is very different, we kindly ask Navi et al. (1) to carry out this subgroup analysis if possible (**Table 1** shows a possible option to group patients according to the International Classification of Diseases for Oncology, 3rd edition, classification), because the knowledge gained would be invaluable and their study offers a truly unique opportunity to do so.

*Marc Sorigue, MD
Edurne Sarrate, MD
Mireia Franch, MD
Juan-Manuel Sancho, MD, PhD

*Department of Hematology
Hospital Germans Trias i Pujol
Ctra Canyet s/n
08916 Badalona
Spain
E-mail: msorigue@iconcologia.net

https://doi.org/10.1016/j.jacc.2017.09.1155

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Navi BB, Reiner AS, Kamel H, et al. Risk of arterial thromboembolism in patients with cancer. J Am Coll Cardiol 2017;70:926–38.

2. Khorana AA, Kuderer NM, Culakova E, et al. Development and validation of a predictive model for chemotherapy-associated thrombosis. Blood 2008;111:4902–7.

3. Santi RM, Ceccarelli M, Bernocco E, et al. Khorana score and histotype predicts incidence of early venous thromboembolism in non-Hodgkin lymphomas. A pooled-data analysis of 12 clinical trials of Fondazione Italiana Linfomi (FIL). Thromb Haemost 2017 Apr 27 [E-pub ahead of print].

4. Caruso V, Di Castelnuovo A, Meschengieser S, et al. Thrombotic complications in adult patients with lymphoma: a meta-analysis of 29 independent cohorts including 18 018 patients and 1149 events. Blood 2010;115:5322–8.

Recurrent Late Bioresorbable Scaffold Thrombosis as a Presenting Symptom of Underlying Cancer

In a recent issue of the *Journal*, Navi et al. (1) demonstrated an increase in short-term risks for arterial thromboembolisms in patients with cancer. We would like to argue that this finding implies that arterial thromboembolisms can be the presenting symptom of an indolent cancer.

Herewith, we present the case of a 50-year-old man with stable coronary artery disease, who experienced 3 angiographically confirmed thromboses of bioresorbable scaffolds (2.5- to 3.5-mm diameter overlapping Absorb, Abbott Vascular, Abbott Park, Illinois) in his left anterior descending artery at 128, 129, and 242 days after implantation. Scaffold thromboses occurred despite treatment with a combination of aspirin, ticagrelor, and either coumarin (with an international normalized ratio in the therapeutic range at time of thrombosis) or therapeutic dose low-molecular-weight heparin. During this period of recurrent scaffold thromboses, the patient also developed multiple unprovoked deep vein thromboses, a pulmonary embolism, and a thrombus in the apex of the left ventricle. No abnormalities could be identified by extensive hematologic analysis, including lupus anticoagulant, anticardiolipin antibodies, antinuclear antibodies, β2-glycoprotein-I antibodies, protein S activity, protein C activity, antithrombin III activity, JAK2 mutations, factor II mutation, and factor V Leiden mutation. Further imaging, including abdominal computed tomography scans, raised the suspicion of a widespread metastasized cancer, the presence of which was confirmed by biopsy of a bone lesion and an esophageal tumor. Due to his deteriorating clinical condition, the patient was offered best supportive care. He died of a hemorrhagic stroke 1 month after the diagnosis of metastasized esophageal cancer was made.

Venous thromboembolism was identified as a common complication of cancer by Trousseau in 1865. Since then, the cancer-induced prothrombotic state leading to venous thromboembolism has been recognized as a well-known presenting symptom of underlying cancer (2). A similar mechanism may explain the observed increased risk of arterial thromboembolisms in patients with cancer (1). Because Absorb bioresorbable scaffolds provide a clear substrate for coronary thrombosis (3), we would like to create awareness among cardiovascular specialists for the occurrence and especially recurrence of late scaffold thrombosis as a potential presenting symptom of an underlying undiagnosed cancer.

*Maarten J.G. Leening, MD, PhD
Auke P.J.D. Weevers, MD
Robert-Jan M. van Geuns, MD, PhD
Jaap W. Deckers, MD, PhD
Mark-David Levin, MD, PhD

*Department of Cardiology
Albert Schweitzer Hospital
PO Box 444
3300 AK Dordrecht
the Netherlands
E-mail: m.leening@erasmusmc.nl

https://doi.org/10.1016/j.jacc.2017.10.086

Please note: Drs. Weevers and van Geuns have received institutional research grants and speaker fees from Abbott Vascular. Dr. Levin has received fees from Janssen, Roche, AbbVie, Celtrion, Amgen, Celgene, and Takeda, all unrelated to the content of the manuscript. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. The patient described in our case provided written consent for publication of materials relating to him.

REFERENCES

1. Navi BB, Reiner AS, Kamel H, et al. Risk of arterial thromboembolism in patients with cancer. J Am Coll Cardiol 2017;70:926–38.

2. Lip GYH, Chin BSP, Blann AD. Cancer and the prothrombotic state. Lancet Oncol 2002;3:27–34.

3. Ali ZA, Serruys PW, Kimura T, et al. 2-year outcomes with the Absorb bioresorbable scaffold for treatment of coronary artery disease: a systematic review and meta-analysis of seven randomised trials with an individual patient data substudy. Lancet 2017;390:760–72.

Risk of Arterial Thrombosis in Cancer Patients

Which Role for Cancer Therapies Vascular Toxicities?

We read with great interest the paper by Navi et al. (1) in a recent issue of the *Journal*. In their work, the authors highlight that patients with incident cancer face a substantially increased short-term risk of myocardial infarction and ischemic stroke, depending on cancer type and stage, which was confined to the first year (1).

Whereas the risk for venous thromboembolism and the benefit/safety of anticoagulants in cancer patients were extensively investigated (2), the association between cancer and arterial thromboembolism was scarcely studied in the published reports. The study by Navi et al. (1) is the largest to raise this important concern, and the authors are to be congratulated for their work.

However, a main limitation of their work is that they neither address nor discuss the role of the vascular toxicities of cancer therapies. The broadly used vascular endothelial growth factor inhibitors were previously demonstrated to be associated with a 3.5-fold increased risk of myocardial infarction and a 1.8-fold increased risk of arterial thrombosis (3), these hazard ratios being consistent with the findings from Navi et al. (1). Vascular endothelial growth factor inhibitors induce an endothelial dysfunction that decreases nitrite oxide and prostacyclin levels, resulting in platelet activation (4). In patients with pre-existing coronary or cerebral artery disease, these mechanisms might contribute to promote thrombosis. Moreover, an increased risk of arterial thromboembolism has been suggested with several other cancer therapies such as lenalidomide or carfilzomib.

The major strengths of this work are to clearly establish the association between cancer and arterial thromboembolism and to highlight the urgent need for coordinated efforts of oncologists and cardiologists in managing patients with cancer. From this perspective, a better knowledge of the risk attributable to cancer therapies constitutes a major outstanding issue.

***Corinne Frere, MD, PhD**
Isabelle Martin-Toutain, MD
Franck Thuny, MD, PhD
Laurent Bonello, MD, PhD

*Haematology Department
Assistance Publique Hôpitaux de Paris
Pitié-Salpêtrière Hospital
47/83 Boulevard de l'Hôpital
F-75013, Paris
France
E-mail: corinne.frere@aphp.fr

https://doi.org/10.1016/j.jacc.2017.10.087

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Navi BB, Reiner AS, Kamel H, et al. Risk of arterial thromboembolism in patients with cancer. J Am Coll Cardiol 2017;70:926–38.

2. Farge D, Bounameaux H, Brenner B, et al. International clinical practice guidelines including guidance for direct oral anticoagulants in the treatment and prophylaxis of venous thromboembolism in patients with cancer. Lancet Oncol 2016;17:e452–66.

3. Faruque LI, Lin M, Battistella M, et al. Systematic review of the risk of adverse outcomes associated with vascular endothelial growth factor inhibitors for the treatment of cancer. PLoS One 2014;9:e101145.

4. Herrmann J, Yang EH, Iliescu CA, et al. Vascular toxicities of cancer therapies: the old and the new–an evolving avenue. Circulation 2016;133:1272–89.

REPLY: Arterial Thromboembolism in Non-Hodgkin Lymphoma, as the Presentation of Occult Cancer, and With Cancer Therapies

We agree with Dr. Sorigue and colleagues that besides cancer stage, cancer histology might also affect arterial thromboembolism risk, particularly in patients with non-Hodgkin lymphoma (NHL). To