Health-Related Quality of Life in Patients With Chronic Thromboembolic Pulmonary Hypertension

Norikazu Yamada, MD, PhD

Chronic thromboembolic pulmonary hypertension (CTEPH) is a progressive disease caused by an increase in pulmonary vascular resistance (PVR) leading to right ventricular failure. Pulmonary endarterectomy (PEA) is recommended as the only curative treatment of choice for eligible patients with CTEPH and should be considered as the first treatment option whenever possible.^{1,2} Successful PEA can dramatically improve the patient's hemodynamics and prognosis.

However, only a proportion of patients fulfill the criteria for surgical intervention and medical treatment has been attempted in cases of inoperable distal-type CTEPH and post-PEA residual PH with a distal lesion. Principal medical treatment for CTEPH consists of life-long anticoagulant, oxygen supply and pulmonary vasodilator. Although off-label use of drugs approved for pulmonary arterial hypertension (PAH), including prostacyclin analogs, endothelin-receptor antagonists, and phospho-

Table. HRQOL Instruments Used in PAH

Instrument	No. of items	No. of domains	Content of domains
Generic measures			
Medical Outcome Study 36-Item Short Form Health Survey (SF-36)	36	8	Physical functioning Role physical Bodily pain General health Vitality Social functioning Role emotional Mental health
Nottingham Health Profile (NHP)	38	6	Physical mobility Pain Sleep Social isolation Emotional reactions Energy
Multi-attributed and preference-based utility measures			
EuroQol (EQ-D) utility index	5	5	Mobility Self-care Usual activity Pain/discomfort Anxiety/depression
Australian Assessment of Quality of Life (AQoL)	15	5	Illness Independent living Physical ability Psychological well-being Social relationships
Condition-specific measures			
Minnesota Living with Heart Failure Questionnaire (MLHFQ)	21	2	Physical Emotional
St. George's Respiratory Questionnaire (SGRQ)	76	3	Symptoms Activity Impact
PAH-specific measures			
Cambridge Pulmonary Hypertension Outcome Review (CAMPOR)	65	3	Symptoms (energy, breathlessness, mood) Functioning QOL

Modified from Rubenfire et al⁴ and Chen et al.⁵ HRQOL, health-related quality of life; PAH, pulmonary arterial hypertension.

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Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan

Mailing address: Norikazu Yamada, MD, PhD, Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, 2-174 Edobashi, Tsu 514-8507, Japan. E-mail: n-yamada@clin.medic.mie-u.ac.jp

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diesterase-5 inhibitors, has been considered for CTEPH treatment in the past,³ the soluble guanylate cyclase agonist, riociguat, was recently approved and available for inoperable CTEPH and persistent or recurrent pulmonary hypertension after PEA.¹ In addition, balloon pulmonary angioplasty (BPA) is recently gaining attention as an effective treatment option for distal-type CTEPH.

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Clinical parameters used to estimate prognosis and response to treatment in PH include the WHO functional class, the Borg dyspnea index, the standardized 6-min walk distance (6MWD), cardiopulmonary exercise testing, right ventricular function by echo Doppler or nuclear imaging, and hemodynamics on right ventricular catheterization including response to pulmonary vasodilator testing. Each parameter (particularly the 6MWD and hemodynamic parameters) has value, but there is only a modest positive correlation between each measure and outcome.⁴ The ultimate goal of PH treatment is to improve survival, but symptom relief and quality of life (QOL) improvement are also important. Clinical research in other diseases has established health-related QOL (HRQOL) to be an important endpoint.⁵ Whether a combination of validated specific measures of QOL, functional and hemodynamic parameters and biomarkers can improve the clinical care of patients needs to be assessed. Such parameters are also needed to assist in the decision for therapy, medical disability support and social welfare.⁴ Although it is known that pulmonary hemodynamics do not correlate well with how PH patients feel and function in their daily lives,⁵ little is known about the relationship between HRQOL and exercise tolerance, hemodynamics and survival in patients with CTEPH.

In this issue of the Journal, Urushibara et al⁶ investigate the predictors of QOL in patients with CTEPH, changes in QOL after surgical and medical treatments, and the relationship between baseline QOL and survival. They demonstrate that PVR and 6MWD were associated with physical functioning (PF) or physical component summary (PCS) in CTEPH patients. And QOL also improved after surgical or medical therapies, with a greater change in the surgical group. PAH-specific therapy such as bosentan and sildenafil improved survival in patients with lower PF at diagnosis. This is the largest study, including 128 patients with CTEPH, to investigate QOL determinants in CTEPH and the influence of QOL on survival in medically-treated CTEPH patients.

Instruments used to assess HRQOL have varied from study to study; for example, generic measures (medical outcome study 36-item short form health survey (SF-36), Nottingham health profile), condition-specific measure (Minnesota Living with Heart Failure Questionnaire) and PAH-specific measure (Cambridge Pulmonary Hypertension Outcome Review) (Table).⁷ Although the SF-36 was used in the current study, which instrument is best to assess HRQOL in CTEPH patients may be unresolved issue. A single standard questionnaire may not be enough to describe the psychological, social, and emotional burdens of CTEPH.

Some studies of PH have demonstrated a correlation between improvement in 6MWD and higher HRQOL scores, but often hemodynamic variables do not correlate with benefits of medical therapy or exercise and respiratory training.⁴ The degree to which physical symptoms of fatigue, weakness, and shortness of breath are induced by anxiety, depression, panic, and hopelessness in CTEPH patients is not clear.⁴ Harzheim et al demonstrated that anxiety and depression were frequently

diagnosed and significantly correlated with QOL in 158 patients with PH, including 20 patients with inoperable CTEPH.⁸ Social support systems such as family, employers, PH support groups, religious belief, and the availability of health insurance can have a major influence on perceived well-being, motivation, confidence, compliance, and even outcome. How each of these variables contributes to the QOL and psychological symptoms in PH is unclear and should be clarified.⁴

It is interesting that mental components significantly improved after both surgical and medical therapies but PCS improved only after surgical therapy in this study. As mentioned, BPA is now expected to be an effective option for CTEPH treatment. BPA has the potential to improve not only the hemodynamic data but also exercise capacity and prognosis, and can be applied to those patients for whom PEA is not an option because of distal surgically inaccessible lesions or residual PH after PEA.^{9–12} Although this study did not include patients undergoing BPA, it is hoped that the change in QOL after BPA will be assessed in the near future.

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