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Chronic Myeloproliferative Disorders

Incidence of pulmonary hypertension in patients with chronic myeloproliferative disorders

Pulmonary hypertension (PH) has been reported to be a common finding in chronic myeloproliferative disorders (CMPD); nevertheless, there is a paucity of data regarding its exact incidence in these patients. We conducted a prospective study in order to assess the incidence of PH in patients with CMPD.

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Twenty-four patients with CMPD were included in the study (Table 1). The diagnosis of CMPD was established according to standard criteria.[1-3] Patients were excluded if any condition known to cause secondary PH was present. Eight patients were male and 16 were female. Their mean (±SD) age was 60.5±15.5 years, the mean age at diagnosis of CMPD was 56.1±16.1 years and the mean duration of CMPD was 4.7±4.5 years. Two patients had polycythemia vera (PV), 14 had essential thrombocythemia (ET), six had agnogenic myeloid metaplasia (AMM), and two had chronic myeloid leukemia (CML). Five patients reported the presence of dyspnea on exertion, which was mild except for in patients #11 and 14. No other symptoms compatible with the diagnosis of PH were reported. None of the patients had signs of right heart failure. All patients underwent transthoracic echocardiography (TTE). Pulmonary hypertension was diagnosed if the estimated right ventricular systolic pressure (RVSP) was higher than 35 mmHg.

Ten patients (41.7%), four males and six females, had PH, with a mean RVSP of 42.2 mmHg (range, 37 to 70 mmHg) (Table 2). Their mean age was 63.8±15.1 years. Six patients

Table 1. Characteristics of patients.

N.	*Sex*	*Age (yr)*	*CMPD*	*Age at diagnosis*	*Thrombosis† of CMPD (yr)*	*Treatment (past/current)‡*	*Hb (g/dL)*	*WBC (x10⁹/L)*	*PLT (x10⁹/L)*	*Splenomegaly*	*Symptoms*
1	F	43	ET	40	(–)	(–)/(–)	14.3	7.5	598	(–)	(+)
2	M	73	AMM	66	(–)	DAN/ EPO, G-CSF	9.9	1.1	66	(+)	(-)
3	M	71	AMM	68	(–)	HU/ DAN, PRE, EPO	10.9	8.4	65	(+)	(+)
4	F	50	ET	40	(–)	TIC, HU/ANA	13.2	8.6	702	(–)	(-)
5	F	50	ET	47	(–)	HU/IFN	13.0	5.0	457	(+)	(-)
6	F	52	ET	44	TIA	HU,TIC/IFN,ASA	10.4	3.0	523	(–)	(-)
7	F	70	ET	58	(–)	IFN/HU	12.8	4.1	607	(–)	(-)
8	F	53	ET	40	(–)	(–)/HU	15.2	6.3	580	(–)	(-)
9	F	72	ET	72	(–)	(–)/(–)	14.1	12.0	862	(–)	(-)
10	M	68	ET	67	(–)	(–)/ASA, ANA	13.2	5.1	500	(–)	(-)
11	M	78	AMM	77	(–)	DAN/EPO,G-CSF	6.2	2.4	600	(–)	(+)
12	F	34	ET	32	(–)	(–)/DIP	13.5	17.4	604	(–)	(-)
13	F	35	ET	34	(–)	(–)/ANA	13.6	14.7	388	(-)	(-)
14	M	65	AMM	63	(–)	DAN/EPO,G-CSF	8.5	2.5	150	(+)	(+)
15	F	77	CML	77	(–)	(–)/IMA	9.9	25.5	1422	(–)*	(+)
16	M	67	PV	66	(–)	(–)/HU, ASA, CLO	14	4.9	137	(–)	(-)
17	F	52	AMM	50	(–)	DAN/EPO,THAL,PRE	9.9	10.3	46	(+)	(-)
18	F	72	CML	72	(–)	IMA	8.3	75.0	590	(+)	(-)
19	F	58	ET	56	(–)	(–)/HU,ASA	12.4	4.8	384	(–)	(-)
20	F	77	ET	65	(–)	IFN/HU	12.6	4.4	367	(–)	(-)
21	M	75	AMM	75	(–)	DAN/EPO, G-CSF,PRE	9.2	2.0	17	(–)	(-)
22	F	51	ET	38	(–)	IFN / HU, ASA	14.5	5.6	354	(–)	(-)
23	F	81	ET	74	(–)	(–)/HU,ASA	12.5	9.8	688	(–)	(-)
24	M	27	PV	26	TMV, IS	(–)/ASA, WAR	15.3	9.8	224	(–)	(-)

*†TIA: transient ischemic attack; TMV: thrombosis of the mesenteric veins; IS: ischemic stroke; ‡DAN: danazol; EPO: erythropoietin; G-CSF: granulocyte colony-stimulating factor; HU: hydroxyurea; PRE: prednisolone; TIC: ticlopidine; ANA: anagrelide; IFN: interferon; ASA: acetylsalicylic acid; DIP: dipyridamole; IMA: imatinib mesylate; CLO: clopidogrel; THAL: thalidomide; WAR: warfarin; *splenectomy prior to the diagnosis of CML because of metastatic gastric carcinoma.*

Table 2. Transthoracic echocardiographic findings.

N.	PH	RVSP (mmHg)	Follow-up (months)
1	(–)	20	3+
2	(+)	45	12+
3	(–)	20	12+
4	(–)	25	9+
5	(+)	40	5+
6	(+)	38	9+
7	(–)	17	9+
8	(+)	37	2+
9	(–)	22	2+
10	(+)	38	6+
11	(+)	70	6
12	(–)	30	4+
13	(+)	37	4+
14	(–)	19	14
15	(+)	37	1+
16	(–)	23	3+
17	(–)	21	1+
18	(–)	25	1+
19	(–)	21	9+
20	(+)	40	4+
21	(+)	40	1
22	(–)	20	4+
23	(–)	30	1+
24	(–)	18	1+

RSVP: right systolic ventricular pressure.

had ET, three had AMM and one had CML. None of the parameters analyzed — age, sex, presence of splenomegaly, type, duration and age at diagnosis of CMPD, presence of symptoms, hemoglobin levels, white blood cell or platelet count — was predictive of the presence of PH. Among the different CMPD there was no correlation between hematologic parameters and presence or severity of PH. Two patients with dyspnea on exertion were found to have PH. One of them had the highest RVSP overall and received treatment with diuretics, but his clinical condition progressively deteriorated and he died from cardiac failure six months later. One patient died of pneumonia one month after the diagnosis of PH. After a mean follow-up of five months (range, 1 to 12 months) all the other patients with PH are alive with no worsening of their status; none of them is receiving treatment for PH. Two patients were already being given acetylsalicylic acid for their CMPD. Until now there have been only case reports and two studies concerning the relationship between PH and CMPD. [4-7]

Nevertheless, the largest cohort reported so far did not comment on the incidence of PH in patients with CMPD, since it was a retrospective search for patients diagnosed with both these disorders.[4] PH is often asymptomatic, so it is possible that a significant proportion of patients with less advanced PH are left undiagnosed. In addition, PH symptoms are not specific and might be attributed to other conditions, especially in more elderly patients. Signs in the early stages of PH are also quite subtle.

The diagnosis of PH in our study was based on measurements obtained from TTE: this non-invasive investigation provides an accurate estimation of pulmonary-artery systolic pressure, comparable to that afforded by cardiac catheterization. The latter is an invasive method frequently contraindicated in these patients.[8]

Furthermore, TTE can reliably rule out congenital, valvular, and myocardial disease as causes of PH. We did not perform transesophageal echocardiography since this would have substantially increased the cost of our study, without significantly altering the management of our patients. Furthermore, since the majority of our patients with PH did not require treatment, we chose not to perform expensive imaging techniques, such as high-resolution CT scanning or ventilation-perfusion scanning, in order to establish the diagnosis of interstitial lung disease or thromboembolism, respectively, as the cause of PH.

Treatment of PH consists of vasodilators, anticoagulants and diuretics; whole-lung radiotherapy is also applied if extramedullary hematopoiesis (EMH) is responsible for the development of PH.[9,10] None of our patients except for one received treatment for PH, because they were asymptomatic: in most cases the RVSP was only mildly elevated. The single patient who was treated with diuretics for PH showed no evidence of EMH on technetium 99m sulphur colloid scintigraphy.

Once PH is diagnosed in patients with CMPD the prognosis is reported to be unfavorable.[4,5] Our study included a preponderance of ET cases; since ET has the best prognosis of all CMPD, this might have contributed to the benign course of our patients. However, the follow-up of the patients in this study is still short, so firm conclusions about the impact of PH on survival cannot be reached.

Although our study included a small number of subjects, it would appear that PH is relatively common in patients with CMPD. More, prospectively designed studies, are needed in order to clarify the impact of PH on the survival of these patients as well as, the optimal treatment.

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