Interplay of cancer and atherothrombotic events

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Disclosure

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I have the following potential conflicts of interest to report:

☑ I do not have any potential conflict of interest

Cancer and cardiovascular diseases

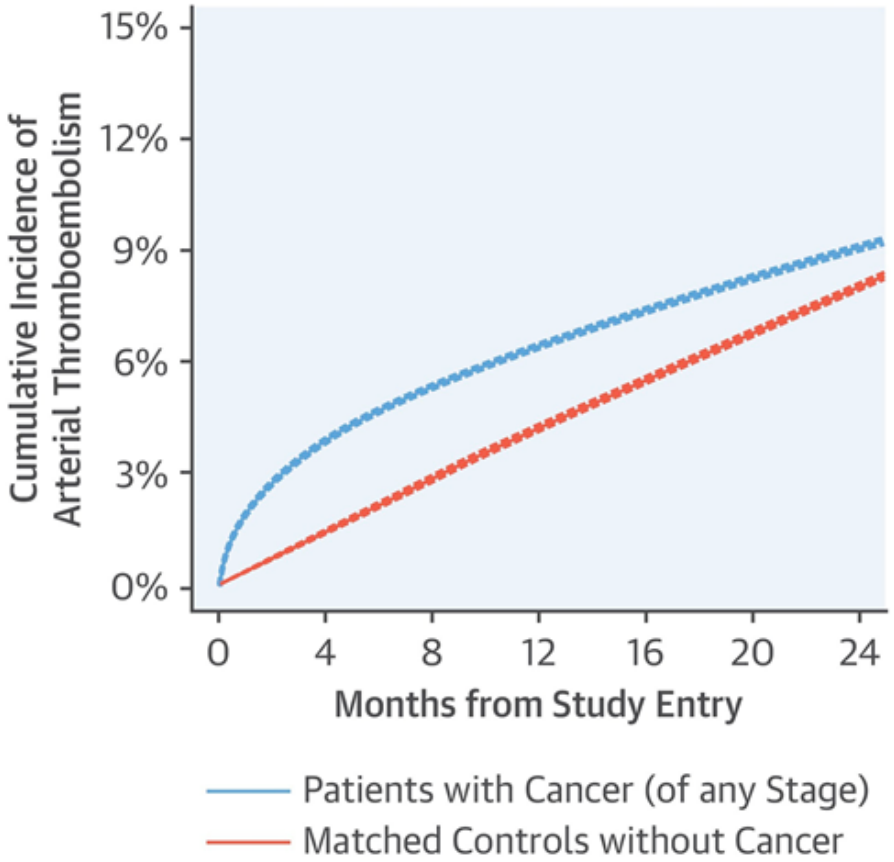
- **Cancer and cardiovascular diseases share similar risk factors**
  - Age
  - Smoking
  - Obesity

- **Cardiovascular diseases are among the most common causes of death in cancer patients**
  - Atherothrombotic events markedly increase mortality in cancer patients (Navi *et al.*, JACC 2017)

- **Cancer patients have a 3-fold greater risk of myocardial infarction compared to age-matched controls** (Navi *et al.*, JACC 2017)

- **The cardiovascular risk of cancer patients is influenced by**
  - Cancer type
  - Cancer stage
  - Therapeutic regimens

Cancer patients have a high risk of atherothrombotic events



Highest risk of atherothrombotic events in the months around diagnosis of cancer

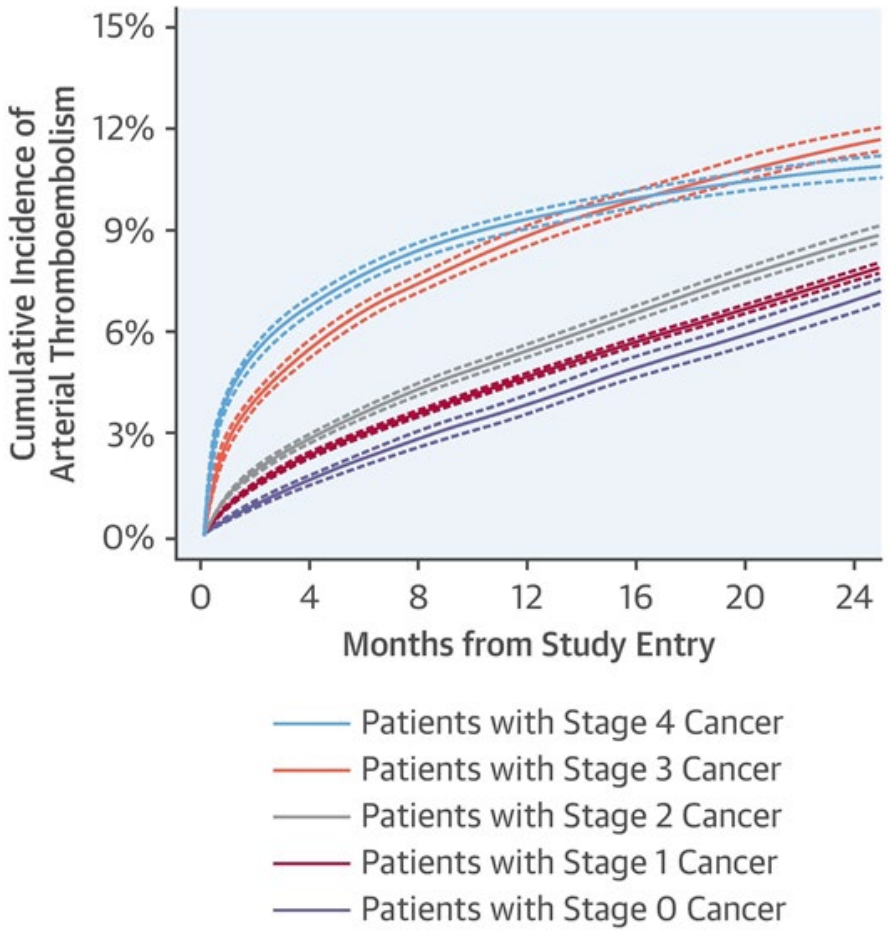
Navi *et al.*, JACC 2017

The incidence of atherothrombotic events depends on cancer type and stage

TABLE 2 Cumulative Incidence of Arterial Thromboembolism, Stratified by Cancer Type

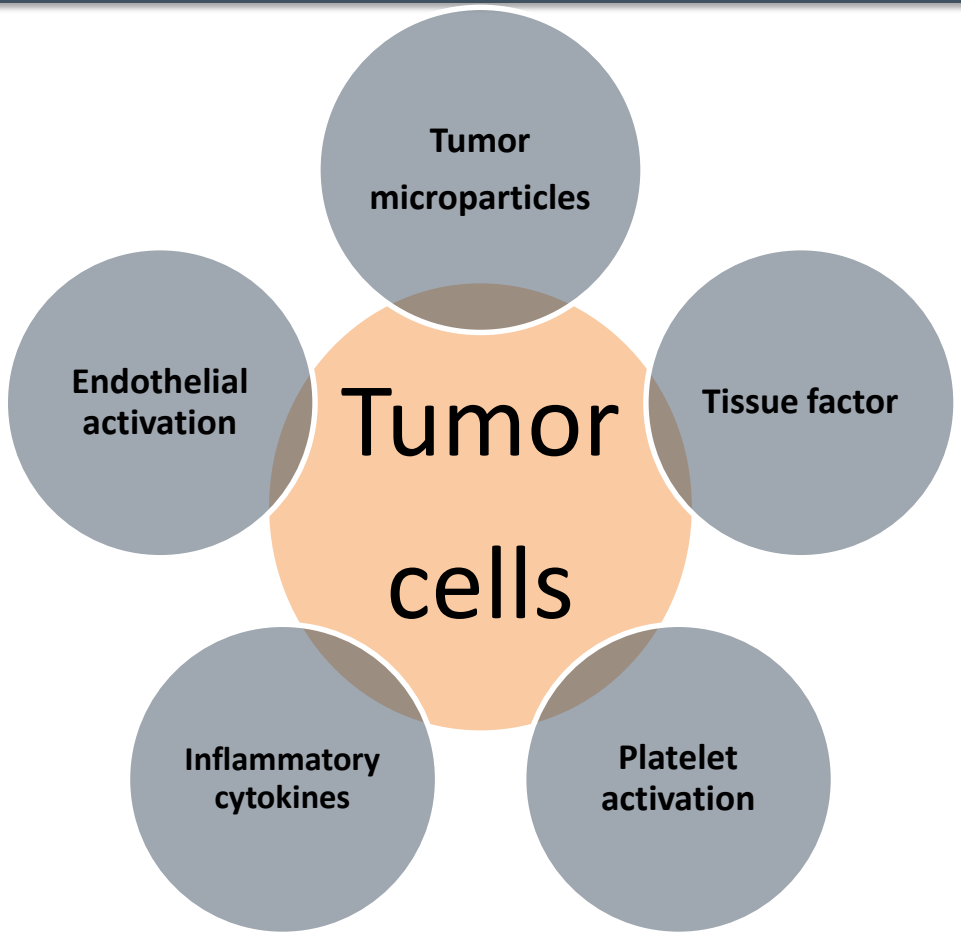
Cancer Type	Time Since Diagnosis of Cancer*			
	3 Months	6 Months	1 Yr	2 Yrs
All cancer				
Patients	3.4 (3.4-3.5)	4.7 (4.6-4.8)	6.5 (6.4-6.6)	9.1 (9.0-9.2)
Control patients	1.1 (1.1-1.1)	2.2 (2.1-2.2)	4.2 (4.2-4.3)	8.1 (8.0-8.2)
Breast				
Patients	1.7 (1.6-1.8)	2.6 (2.5-2.7)	4.2 (4.0-4.3)	7.1 (6.9-7.3)
Control patients	1.0 (1.1-1.1)	1.9 (1.8-2.0)	3.8 (3.6-3.9)	7.3 (7.1-7.5)
Lung				
Patients	6.5 (6.3-6.7)	8.3 (8.0-8.5)	10.3 (10.1-10.6)	–
Control patients	1.2 (1.1-1.3)	2.4 (2.3-2.5)	4.5 (4.3-4.6)	–
Prostate				
Patients	1.3 (1.2-1.4)	2.3 (2.2-2.4)	3.9 (3.8-4.1)	7.0 (6.8-7.2)
Control patients	1.0 (0.9-1.1)	2.0 (1.9-2.1)	3.9 (3.7-4.0)	7.5 (7.3-7.7)
Colorectal				
Patients	4.5 (4.3-4.7)	5.9 (5.7-6.1)	7.7 (7.4-7.9)	10.4 (10.1-10.7)
Control patients	1.3 (1.2-1.4)	2.5 (2.4-2.7)	4.7 (4.5-4.9)	9.0 (8.7-9.3)
Bladder				
Patients	3.2 (2.9-3.5)	4.7 (4.4-5.0)	7.1 (6.7-7.5)	10.4 (9.9-10.9)
Control patients	1.1 (0.9-1.2)	2.3 (2.1-2.5)	4.5 (4.2-4.8)	8.5 (8.1-8.9)
NHL				
Patients	3.7 (3.4-3.9)	5.4 (5.1-5.8)	7.4 (7.0-7.8)	10.3 (9.9-10.8)
Control patients	1.0 (0.9-1.2)	2.2 (2.0-2.4)	4.2 (3.9-4.5)	8.2 (7.8-8.6)
Pancreas				
Patients	4.7 (4.4-5.1)	5.9 (5.5-6.4)	–	–
Control patients	1.2 (1.0-1.3)	2.4 (2.1-2.7)	–	–
Gastric				
Patients	4.9 (4.4-5.5)	6.5 (5.9-7.1)	7.9 (7.3-8.6)	–
Control patients	1.2 (0.9-1.5)	2.2 (1.8-2.5)	4.7 (4.2-5.2)	–

Values are % (95% confidence interval). *Data are shown through the median follow-up period for patients with cancer for each cancer type up to a maximum of 2 yrs.
NHL = non-Hodgkin lymphoma.



Navi *et al.*, JACC 2017

Mechanisms of cancer associated thrombosis



- Procoagulant and proinflammatory environment triggering thrombotic events
- Interaction with vascular toxicity of cancer therapy

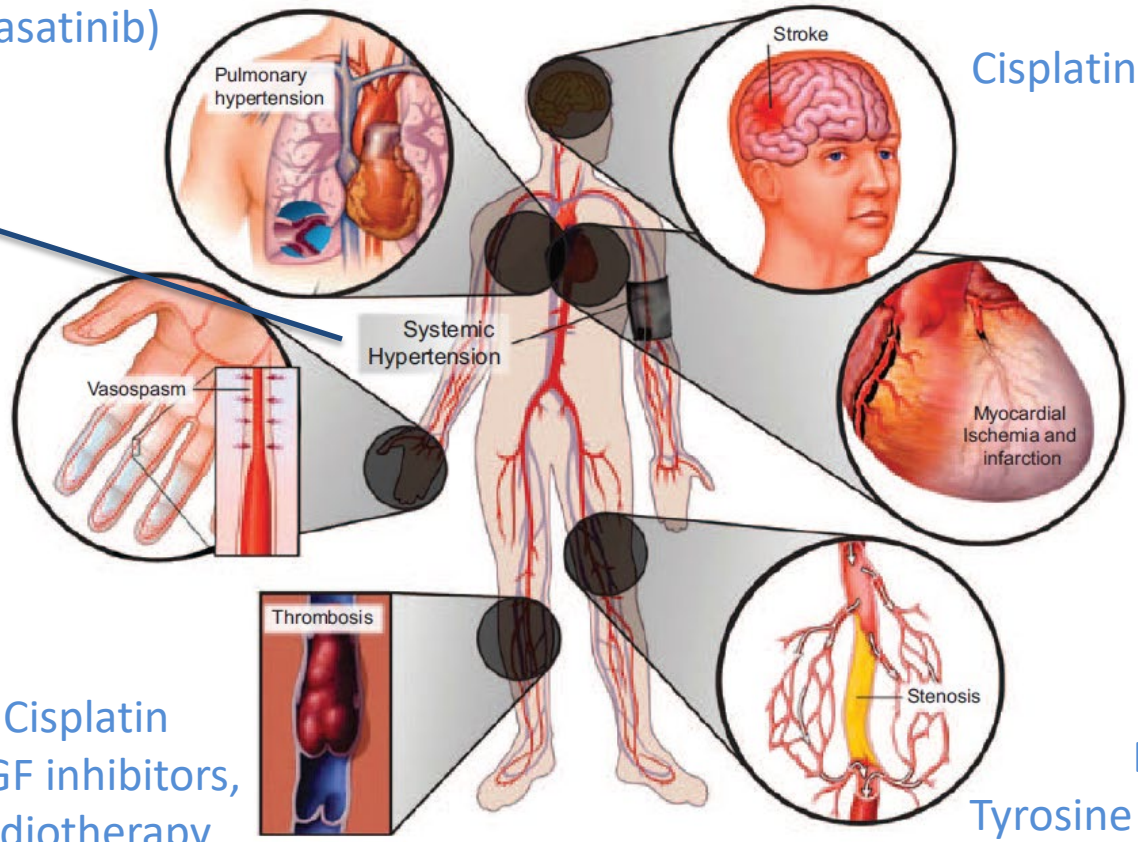
Vascular toxicities of cancer therapies

BCR-ABL
Tyrosine-kinase inhibitor
(Dasatinib)

Inhibitors of
VEGF signaling
(Bevacizumab)

Belomycin,
cisplatin,
gemcitabine

Cisplatin
VEGF inhibitors,
radiotherapy



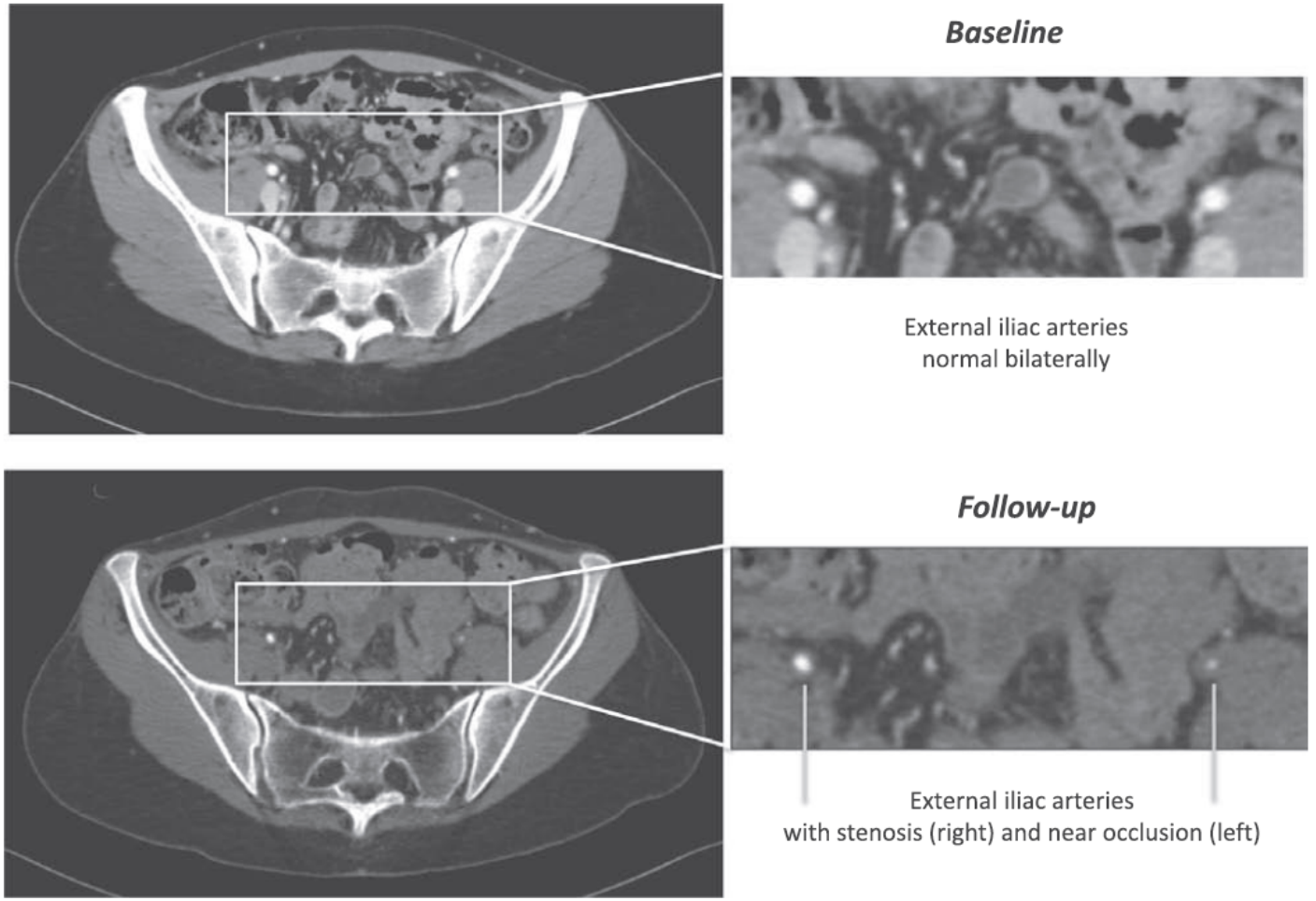
Cisplatin

5-FU, Paclitaxel
Sorafenib

BCR-ABL
Tyrosine kinase inhibitors
(Nilotinib, ponatinib)

Herrmann *et al.*, Circulation 2016

Accelerated peripheral artery diseases associated with Bcr-Abl tyrosin kinase inhibitors



Herrmann *et al.*, Circulation 2016

Cancer therapy increases the risk of atherothrombotic events

Agent	Pathophysiological mechanism	Risk of coronary artery disease and acute coronary syndrome
Fluoropyrimidines (5-FU, capecitabine, gemcitabine)	• Endothelial injury • Vasospasm	• Up to 18% manifest myocardial ischaemia • Up to 7–10%: silent myocardial ischaemia
Platinum compounds (cisplatin)	• Procoagulant status • Arterial thrombosis	• 20-year absolute risk of up to 8% after testicular cancer • 2% risk of arterial thrombosis
VEGF inhibitors (bevacizumab, sorafenib, sunitinib)	• Procoagulant status • Arterial thrombosis • Endothelial injury	• Risk of arterial thrombosis: bevacizumab 3.8%, sorafenib 1.7%, sunitinib 1.4%
Radiotherapy	• Endothelial injury • Plaque rupture • Thrombosis	• 2–7-fold increased relative risk of myocardial infarction • Cumulative 30-year coronary events incidence of 10% in Hogdkin lymphoma survivors • Risk proportional to irradiation dose

5-FU = 5-fluorouracil; VEGF = vascular endothelial growth factor.

2016 ESC position paper

Treatment of cardiovascular diseases in cancer patients – an unmet clinical challenge

- **Cancer patients have a high thrombotic and bleeding risk at the same time**
  - Cancer associated thrombocytopenia
  - Invasive procedures

  } Discontinuation of antithrombotic therapy
  - Bleeding from primary tumor/metastasis (especially brain, gastrointestinal tract)
  - Procoagulant state with high risk of arterial/venous thrombosis
  - Active cancer is associated with stent thrombosis (van Werkum *et al*., JACC 2009)

- **Consideration of overall prognosis of malignancy**
  - Prognostic benefit for most established preventive measures for cardiovascular diseases are uncertain in cancer patients
  - Cancer patients are less likely to receive therapy according to guidelines

- **Lack of randomized clinical trails allows only decision for individual cases based on case series**

Interplay of cancer and atherothrombotic events - an underexplored field

- Cardiovascular diseases are common among cancer patients and contribute to their high mortality

- Cardiovascular risk in cancer patients is determined by the underlying malignancy and the preexisting cardiovascular risk profile

- Cardiovascular toxicity of cancer therapy contributes to the burden of cardiovascular diseases

- Treatment of cardiovascular comorbidities in cancer patients is a field of uncertainty