Author Response 1

We would like to thank the reviewers for their time and for their comments and observations. We believe their suggestions further strengthen our work. We have responded to their comments point-by-point and modified the manuscript accordingly (red text).

REVIEWER 1

Major comments

1. The Authors assert in the abstract lines 61-2 and in the methods that a sample of charts were checked for validity of recall. While this is laudable, no information was provided about the variety of charts, blinding, etc. This is helpful to understand the results of consistency with patient recall presented later in the manuscript.

RESPONSE: The charts were reviewed to assess for hospitalizations and antibiotic use. Charts included clinic notes obtained from prescribing physicians. There was no blinding.

2. In the abstract lines 68 onward and results/conclusions, the biases and any attempts to account for these statistically should be discussed/analyzed.

RESPONSE: The authors feel that an adequate discussion of the limitations of the study would be too extensive for the abstract. These are covered fully in the discussion section, including some additions to the resubmitted version of this manuscript.

3. The last sentence of the introduction and carrying to the methods/results… The authors assert this was a real-world study but present not data on the other concomitant bronchiectasis meds, etc. the patients were on or the protocol followed. Therefore, revision with this data and a discussion are warranted.

RESPONSE: This is one of the limitations of the study. The data patient's drug regimens were not collected for each patient beyond the use of antibiotics. We expanded on this point in the discussion under the limitations of the study.

4. The QOL PRO used (discussed in lines 150-54). Is it validated, published? How was it derived if not validated/published?

RESPONSE: The questionnaire has not been validated or previously published in manuscript form. It was derived using clinically relevant questions regarding the ability of the patient to clear the lungs, overall respiratory health, use of antibiotics and admissions due to respiratory symptoms. Although not validated, the overall responses suggest that the patients had a favorable response to HFCWO therapy. For example, the questionnaire revealed a substantial numerical improvement in the hospitalizations after therapy was started. In parallel to this improvement, the proportion of patients who answered positively to the question "Are you currently taking oral antibiotics for breathing problems?" dropped considerably. Similarly, patients responded favorably to the "How would you rate your overall respiratory health?" and "How would you rate your ability to clear your lungs?" questions favorably, in line with the other answers. Future studies are required to validate these responses. We have expanded on this in the discussion under limitations.

5. Regarding the discussion of bias, can you comment on this concern in lines 168-72 beginning "In all methods…". What was done if a patient stopped using the device due to intolerance and/or

dislike/didn't think it helped?
RESPONSE: Lines 168-172 refer to a specific methodological issue: if the duration of the chart review was longer than duration of HFCWO therapy, and ended with a return, the chart review time interval was restricted to be the same as HFCWO therapy interval. The statistical analysis includes all data regardless of whether a unit was returned prior to the end of the one year post-treatment interval (about 19% of the total). Returns were motivated by a number of reasons, including patient intolerance, physician's orders, entry into a long-term care facility, or death. Any of these could be a source of bias, but the reasons for a return were often not available for analysis. We consider this a limitation of the study.

6. Discussion, lines 280-onward beginning with the sentence "The present study only evaluated the mode of HCFWO that uses triangle-wave pulses" is purely speculative and not the focus of the data/results/methods. I would remove or change this paragraph to harmonize with the remainder of the manuscript.

RESPONSE: We have changed this paragraph as requested to harmonize with the remainder of the manuscript.
7. Conclusion, the sentence "While the cause of this improvement cannot be definitively assigned to HFCWO therapy, the data demonstrate a strong positive association" is not supported by the manuscript findings and needs to be reworded to better reflect the data/individual conclusions.

RESPONSE: For clarity and to be consistent with the results, we have deleted this sentence.
Minor Comments:
1. Abstract line 63, please clarify the phrase "patients who required no respiratory related hospitalizations".

RESPONSE: We have changed this sentence to state the number of patients who had at least one respiratory-related hospitalization the year before and after the initiation of HFCWO. We have also changed this in the results section accordingly.
2. Abstract Line 73, change "in" to "on"

RESPONSE: This has been corrected.
3. Introduction line 106, I believe the explanation for mucociliary impairment is oversimplified in this statement. A broader discussion that better justifies the assessment of HFCWO is warranted.

RESPONSE: We have expanded on the explanation of the pathophysiology of bronchiectasis.
4. Intro, line 108, remove "the" before "pulmonary function"

RESPONSE: This has been corrected.
5. Intro, line 109, consider removing "the goal of…"

RESPONSE: This has been corrected.
6. Intro, line 111, consider adding the phrase "the need for" before "hospitalizations"

RESPONSE: This has been corrected.
7. The authors should present data from medical literature review in the introduction that justifies the assertions that the endpoints they discuss are proper endpoints. The BSI data from Chalmers et al or similar would provide excellent references.

RESPONSE: We have expanded the introduction and included a mention of the BSI to highlight the relevant outcomes that were measured and added the reference by Chalmers et al.
8. Page 4, lines 115-118, is this sentence necessary. IF so (related to comment 3 above), please further justify why HFCWO was chosen.

RESPONSE: We have added a comment that HFCWO is typically utilized if other airway clearance techniques or devices have been ineffective.
9. Introduction, line 124, change "need" to "needed"

RESPONSE: This has been corrected.
10. Methods, line 145, please clarify what the patients were consented for and how. Was this done at a central IRB given that the data comes from patients cared for by numerous providers.

RESPONSE: Informed consent to participate in the registry was obtained from all patients at the time HCFWO was prescribed. The data was stored and managed by an independent actuarial firm and a central was involved in the study: Western Institutional Review Board's (WIRB) IRB Affairs Department.
11. Please clarify the meaning of the sentence in lines 159 that begins "This approach maximized the number of patients…"

RESPONSE: Additional language was added for clarity.
12. In the statistics section, can you comment why ANOVA was not used for these variables with multiple longitudinal time points?

RESPONSE: The biostatistician (coauthor Kraemer) determined a repeated measures model was more appropriate for this data set.
13. Please be more precise with "Approximately 78%" in lines 188

RESPONSE: This has been corrected.
14. Results, lines 198-, please discuss the cohort with details about PsA infection, concomitant meds, etc.

RESPONSE: This is a limitation of the study, these data were not collected for patients beyond the use of antibiotics.
15. The Defined frequent exacerbator discussed in this phrase "Conversely, the percentage of patients who required three or more hospitalizations (frequent exacerbators)" doesn't refer solely to hospital admissions. Please clarify. I suggest that the endpoint be reexamined as the degree/severity of infection/exacerbation.

RESPONSE: Although the frequent exacerbator phenotype may take into consideration exacerbations that did not require a hospital visit, in this study patients classified as "frequent exacerbators" were those that have 3 or more hospitalizations based on the questionnaire base on the question "how many times have you been in the hospital for breathing problems?". The questionnaire did not specifically address the severity of exacerbations, so the severity cannot be analyzed with the current data set. We have added an explanation in the limitations of the study.
16. Results lines 238. Like what this is an important finding? Move findings here, give confidence intervals, and statistical analysis. This is very important!! Also how was baseline FEV1/FVC defined

to define changes?

RESPONSE: The improvement in lung function tests, though evident in the data, require a more thorough analysis that is beyond the original scope of the paper. We chose to remove paragraph.
17. Discussion, lines 263. There is no data in the results section to justify the correlation conclusion offered in this sentence.

RESPONSE: This sentence was changed to more accurately reflect the data presented.
18. The Sentence “Although the breadth of the data recorded, collected in a real-world setting, included a diverse range of practice patterns, the response to HFCWO therapy remained consistent” is confusing, please reword to clarify.

RESPONSE: We have reworded the sentence.

19. Discussion, lines 300-end of the paragraph beginning with the phrase “Second, patients in the study were not randomly selected” is awkward and hard to follow.

RESPONSE: We have reworded the sentence.
20. Discussion, lines 315-, the paragraph beginning “Third, the diagnosis of bronchiectasis was not independently confirmed by the investigators” discuses 2 distinct limitations.

RESPONSE: We have reworded the paragraph.
REVIEWER 2
No additional suggestions.
REVIEWER 3
No additional suggestions.