RESEARCH ARTICLE

# A systematic review of the impact of pulmonary thromboendarterectomy on health-related quality of life

Aarohanan Raguragavan[1] | Dujinthan Jayabalan[1,2] | Sugam Dhakal[1] | Akshat Saxena[3]

[1]Medical School, University of Western Australia, Nedlands, Western Australia, Australia

[2]Department of Hepatology, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia

[3]Department of Cardiothoracic Surgery, Royal Hobart Hospital, Hobart, Tasmania, Australia

**Correspondence**
Dujinthan Jayabalan, The University of Western Australia (M503), 35 Stirling Hwy, Nedlands, WA 6009, Australia.
Email: duji.jayabalan@uwa.edu.au

## Abstract

Pulmonary thromboendarterectomy (PTE) is the current gold standard treatment for chronic thromboembolic pulmonary hypertension (CTEPH) and is a viable treatment option for chronic thromboembolic pulmonary disease (CTEPD). The progressive nature of both diseases severely impacts health-related quality of life (HRQoL) across a variety of domains. This systematic review was performed to evaluate the impact of PTE on short- and long-term HRQoL. A literature search was conducted on PubMed for studies matching the eligibility criteria between January 2000 and September 2022. OVID (MEDLINE), Google Scholar, EBSCOhost (EMBASE), and bibliographies of included studies were reviewed. Inclusion of studies was based on predetermined eligibility criteria. Quality appraisal and data tabulation were performed using predetermined forms. Results were synthesized by narrative review. The structure of this systematic review follows the PRISMA guidelines. This systematic review was prospectively registered in the PROSPERO register (CRD42022342144). Thirteen studies (2184 patients) were included. Within 3 months post-PTE, HRQoL improved in both CTEPD and CTEPH as measured by disease-specific and generic questionnaires. HRQoL improvements were sustained up to 5 years postoperatively in patients with CTEPH post-PTE. PTE remains the gold standard for treating CTEPH and improving HRQoL. Residual pulmonary hypertension and comorbidities such as COPD and coronary artery disease decrement HRQoL over time. The impact of mPAP and PVR on HRQoL outcomes postoperatively remain ambiguous. Pulmonary thromboendarterectomy remains the gold standard for treating CTEPH and has shown to improve HRQoL outcomes at 3-month sustaining

**Abbreviations:** BPA, balloon pulmonary angioplasty; CAMPHOR, Cambridge Pulmonary Hypertension Outcome Review; COPD, chronic obstructive pulmonary disease; CTEPD, chronic thromboembolic pulmonary disease; CTEPH, chronic thromboembolic pulmonary hypertension; HRQoL, health-related quality of life; MeSH, PubMed medical subject headings; MLHFQ, Minnesota Living with Heart Failure Questionnaire; mPAP, mean pulmonary arterial pressure; PRISMA, preferred reporting items for systematic reviews and meta-analyses; PROSPERO, international prospective register of systematic reviews; PTE, pulmonary thromboendarterectomy; PVR, pulmonary vascular resistance; RPH, residual pulmonary hypertension; SF-36, 36-item short form survey; SGRQ, St. George Respiratory Questionnaire.

improvements up to 5-year postoperatively. Residual pulmonary hypertension and comorbidities hinder HRQoL outcomes post-PTE.

# INTRODUCTION

## Rationale

Chronic thromboembolic pulmonary hypertension (CTEPH)[1] and chronic thromboembolic pulmonary disease (CTEPD)[1] represent a failure to resolve thrombotic vascular obstruction in the pulmonary arteries. CTEPH and CTEPD are characterized by differing magnitudes of mechanical obstruction of the major pulmonary arteries with fibro-thrombotic material and concomitant microvascular arteriopathy.[2–4] CTEPH and CTEPD are two current indications for pulmonary thromboendarterectomy (PTE).[4–6]

Untreated, CTEPH typically progresses to right heart failure and death,[4] with reported 3-year mortality of 30%–60%.[7] The progressive nature of the disease severely impacts health-related quality of life (HRQoL) across a variety of domains.[2] PTE is considered the gold standard for all CTEPH patients eligible for surgery.[8] PTE significantly increases long-term survival than medical treatment alone.[9] The improvements yielded by PTE with regard to survival, haemodynamic parameters, and functional status in conjunction with the poor HRQoL associated with CTEPH would suggest that the measurement of HRQoL post-PTE occur frequently.[2,9] However, there have been limited attempts to report health-related quality of life both in patients with CTEPH and following PTE.[2] Recent advancements in medical treatment options for PTE have demonstrated improvements in HRQoL, and evaluation of postoperative HRQoL outcomes remains vital in ensuring clinicians are able to make up to date, evidence-based treatment decisions.[8]

Although PTE is considered the gold standard treatment for CTEPH, the management of patients with symptomatic CTEPD is less clear cut. PTE may impart clinical and haemodynamic improvements at rest and exercise.[10] Understanding HRQoL changes in individuals post-PTE is vital in elucidating the best practice for clinicians and decision-makers.[10]

This systematic review aims to: (i) summarize the literature and clarify strengths and weaknesses of current evidence on HRQoL outcomes post-PTE, (ii) demonstrate and quantify the benefit post-PTE on HRQoL outcomes in patients with CTEPD or CTEPH, (iii) identify factors influencing HRQoL post-PTE, and (iv) provide a foundation for future research into HRQoL in CTEPD or CTEPH patients.

# METHODS

This systematic review followed the structure outlined by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines[11–13] and aligns with the methodology described by Grant and Booth.[14] This systematic review was prospectively registered in the International prospective register of systematic reviews (PROSPERO) register (CRD42022342144). As such this systematic review, was conducted in accordance with PRISMA and PROSPERO guidelines. Institutional review board approval was not required as the data was retrieved from publicly available databases and did not involve collection of patient data.

# Definition and measurement of health-related quality of life

The US Food and Drug Administration[15] define HRQoL as "a multidomain concept that represents the patient's overall perception of the impact of an illness and its treatment."[15] The definition further continues, to state regarding the measurement of HRQoL—"an HRQL measure captures, at a minimum, physical, psychological (including emotional and cognitive), and social functioning."[15]

Accurate HRQoL instruments account for a variety of factors including the presence of symptoms, functioning, affect, and personal relations.[16,17] Best reflecting HRQoL accounts for patients' subjective perceptions and objective health status, effective HRQoL measurement instruments must be reliable, valid, responsive, sensitive, and cover all health domains.[16] Pulmonary hypertension (PH) specific HRQoL instruments such as the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) have been validated in CTEPH and CTEPD.[18] Disease-specific instruments such as the Minnesota Living with

Heart Failure Questionnaire (MLHFQ)[19,20] and the St. George Respiratory Questionnaire (SGRQ),[21] the latter of which having not been validated for CTEPH/CTEPD,[22] are utilized in the literature. A commonly used generic HRQoL instrument in thoracic surgery is the Medical Outcomes Survey Short-Form 36 (SF-36).[23,24]

## Eligibility criteria

Studies considered for review had the following characteristics: (i) adult patients post-PTE, (ii) disease-specific and/or generic HRQoL data recorded using a validated HRQoL assessment instrument, and (iii) postoperative HRQoL scores of PTE patients compared to preoperative, waitlisted/nonwaitlisted patients, general population, and/or other medical management of CTEPD/CTEPH. Studies were restricted according to the following report characteristics: (i) publication date after January 2000, (ii) English language, and (iii) original articles. Only original search manuscripts published in peer-reviewed journals were included. Randomized-control trials, retrospective studies, cross-sectional studies, prospective studies, cohort-studies, and longitudinal studies were deemed suitable for inclusion.

## Information sources and search strategy

A preliminary literature search applying the eligibility criteria outlined above (Figure 1) was conducted using Medical Subject Headings (MeSH) keyword search on PubMed (MEDLINE) in September 2022. Additionally, OVID (MEDLINE), Google Scholar, and EBSCOhost (EMBASE) were manually searched as well as a review of the bibliographies of each included study to identify studies which had not been retrieved in the preliminary MeSH keyword search. All identified articles were retrieved from the above referenced databases.

## Study selection

A. R. and D. J. independently screened titles and abstracts after MeSH keyword and manual searches. Studies were excluded if they did not meet eligibility criteria.

## Data items and extraction

Data items for assessment of study quality (Table 1) and study results (Table 2) were predetermined by A. R. and

A. S. Data extraction was then performed by S. D. and D. J. using standardized pilot forms.

## Synthesis of results

Qualitative analysis was performed per pre-existing guidelines where scores from HRQoL tools were categorized into physical, mental, and functional health domains which were either generic or disease-specific.[2,38]

## Risk of bias

Qualitative analysis based on study quality was used to assess the risk of bias in individual studies with data tabulated in Table 1. Specific tools were not utilized to assess bias within studies due to clinical heterogeneity and unfeasibility of meta-analysis. Each study was assessed for significant selection, performance, detection or reporting bias; supported by the Cochrane guidelines on systematic reviews.[39] Assessment of bias was performed according to the PRISMA guidelines.[11–13] Levels of evidence for individual studies were assessed using previously outlined guidelines (NHMRC Evidence Hierarchy).[40]
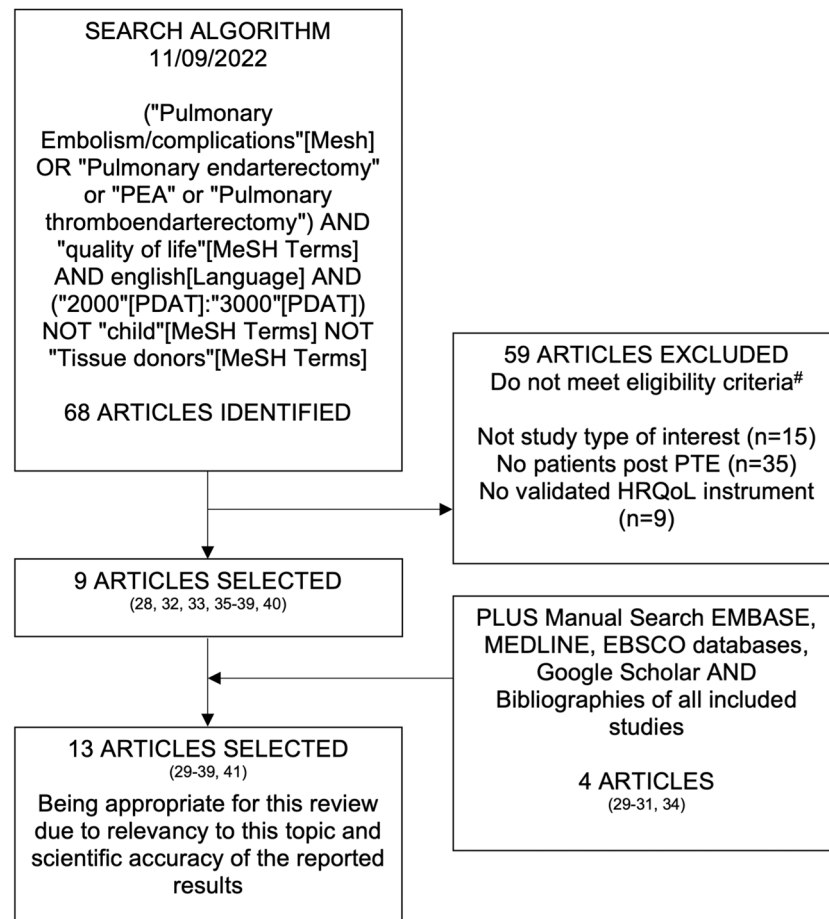
## RESULTS

### Study selection

Following a thorough literature search, 13 studies were chosen to be included in this systematic review (Figure 1). The studies demonstrated significant diversity between comparison groups, used a wide variety of HRQoL instruments, lacked preoperative data, and occasionally did not express data as mean ± standard deviation. The lack of clinical, statistical, and methodological heterogeneity precluded meta-analysis and direct comparison.

### Study characteristics and risk of bias within studies

A systematic review of all literature meeting the eligibility criteria (Figure 1.) was employed to minimize reporting bias. As reported in Table 1, systematic analysis of the resulting studies was undertaken to determine the strength of evidence. Scarcity of comprehensive results and heterogeneity in data presentation precluded detailed and direct comparison of the included studies.

SEARCH ALGORITHM
11/09/2022

("Pulmonary
Embolism/complications"[Mesh]
OR "Pulmonary endarterectomy"
or "PEA" or "Pulmonary
thromboendarterectomy") AND
"quality of life"[MeSH Terms]
AND english[Language] AND
("2000"[PDAT]:"3000"[PDAT])
NOT "child"[MeSH Terms] NOT
"Tissue donors"[MeSH Terms]

**68 ARTICLES IDENTIFIED**

**59 ARTICLES EXCLUDED**
Do not meet eligibility criteria#

Not study type of interest (n=15)
No patients post PTE (n=35)
No validated HRQoL instrument
(n=9)

**9 ARTICLES SELECTED**
(28, 32, 33, 35-39, 40)

PLUS Manual Search EMBASE,
MEDLINE, EBSCO databases,
Google Scholar AND
Bibliographies of all included
studies

**4 ARTICLES**
(29-31, 34)

**13 ARTICLES SELECTED**
(29-39, 41)
Being appropriate for this review
due to relevancy to this topic and
scientific accuracy of the reported
results

#Eligibility criteria outlined in methods section
- adult patients post-pulmonary thromboendarterectomy (PTE)
- disease-specific and/or generic QoL data recorded using a validated HRQoL
  assessment instrument
- postoperative HRQoL scores of PTE patients compared to pre-operative,
  waitlisted/non-waitlisted patients, general population, and/or other medical
  management of CTED/CTEPH.

**FIGURE 1** Search algorithm.

Variation in study design and statistical analysis additionally limited comparison of results. Preclusion of direct and comprehensive comparison represents a source of bias as heterogeneity between studies alters the degree to which exact conclusions can be made.

Twelve studies[25–32,34–37] reported response rates which ranged between 37.5% and 100%. Response rates were variable and poorly reported. Patients who are unable to respond may tend to be more unwell and as such low response rates may skew data more positively.[41] Rates of follow-up varied between studies; length of follow-up ranged between 12 weeks[27] to 5 years,[37] most studies did not report mean follow-up length with one study not reporting follow-up entirely.[33]

All included studies were selected based on the use of HRQoL instruments validated for patients' post-PTE or

with a diagnosis of PH. Instruments were either pulmonary specific, disease-specific, or generic. Nine studies used generic questionnaires with all nine studies using the SF-36.[25,26,29,30,32–36] Four studies used the PH specific CAMPHOR questionnaire.[27,28,31,37] One study used the pulmonary disease-specific SGRQ as well as the heart failure specific MLHFQ.[29]

## Impact of pulmonary thromboendarterectomy on HRQoL in patients with CTEPH

Eleven studies of 2065 patients compared HRQoL scores of patients post-PTE with preoperative HRQoL scores.[25,26,28–35,37] Nine reported[25,26,30,32–35,37] outcomes

**TABLE 1** Quality appraisal.

| References | No. patients | Study design | Generic HRQoL instrument | Disease specific measures | Participation rate / response rate | Level of evidence | Age (mean ± SD or range) | Sex | Location | Aetiology | Study population comparison groups in addition to pre-PEA/post-PEA: No. patients |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Genta et al.[25] | 13 | R | SF-36 | – | PR: NR RR: 100% | IV | 45.7 ± 18.3 | 46.2% M | Brazil | | No additional comparison groups |
| Yoshimi et al.[26] | 83 | R | SF-36 | – | PR: 81.9% RR: 85.3% | IV | 54 ± 13 | 32.5% M | Japan | 33/83 Hx of DVT | PTE central group: 26 PTE relatively peripheral group: 14 Medical central group: 6 Medical relatively peripheral group: 26 Medical mild disease: Group 11 |
| Vuylsteke et al.[27] | 74 | RCT | – | CAMPHOR | PR: 94.6% RR: 89.2% | II | Overall: Deep hypothermic circulatory arrest 53.5 ± 16.8 Antegrade cerebral perfusion 50.7 ± 13.7 | 47.3% M | United Kingdom | | Deep hypothermic circulatory arrest: 35 Antegrade cerebral perfusion: 39 |
| Taboada et al.[28] | 42 | R | – | CAMPHOR | PR: 85.7% RR: 75.0% | IV | 49 ± 16 | 40% M | United Kingdom | 90% Hx of VTE | No additional comparison groups |
| Petrucci et al.[29] | 49 | R | SF-36 | SGRQ MLHFQ | PR: 75.4% RR: 91.8% | IV | 56 ± 15 | 55% M | Italy | | No additional comparison groups |
| Kamenskaya et al.[30] | 128 | P | SF-36 | – | PR: 100% RR: 90.6% | III | 49.0 ± 12.9 range (19–70) | 67.2% M | Russia | 76/128 Hx of VTE | No additional comparison groups |
| Guth et al.[31] | 32 | R | – | CAMPHOR | PR: NR RR: 37.5% | IV | Median (IQR) 34 (24–60) | 50% M | Germany | | No additional comparison groups |
| Kamenskaya et al.[32] | 136 | P | SF-36 | – | PR: NR RR: 89.0% | III | 49.4 ± 12.7 range (21–71) | 57.4% M | Russia | 94/136 Hx of VTE | No additional comparison groups |
| Tamada et al.[33] | 39 | R | SF-36 | – | PR: 81.5% RR: NR | IV | Overall: 63.2 mean Early: 61.8 ± 13.8 Late: 64.6 ± 11.6 | 23.1% M Early: 20% M Late: 26.3% M | Japan | | PTE: 15 BPA: 24 |
| Vanini et al.[34] | 70 | P | SF-36 | – | PR: 73.8% RR: 51.2% | III | 48 ± 10 | 44% M | Italy | | No additional comparison groups |

(Continues)

**TABLE 1** (Continued)

| References | No. patients | Study design | Generic HRQoL instrument | Disease specific measures | Level of evidence | Participation rate response rate | Sex | Age (mean ± SD or range) | Location | Aetiology | Study population comparison groups in addition to pre-PEA/post-PEA: No. patients |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Kamenskaya et al.[35] | 128 | P | SF-36 | SGRQ | III | PR: 100% RR: 83.6% | 67.2% M | 49.0 ± 12.9 range (19–70) | Russia | 76/128 Hx of VTE | No additional comparison groups |
| Nagel et al.[36] | 45 | P | SF-36 | – | III | PR: 83.3% RR: 80.0% | 51.1% M | 57.62 ± 12.44 95% CI (53.89–61.36) median (IQR) 59 (21) | Germany | 17/45 Hx of DVT | No additional comparison groups |
| Newnham et al.[37] | 1342 | R | – | CAMPHOR | IV | PR: 79.5% RR: 74.5% | 53.2% M | Median ± IQR 61 ± 21 | United Kingdom | | No additional comparison groups |

Abbreviations: BPA, balloon pulmonary angioplasty; CAMPHOR, Cambridge Pulmonary Hypertension Outcome Review; CTEPH, chronic thromboembolic pulmonary hypertension; HRQoL, health-related quality of life; Hx, history; IQR, interquartile range; M, male; MLHFQ, Minnesota Living with Heart Failure Questionnaire; NR, not reported; P, prospective; PR, participation rate; PTE, pulmonary thromboendarterectomy; R, Retrospective; RCT, randomised controlled trial; RR, response rate; SD, standard deviation; SF-36, 36-item short form survey; SGRQ, St. George Respiratory Questionnaire; VTE, venous thromboembolism.

for patients with CTEPH, whilst two reported CTEPD patients.[28,31] Eight studies utilized the generic SF-36 HRQoL instrument,[25,26,30,32–35] one in addition to the SGRQ and the MLHFQ.[29] Three studies investigated changes in HRQoL using CAMPHOR.[28,31,37] All studies established that HRQoL was improved by PTE in patients with either CTEPH or CTEPD, the extent and domains of improvement varied between studies.[25,26,28–35,37] Three studies by Kamenskaya et al.[30,32] show some degree of population overlap recruiting participants between September 2011 and February 2016.

Six studies compared HRQoL scores preoperatively with scores within the first year post-PTE using the SF-36. At 3 months patients experience significantly improved mental and physical SF-36 composite scores compared to their preoperative state.[29,34] At 1 year two studies presented improvements across all domains of the SF-36.[29,32] Two studies determined a lack of improvement in mental health, preoperative scores in these studies were reported to show no significant difference from normative population scores.[25,30] Per Kamenskaya and colleagues, by the first year, all domains of HRQoL increased excluding general health, greatest improvements were seen in bodily pain, vitality, role physical, and mental health.[30] A study examining invasive management of CTEPH at 1-year postintervention, which combined results of balloon pulmonary angioplasty (BPA) and PTE, identified that invasive management improved HRQoL across all domains excluding bodily pain.[33] Preoperative results were not provided for comparison.

Yoshimi et al.[26] described HRQoL beyond the first year, stating that physical function, role physical, vitality, social functioning, and mental health domains of HRQoL improved immediately post-PTE with improvements sustained up to 3 years, regardless of the distribution of thromboembolic disease. Kamenskaya et al.[35] determined sustained improvements across all SF-36 domains from 1 year up to 3 years postoperatively. A singular study investigated HRQoL post-PTE utilizing a PH specific instrument, CAMPHOR.[37] Post-PTE patients derive statistically significant improvements in symptoms, activity, and quality of life.[37] All improvements in CAMPHOR score exceeded the minimum clinically important difference defined for the instrument.[37] Pre-PTE CAMPHOR scores reduce significantly, representing an improvement, by 1 year and reduce further by 2-years from which the CAMPHOR score is sustained to 5 years.[37] Using pulmonary disease and heart failure specific instruments Petrucci et al.[29] demonstrate improvements in MLHFQ and SGRQ scores in patients undergoing PTE at 3- and 12-month postoperatively.

**TABLE 2** Results of included studies.

| References | Method of follow-up | Follow-up interval | Comparison groups | | | Other groups |
|---|---|---|---|---|---|---|
| | | | **Pre-PTE** | **Non-PTE** | | |
| Genta et al.[25] | Self-administered questionnaires by researcher initially and by mail post PTE | Baseline, >3 months post PTE  Mean 8.9 months post PTE | YES | N/A | | Controls (normal individuals) |

SF-36 Score: Preoperative (mean ± SD), postoperative (mean ± SD), ($p$ Value postoperative vs. preoperative), controls (mean ± SD), ($p$ Value controls vs. preoperative), ($p$ Value controls vs. postoperative)

- Physical function: 28.9 ± 25.3, 78.5 ± 22.2, ($p = 0.0001$), 92.3 ± 7.5, ($p < 0.001$), ($p > 0.05$)
- Role physical: 11.5 ± 28.2, 68.1 ± 39.0, ($p = 0.0005$), 92.3 ± 27.7, ($p < 0.001$), ($p > 0.05$)
- Bodily pain: 54.8 ± 22.4, 70.0 ± 24.7, ($p = 0.0372$), 77.2 ± 21.1, ($p < 0.05$), ($p > 0.05$)
- General health: 49.1 ± 18.3, 83.4 ± 17.3, ($p = 0.0001$), 86.3 ± 9.1, ($p < 0.001$), ($p > 0.05$)
- Vitality: 42.3 ± 18.3, 78.5 ± 26.8, ($p = 0.0033$), 67.7 ± 16.8, ($p < 0.001$), ($p > 0.05$)
- Social function: 43.3 ± 30.0, 82.3 ± 19.0, ($p = 0.0010$), 84.6 ± 19.6, ($p < 0.001$), ($p > 0.05$)
- Role emotional: 35.9 ± 48.0, 84.5 ± 32.3, ($p = 0.0215$), 76.9 ± 39.4, ($p < 0.05$), ($p > 0.05$)
- Mental health: 61.2 ± 24.2, 77.0 ± 22.3, ($p = 0.0872$), 78.5 ± 19.5, ($p > 0.05$), ($p > 0.05$)

There was a significant improvement in HRQoL postoperatively in the domains: Physical function, role physical, bodily pain, general health, vitality, social function, role emotional when compared to preoperatively. The improvement in the mental health domain was notable but not statistically significant ($p = 0.0872$). Preoperatively, patients had a significantly worse HRQoL compared to the controls in each domain, except for the mental health domain. Postoperatively, patients had a comparable HRQoL to the controls, with no significant difference in any HRQoL domains, except for physical function ($p < 0.05$). We can conclude that PTE improves HRQoL in patients such that they are comparable to a normal population.

| References | Method of follow-up | Follow-up interval | Pre-PTE | Non-PTE | | Other groups |
|---|---|---|---|---|---|---|
| Yoshimi et al.[26] | Self-administered questionnaire | Within 2 weeks of baseline right heart catheterization, and between 12 and 36 months after surgery/medical treatment  Median 1.8 years, range 1.0–3.3 years | YES | YES  Medical vs PTE | | Relatively peripheral vs central arteries affected  Correlation vs. PVR |

HRQoL scores increased across all domains in the SF-36 in the PTE relatively peripheral group when compared to preoperatively. A significant increase was noted in the domains: Physical function ($p < 0.01$), role physical ($p < 0.01$), vitality ($p < 0.05$), social function ($p < 0.05$), and mental health ($p < 0.05$). In contrast to the PTE relatively peripheral group, where five of the eight domains of the SF-36 significantly improved, only two of the six domains in the medical relatively peripheral group significantly improved. The domains in which HRQoL significantly improved in the medical relatively peripheral group were role physical ($p < 0.05$) and vitality ($p < 0.05$). There was a significantly greater improvement in HRQoL in the PTE relatively peripheral group compared to the medical relatively peripheral group in the domains: Physical function ($p < 0.01$), role physical ($p < 0.05$), and general health ($p < 0.01$).

Improvement in SF-36 Score: PTE relatively peripheral group (mean ± SD), medical relatively peripheral group (mean ± SD) ($p$ Value)

- Physical function: 27.0 ± 24.9, 2.7 ± 18.0 ($p < 0.01$)
- Role physical: 60.0 ± 44.4, 20.8 ± 32.4 ($p < 0.05$)
- General health: 20.2 ± 26.0, −3.6 ± 13.3 ($p < 0.01$)

In the PTE central group, seven of the eight SF-36 domains improved at follow-up ($p < 0.05$). Only two patients were remaining in the medical central group with, not large enough for a comparison. In the medical mild disease group, five of the eight SF-36 domains improved significantly at follow-up ($p$ Value not reported). All in all, HRQoL results significantly improved in the PTE group, both central type and relatively peripheral type, when compared to preoperatively. Six of 11 of the relatively peripheral type patient who PTE and survived, did not require oxygen therapy, juxtaposed against the medically treated patients in the relatively peripheral type, in which all of the patients needed to continue oxygen therapy. It has been found that PTE has significantly better HRQoL outcomes when compared to medical treatment in both the central and relatively peripheral types.

(Continues)

**TABLE 2** (Continued)

| References | Method of follow-up | Follow-up interval | Pre-PTE | Non-PTE | Other groups |
|---|---|---|---|---|---|
| | | | | **Comparison groups** | |
| | | SF-36 Score domain correlation with PVR, Spearman correlation coefficient (*p* Value) and decrease in PVR (%), Spearman correlation coefficient (*p* Value) in patients of the relatively peripheral group<br>– Physical function: −0.88 (*p* < 0.01), 0.84 (*p* < 0.01)<br>– Role physical: −0.31 (*p* > 0.05), 0.48 (*p* > 0.05)<br>– Bodily pain: −0.54 (*p* > 0.05), 0.65 (*p* < 0.05)<br>– General health: −0.75 (*p* < 0.01), 0.90 (*p* < 0.01)<br>– Vitality: −0.56 (*p* > 0.05), 0.68 (*p* < 0.05)<br>– Social function: −0.40 (*p* > 0.05), 0.63 (*p* < 0.05)<br>– Role emotional: −0.24 (*p* > 0.05), 0.51(*p* > 0.05)<br>– Mental health: −0.51 (*p* > 0.05), 0.68 (*p* < 0.05)<br>Postoperative PVR had a significant correlation with the domains: physical function (*r* = −0.88, *p* < 0.01) and general health (*r* = −0.75, *p* < 0.01) in patients of the relatively peripheral group. In patients of the relatively peripheral group, the postoperative decrease in PVR as a % had a significant correlation with 6 of the SF-36 domains: Physical function (*p* < 0.01), bodily pain (*p* < 0.05), general health (*p* < 0.05), social function (*p* < 0.05), vitality (*p* < 0.05), and mental health (*p* < 0.05). Postoperative PVR had a significant correlation with the domains: Physical function (*r* = −0.69, *p* < 0.01), role physical (*r* = −0.38, *p* = 0.049), general health (*r* = −0.45, *p* = 0.018), and role emotional (*r* = −0.39, *p* = 0.045) in patients of the central group (nonsignificant data not reported). In patients of the central group, the postoperative decrease in PVR as a % had a significant correlation with six of the SF-36 domains, similarly to the relative peripheral group (complete data not reported). | | | |
| Vuylsteke et al. [27] | Physicians and nurses marked questionnaires | Baseline, 12 weeks, 1 year PTE<br><br>CAMPHOR HRQoL score deep hypothermic circulatory arrest<br>– Pre-PTE: 11 (6–18), 10 (8–17), (*p* = 0.93)<br>– Twelve weeks: 3 (1–9), 4 (1–9), (*p* = 0.97)<br>– One year: 4 (0–9), 1 (0–6), (*p* = 0.26)<br>No significant difference in between the CAMPHOR HRQoL score was identified between the deep hypothermic circulatory arrest and antegrade cerebral perfusion groups at baseline, 12 weeks or 1 year post PTE (*p* > 0.05) | | | Deep hypothermic circulatory arrest vs Antegrade cerebral perfusion<br><br>CAMPHOR HRQoL score deep hypothermic circulatory arrest median (IQR), antegrade cerebral perfusion median (IQR), (*p* Value) |
| Taboada et al. [28] | Self-administered questionnaires | Baseline, 6 months, 1 year post PTE<br><br>The CAMPHOR HRQoL score significantly increased (*p* = 0.0003) from 14 (14) (median [IQR]) before PTE to 2 (11) (median [IQR]) 6-months after PTE. This significant increase compared to baseline (*p* = 0.001) was maintained 1 year post PTE with a HRQoL score of 1 (12). | | | CTEPD patients instead of CTEPH |
| Petrucci et al. [29] | Self-Administered Questionnaire | Before PTE, 3 months post PTE and 1 year post PTE | YES | NO | N/A |
| | SF-36 PCS was significantly associated with all functional parameters. There was no association between the SF-36 MCS or SGRQ and the functional parameters. The PCS was very low before PTE, with the domains physical function, role physical and general health being particularly low. In contrast, the bodily pain domain was closer to the normal mean value. The PCS and all constituent domains increased after PTE at 3 months and 1 year post PTE, approaching values normal of a healthy Italian population. The MCS and its constituent domain scores were all lower before surgery, and all increased at 3 months and 1 year post PTE, approaching values normal of a healthy Italian population. The PCS and MCS significantly improved at 3 months and at 1 year post PTE. The MLHFQ showed a significant improvement in HRQOL by 31 points at 3 months, which was sustained at 1 year post PTE. The SGRQ showed a significant improvement in HRQOL by 30 points at 3 months, which was sustained at 1 year post PTE with no sustained variation. | | | | |

**TABLE 2** (Continued)

| References | Method of follow-up | Follow-up interval | Comparison groups | | |
|---|---|---|---|---|---|
| | | | Pre-PTE | Non-PTE | Other groups |

HRQOL Score: Pre-PTE, 3 months, 12 months, $p$ Value, time change $p$ Value: 3 months vs. pre-PTE, 12 months vs. pre-PTE, 12 months vs. 3 months

- SF-36 PCS: 32 ± 8, 46 ± 8, 48 ± 8, <0.001, <0.001, 0.091
- SF-36 MCS: 43 ± 11, 52 ± 10, 54 ± 8, <0.001, <0.001, 0.261
- MLHFQ: 52 ± 21, 21 ± 19, 17 ± 17, <0.001, <0.001, 0.087
- SGRQ total: 53 ± 15. 22 ± 16, 19 ± 13, <0.001, <0.001, 0.072
- SGRQ symptom: 45 ± 16, 30 ±, 29 ± 13, <0.001, <0.001, 0.549
- SGRQ activity: 68 ± 16, 30 ± 25, 26 ± 23, <0.001, <0.001, 0.126
- SGRQ impact: 48 ± 19, 16 ± 17, 12 ± 12, <0.001, <0.001, 0.107

SF-36 PCS was significantly correlated with the determinants mPAP, PVR, and exercise ability (Δ6MWD meters and Percentage of predicted walk distance). SF-36 MCS had no significantly correlated determinants. MLHFQ was significantly correlated with exercise ability, but no correlation was identified with haemodynamics. No significant correlation was identified between the SGRQ and clinical nor functional data. The extent of dyspnoea was measured using the Modified Borg Scale before and after the 6MWT. The measure was significantly correlated with SF-36 MCS, MLHFQ, and all SGRQ components before the 6MWT, but was only significantly correlated with all SGRQ components after the 6MWT.

Factors associated with HRQOL Score: Δ6MWD metres R (95% CI), $p$ Value, percentage of predicted walk distance R (95% CI), $p$ Value, mPAP R (95% CI), $p$ Value, cardiac output R (95% CI), $p$ Value, PVR R (95% CI), $p$ Value, Modified Borg Scale Pre-R (95% CI), $p$ Value, Modified Borg Scale Post-R (95% CI), $p$ Value

- SF-36 PCS: 39% (6, 64), $p = 0.012$, 36% (21, 27), $p = 0.016$, −52% (−73, −23), $p = 0.001$, 31% (−31, 58), $p = 0.126$, −40% (−65, −71), $p = 0.032$, −21% (−51, 13), $p = 0.079$, −23% (−53, 10), $p = 0.159$
- SF-36 MCS: 15% (−19, 47), $p = 0.363$, 21% (−14, 52), $p = 0.187$, 14% (−19, 45), $p = 0.420$, −32% (−59, 17), $p = 0.091$, 22% (−13, 52), $p = 0.281$, −59% (−77, −31), $p = 0.0000$, −33% (−60, 0), $p = 0.092$
- MLHFQ: −54% (−74, −27), $p = 0.001$, −52% (−73, −24), $p < 0.001$, 25% (−6, 53), $p = 0.119$, −9% (−40, 24), $p = 0.660$, 21% (−12, 50), $p = 0.290$, 42% (11, 65), $p = 0.0013$, 32% (0, 58), $p = 0.086$
- SGRQ total: −30% (−57, 24), $p = 0.072$, −29% (−57, 37), $p = 0.075$, 24% (−80, 52), $p = 0.174$, −20% (−49, 12), $p = 0.366$, 22% (−11, 50), $p = 0.310$, 52% (24, 72), $p = 0.0000$, 51% (23, 72), $p = 0.0006$
- SGRQ symptom: −13% (−33, 31), $p = 0.936$, 11% (−32, 34), $p = 0.947$, 9% (−22, 40), $p = 0.552$, 85% (−24, 40), $p = 0.565$, 19% (−30, 34), $p = 0.926$, 27% (−5, 55), $p = 0.052$, 41% (10, 64), $p = 0.076$
- SGRQ activity: −17% (−47, 15), $p = 0.198$, −13% (−44, 21), $p = 0.408$, 33% (12, 58), $p = 0.024$, −20% (−49, 13), $p = 0.253$, 22% (−10, 51), $p = 0.223$, 36% (5, 61), $p = 0.0004$, 33% (1, 59), $p = 0.015$
- SGRQ impact: −34% (−60, −25), $p = 0.085$, −38% (−63, −59), $p = 0.047$, 11% (−21, 41), $p = 0.546$, −19% (−49, 14), $p = 0.351$, 17% (−16, 46), $p = 0.387$, 47% (17, 69), $p = 0.0000$, 43% (12, 66), $p = 0.006$

| Kamenskaya et al.[30] | Self-Administered Questionnaire via telephone | Before PTE, 1 year post PTE | YES | NO | Determinants of HRQoL 1 year post PTE |

Except for the SF-36 domains: Physical function and social function, all domains had baseline HRQoL scores ≤43. All domains showed an improvement 1 year post PTE when compared to a preoperative state, with statistically significant improvements seen in the domains physical function ($p = 0.00021$), role physical ($p$ −0.00001), bodily pain ($p = 0.00022$), general health ($p = 0.08$), vitality ($p = 0.0001$), social function ($p = 0.0000$), role emotional ($p = 0.00001$) and mental health ($p = 0.00000$), and the component scores PCS ($p = 0.00001$) and MCS ($p = 0.000001$). The only domain to not exceed 40 points post PTE was general health. PCS and MCS fell within the range of 40–50 points post PTE, while five domains (physical function, bodily pain, social function, and role emotional) reached scores above 60 points.

Multivariate linear regression for factors affecting HRQoL in patients 1 year post PTE: Factor, regression coefficient (β) ± standard error, $p$ Value

(Continues)

**TABLE 2** (Continued)

| References | Method of follow-up | Follow-up interval | Comparison groups | | Other groups |
| --- | --- | --- | --- | --- | --- |
| | | | Pre-PTE | Non-PTE | |
| | | | | | – Physical function: RPH, −0.29 ± 0.131, p = 0.034, heart failure, −0.37 ± 0.138, p = 0.009<br>– Role physical: Heart failure, −0.33 ± 0.021, p = 0.021, prolonged ventilation, −0.42 ± 0.151, p = 0.015<br>– Bodily pain: Coronary artery disease, −0.48 ± 0.141, p = 0.042, RPH, −0.29 ± 0.130, p −0.034<br>– General health: Chronic obstructive pulmonary disease, −0.61 ± 0.138, p = 0.021, heart failure, −0.48 ± 0.152, p = 0.042, neurological complications, −0.43 ± 0.149, p = 0.006<br>– Vitality: Heart failure, −0.36 ± 0.137, p = 0.013, prolonged ventilation, −0.36 ± 0.131, p = −0.046<br>– Social function: No significant factors<br>– Role emotional: Prolonged ventilation, −0.57 ± 0.136, p = 0.035, neurological complications, −0.63 ± 0.121, p = 0.003<br>– Mental health: Prolonged ventilation, −0.51 ± 0.217, p = 0.026, neurological complications, −0.55 ± 0.201, p = 0.008<br>– PCS: RPH, 0.27 ± 0.131, p = 0.046, heart failure, −0.34 ± 0.145, p = 0.011<br>– MCS: No significant factors |
| Guth et al.[31] | Self-administered questionnaires<br><br>The CAMPHOR HRQoL score significantly increased (p = 0.02) from 7 (3.5–12) (median [IQR]) before PTE to 2 (0.5–3) (median (IQR)) after PTE | Before PTE, 1 year post PTE | YES | N/A | CTEPD patients instead of CTEPH |
| Kamenskaya et al.[32] | Self-administered questionnaires via telephone survey<br><br>SF-36 Score: Preoperative (mean ± SD), postoperative (mean ± SD), dynamics (Δ) of parameters (mean ± SD) (p Value)<br>– Physical function: 56.43 ± 20.68, 76.70 ± 24.39, 51.17 ± 35.57 (p = 0.001)<br>– Role physical: 16.77 ± 14.97, 51.42 ± 28.02, 61.72 ± 38.67 (p < 0.001)<br>– Bodily pain: 31.39 ± 18.57, 67.91 ± 32.08, 103.72 ± 71.37 (p < 0.001)<br>– General health: 33.21 ± 14.25, 39.02 ± 41.43, 22.55 ± 48.77 (p = 0.071)<br>– Vitality: 31.70 ± 18.15, 52.38 ± 25.21, 84.04 ± 50.26 (p < 0.001)<br>– Social function: 73.21 ± 25.94, 87.28 ± 29.73, 31.79 ± 35.47 (p = 0.002)<br>– Role emotional: 26.19 ± 17.45, 68.45 ± 32.01, 53.90 ± 50.53 (p < 0.001)<br>– Mental health: 39.43 ± 26.26, 64.86 ± 25.58, 65.95 ± 53.75 (p = 0.001)<br>– PCS: 34.33 ± 7.30, 42.59 ± 9.42, 26.34 ± 22.71 (p < 0.001)<br>– MCS: 37.05 ± 7.89, 47.65 ± 7.93, 32.08 ± 24.73 (p < 0.001)<br>The HRQoL of CTPEH is below the national average of 50 across most domains, with the preoperative scores being ≤40 in all domains of the SF-36 with the exceptions of physical function and social function. >80% of the CTEPH patients reported that they did not limit themselves in communication, indicative of high social function preoperatively. The lowest scores in this population of CTPEH patients preoperatively were in the role physical domain. Statistically significantly increases in the PCS, MCS, and domains: Physical health, role physical, bodily pain, vitality, social function, role emotional, and mental health were observed 1 year postoperatively (p ≤ 0.002), while the general health domain approached significance (p = 0.071). With regard to dynamics, the most pronounced positive results were noted in the domains: Bodily pain, vitality, role physical, and mental health. Despite the significant improving in PCS and MCS following PTE, with survival rate of 90%, scores remained below the national average.<br>Dynamics (Δ) of parameters: Affecting factors in regression: β ± standard error (p Value)<br>– Physical function: COPD −0.55 ± 0.157 (p = 0.008)<br>– Role physical: All neurological complications after surgery −0.41 ± 0.114 (p = 0.03), RPH −0.59 ± 0.146 (p = 0.001)<br>– Bodily pain: All neurological complications after surgery −0.39 ± 0.121 (p = 0.04) | Before PTE and 1 year post PTE | YES | N/A | Determinants of HRQoL 1 year post PTE (concomitant diseases and early postoperative complications) |

**TABLE 2** (Continued)

| References | Method of follow-up | Follow-up interval | Comparison groups | | |
|---|---|---|---|---|---|
| | | | Pre-PTE | Non-PTE | Other groups |

Content (from Method of follow-up / Comparison columns):

– General health: COPD −0.60 ± 0.141 (p = 0.02), coronary artery disease -0.45 ± 0.132 (p = 0.03), RPH −0.48 ± 0.127, (p = 0.004), new-onset atrial fibrillation −0.39 ± 0.114 (p = 0.007)
– Vitality: heart failure −0.42 ± 0.136 (p = 0.002)
– Social function: No significant results
– Role emotional: COPD −0.50 ± 0.141 (p = 0.001), all neurological complications after surgery −0.39 ± 0.112 (p = 0.03)
– Mental health: COPD −0.37 ± 0.118 (p = 0.001), all neurological complications after surgery −0.40 ± 0.131 (p = 0.005)
– PCS: COPD −0.36 ± 0.143 (p = 0.03), RPH −0.39 ± 0.148 (p = 0.04)
– MCS: All neurological complications after surgery −0.53 ± 0.111 (p = 0.02)

Upon multivariate regression analysis, the occurrence of, during the hospitalization period, COPD, coronary artery disease, development of neurological complications, RPH, atrial fibrillation, and heart failure lead to significantly worse HRQoL in CTEPH patients 1 year post PTE (p < 0.05). In the long-term period post PTE, there was no significant effect on HQROL by the factors: Age, gender, NYHA functional class, pulmonary artery pressure before surgery, obesity, and diabetes mellitus. No significant relation between the HRQoL domains and in-hospital and 1-year mortality was identified.

Tamada et al.[33] | Self-administered questionnaires | Before and after PTE (unspecified) | YES | N/A | Early vs. Late (time to treatment [TT]) stratification of patients who had invasive treatment (PTE or balloon pulmonary angioplasty [BPA]) Correlation vs. PVR

Following invasive treatment (PTE in 15 patients and BPA in 24 patients), significant improvement was noted in all HRQoL scores, apart from the SF-36 domain, bodily pain. Despite this improvement, except for vitality (50.0 ± 8.9) and mental health (52.0 ± 8.5), all the HRQoL scores were below the national average of 50.

SF-36 Score: Before and after invasive treatment (mean ± SD)
– Physical function: 21.8 ± 18.3, 35.9 ± 14.9 (p < 0.05)
– Role physical: 28.3 ± 17.3, 38.6 ± 13.7 (p < 0.05)
– Bodily pain: 48.1 ± 13.2, 47.3 ± 10.4 (p > 0.05)
– General health: 37.5 ± 10.8, 45.5 ± 9.4 (p < 0.05)
– Vitality: 43.5 ± 12.4, 50.0 ± 8.9 (p < 0.05)
– Social function: 35.7 ± 14.9, 43.8 ± 12.9 (p < 0.05)
– Role emotional: 36.4 ± 17.2, 42.6 ± 16.2 (p < 0.05)
– Mental health: 46.0 ± 11.1, 52.0 ± 8.5 (p < 0.05)
– PCS: 23.2 ± 16.8, 34.0 ± 14.6 (p < 0.05)
– MCS: 50.9 ± 9.0, 54.4 ± 7.4 (p < 0.05)

The current study performed a correlation analysis of HRQoL scores with clinical parameters.

SF-36 Score domain with clinical parameters (Spearman correlation coefficient, p Value)
– Physical function with TT (r = −0.42, p = 0.008), SvO$_2$ (r = 0.35, p = 0.043), 6MWD (r = 0.48, p = 0.003)
– Role physical with age (r = −0.36, p = 0.024), TT (r = −0.34, p = 0.024), PVR (r = −0.37, p = 0.021), SvO$_2$ (r = 0.49, p = 0.003), 6MWD (r = 0.44, p = 0.008)
– Social function with PVR (r = −0.37, p = 0.022)
– Role emotional with SvO$_2$ (r = 0.44, p = 0.008)
– PCS with TT (r = −0.36, p = 0.024), PVR (r = −0.38, p = 0.019), SvO$_2$ (r = 0.53, p = 0.001), 6MWD (r = 0.52, p = 0.001)

Following the correlation analysis, HRQoL analysis was repeated using TT to stratify patients into an early group (TT < median) and a late group (TT ≥ median)

(Continues)

**TABLE 2** (Continued)

| References | Method of follow-up | Follow-up interval | Comparison groups | | |
|---|---|---|---|---|---|
| | | | Pre-PTE | Non-PTE | Other groups |
| | SF-36 Score: Early group normalized score (raw score) (mean ± SD), late group normalized score (raw score) (mean ± SD) (p Value) | | | | |
| | | – Physical function: 42.1 ± 13.7 (76.5 ± 19.4), 29.4 ± 13.6 (58.4 ± 19.3) (p = 0.006) | | | |
| | | – Role physical: 42.6 ± 13.3 (75.0 ± 24.3), 34.3 ± 13.2 (59.9 ± 24.1) (p = 0.044) | | | |
| | | – Bodily pain: 47.9 ± 11.1 (69.3 ± 25.1), 46.7 ± 9.9 (66.6 ± 22.4) (p = 0.749) | | | |
| | | – General health: 48.6 ± 9.6 (61.4 ± 17.8), 42.2 ± 8.2 (49.7 ± 15.2) (p = 0.054) | | | |
| | | – Vitality: 52.7 ± 8.4 (67.5 ± 17.2), 47.2 ± 8.8 (56.3 ± 17.8) (p = 0.044) | | | |
| | | – Social function: 44.3 ± 15.6 (75.6 ± 29.7), 43.3 ± 9.8 (73.7 ± 18.6) (p = 0.411) | | | |
| | | – Role emotional: 46.8 ± 15.7 (80.8 ± 30.8), 38.2 ± 15.9 (64.0 ± 31.2) (p = 0.079) | | | |
| | | – Mental health: 55.1 ± 7.6 (81.3 ± 14.2), 48.7 ± 8.4 (69.2 ± 15.7) (p = 0.016) | | | |
| | | – PCS: 38.8 ± 13.9, 28.9 ± 14.0 (p = 0.015) | | | |
| | | – MCS: 55.6 ± 6.1, 53.1 ± 8.5 (p = 0.247) | | | |
| | | Note: Normalized to general population by scaling to a national average of 50 and a standard deviation of 10. 2 summary scores obtained using normalized scores. HRQoL scores in the late group were significantly lower than the early group in the domains: physical function (p = 0.006), role physical (p = 0.044), vitality (p = 0.044). Mental health (p = 0.016), and in the PCS (p = 0.015). The superior HRQoL performance in the early group is indicative of the improvement invasive therapy can have on the HRQoL of CTEPH patients. | | | |
| Vanini et al.[34] | Self-administered questionnaires | Baseline, 3 months post PTE | YES | N/A | |
| | | SF-36 PCS significantly improved from 35.80 ± 8.63 at baseline to 45.08 ± 9.75 at 3 months post PTE (p < 0.001). SF-36 MCS significantly improved from 47.58 ± 10.70 at baseline to 54.75 ± 8.93 at 3 months post PTE (p < 0.001). No significant correlation between PCS or MCS and cerebral oxygen saturation, anaesthesia duration or time of total circulatory arrest. The correlation between SF-36 PCS and cerebral oxygen saturation, however, approached significance (p < 0.06, 95% CI [−0.70 to 17.81]) in the high-saturation group. | | | |
| Kamenskaya et al.[35] | Self-Administered Questionnaire via telephone | Before PTE, 1 year post PTE and 3 years post PTE | YES | NO | Determinants of HRQoL 3 years post PTE (age and RPH) |
| | | SF-36 Score: Preoperative (median [IQR]), 1-year postoperative (median [IQR]), 3-year postoperative (median [IQR]) (p Value) | | | |
| | | – Physical function: 60.0 (45.0–65.0), 80.0 (70.0–95.0), 75.0 (65.0–87.5) (p = 0.001) | | | |
| | | – Role physical: 10.0 (0.0–35.0), 50.0 (40.0–60.0), 70.0 (65.0–95.0) (p < 0.001) | | | |
| | | – Bodily pain: 32.0 (22.0–44.0), 74.0 (52.0–100.0), 74.0 (62.0–100.0) (p < 0.001) | | | |
| | | – General health: 35.0 (25.0–40.0), 40.0 (25.0–45.0), 56.0 (46.5–67.0) (p = 0.001) | | | |
| | | – Vitality: 35.0 (30.0–40.0), 50.0 (42.5–60.5), 60.0 (52.5–67.5) (p < 0.001) | | | |
| | | – Social function: 72.5 (62.5–82.0), 95.0 (85.0–100.0), 95.0 (81.2–100.0) (p = 0.002) | | | |
| | | – Role emotional: 32.6 (20.0–46.0), 70.0 (60.0–80.0), 85.0 (75.0–95.0) (p < 0.001) | | | |
| | | – Mental health: 48.0 (32.0–56.0), 68.0 (60.0–74.0), 64.0 (60.0–76.0) (p = 0.001) | | | |
| | | – PCS: 32.0 (28.9–36.4), 45.0 (37.8–51.2), 46.3 (38.8–50.4) (p < 0.001) | | | |
| | | – MCS: 37.6 (32.7–41.4), 48.6 (42.5–52.5), 49.7 (43.4–53.7) (p < 0.001) | | | |
| | | Before PTE, all SF-36 domains except for physical function, social function and mental health reported the lowest score. The role physical domain reported scores <40. All scores except for physical function and mental health improved or remained the same across the 1-year postoperative to 3-year postoperative interval. A 3-year postoperative survival rate of 89.8% was achieved, and despite significant | | | |
| | | Statistically significant increases across all domains and PCS and MCS were seen (p ≤ 0.002). | | | |

**TABLE 2** (Continued)

| References | Method of follow-up | Follow-up interval | Comparison groups | | |
|---|---|---|---|---|---|
| | | | Pre-PTE | Non-PTE | Other groups |
| | | improvements in all scores, PCS and MCS remained below the national average of 50 in all intervals. Upon multivariate analysis, RPH led to significantly worse HRQoL in patients 3 years post-PTE ($p \leq 0.004$) in all domains except for social function and mental health. PCS was significantly related ($p \leq 0.001$) while MCS was not reported. Age had a significant negative impact on the physical function domain ($p = 0.02$) and using the age-adjusted Charlson Comorbidity Index (ACCI), age had a significant negative impact on the domains physical function and role physical as well as PCS ($p \leq 0.004$). RPH was a leading factor limiting the patients' improvement in HRQoL post-PTE.<br><br>HRQoL domains: Affecting factors in regression: ß ± standard error (p Value).<br>– Physical function: Age −0.30 ± 0.113 ($p = 0.02$), ACCI −0.46 ± 0.148 ($p < 0.001$), RPH −0.47 ± 0.112 ($p < 0.001$)<br>– Role physical: ACCI −0.40 ± 0.113 ($p = 0.001$), RPH −0.67 ± 0.141 ($p < 0.001$)<br>– Bodily pain: RPH −0.35 ± 0.116 ($p = 0.004$)<br>– General health: RPH −0.43 ± 0.124 ($p < 0.004$)<br>– Vitality: RPH −0.53 ± 0.105 ($p < 0.001$)<br>– Social function: No significant results<br>– Role emotional: RPH −0.45 ± 0.112 ($p < 0.001$)<br>– Mental health: No significant results<br>– PCS: ACCI −0.34 ± 0.115 ($p = 0.004$), RPH −0.81 ± 0.108 ($p < 0.001$)<br>– MCS: No significant results | | |
| Nagel et al.[36] | Self-administered questionnaires | Post PTE: 3 weeks post PTE to 3 weeks post PTE to 22 weeks | Post PTE: 3 weeks (start of rehab), 22 weeks | N/A | PTE patients who underwent rehabilitation (supervised exercise training) |
| | | When comparing the patients HRQoL scores at 22 weeks post PTE to 3 weeks post PTE (the beginning of rehab), there was a statistically significant improvement in the SF-36 domains: Physical function ($p = 0.001$), role physical ($p = 0.001$), bodily pain ($p = 0.004$), and social role function ($p = 0.019$). A significant improvement in the PCS was noted ($p = 0.031$), role emotional ($p = 0.570$) and mental health ($p = 0.623$), not in the MCS ($p = 0.137$). Patients credited the rehabilitation (supervised exercise training) with improving their insight into their improved physical abilities and limitations post PTE.<br><br>SF-36 Score: 3 weeks post PTE, (mean ± SD, 95% CI, median [IQR]), 22 weeks post PTE, (mean ± SD, 95% CI, median [IQR]) (p Value)<br>– Physical function: 37.79 ± 22.39, (29.90–46.04), 37.5 (28.75), 29.78 ± 35.53, (14.42–45.15), 30 (45) ($p = 0.001$)<br>– Role physical: 29.81 ± 40.01, (13.65–45.97), 0 (75), 29.76 ± 37.60, (12.65–46.88), 25 (75) ($p = 0.004$)<br>– Bodily pain: 50.96 ± 17.15, (44.31–57.62), 52 (29.25), 11.05 ± 21.12, (1.43–20.66), 10 (21) ($p = 0.019$)<br>– General health: 45.92 ± 7.55, (42.8–49.04), 45 (7), 4.47 ± 10.51, (−0.59–9.54), 5 (17) ($p = 0.079$)<br>– Vitality: 39.33 ± 12.37, (34.71–43.95), 40 (20), −4.76 ± 14.62, (−11.42-1.89), −5 (15) ($p = 0.212$)<br>– Social function: 60.78 ± 21.32, (52.67–68.89), 62.5 (31.25), 13.13 ± 24.83, (1.51–24.74), 6.25 (37.5) ($p = 0.031$)<br>– Role emotional: 51.89 ± 48.35, (32.76–71.01), 67 (100), 6.70 ± 52.53, (−17.89–31.29), 0 (33) ($p = 0.570$)<br>– Mental health: 54.00 ± 8.71, (50.75–57.25), 52 (12), 1.33 ± 8.52, (−2.54–5.21), 0 (8) ($p = 0.623$)<br>– PCS: 42.78 ± 18.37, (36.16–49.40), 39.5 (32), 19.55 ± 19.42, (10.94–28.16), 23 (31.5) ($p = 0.001$)<br>– MCS: 55.76 ± 23.94, (47.27–64.25), 59 (45.5), 6.36 ± 20.44, (−2.70–15.43), 5 (25.25) ($p = 0.137$) | | |
| Newnham et al.[37] | Self-administered questionnaire | Before PTE and 1, 2, 3, 4, 5-year post PTE Median ± IQR follow-up: 139 ± 79 days | YES | YES | RPH vs. no RPH Correlation vs. PVR |

(Continues)

**TABLE 2** (Continued)

| References | Method of follow-up | Follow-up interval | Comparison groups | | |
| --- | --- | --- | --- | --- | --- |
| | | | Pre-PTE | Non-PTE | Other groups |

CAMPHOR HRQoL score median ± IQR, 95% CI, (p Value compared to baseline)

- Pre-PTE: 11 ± 11, (10–12)
- 1 year: 4 ± 11, (3–4), ($p \le 0.0001$)
- 2 years: 2 ± 9 (2–3), ($p \le 0.0001$)
- 3 years: 2 ± 8 (1–3), ($p \le 0.0001$)
- 4 years: 2 ± 10 (1–4), ($p \le 0.0001$)
- 5 years: 2 ± 9 (14), ($p \le 0.0001$)

Significant improvement in CAMPHOR HRQoL within 1 year that was sustained post PTE for 5 years. This was consistent with multiple-imputation analysis, ensuring missingness was not a significant source of bias.

CAMPHOR No RPH HRQoL score median ± IQR, 95% CI, RPH HRQoL score median ± IQR, 95% CI (p Value)

- Pre-PTE: 10 ± 12, (9–11), 12 ± 10, (11–13), ($p \le 0.05$)
- 1 year: 2 ± 8, (1–2), 7 ± 11, (6–9), ($p \le 0.001$)
- 2 years: 1 ± 6, (1–2), 6 ± 10, (4–7), ($p \le 0.001$)
- 3 years: 1 ± 5, (0–2), 6 ± 10, (4–8), ($p \le 0.001$)
- 4 years: 1 ± 7, (0–2.8), 6 ± 11, (2–10), ($p \le 0.01$)
- 5 years: 1 ± 5, (0–1), 7 ± 10, (5–11), ($p \le 0.001$)

In the CAMPHOR HRQoL score, there was significant improvement ($p < 0.0001$) in both the no RPH and the RPH group at all timepoints when compared to baseline. However, the greatest improvement was in the no RPH group and this improvement was sustained better over the 5 years than the RPH group, which had a negative trend in CAMPHOR HRQoL from 3 to 5 years post PTE.

CAMPHOR No PTE HRQoL score median ± IQR, 95% CI, PTE HRQoL score median ± IQR, 95% CI (p Value)

- Pre-PTE: 10 ± 13, (8–11), 10 ± 11, (9–11), ($p > 0.05$)
- 1 year: 8 ± 13, (6–11), 3 ± 9, (2–3), ($p \le 0.0001$)
- 2 years: 7 ± 10, (6–9), 1 ± 6, (1–2) ($p \le 0.0001$)

Despite no significant difference between the groups being identified at baseline, the PTE group had significantly improved CAMPHOR HRQoL scores at 1 year and 2 years post PTE when compared to the non-PTE group.

- No significant correlation between CAMPHOR HRQoL and sex ($p = 0.97$), 6MWD ($p = 0.107$), CI ($p = 0.912$), mPAP ($p = 0.437$), PVR ($p = 0.602$) was identified. Age was the only factor with a significant correlation ($p = 0.00134$). This is indicative of functional outcomes and physiological measures may not be important determining factors in patients HRQoL.

## Impact of pulmonary thromboendarterectomy on HRQoL in patients with CTEPD

With regard to CTEPD, two studies utilizing CAMPHOR identified that PTE resulted in a statistically significant improvement in HRQoL.[28,31] At 6 months post-operatively, patients experienced improved scores in the domains of activity, symptoms, and quality of life.[28] The improvement in scores was maintained up to 1-year post-PTE across all three domains.[28,31] Minimum clinically important differences were not reported.

## Impact of PTE compared to other treatment modalities

Yoshimi et al.[26] compared PTE to medical treatment with beraprost sodium, bosentan, sildenafil, or epoprostenol, with all patients treated with warfarin and home oxygen therapy. Patients were further separated into having a relatively peripheral distribution of thromboembolic disease or a more central distribution, defined by central disease score less than or equal to one and greater than one, respectively. Patients receiving medical treatment for relatively peripheral disease experienced improvements in the domains of role physical and vitality.[26] Comparatively, surgical management resulted in improvements in physical function, role physical, vitality, social functioning, and mental health.[26] In patients defined as having central disease, seven of eight domains saw improvement post-PTE, while too few medically managed patients survived for comparison.[26] Surgically management also resulted in a lower proportion of patients requiring home oxygen therapy.[26]

Patients who did not undergo surgical management after propensity matching revealed significantly worse CAMPHOR scores across all domains.[37] Reasons for not undergoing PTE included distal, surgically inaccessible disease, comorbidities, declined operation, and a combination of these factors or limited disease/symptoms.[37]

## Factors impacting HRQoL post-PTE

Ten studies investigated factors influencing postoperative HRQoL in patients with CTEPH.[26,27,29,30,32–37]

Residual pulmonary hypertension (RPH) was investigated by four studies.[30,32,35,37] Regardless of the presence of RPH, CAMPHOR scores were significantly improved over baseline.[37] Patients without RPH sustained greater HRQoL over the 5-year follow-up period than patients with RPH, who had a negative trend in CAMPHOR score

from years 3–5.[37] The correlation between RPH and decremented HRQoL domain scores is appreciable at 1- and 3-year post-PTE.[30,32,35] When stratified, patients with increased postoperative mean pulmonary arterial pressure (mPAP) or pulmonary vascular resistance (PVR) experienced worsening CAMPHOR scores.[26,33,37] Percentage decrease in postoperative PVR was correlated with improvements in physical functioning, bodily pain, general health perceptions, vitality, social functioning, and mental health for all PTE patients.[30] There is contention as to whether age, and preoperative mPAP or PVR influence HRQoL improvements post-PTE.[29,30,33,35,37] The studies commenting on the impacts of RPH on HRQoL outcomes post-PTE do not provide insight into whether patients with RPH received further medical or interventional management.[30,32,35]

Patients with reduced time to treatment from initial symptom onset experienced significantly greater scores in physical functioning, role physical, vitality, mental health, and in the overall physical component score.[33] The early group of patients underwent invasive therapy, BPA or PTE, at 12.3 months compared to 72.1 months for the late group.[33]

Patients undergoing 3 weeks of in hospital exercise and respiratory training followed by 19 weeks of home training, achieved significant gains in the domains of physical functioning, role physical, bodily pain, and social role functioning.[36] A significant improvement in the physical component score was also observed.[36] There were no significant improvements in the other domains of HRQoL. Diagnosis of COPD, prolonged ventilation, neurological complications, atrial fibrillation, heart failure, or coronary artery disease hampered improvements in HRQoL.[30,32]

There is no significant minimum clinically important difference with regard to CAMPHOR score between patients who undergo PTE using deep hypothermic circulatory arrest median or antegrade cerebral perfusion at the timepoints 12 weeks or 1-year post-PTE.[34] Moderate hypothermic circulatory arrest did not result in neuropsychological complications.[34]

Studies of patients with CTEPD post-PTE did not investigate factors influencing HRQoL.

## DISCUSSION

### Summary of evidence and interpretation

The key findings of this review include (i) PTE results in increased HRQoL within the first postoperative year for patients with CTEPH or CTEPD, (ii) there exists evidence to show that PTE confers significant HRQoL benefits up

to the fifth year postoperatively for patients with CTEPH, (iii) PTE confers significant HRQoL benefits up to a year postoperatively for patients with CTEPD, (iv) PTE results in greater improvements in HRQoL for patients with CTEPH than nonsurgical management, both BPA or medical management, and (v) clinical factors including time to treatment and RPH, postoperative exercise therapy, and patient demographics modulate HRQoL in patients post-PTE.

## Impact of pulmonary thromboendarterectomy on HRQoL in patients with CTEPH

In addition to poor HRQoL compared to the general population,[2] patients with CTEPH experience significantly poorer survival, and functional and haemodynamic outcomes.[9] Poor HRQoL in CTEPH is considered the result of several factors including difficulty managing the physical burden of disease, unclear prognosis, high cost of treatment, unemployment, financial uncertainty, and impaired social relationships.[2] CTEPH patients report markedly reduced physical and mental HRQoL, with inferior physical functioning, bodily pain, and general health, in addition to poor mental health, vitality, and social functioning.[25,30]

PTE results in a significant improvement in HRQoL for patients diagnosed with CTEPH. A finding consistent across all included studies.[25,26,29,30,32–35,37] In generic, disease-specific, and PH specific HRQoL instruments patients showed improved physical and mental HRQoL as well as reduced symptoms and greater activity levels compared to preoperative scores.[25,26,29,30,32–35,37] Improvement occurred within 3 months and was sustained up to 5 years.[29,34,37] The improvements recorded exceeded the minimum clinically important difference throughout the 5-year period, as such, representing a tangible improvement in HRQoL, an outcome of substantial importance to patients.[37] The interpretation of SF-36 outcomes post-PTE must be taken at the readers discretion as the studies published by Kamenskaya et al.[30,32] exhibit a level of overlap and as such represent increased power with regard to the outcomes in favor of PTE.

Previous reviews have discussed the improvements in functional and haemodynamic outcomes, as well as survival imparted on patients by PTE,[9] however there is currently no systematic review investigating changes in HRQoL. HRQoL represents an important insight that offers valuable information for patients diagnosed with CTEPH. Furthermore, HRQoL is an important patient-reported outcome (PRO) that has been recommended to

be included in PH trials by the World Symposium on Pulmonary Hypertension.[42]

When investigating HRQoL in patients with pulmonary hypertension the SF-36 has been shown to have high ceiling effects, poorer test–retest reliability, with only two of the eight SF-36 domains meeting adequate psychometric criteria for use in research on patients with pulmonary hypertension.[43] Comparatively, three of three CAMPHOR scales met criteria.[43] Evidence also exists to show that the SGRQ is limited in its assessment of HRQoL in patients with pulmonary hypertension.[24] It is recommended that HRQoL be measured using pulmonary hypertension specific measures such as the CAMPHOR,[43] however, only one study assessing HRQoL post-PTE in patients with CTEPH utilized the PH specific CAMPHOR instrument. Future studies assessing CTEPH would find value in reporting PROs such as HRQoL and should utilize validated PH specific instruments.

The evidence comparing PTE to BPA or medical therapy is limited as remains reserved for patients who are either inoperable, have persistent CTEPH, or are undergoing bridging therapy.[44] However, Yoshimi and colleagues revealed that although patients undergoing medical therapy received mildly improved HRQoL, the extent of the improvement was significantly less than that of the cohort of patients who underwent PTE.[26] Regardless of whether patients were diagnosed with relatively peripheral or central distribution of CTEPH, individuals who underwent PTE experience both greater HRQoL as well as reduced need for oxygen therapy.[26] Similarly, Newnham and colleagues identified that propensity matched patients who were not operated on experienced significantly lower HRQoL at up to 2 years postintervention.[37] The analysis, however, was considered exploratory.[37] These findings substantiate PTE as the guideline recommended intervention for CTEPH. There are limited findings that utilize PROs in investigating the impacts of medical management compared to PTE. There is new evidence suggesting the efficacy of BPA in the treatment of CTEPH, BPA patients may have higher survival rates and fewer complications than patients who underwent PTE.[45] However, there is no evidence comparing BPA and PTE reporting HRQoL, and as such, indicating a key point for future research.

RPH significantly decremented HRQoL outcomes post-PTE.[30,32,35,37] RPH resulted in significantly worse HRQoL up to 5 years postoperatively.[37] These findings are also made apparent when stratifying patients by postoperative mPAP and PVR.[26,30,37] Although patients with RPH maintained a statistically significant improvement in HRQoL compared to baseline preoperative states, patients lost their minimum clinically important difference as HRQoL began to decline after 3 years.[37] As

patients without RPH maintained their minimum clinically important difference over the 5 years,[37] treatment of RPH represents an interesting opportunity to improve HRQoL in a large proportion of patients, with current estimates of the incidence of RPH at 25%.[46]

The evidence regarding whether preoperative PVR and mPAP impact HRQoL post-PTE is contentious.[33,37] Studies included in this review indicate that preoperative mPAP and PVR represent physiologic outcome measures that influence postoperative HRQoL.[33] Newnham and colleagues argues that PVR and mPAP have limited impact on HRQoL, and as such reflect the notion that improved physiological and functional outcomes may not be deemed as important to patients as outcomes such as HRQoL.[37] Further investigation is needed to consolidate the findings posed by Newnham and colleagues.

Nagel and colleagues identified the utility of exercise training in patients with CTEPH as early follow-up treatment after PTE in improving several physical domains of HRQoL as well as social functioning.[36] The study was limited as a parallel group design was not feasible. Further investigation into the benefits of exercise rehabilitation is imperative to validating its efficacy in improving HRQoL of patients post-PTE.

## Impact of pulmonary thromboendarterectomy on HRQoL in patients with CTEPD

The evidence discussing the impact of PTE on patients with CTEPD was limited. As CTEPD represents a rare indication for PTE, the evidence evaluating HRQoL outcomes postoperatively was restricted to two studies.[4] HRQoL post-PTE was improved in patients with CTEPD.[28,31] Further investigation is required to compare HRQoL outcomes following PTE as opposed to other treatment methods and to investigate clinical, physiological, and functional factors which modulate HRQoL.

## Review limitations

The clinical heterogeneity of the studies included limited this systematic review. Furthermore, only 13 studies met the eligibility criteria for inclusion, and these studies retain significant bias. Furthermore, given the complexity of PTE surgery, large cohort trials are often limited to a few specialist centers, as such studies reviewed were limited by considerable overlap of patient cohorts. However, this review represents the only evidence available thus far and reflects the state of current available data. Thus, this systematic review adds to the literature for patients being considered for, and currently having had PTE and builds upon the conclusions of pre-existing nonsystematic reviews. Large prospective trials are required to identify long-term HRQoL outcomes in PTE patients.

Variation in age of recipient, surgical expertise, cohort size, and disease severity impact the clinical picture, as such, literature evaluating the outcomes of PTE is inconsistent. Due to the clinical heterogeneity of the studies included, the potential for significant bias should be accounted for in the interpretation of these findings. Studies of HRQoL outcomes post-PTE aim to guide clinicians with surgically relevant recommendations regarding patient outcomes.

## Conclusion

The main finding of this review is that in PTE, improvements in HRQoL from baseline states are obtained at 3 months postoperatively and retained up to 5 years. The improvements are apparent in both PH specific and generic HRQoL measurement tools across all domains measured. PTE represents the gold standard for managing CTEPH, as reflected by the findings of this systematic review. As other interventional and medical management options evolve constant evaluation of PTE must occur, with emphasis placed on PROs such as HRQoL measured with PH specific instruments. RPH presents a major detriment to HRQoL post-PTE, representing a point of future management. Other preoperative and postoperative factors require further research, as do outcomes beyond 5 years. The findings presented should enable surgeons to better understand HRQoL outcomes post-PTE when evaluating patients for surgery and when advising patients regarding their expectations.

### AUTHOR CONTRIBUTIONS
The authors confirm their contribution to the paper as follows: *Study conception and design*: Aarohanan Raguragavan, Dujinthan Jayabalan, and Akshat Saxena. *Data collection*: Aarohanan Raguragavan, Dujinthan Jayabalan, and Sugam Dhakal. *Analysis and interpretation of results*: Aarohanan Raguragavan. *Draft manuscript preparation*: Aarohanan Raguragavan and Dujinthan Jayabalan. All authors reviewed the results and approved the final version of the manuscript.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## ETHICS STATEMENT

This article does not contain any studies involving animals performed by any of the authors. This article does not contain any studies involving human participants performed by any of the authors.

## ORCID

Dujinthan Jayabalan http://orcid.org/0000-0001-9722-661X

## REFERENCES

1. Remy-Jardin M, Hutt A, Remy J. Chronic thromboembolic pulmonary disease and chronic thromboembolic pulmonary hypertension. Semin Respir Crit Care Med. 2022:936–45.

2. Mathai SC, Ghofrani H-A, Mayer E, Pepke-Zaba J, Nikkho S, Simonneau G. Quality of life in patients with chronic thromboembolic pulmonary hypertension. Eur Respir J. 2016;48(2):526–37.

3. Simonneau G, Torbicki A, Dorfmüller P, Kim N. The pathophysiology of chronic thromboembolic pulmonary hypertension. Eur Respir Rev. 2017;26(143):160112.

4. Lang IM, Campean IA, Sadushi-Kolici R, Badr-Eslam R, Gerges C, Skoro-Sajer N. Chronic thromboembolic disease and chronic thromboembolic pulmonary hypertension. Clin Chest Med. 2021;42(1):81–90.

5. Madani MM. Pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension: state-of-the-art 2020. Pulm Circ. 2021;11(2):1–6.

6. Teerapuncharoen K, Bag R. Chronic thromboembolic pulmonary hypertension. Lung. 2022;200(3):283–99.

7. Brookes JDL, Li C, Chung STW, Brookes EM, Williams ML, McNamara N, Martin-Suarez S, Loforte A. Pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension: a systematic review. Ann Cardiothorac Surg. 2022;11(2):68–81.

8. Cannon JE, Jenkins DP, Hoole SP. Chronic thromboembolic pulmonary hypertension: a review of risk factors, management and current challenges. Expert Rev Cardiovasc Ther. 2022;20(1):35–43.

9. Rahnavardi M, Yan TD, Cao C, Vallely MP, Bannon PG, Wilson MK. Pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension: a systematic review. Ann Thorac Cardiovasc Surg. 2011;17(5):435–45.

10. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger R, Brida M, Carlsen J, Coats A, Escribano-Subias P, Ferrari P, Ferreira DS, Ghofrani HA, Giannakoulas G, Kiely DG, Mayer E, Meszaros G, Nagavci B, Olsson KM, Pepke-Zaba J, Quint JK, Rådegran G, Simonneau G, Sitbon O, Tonia T, Toshner M, Vachiery JL, Vonk Noordegraaf A, Delcroix M,

11. Rosenkranz S, ESC/ERS Scientific Document G. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022;43(38):3618–731.

11. Moher D, Altman DG, Liberati A, Tetzlaff J. PRISMA statement. Epidemiology. 2011;22(1):128.

12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336–41.

13. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.

14. Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. Health Info Libr J. 2009;26(2):91–108.

15. U.S. Department of Health and Human Services FDA Center for Drug Evaluation and Research, U.S. Department of Health and Human Services FDA Center for Biologics Evaluation and Research, U.S. Department of Health and Human Services FDA Center for Devices and Radiological Health. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. Health Qual Life Outcomes. 2006;4(1):79.

16. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. N Engl J Med. 1996;334(13):835–40.

17. Guyatt GH. Measuring health-related quality of life. Ann Intern Med. 1993;118(8):622–9.

18. McCabe C, Bennett M, Doughty N, MacKenzie Ross R, Sharples L, Pepke-Zaba J. Patient-reported outcomes assessed by the CAMPHOR questionnaire predict clinical deterioration in idiopathic pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension. Chest. 2013;144(2):522–30.

19. Bilbao A, Escobar A, García-Perez L, Navarro G, Quirós R. The Minnesota living with heart failure questionnaire: comparison of different factor structures. Health Qual Life Outcomes. 2016;14(1):23.

20. Cenedese E. Measurement of quality of life in pulmonary hypertension and its significance. Eur Respir J. 2006;28(4):808–15. https://doi.org/10.1183/09031936.06.00130405

21. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. Am Rev Respir Dis. 1992;145(6):1321–7.

22. Condliffe R. Living with pulmonary hypertension: quality not just quantity. Eur Respir J. 2011;38(3):512–3. https://doi.org/10.1183/09031936.00027911

23. Ware Jr., JE SF-36 health survey. In: Maruish ME, editors. The use of psychological testing for treatment planning and outcomes assessment. 2nd ed. Lawrence Erlbaum Associates Publishers; 1999. pp. 1227–46.

24. Taichman DB, Shin J, Hud L, Archer-Chicko C, Kaplan S, Sager JS, Gallop R, Christie J, Hansen-Flaschen J, Palevsky H. Health-related quality of life in patients with pulmonary arterial hypertension. Respir Res. 2005;6(1):92. https://doi.org/10.1186/1465-9921-6-92

25. Genta PR, Jatene FB, Terra-Filho M. Quality of life before and after pulmonary thromboendarterectomy: Preliminary results. Jornal Brasileiro de Pneumologia. 2005;31:48–51.

26. Yoshimi S, Tanabe N, Masuda M, Sakao S, Uruma T, Shimizu H, Kasahara Y, Takiguchi Y, Tatsumi K, Nakajima N, Kuriyama T. Survival and quality of life for

patients with peripheral type chronic thromboembolic pulmonary hypertension. Circ J. 2008;72(6):958–65.

27. Vuylsteke A, Sharples L, Charman G, Kneeshaw J, Tsui S, Dunning J, Wheaton E, Klein A, Arrowsmith J, Hall R, Jenkins D. Circulatory arrest versus cerebral perfusion during pulmonary endarterectomy surgery (PEACOG): a randomised controlled trial. Lancet. 2011;378(9800):1379–87.

28. Taboada D, Pepke-Zaba J, Jenkins DP, Berman M, Treacy CM, Cannon JE, Toshner M, Dunning JJ, Ng C, Tsui SS, Sheares KK. Outcome of pulmonary endarterectomy in symptomatic chronic thromboembolic disease. Eur Respir J. 2014;44(6):1635–45.

29. Petrucci L, Carlisi E, Ricotti S, Zanellato S, Klersy C, D'Armini AM, Nicolardi S, Morsolini M, Viganò M, Dalla Toffola E. Functional assessment and quality of life before and after pulmonary endoarterectomy. G Ital Med Lav Ergon. 2015;37(3):170–5.

30. Kamenskaya O, Klinkova A, Loginova I, Chernyavskiy A, Edemskiy A, Lomivorotov VV, Karaskov A. Determinants of health-related quality of life 1 year after pulmonary thromboendarterectomy. Ann Vasc Surg. 2018;51:254–61.

31. Guth S, Wiedenroth CB, Rieth A, Richter MJ, Gruenig E, Ghofrani HA, Arlt M, Liebetrau C, Prüfer D, Rolf A, Hamm CW, Mayer E. Exercise right heart catheterisation before and after pulmonary endarterectomy in patients with chronic thromboembolic disease. Eur Respir J. 2018;52(3):1800458.

32. Kamenskaya O, Klinkova A, Loginova I, Chernyavskiy A, Lomivorotov VV, Karaskov A. Factors affecting the quality of life before and after surgery in patients with chronic thromboembolic pulmonary hypertension. Qual Life Res. 2018;27(3):747–54.

33. Tamada N, Nakayama K, Yanaka K, Onishi H, Shinkura Y, Tsuboi Y, Izawa KP, Satomi-Kobayashi S, Otake H, Tanaka H, Shinke T, Okita Y, Emoto N, Hirata K. Early introduction of pulmonary endarterectomy or balloon pulmonary angioplasty contributes to better health-related quality of life in patients with chronic thromboembolic pulmonary hypertension. JACC Cardiovasc Interv. 2018;11(11):1114–6.

34. Vanini B, Grazioli V, Sciortino A, Pin M, Merli VN, Celentano A, Parisi I, Klersy C, Petrucci L, Salati M, Politi P, D'Armini AM. Neuropsychological outcomes after pulmonary endarterectomy using moderate hypothermia and periodic circulatory arrest. J Heart Lung Transplant. 2018;37(7):860–4.

35. Kamenskaya O, Klinkova A, Chernyavskiy A, Lomivorotov VV, Edemskiy A, Shmyrev V. Long-term health-related quality of life after surgery in patients with chronic thromboembolic pulmonary hypertension. Qual Life Res. 2020;29(8):2111–8. https://doi.org/10.1007/s11136-020-02471-z

36. Nagel C, Nasereddin M, Benjamin N, Egenlauf B, Harutyunova S, Eichstaedt CA, Xanthouli P, Mayer E, Grünig E, Guth S. Supervised exercise training in patients with chronic thromboembolic pulmonary hypertension as early follow-up treatment after pulmonary endarterectomy: a prospective cohort study. Respiration. 2020;99(7):577–88.

37. Newnham M, Bunclark K, Abraham N, Ali S, Amaral-Almeida L, Cannon JE, Doughty N, Ng C, Ponnaberanam A, Sheares K, Speed N, Taboada D, Toshner M, Tsui S,
Jenkins DP, Pepke-Zaba J. CAMPHOR score: patient-reported outcomes are improved by pulmonary endarterectomy in chronic thromboembolic pulmonary hypertension. Eur Respir J. 2020;56(4):1902096.

38. Patrick DL, Deyo RA. Generic and disease-specific measures in assessing health status and quality of life. Med Care. 1989;27: S217–32.

39. Furlan AD, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine. 2009;34(18):1929–41.

40. Health N, Council MR NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. NHMRC Canberra, Australia; 2009.

41. Coste J, Quinquis L, Audureau E, Pouchot J. Non response, incomplete and inconsistent responses to self-administered health-related quality of life measures in the general population: patterns, determinants and impact on the validity of estimates—a population-based study in France using the MOS SF-36. Health Qual Life Outcomes. 2013;11(1):44.

42. McGoon MD, Ferrari P, Armstrong I, Denis M, Howard LS, Lowe G, Mehta S, Murakami N, Wong BA. The importance of patient perspectives in pulmonary hypertension. Eur Respir J. 2019;53(1):1801919.

43. Twiss J, McKenna S, Ganderton L, Jenkins S, Ben-L'amri M, Gain K, Fowler R, Gabbay E. Psychometric performance of the CAMPHOR and SF-36 in pulmonary hypertension. BMC Pulm Med. 2013;13(1):45.

44. Kim NH, Delcroix M, Jais X, Madani MM, Matsubara H, Mayer E, Ogo T, Tapson VF, Ghofrani HA, Jenkins DP. Chronic thromboembolic pulmonary hypertension. Eur Respir J. 2019;53(1):1801915. https://doi.org/10.1183/13993003.01915-2018

45. Zhang L, Bai Y, Yan P, He T, Liu B, Wu S, Qian Z, Li C, Cao Y, Zhang M. Balloon pulmonary angioplasty vs. pulmonary endarterectomy in patients with chronic thromboembolic pulmonary hypertension: a systematic review and meta-analysis. Heart Fail Rev. 2021;26(4):897–917.

46. Hsieh WC, Jansa P, Huang WC, Nižnanský M, Omara M, Lindner J. Residual pulmonary hypertension after pulmonary endarterectomy: a meta-analysis. J Thorac Cardiovasc Surg. 2018;156(3):1275–87.

## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.