

## Preface

# Cardiovascular and Thromboembolic Diseases in Oncology: Novel Aspects and Revisited Issues

Massimo Franchini, MD<sup>1</sup> Antonella Tufano, MD, PhD<sup>2</sup> Antonio Coppola, MD<sup>3</sup>

<sup>1</sup>Department of Haematology and Transfusion Medicine, Carlo Poma Hospital, Mantova, Italy

<sup>2</sup>Department of Clinical Medicine and Surgery, Federico II University Hospital, Naples, Italy

<sup>3</sup>Department of General and Specialist Medicine, Hub Center for Inherited Bleeding Disorders, University Hospital, Parma, Italy

Semin Thromb Hemost 2021;47:896–898.

Welcome to the latest issue of *Seminars in Thrombosis and Hemostasis* (STH), which is dedicated to a very challenging and topical subject, from both clinical and research point of view. Cardiovascular and thromboembolic disorders are closely linked to cancer, being that a hypercoagulable state is an essential component of the pathophysiology of the disease. In addition, cardiovascular complications, including heart failure, arterial hypertension, coronary artery disease, venous thromboembolism (VTE), peripheral vascular disease, arrhythmias, pericardial disease, and pulmonary hypertension, are related to cancer itself or may complicate anticancer treatments, worsening patients' prognosis. Moreover, these cardiovascular diseases increasingly affect the growing numbers of cancer survivors including those becoming elders. These multilevel interrelationships are now addressed by the multidisciplinary approach of *cardiovascular oncology*, aimed at the holistic assessment of cardiovascular risk and diseases of patients over all phases of cancer treatment and clinical course, including subsequent long-term follow-up, requiring the close collaboration of oncologists, cardiologists, internal medicine and other specialists. These issues are deeply analyzed by some of the most distinguished international experts in this field.

The contributions begin with a narrative review from Tufano and colleagues, which introduces the emerging field of cardiovascular oncology.<sup>1</sup> The authors report the most relevant data about epidemiology and pathophysiology of cardiovascular oncology, and in particular, the mechanisms of cardiovascular complications in cancer and the pathophysiology of cardiotoxicity related to chemotherapeutic agents, targeted therapies, immunotherapies, and radiotherapy.

Next, Ortega Pérez and colleagues<sup>2</sup> recognize in their article the increased incidence of cardiovascular complications in the oncologic population and emphasize the need for a multidisciplinary approach, to offer to cancer patients the

best management, which includes prevention, early detection, treatment, and surveillance of cardiovascular events. This is the background for the cardio-oncology discipline, which enables to provide the best balance between cancer treatment and cardiovascular health protection with a patient-tailored approach.

This issue of STH continues with three contributions about VTE in oncology. Prandoni and Campello<sup>3</sup> focus on the setting of ambulatory cancer patients undergoing chemotherapy and analyze the risk factors for VTE, the most important including activation of extrinsic and intrinsic coagulation pathways, platelet activation, impaired fibrinolysis, the use of catheters, the infusion of blood products, and the thrombogenic potential of chemotherapeutic agents. Notably, a section of this review is devoted to prevention strategies for chemotherapy-associated VTE, and the authors conclude that low-dose novel direct oral anticoagulants (DOACs) are the most promising drugs, having the potential to offer an effective and safe protection against VTE.

The challenging issue of VTE in pediatric cancer patients with central venous catheter (CVC) is systematically analyzed by Hansen and colleagues.<sup>4</sup> After reviewing 25 studies including 2,318 pediatric cancer patients, the authors observed that 20% of children with tunneled or nontunneled CVC, and 12% of children with implantable ports, suffer from VTE. The investigators conclude that such patients are at a substantially increased risk of VTE, with children having acute lymphoblastic leukemia and CVC having higher VTE incidence than children with solid tumors and CVC.

The subsequent contribution from Cohen and colleagues deals with cancer-associated splanchnic vein thrombosis (SVT),<sup>5</sup> which includes portal, mesenteric, and splenic vein thrombosis and the Budd-Chiari syndrome. Like typical-site VTE, SVT is also frequently associated with cancer, particularly intra-abdominal solid malignancies and

**Address for correspondence**  
Massimo Franchini, MD,  
Department of Haematology and  
Transfusion Medicine, Carlo Poma  
Hospital, Mantova 46100, Italy  
(e-mail: massimo.franchini@  
asst-mantova.it).

**Issue Theme** Cardiovascular and  
Thromboembolic Diseases in  
Oncology: Novel Aspects and  
Revisited Issues; Antonella  
Tufano, MD, PhD, Antonio  
Coppola, MD, Maurizio Galderisi,  
MD, and Massimo Franchini, MD

© 2021. Thieme. All rights reserved.  
Thieme Medical Publishers, Inc.,  
333 Seventh Avenue, 18th Floor,  
New York, NY 10001, USA

DOI <https://doi.org/10.1055/s-0041-1733926>.  
ISSN 0094-6176.

myeloproliferative neoplasms. In this narrative review, the authors summarize the epidemiological and clinical aspects, pathogenesis, risk factors, and diagnosis of cancer-associated SVT, focusing on the current knowledge regarding the management of this challenging (and often poorly known) condition.

This issue of STH continues with an update of arterial thrombosis in cancer patients by Franchini and colleagues.<sup>6</sup> Cancer-associated arterial thrombotic events are less well studied than VTE, but are increasingly recognized, particularly in some types of malignancies and in association with specific anticancer therapies. The complex pathogenesis, with the interrelationships between cancer-related and patient-specific risk factors, the most relevant clinical evidence and treatment considerations on cancer-associated arterial thrombosis are addressed by the authors in this narrative review.

The seventh article in this issue analyzes another perspective of cardiovascular oncology, being focused on the antithrombotic treatment of patients with cardiovascular diseases and concomitant malignancies.<sup>7</sup> Santoro and colleagues collected all the scientific evidence, including the most updated clinical trials and guidelines, to provide recommendations on the management of antithrombotic treatment (both antiplatelet and anticoagulant therapy) in cancer patients with either pre-existent or new-onset coronary artery disease. The authors conclude on the need for further studies in this specific population of patients, so far excluded from clinical trials, to answer the many questions still not addressed on this topic.

Two further articles deal with prognostic assessments of outcomes in cancer patients, from different perspectives. Falanga and colleagues<sup>8</sup> focus on a particularly critical issue, i.e., the hemostatic imbalance existing in malignant disease, which is shifted toward a procoagulant direction and is responsible for the increased incidence of thrombotic complications. The authors analyze the hemostatic biomarkers in different types of cancers, evaluating their potential utility in predicting cancer outcomes, including overall and disease-specific survival, disease recurrence, and progression. The investigators conclude, however, that available literature data, although intriguing, are scarce and further prospective trials on larger population of patients are needed to validate the prognostic role of such hemostatic biomarkers in cancer.

In the ninth article of this STH issue, Candeloro and colleagues<sup>9</sup> address their research on the risk of ambulatory cancer patients of developing arterial/thrombotic complications or anticoagulant therapy-related bleeding events. In particular, the authors summarize the characteristics and performance of risk assessment scores for recurrent VTE and discuss available data on risk assessment for bleeding and arterial thrombosis in the cancer population. The identification and improvement of such scores would help clinicians in daily practice to make balanced decisions on the treatment of their cancer patients.

The last full article in this issue is a theme-unrelated contribution by Rossetti and colleagues, who nevertheless address an important topic, regarding the interrelationships between coagulation and inflammatory/immunologic

responses.<sup>10</sup> The authors report a pilot study of 23 non-oncological VTE patients in which they evaluated several interleukins and microRNAs (miRNAs) as early biomarkers of pathology to predict the outcome of VTE. Notably, the authors identify miRNA 126, a molecule highly active in mediating endothelial activation, as a diagnostic biomarker of VTE and a prognostic biomarker of poor early recanalization. This novel finding is discussed in the frame of the increasing number of clinical, animal model and in vitro studies, also reviewed by the authors, which suggest the potential role of miRNAs in modulating the cellular and biohumoral responses involved in VTE.

Finally, the last contribution in this issue is a Letter to the Editor, in which Franchini et al report the case of an acquired factor VII deficiency in a patient with bronchogenic carcinoma.<sup>11</sup> This case is challenging from a diagnostic and therapeutic point of view. The prophylactic use of low-dose of recombinant activated factor VII permitted the safe endoscopic removal of the tumoral mass and the restoration of normal hemostasis.

While wishing all our readership enjoyable reading, we would like to warmly thank all the authors who were able to provide such excellent contributions in these difficult times, and to dedicate this issue to our beloved co-editor Maurizio Galderisi. He was among the first to address and highlight the importance of cardiovascular oncology and therefore enthusiastically became involved in this editorial project. Unfortunately, he did not complete this exciting journey, losing his battle against coronavirus disease 2019 (COVID-19). It was very difficult for the residual members of the Guest Editor team to continue with the development of this issue without Maurizio, but now, at the finish line we have achieved another valuable piece of his precious legacy.

#### Conflict of Interest

None declared.

#### References

- 1 Tufano A, Coppola A, Galderisi M. The growing impact of cardiovascular oncology: epidemiology and pathophysiology. *Semin Thromb Hemost* 2021;47(08):899–906
- 2 Ortega Pérez R, Sanz AP, Gutiérrez VG, Zamorano Gómez JL. Cardiovascular oncology: the need for a multidisciplinary approach? *Semin Thromb Hemost* 2021;47(08):907–913
- 3 Prandoni P, Campello E. Venous thromboembolism in cancer patients undergoing chemotherapy: risk factors and prevention. *Semin Thromb Hemost* 2021;47(08):914–919
- 4 Hansen RS, Nybo M, Hvas A-M. Venous thromboembolism in pediatric cancer patients with central venous catheter—a systematic review and meta-analysis. *Semin Thromb Hemost* 2021;47(08):920–930
- 5 Cohen O, Caiano LM, Tufano A, Ageno W. Cancer-associated splanchnic vein thrombosis. *Semin Thromb Hemost* 2021;47(08):931–941
- 6 Franchini M, Tufano A, Casoria A, Coppola A. Arterial thrombosis in cancer patients: an update. *Semin Thromb Hemost* 2021;47(08):942–949
- 7 Santoro C, Capone V, Canonico ME, et al. Single, dual and triple antithrombotic therapy in cancer patients with coronary artery disease: searching for evidence and personalized approaches. *Semin Thromb Hemost* 2021;47(08):950–961

- 8 Falanga A, Marchetti M, Russo L. Hemostatic biomarkers and cancer prognosis: where do we stand? *Semin Thromb Hemost* 2021;47(08):962–971
- 9 Candeloro M, Guman NAM, Kraaijpoel N, Di Nisio M. Risk assessment models for thrombosis and anticoagulant-related bleeding in ambulatory cancer patients. *Semin Thromb Hemost* 2021;47(08):972–981
- 10 Rossetti P, Goldoni M, Pengo V, et al. MiRNA 126 as a new predictor biomarker in venous thromboembolism of persistent residual vein obstruction: a pilot study. *Semin Thromb Hemost* 2021;47(08):982–991
- 11 Franchini M, Bezzi M, Spreafico F, et al. Acquired factor VII deficiency associated with bronchogenic carcinoma: a case report. *Semin Thromb Hemost* 2021;47(08):992–994