

How well do European patients understand cancer-associated thrombosis? A patient survey

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ABSTRACT

Ongoing concerns regarding the morbidity and mortality from cancer-associated thrombosis led the European Cancer Patient Coalition (ECPC), the voice of cancer patients across Europe, to create a pan-European cancer-associated awareness patient survey to assess cancer-associated thrombosis (CAT) knowledge among a large population of patients with cancer. The ECPC survey represents the largest of its kind among patients/caregivers with CAT. It identified significant gaps in patient awareness and knowledge of CAT as well as a need for educational CAT-related discussions and interventions between healthcare professionals and patients with cancer and their caregivers. The aim of this paper is to highlight these gaps and to provide awareness of what/when information should be shared with patients/caregivers. Notably, the importance of providing information on how to reduce their risk of CAT, the role of anticoagulant prophylaxis and treatment (short- and long-term) including possible side-effects, and finally how to identify CAT symptoms early. Here we outline what type of information should be provided, as well as when and how to best discuss CAT with our oncology patients and their caregivers along the cancer care continuum, to reduce the risk of CAT and associated complications with a goal of improving patient outcomes.

Abbreviations

CAT	cancer-associated thrombosis
ECPC	European Cancer Patient Coalition
VTE	venous thromboembolism
CA	cancer

Simple summary

Patients with cancer are living longer with an increased risk for cancer- and treatment-related side-effects, including an increased risk for cancer-associated thrombosis (CAT). The aim of this pan-European patient survey was to assess patient awareness and knowledge about CAT, including risk factors, signs and symptoms and interventions, to better prevent and treat CAT. Highlighting key findings from the survey,

we outline the gaps and needs regarding who, when, and how information should be provided, as well as what type of information should be provided, to cancer patients and their caregivers to reduce the risk of CAT. It is important that the entire oncology multidisciplinary team participate in educating patients about CAT to help them participate in decision-making process and to improve patient outcomes. Education is best provided in a variety of approaches including a healthcare professional-patient encounter, printed material and digital/electronic/web based material. Speaking about CAT between patient, caregiver and healthcare professional along the whole continuum of cancer care provides a good model for prevention and treatment of CAT.

Introduction

The introduction of new treatments has contributed to improved

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overall survival for cancer patients. Many patients are living longer with their cancer and remain on systemic anticancer therapies longer (approximately two times longer), resulting in an increased risk for treatment-related long-term and latent side-effects, including blood clots [1]. Despite the fact that both cancer and its various treatments are well recognized risk factors for venous thromboembolism (VTE), thrombosis remains a major cause of morbidity and mortality in this population [2,3]. Data support that up to 20% of patients with cancer will experience VTE, which is approximately 4–5 times higher than the general population [4]. Unfortunately, despite the large body of evidence demonstrating the safety and efficacy of anticoagulants in the prevention and treatment of venous thrombosis in this population [5,6], it is well recognized that patients with cancer associated thrombosis (CAT) continue to have higher hospitalization rates with an increased risk of mortality, and decreased rates of thrombolysis, than in the general population [2,7,8]. The high rate of CAT suggests that, despite the clinical evidence and clear guideline recommendations for patients with cancer (ISTH, ASCO, ESMO, ASH), CAT prevention and recognition remain low among healthcare professionals [3,9,10]. Further, several patient surveys conducted between 2010 and 2017 have revealed that patients and their families were unaware of VTE as a complication of cancer and its treatment. Those surveyed expressed a desire to be educated about VTE symptoms, risk factors, prevention strategies and complications to better equip themselves in their cancer journey and improve their overall cancer outcomes [11,12]. Of note, while patients wanted to learn about the harm associated with VTE most indicated they preferred to receive the education in the context of a physician-patient encounter [11].

A roundtable including oncology healthcare professionals, policy-makers and patient advocates was convened to discuss and review the evidence regarding their ongoing concerns of excessive CAT associated morbidity and mortality, as well as patients' desire for greater CAT awareness. These discussions demonstrated that very little change had occurred over the years and that greater knowledge about CAT was still needed across the spectrum of healthcare practitioners and patients, particularly regarding primary and secondary prevention of thrombosis. Additionally, it was noted that improved communication throughout the entire cancer care pathway was required to raise awareness regarding CAT.

As a follow-up to this roundtable, the European Cancer Patient Coalition (ECPC), considered by many to be the voice of cancer patients across Europe, in collaboration with healthcare professionals and industry, created the first ever pan-European survey to assess the level of awareness of CAT risk, symptoms, treatments, and desired attributes for anticoagulation treatment among patients with cancer. This survey was designed to act as a baseline of CAT knowledge which could then inform and enable conversations about CAT with healthcare professionals as well as with patients with cancer. Future educational CAT-related interventions could then be compared to this baseline.

The entire ECPC survey result was originally released at World Thrombosis Day in October 2018 ([ECPC_2018_Cancer_associated_thrombosis_awareness_survey_report.pdf](#))

Here we focus on aspects of the survey that identify significant gaps in patient awareness and knowledge of CAT. Novel findings to communicate are further highlighted; specifically, these data suggest that patients have a poor understanding of their own CAT risk, symptoms of CAT, prevention, and treatment options for CAT. Hearing the patient and caregiver voice, healthcare professionals along the entire continuum of cancer care are encouraged to speak directly with greater frequency to their patients to educate them about CAT [13].

Results

Patient characteristics

There were 1365 cancer patients/survivors or caregivers who

responded to the survey.

Responses were received from 6 countries; Spain and the UK provided the highest proportion of responders (Germany ($n = 175$), Greece ($n = 267$), Italy ($n = 246$), Spain ($n = 332$), UK ($n = 324$), and France* ($n = 21$)). Of the responders, the majority (76%; $n = 966$) were cancer patients/survivors and were female (75%). About two-thirds of patients had cancer for > 1 year and $> 90\%$ were 45 years of age or older. Twenty four percent ($n = 299$) of survey participants had suffered from thrombosis associated with their cancer.

The dissemination of the survey was primarily through various online mechanisms (social media, email newsletters, website posts and media) with the majority of responders (68%; $n = 926$) hearing about the survey online. As information on the survey was widely disseminated online, it was not possible to calculate a response rate [13].

New findings from the 35-question survey are highlighted with a focus on the combined data from all survey respondents across countries. Overall, results are similar in the different countries surveyed.

Patient's awareness of CAT and CAT risk

The survey found that 72% ($n = 957$) of survey participants were unaware of the higher than normal risk of developing thrombosis in cancer patients. When asked to rate their overall understanding of CAT on a scale of 1 (low) to 10 (high), the mean score was 4.1/10. In fact, over half of respondents (55%) gave a rating of 4 or below (low understanding) and only 21% gave a rating of 7 or above (high understanding), (Fig. 1) [13]. The average rating was very similar in the different countries surveyed [13].

When asked about the risk factors for VTE, inactivity was the only risk factor that was recognized by more than half of the respondents. Less than half were aware of other risk factors, which were listed, that also increase the risk of thrombosis (Table 1). The average rating was very similar in the different countries surveyed [13].

First information about CAT

Survey participants responded that they had received information on CAT at a variety of time points through their cancer journey, with 35% of patients being made aware either immediately before or at their cancer diagnosis. Of particular concern, one quarter (26%) of respondents (the largest proportion) noted that they first became aware of cancer-associated thrombosis when they suffered a blood clot (Fig. 2 [13]). The average rating was very similar in the different countries surveyed [13].

CAT prevention and symptoms

Among those completing the survey, awareness of actions they could take to reduce the risk of thrombosis varied substantially with 87% ($n =$

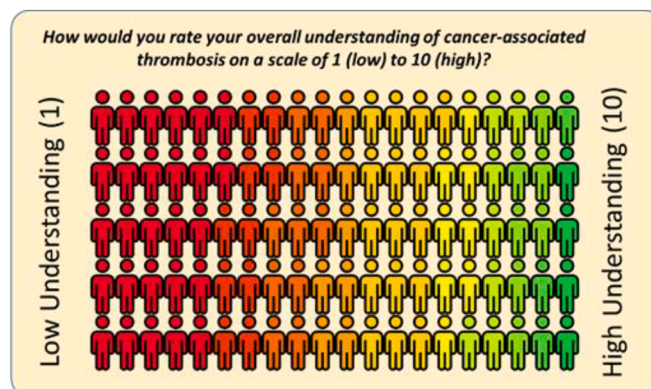


Fig. 1. Survey participant rating of their understanding of CAT.

Table 1
Participant understanding of risk factors for CAT.

Risk factor for cancer-associated thrombosis	Percentage of respondents completely aware
Inactivity for long periods of time*	65%
Previous thromboses	46%
Cancer surgery	35%
Chemotherapy	33%
Central venous catheter (central line)	23%
Radiotherapy	17%
Certain cancer types†	15%

* in bed \geq 4 days

† certain cancer types including cancers of the stomach, brain, kidneys, ovaries

325) of respondents indicating they were aware that taking a walk could reduce their risk (Fig. 3) [13].

Symptoms of CAT appeared to be relatively well known, with 73% ($n = 270$) of survey participants indicating that they were aware that swelling in the foot, ankle or leg could be a sign of deep vein thrombosis (DVT) and 71% indicating that shortness of breath could be a sign of

pulmonary embolism (PE) (Fig. 4). Other symptoms, however, were less well known with just over half (57%) of participants being aware that pain, cramping, and tenderness could be a sign of DVT. About one third (33%) knew that irregular heartbeat could be a sign of PE [13]. These results varied between countries, across conditions and between different symptoms; however, there was no discernable overall pattern [13].

Treating CAT

Over a third of respondents (37%) stated that they were currently using anticoagulants. Within this group, 60% were being treated for an existing clot and the remainder as VTE prophylaxis. It was noted that an equal number used an oral vs an injectable anticoagulant. Virtually all (96%; $n = 371$) knew that anticoagulants could be used to effectively treat thrombosis. However, only 41% ($n = 136$) had been informed about possible side-effects including increased bleeding risk. For those patients taking an anticoagulant, 22% had experienced side-effects from their anticoagulants and 9% had not been informed about what to do if

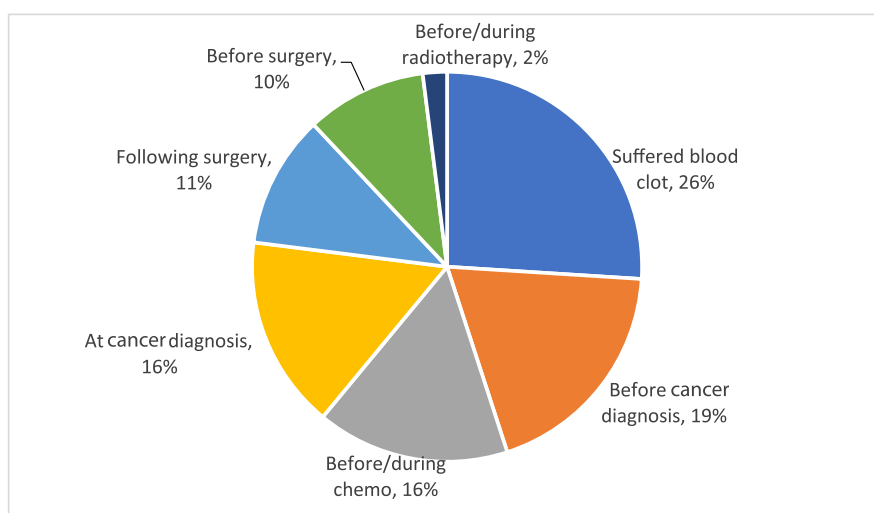


Fig. 2. First awareness of CAT.

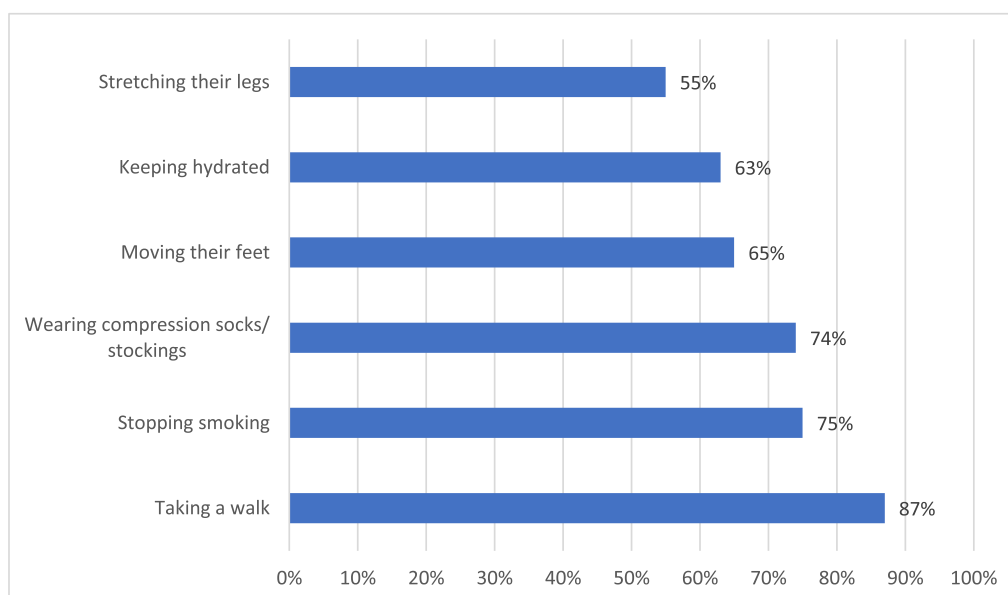


Fig. 3. Aware that action could reduce risk of CAT.

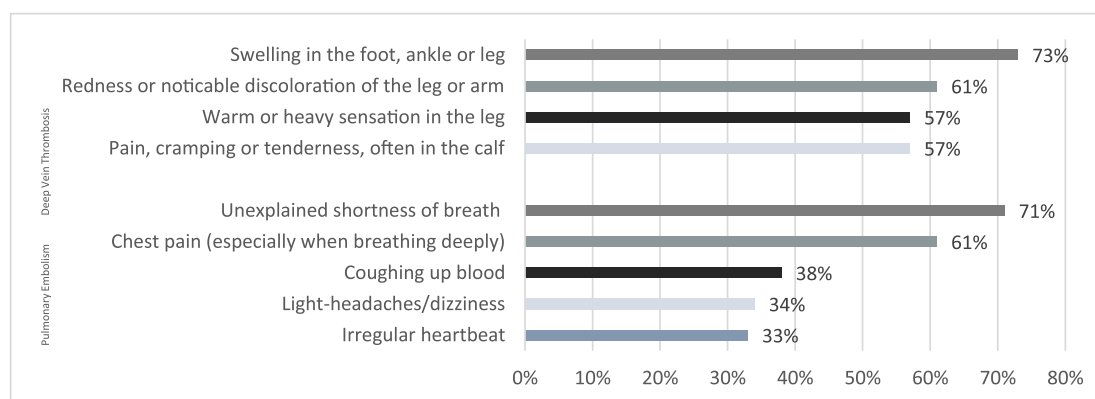


Fig. 4. Understanding of DVT/PE symptoms and what to look for.

side-effects occurred [13]. Some of these results varied between countries with the differences primarily related to how side-effects are reported within their healthcare system, i.e. contacting emergency services vs speaking to the patient's physician or nurse [13].

Discussion

Prior to the ECPC survey, little was known about European cancer patient awareness of thrombosis. The first key finding was that the vast majority of respondents reported that they were completely unaware that cancer patients have a higher-than-normal risk of developing cancer-related thrombosis. In fact, only 21% of patients indicated that they had a good understanding of CAT, supporting the need for improved CAT-related education throughout their cancer journey. The second key finding was that up to two-thirds of patients with cancer were not informed about their CAT risk nor educated by a healthcare professional on risk factors or signs and symptoms of CAT [13].

The data uncovered in this large ECPC survey ($N = 1365$) substantiate what has been found in previous evidence from both hospitalized patients and outpatients in the UK and USA. Despite the different methodologies used (survey of stakeholder organizations and qualitative patient interviews), these reports confirm that patients neither receive adequate teaching regarding thrombosis nor the potential harm associated with thromboses [11,12,14]. The PELICAN qualitative patient interviews ($N = 10$) further identified that CAT has not been afforded the same priority as other cancer complications which may be related to the long-term distress associated with CAT and may contribute to increased morbidity and mortality [12]. Similarly, a qualitative substudy of the select-d trial found that the majority of patient-participants were unaware of their increased CAT risk and attributed their CAT symptoms to side-effects of their cancer or its treatment. This led to a delay in presentation, diagnosis, and treatment for CAT [14]. Overall, those surveyed or interviewed received or preferred to receive education in the context of a doctor/healthcare professional-patient encounter [11,13,14].

More specifically, data uncovered in the ECPC survey suggest that information given regarding VTE risk, signs and symptoms, and treatment as well as treatment-related side effects must be provided at regular intervals by the entire oncology care team which includes physicians, nurses, and pharmacists. In addition, contact with patients during in-person and virtual clinical encounters, self-learning (e.g., internet resources and printed leaflets) should also be encouraged. This can be done through a local CAT pathway along the continuum of care (e.g., pre-surgery and chemotherapy encounters). There also exists a significant amount of online education material, although patients should be given guidance on which internet sites offer the most reputable information [15].

As previously uncovered in the PELICAN and select-d studies [12,14,

16,17] patients' experiences are an education in themselves, particularly for the oncology care team. Once the patient has a thrombosis, the opportunity for thrombosis prevention, which should be the most crucial focus of the care clinics (surgical, oncology and palliative care), is gone. Through this ECPC survey, we have learned about patient awareness and knowledge of CAT and their experiences with CAT prevention and treatment [13]. Oncology professionals, as well as other members of the patient's care team (e.g. internists, surgeons, nurses), need to perform better, at every stage of the patient's cancer pathway, to ensure patients are aware of CAT and their individual risk to develop a blood clot.

Importantly, the data from the ECPC survey has revealed that there needs to be clear communication between oncology professionals regarding who will provide CAT education, including when, and how often that education should be delivered along the continuum of cancer care. One successful model for CAT guideline implementation was the Venous Thromboembolism Prevention in the Ambulatory Cancer Clinic (VTE-PACC) program which incorporated a multidisciplinary team of oncologists, hematologists, pharmacists, and nurses, and an electronic health record-based risk assessment that was nursing driven. This care model used a multidisciplinary approach to focus on VTE risk assessment and prophylaxis in oncology patients leveraging multiple areas of expertise to ensure patients at high risk for developing a VTE were identified and educated about their risk and risk reduction options with a focus on optimizing clinical outcomes for each patient. This model led to an increase in VTE education and risk assessment from $< 5\%$ to $> 95\%$ of outpatients with cancer. Furthermore, 94% of high-risk patients received additional evaluation and recommendations for thromboprophylaxis. Successful implementation of VTE guidelines using a model such as this may significantly impact patient morbidity and mortality [18]. Data also support that the multi-disciplinary team approach ensures that patients are provided with the education and information to help them share in the decision-making process, and with improved patient engagement comes improved patient experience and outcomes [19].

Examples of Excellent CAT Patient Material vetted for UK and European Patients:

- [ECPC CAT- Be clot conscious](#)
- [Thrombosis UK](#)

CAT education tips

- In clinic, listening and teaching moments, followed by recommendations for websites to enable self-learning.
- Enabling multidisciplinary team, including community pharmacists, to provide VTE disease education (ClotAssist program) [20].

It is important that appropriate information about CAT risk should

also include lesser known but equally important factors, including cancer surgery, the use of central lines, and the increased CAT risks associated with specific cancers, chemotherapeutics, and radiotherapy. Patients need more information about actions they can take to reduce their risk of CAT, particularly those that are relatively easy and low cost to implement such as walking if possible and keeping hydrated. Further, patients should also be fully informed about symptoms of CAT and who to contact if they experience symptoms such as warmth, pain, swelling tenderness or redness in any extremity, particularly the calf or leg. For pulmonary embolism, symptom awareness should include chest discomfort, shortness of breath coughing blood, light-headedness/dizziness, and an irregular heartbeat [3].

Specific limitations with this survey have been identified. First, this was a self-reported assessment of cancer diagnosis and CAT awareness and, being voluntary, it may be that those who participated had a particular interest in VTE, possibly because of their experience as a patient or caregiver. Further, as the survey was only available to those in the UK and certain European countries, differences in the healthcare systems between countries may also impact the responses. The survey was primarily completed online (2% of completed surveys were paper copies), favouring patients with access to a computer, suggesting affordability and health status. As well, not all questions were answered by all respondents, resulting in missing data which could potentially have impacted analysis, and finally there is a lack of comparator population. However, similarities between the answers from participants across multiple countries lends credibility to the understanding and development of consistent themes [13].

Materials and methods

The cancer-associated awareness patient survey was initiated by the ECPC in conjunction with other relevant member organizations to identify themes and develop questions to better understand awareness of CAT. The survey, consisting of 35 questions, was conducted by Quality Health on behalf of the ECPC between April and Sept 2018 in 6 countries (UK, France, Germany, Greece, Italy and Spain). The survey questions included contextual questions (demographic information/status of treatment) as well as questions aligned along treatment pathways (diagnosis, testing, status of treatment) regarding from whom and how information on CAT was acquired and could be answered by cancer patients/survivors or their caregivers. The questions provided pre-defined answer options based on best principles for surveys to ensure optimal responses. The survey was set up on Quality Health's bespoke on-line survey system, with the survey and accompanying introduction information translated to French, German, Greek, Italian and Spanish. Dissemination of the survey was carried out through ECPC's membership network using social media, email newsletters, website posts, and through media work. Completion of the survey implied informed consent. The research was considered ethics review (IRB) exempt as it involved research in which persons chose to anonymously complete an online survey [13].

Data analysis: A three-stage process was undertaken in the development and analysis of the survey including development and beta-testing of the questions and platform, patient completion in 6 EU countries, followed by a thorough analysis and reporting of the findings with an overall summary (combined data from all respondents in all countries) as well as an analysis by country. Percentages are calculated after excluding those participants that did not answer that particular question. All percentages are rounded to the nearest whole number. When added together, the percentages for all answers to a particular question may not total 100% because of this rounding. Data is included in the overall findings; a separate analysis of the French findings was not completed as numbers would not allow for robust statistical analysis [13].

Conclusion

It is evident from this large survey of cancer patient/survivors that oncology professionals need to better understand the gaps in patient knowledge regarding cancer-associated thrombosis. Further, healthcare professionals need to provide education to patients across the continuum of care to improve patient outcomes. We have a collective responsibility using the ECPC patient survey as a baseline to inform patients with cancer on how to identify signs and symptoms of CAT to enable faster diagnosis and treatment. Improved education regarding the benefits and risks of using anticoagulant therapy also needs to be emphasized. An example of a successful patient education model implemented throughout the continuum of care that could be adapted and implemented in cancer centers across Europe, has been provided. We have also suggested excellent evidence-based online resources that be readily accessed by healthcare professionals. Ultimately, patient outcomes will be improved if we recognize and develop cogent strategies to educate our patients on the risk factors, treatment and treatment-related side effects associated with blood clots in cancer patients.

CRediT authorship contribution statement

Anna Falanga: Conceptualization, Visualization, Methodology, Writing – review & editing. **Charis Girvalaki:** Visualization, Writing – review & editing. **Manuel Monreal:** Conceptualization, Visualization, Methodology, Writing – review & editing. **Jacob C Easaw:** Conceptualization, Visualization, Methodology, Writing – original draft, Writing – review & editing. **Annie Young:** Conceptualization, Visualization, Methodology, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Anna Falanga, declaration of conflicts: participation in corporate symposia and advisory board meetings for Sanofi, Bayer, LEO Pharma, and Pfizer. Charis Girvalaki, no conflicts of interest to declare. Manuel Monreal, has received unrestricted educational grants for research from Sanofi, LEO Pharma and Rovi, as well as honoraria for advisory meetings from Sanofi and LEO Pharma and fees for lectures or presentations from Sanofi, LEO Pharma, Pfizer and Alfa-Sigma. Jacob C. Easaw, has received honoraria for speaking from Amgen, Elvium, and LEO Pharma. Annie Young, has received honoraria from LEO Pharma, BMS/Pfizer Alliance, and Chugai, as well as an unrestricted educational grant from Bayer.

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