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Early View

Research letter

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RESEARCH LETTER

The minimal clinically important difference of the Severe Respiratory Insufficiency questionnaire in severe COPD.

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TAKE HOME MESSAGE;

The SRI is frequently used to measure quality of life in severe COPD patients treated with NIV, however its MCID is unknown. This paper shows MCID estimates between 4.5 - 6.2, so that we suggest an increase of approximately 5 points is clinically relevant.

INTRODUCTION

The Severe Respiratory Insufficiency Questionnaire (SRI) is developed to measure health-related quality of life (HRQL) specifically in patients with chronic hypercapnic respiratory failure (CHRF) [1]. It has been validated for patients with a broad spectrum of underlying diseases, including patients with chronic obstructive pulmonary disease (COPD) [2], and has been used extensively in trials investigating noninvasive ventilation (NIV) for CHRF due to different aetiologies. Furthermore, its use in clinical practice for care quality monitoring is increasing, and might increase further since convenient applications for mobile devices recently became available. Unfortunately, the minimal clinically important difference (MCID) has not been determined. Therefore, it remains difficult to interpret the improvements in HRQL or to use the SRI as a primary outcome in clinical trials as the MCID determinates the sample size needed. Therefore, we aimed to estimate the MCID of the SRI in a group of severe COPD patients treated with NIV.

METHOD

Data were collected prospectively in 3 trials on chronic NIV in COPD. All trials were approved by our Ethical Review Board and patients gave written informed consent to participate. The study designs of these trials are described elsewhere [3-5]. The following parameters were collected at baseline and after 6 months of NIV; room air blood gasses, lung function, the 6-minute walking distance (6-MWD), the SRI and the Hospital Anxiety and Depression Scale (HADS) [6]. Additionally, patients were retrospectively asked for their perceived change in health after 6 months of NIV, using an 11-point global rating scale of change (GRC), ranging from -5 (health deteriorated) to +5 (health improved) [7].

Data are presented as mean ± standard deviation (SD). To determine the MCID of the SRI, we used a combination of anchor- and distribution-based approaches. To be included as anchor, the Pearson correlation coefficient (or non-parametric equivalent) between the change (Δ) in the SRI scores and the Δanchor required to be >0.3. If this condition was satisfied, we conducted univariate linear regression analyses with the ΔSRI scores as dependent variables, and the Δanchor as independent variables. For the GRC, we calculated the average ΔSRI of the participants scoring +2 and +3 as estimate for the MCID, as only these scores were considered minimally clinically relevant [7]. For the distribution approach, the MCID was calculated as 0.5 times the SD of the ΔSRI scores.

RESULTS

This analysis included 108 patients with severe COPD *(forced expiratory volume in 1 second (FEV_1) 0.69±0.27L)* and CHRF *(arterial partial pressure of carbon dioxide ($PaCO_2$) 7.2±0.8kPa / 54±6mmHg)*. Patients experienced poor exercise capacity *(6-MWD 238±121m)*. The mean SRI summary score (SRI-SS) was 52±15, and ranged between 37 and 62 for the subdomains. The mean HADS scores were 6.6±4.8 and 7.6±4.5 points respectively. The Δ$PaCO_2$ and Δbicarbonate were not correlated sufficiently with the ΔSRI (r=-0.21 and r=-0.13 for the SRI-SS) and therefore could not be used as anchor. According to the GRC, 76% experienced an improved health, of which 38% (n=30) experienced a minimal relevant improvement (GRC +2/+3). Table 1 presents the correlations between the Δanchors and ΔSRI scores, and the MCID estimates of the SRI subdomain and SRI-SS.

Table 1: MCID estimates for the SRI domain and summary scores, separately for the different approaches.

		Anchor approach					Distribution approach
		6-MWD	**FEV_1** [1]	**HADS-a**	**HADS-d**	**GRC** [2]	
SRI-RC	*R*	0.33**	0.44**	*-0.26***	-0.27**	0.35**	
	MCID estimate	8.6 *(7.6–9.7)*	11.2 *(9.3–13.1)*			10.3 *(5.3–15.3)*	7.5
SRI-PF	*R*	0.44**	0.19	*-0.24**	-0.33**	0.18	
	MCID estimate	2.3 *(1.3–3.4)*			3.1 *(2.0–4.1)*		8.0
SRI-AS	*R*	0.19	0.27**	*-0.25***	-0.22*	0.31**	
	MCID estimate					7.4 *(0.6–14.2)*	8.6
SRI-SR	*R*	0.21*	0.15	*-0.25***	-0.23*	0.25*	
	MCID estimate						6.3
SRI-AX	*R*	0.21*	0.33**	*-0.48***	-0.39**	0.24*	
	MCID estimate		9.6 *(7.0–12.2)*	7.8 *(6.5–9.0)*	8.0 *(6.7–9.3)*		10.2
SRI-WB	*R*	0.18	0.20*	*-0.53***	-0.52**	0.24*	
	MCID estimate			3.9 *(2.9–5.0)*	4.6 *(3.5–5.6)*		8.8
SRI-SF	*R*	0.39**	0.21*	*-0.32***	-0.38**	0.26*	
	MCID estimate	1.7 *(0.5–2.8)*		2.1 *(1.0–3.3)*	2.8 *(1.8–3.9)*		8.5
SRI-SS	*R*	0.39**	0.35**	*-0.48***	-0.48**	0.35**	
	MCID estimate	4.5 *(3.7–5.3)*	6.2 *(4.7–7.7)*	5.1 *(4.4–5.9)*	5.5 *(4.8–6.2)*	5.0 *(0.6–9.3)*	6.0

R: correlations between the change in the SRI and the change in the anchors after 6 months, correlation data are Pearson correlation coefficient, except for [1], Spearman correlation coefficient; MCID estimate: estimate (95% confidence interval). For the anchor approach, only anchors that correlated >0.3 were used; [2], n=30; *; $p<0.05$; **, $p<0.01$.

6-MWD, 6-minute walking distance; FEV_1, forced expiratory volume in 1 second; GRC, global rating scale of change; HADS-a/HADS-d, anxiety, respectively depression domains of the Hospital Anxiety and Depression Scale (a higher score indicates more symptoms of anxiety or depression); SRI-RC, SRI respiratory complains; SRI-PF, SRI physical functioning; SRI-AS, SRI attendant symptoms and sleep; SRI-SR, SRI social relationships; SRI-AX, SRI anxiety; SRI-WB, SRI psychological well-being; SRI-SF, SRI social functioning; SRI-SS, SRI summary score.

DISCUSSION

We present the first MCID estimate of the SRI in a population of severe COPD patients treated with NIV. Using different clinical and patient reported anchors with established MCIDs in patients with severe COPD and a distribution estimate, our results indicate MCID estimates between 4.5 and 6.2 points. We therefore suggest that an increase of approximately 5 points on the SRI-SS can be considered clinically relevant in this population.

In this study, we have estimated the MCID of both the summary and subdomains scores. It is important to get insight in the MCID of the subdomains as the SRI measures different HRQL aspects. These aspects are impaired to a varying degree and NIV may affect these aspects differently. Our MCID estimates of certain subdomains are considerably aberrant to the 5 points of the SRI-SS. Although this might reflect that for these subdomains a relevant change is truly different, it should be noted that the MCID estimates were probably less precise as the number of available anchors, i.e. measures that correlated with the subdomains, was more limited.

To reach a precise estimate of a MCID, it is recommended to use multiple patient and disease centred anchors [8]. Anchors should be correlated with the outcome, be relevant and reflect the content of the measure and should have an established MCID derived from comparable populations. First, we used measures as anchors if they were sufficiently correlated (>0.3) to the change in the SRI [8]. Second, our anchors are relevant and reflected the change in HRQL: physical anchors correlated with physical domains (respiratory complaints and physical functioning) and psychological domains correlated well with the HADS scores. This is in line with an earlier paper which showed that the HADS explained over 50% of the variance of the SRI-SS [9]. Also, domains that require more mixed competencies such as social functioning, correlated well with both a physical- and psychological anchor. The GRC was used as an additional anchor, as this specifically represents a patient rated change in their HRQL. The convergent results confirm the reflection of these anchors to changes in the specific SRI scores.

Finally, our anchors have an established MCID derived from comparable populations. For the 6-MWD, we have used the MCID of 26m estimated from a cohort of severe emphysema patients *(FEV_1 26.9% predicted) [10].* The MCID of the HADS of -1.5 points per domain was estimated in a population of moderate to severe COPD *(FEV_1 34.3% predicted)* with comparable baseline HADS scores [11]. The MCID of the FEV_1 of 100ml was based on multiple studies with varying severity of COPD [12]. A concern with this MCID is that the initial FEV_1 might influence the potential for improvement, so a single MCID might be inappropriate [13]. A relative change has also been proposed for patients with severe airflow obstruction, but what percentage would be of minimal importance is not yet determined. Experts have proposed a 12% improvement to be clinically relevant, which in our cohort would imply that an improvement of only 78ml would be relevant, resulting in a smaller MCID [13]. We therefore hypothesize that the MCID of 100ml overestimates the MCID of the SRI. For the GRC, we used a +2/+3 score as minimally relevant, in line with previous studies using this method.

Interestingly, we could not demonstrate a correlation between the change in $PaCO_2$/bicarbonate and the change in the SRI score. Trials that have shown HRQL benefits of chronic NIV in COPD patients all targeted and achieved a significant reduction in $PaCO_2$ [3, 14]. This reduction has therefore been advocated to be responsible for the benefits of NIV [15]. Although $PaCO_2$

certainly reflects ventilatory efficacy, our results suggest that a change in other parameters might have more influence on the change in HRQL. Whether these parameters are actual targets of NIV is still to be determined.

We have established the first MCID estimate of the SRI in COPD patients with CHRF. Using a combination of clinical and patient reported anchors, we precisely estimated the MCID of the SRI summary score between 4.5 and 6.2 points. The estimates of the subdomains might however be more imprecise and future studies need to determine the accuracy of these estimates. We emphasize that our estimates are only applicable to a selected group of stable hypercapnic COPD patients. The validity of our estimates should be further investigated for other populations with CHRF, including COPD patients initiated on chronic NIV following an exacerbation. Our MCID should be used to value significant results of clinical trials and to determine the sample size of future trials in this population with severely impaired HRQL.

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DISCLOSURE STATEMENT

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The other authors state that they have no conflicts of interest.

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