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Management of cancer-associated thromboembolism: Introduction

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Venous thromboembolism (VTE) is a common complication in patients with cancer, associated with a high risk of morbidity, including VTE recurrence and bleeding, and mortality [1]. The challenges of managing cancer-associated thrombosis (CAT) are evolving all the time and new management approaches are regularly proposed and validated. Thanks to progress in anticancer treatment and supportive care, the life expectancy of patients with CAT is improving, reaching many months and years. Recent studies have shown that the incidence of CAT is increasing over time, whereas the risk of CAT-related death is declining, even if it remains high [2]. As a result of these trends, a growing number of patients with CAT need to be managed in everyday care for increasing periods of time. Consequently, the care pathway for these patients is evolving and many professionals and specialties are involved over the course of the patient's journey with CAT, which raising new issues. Several clinical guidelines have been published summarizing the results of the available literature, mainly focusing on treatment of CAT [3–6].

In this context, it seemed important to us to identify those situations which pose challenges to manage in everyday clinical practice, including unresolved issues, and to share the views and experience of different types of healthcare professionals who have to face those issues. Coordinated by the Investigation Network On Venous ThromboEmbolism (INNOVTE), a national network accredited by the French Clinical Research Infrastructure Network (F-CRIN), and with the collaboration of French scientific societies of various specialties involved in the management of patients with CAT (see below), we established a multidisciplinary working group who identified the challenges, reviewed the available data and put forward proposals for clinical practice. This multidisciplinary group involved clinicians from various specialties (including oncology, pulmonology, vascular medicine, cardiology, geriatrics, internal medicine, palliative care, emergency medicine and general practitioners) as well as nurses and pharmacists.

The first issue we decided to consider is the care pathway of patients with CAT, putting into perspective the journey of the patients from diagnosis to resolution, and the different health partners involved (Fig. 1). Next, the question of home treatment was proposed and where we are in the identification of patients with CAT who could be managed at home. The treatment of CAT is crucial and should be considered from a global perspective, taking into account patient-related, VTE-related, cancer-related, and treatment-related factors. Here, we decided to focus only on treatment of patients who develop CAT and we did not address the more general issue of thromboprophylaxis in patients with cancer. Due to the improving prognosis of patients with CAT, the question of anticoagulant treatment has to focus both on the initial post-diagnosis period and on the extended maintenance period. Many complex patient-related issues are relevant to the management of CAT. For example, the incidence of cancer increases with age, which may also impact the effectiveness of treatment. Renal impairment, extremes of body weight and thrombocytopenia are frequent con-

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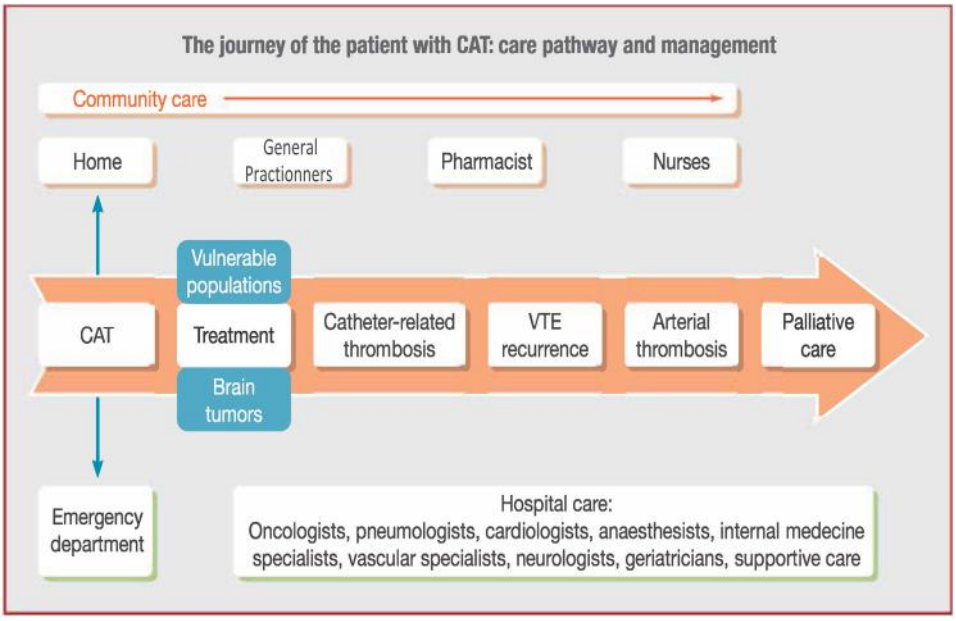

Fig. 1. The journey of the patient with Cancer-Associated Thrombosis (CAT).

ditions seen in cancer, and may also influence the benefit-risk profile of anticoagulant treatments. However, such patient groups have not been investigated specifically in prospective clinical trials of anticoagulant treatments for CAT. Similarly, very limited data is available from clinical trials on patients with CAT and brain tumours, and concerns have been raised about the risk of bleeding with anticoagulant treatment in this patient population. The number of patients with brain tumours receiving anticoagulants is probably underestimated, since cerebral imaging is not systematically performed before initiating anticoagulant treatment after a CAT diagnosis.

Patients with CAT frequently undergo a central venous catheter (CVC) placement for anticancer treatment administration and CVC thrombosis is a frequent complication, raising questions about catheter management and the anticoagulant treatment. Once patients are treated, they remain at risk for experiencing a VTE recurrence. Once again, this is a relatively common situation which has not been explored to any extent in randomised clinical trials. The available data may make different alternatives such as anticoagulant switch or dose increase/escalation. The bleeding risk associated with CAT treatment is also higher compared to VTE treatment in patients without cancer. The management of these bleeding complications is not discussed in the present proposals, but is subject of separate updated guidelines of the French Society of Anaesthesia and Intensive Care (SFAR) and the French Society of Emergency Medicine (SFMU). In the same way, the perioperative management of CAT treatment is not discussed herein, but is specifically addressed in updated guidelines of the French Society of Anaesthesia and Intensive Care (SFAR) and Groupe d'Intérêt en Hémostase Périopératoire (GIHP).

Patients with cancer now have a longer life expectancy, even at an advanced stage of cancer, and this raises questions about the duration of anticoagulant treatment, as well as the decision to discontinue treatment at the end of life. Palliative care is a situation where anticoagulant treatment may be associated with more constraints and risks than benefit.

Lastly, in relation with the improved prognosis of patients with CAT, the risk of arterial complications, such as acute coronary syndrome, stroke, peripheral arterial disease and atrial fibrillation, have been identified in these patients. Hypercoagulability is the main mechanism suspected, but it is possible that certain anticancer treatments also play a role.

We are progressively moving from an era where CAT was considered as a single entity with a single reference treatment proposed, to an era of shared care plans tailored to each individualised patient's needs and expectations. This approach should be a dynamic one in order to adapt to frequent changes in the state of patients with CAT over time. All partners in the care pathway have to be involved in this partnership.

All these situations will be discussed in this issue of *Archives of Cardiovascular Diseases*, with an overview of the available literature and proposals for clinical practice. For each question, a writing group analysed the published literature and drafted a first version of the manuscript providing arguments for the proposals for clinical practice which was discussed with all members of the working group in a plenary meeting. Each proposal was drafted as followed: "we recommend" when it was supported by solid evidence (such as randomised controlled trials or meta-analyses) or "we suggest" when the proposal was supported by less evidence (such as cohort studies or small trials) and "we propose" in the absence of any clear scientific evidence (such as case reports, case series...). The manuscript was then critically reviewed by independent multidisciplinary experts who were designated by each national scientific society associated with this work. The writing group then drafted a revised version of the manuscript and the revised version of the proposals was then submitted to the whole working group who voted for the proposals in a secret ballot. For each proposal, the members had to vote for one of the following five propositions: "I strongly disagree", "I tend to disagree", "I tend to agree", "I fully agree" or "I am not able to give an opinion". In the chapters that follow, the results of the vote are presented after each proposal.

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française (ANOCEF), Société française de gériatrie et gérontologie (SFGG), Association francophone des soins oncologiques de support (AFSOS), Société française d'hématologie (SFH), Société française d'anesthésie et de réanimation (SFAR) and ONCORIF (Regional oncology network in Île-de-France). Last, but not least, we would like to express our gratitude to Lead Up (Yasmina Dehane and Gildas Auffret) for coordination of the working group meetings and overall logistical support and Adam Doble for his invaluable help in medical writing.

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Disclosure of interest

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References

[1] Crobach MJT, Anijs RJS, Braekkan SK, Severinsen MT, Hammerstrom J, Skille H, et al. Survival after cancer-related venous thrombosis: the Scandinavian thrombosis and cancer study. Blood Adv 2023;7(15):4072–9.
[2] Ording AG, Skjoth F, Sogaard M, Hojen AA, Overvad TF, Noble S, et al. Increasing incidence and declining mortality after cancer-associated venous thromboembolism: a nationwide cohort study. Am J Med 2021;134(7):868–76.e5.
[3] Farge D, Frere C, Connors JM, Khorana AA, Kakkar A, Ay C, et al. 2022 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer, including patients with COVID-19. Lancet Oncol 2022;23(7):e334–47.
[4] Lyon AR, Lopez-Fernandez T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al. 2022 ESC guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Eur Heart J 2022;43(41):4229–361.
[5] Falanga A, Ay C, Di Nisio M, Gerotziafas G, Jara-Palomares L, Langer F, et al. Venous thromboembolism in cancer patients: ESMO clinical practice guideline. Ann Oncol 2023;34(5):452–67.
[6] Mahé I, Meyer G, Girard P, Bertoletti L, Laporte S, Couturaud F, et al. French guidelines for the treatment of cancer-associated venous thromboembolism – 2023 update. Respir Med Res 2023;84:101056.