 134)			Without AF <sup>a</sup> (n = 134)			P
	N	% column	Median (IQR)	N	% column	Median (IQR)	
CHA2DS2-VASc (n = 268)	No <sup>d</sup>	57	47.5	48	41.0		
	M ≤ 1, F ≤ 2	17	12.7	32	23.9	3.0 (2–4)	0.025*
	M > 1, F > 2	117	87.3	102	76.1		0.026 <sup>b,*</sup>
HAS-BLED (n = 268)	≤ 2	74	55.2	105	78.4	2.0 (1–2)	<0.001*
	> 2	60	44.8	29	21.6		<0.001 <sup>b,*</sup>
	Yes	21	15.7	17	12.7		0.600 <sup>b</sup>
TE at or after diagnosis (n = 268)	No <sup>d</sup>	113	84.3	117	87.3		
TE regardless of time (n = 251)	Yes	63	48.5	70	57.9		0.164 <sup>b</sup>
Types of TE (n = 118)	No	67	51.5	51	42.1		
	Arterial	46	68.7	34	66.7		0.960 <sup>b</sup>
	Venous	13	19.4	10	19.6		
Bleeding at or after diagnosis (n = 268)	Both	8	11.9	7	13.7		
	Yes	11	8.2	6	4.5		0.316 <sup>b</sup>
	No	123	91.8	128	95.5		
Bleeding event regardless of time (n = 250)	Yes	13	10.2	8	6.5		0.364 <sup>b</sup>
	No <sup>d</sup>	114	89.8	115	93.5		
	Antiplatelet therapy	51	38.1	78	58.2		0.001 <sup>b,*</sup>
Antithrombotic therapy (n = 268)	Yes	83	61.9	56	41.8		
	No	47	35.1	10	7.5		<0.001 <sup>b,*</sup>
	VKA	87	64.9	124	92.5		
DOAK	Yes	50	37.3	12	9.0		<0.001 <sup>b,*</sup>
	No	84	62.7	122	91.0		
	Heparin	6	4.5	3	2.2		0.500 <sup>b</sup>
MPN therapy (n = 268)	No	128	95.5	131	97.8		
	Yes	115	85.8	92	68.7		0.001 <sup>b,*</sup>
	Any type of antithrombotic <sup>e</sup>	19	14.2	42	31.3		
Anagrelide	Yes	23	17.2	21	15.7		0.869 <sup>b</sup>
	No	111	82.8	113	84.3		
	HU	86	64.2	74	55.2		0.171 <sup>b</sup>
Ruxolitinib	No	48	35.8	60	44.8		
	Yes	35	26.1	49	36.6		0.087 <sup>b,*</sup>

TABLE 1 (Continued)

Variables	With AF <sup>a</sup> (n = 134)		Without AF <sup>a</sup> (n = 134)		P
	N	% column	N	% column	
	No	73.9	85	63.4	
	Yes	9.7	12	9.0	>0.999
Interferon	No	90.3	122	91.0	b
	Yes	2.2	4	3.0	>0.999
Imide	No	97.8	130	97.0	b
	Yes	76.1	105	78.4	0.771
Any type of MPN Therapy <sup>c</sup>	No	23.9	29	21.6	b
	Yes	74.6	103	83.7	b, #
JAK2 (n = 249)	No	25.4	20	16.3	
	Yes	18.8	10	20.0	>0.999
CalR (n = 98)	No	81.3	40	80.0	b
	Yes	12.2	5	11.4	>0.999
MPL (n = 93)	No	87.8	39	88.6	b

Abbreviations: AF, atrial fibrillation; LDH, lactate dehydrogenase; TE, thromboembolic events.

<sup>a</sup>Patients with a history of successful cardioversion before the date of MPN diagnosis were not considered to have AF.

<sup>b</sup>Fisher's Exact test for categorized variables.

<sup>c</sup>Polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF), MPN unclassifiable (MPN-U), postPV-myelofibrosis (postPV-MF), post-ET myelofibrosis (postET-MF).

<sup>d</sup>No or not documented.

<sup>e</sup>Any type of therapy; these pts could have been treated with several therapies, either simultaneously or separately.

\*  $P < 0.05$ .

# Borderline significance  $P < 0.09$ .

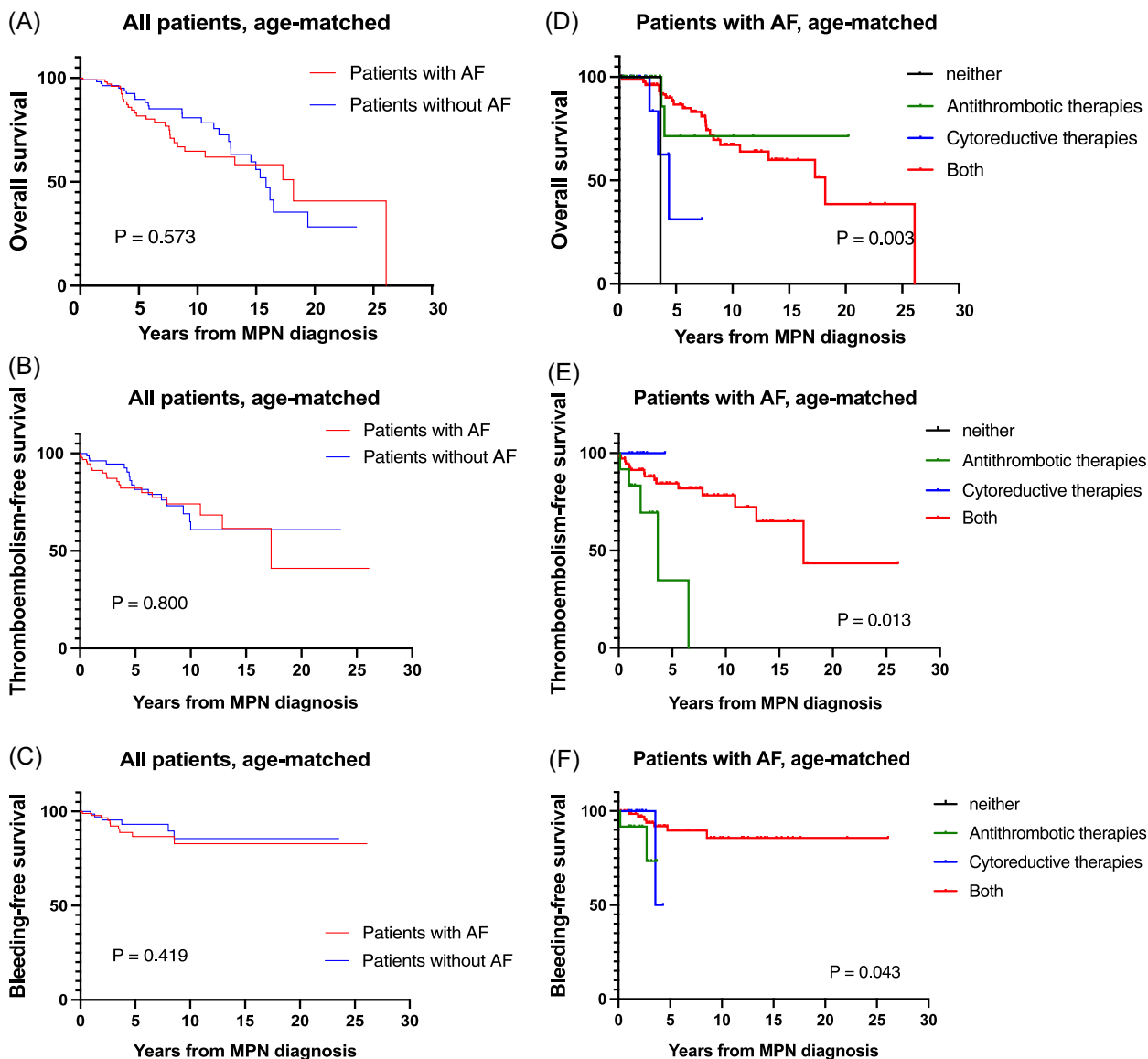
(GSG-MPN bioregistry) is an ambispective observational study of MPN pts, with over 70 centers participating. Recruitment started in August 2012, with a data cut-off date of January 2020.

As in the general population,<sup>6</sup> the median age of AF pts in our MPN cohort was higher than those without AF (Supporting Information S1: Table S3). The prevalence of AF in pts older than 80 years of age in our MPN cohort was higher than that in the general population (18.2% [Supporting Information S1: Figure S1] vs. 8.8% in the FRAMINGHAM study<sup>8</sup>).

Since the incidence and complication rate of MPN pts increase with age and since CRT is recommended in an age-adapted manner, we performed a case-control analysis following a 1:1 pattern, with age as

a matching factor (Table 1,  $n = 134$  with AF vs.  $n = 134$  without AF). Here, unlike in non-age-matched analyses (Supporting Information S1: Table S3), which showed higher incidence of TEs and BEs in AF pts, no significant difference in the prevalence of TEs and BEs was observed after age-matching. Also, the higher percentage of arterial TE in AF pts was no longer observed after age-matching, suggesting that all pts (MPN pts as well as non-MPN pts) develop a preponderance of arterial over venous TE with increasing age, as has been described before.<sup>1,9,10</sup>

While cardiovascular comorbidities are reported to be risk factors for the development of AF,<sup>8,11</sup> in our age-matched cohort, it was revealed that AF pts had more cardiac comorbidities than non-AF pts. In addition, use of any type of ATT, including vitamin K antagonists (VKAs) and direct



**FIGURE 1** Analyses in the age-matched cohort. (A) Age-matched OS of pts with MPN ( $n = 134$  each). (B) Age-matched TE-free survival ( $n = 134$  each). (C) Age-matched bleeding event-free survival ( $n = 134$  each). (D) OS stratified by antithrombotic and cytoreductive therapy in MPN pts with AF with antithrombotic or cytoreductive therapy, neither or both. Cox regression analyses: neither versus both (HR = 12.313; 95% CI 1.494–101.453,  $P = 0.020$ ), antithrombotic therapies versus both (HR = 0.778, 95% CI 0.182–3.335,  $P = 0.736$ ), cytoreductive therapies versus both (HR = 4.665, 95% CI 1.289–16.880,  $P = 0.019$ ). (E) TE-free survival stratified by antithrombotic and cytoreductive therapy in MPN pts with AF with antithrombotic or cytoreductive therapy, neither or both. Cox regression analyses: neither versus both (HR = 0.000, 95% CI 0.000–NE,  $P = 0.993$ ), antithrombotic therapies versus both (HR = 4.351, 95% CI 1.465–12.926,  $P = 0.008$ ), cytoreductive therapies versus both (HR = 0.000, 95% CI 0.000–NE,  $P = 0.982$ ). (F) Bleeding-free survival stratified by antithrombotic and cytoreductive therapy in MPN pts with AF with antithrombotic or cytoreductive therapy, neither or both. Cox regression analyses: neither versus both (HR = 0.000, 95% CI 0.000–NE,  $P = 0.988$ ), antithrombotic therapies vs both (HR = 6.567, 95% CI 1.49–28.97,  $P = 0.013$ ), cytoreductive therapies vs both (HR = 2.857, 95% CI 0.32–25.35,  $P = 0.346$ ). NE, non-estimable.

oral anticoagulant (DOAC), was more prominent in AF pts. Conversely, a higher percentage of non-AF pts were treated with APA.

When analyzing the entire cohort of MPN pts without age-matching, our Kaplan–Meier survival analyses showed significantly inferior OS in pts with coexisting AF (Supplemental Figure 4A). 5-year OS was 92% in pts without AF and 82% in pts with AF. When focusing on the time after diagnosis of MPN (as opposed to the lifetime of a patient), the incidence of events in AF pts was higher only for BEs but not for TEs when compared to non-AF pts (Supporting Information S1: Figure S4B,C). 10-year BEFS was 97% in pts without AF and 89% in pts with AF. In current guidelines on the management of pts with AF in the general population, anticoagulants are recommended for pts with AF and an elevated CHA2DS2-VASc score of  $\geq 2$  in men or  $\geq 3$  in women.<sup>12</sup> Thus, it is likely that the increased incidence of cardiovascular comorbidities in our MPN pts with AF led to higher CHA2DS2-VASc scores and to a higher rate of prophylactic ATTs, independently from the MPN management. The increased prevalence of bleeding after but rarely before the MPN diagnosis in this group of pts (Supporting Information S1: Figure 4C) may at least in part be explained by this increase in ATTs, as described earlier.<sup>9</sup> Importantly, the fact that no difference in thromboembolic event-free survival (TEFS) was observed between our MPN pts with AF vs. those without AF (Supporting Information S1: Figure 4B) suggests that management of AF pts in our cohort successfully prevented excess TEs in these pts. The definition of TEFS and bleeding event-free survival (BEFS) is provided in the methods section of the supplemental file.

We then performed survival analysis after age-matching of the cohort to reduce the influence of differences in the sample size and the age difference between the pts with vs without AF. The inferior survival outcomes were no longer observed in age-matched analyses. The presence of AF did not have a significant overall influence on the OS, TEFS, or BEFS in MPN pts (Figure 1A–C). We speculate that this was due to the success of the combined use of ATTs and CRT in an aging MPN population at high risk for TEs due to coexisting AF. The difference in BEFS was no longer significant in age-matched analysis, which may indicate that management of anticoagulation has become better tolerated during the past few years, possibly through the increased use of DOACs instead of VKAs, also shown in more recent MPN cohort analyses.<sup>13,14</sup>

The importance of ATTs and CRTs was evident from our study, particularly in pts with coexisting AF. OS was worse when AF pts received neither of the therapies, or when they were treated only with CRTs (Figure 1D). Compared to patients who received both therapies, patients who received neither therapy or only CRTs had significantly inferior OS (5-year OS for neither: not obtainable, for only CRTs: 31.3%, for Both: 86.7%). These significant differences were observed only in the AF group ( $P = 0.003$ ). The result of the analysis of the non-AF group is shown in Supporting Information S1: Figure S5A.

An additional OS analysis was conducted using a 1:1 matched data set with a larger number of matching factors, including age, congestive heart failure, diabetes mellitus, arterial hypertension, abnormal renal function, and a history of thromboembolic and vascular events. This analysis yielded a similar result as the matching analysis using age alone (Supporting Information S1: Figure S9).

Similarly, the worst TEFS and BEFS was observed in pts with AF who were treated only with ATT (Figure 1E,F) compared to pts treated with combined therapy with ATT and CRT.

Through age-matched OS, TEFS, and BEFS analyses, we observed that MPN pts with AF treated with combined ATT and CRTs have better prognoses than those with ATT or CRT alone. We would like to emphasize that all age-matched survival analyses stratified by ATT and CRT were significant only in AF patients. In non-AF patients, OS, TEFS, and BEFS stratified by ATT and CRT showed no significance, as shown in Supporting Information S1: Figure S5. OS,

TEFS, and BEFS analyses, separate for ATT and CRT, can be found in Supporting Information S1: Figures S6–S8.

Our data demonstrate the beneficial effects of MPN-specific CRT in addition to ATT for the prevention of TEs and BEs in MPN pts with coexisting AF. As outlined in current management guidelines for MPN, the risks of thromboembolism and bleeding have to be carefully balanced.<sup>2,15</sup> One of the limitations of our study is that the prevalence of newly developed AF along with MPN over time could not be assessed in our study. AF was recorded at the time of registration, and it is hence unclear if the AF occurred before or after the MPN diagnosis. Moreover, while we observed a higher prevalence of AF in the MPN population compared to the non-MPN population, due to the observational nature of our study, we cannot prove a causal relationship, but can only suggest this interesting association. Finally, whether the ATTs were discontinued after the initiation of CRT was not consistently documented in this study. In future studies, such data could enable more nuanced analyses and offer deeper insights into the interplay between AF and MPN.

However, one of the strengths of our study is the large number of pts and the inclusion of all major MPN subtypes. It adds significant data on the management of AF in MPN pts, which are urgently needed in the absence of controlled clinical trials on this topic.

In conclusion, our study provides evidence for beneficial effects of CRT as additional treatment for MPN pts with coexisting AF, including not only elderly pts older than 60 years of age but also younger pts. Prospective studies are needed to validate these findings and determine whether pts with different MPN subtypes need to be managed differently.

## ACKNOWLEDGMENTS

The authors would like to thank all colleagues and members of the research groups and participating centers for their work and continued support. The data presented here are part of the MD thesis of Hyunyeon Rosa Cho. Open Access funding enabled and organized by Projekt DEAL.

## AUTHOR CONTRIBUTIONS

The authors confirm their individual contributions to the manuscript as follows: Hyunyeon Rosa Cho (Submitting author): Conceptualized and designed the study, collected the data, performed the statistical analyses, performed most of the data interpretation, drafted the original manuscript, and contributed to the critical review and revision of the manuscript. Steffen Koschmieder (Corresponding Author): Contributed to the collection of bioregistry data, contributed to interpretation of data evaluation, secured funding, provided supervision throughout the project, and participated in the review and revision of the manuscript. Susanne Isfort, Kim Kricheldorf, Frank Stegelmann, Martine Klausmann, Florian Heidele, Martin Griesshammer, Holger Schulz, Andreas Hochhaus, Joachim Göthert, Rudolf Schlag, Wiebke Hollburg, Lino Teichmann, Katja Sockel, Stefan Wilop, Deniz Gezer, Martin Kirschner, Konstanze Döhner, and Tim H. Brümmendorf contributed to the collection of bioregistry data, contributed to interpretation of data evaluation, and participated in the review of the manuscript. Each author reviewed the manuscript, believes it represents valid work, and approves it for submission.

## CONFLICT OF INTEREST STATEMENT

Susanne Isfort reports advisory board honoraria from GSK, Pfizer, Incyte, and Novartis, honoraria from Novartis, BMS, Pfizer, Incyte, AOP Orphan; and other financial support (e.g., travel support) from Alexion, Novartis, Pfizer, Mundipharma, Roche, Hexal, and AOP Orphan. Frank Stegelmann reports consulting fees from BMS/Celgene, Incyte,

MorphoSys, Novartis and received honoraria from AbbVie, AOP Orphan, Incyte, Novartis, and Pfizer. Florian H. Heidel has received research funding from Novartis, Celgene/BMS, and CTI BioPharma and has served as a consultant for Novartis, BMS, AOP, Janssen, Abbvie, GSK, and Kartos. Martin Grieshammer received consulting fees from AOP Orphan, Novartis, BMS, AbbVie, Pfizer, Roche, Janssen, Gilead, AstraZeneca, Sierra, Lilly, GSK and reports honoraria from AOP Orphan, Novartis, BMS, AbbVie, Pfizer, Roche, Janssen, Gilead, AstraZeneca, Sierra, Lilly, and GSK. Andreas Hochhaus reports Research support by Novartis, BMS, Pfizer, Incyte, Enliven, TERNIS. Lino Teichmann reports honoraria from AOP Pharma, BMS, Jazz. Pharmaceuticals, Novartis, and Sobi and consultancy for Astellas, Blueprint. Medicines, BMS, GSK, Pfizer, and Sobi. Katja Sockel received lecture fees from BMS, Novartis, GSK, AbbVie, Jazz, advisory fees from BMS, Novartis, GSK, Blueprint, and SOBI R, and reports research support from Active Biotech. Stefan Wilop reports advisory board honoraria and presentation fees from BMS. Deniz Gezer reports advisory board activity for AMGEN, Takeda and Celgene and travel money from AMGEN, Celgene, and Bristol-Myers Squibb. Konstanze Döhner received research support from Novartis, Celgene/BMS, Astellas and Agios, received honoraria from Novartis, Janssen, Celgene/BMS, Daiichi Sankyo, JAZZ, Rosche and GSK. Reports advisory board honoraria from Novartis, Janssen, Celgene/BMS, Daiichi Sankyo, JAZZ, Rosche, AbbVie, and GSK. Tim H. Brümmendorf reports COI from Novartis, Pfiyer, Synlab, Incyte, Merck, and Rosche. Steffen Koschmieder received research funding from Geron, Janssen, AOP Pharma, and Novartis; received consulting fees from Pfizer, Incyte, Ariad, Novartis, AOP Pharma, Bristol Myers Squibb, Celgene, Geron, Janssen, CTI BioPharma, Roche, Bayer, GSK, Sierra Oncology, and PharmaEssentia; received payment or honoraria from Novartis, BMS/Celgene, and Pfizer; received travel/accommodation support from Alexion, Novartis, Bristol Myers Squibb, Incyte, AOP Pharma, CTI BioPharma, Pfizer, Celgene, Janssen, Geron, Roche, AbbVie, GSK, Sierra Oncology, and Kartos; had a patent issued for a BET inhibitor at RWTH Aachen University; participated on advisory boards for Pfizer, Incyte, Ariad, Novartis, AOP Pharma, BMS, Celgene, Geron, Janssen, CTI BioPharma, Roche, Bayer, GSK, Sierra Oncology, and PharmaEssentia, and is an Editor of *HemaSphere*. The remaining authors declare no conflict of interest.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supplementary material of this article.

#### FUNDING

This work was supported by the German Research Foundation (DFG) within the Clinical Research Unit CRU344 to S.K. (KO 2155/9-2, project number 417911533) and T.B. (BR 1782/5-2 and BR 1782/6-1, project number 428857858) and Center for Integrated Oncology, CIO-Aachen.

#### ORCID

Hyunye Rosa Cho  <http://orcid.org/0009-0004-9750-5554>

Lino Teichmann  <http://orcid.org/0000-0001-9489-7282>

Konstanze Döhner  <http://orcid.org/0000-0002-2261-9862>

Steffen Koschmieder  <http://orcid.org/0000-0002-1011-8171>

#### SUPPORTING INFORMATION

Additional supporting information can be found in the online version of this article.

#### REFERENCES

- Rungjirajittranon T, Owattanapanich W, Ungprasert P, Siritanaratkul N, Ruchutrakool T. A systematic review and meta-analysis of the prevalence of thrombosis and bleeding at diagnosis of Philadelphia-negative myeloproliferative neoplasms. *BMC Cancer*. 2019;19:184.
- Appelmann I, Kreher S, Parmentier S, et al. Diagnosis, prevention, and management of bleeding episodes in Philadelphia-negative myeloproliferative neoplasms: recommendations by the Hemostasis Working Party of the German Society of Hematology and Medical Oncology (DGHO) and the Society of Thrombosis and Hemostasis Research (GTH). *Ann Hematol*. 2016;95:707-718.
- Vener C, Artoni A, Boschetti C, et al. An acquired factor VIII inhibitor in a myeloproliferative neoplasm presenting with severe retroperitoneal hemorrhage. *Leuk Lymphoma*. 2012;53:2296-2298.
- Camm AJ, Kirchhof P, Lip GYH, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31:2369-2429.
- Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *Eur Heart J*. 2012;33:2719-2747.
- Mahé K, Delluc A, Chauveau A, et al. Incidence and impact of atrial arrhythmias on thrombotic events in MPNs. *Ann Hematol*. 2018;97:101-107.
- De Freitas AS, Alvarez-Larrán A. Risk of thrombosis and hemorrhage in patients with polycythemia vera and atrial fibrillation treated with prophylactic oral anticoagulants. *Ann Hematol*. 2016;95:1903-1904.
- Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham study. *N Engl J Med*. 1982;306:1018-1022.
- Kaifia A, Kirschner M, Wolf D, et al. Bleeding, thrombosis, and anticoagulation in myeloproliferative neoplasms (MPN): analysis from the German SAL-MPN-registry. *J Hematol Oncol*. 2016;9:18. doi:10.1186/s13045-016-0242-9
- Hultcrantz M, Björkholm M, Dickman PW, et al. Risk for arterial and venous thrombosis in patients with myeloproliferative neoplasms: a population-based cohort study. *Ann Intern Med*. 2018;168:317-325.
- Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation: analysis of pooled data from five randomized controlled trials. *Arch Intern Med*. 1994;154:1449-1457.
- January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. *Circulation*. 2019;140(6):e285.
- Gecht J, Tsoukakis I, Kricheldorf K, et al. Kidney dysfunction is associated with thrombosis and disease severity in myeloproliferative neoplasms: implications from the German study group for MPN bioregistry. *Cancers*. 2021;13:4086.
- Barbui T, De Stefano V, Carobbio A, et al. Direct oral anticoagulants for myeloproliferative neoplasms: results from an international study on 442 patients. *Leukemia*. 2021;35:2989-2993.
- Kreher S, Ochseneither S, Trappe RU, et al. Prophylaxis and management of venous thromboembolism in patients with myeloproliferative neoplasms: consensus statement of the Haemostasis Working Party of the German Society of Hematology and Oncology (DGHO), the Austrian Society of Hematology and Oncology (ÖGHO) and Society of Thrombosis and Haemostasis Research (GTH e.V.). *Ann Hematol*. 2014;93:1953-1963.