Clinicians' and Researchers' Perspectives on a New Chronic Obstructive Pulmonary Disease Exacerbation Definition: Rome Wasn't Built in a Day

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To the Editor:

Current definitions of, and severity classifications for exacerbations of chronic obstructive pulmonary disease (COPD), are imperfect. Severity criteria have most commonly been classified by the level of treatment received, whereas definitions of exacerbation were not time bound and poorly discriminated exacerbation pathophysiology from alternative conditions that could mimic or complicate exacerbations (1). In an attempt to progress the field, a new definition and severity classification called the Rome proposal was developed using a Delphi process of over 80 items, literature review, and expert consensus (2). The definition and severity classification have now been adopted by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) (1). The Rome definition of exacerbation in a patient with COPD is "an event characterized by dyspnea and/or cough and sputum that worsen over ⩽14 days, which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insult to the airways" (2). The new severity classification includes the quantification of breathlessness, as well as physiological and biochemical measures. The Rome proposal has not yet been validated. Therefore, we undertook an international survey to assess the views of clinicians and researchers about the Rome proposal and how it might be implemented in clinical practice and research.

Methods

We designed a 12-question survey on SurveyMonkey, which was open for responses between June 6 and December 15, 2022. A convenience sample of clinicians was invited through personal contacts, and the survey was also distributed through social media, including Twitter, LinkedIn, and Facebook. Analysis was conducted using Statistical Package for the Social Sciences, version 28) and the qualitative data acquired were analyzed using NVIVO software. Descriptive statistics were used, and the characteristics

Table 1. Demographic Data of Participants in this Study

Demographic Data	Frequency (%)
Age, yr*	
18–24	14 (10)
25–34	41 (30)
35–44	33 (24)
45–54	33 (24)
55–64	15 (11)
65+	2 (1)
Gender*	
Male/female	78 (57)/60 (44)
Region*	
Europe	63 (46)
North America	32 (23)
Middle East	21 (15)
Asia	9 (7)
South America	8 (6)
Africa	4 (3)
Australasia	1 (1)
Profession*	
Doctor	61 (44)
Respiratory therapist or physiologist	35 (25)
Nurse	18 (13)
Other clinicians	24 (17)
Have you already heard about the Rome proposal?*	
No	88 (64)
Yes	50 (36)
Do you agree or disagree with the Rome proposal?†	
Strongly agree or agree	60 (73)
Neither agree nor disagree	15 (18)
Disagree or strongly disagree	7 (9)
How familiar are you with the Rome proposal?‡	
Familiar	33 (91)
Not familiar	3 (9)
Do you use the Rome severity classification of COPD exacerbations in clinical practice?§	
No	25 (69)
Yes	11 (31)
Do you use the Rome severity classification of COPD exacerbations in research?§	
No	8 (22)
Yes	28 (78)
How likely is it that you would use the Rome severity classification in clinical practice in the future?‖	
Very likely or likely	63 (68)
Neither likely nor unlikely	14 (15)
Unlikely or very unlikely	15 (17)
How likely is it that you would use the Rome severity classification in research in the future?‖	
Very likely or likely	66 (72)
Neither likely nor unlikely	8 (9)
Unlikely or very unlikely	18 (19)
Do you agree that the Rome definition addresses the shortcomings of current definitions of exacerbation?‖	
Strongly agree or agree	56 (61)
Neither agree nor disagree	23 (25)
Disagree or strongly disagree	13 (14)

Definition of abbreviation: COPD = chronic obstructive pulmonary disease.
*$n = 138$.
†$n = 82$.
‡$n = 36$. The question was asked to those participants who had already heard about the Rome proposal.
§$n = 36$. The question was asked only to those participants who were already familiar with the Rome proposal.
‖$n = 92$. The question was asked to all participants, having been provided information on the Rome proposal.

Supported by King Abdulaziz University, Saudi Arabia (M.A.A.).

Author Contributions: Conception, design, data collection, analysis, interpretation, and drafting of the manuscript: M.M.A. and J.R.H. Manuscript review: A.J.S. and B.K. Supervision: J.R.H.

Originally Published in Press as DOI: 10.1164/rccm.202210-1949LE on January 19, 2023

Table 2. Positive and Negative Opinions toward the Adoption of the Rome Proposal in Clinical Practice and Research

Barriers and Concerns	Facilitators and Positive Aspects
"Not recommended by local governing medical research societies."	"I like the specificity around duration, triggers, and symptoms."
"Quite secondary care oriented. Requires more tests. Difficult to make a clinical decision on it in the community if blood gases and CRP are involved."	"Clarification of provoking insult categories is interesting."
"VAS, ABG, and CRP may not always be available and too complex."	"It is simple to use in everyday clinical practice, including both event and symptoms."
"Too vague, will lead to significant study heterogeneity."	"Covered most of the aspects."
"[need] Clinical evidence of using this concept and outcomes of following the diagnostic tool."	"Time frame and severity classification."
"In addition to CRP, I want an eosinophil count and ECG (DECAF score). I would want VAS for cough, wheeze, [and] sputum in addition to dyspnea. Severity score is not practical enough for clinical practice but also not detailed enough for research."	"Integration of many pertinent variables."
"There is no global diversity in the approach to define this – with authors from North America and Europe only and lack of diversity in authors."	"Captures exacerbations that are more clinically important than purely symptom-based exacerbations."
"There is a lack of patient input."	"The cardinal symptoms of a COPD exacerbation are nonspecific and can represent many disorders, including but not limited to pneumonia, congestive heart failure, acute coronary syndrome, and pulmonary embolism."
"Needs wider dissemination [among] colleagues."	

Definition of abbreviations: ABG = arterial blood gas; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; DECAF = Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation; VAS = visual analog scale.

of the participants were summarized using frequency and percentages. Information about the Rome proposal was provided to participants.

Results

One hundred and thirty-eight healthcare professionals from 25 countries participated in the survey. Not everyone answered every question; skip-logic was used to provide additional questions to those who were already familiar with the Rome proposal. Because the response rate varied per question, the percentages of respondents are displayed. The demographics of the respondents and the responses to the questions are provided in Table 1.

We asked all participants whether they agreed or disagreed with the Rome proposal; the response rate was 82/138 (59%). Among the participants who responded to this question, 60/82 (73%) reported agreeing or strongly agreeing with the proposed definition. The response rate was 92/138 (67%) when participants were asked if the Rome proposal addressed the shortcomings of previous definitions of COPD exacerbation. Of those who responded, 56/92 (61%) agreed or strongly agreed that the Rome definition did address many of the shortcomings of previous definitions of COPD exacerbations.

The majority of respondents, 88/138 (64%), reported not being previously aware of the Rome definition; thus, they did not currently use the Rome severity classification of COPD exacerbation in clinical practice or in research. Nevertheless, the majority, 63/92 (68%), of clinicians reported that they would likely use the Rome proposal in future clinical practice, and 66/92 (72%) would use the Rome proposal in future research.

In qualitative responses, participants described the Rome proposal as useful, practical, specific, clear, objective, and comprehensive. In contrast, participants noted barriers that could potentially prevent the use of the Rome classification in clinical practice and research. External factors included lack of awareness, lack of resources, lack of validation, complexity, and impracticality. Example quotes are provided in Table 2.

Discussion

Dissatisfaction with current definitions of exacerbation and exacerbation severity criteria led to the development of the Rome proposal, now adopted by GOLD (1). The Rome proposal requires prospective validation against outcomes such as mortality, recovery, and hospital admission. While such studies are being completed, we sought to survey the views of clinicians and researchers about the Rome proposal in the context of clinical practice and clinical trials.

Although we found good support for the proposal, there was a lack of awareness, and this lack of validation was seen as a barrier to implementation. Participants felt that the dyspnea visual analog scale could be impractical and that the C-reactive protein and blood gas are impractical outside of a hospital setting. This suggests some misunderstanding, as the C-reactive protein and blood gas analysis were not mandated in the Rome proposal.

This study has some limitations. Although there were participants from 25 countries, the responses were mainly from three countries and thus may not reflect the opinions of clinicians more widely.

Conclusion. This study indicates enthusiasm from clinicians for using new definitions of exacerbation and a new exacerbation severity classification in clinical practice and research. Validation studies are urgently required, both for Rome and for alternatives such as the Spanish COPD Guidelines, or GesESPOC (3) to demonstrate their utility in clinical practice and research. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Quantitative Effects of Ansa Cervicalis Stimulation in Obstructive Sleep Apnea

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To the Editor:

Obstructive sleep apnea (OSA) is estimated to affect 15–30% of U.S. adults (1). Hypoglossal nerve stimulation (HNS) is an alternative treatment to positive airway pressure (PAP) for select patients, but a substantial subset experience inadequate therapeutic efficacy (2), suggesting that additional respiratory neurostimulation (RNS) strategies are required.

Caudal tracheal traction on the pharynx is mediated by changes in end-expiratory lung volume and has been documented to decrease pharyngeal collapsibility (3, 4). The infrahyoid strap muscles, innervated by the ansa cervicalis nerve plexus, also pull the pharynx caudally. Early studies of ansa cervicalis stimulation (ACS) of the sternothyroid muscle have demonstrated stabilization of pharyngeal patency (5, 6). Nevertheless, ACS effects on human pharyngeal collapsibility have not yet been rigorously quantified.

The pharyngeal airway obstructs completely when the nasal pressure drops below a critical closing pressure (P_{CRIT}), and inspiratory airflow limitation is abolished when nasal pressure exceeds that of external collapsing forces (P_{OPEN}). The magnitude of the effect of therapeutic interventions on pharyngeal collapsibility can thus be quantified by estimating changes in P_{CRIT} and P_{OPEN} (7). The primary objective of the present study was to quantify the effect of sternothyroid muscle contraction via ACS on measures of pharyngeal collapsibility in patients with OSA.

Methods

This study was approved by the Vanderbilt University Medical Center Institutional Review Board (IRB 181078). Participants underwent uni- or bilateral ACS with percutaneous fine-wire electrodes under propofol anesthesia using a modified version of a previously described drug-induced sleep endoscopy protocol (5, 6, 8). Modifications included maintaining jaw, head, and neck postures in a constant neutral position and controlling upstream nasal pressure with a PAP device. PAP was decreased from non–flow-limited inspirations to apnea in 1-cm H_2O decrements with uni- or bilateral ACS applied in a three-breath on/off stimulation regime (Figure 1). P_{CRIT} (apnea) and P_{OPEN} (non–flow-limited inspirations) were ascertained for each stimulation condition by plotting a regression line through the peak inspiratory flow rates measured across varying nasal pressures (7).

Results

Nineteen participants underwent one or more bilateral ACS neurostimulation experiments ($n = 23$) with an additional unilateral ACS experiment successfully completed in 12 of the participants. There were no significant differences in age, sex, body mass index (BMI), or apnea–hypopnea index (AHI) between the two groups ($P > 0.1$). Participants were primarily middle-aged (mean ± SD, 52.8 ± 10.7 y), obese (31.6 ± 2.4 kg/m^2) males ($n = 18$) with severe OSA (43.1 ± 19.1 events/h).

Unilateral ACS decreased mean P_{CRIT} and P_{OPEN} from baseline by 1.6 ± 1.5 cm H_2O and 1.9 ± 1.1 cm H_2O, respectively ($P < 0.001$). Bilateral ACS decreased mean P_{CRIT} and P_{OPEN} by 2.1 ± 1.6 cm H_2O and 3.1 ± 1.6 cm H_2O, respectively ($P < 0.001$) (Figure 2). The magnitude of ΔP_{OPEN} with bilateral ACS was significantly greater than with unilateral ACS ($P = 0.02$), but ΔP_{CRIT} was not ($P = 0.37$).

Median ΔP_{CRIT} and ΔP_{OPEN} values were calculated from the bilateral ACS experiment, and characteristics for participants at or

Supported by the NHLBI (R01HL161635) and the American Academy of Sleep Medicine Foundation ABSM 2019 Junior Faculty Award (219-JF-19).

Author Contributions: Y.L.: methodology, software, formal analysis, investigation, data curation, writing–original draft, review and editing, and visualization. K.E.R.: investigation, writing–review and editing. A.R.S.: conceptualization, methodology, investigation, and writing–review and editing. D.Z.: conceptualization, methodology, investigation, resources, and writing–review and editing. C.J.L.: methodology, formal analysis, and writing–review and editing. H.A.B.: investigation. D.T.K.: conceptualization, methodology, validation, investigation, resources, visualization, supervision, funding acquisition, and writing–review and editing. All authors discussed and approved the manuscript.

Originally Published in Press as DOI: 10.1164/rccm.202212-2318LE on January 19, 2023