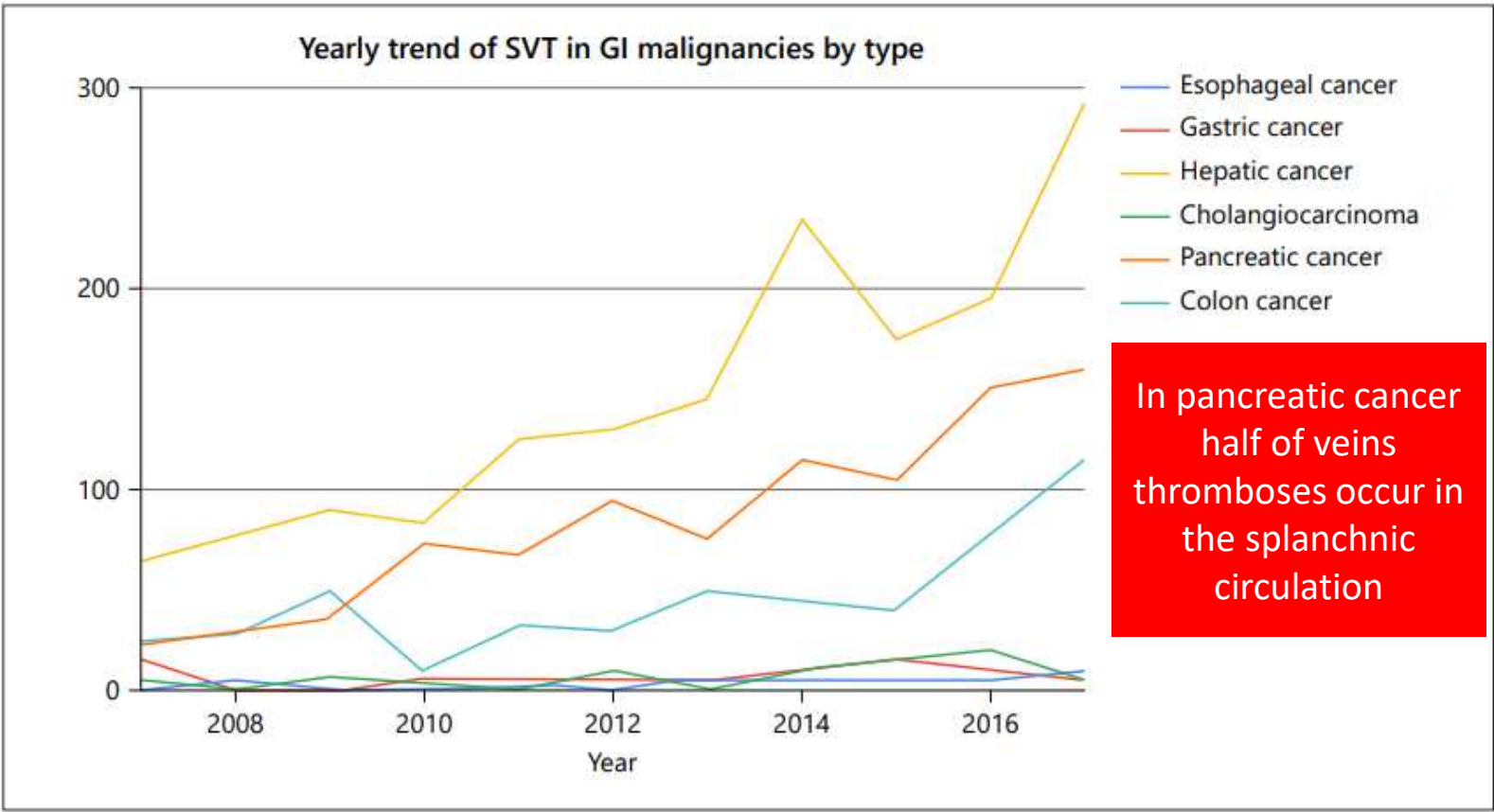


VALDIG Portal Vein Thrombosis Meeting
Hôtel de Ville de Paris
November 29th-30th 2022

Management of PVT in patients
with Pancreatic Cancer and Pancreatitis
Massimo Primignani, Milan Italy



Yearly trend of hospitalizations for SVT in GI malignancies 2007- 2017



In pancreatic cancer half of veins thromboses occur in the splanchnic circulation

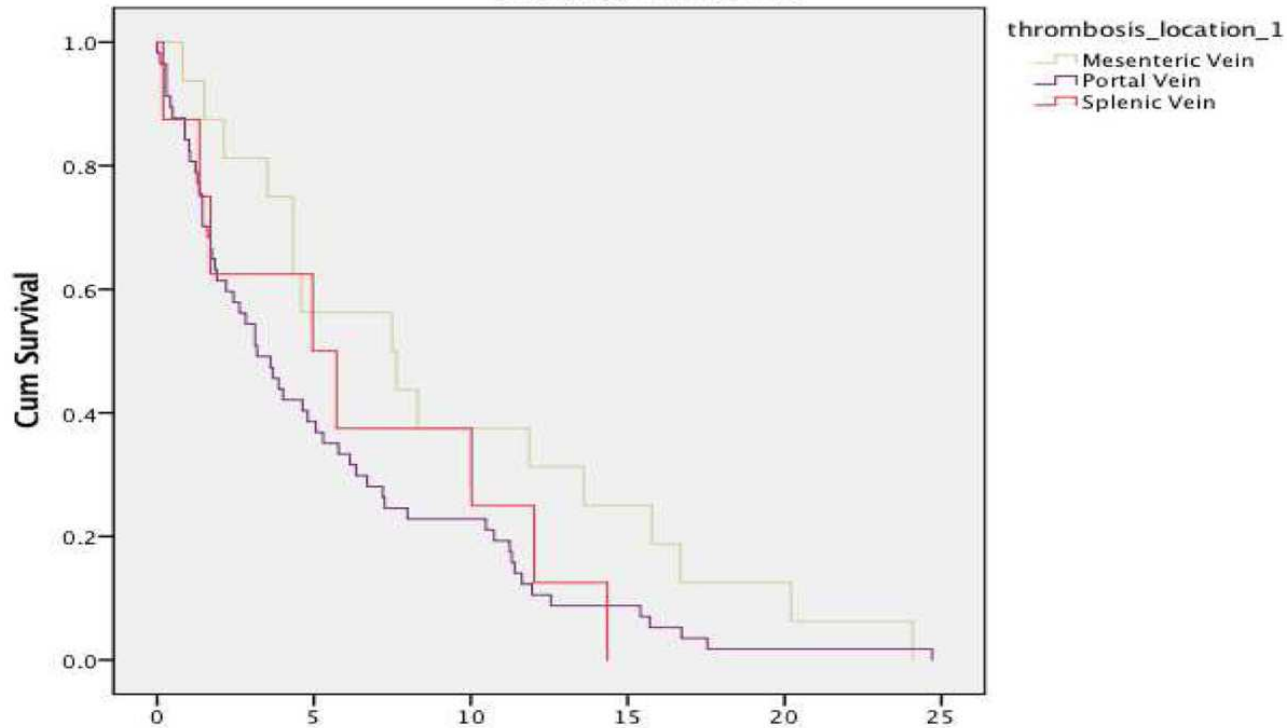
Out of 32,324 hospitalizations for SVT, 10% are associated with GI cancer.
HCC and pancreatic cancer are the most common

Khorana score identifies cancer patients at high risk of VTE

Patients' characteristics	Risk score
Site of cancer	
Very high risk (stomach, pancreatic, biliary)	2
High risk (lung, lymphoma, testicular)	1
Prechemotherapy platelet count < 100,000	1
Prechemotherapy hemoglobin < 10 g/dL or use of red cell growth factors	1
Prechemotherapy leukocyte count < 4,000	1
Body Mass Index ≥ 35 kg/m ²	1

Does thromboprophylaxis for VTE prevent SVT?
Unsettled (but plausible)

Splanchnic vein thrombosis in Pancreatic Cancer



- 95 patients
- 153 SVT
- frequent incidental finding:

PVT 45%
MVT 26%
SVT 17%

OS: PVT 3.6m, SVT 5.7m, MVT 7.4m

Hicks AM, Clin Colorectal Cancer. 2018

Splanchnic vein thrombosis in Pancreatic Cancer

SVT is a poor prognostic indicator for short term survival



LMWH if no contraindications

(active bleeding, severe thrombocytopenia or end of life care)

The role of anticoagulation with regard to oncologic outcome and prevention of complications remains to be fully defined

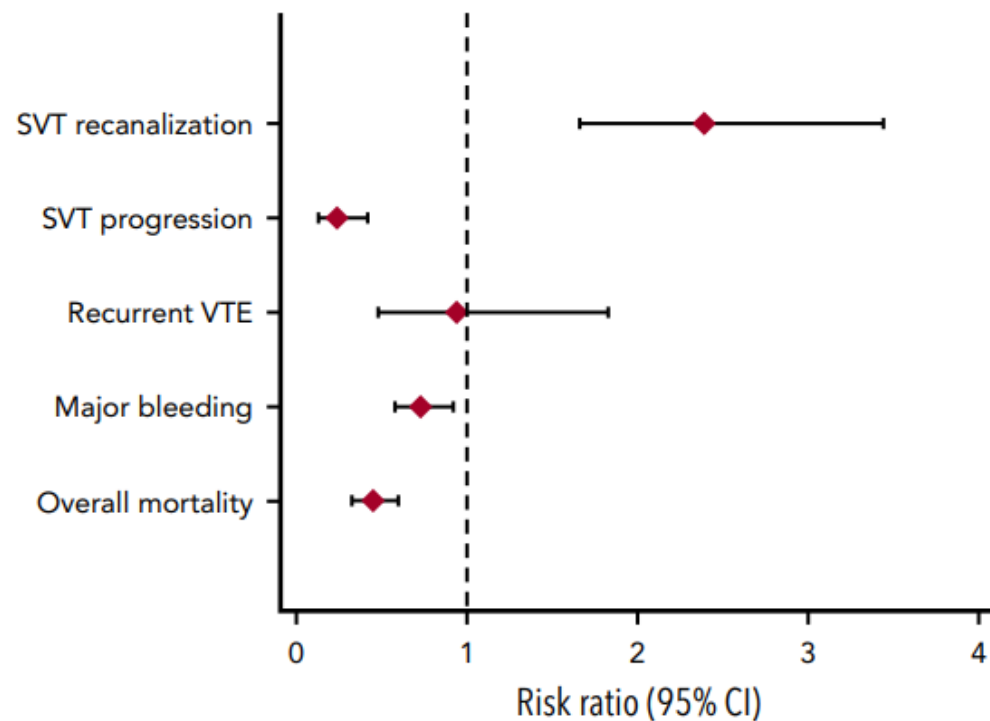
Anticoagulant therapy for splanchnic vein thrombosis: A systematic review and meta-analysis

7969 patients from 97 studies

Risk factors

Liver cirrhosis, n/N (%)	2578/5518 (46.7)
Myeloproliferative neoplasm, n/N (%)	1429/4598 (31.1)
Unprovoked, n/N (%)	770/3070 (25.1)
Solid cancer, n/N (%)	1108/4787 (23.1)
Surgery, n/N (%)	642/3762 (17.1)
Abdominal inflammation/infection, n/N (%)	726/4346 (16.7)
Hormonal replacement therapy, n/N (%)	297/3250 (9.1)

Anticoagulant therapy for splanchnic vein thrombosis: A systematic review and meta-analysis



- Anticoagulant therapy was associated with a high rate of splanchnic vein recanalization and a low rate of

Effects consistent across different etiologies

thrombosis were reduced by anticoagulant therapy.

Anticoagulant therapy for SVT: an individual patient data meta-analysis

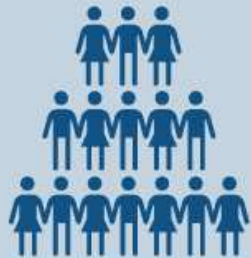
3 studies, none RCT, 1635 patients, 80% received anticoagulation for a median duration of 316 days

Risk factors	
Unprovoked	462 (28.3)
Solid cancer	523 (32.0)
Liver cirrhosis	287 (17.6)
Myeloproliferative neoplasm	118 (7.2)
Recent surgery	155 (9.5)
Hormonal therapy	57 (3.5)
Inflammatory bowel disease	24 (1.5)
Pregnancy or puerperium	15 (0.9)
Pancreatitis/abdominal infection	155 (7.0)
Leukemia, lymphoma, myeloma	20 (1.2)

Anticoagulant therapy for splanchnic vein thrombosis: an individual patient data meta-analysis

Anticoagulant treatment in splanchnic vein thrombosis

1635
Patients with
splanchnic vein
thrombosis



Effects consistent
across different
etiologies

Anticoagulant
treatment

 **325**

Anticoagulant treatment resulted in:



Major bleeding

HR 0.47 (95%CI 0.30 to 0.74)



Recurrent VTE

HR 0.42 (95%CI 0.27 to 0.64)



All-cause mortality

HR 0.23 (95%CI 0.17 to 0.31)

Splanchnic vein thrombosis predicts worse survival in patients with advanced pancreatic cancer

- 6164 patients with advanced pancreatic cancer identified through the Veterans Health Administration database
- SVT in 122 → two-fold increase in mortality : aHR 2.02 (95% CI 1.65-2.47)

Anticoagulant therapy
Did not affect mortality: aHR 0.99
Increased the risk of hemorrhage : aHR 2.7

Role of Anticoagulation in Pancreatic Cancer-related SVT

- SVT in Pancreatic Cancer is a frequent finding at diagnosis or during disease progression and is a marker of poor outcome in the short-term.
- Results of clinical studies and meta-analysis are heterogeneous

Research Agenda

A prospective multicenter study to assess role of anticoagulation in pancreatic cancer-related SVT, regarding survival and prevention of complications

Pancreatitis-related Splanchnic Vein Thrombosis

EPIDEMIOLOGY 1

- The incidence of SVT in acute pancreatitis is 1%-24% (depending on the severity of pancreatitis and the diagnostic tools, often incidental finding).
- SVT develops within 1 to 2 weeks after the onset of moderate or severe acute pancreatitis.
- **SVT is closely associated with the extent of pancreatic necrosis**

Pancreatitis-related Splanchnic Vein Thrombosis

EPIDEMIOLOGY 2

- Splenic vein is most frequently involved, PV is the second, SMV is the third
- In the absence of recanalization, most patients develop collateral circulation.
- 40–100% of patients with PV thrombosis develop cavernous transformation within few weeks

Balthazar Score/Computed Tomography Severity Index (CTSI) for Risk Assessment of SVT

1 Balthazar Grade

- Grade A Normal CT (0 points)
- Grade B Focal or diffuse enlargement (1 point)
- Grade C Pancreatic gland abnormalities (2 points)
- Grade D Fluid Collection (3 points)
- Grade E Two or more fluid collections (4 points)

2 Necrosis score

- No necrosis (0 points)
- 0 to 30% necrosis (2 points)
- 30 to 50% necrosis (4 points)
- Over 50% necrosis (6 points)

Both SVT risk and
bleeding risk increase
with the severity of
acute pancreatitis

Practice guidance for diagnosis and treatment of pancreatitis-related splanchnic vein thrombosis (Shenyang 2020)

Management (1)

Most patients with isolated splenic vein thrombosis are asymptomatic and the spontaneous recanalization rate is high



No anticoagulation, but close monitoring of SVT progression

Practice guidance for diagnosis and treatment of pancreatitis-related splanchnic vein thrombosis (Shenyang 2020)

Management (2)

The risk of development of splanchnic vein thrombosis is if the thrombosis is acute.

The risk of intestinal bleeding is if the thrombus is acute.

Appropriate for patients with a recent history of gastrointestinal bleeding or impending risk of bleeding ?

Anticoagulation in case of thrombosis progression

Current practice of anticoagulant in the treatment of SVT secondary to acute pancreatitis

Systematic review

No randomized trials, 2 case series, 5 retrospective studies, 9 case reports.

198 patients with SVT, 92 (46%) received anticoagulation.

- **Recanalization** : treated 14%
non-treated 11%
- **Bleeding** : treated 16%
non-treated 5%

Perform a RCT

Studies too heterogeneous to undertake a meta-analysis

Use of therapeutic anticoagulation in splanchnic vein thrombosis associated with acute pancreatitis: a systematic review and meta-analysis

Seven studies (6 retrospective, 1 prospective multicenter)
8353 patients, **339 with SVT**

Recanalization:	51.5 vs 28%	RR 1.6, 95%CI 1.17-2.27; P=0.004
Bleeding:	21% vs 11%	RR 1.95, 95%CI 0.98-3.88; P=0.06
Collateral formation:	43% vs 46%	RR 1.24, 95%CI 0.75-2.05; P=0.4
Death:	13% vs 7%	RR 2.02, 95%CI 0.85-4.8; P=0.1

Anticoagulation resulted in recanalization of the involved vessels without significantly increasing the risk of bleeding complications

Anticoagulant therapy for SVT: an individual patient data meta-analysis

3 studies, none RCT, 1635 patients, 80% received anticoagulation for a median duration of 316 days

Risk factors	
Unprovoked	462 (28.3)
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Anticoagulant therapy for SVT: an individual patient data meta-analysis

3 studies, no RCT, 1635 patients, 80% received anticoagulation for a median duration of 316 days

Anticoagulation associated with :



**Recurrence of SVT
Major bleeding
Mortality**

Results consistent in subgroups



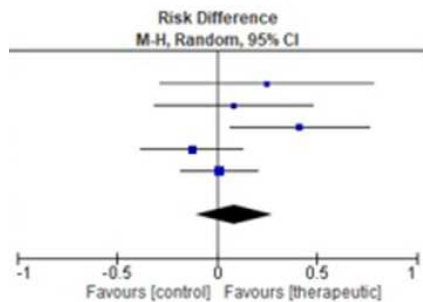
**In favor of
Anticoagulation**

Therapeutic anticoagulation for splanchnic vein thrombosis in acute pancreatitis: A systematic review and meta-analysis

- Seven retrospective cohort studies (3495 patients).
- SVT in 233 patients (7%), most frequent the splenic vein (44%).
- AC to 109 patients (47%), most frequent if triple vessel thrombosis (72%) and least if isolated splenic vein (22%) or superior mesenteric vein thrombosis (0%).
- In most studies LMWH followed by warfarin (duration 1.5 -12 months).

Therapeutic anticoagulation for splanchnic vein thrombosis in acute pancreatitis: A systematic review and meta-analysis

Recanalization



risk difference 9%

Varices/Collaterals/Cavernoma

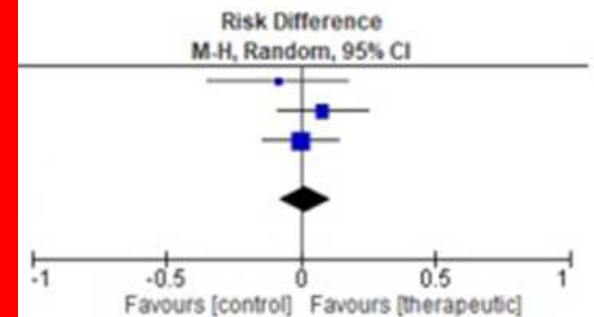
No benefit of anticoagulation
But...
Low quality data
Need for high-quality studies

risk difference -3%

Haemorrhage

risk difference 3%

Mortality



risk difference 2%

Anticoagulation in Acute Pancreatitis-related SVT

Conclusions

- SVT in Acute Pancreatitis is frequent in severe forms, associated with pancreatic/peripancreatic necrosis.
- Anticoagulation is often not performed, because of perceived high bleeding risk (pseudoaneurysm, portal hypertensive bleed) or need of invasive treatments (drainage of fluid collections/endoscopic or surgical necrosectomy)
- Results of clinical studies and meta-analyses are heterogeneous

Research Agenda 1

A large multicenter RCT of Anticoagulation therapy in patients with Acute Pancreatitis and SVT

Requirements

- Pre-defined diagnostic tools for SVT diagnosis
- Define type, dose and duration of treatment, follow-up and outcomes

Final Question: Anticoagulation for **Preventing** SVT
in Acute Necrotizing Pancreatitis ?

Compared with a historic cohort of patients not receiving anticoagulation, patients receiving anticoagulation had

Research Agenda

RCT to confirm these findings
LMWH: Therapeutic dose?
Prophylactic dose?



THANK YOU