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Epidemiology and Clinical Features of portal vein thrombosis: a multicenter study.

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7 **Epidemiology and Clinical Features of Portal vein thrombosis:**
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10 **a multicenter study**
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56 **Short title:** Portal vein thrombosis in Sweden
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ABSTRACT

Background

Reliable epidemiological data for portal vein thrombosis (PVT) are lacking.

Aims

To investigate the incidence, prevalence and survival rates for patients with PVT.

Methods

Retrospective multicentre study of all patients registered with the diagnosis of PVT between 1995-2004.

Results

173 patients (median age 57 years, 93 men) with PVT were identified and followed for a median of 2.5 years (range 0-9.7). The mean age-standardised incidence and prevalence rates were 0.7 per 100,000 per year and 3.7 per 100,000 inhabitants, respectively. Liver disease was present in 70 patients (40%), malignancy in 27%, thrombophilic factors in 22% and myeloproliferative disorders 11%. Two or more risk factors were identified in 80 patients (46%). At diagnosis 65% were put on anticoagulant therapy. Thrombolysis, TIPS, surgical shunting and liver transplantation was performed in 6, 3, 2 and 8 patients, respectively. The overall survival at 1 and 5 years was 69% and 54%. In the absence of malignancy and cirrhosis the survival was 92% and 76%, respectively.

Conclusions

The incidence and prevalence rates of PVT were 0.7 per 100,000 per year and 3.7 per 100,000 inhabitants, respectively. Concurrent prothrombotic risk factors are common. The prognosis is variable and highly dependent on underlying disease.

Key words: Venous Thrombosis, Portal Hypertension, Epidemiology, Risk Factors, Cirrhosis, Cancer.

INTRODUCTION

Portal vein thrombosis (PVT), considered a rare disorder in developed countries¹, is becoming increasingly recognised as a clinical entity. Reliable data on the incidence and prevalence of PVT in the general population or in selected patient groups are lacking. Some attempts have been made using autopsy or inpatient hospital registers from the 1970s and early 1980s²⁻⁴ with varied results. In retrospective studies of patients with liver cirrhosis, the prevalence has been reported to lie between 0.6 and 25 with an increased frequency in decompensated disease^{3,5-7}. In cases with cirrhosis and hepatocellular cancer the occurrence of PVT has reached 44%⁸. The aetiology of PVT is diverse^{1,9}, often with multiple concurrent factors implicated^{10,11}. Local risk factors e.g. liver cirrhosis, hepatobiliary malignancy, abdominal inflammation, infection and surgical intervention are the most common predisposing factors^{1,9}. New insights into systemic factors such as inherited or acquired thrombophilia^{6,10,12-15} and primary myeloproliferative disorders (MPD)¹⁶⁻¹⁸ have improved our understanding of portal vein obstruction especially in non-cirrhotic and patients without neoplasia. The frequencies and distribution of etiologic factors differ in reported case series due to different diagnostic criteria, referral patterns, ethnic groups and geographical regions^{4-6,9,10,15,17,19}. In the absence of randomised controlled trials the optimal management of PVT is not known although some consensus, based on expert opinion derived from retrospective studies, exists²⁰⁻²².

The aim of this study was to investigate the epidemiology, clinical presentation and survival in an unselected cohort of adult patients with PVT in Sweden.

PATIENTS AND METHODS

Patients

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2
3 This retrospective study was performed in collaboration with the Swedish Internal Medicine
4 Liver Club, a nation-wide network of university hepatologists. We searched the computerised
5
6 diagnosis databases of eleven hospitals, comprising all nine university hospitals, including the
7
8 liver transplantation centres in Sweden. The background population of these centres was 4.4
9
10 million, which constitutes approximately half of the Swedish population. Consecutive patients
11
12 between January 1995 and October 2004 registered with the ICD-9 (452 and 572B) or ICD-10
13
14 (I81, and K75.1) diagnosis codes suggestive of PVT were identified. All patients with partial
15
16 or complete thrombotic obstruction of the portal vein visualised at imaging, were included.
17
18 The date of diagnosis was defined as the year and month on which the obstruction was
19
20 evident on at least one of the following imaging modalities: ultrasonography (performed in
21
22 156 patients), computerised tomography (n=129), angiography (n=20) or magnetic resonance
23
24 imaging (n=16). The thrombosis was classified as acute if a recent intraluminal obstruction
25
26 was visualised, and chronic if a portal cavernoma, i.e. portoportal collaterals were present²³.
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36 Information on clinical characteristics, catchment area, investigations undertaken, laboratory
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38 findings, treatment, as well as the outcome was extracted from the medical records using
39
40 structured case record forms. The presence of cirrhosis or not was based on clinical data, i.e.
41
42 past history of liver disease, results of imaging and laboratory studies and by liver biopsy
43
44 when performed. Child-Pugh scores were assessed in cirrhotic patients. The presence of any
45
46 liver disease, intra-abdominal malignancy, gastrointestinal inflammation, abdominal infection
47
48 or abdominal surgery performed less than three months prior to diagnosis, were categorised as
49
50 local risk factors. Thrombophilias, blood disorders, any previous thrombosis, extra-abdominal
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52 malignancy, hormone therapy, systemic infection, rheumatoid disorders and pregnancy were
53
54 considered systemic aetiological factors.
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3 Follow-up was from the date of diagnosis until either death or study closure in October 2004,
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5 or, in the case of loss to follow-up, the last visit. Causes of death were acquired from the
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7 medical records, or if absent, from the Cause-of-death register, the National board of health
8
9 and welfare, Stockholm. Register search was made possible through the national registration
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11 number, unique for each citizen²⁴.
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17 **Epidemiology**

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19 Patient care during the study period was almost solely public and population based, and the
20
21 referral patterns based on geographic grounds. To assure full catchment of PVT cases,
22
23 analysis of epidemiology was restricted to primary catchment area-patients in six centres
24
25 which had used both in- and outpatient registers to identify patients. The mean population
26
27 figure for each year and each primary catchment area were available from 1995 and onwards
28
29 from Statistics Sweden, Stockholm. The combined population of these six centres was 1.3
30
31 million, comprising approximately 15% of the Swedish population in 2001. The mean
32
33 incidence rate was calculated for the years 1995-2003 and the mean prevalence rate for the
34
35 years 2001-2003. Crude rates were age-standardised according to the population census in
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37 1970. Patients were not included in the analysis of prevalence rates following orthotopic liver
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39 transplantation.
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48 **Statistics**

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50 Comparisons between independent groups were made by Mann-Whitney U-test and Kruskal-
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52 Wallis one-way analysis of variance as appropriate for continuous variables. For categorical
53
54 variables chi-squared tests were performed and Fisher's exact test used when more than 20%
55
56 of the expected values were less than five. The Kaplan-Meier estimate was applied for
57
58 calculating overall and transplantation-free survival rates. Univariate analysis of factors at
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3 diagnosis influencing survival was assessed using the log-rank test. Multivariate analysis was
4
5 carried out using Cox's proportional hazard model. Results were expressed as medians and
6
7 range. All analyses were carried out in SPSS for Windows version 16.0 (SPSS Inc, Chicago,
8
9 IL). Two-tailed p values < 0.05 were considered statistically significant.
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12 13 14 15 **Ethics**

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17 The study was approved by the committee of human ethics at all participating centres.
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20 21 22 **RESULTS**

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24 173 patients (93 men) with a median of 17 cases per hospital (range 1-33) were identified and
25
26 grouped into three strata; N-PVT, non-malignant, non-cirrhotic PVT (n=89), C-PVT, non-
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28 malignant, cirrhotic PVT (n=38), and, M-PVT, malignant PVT (n=46). Fifty-five patients
29
30 (32%) were diagnosed at the two transplantation centres. The median age at diagnosis was 57
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32 years (range 15-94). One patient (0.6%) was lost to follow-up due to migration when the
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34 study ended in October 2004.
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40 41 **Epidemiology**

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43 124 new cases of PVT were diagnosed at the six centres eligible for analysis of
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45 epidemiological data, of whom 97 patients (56% of all patients) were from the primary
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47 catchment areas. The mean age-standardised incidence and prevalence rates of PVT were
48
49 calculated to be 0.7 (95% CI 0.3-1.2) per 100,000 inhabitants per year and 3.7 (95% CI 2.6-
50
51 4.8) per 100,000 inhabitants, respectively. The percentage of patients living in the primary
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53 catchment area of liver transplantation and non-liver transplantation centres were comparable,
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55 81% and 78%, respectively (NS).
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Risk factors

The spectrum of risk factors is listed in Table 1. The most prevalent risk factor was a liver disorder, present in 70 patients (40%) of whom 54 (76%) had liver cirrhosis. Alcoholic liver disease was present in 21 patients (12%), viral hepatitis in 15 (9%), cryptogenic cirrhosis in 14 (8%), autoimmune hepatitis in 6 (3%), NAFLD in 4 (2%) and other liver disorders in 10 (6%).

Of systemic factors, thrombophilic conditions were present in 22% of patients and 19% of all patients had a previous history of any extra-splanchnic thrombotic event with a trend to concurrent presence of these two (chi-square 3.3; df 1, $p=0.07$). Eighteen patients (11%) had an underlying MPD. The occurrence of thrombophilia and MPD was 26% and 18% in N-PVT, 17% and 6% in C-PVT and, 18% and 2% in M-PVT patients, respectively. MPD and severe infections were more common in N-PVT compared to the two other groups ($p=0.015$ and $p=0.046$, respectively).

Overall, 76 patients (44%) had one or more local precipitating factors, 42 patients (24%) had a systemic risk factor, and 38 (22%) had a combination of both. Considering the presence of any risk factor 76 patients (44%) had one risk factor identified; two or more risk factors were present in 80 patients (46%). No obvious risk factor was evident in 17 patients (10%).

Clinical characteristics

N-PVT patients were younger at the time of diagnosis (median age 54 years) compared to patients with C-PVT (60 years) or M-PVT (67 years), $p<0.001$ (for both comparisons) and presented more often with fever, 48% ($p=0.004$). On the other hand were ascites ($p<0.001$), splenomegaly ($p<0.001$), oesophageal varices ($p=0.001$), jaundice ($p=0.005$) and signs of

1
2
3 hypertensive gastropathy ($p=0.017$) more prevalent in C-PVT and M-PVT. Abdominal pain
4
5 was a common complaint in N-PVT (78%) and M-PVT patients (70%), but less frequent in C-
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7 PVT (46%) ($p=0.002$). Ileus was diagnosed in 6 cases (4%). Eight patients (5%) were
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9 asymptomatic of whom six were N-PVT patients.
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15 Classification according to Child-Pugh was, for the cirrhotic patients ($n=38$) grade A 14%,
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17 grade B 61% and grade C 25%, and, for patients with malignancy ($n=46$), 0%, 87% and 13%,
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19 respectively.
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24 The median C-reactive protein (CRP) in N-PVT (67mg/L) and M-PVT (44mg/L) was higher
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26 than in C-PVT patients (13mg/L) ($p=0.003$). Few patients had an increase in prothrombin
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28 INR and the transaminase levels were generally normal or slightly elevated.
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32 33 34 **Diagnosis**

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36 An acute thrombosis was present in 128 patients (74 %), chronic thrombosis in 32 (18%) and
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38 was unspecified in 13 (8%). The thrombosis was limited to the portal vein in 102 patients
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40 (59%) and in the remaining 71 patients (41%) one or more accessory veins, i.e. the mesenteric
41
42 and/or splenic veins were also involved. PVT engaging accessory veins, were found in 49%
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44 N-PVT, 29% C-PVT and 35% M-PVT patients (NS).
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50 51 **Medical treatment and interventions**

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53 Details of interventions performed at diagnosis and during follow-up are given in Table 2. At
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55 diagnosis 113 patients (65%) were administered anticoagulant therapy with additionally three
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57 patients during follow-up. Treatment was usually started with LMWH and followed by oral
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59 anticoagulation. Of the 116 anticoagulated patients, 94 had an acute thrombosis, 15 chronic
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3 thrombosis and in seven the nature of the thrombosis was not specified. The median duration
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5 of treatment was 6.4 (range 0.1-114) months and the mean duration was 16 months.
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10 Anticoagulant therapy was more common in N-PVT patients (85%) than those with C-PVT
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12 (70%) or M-PVT (50%), ($p=0.004$) while diuretics were less frequent in N-PVT patients
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14 ($p<0.001$). All six patients (4%) given thrombolysis (one local and five systemically) were
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16 non-malignant non-cirrhotic; five of these cases had an acute PVT and three of them had a
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18 thrombosis involving accessory veins as well. Three patients (2%) underwent TIPS at
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20 diagnosis, all of which had an underlying liver disease. In two patients (both N-PVT) surgical
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22 shunting procedures were performed during the first year (portosystemic shunt $n=1$) or the
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24 third year (splenorenal shunt $n=1$) after diagnosis due to GI-bleeding and varices. Eight
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26 patients (5%) underwent liver transplantation (secondary to an underlying hepatic disorder),
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28 of whom one ultimately died, six days after transplantation. Not more than six patients (3%)
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30 underwent bowel resection due to ischemia.
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39 Information on recanalisation was available in 61 patients (35%). Partial or complete
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41 recanalisation was seen in 70% during the first year of follow-up and 72% at the last follow-
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43 up visit. 36 of 44 patients (82%) with recanalisation had received anticoagulation. An
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45 increased obstruction in the portal venous tract was observed in 7% and remained unchanged
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47 in 21%. Recanalisation frequencies did not differ between N-PVT, C-PVT and M-PVT
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49 patients (data not shown).
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55 **Survival**

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57 The median follow-up was 2.5 years (range 0–9.7). A total of 74 patients (43%) died during
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59 the follow-up period. Causes of death are listed in Table 3. Two patients that had not received
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3 anticoagulation died from variceal bleeding. There was one fatality (0.6%) due to intestinal
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5 ischemia.
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10 The overall survival at 1 and 5 years was 69% (95% CI 61–76) and 54% (95% CI 46–62),
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12 respectively (Figure 1). In N-PVT (n=89) the survival at 1 and 5 years was 92% (95% CI 86–
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14 98) and 76% (95% CI 66–86), respectively. For C-PVT (n=38) the survival at 1 and 5 years
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16 was 53% (95% CI 37–69) and 38% (95% CI 19–58), respectively and those with M-PVT,
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18 n=46) the 1 and 5 year survival was 37% (95% CI 23–51) and 24% (95% CI 11–37),
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20
21
22 respectively.
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27 Factors at diagnosis that influenced the transplantation-free survival were assessed by using
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29 univariate analysis. The use of anticoagulants at diagnosis or during the first follow-up year
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31 was not significantly related to survival (p=0.31 and p=0.11, respectively). Age, ascites,
32
33 encephalopathy, albumin, bilirubin, prothromin time, cirrhosis, malignancy and ALP had an
34
35 impact on survival (p<0.001) as also ALT (p=0.002), platelet count (p=0.003), presence of
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37 oesophageal varices (p=0.005) and splenomegaly (p=0.007). The presence of a thrombotic
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39 extension into the mesenteric vein did not significantly influence the survival.
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45 The results of a multivariate analysis for the total cohort and for patients with non-malignant
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47 PVT (n=127) are presented in Table 4, showing that age, bilirubin, cirrhosis and malignancy
48
49 independently influenced survival (p<0.001). Male sex had an independent prognostic value
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51 for decreased survival in the total cohort (p=0.029) but not for patients with non-malignant
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54
55 PVT.
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DISCUSSION

We report the epidemiology, risk factors and outcomes of a large group of unselected patients with PVT. The study is the first in which both incidence and prevalence rates of PVT are reported in a population-based cohort. We used in- and outpatient registers and calculated the mean age-standardised incidence and prevalence rates to be 0.7 per 100,000 inhabitants per year and 3.7 per 100,000 inhabitants, respectively. The inpatient register contains individual-based information on a nationwide level since 1987 and a discharge diagnosis is available in 99% of all hospitalised patients²⁵. The diagnosis of PVT has not been validated but results on other disorders have shown a 85-90% accuracy²⁵.

Nationwide register data limited to in-patients for the years 1981-85 in Denmark gave an estimated incidence rate of 0.27 per 100,000 inhabitants and year², i.e. half the rate reported herein. In contrast to that study, we also included data from out-patient registers and covered a later time period, 1995-2004, during which the diagnostic awareness of this condition has increased and better imaging modalities have become available.

Population-based prevalence rates for PVT have been addressed in two older autopsy studies. In the Japan Autopsy Register of 1975-1982 (n=247,728) PVT was found in 0.05% (\approx 50 per 100,000) (adapted from Okuda et al in ³), whereas in Malmö city, Sweden, the prevalence was as high as 1.0% (\approx 1000 per 100,000) in 1970-1982 (n=23,796 representing 84% of all in-hospital deaths)⁴. The difference between these results are striking and could be due to a lower occurrence of PVT in Japan compared to Europe. However, considering that both studies originate from necropsy results, in which there is a selection for the more severe cases per se, variable autopsy rates in different centres as well as ascertainment bias⁴, our lower prevalence rate should be considered more reliable. This assumption is underlined by the high

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3 proportion of patients with intra-abdominal neoplasia (67%) in one of the autopsy studies⁴ as
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5 compared to in our study (21%) and in a previous large case series (24%)¹⁷. Although a
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7 thorough search of the in- and outpatient registers was performed it cannot be excluded that
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9 we might have missed some patients with advanced malignancy as well as asymptomatic
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11 cases with underlying cirrhosis. At the time of our study screening for hepatocellular
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13 carcinoma was not routinely performed in the participating centres. Thus, the incidence and
14
15 prevalence rates of PVT here are possibly underestimated.
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22 New insights in the aetiology of PVT have revealed the presence of more than one risk factor
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24 in a high proportion of patients^{10, 17, 26}. This was confirmed in our study with 23% having a
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26 combination of a local and a systemic risk factor compared to 16% in a study from the
27
28 Netherlands¹⁷. Moreover, and despite that not all patients had undergone a full diagnostic
29
30 work-up for thrombophilic disorders and MPD, almost half of the patients (46%) had two or
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32 more risk factors (regardless of if local or systemic). In an Italian single center study of non-
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34 cirrhotic non-malignant patients with thrombosis confined to the splanchnic veins, the
35
36 occurrence of two or more risk factors was 27%²⁶ compared to 37% in our N-PVT patients.
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38 Cultures of progenitors¹⁹ were not performed and the JAK2-V617F mutation analysis¹⁶ was
39
40 not available at the time of study closure. We have recently observed the presence of the
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42 JAK2-mutation in 19% of PVT patients without malignancy or cirrhosis (unpublished
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44 observation). These findings suggest that a thorough diagnostic work-up in order to optimise
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46 the management of patients is warranted irrespective of the presence of a local precipitating
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48 factor.
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58 Local factors were more common in men (p=0.005) than in women in whom systemic factors
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60 (e.g. rheumatoid disorders) dominated (p=0.019), which has not previously been reported.

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3 This observation is probably due to that liver cirrhosis and hepatocellular carcinoma are more
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5 common in men.
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10 The prevalence of inherited or acquired thrombophilia was 22%. Although the highest
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12 frequency was seen in N-PVT patients (26%), there was no statistically significant difference
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14 compared to C-PVT (17%) and M-PVT (18%) patients. The presence of thrombophilia and
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16 MPD at diagnosis did not significantly effect survival in our univariate analysis (p=0.86 and
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18 p=0.36, respectively).
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24 Due to the lack of randomised controlled trials the best treatment for PVT is mainly empirical
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26 [7, 20-22](#).
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29 Partly based on retrospective studies from France, in which 90% achieved partial or complete
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31 recanalisation²³ without an increased risk of bleeding²⁷, anticoagulant therapy has been
32
33 advocated for patients with acute non-malignant and non-cirrhotic PVT²⁰⁻²². Recanalisation
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35 was however achieved only in 66% (31% partial and 34% complete) of our N-PVT patients
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37 during the first year after diagnosis, with a minor increase to 68% when analysing the total
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39 follow-up period. Although, these results must be interpreted with caution as data on
40
41 recanalisation was limited, they are in line with a recently published retrospective Italian
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43 series in which 45% of N-PVT patients achieved complete recanalisation. However, findings
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45 in a prospective study have furthermore indicated a limited recanalisation rate of 44%²⁸.
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53 Our overall survival rates at 1 and 5 years were consistent with the findings in a similar
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55 multicentre series from the Netherlands¹⁷, being 69% vs. 70%, and, 54% vs. 61%,
56
57 respectively. A slightly lower survival in our study could be attributed to a higher frequency
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3 of concomitant mesenteric vein thrombosis (31% vs. 11%), which has been associated with
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5 decreased survival^{17, 29, 30}, although this was not evident in our univariate analysis.
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10 The survival rates for N-PVT patients were good and similar to findings in previous series¹⁷,
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12 ²⁶. However, the 5-year survival for such patients was higher in an Italian cohort being 93%²⁶
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14 compared to 76% in our study. A more favourable outcome could be explained by their single
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16 tertiary referral centre holding a liver transplantation unit, and by a uniform management
17
18 strategy in younger patients (median age at diagnosis was 45 compared to 54 year in our
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20 study). Reports comparing the survival in cirrhotic patients with and without PVT are lacking
21
22 in the literature. The median one-year cumulative survival for C-PVT was 53% in our study,
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24
25 i.e. worse than the 78% reported for cirrhotic patients in general³¹.
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31 Although the use of anticoagulants during the first year after diagnosis was high (65%)
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33 (compared to 34% in the Italian and 25% in the Dutch study), we did not observe an increased
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35 survival with anticoagulation, nor has this been evident in other studies except for one study
36
37 on chronic portomesenteric thrombosis patients (n=60)²⁹. In that report, mortality was
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39 secondary to portal hypertension, in contrast to our study in which the cause of death
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41 primarily was related to the underlying condition¹⁷. We had two deaths due to variceal
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43 bleeding in patients who had not been anticoagulated. Bowel resection was performed in six
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45 patients (3%); death due to intestinal ischemia was very rare and occurred in only one (0.6%)
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51 patient.
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55 There are some limitations and strengths to our study. It is a retrospective analysis of a
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57 heterogeneous, although large patient cohort, and, a standardized diagnostic work-up had not
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59
60 been applied. To exclude an undue selection and referral bias as much as possible, we

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3 included all PVT patients treated at both academic and non-academic hospitals. It is possible
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5 that some patients with thrombophilia or MPD went undetected. To assure full catchment of
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7 all PVT cases, analysis of epidemiology was restricted to primary catchment area-patients in
8
9 the six centres which had used both in- and outpatient registers to identify patients. Treatment
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11 bias is possibly reduced by a more recent study period during which dramatic changes in
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13 therapeutic options have evolved.
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20 In conclusion, the mean age-standardised incidence and prevalence rates of PVT in Sweden
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22 were calculated to be 0.7 per 100,000 inhabitants per year and 3.7 per 100,000 inhabitants,
23
24 respectively. A liver disorder is a frequent risk factor and the presence of concurrent
25
26 prothrombotic factors is common. The prognosis is variable and highly dependent on
27
28 underlying disease. The survival rate is high in the absence of cirrhosis and/or malignancy.
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34 **STATEMENT OF INTERESTS**

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36 This study was supported by unrestricted grants from Futurum – the academy of health care;
37
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39
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42 form in *Scand J Gastroenterol* 2006;41(suppl. 242):32 and in *Gut* 2006; 55 (Suppl V) A35.
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Table 1a.

Local risk factors in Portal vein thrombosis (n=173). Patients can have more than one factor.

| | N | % |
|---------------------------------|----|----|
| Liver disease | 70 | 40 |
| With cirrhosis | 54 | |
| Without cirrhosis | 16 | |
| Intra-abdominal malignancy | 37 | 21 |
| Hepatocellular cancer | 21 | |
| Colorectal cancer | 4 | |
| Other | 12 | |
| GI-inflammation (n=166)* | 24 | 14 |
| Abdominal surgery# | 8 | 5 |
| Severe local infection (n=169)* | 5 | 3 |
| No local factor identified | 59 | 34 |

*One patient had alcoholic liver disease and viral hepatitis.

*Denotes number of evaluable cases.

#Within three months prior to diagnosis.

Table 1b.

Systemic risk factors in Portal vein thrombosis (n=173). Patients can have more than one factor.

| | N | % |
|--|----|----|
| Thrombophilic factor† (n=126)* | 28 | 22 |
| Factor V Leiden mutation | 13 | |
| Hyperfibrinogenemia | 4 | |
| Lupus anticoagulant | 4 | |
| Cardiolipin antibodies | 3 | |
| Antithrombin deficiency‡ | 3 | |
| Prothombin gene mutation | 2 | |
| Protein S deficiency‡ | 1 | |
| Previous thrombosis (n=156)* | 29 | 19 |
| Venous | 19 | |
| Arterial | 10 | |
| Myeloproliferative disorder (n=158)* | 18 | 11 |
| Polycytemia vera rubra | 12 | |
| Essential Thrombocythemia | 5 | |
| Chronic Myeloid Leukaemia | 1 | |
| Severe systemic infection (n=169)* | 14 | 8 |
| Hormone replacement therapy (n=75/80)* | 9 | 12 |
| Rheumatoid disorder (n=165)* | 8 | 5 |
| Blood malignancy | 6 | 13 |
| Lymphoma | 4 | |
| Leukaemia | 2 | |
| Extra-abdominal malignancy | 3 | 7 |
| Oral contraceptives (n=74/80)* | 3 | 4 |
| Pregnancy (n=79/80)* | 3 | 4 |
| No systemic factor identified | 93 | 54 |

†Two patients had more than one factor (antithrombin deficiency and hyperfibrinogenemia, protein S deficiency and lupus anticoagulant, respectively).

*Denotes number of evaluable cases.

‡Deficiency due to liver failure not included i.e. patients with combined low levels of protein S and protein C and/or antithrombin were excluded.

Table 2.

Interventions in 173 patients with portal vein thrombosis.

| | At diagnosis | | During follow-up | |
|---------------------------|--------------|----|------------------|----|
| | n | % | n | % |
| Anticoagulants | 113 | 65 | 116 | 67 |
| Heparin/LMWH | 102 | | 103 | |
| Coumarin derivatives | 63 | | 70 | |
| Thrombolysis | 6 | 3 | 6 | 3 |
| Acetylsalicylic acid | 11 | 6 | 14 | 8 |
| Other antiplatelet drugs | 2 | 1 | 2 | 1 |
| Diuretics | 64 | 37 | 71 | 41 |
| Betablockers | 64 | 37 | 72 | 42 |
| Isosorbide mononitrate | 11 | 6 | 13 | 8 |
| Band ligation | 26 | 15 | 36 | 21 |
| Sclerotherapy | 20 | 12 | 23 | 13 |
| TIPS or surgical shunting | 3 | 2 | 5 | 3 |
| Liver transplantation* | 1 | 1 | 8 | 5 |
| Splenectomy | 0 | 0 | 5 | 3 |
| Bowel resection | 4 | 2 | 6 | 3 |

*Due to underlying liver disease

FU, Follow-up; LMWH, low-molecular-weight heparin; TIPS, transjugular intrahepatic portosystemic shunting.

Table 3.

Cause of death in patients with portal vein thrombosis (n=74).

| | PVT (n=74) | |
|--------------------------|------------|----|
| | n | % |
| Malignancy | 31 | 42 |
| Intra-abdominal* | 28 | |
| Other | 3 | |
| Liver failure | 16 | 22 |
| Cardiac failure | 9 | 12 |
| Multiorgan failure | 6 | 8 |
| Infection | 4 | 5 |
| Variceal bleeding | 2 | 3 |
| Intestinal ischemia | 1 | 1 |
| Other, non-liver related | 5 | 7 |

* Hepatocellular cancer (n=18), liver metastasis (n=4), biliary (n=2), colorectal (n=2), pancreatic (n=1) and gastric cancer (n=1).

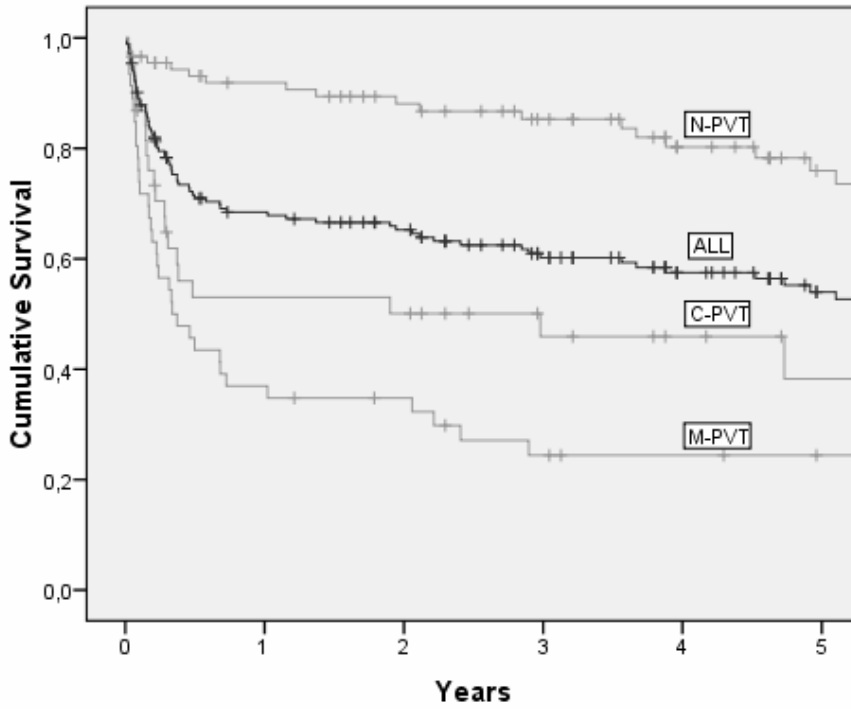
Table 4.

Multivariate survival analysis of characteristics at diagnosis in 173 patients with portal vein thrombosis. Relative risk (RR) of death is given for the total cohort and separately for those with non-malignant portal vein thrombosis (n=127).

| | PVT (n=173) | | | | | Non-malignant PVT (n=127) | | | | |
|-----------------------------------|-------------|--------|---|-----|--------|---------------------------|--------|---|------|--------|
| | RR | 95% CI | | p | | RR | 95% CI | | p | |
| Age | | | | | | | | | | |
| <=50 | 1.0 | | | | | 1.0 | | | | |
| 51-60 | 1.9 | 0.8 | - | 4.3 | 0.14 | 2.9 | 1.0 | - | 8.4 | 0.06 |
| > 60 | 4.2 | 2.0 | - | 8.6 | <0.001 | 12.0 | 4.1 | - | 34.9 | <0.001 |
| Sex | | | | | | | | | | |
| Female | 1.0 | | | | | 1.0 | | | | |
| Male | 1.9 | 1.1 | - | 3.5 | 0.03 | 1.1 | 0.6 | - | 2.3 | 0.72 |
| Bilirubin (µmol/L) | | | | | | | | | | |
| <= 20 | 1.0 | | | | | 1.0 | | | | |
| > 20 | 4.8 | 2.6 | - | 8.8 | <0.001 | 3.8 | 1.7 | - | 8.6 | 0.00 |
| Albumin (g/L) | | | | | | | | | | |
| <= 30 | 1.0 | | | | | 1.0 | | | | |
| > 30 | 0.9 | 0.5 | - | 1.5 | 0.58 | 1.2 | 0.5 | - | 2.8 | 0.62 |
| Mesenteric vein thrombosis | | | | | | | | | | |
| Absent | 1.0 | | | | | 1.0 | | | | |
| Present | 1.2 | 0.7 | - | 2.2 | 0.55 | 0.8 | 0.4 | - | 1.8 | 0.61 |
| Cirrhosis | | | | | | | | | | |
| Absent | 1.0 | | | | | 1.0 | | | | |
| Present | 2.7 | 1.6 | - | 4.7 | <0.001 | 7.3 | 2.9 | - | 18.3 | <0.001 |
| Abdominal inflammation | | | | | | | | | | |
| Absent | 1.0 | | | | | 1.0 | | | | |
| Present | 0.5 | 0.2 | - | 1.2 | 0.11 | 1.1 | 0.3 | - | 3.7 | 0.88 |
| Malignancy | | | | | | | | | | |
| Absent | 1.0 | | | | | | | | | |
| Present | 3.5 | 1.9 | - | 6.6 | <0.001 | | | | | |

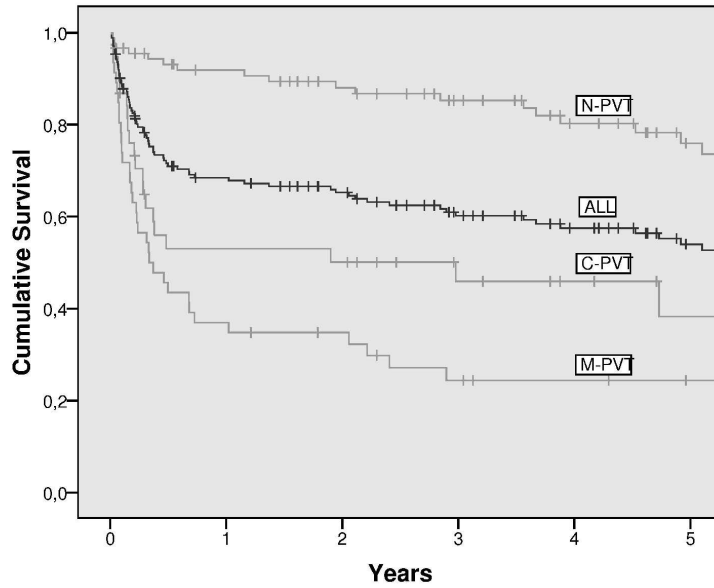
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Figure 1. Overall survival rates for all patients with portal vein thrombosis, for patients with non-malignant, non cirrhotic portal vein thrombosis, N-PVT, for patients with cirrhosis but no malignancy, C-PVT, and for patients with malignancy with or without cirrhosis, M-PVT.



| Patients at risk: | | | |
|-------------------|-----|-----|----|
| All | 173 | 110 | 44 |
| N-PVT | 89 | 75 | 33 |
| C-PVT | 38 | 18 | 5 |
| M-PVT | 46 | 17 | 9 |



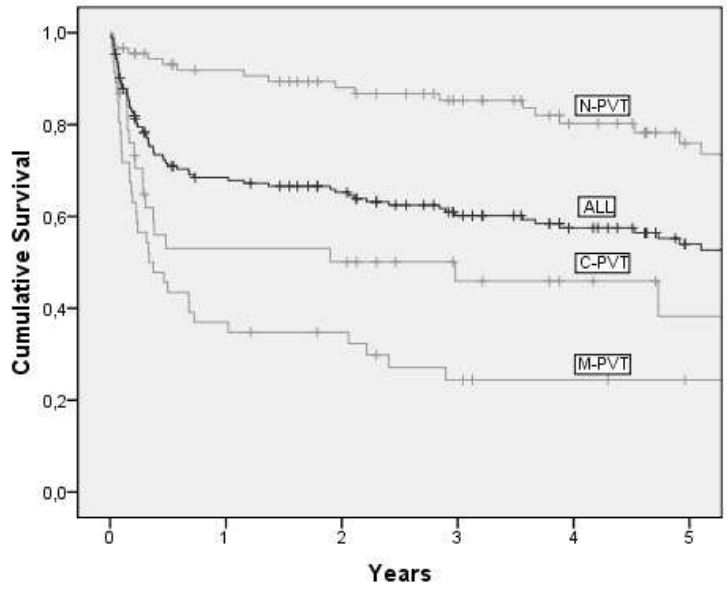


| Patients at risk: | | | |
|-------------------|-----|-----|----|
| All | 173 | 110 | 44 |
| N-PVT | 89 | 75 | 33 |
| C-PVT | 38 | 18 | 5 |
| M-PVT | 46 | 17 | 9 |

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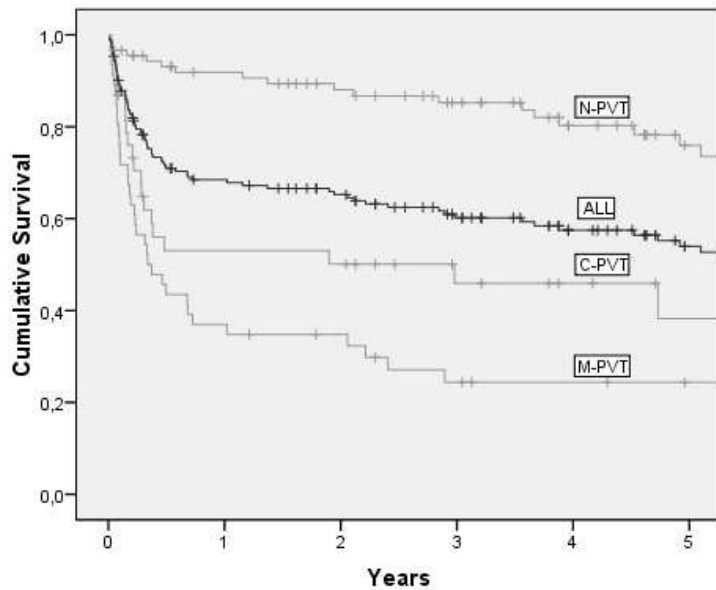


| Patients at risk: | | | |
|-------------------|-----|-----|----|
| All | 173 | 110 | 44 |
| N-PVT | 89 | 75 | 33 |
| C-PVT | 38 | 18 | 5 |
| M-PVT | 46 | 17 | 9 |

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| Patients at risk: | | | |
|-------------------|-----|-----|----|
| All | 173 | 110 | 44 |
| N-PVT | 89 | 75 | 33 |
| C-PVT | 38 | 18 | 5 |
| M-PVT | 46 | 17 | 9 |

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