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RESEARCH ARTICLE

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Recognition, diagnosis, and operability assessment of chronic thromboembolic pulmonary hypertension (CTEPH): A global cross-sectional scientific survey (CLARITY)

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Abstract

Early recognition and diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) is crucial for improving prognosis and reducing the disease burden. Established clinical practice guidelines describe interventions for the diagnosis and evaluation of CTEPH, yet limited insight remains into clinical practice variation and barriers to care. The CTEPH global cross-sectional scientific survey (CLARITY) was developed to gather insights into the current diagnosis,

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treatment, and management of CTEPH and to identify unmet medical needs. This paper focuses on the recognition and diagnosis of CTEPH and the referral and evaluation of these patients. The survey was offered to hospital-based medical specialists through Scientific Societies and other medical organizations, from September 2021 to May 2022. Response data from 353 physicians showed that self-reported awareness of CTEPH increased over the past 10 years among 96% of respondents. Clinical practices in acute pulmonary embolism (PE) follow-up and CTEPH diagnosis differed among respondents. While 50% of respondents working in a nonexpert center reported to refer patients to an expert pulmonary hypertension/CTEPH center when CTEPH is suspected, 51% of these physicians did not report referral of patients with a confirmed diagnosis for further evaluation. Up to 50% of respondents involved in the evaluation of referred patients have concluded a different operability status than that indicated by the referring center. This study indicates that early diagnosis and timely treatment of CTEPH is challenged by suboptimal acute PE follow-up and patient referral practices. Nonadherence to guideline recommendations may be impacted by various barriers to care, which were shown to vary by geographical region.

KEYWORDS
chronic thromboembolic pulmonary hypertension, clinical practice, diagnosis, pulmonary embolism, pulmonary hypertension

INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare form of pulmonary hypertension (PH).[1,2] It is caused by the occlusion of proximal pulmonary arteries by fibrotic intravascular material, in combination with a secondary microvasculopathy, that lead to increased pulmonary vascular resistance and progressive right heart failure.[3] While CTEPH remains underrecognized and underdiagnosed,[4] current estimates of the annual incidence of CTEPH lie between 3.1 and 6.0 cases per million population, and prevalence between 25.8 and 38.4 cases per million population.[5] Generally, CTEPH is considered a rare complication of acute pulmonary embolism (PE), with a reported incidence of 0.6% in all patients with acute PE and 3.2% in those who were alive after an initial treatment period of 6 months.[1,2,6] A recent prospective observational study showed a cumulative incidence of 2.3% for CTEPH after acute PE.[1,2,7] However, up to 35% of patients with CTEPH have no reported history of acute PE.[8,9] A growing amount of data suggests that the true incidence of disease may be underestimated by three-fold.[4]

Although CTEPH has a poor prognosis if left untreated,[10] it is a treatable form of PH, which is why early recognition and diagnosis is crucial.[11] Pulmonary endarterectomy (PEA) is established as the treatment of choice for eligible patients.[3] Over the past decade, additional treatment options have become available, including drug therapy and balloon pulmonary angioplasty (BPA). Nowadays, a multimodal treatment approach is commonly adopted, with a combination of PEA, BPA, and drug therapy to target the mixed anatomical lesions: proximal, distal, and microvasculopathy, respectively.[1,2]

However, the diagnosis of CTEPH is often delayed and is commonly overlooked in the evaluation of patients with exertional dyspnea due to the nonspecific nature of symptoms and lack of disease awareness among health-care professionals. In a UK cross-sectional study of 567 adult patients with PH, diagnosis was delayed by at least 1 year in 48% of patients, where 40% of patients had consulted at least four different healthcare practitioners before diagnosis.[12] Recent international registry data showed that the median time from onset of symptoms to CTEPH diagnosis was 15 months, where majority of patients (approximately 75%) were diagnosed at an advanced stage of disease (New York Heart Association functional class III–IV).[9] Taking into consideration previous registry data,[8] the median time to diagnosis has not improved over the past decade.[9]

Despite advancements in the treatment and management of CTEPH,[1,2] there is scarce information on clinical

decision-making patterns and challenges in adhering to guideline recommendations. Recent international registry data from mainly Europe and Japan, as well as America and other countries, revealed regional differences in the use of diagnostic imaging modalities and therapeutic approaches.[9] Clinical practice variation and barriers to care among medical specialists and across other regions of the world remain largely undescribed.

The CTEPH global cross-sectional scientific survey (CLARITY) was developed to gather insights from the physician's perspective into the current diagnosis, treatment, and management of CTEPH and to identify unmet medical needs.

METHODS

Survey development

A Scientific Committee of 11 international CTEPH experts from the regions of Europe, North America, Latin America, and Asia-Pacific was established to support the development of the survey. A modified Delphi Technique,[13] consisting of two questionnaire rounds, was used to reach consensus on the research topics for the survey (Figure 1). Initial preliminary research topics were identified through a targeted literature search via PubMed, and informed by the expert opinion of the Scientific Committee. In the first Delphi round, the Scientific Committee was asked to rate the preliminary research topics for inclusion in the survey based on a five-point Likert scale and to provide suggestions for improvement. Research topics that reached consensus agreement for inclusion, based on an a priori-defined threshold of 78%,[14] and revised research topics were shared with the Scientific Committee for a second round of assessment. Research topics that met the final consensus agreement, based on an a priori-defined threshold of 89%,[14] were included in the survey: (1) recognition of CTEPH, (2) diagnosis of CTEPH (following acute PE or otherwise), (3) operability assessment, (4) surgical and interventional treatment, (5) drug therapy, (6) multimodal treatment approach for CTEPH, and (7) practices and perceptions toward anticoagulation.

For each research topic, survey questions were drafted and reviewed by the Scientific Committee for content and face validity. Afterward, the survey was piloted with a small group of CTEPH experts ($n = 4$) and revised to develop the final questionnaire. The online survey was programmed using the Qualtrics software and hosted on a server with controlled access. The English survey was translated into 11 languages (French, German, Italian, Spanish, Portuguese, Polish, Russian, Turkish, simplified Chinese, Japanese, and Korean). The final survey consisted of 110 closed- and open-ended questions (see Supporting Information). Conditions and display logic were used to ensure respondents only answered questions relevant to their clinical practice and elicited previous responses.

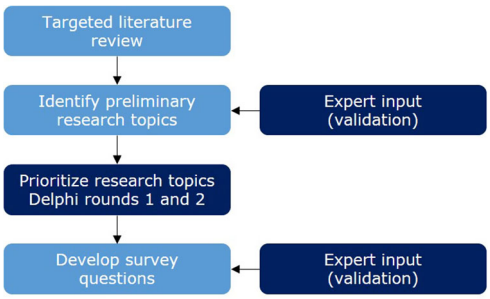

FIGURE 1 Survey development process.

Survey distribution

The target respondents for the survey were hospital-based medical specialists, likely to intervene in the clinical management of a PE or CTEPH patient, across different clinical settings, including expert PH/CTEPH centers and nonexpert centers. No formal sample size was set; potential respondents were invited to participate through 21 international, regional, and national Scientific Societies and other medical organizations recommended by the Scientific Committee (see Acknowledgments). These organizations were free to choose how to distribute the survey to their membership (e.g., email newsletter, website announcement, social media posts). Respondents were not compensated for their time. Response collection occurred from September 10, 2021 to May 1, 2022.

Data analysis

Categorical responses from the closed-ended questions were reported as proportions. Qualitative data from the open-ended questions were analyzed, recoded into categorical variables, and reported as proportions. Subanalyses were performed by region and to further explore the impact of medical specialty and affiliation with an expert PH/CTEPH center.

RESULTS

This paper presents the findings on contemporary clinical practices and challenges in the recognition and diagnosis of CTEPH and in the referral and evaluation of these patients.

Respondent characteristics

Out of 416 responses collected, 353 were included in this analysis. A total of 63 responses were excluded because the respondents indicated no involvement in PE diagnosis and/or follow-up, CTEPH diagnosis, or CTEPH operability assessment, treatment, and/or follow-up (27%, $n = 17$) or were general practitioners (73%, $n = 46$). Included respondents were from Europe (44%, $n = 155$), Asia-Pacific (32%, $n = 113$), North and South America (both 11%, $n = 38$ and $n = 40$, respectively), and Middle East and Africa (2%, $n = 7$). Most respondents specialized in pulmonology (44%, $n = 156$) or cardiology (41%, $n = 146$). Others specialized in cardiothoracic surgery, internal medicine, vascular medicine, hematology, radiology, or other medical specialties (14%, $n = 51$). Majority of respondents had between 5 and 14 (35%, $n = 123$) or 15–29 (39%, $n = 138$) years of working experience. Most respondents (53%, $n = 187$) were involved in PE diagnosis and/or follow-up as well as CTEPH diagnosis, operability assessment, treatment, and/or follow-up and were working in a unit or department dedicated to acute PE management (22%, $n = 77$), an expert PH/CTEPH center (37%, $n = 130$), or both (12%, $n = 41$). Of the 182 respondents who did not work in an expert PH/CTEPH center, only 30% were affiliated with such a center ($n = 54$). Further details on respondent characteristics are presented in Table 1. In addition, respondent extent of involvement in acute PE and CTEPH, by region, is shown in Supporting Information S1: Table 1.

TABLE 1 Respondent demographics and characteristics.

Parameter	Respondents ($N = 353$)
Geography, *n* (%)	
Europe	155 (44)
Asia-Pacific	113 (32)
South America	40 (11)
North America	38 (11)
Middle East and Africa	7 (2)
Medical specialty, *n* (%)	
Pulmonology	156 (44)
Cardiology	146 (41)
Cardiothoracic surgery	14 (4)
Internal medicine	15 (4)
Vascular medicine	10 (3)
Hematology	5 (1)
Radiology	1 (<1)
Other	6 (2)
Years of working experience in specialization, *n* (%)	
<5 years	34 (10)
5–14 years	123 (35)
15–29 years	138 (39)
≥30 years	58 (16)
Level of involvement in acute PE and CTEPH, *n* (%)	
PE diagnosis and/or follow-up, CTEPH diagnosis, and CTEPH operability assessment, treatment, and/or follow-up	187 (53)
PE diagnosis and/or follow-up and CTEPH diagnosis	77 (22)
PE diagnosis and/or follow-up only	49 (14)
CTEPH diagnosis, and CTEPH operability assessment, treatment, and/or follow-up	20 (6)
CTEPH diagnosis only	15 (4)
CTEPH operability assessment, treatment, and/or follow-up only	5 (1)
Care setting and affiliation, *n* (%)	
Working in a unit or department that is dedicated to acute PE management	77 (22)
Working in a PH/CTEPH expert center	130 (37)
Working in a unit or department dedicated to acute PE management and a PH/CTEPH expert center	41 (12)
None of the above	105 (30)

Awareness

Self-reported awareness of CTEPH increased over the past 10 years among 96% ($n = 339$) of respondents. Frequently reported contributing factors for this evolution (Supporting Information S1: Table 2) were attendance to disease education activities and conferences (78%, $n = 265$), the availability of drug therapy for CTEPH (64%, $n = 216$), and advances in understanding disease pathophysiology and epidemiology (57%, $n = 192$).

CTEPH detection after PE

Clinical practices in CTEPH detection after PE differed among the 313 respondents involved in PE diagnosis and/or follow-up. The majority of respondents reported that following acute PE, patients in their hospital receive anticoagulation for 3–6 months with clinical follow-up (91%, $n = 285$), whereas 4% ($n = 14$) did not report

TABLE 1 (Continued)

Parameter	Respondents ($N = 353$)
If not working in a PH/CTEPH expert center ($n = 182$)	
Affiliated with a PH/CTEPH expert center	54 (30)
Not affiliated with a PH/CTEPH expert center	85 (47)
Unknown/uncertain	43 (24)

Note: Number of responses, by country: Europe (Czech Republic (1); Denmark (1); Finland (1); France (16); Georgia (1); Germany (4); Greece (2); Italy (2); Latvia (1); Poland (54); Portugal (2); Romania (1); Russia (49); Serbia (1); Slovakia (1); Spain (1); Sweden (1); United Kingdom (16)), Asia-Pacific (Australia (5); China (74); India (2); Indonesia (1); Japan (28); Singapore (2); Thailand (1)), Latin America (Argentina (8); Brazil (15); Colombia (8); Dominican Republic (1); Guatemala (1); Mexico (3); Nicaragua (1); Paraguay (1); Venezuela (2)), North America (Canada (4); United States (34)), Middle East and Africa ([Algeria (2); Iran (2); Kenya (1); Morocco (1); Oman (1)].

Abbreviations: CTEPH, chronic thromboembolic pulmonary hypertension; PE, pulmonary embolism; PH, pulmonary hypertension.

TABLE 2 Barriers affecting CTEPH detection after PE.

Reported barriers, *n* (%)	Respondents ($N = 313$)
Lack of disease awareness among non-experts	242 (77)
Lack of structured follow-up post-acute PE	175 (56)
Nonspecific presentation of disease and diagnostic misclassification	136 (44)
Incomplete understanding of the natural history of disease (disease progression)	121 (39)
Lack of clinical guidelines/algorithms to screen for possible CTEPH	73 (23)
Other	7 (2)
Unknown/uncertain	7 (2)
No perceived barriers	6 (2)

Note: Total does not equal 100% due to multiple response options.

Abbreviations: CTEPH, chronic thromboembolic pulmonary hypertension; PE, pulmonary embolism.

further follow-up following anticoagulation for 3–6 months. Another standard follow-up approach after acute PE was to perform echocardiography (77%, $n = 240$), always (49%, $n = 153$), or in symptomatic patients only (28%, $n = 87$). Respondents indicated that when using echocardiography during acute PE follow-up, it is typically performed in patients who had right ventricular dysfunction at the time of acute PE (65%, $n = 204$), in patients with dyspnea (63%, $n = 197$), and in patients with functional limitation (54%, $n = 168$). Only a minority of respondents (11%, $n = 34$) reported that echocardiography would be performed in *all patients* during follow-up after acute PE. In terms of other imaging tests, respondents reported that their standard follow-up approach was to repeat imaging to ensure resolution of clots, always (30%, $n = 93$) or in symptomatic patients only (33%, $n = 102$). Majority of respondents (85%, $n = 265$) reported using the 2019 european society of cardiology (ESC)/european respiratory society (ERS) Guidelines for the diagnosis and management of acute PE for follow-up after acute PE.

The most frequently reported barriers for CTEPH detection after PE were lack of disease awareness among nonexperts (77%, $n = 242$), followed by lack of structured follow-up postacute PE (56%, $n = 175$), and nonspecific presentation of disease and diagnostic misclassification (44%, $n = 136$), among others (Table 2). Further analysis of these reported barriers did not suggest evident differences between regions.

CTEPH diagnosis

Of the 299 respondents involved in the diagnosis of CTEPH, ventilation–perfusion (V/Q) scan (75%, $n = 225$) and computed tomography pulmonary angiography (CTPA) (66%, $n = 197$) were the most commonly used tools to screen patients with PH for CTEPH. The reported availability of different tools and tests for the evaluation of patients with suspected CTEPH is shown in Supporting Information S1: Figure 1. With regard to the sequence of diagnostic procedures, echocardiography was most commonly reported to be performed first (Figure 2). Majority of respondents (69%, $n = 207$) reported using the 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension.

Frequently reported barriers to diagnose CTEPH included lack of CTEPH awareness (following PE or otherwise) (70%, $n = 208$), delayed referral (58%, $n = 172$), and lack of expertise in performing diagnostic procedures (36%, $n = 107$), among others (Table 3). Regional-level analysis suggested that lack of expertise in performing diagnostic procedures was more common in South America and Asia-Pacific and that delayed referral was more common in North and South America, whereas lack of CTEPH awareness was relatively common across regions (data not shown). Lack of availability of diagnostic tools was reported by 28% ($n = 84$) of respondents. This was further exemplified by the more frequent reported availability of V/Q scan among pulmonologists (85%, $n = 126$) compared to

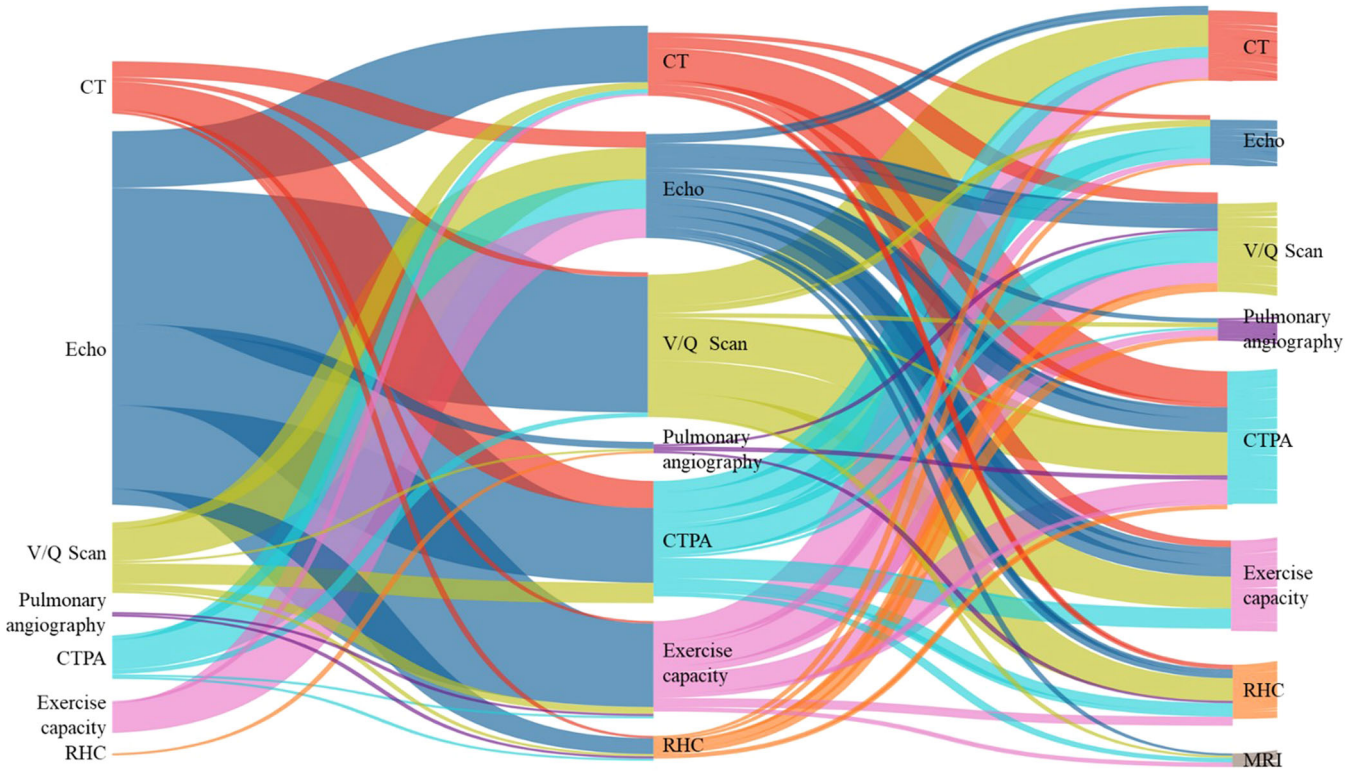

FIGURE 2 Sankey chart for order of diagnostic procedures. Sankey chart illustrating the sequence of diagnostic tools and tests performed by respondents involved in the diagnosis of chronic thromboembolic pulmonary hypertension ($n = 299$). The order of the first three diagnostic procedures, in sequential order, is shown here. The thickness of the lines indicates higher level of use of a particular diagnostic pathway. CT, computed tomography; CTPA, computed tomography pulmonary angiogram; MRI, magnetic resonance imaging; RHC, right heart catheterization; V/Q, ventilation–perfusion.

cardiologists (54%, $n = 67$) (Supporting Information S1: Figure 1).

Referral from nonexpert to expert center

Out of the 182 respondents that did not work in an expert PH/CTEPH center, 50% ($n = 90$) and 49% ($n = 89$) reported referring patients to an expert center when CTEPH is suspected and when the diagnosis of CTEPH is established, respectively, where 13% ($n = 23$) reported referring both patients with suspected and confirmed CTEPH. Among respondents that were reportedly affiliated with an expert PH/CTEPH center ($n = 54$), these proportions increased to 65% ($n = 35$), 56% ($n = 30$), and 22% ($n = 12$), respectively.

Among factors driving referral decisions (Supporting Information S1: Figure 2), the most commonly reported factors were guideline recommendations when CTEPH is suspected (56%, $n = 50$) and lack of access to PEA when the diagnosis of CTEPH is established (57%, $n = 51$). Respondents that were affiliated with an expert PH/CTEPH center were more likely to report that guidelines recommendations and lack of expertise in performing BPA drive referral decisions when CTEPH is suspected compared to respondents that were not affiliated with an expert PH/CTEPH center (66%, $n = 23$ vs. 49%, $n = 20$; 43%, $n = 15$ vs. 24%, $n = 10$). When the diagnosis of CTEPH is established, respondents that were affiliated with an expert PH/CTEPH center were more likely to report that guideline recommendations drive referral decisions compared to respondents that were not affiliated with an expert PH/CTEPH center (53%, $n = 16$ vs. 33%, $n = 12$), followed by lack of available experts to perform diagnostic workup/operability assessment and lack of expertise in performing BPA (both 43%, $n = 13$ vs. 28%, $n = 10$).

Operability assessment

Respondents who were involved in CTEPH operability assessment, treatment, and/or follow-up, and who were working in a hospital performing PEA, reported that referred CTEPH patients are usually (90%, $n = 148$) assessed for operability. Following assessment, these respondents have observed the following:

TABLE 3 Barriers to (optimal) diagnosis of suspected CTEPH.

Reported barriers, *n* (%)	Respondents (*N* = 299)
Lack of CTEPH awareness (following acute PE or otherwise)	208 (70)
Delayed referral	172 (58)
Lack of expertise in performing diagnostic procedures	107 (36)
Lack of expertise in reading images	104 (35)
Low level of adherence to clinical guidelines/algorithms	86 (29)
Lack of availability of diagnostic tools	84 (28)
Lack of available experts to perform diagnostic workup	75 (25)
Under- and/or over-utilization of certain diagnostic tools	67 (22)
Lack of patient access to diagnostic testing (i.e., patient out-of-pocket expenses or absence of reimbursement)	51 (17)
Lack of a national expert PH/CTEPH center	44 (15)
Patient refusal for referral to an expert PH/CTEPH center	38 (13)
No perceived barriers	9 (3)
Other	5 (2)
Unknown/uncertain	3 (1)

Note: Total does not equal 100% due to multiple response options.

Abbreviations: CTEPH, chronic thromboembolic pulmonary hypertension; PE, pulmonary embolism; PH, pulmonary hypertension.

TABLE 4 Barriers to (optimal) operability assessment of CTEPH patients.

Reported barriers, *n* (%)	Respondents (*N* = 212)
Lack of standardized operability assessment criteria	67 (32)
Lack of a multidisciplinary CTEPH team	64 (30)
No perceived barriers	50 (24)
Lack of a national reference center for CTEPH	48 (23)
Patient refusal for referral to an expert PH/CTEPH center	44 (21)
Lack of patient access to operability assessment	42 (20)
Lack of availability of operability assessment tools	39 (18)
Lack of or delayed access to a second opinion	30 (14)
Other	8 (4)
Unknown/uncertain	7 (3)

Note: Total does not equal 100% due to multiple response options.

Abbreviations: CTEPH, chronic thromboembolic pulmonary hypertension; PH, pulmonary hypertension.

- Patients deemed inoperable by the referring center were operable following operability assessment (49%, $n = 72$),
- Patients deemed operable by the referring center were inoperable following operability assessment (38%, $n = 56$),
- Referring center did not conduct operability assessment (38%, $n = 56$),
- Patients have delayed operability assessment (37%, $n = 54$).

Of the 204 respondents involved in operability assessment, the key factors considered when deciding whether a patient is operable or not were, by order of most commonly reported, (1) accessibility of thrombi (88%, $n = 179$), (2) comorbidities (86%, $n = 176$), and (3) benefit/risk ratio (72%, $n = 147$), among others (Supporting Information S1: Table 3). Respondents reported seeking a second opinion on the surgical status of the patients when the patient is deemed operable but the surgical risk is high (53%, $n = 109$), when the surgical accessibility of thrombotic material is uncertain (45%, $n = 92$), when requested by the patient/family (31%, $n = 64$), when the previous operability assessment is outdated (18%, $n = 37$), or when the operating center performs ≤ 50 PEAs per year (18%, $n = 36$).

Frequently reported barriers to optimal CTEPH operability assessment included lack of standardized operability assessment criteria (32%, $n = 67$), lack of a multidisciplinary CTEPH team (30%, $n = 64$), and lack of a national reference center for CTEPH (23%, $n = 48$) (Table 4). Regional-level analysis suggested that there were less perceived barriers to operability assessment among respondents from Europe, where 14% ($n = 30$) of these respondents did not report any barriers (data not shown).

DISCUSSION

Our research showed that CTEPH awareness increased over the past 10 years across medical specialists and clinical settings, mainly due to educational efforts. This trend was anticipated on the basis of newly approved pharmacotherapy for CTEPH[15] and the emergence of

BPA as an effective treatment option, especially for patients with inoperable disease.[1,2] Despite the availability and reported use of clinical practice guidelines to facilitate the detection of CTEPH after PE and to confirm the diagnosis of suspected CTEPH,[16] our findings suggest considerable nonadherence to the guidelines in terms of diagnostic strategies and decision-making processes. For instance, current guidelines recommend using echocardiography as the first-line diagnostic test in patients with suspected CTEPH following acute PE.[1,2] However, at least 20% of respondents did not report using echocardiography as a standard follow-up approach after acute PE in *any* patient. In relation to patient referral, half of the respondents working in a nonexpert center reported to refer patients to an expert PH/CTEPH center when CTEPH is suspected according to guideline recommendations. However, our research also found that many of these medical specialists did not report to refer patients with a confirmed diagnosis of CTEPH to an expert center for further evaluation (51%). Finally, our research suggests considerable discrepancy in terms of operability assessment between referring and expert centers, where up to 50% of respondents involved in the evaluation of referred patients have concluded a different operability status than that indicated by the referring center.

Imaging (primarily V/Q scan and CTPA) plays a central role in the diagnosis of CTEPH to document the perfusion defects and the chronic occlusions of proximal pulmonary arteries by organized fibrotic clots.[17] It is important to note that a negative CTPA does not exclude CTEPH.[3] Therefore, there is an inherent risk among non-CTEPH specialized physicians, who rely on CTPA to screen patients with PH, to miss the disease. Furthermore, early recognition of CTEPH is challenged by knowledge gaps within the imaging community.[17] In a separate subanalysis among 160 cardiologists and 156 pulmonologists, the sequence of diagnostic procedures performed to diagnose CTEPH was shown to differ.[18] Whether procedures were planned simultaneously was not captured by our survey.

Our findings confirm earlier observations on the underutilization of V/Q scanning for the diagnosis of CTEPH,[19,20] driven by lack of availability or expertise.[19] Although V/Q scanning was the screening test of choice among respondents involved in the diagnosis of CTEPH, as little as 54% of cardiologists reported availability of V/Q scanning in their hospital.

In addition, our findings regarding patient referral to expert centers are in line with previous research. Gall et al. observed that referral rates for PEA evaluation ranged from 25% in Japan to 44% in Europe. The authors reported higher referral rates among PH centers, with the main reasons for lack of referral being that surgery was not considered unless medical treatment was failing and patient refusal.[19] Another study in the United Kingdom demonstrated wide geographical variation in referral rates for PEA evaluation on the basis of proximity to nationally designated expert centers.[21] Although our research did not investigate reasons for the lack of referral, the findings highlight that main driving factors for patient referral were guideline recommendations when CTEPH is suspected and lack of access to PEA when the diagnosis of CTEPH is established. The observed discrepancy in operability status evaluation between referring and expert centers further highlights the importance of referring both patients with suspected and confirmed CTEPH to an expert center with a multidisciplinary team, including multimodality expertise, for further evaluation.

As shown by our findings, key barriers remain, necessitating a variety of approaches, ideally tailored to medical specialists. Education of healthcare professionals, especially those involved in the care of patients with acute PE and radiologists, remains imperative to improve disease awareness and timely diagnosis.[17] Early diagnosis and referral of patients with CTEPH can furthermore be facilitated through the organization of PE clinics, through structured follow-up of acute PE patients[22] as well as the development and validation of screening algorithms to support clinical decision-making.[3]

It is important to acknowledge the limitations of this research. While our survey sought broad representation through distribution by 21 Scientific Societies and other medical organizations, the voluntary nature of the survey may have introduced self-selection bias among respondents. Furthermore, the organizations independently determined how to circulate the survey among their members, potentially influencing the survey's reach and sample size, resulting in variations in response rates among different physicians and geographic locations. These considerations are important when interpreting the generalizability of our findings. Furthermore, working at or affiliation with an expert PH/CTEPH center was self-reported by the respondents. "Affiliation" was not defined in the survey but was understood as "having established connections with an expert center." It should be acknowledged that not all countries will have a shared definition of an expert PH/CTEPH center. Furthermore, no verification was performed against established criteria, such as those outlined for PH referral and CTEPH centers by the recent 2022 ESC/ERS Guidelines for the diagnosis and treatment of PH,[1,2] meaning that the expertise of respondents could not be confirmed. In addition, survey-related variables such as survey length

may have contributed to participant fatigue and impacted the overall response rate. Further research on the contemporary management of CTEPH should also consider the perspectives of general practitioners considering their crucial role in referring patients presenting with dyspnea and suspicion of PH to a cardiologist and/or a pulmonologist for further assessment.

In conclusion, CLARITY provided global insights from the physician's perspective into the recognition and diagnosis of CTEPH and the referral and evaluation of these patients. The results show that the awareness of CTEPH has increased across medical specialists and clinical settings over time, and although detection is facilitated through the use of established clinical practice guidelines, structured follow-up after acute PE appears suboptimal. Identified barriers to care may impact the ability to diagnose CTEPH early. There is a need for further education of physicians, with a focus on symptomatic patients following acute PE, to enable early detection and diagnosis of CTEPH patients. Furthermore, patient referral processes should be improved to ensure operability assessment by a multidisciplinary team, as recommended by the guidelines. However, appropriate measures to improve guideline implementation as well as diagnostic and operability assessment may vary by geographical region, depending in particular on the organization of care.

AUTHOR CONTRIBUTIONS

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ETHICS STATEMENT

The authors have nothing to report.

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SUPPORTING INFORMATION

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