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Full Length Article

“No one told me anything about it and I cannot explain it”: Illness perception in symptomatic and asymptomatic patients with cancer-associated thrombosis

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ABSTRACT

Introduction: Patients with cancer, have reported cancer-associated thrombosis (CAT), a distressing event in their overall illness. However, whether the clinical presentation of CAT; symptomatic versus asymptomatic, impacts illness perception is poorly elucidated. The aim of this study was to explore illness perception in patients with CAT, stratified by the clinical presentation.

Materials and methods: In a qualitative design, we conducted a three-step workshop. Patients were included from a specialised cardiology care unit for oncology patients. Data analysis was performed using framework analysis. The analytic framework was based on the five components of illness perception: (1) identity of illness, (2) causal beliefs, (3) timeline beliefs, (4) beliefs about control/cure and (5) consequences.

Results: Eleven patients with CAT participated in the workshop; five symptomatic and six asymptomatic. Within each category of illness perception following notions emerged (1) the identity of CAT was *only* tangible for symptomatic participants, (2) the aetiology was considered important information for symptomatic participants, which was in contrast to asymptomatic participants, (3) asymptomatic participant did not consider recurrent CAT a threat towards their health, (4) asymptomatic participants were prone to information overload, whilst information was imperative to the sense of control in symptomatic participants, (5) low molecular weight heparin treatment was accepted in symptomatic participants due to remission of symptoms.

Conclusions: The clinical presentation of CAT (asymptomatic/symptomatic) proved essential to illness perception. These findings indicate that information level and communication within the medical consultation, should actively consider the clinical presentation of CAT in order to optimize management and compliance.

1. Introduction

Cancer associated thrombosis (CAT) remains the number one cause of mortality during chemotherapy treatment and the second most common cause of mortality in all cancer patients [1,2].

However, with the widespread use of high-resolution computed tomography (CT) in disease staging and monitoring, the frequency of incidental, clinically unsuspected, and usually asymptomatic pulmonary embolism (PE) is increasing [3]. Studies have shown that patients with cancer consider venous thromboembolism (VTE) a distressing experience within the context of their cancer disease [4]. However, whether the clinical presentation of CAT (symptomatic versus asymptomatic) impacts illness perception in these patients is poorly elucidated. Illness

perception is typically influenced by symptoms, which usually initiates a quest towards a diagnosis that matches the symptoms. Conversely, when given a diagnosis, the pursuit for symptoms initiates – even when the illness may be asymptomatic. Hence, symptoms are a tangible way for patients to monitor their illness and guide medication use [5]. When absent, engagement in self-care behaviour can be a challenge, e.g. as shown in patients with hypertension, where non-adherence and unwillingness to make behavioural changes is notable [6–8]. The coping strategies activated by such health issues are based on personal experience and medical knowledge. However, these are not always appropriate, given the rudimentary nature of knowledge patients possess on medical issues [9]. Indeed, one study, which randomized CAT patients after six months anticoagulation to low molecular weight heparin

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(LMWH) or no anticoagulant, found cancer patients with little or no VTE symptom burden to decline participation because they did not want to receive LMWH [10]. This insinuates a difference in illness perception driven by the clinical presentation of CAT. Alignment of illness perception between physicians and patients is the key to improved communication in medical consultations and adherence to treatment [11]. Thus, exploring and identifying possible differences in illness perception is crucial for optimal management and compliance, especially in a complex clinical situation as CAT [4].

Thus, the aim of this study was to explore illness perception in patients with CAT, according to clinical presentation; symptomatic versus asymptomatic.

2. Methods

Since the aim of the study was exploratory, a qualitative design with a workshop in three steps was chosen (Fig. 1). This approach provided a platform for interactive communication, which allowed participants to use the ideas of others as cues to express their own views and facilitated discussion on opposing views. Thus, experiences are shared and opinions voiced, that might not surface during individual interviews. The study was designed and reported according to the Consolidated criteria for reporting qualitative research [12].

2.1. Participants

Workshop participants were recruited from the thrombosis unit at Herlev-Gentofte University Hospital, Denmark. Patients with an outpatient contact from September 1st 2021 to December 1st 2021 were eligible for inclusion and approached by telephone. Inclusion criterions were met if patients were diagnosed with a CAT and treated with either LMWH or direct oral anticoagulants (DOAC). Exclusion criterions included cognitive impairment or/and inability to speak- or understand Danish. Maximum variation in sampling was sought to ensure a population covering the multiple perspectives and complexities of illness-perception. Hence, a purposeful sampling was performed with respect

to gender, age, cancer type and clinical presentation of CAT. Sample size was determined based on standards of qualitative analyses; meaning that a sample rich on information relevant to a specific subject, requires fewer participants [13].

2.2. Data collection

The workshop was conducted at Herlev-Gentofte University Hospital for a duration of 120 min. The workshop was directed and facilitated by three of the authors (NN, CS and AH). The workshop was conducted in three steps, following a brief introduction by the facilitators (Fig. 1). In *step one*, participants created cognitive maps, visualising mental hurdles in their course of illness. Participants were provided pictures representing different emotions and events, along with blank cards to fill as desired. The participants choose pictures, which they felt were related to their course of illness and placed them on a piece of paper. Participants were, hereafter, instructed to draw lines between pictures, indicating associations. Lastly, patients were instructed to draw circles or plus signs, in which the size of the circles or the number of plusses, indicated the significance of a given event or emotion (Fig. 2). In *step two* participants were divided into groups based on the clinical presentation of CAT. Within these groups participants shared elements from their cognitive maps and elaborated on the thoughts behind. The facilitators stimulated the dialogue within the groups. *Step three*, included a collaborative discussion, led by NN and AH, between all participants, so the nuances of the clinical presentation of CAT could emerge.

2.3. Data analysis

Transcripts were typed into a Word document and uploaded to NVivo 20 computer software for data management and analysis [14]. Data analysis was performed by NN, CS and AH using framework analysis. This was considered the most appropriate analytic method, enabling a deductive approach when creating an analytic framework based on the components of illness perception (comprising five components: identity of illness, causal beliefs, timeline beliefs, beliefs about

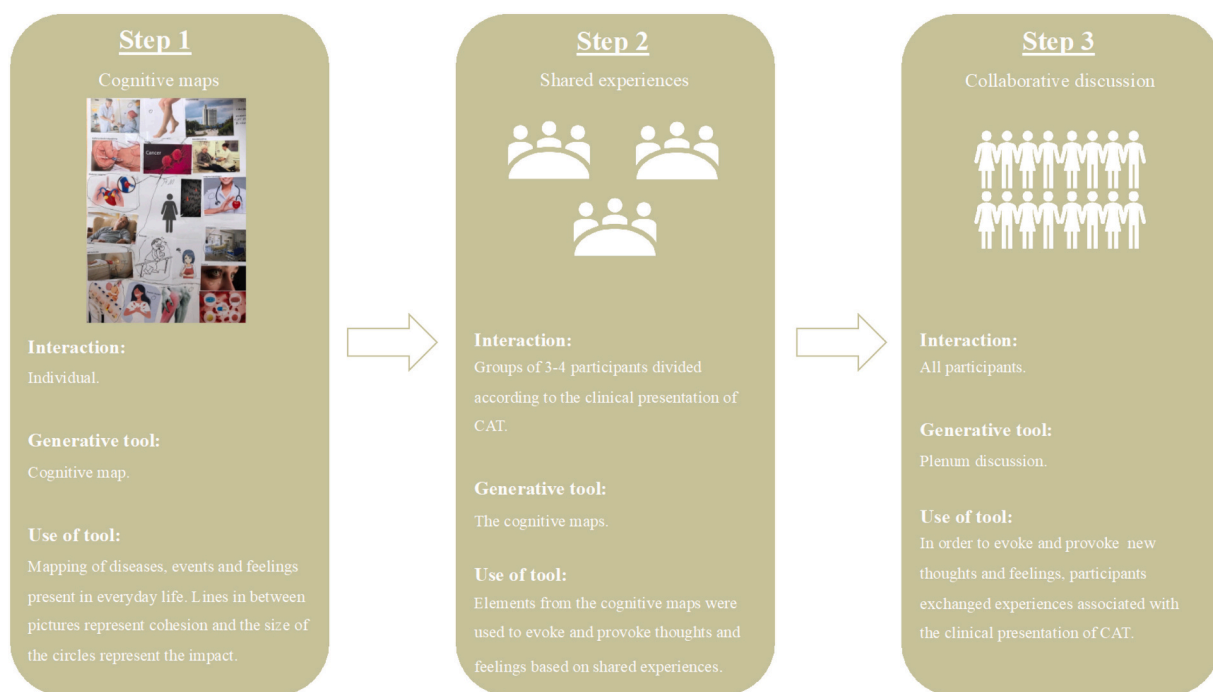


Fig. 1. Description of the elements in the workshop process. The workshop was conducted in three steps. In the first step, participants developed cognitive maps. In the second step, participants shared their experiences using their cognitive maps. In the third step all participants participated in a collaborative discussion.

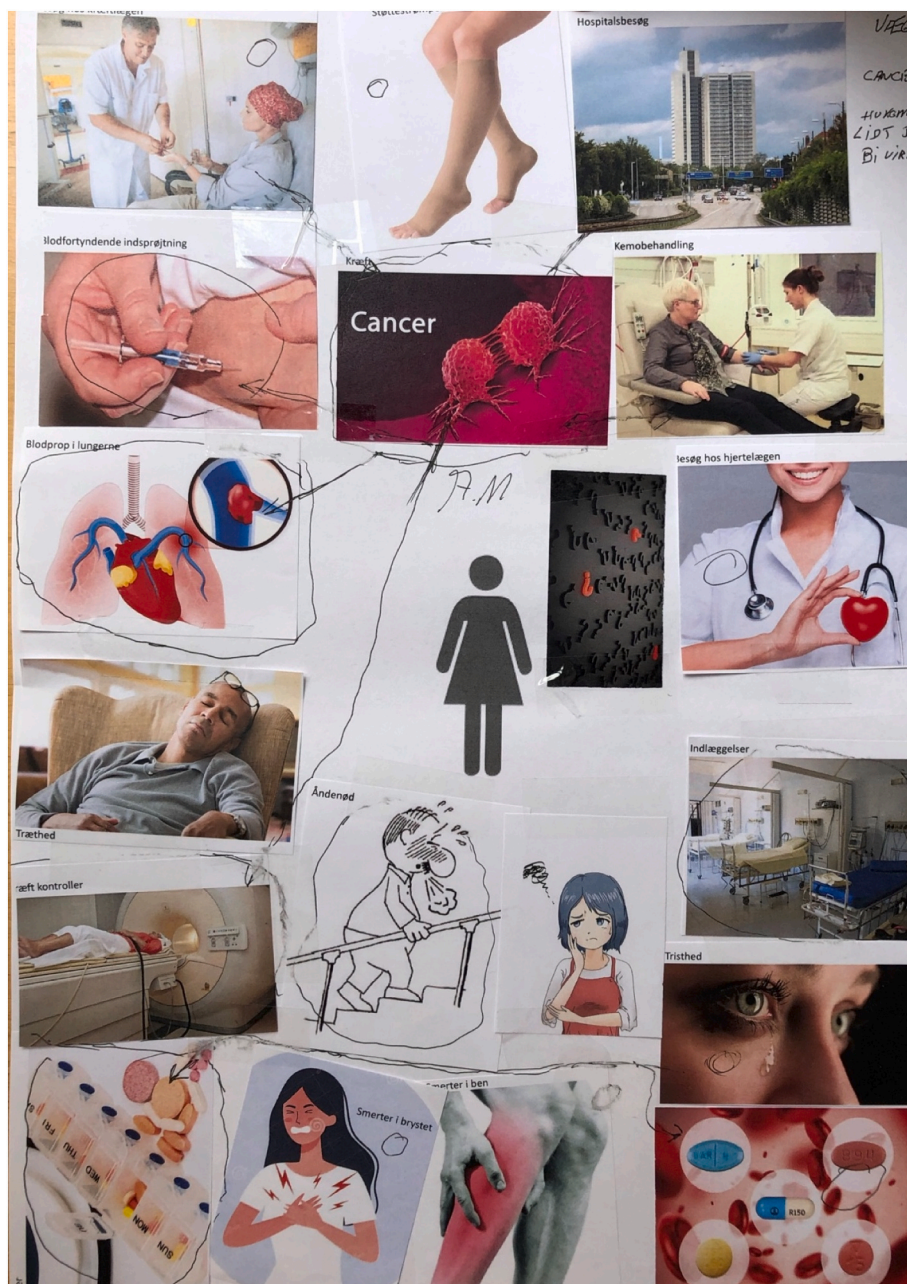


Fig. 2. Example of a cognitive map. An example of a cognitive map developed by one participant.

control or cure and consequences [11]), whilst also allowing room for inductive observations [15]. Framework analysis is comprised of five interconnected stages that provide clear guidance of data analysis:

1. Familiarization with data: Listening to recordings, re-reading transcripts and cognitive-maps, and listing key ideas and recurrent themes.
2. Identifying themes: In our study the thematic framework was given by the components of illness perception. Nonetheless, we identified subthemes by an inductive approach by reviewing data and identifying key issues and concepts raised by the respondents.
3. Indexing data: At this stage, we took the themes and subthemes and applied them to our transcripts using qualitative coding. Hence, we divided our transcripts into manageable portions and coded these sections with themes and sub-themes developed in the previous step.

4. Charting and summarizing data: A matrix in which, each column is a theme/subtheme and each row is a transcript linked to a theme/subtheme. The last column of the matrix is a summary of the findings from each participant and the last row of the matrix is a summary of the theme/subtheme.
5. Mapping and interpretation of data: This step involves an overview across the transcripts to obtain a more thorough understanding of the aim of the study. Lastly, this step includes a selection of relevant and appropriate quotes (see supplementary Table 1)

To ensure trustworthiness of our findings, the analysis was conducted in Danish before translating quotations into English. Danish quotations and English translations are presented in Supplementary Table 2.

2.4. Ethics

All participants were informed of the study aim and process. Oral consent was retrieved at inclusion, followed by a written consent prior to the workshop. Participants preserved the right to withdraw their consent at any given time. The study was conducted in compliance with the Capital Region at Knowledge Center for Data reviews (File no. P-2021-653). Other approvals were not necessary according to Danish legislation.

3. Results

We contacted 32 patients from the thrombosis unit at Herlev-Gentofte University Hospital, Denmark. Of these, 11 patients agreed to participate in the workshop; six participants had asymptomatic CAT and five had symptomatic CAT. Participant characteristics are presented in Table 1. Median age was 74.5 [67.0–77.5] for the asymptomatic participants and 66.0 [65.0–70.0] for the symptomatic participants. The median year since cancer diagnosis was 6.0 [1.8–11.0] for asymptomatic participants and 2.5 [1.5–8.0] for symptomatic participants. The majority of patients were treated with a DOAC (83.3 % of asymptomatic participants and 40 % of symptomatic participants), however for all participants anticoagulant treatment was initiated with LMWH.

The five themes given by the components of illness perception constructed our thematic framework; (1) identity of illness, (2) causal beliefs, (3) timeline beliefs, (4) beliefs about control or cure and (5) consequences.

3.1. Identity of illness

The sense that CAT was a secondary disease in comparison to the cancer disease was prominent in the participants illness perception regardless of CAT presentation (symptomatic/asymptomatic). Nevertheless, the symptomatic participants defined CAT through their symptoms and saw it as a consequence of their cancer disease and a sign of progression of their cancer. A symptomatic participant explained: “[...] I was surprised by it [CAT], to have it in addition to the cancer diagnosis, has been a mental burden, in the sense that it is downhill from here”. Whilst the asymptomatic participants found it challenging to identify the CAT, one participant said: “I did not think of it [CAT] as anything special, not that I do now, but I am more aware of what it is”. Thus, the identity of CAT was tangible for participants with symptomatic CAT, whilst it seemed as if CAT did not really exist in the illness perception of asymptomatic

participants.

3.2. Causal beliefs

All together there was a notion that the participants, themselves, had to be proactive in order to understand the aetiology behind the CAT regardless of the clinical presentation. However, the symptomatic participants presented very plausible aetiologies, such as cancer, immobility and side-effects to chemotherapy, whilst the asymptomatic participants expressed that they did not know what might have caused the VTE. One asymptomatic participant said: “No one told me and I cannot explain it. I didn't feel it at all”. Thus, for the symptomatic participants it was important to understand the aetiology, hence they searched for answers themselves. On the contrary, asymptomatic participants seemed unconcerned towards the aetiology.

3.3. Timeline beliefs

There was a rather short timeline belief, in the sense that all participants believed they were cured from the CAT, however this was based on different perceptions. Symptomatic participants made the assessment based on the regression of symptoms, as one participant said: “I believe I am cured now. The swelling is gone, so I believe the medication has worked”, while asymptomatic participants simply trusted that the given medicine was efficient.

Another aspect of timeline beliefs was the possibility of recurrent events. Symptomatic participants thought anxiously of recurrent events, though there was a perception that this would not occur with continuous treatments. The asymptomatic participants almost unitedly agreed that the CAT was irrelevant to their prognosis and they were neither anxious or afraid of recurrent events. One asymptomatic participant explained:

“When I ask about the treatment [anti-cancer treatment], they say: ‘It's experimental treatment’, that's why the cancer consumes a lot. The blood cloths, well, I'll take my medicine and we'll see how it goes. The other thing [cancer], will be my death”.

Thus, the symptomatic participants, acknowledged the dangers of VTE and potential recurrent events, whilst asymptomatic patients did not consider the VTE as a serious threat towards their health, hence recurrent events were only discussed in the context of continuous treatment.

Table 1
Characteristics of participants.

Informant	Presentation	Age	Gender	Living status	Smoking	Cancer type	Year of cancer diagnosis	Metastasis	Location of VTE	Current treatment
Informant 1	Asymptomatic	42	Female	Not alone	Former smoker	Malignant melanoma	2013	Yes	Legs	DOAC
Informant 2	Asymptomatic	78	Male	Not alone	Never	Prostate	2009	Yes	Lungs	DOAC
Informant 3	Symptomatic	74	Female	Not alone	Smoker	Lymphoma	2006	No	Legs	DOAC
Informant 4	Symptomatic	63	Female	Not alone	Former smoker	Lung	2019	Yes	Lungs	LMWH
Informant 5	Symptomatic	66	Female	Not alone	Former smoker	Breast	1998	Yes	Lungs	LMWH
Informant 6	Asymptomatic	73	Female	Not alone	Former smoker	Kidney	2017	Yes	Lungs	LMWH
Informant 7	Symptomatic	70	Male	Not alone	Former smoker	Prostate	2018	Yes	Legs and lungs	LMWH
Informant 8	Symptomatic	65	Male	Alone	Former smoker	Gastrointestinal	2021	No	Lungs	DOAC
Informant 9	Asymptomatic	78	Female	Alone	Former smoker	Ovarian	2020	Yes	Lungs	DOAC
Informant 10	Asymptomatic	76	Female	Not alone	Never	Ovarian	2000	No	Lungs	DOAC
Informant 11	Asymptomatic	65	Male	Not alone	Smoker	Lung	2021	No	Lungs	DOAC

3.4. Beliefs about control or cure

Altogether there was a notion that information on CAT *after* the event was imperative to the sense of control regardless of the clinical presentation of CAT. In the absence of information, participants required supporting imaging to reassure that the given anticoagulant treatment was effective. A participant said:

“This is why information is so important; what is the situation I am currently in and why am I in it? If I understand that, then I feel safer and I can act based on knowledge, right?”

For the symptomatic participants knowledge *prior* to the event was also important, because there was a sense that this would have reduced the time to diagnosis. As explained by a symptomatic participant: “*If I knew I was at risk or if I knew the symptoms, then I would not have waited for the swelling to clear itself*”. However, the asymptomatic participants were more ambiguous towards information regarding the VTE prior to the event:

“I think there is a reason for the reluctance in giving us all the information. Yes, my adrenal gland is not working now, I can't taste anything and I was suddenly diagnosed with a blood clot, which apparently came from the medication that fights the cancer, but if they were to inform us of all that...”

Thus, for the symptomatic patients, information about VTE prior to the event was imperative to their sense of control, conversely asymptomatic patients were more ambiguous towards information regarding VTE prior to the event.

3.5. Consequences

Regardless of the presentation of CAT, participants expressed that the transdisciplinary collaboration between oncologists and cardiologists failed, forcing them to take charge. As a participant voiced: “[...] *It is really hard. It forces you to be the project manager of your own disease, juggling all balls at once. It affects my everyday life*”.

Another subject of interest was the LMWH injections. Most participants described the treatment as intrusive, however, there was a sense of acceptance in participants with symptoms. One symptomatic participant said “*It [injections] was intrusive, however I could see my symptoms wear off, so there was definitely an effect*”. In contrast, asymptomatic participants had a hard time accepting the injections and there was a sense of frustration in having to engage in yet another disease and treatment. One of the asymptomatic participants voiced:

“[...] But I couldn't feel any difference, not before the incidence, not after and not now. So, it is a bit, well okay, is it [blot clot] still there or what? I certainly don't know. When you don't feel anything, it is like, well okay...”

Thus, the symptomatic participants expressed acceptance of the treatment, because they could see their symptoms regress, whilst the asymptomatic participants saw no effect, making them reluctant towards the treatment.

4. Discussion

In this study of illness perception in patients with CAT, we found the components of illness perception to be influenced by the clinical presentation of CAT (symptomatic/asymptomatic). In a setting where another serious condition co-exists with the VTE, we found asymptomatic participants to perceive CAT as a minor event in the overall course of their cancer disease, which was in contrast to the symptomatic participants who perceived CAT as a significant event.

When asked to explain the identity of CAT, we found symptomatic participants to define CAT through the relevant symptoms, indicating that for symptomatic participants, CAT was made tangible through their

symptoms. Conversely, for the asymptomatic participants CAT did not have an identity nor did it consume any thoughts. The asymptomatic participants made no effort in identifying symptoms which they believed were associated with their disease. This is in contrast to previous findings, where asymptomatic participants are consumed by the need to find symptoms or labels that match their disease [5]. This discordant finding may reflect that the theory on illness perception provided by Leventhal et al. does not assess the clinical situation in which another serious condition co-exists.

Moreover, symptomatic participants were proactive in terms of understanding why they had a CAT, in order to control and prevent recurrent events. The asymptomatic participants were indifferent in regards to the aetiology, since the thought of recurrent events did not occupy their minds. Our observations in the symptomatic participants were in line with previous findings, in which the primary concern was the cancer diagnosis and secondly a low recurrence rate [16], and thus differed significantly from our findings in the asymptomatic participants. These findings emphasize, the importance of implementing the clinical presentation of CAT, when informing of- and treating patients with CAT, because the level of information needed in the medical consultation differs accordingly.

The sense of control in these participants was highly associated to the level of information they received. However, we found an element of information-overload predominately in the asymptomatic participants. Information overload is a complex phenomenon and the factors it comprises is not fully investigated [17,18]. In this context, the clinical presentation of CAT seemed to influence the limit to which information overload was reached. In the symptomatic participants, information seemed imperative to the sense of control and the limit of information overload was never reached, whereas symptomatic participants were more comfortable being on a need-to-know basis.

In the study by Noble et al., patients reported administration form as the fourth most important attribute of their VTE treatment [16]. This challenged previous perception of LMWH being unacceptable and burdensome to some patients [19–21]. Our study further complicates these notions, by adding an extra element; the clinical presentation of CAT. We found symptomatic participants to be more accepting and understanding of the treatment they were offered, which mainly relied on the regression of symptoms. The asymptomatic patients were more reluctant to use LMWH, because the disease itself and the effects of the treatment were invisible, hence in these participants tablet treatment wins primacy.

The participants voiced discontent in regards to the transdisciplinary collaboration between cardiologist and oncologists. The unit from which the participants were recruited, is a specialised cardiology care unit for oncology patients. Nonetheless, participants still felt they had to take charge themselves, in order to be adequately treated and informed. Altogether, indicating that this issue could be more pronounced in non-specialised units, whilst emphasizing the importance of a well-developed transdisciplinary collaborations, which is homogenous and well-coordinated.

4.1. Clinical implications

The differences in illness perception calls upon a more individualized approach when encountering patients with CAT. We know that there is not a one-size-fits-all model and likewise it is very difficult to tailor the medical consultation completely to accommodate each individual. However, our findings provide insights which can help the medical consultation by a simple stratification of the clinical presentation. In this population, recurrence rates are and compliance is a key factor [1,22]. Thus, patient education and counseling are crucial, especially in patients with asymptomatic CAT, to reduce recurrence rates, by both enhancing compliance and reducing modifiable risk factors. Patients with symptomatic CAT are more mentally burdened by the diagnosis, hence psychological support to assist coping strategies are relevant.

4.2. Strengths and limitations

The qualitative exploratory design applied in this study is a well-established method to gain insight into patients' thoughts, experiences, perceptions and attitudes [23] and this is the first study investigating illness perception in patients with CAT stratified by the clinical presentation (asymptomatic/symptomatic). Nonetheless, this design has limitations. Firstly, the findings of this study are not generalizable, but transferrable to similar settings and to patient groups where two serious conditions co-exist.

One-third of patients recruited from the thrombosis clinic were included in the study. The low inclusion rate, was primarily due to the frailty of the patient population. A substantial number of these patients were terminal, making attendance strenuous.

The notion that the clinical presentation of a diagnosis is essential for illness perception is not well-sought out in the literature and studies from more heterogeneous populations are needed to generalize our findings.

5. Conclusion

In conclusion, the clinical presentation of CAT (asymptomatic/symptomatic) proved essential to illness perception. The findings of this study indicates that the information level and communication within the medical consultation, should actively consider the clinical presentation of CAT. There is no one-size-fits-all solution to obtain the optimal consultation, but this study provides insights into an overlooked aspect which sought to be considered.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: AAH reports consulting fees from Bayer and The Bristol-Myers Squibb-Pfizer Alliance, and speaker bureaus from Bayer, The Bristol-Myers Squibb-Pfizer Alliance, and MSD, ML reports Speaker fees from BMS and Bayer.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.thromres.2022.10.013>.

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