

Depression, anxiety and psychological distress in patients with pulmonary hypertension: a mixed-methods study

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ABSTRACT

Introduction Pulmonary hypertension (PH) is a chronic and progressive disease. While prognoses have improved, PH patients still experience side effects and activity restrictions. Accordingly, the key questions asked by this study are ‘How many PH patients have depression/anxiety symptoms?’ and ‘Is there a difference in the symptoms and distress factors between pulmonary arterial hypertension (PAH) and chronic thromboembolic PH (CTEPH) patients, and how are they experiencing distress?’

Methods A mixed-methods study was conducted to collect and analyse quantitative and qualitative data. We administered questionnaires (Patient Health Questionnaire (PHQ-9) and Generalised Anxiety Disorder-7) and then conducted interviews with participants who reported moderate to severe depressive symptoms (PHQ-9 ≥ 10).

Results Seventy-four participants were enrolled in the study, 25 with idiopathic PAH and 49 with CTEPH. Their average age was 55.2 years (PAH 42.7 years, CTEPH 61.5 years). Overall, 44.6% of participants had mild or more severe depressive symptoms (PHQ-9 ≥ 5) and 17.6% had moderate or more severe depressive symptoms (PHQ-9 ≥ 10). PAH patients had particularly high depressive symptoms (PHQ-9 ≥ 5 : PAH 64.0%, CTEPH 34.7%; PHQ-9 ≥ 10 : PAH 24%, CTEPH 14.3%). We extracted four common themes from the qualitative interview data on participants’ experience of psychological distress: ‘Loss of myself,’ ‘Isolation from my surroundings,’ ‘Hassle associated with oxygen therapy,’ and ‘Fear of illness progression/deterioration.’ One theme—‘Suffering from side effects’—was extracted only for PAH patients, while another—‘Rumination on illness due to breathlessness’—was extracted only for CTEPH patients.

Discussion and conclusion The study found that PH patients are prone to depression. The identification of factors and themes that influence the psychological distress of PH patients is important information that can be used to improve the support for the physical and mental health of these patients. Interventions for these distress may contribute to improving the mental status of PH patients.

BACKGROUND

Pulmonary hypertension (PH), defined as a mean pulmonary arterial pressure (PAP) of 25 mm Hg or greater, is a chronic and progressive disease resulting in symptoms

Key messages

- ▶ The key questions asked by this study are ‘How many pulmonary hypertension (PH) patients have depression/anxiety symptoms?’ and ‘Is there a difference in the incidence of depressive and anxiety symptoms and distress factors between pulmonary arterial hypertension and chronic thromboembolic PH patients, and how are they experiencing distress?’
- ▶ Our study found that patients with PH are prone to depression and identified factors and themes that affect these patients’ psychological distress.
- ▶ Because the identification of factors and themes that influence the psychological distress of PH patients in this study is important information that can be used to improve the support of healthcare providers for the physical and mental health of these patients. Interventions for the components of distress identified in this study may contribute to improving the mental status of PH patients.

such as shortness of breath on exertion, fatigue, chest pain and syncope.^{1–3} PH is classified into five groups according to similarities in clinical symptoms, pathological findings, haemodynamics and treatment strategies. Pulmonary arterial hypertension (PAH) is a lesion at the level of fine pulmonary artery capillaries. Chronic thromboembolic PH (CTEPH) is a specific type of PH that is characterised by stenosis or occlusion of subsegmental, segmental or larger pulmonary arteries by organic thrombus.^{4,5} CTEPH can be cured by surgical pulmonary endarterectomy or balloon pulmonary angioplasty (BPA), but there is no surgical treatment for PAH other than lung transplantation to normalise pulmonary artery pressure. In addition, although drug therapy is rapidly developing and improving the prognosis for PAH, self-management of drug therapy is very complicated and side effects occur at a fairly high rate. Therefore, the pathogenesis, epidemiology and treatment of PAH and CTEPH are different.



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Overall, patients with PH have previously experienced high mortality; however, advances in catheter treatment and surgery have made it possible for CTEPH patients to restore PAP to within the normal range and improved life prognosis,^{6–10} and treatment of PAH has also dramatically improved, with new developments in therapy increasing the 3 year survival rate from 63% to 96%.¹¹ Thus, understanding of PH outcomes is currently shifting from ‘high mortality’ to ‘chronic disease’ or ‘living with the disease.’

Although better management is now available for individuals with PH, they still experience a high risk of right-sided heart failure and sudden death. Moreover, because PAP is easily elevated, many PH patients must greatly adjust their activity levels. They also must learn to self-manage complicated therapies such as continuous intravenous therapy, subcutaneous injection therapy and/or inhalation therapy, all of which have side effects. In other words, the dramatic improvements in PH prognoses coexist with significant side effects and activity restrictions. In order to tailor nursing support to a PH patient’s individual needs, the patient’s actual life condition must be clarified.

Anecdotally, patients with PH have been known to experience depression and anxiety, which lead to decreased quality of life (QoL). However, we found only seven prior studies on depression and anxiety among PH patients. McCollister *et al* reported that 40% of PAH patients in their study had mild/moderate depression and 15% had major depression.¹² Harzheim *et al* reported that, in a sample of 138 PAH patients and 20 CTEPH patients, 55.1% of participants had depression and 45.5% had anxiety.¹³ Participants with depression or anxiety had significantly lower QoL, and QoL impairment significantly correlated with the severity of the depression ($p<0.01$) and anxiety ($p<0.05$).¹³ M M Vanhoof *et al* reported that 32.6% of the PAH/CTEPH patients in their study had depression, 48% had anxiety and 27.6% had stress symptoms. Overall, reduced QoL correlated with the severity of physical symptoms of PH, and decreased 6 min walking distance.¹⁴ Somaini *et al* reported that 33% of the PH patients in their study had depression and 34% had anxiety. The proportion of depression was higher in patients who had not yet received treatment than in those who were receiving treatment.¹⁵ Halimi *et al* reported that 41% of PAH patients had probable or possible depression and 58% had probable or possible anxiety as measured using the Hospital Anxiety and Depression Scale. Overall, 51% of the sample had an anxiety-depression disorder.¹⁶ Funabashi *et al* reported that 37.5% of CTEPH patients in their study had depression and that CTEPH patients were significantly more depressed than healthy individuals (37.5% vs 8.9%).¹⁷ A study conducted by Pfeuffer *et al* compared PAH and CTEPH patients, reporting that the rate of depression was higher among those with CTEPH than those with PAH (56% vs 30%; $p=0.03$).¹⁸

We found only one mixed-method study on PH patients and their symptom distress: in a study conducted by

Muntingh *et al* of 67 PAH patients, participants reported low and fluctuating energy levels, difficulty with loss of abilities, worries about the future, restricted ability to fulfil their roles, and being misunderstood by others. Age correlated significantly with distress levels, with younger participants reporting higher scores on the Distress Thermometer. Female patients reported a higher distress level ($M=5.6$; $SD=2.4$) than male patients ($M=4.8$, $SD=2.3$), but this difference was not significant.¹⁹ But we found no mixed-method studies comparing PAH and CTEPH patients.

There remains a need to investigate not only rates of depression and anxiety among individuals living with PAH or CTEPH, but also their experiences of psychological distress, difficulties and care needs in daily life. The key questions asked by this study are ‘How many PH patients have depression/anxiety symptoms?’ and ‘Is there a difference in the incidence of depressive and anxiety symptoms and distress factors between PAH and CTEPH patients, and how are they experiencing distress?’ These findings can suggest interventions for PH-specific distress and lead to improved comprehensive healthcare.

Accordingly, this study aimed to clarify both the psychological states of PAH/CTEPH patients (depression, anxiety) and the experiences of these patients that are related to psychological distress in their daily lives.

METHODS

Study design

This study used an explanatory sequential mixed-method design.^{20–22} First, we conducted a quantitative investigation to evaluate the incidence of depression and anxiety in a sample of PH patients. Second, we conducted qualitative analyses (structured interviews) with a subsample of patients who reported depression and/or anxiety symptoms in order to clarify how those patients were feeling.

Participants and procedures

All study participants met the following inclusion criteria: (1) diagnosis of PAH or CTEPH; (2) aged 20 years or older and (3) currently a patient at Keio University Hospital’s Pulmonary Hypertension Clinic in Japan. Exclusion criteria were (1) Impaired cognition and judgement, unable to obtain understanding and consent to research and (2) PH associated with other diseases such as collagen disease and lung disease.

Participants were recruited at the Pulmonary Hypertension Clinic at Keio University Hospital—which is a tertiary medical facility in central Tokyo, Japan—during the period between December 2016 and March 2019, as well as through consecutive sampling.

The clinic’s physicians (MK and TK) selected eligible patients for the study from among the clinic’s patients and the nurse (YTaki) explained the study to the patients and obtained their written consent. All participants who visited the outpatient clinic during the study period were approached and recruited.

Quantitative and qualitative data collection

Participants who provided written consent to the study were asked to complete a set of questionnaires. Individual interviews were also conducted with a subset of participants, with 30–60 min interviews. The participants' demographic and clinical data (age, gender, type of PH, WHO functional class, oxygen use, PAP, 6 min walking distance and type of therapy) were obtained from their electronic medical records.

Depression was measured using the Patient Health Questionnaire (PHQ-9) a self-report questionnaire consisting of nine items measuring the severity of depressive symptoms. PHQ-9 scores can range from 0 to 27 since each of the nine items can be scored from 0 (not at all) to 3 (nearly every day).²³ Anxiety was assessed using the Generalised Anxiety Disorder questionnaire (GAD-7), a self-report questionnaire that uses seven items to measure the severity of anxiety. GAD-7 scores can range from 0 to 21 since each of the seven items can be scored from 0 (not at all) to 3 (nearly every day).²⁴ Both the PHQ-9 and GAD-7 have been validated using a Japanese clinical sample.

Individual face-to-face interviews were conducted using a semi-structured interview guide among a subsample of participants with moderate-to-severe depression or anxiety (PHQ-9 or GAD-7 scores ≥ 10). The interview guide was created through discussion among PH physicians (MK and TK), a psychiatrist (DF) and nurses (YTake, YTake) and included two questions: '(1) Do you have any symptoms, side effects, or activity restrictions due to PH?' and '(2) Do you have any feeling of difficulty, distress, or pain in your life while undergoing PH treatment?' The interviews were conducted by one researcher (YTake), who has extensive experience and was trained and supervised by a psychiatrist (DF), to ensure consistent quality.

The interviews were conducted in a private room during routine clinic visits or during admission for right-heart catheter examination. All interviews were recorded and transcribed verbatim.

There was no patient or public involvement in the design, conduct, reporting or dissemination plans of this study.

DATA ANALYSIS

Quantitative data

Descriptive statistics were expressed as means and SD for continuous variables, and as frequencies and proportions for dichotomous and nominal variables.

Both the PHQ-9 and GAD-7 scores were categorised into four severity levels of depression/anxiety: severe (15 or higher); moderate (10–14); mild (5–9) and no symptoms (0–4). Potential differences in depression and anxiety related to factors such as oxygen therapy, symptoms, symptom severity (WHO functional class), treatment, side effects and haemodynamics were analysed using the χ^2 test or Fisher's exact test. SPSS V.25.0 was used for all statistical analyses.

Qualitative data

Participants with moderate to severe depression or anxiety (PHQ-9 or GAD-7 scores ≥ 10) were selected for qualitative interviews. All qualitative data was anonymised. The data focused on psychological distress and pain and were analysed using thematic analysis.^{25–26} Analysis of the interview data was conducted by three researchers (YTake, YTake and AZD), including a supervisor with extensive qualitative research experience. Having three researchers review and come to agreement on the qualitative analysis ensured the trustworthiness of the analysis.^{27–28} The qualitative analysis software MAXQDA (Verbi, Berlin) was used to organise the data coding.^{29–31} First, the interview transcripts were analysed line by line, and initial codes were identified, then the codes were sorted into subthemes based on differences and similarities. Finally, the subthemes were grouped into themes, with definitions stated for each theme.

Since PAH and CTEPH have different disease mechanisms, prognoses, and treatment methods, we analysed data for each disease separately and then compared the results.

RESULTS

Quantitative data

Participant demographics

We approached 78 patients and obtained written consent from 74 participants (25 PAH and 49 CTEPH patients) (consent rate=94.9%). The participants' demographics are shown in [table 1](#). The mean age of the participants was 55.2 years (PAH, 42.7 years; CTEPH, 61.5 years) and 70.3% were women. The majority of the participants were class II according to WHO functional classifications. No PAH patients were class III, but approximately a quarter of the CTEPH patients were class III. The PAH patients had higher mean PAP than the CTEPH patients. Approximately a quarter of both the PAH and CTEPH participants used oxygen inhalation all day, while 13.5% used oxygen inhalation only at night (PAH, 8.0%; CTEPH, 16.3%).

Shortness of breath was the most common symptom among CTEPH patients (57.1%), while pain (jaw pain, puncture-site pain from subcutaneous injections and plantar pain), which was a side effect of the PH therapies, was the most common symptom among PAH patients (64.0%).

The most common treatment was oral medicine only (40.0% of participants), followed by continuous intravenous injection therapy (32.0%) and continuous subcutaneous injection therapy (24.0%), which was specific to PAH patients; 49.0% of the CTEPH patients were post-BPA. Mean PAP was lower for the post-BPA group (23.1 \pm 7.6 mm Hg) than for the pre-BPA group (36.8 \pm 11.4 mm Hg).

Depression and anxiety symptoms

Of the total participants, 44.6% had some depressive symptoms (PHQ-9 ≥ 5). Of these, 17.6% had moderate to severe depressive symptoms (PHQ-9 ≥ 10). The incidence of depressive symptoms was higher among PAH patients than CTEPH patients ([table 2](#)). The incidence

**Table 1** Participant demographics

Characteristics	Participants		
	PAH (n=25)	CTEPH (n=49)	All (n=74)
Age in years, mean (SD), range	42.7 (14.6), 20–69	61.5 (10.2), 41–83	55.2 (14.8), 20–83
Sex, male/female n (%)	7 (28.0)/18 (72.0)	15 (30.6)/ 34 (69.4)	22 (29.7)/ 52 (70.3)
WHO functional class, n (%)			
Class I	3 (12.0)	13 (26.5)	16 (21.6)
Class II	22 (88.0)	23 (46.9)	45 (60.8)
Class III	0 (0.0)	13 (26.5)	13 (17.6)
Class IV	0 (0.0)	0 (0.0)	0 (0.0)
Oxygen, n (%)			
All day	7 (28.0)	12 (24.5)	19 (25.7)
At night only	2 (8.0)	8 (16.3)	10 (13.5)
No oxygen	16 (64.0)	29 (59.2)	45 (60.8)
Symptoms or side effects, n (%)			
Shortness of breath (symptom)	9 (36.0)	28 (57.1)	37 (50.0)
Side effects	21 (84.0)	5 (10.2)	26 (35.1)
Pain	16 (64.0)	5 (10.2)	21 (28.4)
Nausea	6 (24.0)	3 (6.1)	9 (12.2)
Diarrhoea	10 (40.0)	0 (0.0)	10 (13.5)
Treatment, n (%)			
Only oral	10 (40.0)	25 (51.0)	–
Intravenous	8 (32.0)	–	–
Subcutaneous	6 (24.0)	–	–
Inhalation	1 (4.0)	–	–
Post-BPA or ongoing BPA	–	24 (49.0%)	–
Mean PAP, mm Hg (SD), range	42.5 (12.3), 22–67	30.1 (11.9), 16–64	34.3 (13.3), 16–67
Only oral	39.0 (12.3), 22–66	36.8 (11.4), 21–64	–
Intravenous	43.1 (13.3), 23–63	–	–
Subcutaneous	48.2 (11.7), 37–67	–	–
Inhalation	38.0(-), 38	–	–
Post-BPA or ongoing BPA	–	23.1 (7.6), 16–51	–

BPA, balloon pulmonary angioplasty; CTEPH, chronic thromboembolic pulmonary hypertension; GAD-7, Generalised Anxiety Disorder 7-item questionnaire; PAH, pulmonary arterial hypertension; PAP, pulmonary arterial pressure; PHQ-9, 9-item Patient Health Questionnaire.

of depressive symptoms in the post-BPA CTEPH group was 29.2% compared with the CTEPH (40.0%) and PAH(64.0%) groups with only medical treatment. The participants who were classified as WHO Functional Class II or higher were more likely to have moderate to severe depressive symptoms ($p=0.030$) than those classified as Class I or lower. Moderate-to-severe depression was significantly higher ($p=0.017$) among participants who used oxygen therapy all day (36.8%) compared with those using oxygen only at night or not at all (10.9%). The PAH patients showed similar levels of depression across all levels of oxygen therapy (all-day oxygen use, 21.0%; oxygen only at night/no oxygen, 28.6%), while the moderate to severe depression was higher among the

CTEPH patients who used oxygen all day (all-day oxygen use, 41.7%; oxygen only at night/no oxygen, 5.4%; $p=0.007$).

Overall, there was a significantly higher rate of more than mild depression among the participants with side effects (65.4%) than those without (33.3%, $p=0.008$).

Moderate depression was observed in 50.0% of the users of Selexipag, a drug used only for PAH, while the depressive symptoms were low among the patients who were not using Selexipag (11.8%; $p=0.059$). Also, patients experiencing pain had mild or greater levels of depressive symptoms than those without pain ($p=0.025$). Anxiety (GAD-7 ≥ 5) was reported by 24.3% of the participants (PAH, 28.0%; CTEPH, 22.4%), while moderate or greater anxiety (GAD-7

Table 2 Depression and anxiety symptoms

Characteristics	PAH (n=25)	CTEPH (n=49)	All (n=74)
Depression (PHQ-9 score), mean (SD), range	5.9 (4.7), 0–15	4.4 (4.6), 0–19	4.9 (4.6), 0–19
Minimal (0–4), n (%)	9 (36.0)	32 (65.3)	41 (55.4)
Mild (5–9), n (%)	10 (40.0)	10 (20.4)	20 (27.0)
Moderate to severe (10–27), n (%)	6 (24.0)	7 (14.3)	13 (17.6)
Anxiety (GAD-7 score), mean (SD), range	3.3 (4.9), 0–20	2.8 (2.9), 0–11	3.0 (3.7), 0–20
Minimal (0–4), n (%)	18 (72.0)	38 (77.6)	56 (75.7)
Mild (5–9), n (%)	4 (16.0)	9 (18.4)	13 (17.6)
Moderate to severe (10–21), n (%)	3 (12.0)	2 (4.1)	5 (6.8)

CTEPH, chronic thromboembolic pulmonary hypertension; GAD-7, Generalised Anxiety Disorder 7; PAH, pulmonary arterial hypertension; PHQ-9, Patient Health Questionnaire 9.

≥10) was reported by only 6.8% (PAH, 12.0%; CTEPH, 4.1%). However, no statistically significant differences were found for disease and treatment variables.

Qualitative data

Of the 74 total participants, 13 reported moderate to severe depression and/or anxiety symptoms and were interviewed individually. [Table 3](#) shows the characteristics of the six PAH patients, and [table 4](#) shows the characteristics of the seven CTEPH patients.

Six themes were extracted: four common to both PAH and CTEPH, one specific to CTEPH, and one specific to PAH. The four common themes were ‘Loss of myself,’ ‘Isolation from my surroundings,’ ‘Hassle associated with oxygen therapy,’ and ‘Fear of illness progression/deterioration.’ The theme specific to PAH was ‘Suffering from side effects,’ and the theme specific to CTEPH was ‘Rumination on illness due to breathlessness.’ Themes and subthemes are shown in [table 5](#). The following sections describe each theme, with examples.

Theme 1: Loss of myself

Definition

Participants could not do things they had previously done as a matter of course before the onset of the illness (eg, maternal role, work, hobbies); they felt pain such as feelings of loss, conflict, or irritability, and they searched constantly for reasons for their situation, regretting their past behaviour. PAH patients felt stressed that their activities were so strictly restricted.

Examples

I can't do the work I've always been doing. I have no purpose in life. (A)

I can't do things that other people can do easily. It's very stressful. (F)

If I had gone to a large hospital with specialists right away, I wouldn't have gotten worse. (D)

Theme 2: Isolation from my surroundings

Definition

Participants felt it was difficult for others to understand their situation, especially when they did not look sick.

Table 3 Characteristics of six PAH patients and psychological distress

ID	Age (years)	Sex	Treatment	Side-effects	Mean PAP	WHO-FC	All-day oxygen	PHQ-9 score	GAD-7 score
A	60s	M	Oral	None	38	II	+	11	6
B	30s	M	Subcutaneous injection + oral	Subcu-taneous injection-site pain	42	II	–	13	7
C	40s	M	Oral	Fatigue	45	II	–	10	10
D	50s	F	Oral	Nausea, foot-pain, fatigue	34	II	–	14	20
E	20s	F	Intravenous + oral	Foot pain, jaw pain, Hot-flushes	49	II	+	15	13
F	20s	F	Oral	nausea	66	II	–	12	2
								Mean12.5 SD1.9	Mean9.7 SD6.3
								Mean45.7 SD11.3	

F, female; GAD-7, 7-item Generalised Anxiety Disorder questionnaire; M, male; PAH, pulmonary arterial hypertension; PAP, pulmonary arterial pressure; PHQ-9, 9-item Patient Health Questionnaire; WHO-FC, WHO-Functional Class.

**Table 4** Characteristics of seven CTEPH patients and psychological distress

ID	Age (years)	Sex	Treatment	Side effects	Mean PAP	WHO-FC	All-day oxygen	PHQ-9 score	GAD-7 score
G	70s	F	Oral	None	53	III	+	12	2
H	70s	F	Oral	None	25	II	+	15	4
I	50s	F	Post-BPA	None	24	II	-	11	2
J	60s	F	Oral	Headache	31	II	+	14	11
K	70s	F	Oral	None	31	III	+	13	6
L	60s	F	Ongoing-BPA	None	51	III	+	13	9
M	50s	M	Oral	None	42	III	-	19	6
								Mean13.9	Mean6.9
								SD2.6	SD3.3

BPA, balloon pulmonary angioplasty; CTEPH, chronic thromboembolic pulmonary hypertension; GAD-7, 7-item Generalised Anxiety Disorder questionnaire; PAP, pulmonary arterial pressure; PHQ-9, 9-item Patient Health Questionnaire; WHO-FC, WHO-Functional Class.

They felt isolated, unable to confide in friends, family or medical staff about their distress; alienated; and unable to join groups.

Examples

My disease is severe, but because I look fine, my co-workers don't understand my situation. (B)

I used to have many friends, but we lost contact when I became sick. I have no one to confide in, so it's tough. (A)

My husband helps me, but I feel bad having to ask him. (K)

Theme 3: Hassle associated with oxygen therapy

Definition

Participants felt distressed by the changes in their appearance associated with the oxygen tube and by the burden of having to cart around their oxygen cylinder. The CTEPH patients in particular suffered from the feeling of being restricted by the oxygen tube and the pain caused by the tube when pulled.

Examples

The sense of always being tied to this oxygen tube is really distressing. (G)

Because I live in the countryside, people stare at me when I go out with the oxygen. (E)

If I just didn't need the oxygen, things would be very different....I tell myself, 'It can't be helped' but really, it's a terrible burden. (J)

Theme 4: Fear of illness progression/deterioration

Definition

Participants constantly felt anxious that their condition may worsen. When their physical condition deteriorated, they felt shocked and disappointed. When their doctor talked about the possibility of initiating injection therapies because of their deteriorating health, they felt anxiety, conflict, and despair.

Examples

My doctor said that my heart is getting swollen.... I became very dejected because I thought my condition would only get worse in the future. (E)

My doctor said I need subcutaneous injections. I became so depressed, I thought I would be better off dead, and imagined a hanging rope dropping down towards me. (C)

I worry about what will happen in the future. I wonder things like, 'Will the pain always be like this?' (G)

Theme 5: Suffering from side effects (PAH only)

Definition

The side effects of treatment experienced by the participants (eg, nausea, foot pain, jaw pain and injection-site pain). Generally, side effects increased as patients' medication dosage increased. Pain could become intolerable. The side effects caused negative experiences such as mental lethargy and depression, resulting in decreased activity in daily living (eg, going outside or doing housework).

Examples

Subcutaneous injection-site pain is the worst pain that I have ever experienced. (B)

If I complain that my feet hurt, my doctor says, 'It's important that you take the medicine, be tough!' (E)

I don't want to move because of pain and nausea. (D)

Theme 6: Rumination on illness due to breathlessness (CTEPH only)

Definition

Physical distress caused psychological distress. The CTEPH patients experienced shortness of breath and fatigue associated with their illness. These symptoms worsened when the patients walked up or down the stairs, did housework, or talked while walking.

Examples

Breathlessness is the hardest thing. It is tough for me to do anything without oxygen. (G)

Table 5 Themes and subthemes

Theme	Subtheme	
	PAH	CTEPH
Loss of myself	Disappointment in self when unable to play a social role	
	Loss of independence	
	Irritability regarding physical disability	
	Loss of purpose of life	
	Hopelessness	
	Anxiety about finances that is increasing because I cannot work	
	Seeking reasons for the current situation	
	Stress about activity limitations	
	Discouragement and regret for past actions	
Isolation from my surroundings	Having no one who listens to my feelings	
	Not wanting to be a burden to others	
	Lack of understanding from others	
	Hard to move like others	
	Feeling of alienation from friends	
Hassle associated with oxygen therapy	Appearance with oxygen	
	Burden of going out with oxygen	
	Difficulty in moving because of pulling oxygen cylinder	Sense of restraint linked to oxygen
		Pain when oxygen tube is pulled
Fear of illness progression/deterioration	Fear of disease progression	Anxiety that illness will last for a lifetime
	Shock of getting worse	Anxiety about physical weakness
	Anxiety and conflict regarding injection therapy	Anxiety about breathlessness
	Despair due to the possibility of starting injection therapy	
Suffering from side effects	Balance between strong side effects and life	
	Endurance of side effects that cannot be tolerated due to deterioration of health	
	Distress due to side effects	
	Lethargy caused by side effects	
	Negative emotions caused by side effects	
	Decrease in ADL due to side effects	
	Ineffective countermeasures for pain	
	Resignation to having to cope with side effects	
Rumination on illness due to breathlessness		Associating illness with breathlessness
		Emotional pain by dyspnea on exertion

ADL, activities of daily living; CTEPH, chronic thromboembolic pulmonary hypertension; PAH, pulmonary arterial hypertension.

I feel suffocated, which makes me think about my illness more intensely—it's so depressing. (J)
 When I take a walk with my wife, I sometimes forget my physical condition and start chatting, which causes breathlessness. (M)

DISCUSSION

Integration of the quantitative and qualitative data

We demonstrated that 44.6% of the participants reported some levels of depressive symptoms (PHQ-9 ≥ 5). This finding was similar to the findings of prior research.^{12–18} This suggests, that despite dramatic advances in

treatment methods that have improved life expectancy, mental health has not improved. To better understand these results, we conducted qualitative interviews with participants who had depressive symptoms. Analysis of the interviews identified four common themes: 'Loss of myself,' 'Isolation from my surroundings,' 'Hassle associated with oxygen therapy,' and 'Fear of illness progression/deterioration.' By integrating the qualitative data, it became clear that the sense of loss and alienation associated with the onset of the disease, as well as the side effects and hardships associated with treatment such as oxygen therapy, affected the mental state of the patients,



indicating the need for interventions to address these issues. Similarly, Muntingh *et al* reported that patients with PAH mentioned low and fluctuating energy levels, difficulties with loss of abilities, worries about the future, restricted ability to fulfil their social roles and being misunderstood by others.¹⁹ It should be noted that their study focused on PAH patients only, while our study extracted similar themes from both the CTEPH and the PAH patients. In our study, integrating qualitative and quantitative data led to the elucidation of common and disease-specific factors in PAH and CTEPH.

Almost all of the previous studies on psychological distress in PH patients were quantitative studies. Since our study used mixed-methods, it was possible to clarify patients' experiences that are related to depression and anxiety.

Although PAH and CTEPH both belong to the larger category of PH, their epidemiological characteristics, treatment methods, and prognoses differ; we, therefore, analysed them separately. Our analyses showed that the majority of themes are common to both PAH and CTEPH, but that there are themes that are specific to each disease ('Suffering from side effects' for PAH and 'Rumination on illness due to breathlessness' for CTEPH). This new knowledge contributes to a better understanding of the lived experience of patients with PAH and CTEPH and thus to the provision of better healthcare.

Depression, anxiety and psychological distress with PAH

The incidence of depression in our PH sample was comparable to other critical illnesses such as heart failure (42.1%)³² and cancer (50.2%),³³ indicating that systematic psychological support is needed. The proportion of PAH patients with depressive symptoms was higher than that of CTEPH patients.

Four out of six PAH patients who had moderate to severe depression were taking Selexipag, and their depressive symptoms were more severe than the symptoms experienced by the two patients who were not taking Selexipag. Selexipag is an oral PAH medicine that is widely used as it decreases shortness of breath. In Japan, nursing consultation support is not currently available to patients undergoing only oral therapy. Unlike with CTEPH, there is no surgical treatment for PAH, and therefore, no way to completely cure the disease except lung transplantation, and so drug therapy remains the main treatment. Thus, PAH patients are in a situation where side effects are almost inevitable. Compared to before 2000, current drug therapies have led to greater patient survival, and some healthcare providers may think that patients should endure the drugs' side effects because they improve their prognosis. Our findings make it clear that patients are suffering from these side effects, and that support for PAH patients experiencing side effects is of paramount importance; thus, nursing consultation, systematic support and interventions that enable patients to manage symptoms on their own for such patients are

strongly recommended. This study was conducted on all the participants during outpatient visits, but since it was conducted at only one facility and the number of participants was only 25, it cannot be generalised. In the future, it will be necessary to conduct the research at more facilities and verify the results.

Depression, anxiety and psychological distress with CTEPH

CTEPH patients had a lower rate of depressive symptoms than PAH patients. This finding contradicts that of Pfeuffer *et al*, who reported greater depression among CTEPH patients (56%) than PAH patients (30%).¹⁸ A possible explanation is the use of BPA to treat CTEPH is widespread in Japan, and the facility where this research was conducted performs BPA as a standard treatment for patients with peripheral CTEPH. About half of the CTEPH patients participating in the study had already received BPA, and this group had significantly lower mean PAP, higher functional status (WHO Functional class I or II only), and lower PHQ-9/GAD-7 scores. Five out of seven CTEPH patients who reported moderate to severe depression were in the pre-BPA group, and one patient had just started BPA. These results suggest that BPA contributes to the improvement of psychological status, and that CTEPH patients who have not undergone BPA are at high risk for depression and anxiety.

Overall, participants who were post-BPA had improved haemodynamics and lower depression and anxiety scores. However, one participant had moderate depression despite low mean PAP and withdrawal from oxygen therapy. This participant's depression scores may have related to other confounding factors, but may also have resulted from a gap between expectations and reality: the participant in question said that she 'did not feel as recovered as I thought I would' after the BPA. Our results indicate it is important to screen for depressive symptoms even among post-BPA patients, ideally using simple indicators during regular visits. Five out of seven CTEPH patients with moderate to severe depression used oxygen all day, and the use of all-day oxygen therapy was significantly associated with poor psychological status. In addition, the theme 'Hassle associated with oxygen therapy' was extracted from the analysis of the qualitative interview data. These results suggest that the CTEPH patients who are under oxygen therapy are at a higher risk of psychological distress, requiring extra care in this regard. We found no statistically significant difference in the incidence of moderate to severe depression between WHO functional classifications. However, in the qualitative analysis, we extracted the theme of 'Rumination on illness due to breathlessness' as an important issue among patients with CTEPH. This indicates a need to assess the situation regarding shortness of breath and rapid fatigue among CTEPH patients, listen to patients' thoughts about their situations and provide guidance on how to manage their lives while reducing the burden associated with oxygen therapy.

In our clinical sample, anxiety was less prevalent than depression. This contrasts with the past studies, which found anxiety to be more prevalent than depression, or anxiety being comparable to depression.¹⁴ This difference is partly due to the high proportion of our study participants with post-BPA. BPA is expected to restore PAP within the normal range, which leads to reduced anxiety. The theme ‘fear of illness progression/deterioration’ was extracted from both the PAH and the CTEPH groups. It is important to keep in mind that even though the proportion of patients with anxiety was small, there are still patients who experience anxiety and fear of deterioration. Since this survey was a cross-sectional study of the state of affairs at a given point in time, it was not possible to compare mental states before and after the introduction of BPA. In addition, the analysis was limited to focusing only on psychological states such as depression and anxiety. In the future, it will be necessary to conduct comparative studies before and after BPA and to analyse the association between mental status and QOL in order to clarify the actual situation.

CONCLUSION

The study found that patients with PH are prone to depression. The factors and themes identified in this study as affecting PH patients’ psychological distress. The identification of factors and themes that influence the psychological distress of PH patients in this study is important information that can be used to improve the support of healthcare providers for the physical and mental health of these patients. Interventions for the components of distress identified in this study may contribute to improving the mental status of PH patients. Based on the study results, it is necessary to develop support programmes for patients’ mental and physical self-management.

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