PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Quality of life and disease experience in patients with heart failure with reduced ejection fraction in Spain: a mixed-methods study
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VERSION 1 – REVIEW

REVIEWER	Austin, Rosalynn Portsmouth Hospitals University NHS Trust
REVIEW RETURNED	02-Jun-2021

GENERAL COMMENTS	Thank you for inviting me to review this interesting paper on the HF experience. It highlights an interesting topic area quality of life (QoL) perspectives between patients and their caregivers. In heart failure. It also presents a complex study design incorporating multiple methods. The results highlight how while the tools used are valid and reliable, they may not completely capture or reflect a full understanding of the patient experience. Main suggestions and questions are below. Suggestions: 1) Title: consider changing the title to include more than just ethnographic as you have used multiple methods (quantitative and qualitative (interviews and observation). 2) Abstract: Within the results add in the main scores from the standardized PROMS used. Connect these scores to your qualitative findings more clearly. Highlight where caregivers disagreed with patients in relation to their QoL 3) The introduction of PREMS is not clear within the manuscript, as not used within this study. 4) Methods: There are multiple methods and multiple stages to this study, which need clarification in a better outlined study design. No details are provided about the consent of or interview content for relative/caregivers. “Selected patients” (line 35) How these were they selected and why is not outlined. 5) Data analysis: Recommend a separation of the analysis plan into qualitative and quantitative rather than grouping all together into a single section of “statistical methods”. Together with

	providing more details into qualitative analysis, triangulation and saturation. 6) Pg 19 line 8 and “M” is missing from PROM 7) Results: The reflections by patients and caregivers is interesting but the connection to PROMS scores the results sometimes is not always clear. A better illustration of the triangulation between the different data types would be helpful. Correlations are discussed but no correlation results are provided in the table indicated. Minimal results are shared around the caregiver perspective and the healthcare interaction observations. I feel this paper addresses an important issue within HF, but more clarity in methods and more details within the results are needed to fully evaluate this work. Their key findings around how patients with HF may struggle with the two week recall for PROMS has interesting implications for research and clinical applications of PROMS in HF.

REVIEWER	Hill, Loreena Queen's University Belfast, School of Nursing and Midwifery
REVIEW RETURNED	08-Sep-2021

GENERAL COMMENTS	Dear Author, Many thanks for the opportunity to review this interesting manuscript. In recent years there has been increased attention on the reliability and implementation of PROMS. In general I was fascinated by the research design and how ethnographic data would be analyzed with quantitative (PROMS questionnaire). Unfortunately I feel the latter received greater attention and the many nuances of patient experiences took second place. I would like to make a few more specific comments: Research Design: This is more a concurrent Mixed Methods study using interviews, observation and questionnaires. Please explain why 'Observational, descriptive, multicenter, cross-sectional, qualitative study' was selected. Introduction: please update terminology on page 5 line 22, HF with mildly reduced EF as per 2021 ESC guidelines. In page 6 you mention 'little is know about patient and caregiver experience living with HF' . This is not entirely correct, so please re-phrase. See one example - see PLoS One. 2020 Dec 14;15(12):e0243974. doi: 10.1371/journal.pone.0243974. Please amend line 54 page 6 as your analysis was not a qualitative comparison, but mixed methods Methods: Please provide more details on sample size- how it was obtained. Who carried out the interviews? Rephrase page 9 line 37 as unclear who were the "selected patients", who accompanied the patient, how was the observational data obtained? Finally how was the Quant:Qual data triangulated and analyzed. Results: Table 3 summarized key themes, however I believe there is a higher level of analysis warranted. for example 'impact of demographic factors' is descriptive. This would have added patient narratives to the results. Interesting study, worthy of publication

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Mrs. Rosalynn Austin, Portsmouth Hospitals University NHS Trust, University of Southampton Faculty of Health Sciences Comments to the Author:

Thank you for inviting me to review this interesting paper on the HF experience. It highlights an interesting topic area quality of life (QoL) perspectives between patients and their caregivers. In heart failure. It also presents a complex study design incorporating multiple methods. The results highlight how while the tools used are valid and reliable, they may not completely capture or reflect a full understanding of the patient experience. Main suggestions and questions are below.

Suggestions:

1) Title: consider changing the title to include more than just ethnographic as you have used multiple methods (quantitative and qualitative (interviews and observation).

RESPONSE: Thank you for the suggestion. Indeed, the study includes multiple methods and not only qualitative research. We have changed the title to “Quality of life and disease experience in patients with heart failure with reduced ejection fraction in Spain: a mixed methods approach to go beyond standardized data” to reflect this fact.

2) Abstract: Within the results add in the main scores from the standardized PROMS used. Connect these scores to your qualitative findings more clearly. Highlight where caregivers disagreed with patients in relation to their QoL

RESPONSE: We have re-structured the abstract to include some of the information proposed. We expanded on the Results section, now including the PROMS main scores and highlighting where caregivers disagreed with patients in relation to their QoL.

3) The introduction of PREMS is not clear within the manuscript, as not used within this study.

RESPONSE: We have removed all references to PREMs, as well as the citation to Lagha E et al. Patient Reported Experience Measures (PREMs) in chronic heart failure. J R Coll Physicians Edinb. 2012;42(4):301-305.

4) Methods: There are multiple methods and multiple stages to this study, which need clarification in a better outlined study design. No details are provided about the consent of or interview content for relative/caregivers. “Selected patients” (line 35) How these were they selected and why is not outlined.

RESPONSE: We have made numerous modifications to the Methods section to better outline the mixed-methods design. Also, we have included a reference to the authorization by the patients (line 181). We have rewritten and extended the description of the section on the visits with patients to their healthcare providers. Patients were selected for these visits based on their NYHA status (two patients per NYHA class).

5) Data analysis: Recommend a separation of the analysis plan into qualitative and quantitative rather than grouping all together into a single section of “statistical methods”. Together with providing more details into qualitative analysis, triangulation and saturation.

RESPONSE: Thank you for the suggestion. We have now reorganized the information in the sections previously titled ‘Outcomes and assessments’ and ‘Statistical Methods’ into two sections on ‘Qualitative outcomes and analyses’ and ‘Quantitative outcomes and analyses’. We have added additional detailed information on how the qualitative analysis was carried out, triangulation and saturation.

6) Pg 19 line 8 and “M” is missing from PROM

RESPONSE: Corrected, thank you (page 17, line 8).

7) Results: The reflections by patients and caregivers is interesting but the connection to PROMS scores the results sometimes is not always clear. A better illustration of the triangulation between the different data types would be helpful. Correlations are discussed but no correlation results are provided in the table indicated. Minimal results are shared around the caregiver perspective and the healthcare interaction observations.

RESPONSE: To establish a direct connection between the reflections by patients/caregivers and PROMs scores is challenging. Indeed, rather than seeking corroboration of results from different data sources, the mixed methods approach intended to highlight the complementarity of ethnographic data and PROMs. We have added an additional row in Table 3 to provide two revealing examples from the interviews in which the PROMs were clearly insufficient to describe the true situation of the patient.

With regards to the triangulation of data, we have expanded the description of the methodology in the Materials and Methods (lines 267-279).

The reviewer is correct that no quantification of the correlation between the scores of the PROMs and the NYHA is presented in Table 2. To avoid misinterpretations, we changed the sentence in page 12 (section on PROMs and health status) to “The results of the EQ-5D-5L and KCCQ showed a strong correspondence with the NYHA functional classes, and also between the two PROMs (Table 2). We found that scores from PROMs dropped as the NYHA increased (i.e., the higher the NYHA class and the HF symptoms, the worse their perceived health status was).”

We have now added citations to Table 3 in the sections on the caregiver perspective and the healthcare interaction observations, and we have expanded with new examples of the interactions supporting our conclusions.

I feel this paper addresses an important issue within HF, but more clarity in methods and more details within the results are needed to fully evaluate this work. Their key findings around how patients with HF may struggle with the two week recall for PROMS has interesting implications for research and clinical applications of PROMS in HF.

RESPONSE: We appreciate the reviewer’s insights and hope that the corrections and additions better support the conclusions reached.

Reviewer: 2
Dr. Loreena Hill, Queen's University Belfast Comments to the Author:

Dear Author, Many thanks for the opportunity to review this interesting manuscript. In recent years there has been increased attention on the reliability and implementation of PROMS. In general I was fascinated by the research design and how ethnographic data would be analyzed with quantitative (PROMS

questionnaire). Unfortunately I feel the latter received greater attention and the many nuances of patient experiences took second place. I would like to make a few more specific comments:

Research Design: This is more a concurrent Mixed Methods study using interviews, observation and questionnaires. Please explain why 'Observational, descriptive, multicenter, cross-sectional, qualitative study' was selected.

RESPONSE: We have now changed the overall description of the study to “observational, cross-sectional, descriptive, multicenter, and mixed methods study”.

Introduction: please update terminology on page 5 line 22, HF with mildly reduced EF as per 2021 ESC guidelines. In page 6 you mention 'little is know about patient and caregiver experience living with HF' . This is not entirely correct, so please re-phrase. See one example - see PLoS One. 2020 Dec 14;15(12):e0243974. doi: 10.1371/journal.pone.0243974. Please amend line 54 page 6 as your analysis was not a qualitative comparison, but mixed methods

RESPONSE: Thank you for alerting us on the recent change in terminology. We have corrected the term to mildly-reduced ejection fraction (HFmrEF). We have also changed reference 8 to McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal. 2021;42(36):3599-3726.

Thank you for bringing our attention to the study by Checa et al PLoS One. We have included this reference and reworded the sentence as follows: “Little is known about the patient’s and caregiver’s perspective of living with HF in Spain, and previous studies did not differentiate by LVEF.”

We amended the sentences explaining the rationale of the study as follows (originally page 6, line 54; now lines 150-154): “We used a mixed methods approach involving the parallel use of an ethnographic approach with PROMs for the assessment of health status (EQ-5D-5L and KCCQ). Rather than seeking corroboration of results from different data sources, the mixed methods approach intended to highlight the complementarity of ethnographic data and PROMs”. This was also reworded in the Objectives of the Abstract.

Methods: Please provide more details on sample size- how it was obtained. Who carried out the interviews? Rephrase page 9 line 37 as unclear who were the "selected patients", who accompanied the patient, how was the observational data obtained? Finally how was the Quant:Qual data triangulated and analyzed.

RESPONSE: We have added additional information related to the sample size in the patient selection of the Methods (lines 194): “A sample size of 20 patients was selected to have sufficient representation of the 3 major NYHA classes. Purposeful sampling was based on the characteristics of potential participants extracted from medical records to obtain optimal variety.”

Regarding the methodology used for the visits to the healthcare providers, we have rewritten the whole paragraph, describing in more detail who were the selected patients, who accompanied the patient, and how was the data obtained and analyzed.

Results: Table 3 summarized key themes, however I believe there is a higher level of analysis warranted. for example 'impact of demographic factors' is descriptive. This would have added patient narratives to the results.

RESPONSE: We have removed the section on “Impact of demographic factors” from Table 3, as the reviewer is correct that this is descriptive. We have added a section on the topic of filling PROM questionnaires, which is an additional key theme of the study. We thank the reviewer for the insightful comments.

VERSION 2 – REVIEW

REVIEWER	Hill, Loreena Queen's University Belfast, School of Nursing and Midwifery
REVIEW RETURNED	16-Oct-2021

GENERAL COMMENTS	Dear Author, Many thanks for the opportunity to review this revised manuscript. It is much improved, however there are a two outstanding concerns which require to be addressed. Abstract: the design outlined in the abstract (page 61) is not consistent with that documented in the methods (line 168). Results: In table 2 replace one of the caregiver quotes with that of a patient, for example use of patient noted in line 355 Minor comments which will be easily rectified. Best wishes as you progress your submission

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Dr. Loreena Hill, Queen's University Belfast Comments to the Author:

Dear Author,

Many thanks for the opportunity to review this revised manuscript. It is much improved, however there are a two outstanding concerns which require to be addressed.

*Abstract: the design outlined in the abstract (page 61) is not consistent with that documented in the methods (line 168).

RESPONSE: We have indicated “mixed-methods study” in the abstract to make it consistent with the description of the design in Methods.

*Results: In table 2 replace one of the caregiver quotes with that of a patient, for example use of patient noted in line 355

RESPONSE: Thank you for the suggestion. We have added new quotes from the patient noted in line 355 to complement caregiver quotes in Table 2.