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Recidief buikvenetrombose onder VKA: Wat nu?

Casus Nederlandse Trombose Congres 1 juli 2022

Dr. M.M.C. Hovens, internist-vasculair geneeskundige

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Mw. D, 56 jr

SEH 26/5

Sinds paar uur toenemend buikpijn, gehele buik, braken. Deze klachten nieuw!

Ziek, opgekruld in bed liggend, temp 37
Hemodynamisch stabiel
Gespannen buik, spaarzame peristaltiek, geprikkeld

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Test	26-05-2022 22:41 KCL X Maur... 998220379852 SEH
Hematologie algemeen	
Volledig bloedbeeld	
Hemoglobine	9.3
Hemoglobine POCT	-
Hematocriet	0.49
Hematocriet (POCT)	-
Erytrocyten	6.2
MCV	80
MCH	1.5
MCHC	18.9
Leucocyten	12.1
Trombocyten	443

Test	26-05-2022 22:41 KCL X Maur... 998220379852 SEH	27-05-2022 00:42 KCL Rashaan 998220379877 CHI
PTT	-	-
INR	3.4	-
INR (POCT)	-	-
Fibrinogeen	-	-
D-Dimeer	-	-
Chemie		
Chemie algemeen		
Natrium	143	-
Natrium (POCT)	-	-
Kalium	3.2	-
Kalium (POCT)	-	-
Chloride (POCT)	-	-
Bicarbonaat	-	-
Anion gap, alb gecorr.	-	-
Ureum	3.7	-
Kreatinine	57	-
GFS (CKD-epi)	>90	-
Fosfaat	-	-
Calcium ion. (BG)	-	-
Albumine	-	-
Magnesium	-	-
Bilirubine Totaal	30	-
Bilirubine Direct	14	-
Alkalische Fosfatase (AF)	133	-
Y-GT	31	-
ALAT	61	-
ASAT	73	-
LD	421	-
Lipase	44	-
Lactaat	-	2.7

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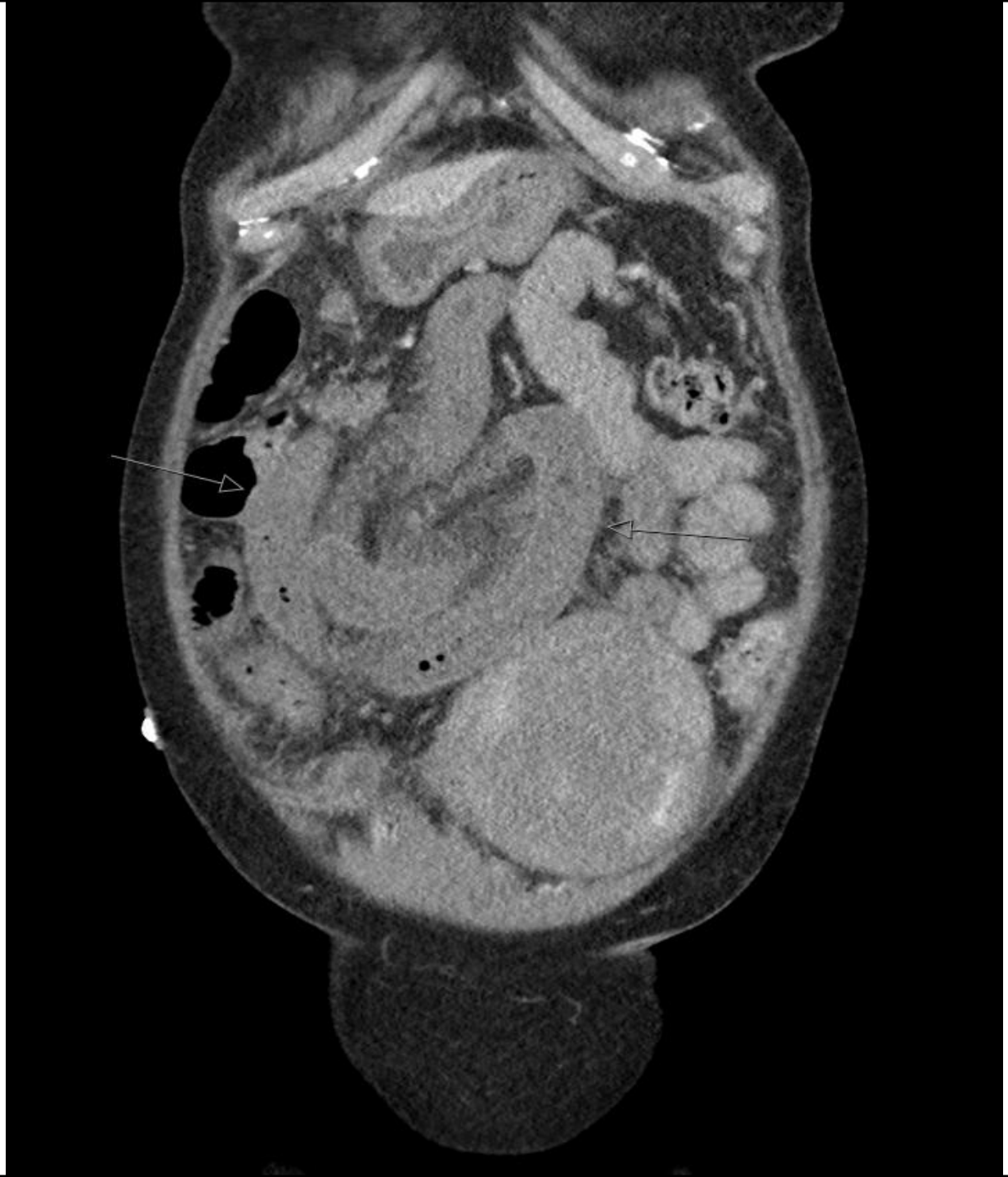

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- Acuut laparotomie:

  laparotomie, adhesiolysis bij status na rives stoppa, lastig vanwege abdominale varices 2L bloedverlies. Resectie 80cm necrotische darm op basis van veneuze trombose. Geen anastomoses aangelegd. 320cm dunne darm nog aanwezig.

- Beloop:

  relaparotomie op 28/5, anastomose aangelegd
  IC verblijf, UFH
  vanaf begin juni afdeling heelkunde

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- Voorgeschiedenis:
  - hypertensie
  - 2013 essentiële trombocytose
    - trombo 637
    - JAK2 V617F mutatie positief
    - -> ASA / cytoreductieve therapie
  - 2017 trombose v porta / mesenterica
    - ASA -> VKA, streefwaarde INR 2-3

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Conclusie

56 jarige patiënte met myeloproliferatieve aandoening (ET) met recidief splanchnicustrombose onder VKA

-> wat nu?

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Diagnostische overwegingen

- Therapietrouw?
- Obstructie darm?
- Bijkomende hypercoagubiliteit?
- Maligniteit?
- Beloop MPN?

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MPN & SVT

- Relatief vaak voorkomende oorzaak SVT

  tot 40% in cohortstudies

  ook met normaal bloedbeeld! (JAK2+)

Table 1. *Aetiological factors in Budd Chiari syndrome and portal vein thrombosis based on the result of the En-Vie study cohorts*[5,7]

Risk factor	BCS Frequency (%)	PVT Frequency (%)
Inherited thrombophilia	21	35
Acquired thrombophilia	44	19
Myeloproliferative neoplasm	49	21
JAK2 pos	29	16
Hormonal factors	38	44
Oral contraceptives	33	44
Pregnancy	6	0
PNH	19	0
Other systemic factors	23	n.d.
Local factors	0	21

BCS = Budd Chiari syndrome; PVT = portal vein thrombosis; PNH = paroxysmal nocturnal haemoglobinuria.

Leebeek Neth J Med 2012

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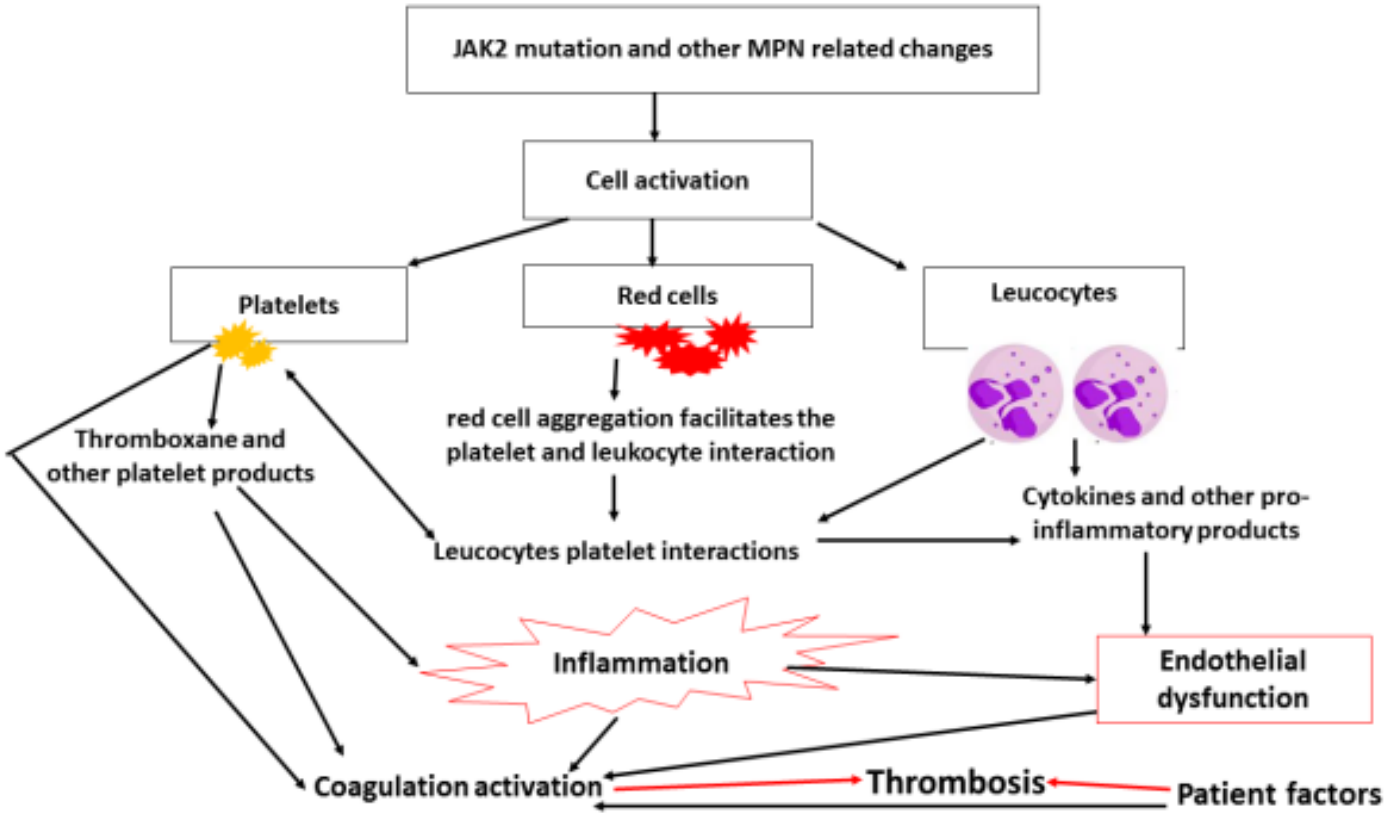

Arachchillage Semin Thromb Hemost 2019

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Behandeling SVT bij MPN

- Cytoreductieve therapie indien trombocyten >450 x109 /l en streef bij behandeling naar trombocyten aantal <400 x 109 /l
- Levenslang therapeutisch antistolling
- Overweeg TAR

ETrichtlijn HOVON werkgroep 2019

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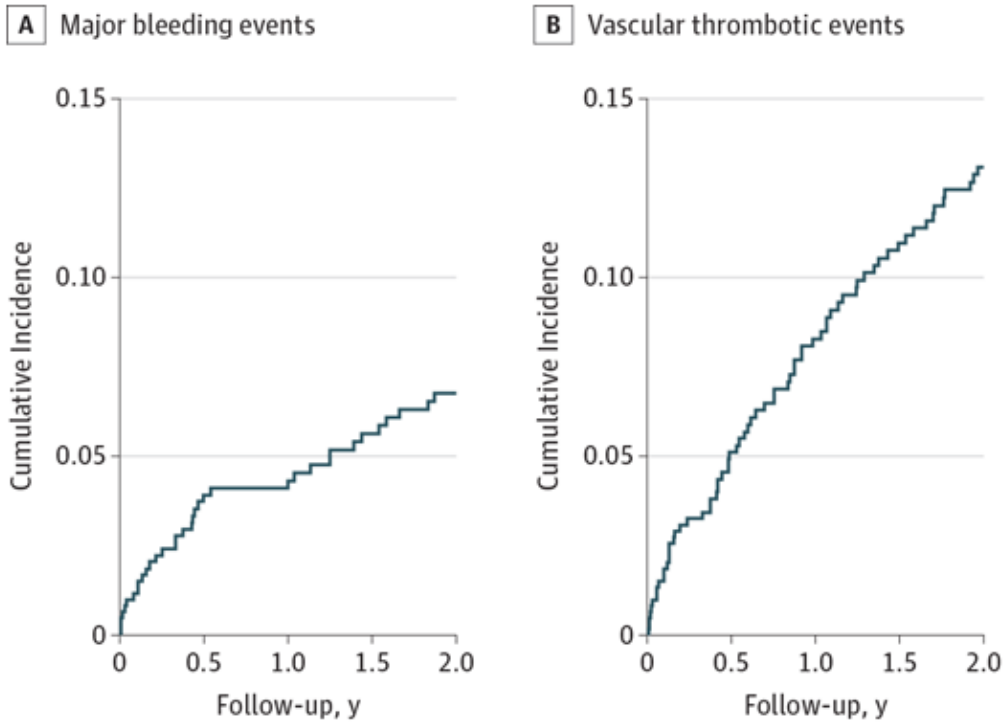
Beloop : toch hoge recidiefkans!

Figure 1. Cumulative Incidence of Major Bleeding and Thrombotic Events in the Entire Cohort of Patients With Splanchnic Vein Thrombosis



Ageno. JAMA Int Med 2015

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Beloop : toch hoge recidiefkans!

TABLE 1 Incidence rate of recurrent thrombosis and bleeding in MPN patients with DVT at common sites or with splanchnic vein thrombosis treated with VKAs or DOACs

Treatment	Patients (*N*)	IR of recurrent thrombosis /100 person-years (95% CI)	IR of bleedings /100 person-years (95% CI)
VKAs60	DVT of legs ± PE (206)	5.3 (3.2–8.4)	2.4 (1.1–4.5)
DOACs67	DVT of legs ± PE (158)	4.5 (2.9–6.8)	2.7 (1.4–5.2)
VKAs62	SVT (139)	3.9 (2.4–5.8)	2.0 (1.1–3.5)
DOACs67	SVT (51)	3.2 (1.2–8.6)	0.8 (0.1–5.5)

Abbreviations: CI, confidence interval; DOAC, direct oral anticoagulant; DVT, deep vein thrombosis; IR, incidence rate; PE, pulmonary embolism; SVT, splanchnic vein thrombosis; VKA, vitamin K antagonist.

Barbui RPTH 2022

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SYSTEMATIC REVIEW

blood advances

A systematic review of antithrombotic treatment of venous thromboembolism in patients with myeloproliferative neoplasms

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Table 3. Recurrent thrombotic events (arterial or venous) per treatment strategy

Antithrombotic treatment	Recurrent events n/N	Recurrent events %	Relative risk (95% CI); I^2
Antiplatelet therapy only	36/118	30.5	
Antiplatelet + cytoreduction	84/452	18.6	0.27 (0.07-1.04); 80.9%
Oral anticoagulation (any)	42/120	35.0	
Oral anticoagulation (any) + cytoreduction	60/376	16.0	0.42 (0.19-0.92); 62.7%
Oral anticoagulation + antiplatelet therapy	4/16	25.0	
Oral anticoagulation + antiplatelet + cytoreduction	9/37	24.3	0.60 (0.18-2.01); 36.3%
No antithrombotic treatment or cytoreduction	12/33	36.4	
Cytoreduction only	31/101	30.7	0.50 (0.37-0.67); 0.0%
Recurrent thrombosis per type of oral anticoagulant			
VKA only	39/106	36.8	
VKA + cytoreduction	55/313	17.6	0.51 (0.23-1.14); 62.2%
DOAC only	3/14	21.4	
DOAC + cytoreduction	5/63	7.9	0.21 (0.08-0.60); 16.9%
VKA + antiplatelet therapy	4/11	36.4	
VKA + antiplatelet + cytoreduction	9/37	24.3	0.43 (0.16-1.15); 0%
DOAC + antiplatelet therapy	0/5	0%	—

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Wat nu te doen?

- LMWH monotherapie?
- Switch naar DOAC?
- TAR toevoegen?
- VKA doorgaan, hogere streefwaarde?
- Cytoreductieve therapie veranderen?

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Beloop Mw. D.

- Huidige dosering hydroxycarbamide voortgezet
  trombocyten stabiel <400 x 109 /l

- LMWH klinisch, instellen VKA streefwaarde 3-4

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rpth research & practice in thrombosis & haemostasis

STATE OF THE ART ISTH 2021

Thrombosis in myeloproliferative neoplasms during cytoreductive and antithrombotic drug treatment

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Abstract

A state-of-the-art lecture titled "Myeloproliferative Neoplasm-associated Thrombosis" was presented at the ISTH congress in 2021. We summarize here the main points of the lecture with two purposes: to report the incidence rates of major thrombosis in polycythemia vera and essential thrombocythemia and to discuss to what extent cytoreductive therapy and antithrombotic drugs have reduced the incidence of these events. Unfortunately, the incidence rate of thrombosis remains high, ranging between 2 and 5/100 person-years. It is likely that new drugs such as interferon and ruxolitinib can be more efficacious given their cytoreductive and anti-inflammatory activities. Despite prophylaxis with vitamin K antagonists and direct oral anticoagulants after venous thrombosis in either common sites or splanchnic or cerebral sites, the incidence rate is still elevated, as high as 4 to 5/100 person-years. Future studies with new drugs or new strategies should consider thrombosis as the primary endpoint or surrogate biomarkers only if previously validated.

KEYWORDS
antithrombotic drugs, cytoreduction, epidemiology, myeloproliferative neoplasm, thrombosis

Essentials

- The risk of arterial and venous thrombosis is increased in myeloproliferative neoplasms.
- Hydroxyurea and thromboprophylaxis have a partially favorable risk-benefit profile.
- New formulations of interferon and JAK2 inhibitors will hopefully improve the thrombotic burden.
- New intervention trials should assess surrogate biomarkers of thrombosis with proven validation.

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