

REVIEW

Quality of life in oncological patients with venous thromboembolic disease

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Abstract

Venous thromboembolic disease (VTE) is a significant medical problem in cancer patients, as it is associated with substantial morbidity and increased mortality. Cancer survivors with VTE experience important changes in their health-related quality of life (HRQOL). Over the past few years, HRQOL and its measurement have been incorporated in clinical studies of anticoagulation therapy, as well as in qualitative and quantitative studies for the examination of the impact of VTE in cancer patients. While there are several tools available to assess HRQOL, few are specific to cancer patients and VTE. More importantly, those same tools are yet to be incorporated in routine clinical practice. The purpose of this review is to describe the available tools for the assessment of HRQOL in cancer patients with a focus on VTE, as well as the characteristics of those tools, their strengths, limitations, and potential applicability in clinical practice.

KEYWORDS

anticoagulation, cancer, outcomes, quality of life, venous thrombosis

Essentials

- Venous thrombosis (VTE) in cancer can lead to significant impairment in quality of life (QOL).
- Few instruments to measure QOL in cancer explore the impact of VTE.
- The impact of VTE on the QOL of cancer patients has been explored using qualitative methods.
- Research is needed to guide interventions to improve care and QOL in cancer-associated VTE.

1 | INTRODUCTION

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), affects about 1 to 2 individuals per 1000 person-years in Europe and the United States. About 20% of these patients die within a year after VTE, and among survivors, complications occur frequently [1]. The high mortality and complication rates dictate timely diagnosis and proper treatment of VTE. Moreover, evaluation of quality of life in patients with VTE deserves attention given that the number of VTE survivors worldwide is large.

Over the past few years, the concept of health-related quality of life (HRQOL) has been increasingly reported in the scientific literature. Researchers and clinicians have reached a broad consensus regarding what should be considered in HRQOL measurement. HRQOL is an individual's perception of health in 5 different domains: physical, functional, psychological, social, and spiritual [2,3]. Given that researchers have developed a wide variety of scales for measurement of HRQOL over the past decade, comparison of studies of HRQOL has become more difficult, as has selection of the most appropriate instruments for HRQOL assessment in clinical practice. Additionally, a

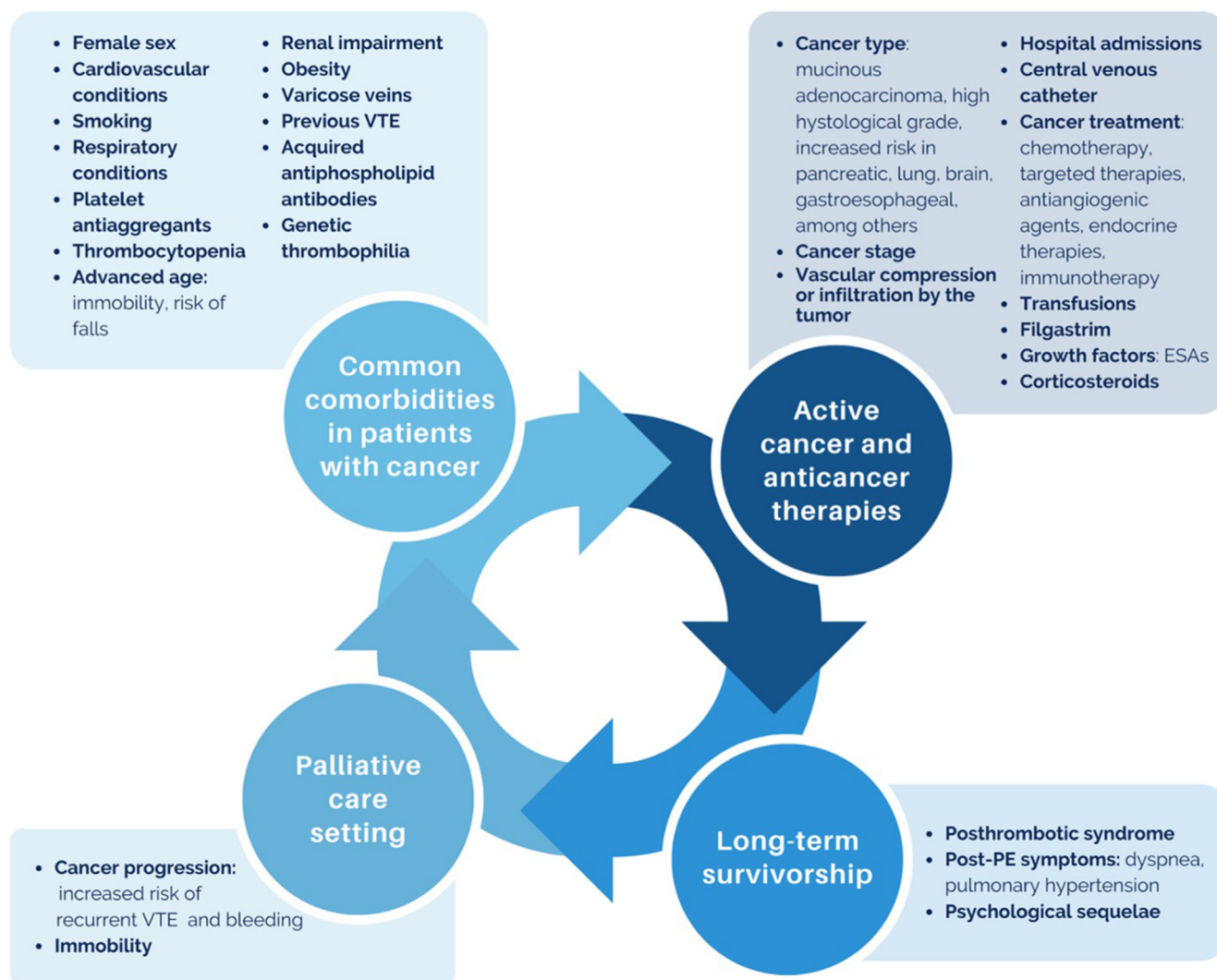


FIGURE Several concomitant risk factors for both cancer-associated thrombosis and bleeding may occur in patients with cancer that vary during the patient's journey overall influencing quality of life. ESAs, erythropoietic stimulating agents; PE, pulmonary embolism; VTE, venous thromboembolism.

much lesser consensus exists regarding which tool should be used for the evaluation of HRQOL for specific pathologies or targeted population groups [2].

Regarding HRQOL assessment tools for VTE patients, a recent systematic review of questionnaire development and methodology for HRQOL instruments demonstrated that no instrument fulfills all of the basic requirements for this type of questionnaire [4]. Focusing particularly on patients with cancer-associated thrombosis (CAT), a specific instrument aimed at evaluating the impact of VTE on HRQOL has yet to be developed. In recent years, researchers and clinicians have tended to differentiate CAT from VTE in the general population for several reasons, including aspects of underlying biological characteristics, epidemiology, and research, as well as their clinical features and treatment. Highlighted below are some of the factors that justify the differential study of patients with CAT.

- There is an increased and growing epidemiologic burden of CAT [5]. At least 1 in 5 VTE events is associated with cancer, and the

incidence of VTE is increasing in cancer patients, whereas it has remained steady in the general population [6,7]. VTE is diagnosed in 5% to 20% of cancer patients during their disease courses, which has resulted in an increase in morbidity [8]. Moreover, thrombosis is a leading cause of death in patients with cancer [6,9].

- There is a greater difficulty in managing VTE in patients with cancer owing to increased risk of death, recurrence of VTE, and bleeding complications than in patients without cancer [10,11]. This has led to the development of specific clinical trials of anticoagulation therapy for VTE in this population and to the current indications for extended treatment durations (>3 months, usually years) with low-molecular-weight heparin (LMWH) [12] and, in recent years, direct oral anticoagulants [8,13–15].
- Multiple varied prothrombotic risk factors exist related to the type and extension of the tumor and to the cancer treatment performed (eg, surgery, chemotherapy, hormone therapy, antiangiogenic treatments, erythropoietin administration, central venous catheter use, and hospitalization). Furthermore, many cancer patients in the

TABLE 1 Factors influencing the decision for extended anticoagulation beyond 3 to 6 months in patients with cancer-associated VTE.

Favors continuation of anticoagulation	Favors stopping anticoagulation
High prothrombotic malignancy-specific risk (ie, metastatic pancreatic or lung cancer, active cancer, cancer progression)	Low prothrombotic malignancy-specific risk (ie, localized breast or prostate cancer, cancer remission)
Systemic prothrombotic therapies (ie, chemotherapy and/or ESA, tamoxifen)	VTE burden (non-life-threatening symptoms, incidental asymptomatic VTE, absence of residual vein thrombosis)
VTE burden (previous history or recurrent VTE, acute symptomatic PE, massive DVT, severe postthrombotic syndrome)	
Low bleeding risk	Primary concern is bleeding or high bleeding risk
Primary concern is recurrence	(previous history of bleeding, anemia, renal impairment, concomitant antiplatelet use)
Additional prothrombotic conditions (obesity, female sex, poor performance status, central venous catheter)	Provoked index VTE event (related to a factor that reversed; ie, surgery, prolonged hospital admission)

Adapted from Zwicker and Bauer [17] and Sanfilippo et al. [11].

DVT, deep vein thrombosis; ESA, erythropoietic stimulating agent; PE, pulmonary embolism; VTE, venous thromboembolism.

Western world have additional thrombotic risk factors, such as advanced age, immobility, and obesity [16]. Cancer patients may also have multiple varied bleeding risk factors related to tumoral hypervascularization, thrombocytopenia, and/or invasive diagnostic and treatment procedures. The number and variability of the thrombotic and bleeding risk factors hinder decision-making regarding primary and secondary thromboprophylaxis and may affect issues related to HRQOL in this population (Figure) [11,17].

- Incidental VTE and VTE in other atypical locations, such as in association with a central venous catheter or involving cerebral veins or splanchnic territories, occur more frequently in cancer patients [11,18].
- Exponential development of new antitumor treatments over the past decade has contributed to progressive increases in the survival and clinical complexity of cancer patients, particularly those who have CAT. The management of CAT requires constant dialogue with their primary oncologists and, frequently, other specialists (eg, radiologists, hematologists, internists, and vascular surgeons). CAT should be managed with a medium- to long-term perspective for a growing number of surviving patients with advanced metastatic cancer. Moreover, in particular for patients with advanced cancer, CAT prevention and treatment should be established considering the patient's values and preferences and in coordination with supportive and palliative care professionals with the aim of periodically reassessing the optimal CAT treatment during the cancer disease course [8,11,12,14].

Given these factors, the significant clinical impact of VTE events (eg, potentially life-threatening events and physical and psychological sequelae) and the burden associated with anticoagulant therapy (bleeding risk, drug-drug interactions, and high costs), development of specific instruments for the measurement of HRQOL in patients with CAT would be justifiable. The ability to measure and consider HRQOL in this context may contribute to an adjustment in shared decision-making for anticoagulation therapy, especially in situations in which clinical evidence of safety and effectiveness is limited (Table 1) [11,17].

In the following sections, we provide a general overview of the development and selection of tools used for HRQOL measurement in oncology, review the instruments developed for evaluation of the impact of VTE on HRQOL, describe data about HRQOL and patients' experiences and preferences for anticoagulation therapy in patients with CAT, and summarize current gaps in knowledge and future directions for HRQOL research and clinical applications in CAT.

2 | MEASUREMENT OF HRQOL IN ONCOLOGY

During treatment decision-making in clinical practice, clinicians and patients usually consider the potential impact of therapies on HRQOL intuitively and implicitly. However, including validated instruments that allow for objectifying and standardizing evaluation of HRQOL [2,19] via traditional quantitative scientific methodology is recommended. The goals of this are to compare the changes in HRQOL in the same patient, quantify the differences in HRQOL among individuals in the same group, and confirm the validity of analysis of HRQOL in external groups with the same disease but with cultural and linguistic differences.

Knowledge regarding the design and validation of instruments for HRQOL measurement has increased extraordinarily over the past few years. Their development demands the expertise of and close collaboration among mathematicians, statisticians, and physicians/clinicians to integrate biomedical and social science approaches. The complex methodology behind the development of HRQOL scales goes beyond the objectives of this review.

Moreover, once these instruments are developed, their applicability in other groups or countries should be tested in different settings after a meticulous language translation and cultural adaptation process, in order to ensure its usefulness in research and, ideally, clinical practice [2,19].

Regarding the HRQOL instruments developed in oncology, they can be classified into 2 major groups: generic instruments used to

TABLE 2 Summary of specific instruments for the measurement of HRQOL in patients with venous disease and DVT/PE and general VTE studies evaluating HRQOL.

	Author (year)	Instrument	Original language
Venous disease	Franks (1992)	Health questionnaire for venous disease [65]	English
	Garratt (1993)	Aberdeen Varicose Vein Questionnaire [66]	English
	Launois (1996)	Chronic Lower Limb Venous Insufficiency [67] Questionnaire	French
	Augustin (1997)	Freiburger Questionnaire [68]	German
	Kyszcz (1998)	Tübingen Questionnaire [69]	German
	Lamping (1998)	VEINES-QOL [70]	English
	Belcaro (2006)	Venous Quality of Life Score [71]	Italian
	Guex (2007)	Quality of Life Outcome Response-Venous [72]	French
DVT	Mathias (1999)	Health-Related Quality of Life Questionnaire for Deep Venous Thrombosis [73]	English
	Van Korlaar (2004)	Venous Thrombosis Quality of Life [74]	English
	Hedner (2004)	Deep Venous Thrombosis Quality of Life [75]	Swedish
	Kahn (2006)	Adapted from the VEINES-QOL/Sym de Lamping (1998) [20]	English
PE	Cohn (2009)	PEmb-QoL questionnaire [76]	Dutch
	Author (year)	Instrument (study)	Number of patients (proportion of patients with cancer)
VTE studies	Kline et al. (2016) [30]	VEINES-QOL/Sym and SF-36 [30]	253 (2.8%)
	Hogg et al. (2013) [31]	Standard Gamble Method [31]	215 (23%)
	Hogg et al. (2014) [32]	SF-36, PEmb-QoL, and VEINES-QOL/Sym [33]	44 (18)
	Hunter et al. (2019) [34]	Audio-recorded semistructured interviews [34]	11 (0%)
	Monreal et al. (2019) [35]	EQ-5D-5L [35,36]	2056 (8.5%)
	Chuang et al. (2019) [28]	EQ-5D-5L [28]	1399 (8.5%)

DVT, deep vein thrombosis; HRQOL, Health-Related Quality of Life; PE, pulmonary embolism; PEmb-QoL, Pulmonary Embolism Quality of Life; VEINES-QOL, Venous Insufficiency Epidemiologic Economic Study Quality of Life; VTE, venous thromboembolism.

measure an individual's well-being from a broad, general point of view and specific instruments focused in populations with particular pathologies (see the [Supplementary material](#)).

3 | SPECIFIC SCALES FOR THE EVALUATION OF HRQOL IN PATIENTS WITH VTE

Clinicians and researchers have developed multiple HRQOL instruments to assess QOL in patients with venous disorders including DVT and/or PE (Table 2) [20,28,30–36,62–72]. Among them is the VEINES-QOL/Sym questionnaire, which Kahn et al. [20,21] adapted from the VEINES-QOL instrument originally developed for the evaluation of QOL in patients with venous diseases. The VEINES-QOL/Sym questionnaire has been validated in multiple countries in both geriatric patients with DVT and patients with vein ulcers [22].

Regarding the quantification of the impact of PE on patients' QOL, physicians have used generic scales such as the 36-Item Short Form Health Survey [23], the Chronic Respiratory Disease Questionnaire

[24], and the Cambridge Pulmonary Hypertension Outcome Review [25]. Furthermore, over the past few years, came the Pulmonary Embolism Quality of Life (PEmb-QoL) questionnaire that examines several dimensions of the symptoms. The higher the score, the lesser the impact on QOL [26,27].

In general VTE studies, HRQOL has been assessed by generic and specific instruments, with cancer population being underrepresented on those studies (Table 2) [28–36].

Recently, International Consortium for Health Outcomes Measurement (ICHOM) Connect developed an international standard set of patient-centered outcome measures for the evaluation of VTE [37]. The goal is to standardize outcomes in VTE patients, including both disease-specific and general aspects of QOL (psychological and physical). The tools used for outcome measurement by ICHOM Connect were the PEmb-QoL and VEINES-QOL questionnaires, Patient-Reported Outcome Measurement Information System, and Post-VTE Functional Status scale. Outcomes were measured prospectively at 0, 3, 6, and 12 months after VTE. The ICHOM Connect VTE instrument is the newest one developed for this population as of July 2023. It has some limitations regarding QOL evaluation because it

TABLE 3 Studies on HRQOL and patients' experiences in the setting of CAT.

Study	HRQOL instrument	Number of patients	Main conclusions	
Quantitative research				
CATCH [38,39]	Dewilde et al. [40]	EQ-5D-3L	900	Cancer patients with VTE experience greater distress due to the additional CAT diagnosis [60]
	Lloyd et al. [41]		833	Recurrent VTE in cancer patients is associated with a negative impact on HRQOL
ADAM VTE [42]	Duke Anticoagulation Satisfaction Scale		287	Direct oral anticoagulant (apixaban) use has lesser probability of recurrent VTE development and major bleeding than low-molecular-weight heparin (dalteparin) use in cancer patients. Parenteral therapy generated additional stress, anxiety, and frustration in cancer patients, indicating a negative impact on their HRQOL.
CANVAS [43]	SF-12		671	Cancer patients with new clinical or radiological diagnosis of VTE.
	Anti-Clot Treatment Scales PRO measures			Incidental VTE was included. HRQOL and ACTS (assessment of perceptions of anticoagulation therapy) were secondary outcomes and the study is not powered for those. No clinically meaningful differences in the benefits or burdens of treatment between LMWH and DOAC.
QCa [43]	VEINES-QOL/Sym		425	Symptomatic VTE significantly reduces HRQOL in cancer patients.
	PEmb-QoL	(128 cases and 297 controls)		
	EORTC QLQ-C30			
	EQ-5D			
QUAVITEC [29]	MOS SF-36		417	Factors related to a negative impact on quality of life include symptomatic thrombosis, disseminated cancer, histologic type, ECOG score of >2, and immobilization.
	EORTC QLQ-C30	(120 cases and 297 controls)		
	VEINES-QOL			
Napolitano et al. [44]	EORTC-C30		128	LMWH is generally well-tolerated in the long-term treatment, and it did not have a negative impact on HRQOL.
Font et al. [45]	Deep Venous Thrombosis Quality of Life		74	VTE caused a significant impairment in HRQOL. Increased distress was associated with a better treatment adherence.
Qualitative research				
PELICAN, UK [54]	Semistructured interviews		20	Patients receive little information about signs and symptoms to timely identify CAT. The diagnosis causes physical and emotional distress.
PELICANOS, Spain [55]			20	CAT diagnosis causes distress in both cancer patients and their families.
PELICANADA, Canada [56]			20	Distress concerning CAT is common among cancer patients and is often added to the previous anxiety generated by cancer diagnosis.

(Continues)

TABLE 3 (Continued)

Study	HRQOL instrument	Number of patients	Main conclusions
Le PELICAN, France [57]		24	Patients showed little distress about the diagnosis of VTE possibly due to the lack of information about the CAT. More education about CAT is needed among patients.
PELICANZ, New Zealand [58]		20	Patients did not consider lack of information on CAT a causative factor in developing emotional distress. Education about CAT is needed among cancer patients.
Hutchinson et al. [57]	Semistructured interviews	37	Cancer patients lack awareness of increased VTE risk and symptoms. Patients find easier to take oral anticoagulant treatment than parenteral therapy, however, they would only take tablets if they were found to be as safe and effective as injections.
Benelhaj et al. [58]	Qualitative data exploring the experience of patients with incidental PE	11	Patients considered upsetting and unexpected the diagnosis of incidental PE. Information was appreciated when given timely and from experts. There is a need for more education regarding the increased risk of developing VTE in cancer patients.

CAT, cancer-associated thrombosis; CANVAS, Canagliflozin Cardiovascular Assessment Study; ECOG, Eastern Cooperative Oncology Group; HRQOL, Health-Related Quality of Life; LMWH, low-molecular-weight heparin; PE, pulmonary embolism; PRO, Patient-Reported Outcomes; VTE, venous thromboembolism.

disregards the obtention of baseline QOL data, which does not allow for evaluation of its progression. Moreover, given that it is a new instrument, validation for this type of tool is recommended [4].

4 | HRQOL, EXPERIENCES, AND PREFERENCES IN PATIENTS WITH CAT

Information regarding evaluation of HRQOL in randomized clinical trials for the CAT population is limited (Table 3). This is particularly true regarding evaluation using the scales described above.

In the Comparison of Acute Treatments in Cancer Haemostasis study [38,39], multiple aspects of HRQOL (using the EQ-5D-3L questionnaire) were analyzed at randomization in 833 enrolled CAT patients taking tinzaparin or vitamin K antagonists as anticoagulant therapy [40,41]. HRQOL was assessed every month until the seventh month of follow-up. Additionally, the impact of VTE recurrence ($n = 76$ events) and bleeding complications ($n = 159$) on HRQOL were evaluated, with the latter having a greater impact than the former in patients with recurrent VTE. Variability among the study patients was seen. In particular, women and patients with the highest Eastern Cooperative Oncology Group performance status had the worst HRQOL scores. Also, HRQOL diminished progressively in all patients.

Notably, the ADAM trial [42] demonstrated that the use of apixaban is safer than that of LMWH (eg, dalteparin) in cancer patients, with a lower probability of recurrent VTE and major bleeding. At baseline, researchers saw no differences in HRQOL between anticoagulant groups. Nonetheless, during follow-up, use of the Duke Anticoagulation Satisfaction Scale demonstrated that parenteral therapy generated additional stress, anxiety, and frustration in these cancer patients, indicating a negative impact on their HRQOL. Therefore, this increased distress induced treatment abandonment by several patients, which may have reduced their HRQOL even more.

The Canagliflozin Cardiovascular Assessment Study trial [43], aimed to compare the use of DOACs vs LMWH for preventing recurrent VTE and for rates of bleeding in patients with CAT, included as secondary outcomes the measure of HRQOL with the 12-Item Short Form Health Survey (SF-12) [44], participants' perceptions of the burdens and benefits of anticoagulation treatment on the Anti-Clot Treatment Scale [45], and Patient-Reported Outcomes measures at 3-month and 6-month follow-up. Interestingly, among the survivors that were able to complete tests at 3- and 6-month follow-up, no differences were found on comparing patients treated with DOACs or LMWH by the SF-12, the 12-item burdens and the 3-item benefits included in the Anti-Clot Treatment Scale and the additional Patient-Reported Outcomes measures were evaluated.

In the QCa study [46], a Spanish multicentric prospective study performed in 2015-2018, researchers evaluated HRQOL using both VTE-specific (VEINES-QOL/Sym and PEmb-QoL) and VTE-general (European Organization for Research and Treatment of Cancer

TABLE 4 Summary of current gaps in the knowledge of health-related quality of life in patients with CAT and current available instruments for further clinical research.

<p>Current gaps in the knowledge of HRQOL measurements in patients with CAT</p> <ul style="list-style-type: none"> • Short (first 3-6 mo) and long-term (beyond 6 months) impact in HRQOL of different anticoagulant therapies (LMWH, DOAC, VKA). • Prospective assessment of HRQOL measures in patients with acute symptomatic or incidental VTE events. • Short- and long-term impact in HRQOL of residual venous thrombosis and postthrombotic syndrome in the lower and upper limbs. • Impact of bleeding events in HRQOL in patients with CAT. • Management of CAT in patients with advanced cancer in the palliative care setting and at the end of life. 	<p>Quantitative instruments</p> <p>EQ-5D; EQ-5D-3L EORTC QLQ-C30 DASS VEINES-QOL/Sym PEmb-QoL MOS SF-36 Self-reported adherence Morisky-Green tool DVTQOL</p> <p>Qualitative research methods</p> <p>Semistructured interviews In-depth interviews Focus groups Open-ended surveys Projective technics Case studies Case interpretive analysis Thematic coding Grounded theory Direct observation Ethnography</p>	<p>Advantages:</p> <p>Test a hypothesis or Theory Standardized and structured data collection Use of objective statistical analysis Large sample representative Deductive methods of presenting data</p> <p>Limitations:</p> <p>Close-ended questions Crosscultural validation</p> <p>Advantages:</p> <p>New theory based on the gathered data Small judgment sampling Open-ended questions</p> <p>Limitations:</p> <p>Inductive methods of presenting data Subjective understanding</p>
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CAT, cancer-associated thrombosis; DASS, Duke Anticoagulation Satisfaction Scale; DOAC, direct oral anticoagulants; DVTQOL, Deep Venous Thrombosis Quality of Life; HRQOL, Health-Related Quality of Life; LMWH, low-molecular-weight heparin; VKA, vitamin K antagonists; VTE, venous thromboembolism.

QLQ-C30 and EQ-5D-3L instruments). They performed the assessment with 2 cancer patient groups: those with acute symptomatic VTE and those without VTE (control group). The mean (\pm SD) age of the enrolled patients (120 with VTE and 297 without VTE) was 60.2 \pm 18.4 years. The most prevalent tumors in this cohort were of gastrointestinal (23.5%) and pulmonary (19.8%) origin. The investigators found marked differences in global health status according to the EQ-5D-3L score (cases vs controls, 0.55 vs 0.77; mean difference: -0.22) and QLQ-C30 score (cases vs controls, 47.7 vs 58.4; mean difference: -10.3). Moreover, they found a difference in the scores for the PEmb-QoL questionnaire (cases vs controls, 44.4 vs 23.0; mean difference: -21.4) [36]. Also, the HRQOL score using VEINES-QOL/Sym was considerably lower in the cases (42.7) than in the controls (51.7; mean difference: -9.0). Marin-Barrera et al. [46] concluded that symptomatic VTE significantly reduces HRQOL in cancer patients.

In 2018, the results of the prospective observational QUAVITEC (Quality of Life in Cancer Patients Undergoing Anticoagulant Treatment with LMWH for Venous Thromboembolism) study were published [29]. It was designed to evaluate the impact of prolonged LMWH-based treatment on general QOL in CAT patients using both general (36-Item Short Form Health Survey and QLQ-C30) and specific (VEINES-QOL/Sym) scales. In a logistic regression analysis including time as a covariable, QOL scores improved progressively from the time of diagnosis to 3 and 6 months of follow-up. Factors related to increased negative impact on QOL included symptomatic thrombosis, disseminated cancer, histologic cancer type, Eastern

Cooperative Oncology Group score of greater than 2, and immobilization.

In a recent observational study [47], HRQOL was analyzed in 128 cancer patients with residual VTE previously detected via ultrasound 6 months after initiating anticoagulant therapy. Patients continued receiving long-term LMWH therapy (75% of full-dose adjustment by body weight), attending follow-up visits every 3 months for at least 2 years. The tool used for this evaluation was the EORTC-C30 (European Organization for Research and Treatment of Cancer) questionnaire, which was applied by a psychologist at the moment of inclusion in the study and 6, 12, and 24 months thereafter. The global EORTC-C30 scores at inclusion and 6, 12, and 24 months were 52.1, 51.4, 50.8, and 50.1, respectively. No significant differences were observed in scores between study entry and last available follow-up ($P = .1$). Finally, LMWH was generally well-tolerated during the long-term treatment, and it did not have a negative impact on HRQOL.

Font et al. [48] performed a multicenter quantitative study to assess treatment adherence and HRQOL during anticoagulation therapy for CAT at 30 days and 3 months after enrollment. The participants included 74 adults with both cancer and confirmed acute lower extremity DVT. The most negatively affected domains of HRQOL were emotional and physical symptoms, sleep disturbances, and physical activity limitations. The authors reported a correlation between increased distress and improved treatment adherence.

Regarding the experiences with CAT and preferences for anticoagulation therapy of patients with CAT, several studies using qualitative and mixed model research methodologies must be

mentioned [49–51]. Some of these studies centered on patients with advanced cancer and the palliative care/hospice environment [52]. Others focused on how patients' experiences and preferences may influence the type and duration of anticoagulant therapy for CAT [48,53]. The knowledge provided by these studies has helped physicians better enhance shared decision-making in the management of patients with CAT. Among the qualitative studies performed with CAT patients are the PELICAN series of studies aimed at exploring the experiences and preferences of patients with data collected in the United Kingdom [54], Spain [55], Canada [56], France [57], and New Zealand [58].

Qualitative data from the SELECT-D (Anticoagulation Therapy in Selected Cancer Patients at Risk of Recurrence of Venous Thromboembolism) trial [59] comparing the efficacy and safety of rivaroxaban and dalteparin in patients with CAT were assessed by Hutchinson et al. [60]. Their main conclusions were that education about CAT is needed before it develops and that patients prefer oral over parenteral drugs but only if their efficacy and security are equivalent. Along the same lines, a recent study performed in the United Kingdom [61] involving 11 cancer patients with incidentally diagnosed PE exposed experiences in the interviewed patients similar to those identified in the PELICANADA study [56].

5 | GAPS IN KNOWLEDGE AND FUTURE DIRECTIONS

The need for development of standardized instruments for the measurement of HRQOL has increased over the past decade. Overall, this represents an opportunity regarding future standardization of the current HRQOL measurement instruments in oncology. However, a gap in knowledge remains in the evaluation of HRQOL in CAT, as summarized in Table 4. Further studies are needed to assess the acceptability, internal consistency reliability, validity, and reproducibility of the explored scales in different settings.

The use of mixed quantitative and qualitative methodologies seems to be the most appropriate tools to apply in future studies. Findings may eventually lead to the application of HRQOL measurement tools that can facilitate shared decision-making of CAT treatment in daily practice [62–64].

Additionally, future studies in HRQOL in CAT may need to include catheter related venous thrombosis and postthrombotic syndrome. To the best of our knowledge, there are no prospective studies specific to those scenarios in cancer population.

6 | CONCLUSION

Specific validated tools for the evaluation of HRQOL in patients with CAT are needed. In our opinion, there is not currently a single tool that satisfies the clinical and/or research needs for the evaluation of HRQOL in CAT. We recommend that future prospective studies in CAT apply and evaluate the performance of the tools presented in this

review, and we suggest the use of combined qualitative and quantitative instruments.

Finally, the implementation of HRQOL measurement instruments in routine clinical practice will require overcoming existing limitations, such as time investment by both physicians and patients, administration, and analysis of results; moreover, reliability and validity issues can only be addressed by clinical studies focused on HRQOL in CAT.

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SUPPLEMENTARY MATERIAL

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