

References

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Familial polycythemia vera: results from the Swedish Family-Cancer Database

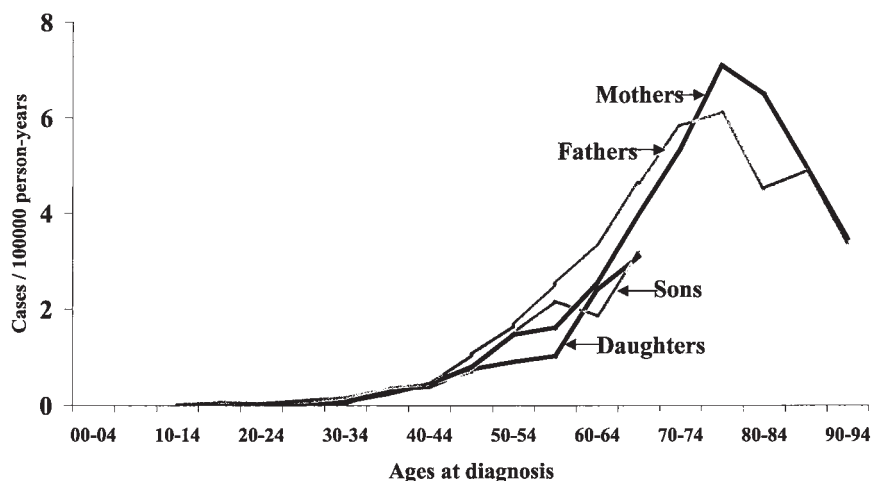


Figure 1 Age-specific incidence rates of polycythemia vera in parents and offspring in the Swedish Family-Cancer Database.

TO THE EDITOR

Polycythemia vera (PV) is a rare chronic myeloproliferative disorder due to the clonal expansion of a multipotent hemopoietic stem cell. Other related myeloproliferative disorders are chronic myeloid leukemia, myeloid metaplasia with myelofibrosis and essential thrombocythemia.¹ The clinical course of PV is characterized by hyperproliferation of the erythroid, myeloid and megakaryocyte cell lineages in the acute phase, anemia and fibrosis in the spent phase, and a risk of developing acute myeloid leukemia (AML) in the final phase. Little is known about familial predisposition to PV. Only case reports, but no analytical epidemiological studies on familial aggregation of PV, are available.^{2–4} The case reports included parent–child pairs of PV. Because of lack of population-based data on familial PV, we examine here these neoplasms using the nationwide Swedish Family-Cancer Database including all Swedes, ‘offspring’ born since 1932 with their parents recorded at birth. The parental population can assume any

age in the database, but the offspring population ranges between 0 and 66 years. The database has been updated in 2001 to include over 10 million individuals and over 1 million malignancies notified to the Swedish Cancer Registry between 1958 to 1998.⁵ However, data for PV are only available since 1975. In addition to familial relationships and neoplasms, the database contains information on residential area and socio-economic status. Familial risks were calculated for offspring separately for families where only a parent or only a sibling was affected with PV or with any other malignancy. There were no families where a parent and two siblings were affected by PV. Standardized incidence ratios (SIRs) were calculated by dividing the observed numbers (O) of cases by the expected (E) ones, calculated as person-years at risk based on age (5-year age-groups), period (5-year periods), area of residence (two categories), socio-economic status (four categories) and sex-specific incidence rates for all persons in the database.⁶ Confidence intervals (95%CI) were calculated assuming a Poisson distribution.⁶

The annual number of PV cases notified to the Swedish Cancer Registry has ranged from 90 to 170 with no evidence of a systematic trend. In the Family-Cancer Database the total number of affected offspring, fathers and mothers were 386, 1332 and 1231, respectively. The respective crude incidence rates were 0.23, 1.30 and

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Table 1 Familial risks for polycythemia vera

Familial cancer sites	Status of familial cancer									
	Parent only					Sibling only				
	O	E	SIR	95% CI		O	E	SIR	95% CI	
Oral	2	1.96	1.02	0.10	2.92		0.41			
Stomach	6	6.32	0.95	0.34	1.86		0.44			
Colon	10	8.68	1.15	0.55	1.98	2	1.12	1.79	0.17	5.12
Rectum	4	5.08	0.79	0.20	1.75	1	0.67	1.49	0.00	5.83
Pancreas	6	3.91	1.54	0.55	3.01		0.35			
Lung	13	8.36	1.55	0.82	2.51	1	1.30	0.77	0.00	3.02
Breast	21	13.01	1.61	1.00	2.38	7	5.49	1.27	0.51	2.39
Cervix	4	2.92	1.37	0.36	3.04	1	1.05	0.95	0.00	3.73
Endometrium	3	3.23	0.93	0.18	2.28	1	0.75	1.33	0.00	5.22
Prostate	15	18.05	0.83	0.46	1.30		0.87			
Kidney	3	4.55	0.66	0.12	1.62	1	0.68	1.47	0.00	5.75
Bladder	7	6.18	1.13	0.45	2.13	2	0.85	2.37	0.22	6.78
Melanoma	3	2.65	1.13	0.21	2.78	1	1.79	0.56	0.00	2.19
Skin	5	4.47	1.12	0.35	2.32	1	0.45	2.21	0.00	8.66
Nervous system	3	3.62	0.83	0.16	2.03	4	1.59	2.52	0.65	5.58
Connective tissue	2	0.86	2.33	0.22	6.69	1	0.26	3.81	0.00	14.93
Non-Hodgkin	3	3.69	0.81	0.15	1.99		1.03			
Hodgkin	5	2.24	2.23	0.70	4.62		0.24			
Lymphatic and myeloid leukemia	7	2.78	2.52	1.00	4.73		0.54			
Polycythemia vera	6	0.55	10.89	3.92	21.34		0.07			
All	133	118.35	1.12	0.94	1.32	26	24.48	1.06	0.69	1.51

All expected numbers were calculated based on site, age, period, residence and socioeconomic level-specific incidence. Bold shows that 95% CI \geq 1.00.

Table 2 Tumors in families were an offspring presented with PV

Family	Sex	Offspring		Mother		Father	
		Diagnosis	Age at diagnosis	Diagnosis	Age at diagnosis	Diagnosis	Age at diagnosis
1	Male	PV	63			PV	65
2	Male	PV	41	PV	65		
3	Male	PV	58	PV	52		
4	Female	PV	46	PV	50	CML	60
5	Male	PV	13	PV	71		
6	Male	PV	38	PV	50		
7	Female	PV	41	CLL	83	Prostate cancer	84
8	Female	PV	58	AML	57		
9	Male	PV	48			CLL	76
10	Female	PV	54	CML	75	Stomach cancer	53
11	Male	PV	51	CLL	59	Brain astrocytoma	68
12	Male	PV	32	AML	75	Lung cancer	52
13	Female	PV	44	AML	62		

1.13/100000 person-years. The age-specific incidence rates are shown in Figure 1. PV is mainly an old-age disease, with a maximal incidence at 75–79 years among men and women. No gender difference can be noted.

Familial risks for offspring PV are shown in Table 1 by any malignancy in a family member. PV was diagnosed in six parent–offspring pairs, giving a highly significant SIR of 10.89, whereas no sibling pairs were affected. In seven families, parents had leukemia and offspring PV; the SIR was 2.52 of borderline significance. The parental leukemias were three chronic lymphoid leukemias (CLL, SIR = 2.10, 95%CI 0.40–5.16), three AMLs (SIR = 3.89, 95%CI 0.73–9.53) and one chronic myeloid leukemia (CML, SIR 2.30, 95%CI 0–9.02). PV in offspring associated with no other parental or sibling tumor. In the database one sibling pair presented with a disorder, related to PV, of myelofibrosis, SIR 173 (95%CI 16–498); no parent–offspring pairs were

found. The sex and age at diagnosis data on the familial pairs are cited in Table 2. Among the 13 affected offspring, eight were male and five female. All but one of the parents with PV or leukemia were mothers. The ages at diagnosis ranged from 32 to 84, with one exceptionally young offspring diagnosed at age 13 years. Only in one family was more than one sibling affected with any malignancy; in family 2 a brother presented with renal cancer at age 58 years and a sister with breast cancer at age 55 years. In family 4, mother presented with PV and father with CML. When mothers were diagnosed with leukemia, four fathers had a cancer, yet all with different types (Table 2). This is more than expected because in the database only some 10% of the offspring with any parental cancer have two affected parents.

To our knowledge, this is the only analytical epidemiological study on familial risks in PV. We found a large risk of 10.89 for offspring from affected parents. No affected sibling pairs were observed but the

expected number was only 0.07. PV in offspring was also increased from parental leukemias. Among these seven cases, three parents had AML, which is a disease related to PV. The data suggest that even other leukemias share risk factors with PV, but this remains tentative because of the small number of cases.

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