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Original research

Quality of life and disease experience in patients with heart failure with reduced ejection fraction in Spain: an ethnographic study

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ABSTRACT

Objectives: To gather insights on the disease experience of patients with heart failure with reduced ejection fraction (HFrEF), assessing the correlation between patients' experiences and narratives related to the disease and data collected through standardized patient-reported outcome measures (PROMs). Also, to explore new ways of evaluating the burden experienced by patients and caregivers.

Design: Observational, descriptive, multicenter, cross-sectional, qualitative study.

Setting: Secondary care, patient's homes.

Participants: Twenty patients with HFrEF (NYHAs I-III) aged 38-85 years.

Measures: PROMs EuroQoL 5D-5L and Kansas City Cardiomyopathy Questionnaire and patient interview and observation.

Results: A total of 20 patients with HFrEF participated in the study. The patients' mean (SD) age was 72.5 (11.4) years, 65% were male, and were classified in NYHA functional classes I (N=4), II (N=7) and III (N=9). The study showed a strong impact of HF in the patients' quality of life (QoL) and disease experience, as revealed by the in-depth interviews and the standardized PROMs. Patients and caregivers often disagreed describing and evaluating perceived QoL. Patients related current QoL to distant life experiences or to critical moments in their disease, such as hospitalizations. Anxiety over the disease progression is apparent in both patients and caregivers, suggesting that caregiver-specific tools should be developed.

Conclusions: PROMs are an effective way of assessing symptoms over the most recent time period. However, especially in chronic diseases such as HFrEF, PROM scores could be complemented with additional tools to gain a better understanding of the patient's status. New PROMs designed to evaluate and compare specific points in the life of the patient could be clinically more useful to assess changes in health status.

Strengths and limitations of this study

- This study followed an ethnographic approach to collect data on patient's experiences and narratives related to heart failure, a type of study not before carried out in Spain and with scarce reports worldwide.
- Both patients and caregivers could discuss freely and explain in detail the aspects of the disease that they considered under control and those where change was deemed necessary.
- The often-contrasting views of patients and caregivers highlighted the difficulties in obtaining accurate and objective evaluations of quality of life.
- Although the selection of patients aimed for inclusiveness and diversity, the limited number of HFrEF patients selected for in-depth analysis may not be fully representative of the population of HFrEF patients in Spain.
- The ethnographic interviews took place in the context of the COVID-19 pandemic, which transformed the daily routines of patients and caregivers and may have to a certain extent altered their perspective of living with HFrEF.

INTRODUCTION

Despite advances in treatment, heart failure (HF) remains one of the leading causes of hospitalization and readmissions, death and disability worldwide.[1,2] The economic burden of HF, mainly driven by recurrent hospitalizations, consumes an estimated 1-2% of healthcare budgets.[3,4] The progressive aging of the population in some Western countries, such as Spain, and increasing HF prevalence, have positioned this disease as a major public health problem.[5–7]

Clinically, HF can be classified based on the left ventricular ejection fraction (LVEF) into HF with reduced ejection fraction (HFrEF), defined as an EF ≤40%, mid-range ejection fraction (HFmrEF), defined as EF >40% and <50%, and HF with preserved ejection fraction (HFpEF), defined as an ejection fraction ≥50%.[8] Patients in these subgroups often have distinct underlying etiologies, demographics, co-morbidities and response to therapies.[9,10] Additionally, the presence and severity of symptoms and exercise intolerance of patients with HF is usually categorized following the New York Heart Association (NYHA) classification into four functional classes (I-IV), being class IV the worst.[11]

HF can severely affect the quality of life (QoL) of the patient by reducing their independence and ability to undertake daily living activities, and can also disturb their mental health and psychosocial well-being.[12,13] Prior studies have shown that patients with HF had an even higher incidence of limitations than patients with chronic diseases such as diabetes, cancer, or Alzheimer's disease.[13] Several patient-reported outcome measures (PROMs) have been used to quantify health status in patients with HF, such as the generic EuroQoL 5D-5L (EQ-5D-5L) and the disease-specific Kansas City Cardiomyopathy Questionnaire (KCCQ).[13–17] PROMs such as the KCCQ have a good correlation with prognosis and their use has been encouraged by the American Heart Association in both routine clinical practice and clinical trials of new therapies.[18,19] However, although these PROMs can be useful indicators of health status and how HF

impacts patients' QoL within a 2-week recall period, they have not been designed to reflect some of the patient's and caregiver's perspectives on living with HF, including aspects such as the importance of interactions with family or healthcare providers, feelings related to the course of their disease, or barriers to accessing healthcare resources.[20] These unique aspects of culture, preferences, customs, values and attitudes, could have an impact on treatment effectiveness and outcomes. Complementary to PROMs, patient-reported experience measures (PREMs) are useful to evaluate quality of patient care and the interaction between the patient and the healthcare system.[21,22] However, neglecting the limitations of both PREMs and PROMs could hinder our understanding of the patient's attitudes and real-life disease experiences.

Ethnographic qualitative studies involve observation of the patients and caregivers in their real-world settings to determine how they behave in specific contexts. Ethnographic research collects comprehensive information from multiple sources such as interviews, caregiver perspectives, non-participant observation of healthcare visits and home tours, among others, and has previously been carried out to investigate QoL in patients with HF.[12,23–28] Previous ethnographic studies conducted in patients from the United Kingdom identified barriers to interventions for HF and critical points on disease pathways which resulted in an increase in the risk of admission.[29–31]

Little is known about the patient's and caregiver's perspective of living with HF, and no study in this context has been performed in Spain. The objective of this study was to gather insights on the disease experiences of patients with HFrEF and their caregivers, and the impact on their everyday life. The parallel use of an ethnographic approach with PROMs for the assessment of health status (EQ-5D-5L and KCCQ) allowed qualitative comparison of both types of results. The goal was to improve awareness of healthcare professionals, service providers, policy makers and educators on the factors that can potentially influence treatment effectiveness, and the existence of aspects of the patient's experience that are not covered by existing tools. In turn, this may encourage firstly, a more active participation of healthcare providers, patients and caregivers in clinical decisions considering not only the disease state, but also cultural factors and individual values and attitudes, and secondly, the development of instruments for the evaluation of healthcare interventions.

METHODS

This was an observational, descriptive, multicenter, cross-sectional, qualitative study to obtain insights regarding HFrEF patients' perception and attitudes towards their disease. The patients in the study were recruited at the Departments of Cardiology of 2 large tertiary-level hospitals, namely, the Puerta del Hierro University Hospital (Majadahonda, Madrid, Spain) and the Bellvitge University Hospital (Hospitalet de Llobregat, Barcelona, Spain). The patient populations attended by these hospitals were socioeconomically very distinct, as the Puerta del Hierro University Hospital is located at a high-income district of Madrid, and the Bellvitge University Hospital covers a suburban area of mostly low or very low-income patients. Due to the qualitative and observational design of the study, there was no masking or randomization. Clinical management of the patients followed routine clinical practice, with no changes in treatment or additional clinical assessments specific for this study. All decisions related to disease management were made at the discretion of the treating physician without interference by the sponsor. Informed consent was obtained from each patient prior to study initiation. The study protocol was approved by the Ethics Review Board of the Bellvitge University Hospital on March 12th, 2020 with number PR062/20.

Patients

Patients were assessed for eligibility by local clinical staff according to selection criteria at each participating center. Patients were classified by NYHA class and could be belong to any of the 4 classes I to IV. The inclusion criteria were ≥18 years at the time of consent, established documented diagnosis of HFrEF (LVEF ≤40%), and signed consent to participate. Patients unable to complete the PROMs because of any psychological or physical condition and patients hospitalized at inclusion were excluded.

Data collection

The patient's demographic information and medical history were collected from medical records at the selection visit. On the day of the home visit the patients first completed two health status questionnaires and then a multidisciplinary team composed of social scientists conducted a semi-structured interview following a topic guide to allow respondents to express their experiences and feelings related to HF. The topic guide was organized in 6 domains: 1, personal life account and current context; 2, life experience with previous diseases and current comorbidities; 3, living and personal experience with HF; 4, perception of QoL before and after diagnosis of the disease; 5, relationship with the caregiver and its environment; and 6, relationship with healthcare providers. The interview conducted at the patient's home lasted approximately 90 minutes. In some instances, with the consent of the patient, his/her closest caregivers were interviewed at the patient's home on the same day for about 30 min. The interview with the caregivers aimed at understanding their perception of the patient's status and evaluating their social and emotional relationship with the patient.

Selected patients were accompanied to the first healthcare appointment after the interview. In the interaction with healthcare providers researchers focused on the initial and main topics of conversation with healthcare provider, questions by patients and caregivers, and general attitude of patients. Also patients and caregivers were asked to evaluate the medical visit. Researchers added analytical and reflexive comments to field notes immediately after conducting interviews and observations.

The in-depth interview aimed to capture the patients' experience with the disease from their own point of view, whereas the non-participant observation during the medical visits allowed to investigate the relationship with the healthcare practitioners for both of patients and family members.

Data were collected by audio recording and notes, taking into consideration all aspects of the patient's life and in all cases protecting the patient's data privacy. Subsequently, data triangulation was used to integrate quantitative and qualitative information by ethnographers, individually and in joint sessions. The analytical process aimed to reach theoretical saturation.

Outcomes and assessments

The following primary variables were assessed: the patient's profile; the patient's emotional perception (values, attitude, frustration, fear) during the HFrEF journey, including the role of the caregiver; key relationships and communication processes during the patient HFrEF journey (patient-doctor, patient-carer/family); main barriers to accessing healthcare services experienced by patients during the HFrEF journey; and the patient's unmet needs (cognitive, emotional and functional) associated with HF.

Secondary variables assessed included PROMs by using the EQ-5D-5L and KCCQ. The EQ-5D-5L is a self-reported questionnaire used to derive a standardized measure of health status, also referred to as a utility score.[32] The KCCQ is a self-administered HF-specific instrument and has shown to be a valid, reliable and responsive measure for patients with HF.[14] Spanish validated versions of these questionnaires were used.[33,34] For the EQ-5D-5L, the number and percentage of patients reporting any type of limitation for each questionnaire dimension, the number and percentage of patients reporting "severe" or "extreme" responses for each questionnaire dimension, as well as the index value and the visual analogue scale (VAS) score, were assessed; for the KCCQ, the score for each domain/subdomain, and a summary score for the total symptom score, clinical symptom score and overall summary score were assessed.

Statistical methods

Observational data, interviews and documentary materials were analyzed at three levels: individual patient cases, across cases within research centers, and across research centers to synthesis. The PROMs were analyzed descriptively.

RESULTS

Patient characteristics

A total of 20 patients with HFrEF participated in the study (Table 1). The mean (SD) age of the patients was 72.5 (11.4) years (range, 38-85 years), and 13 (65.0%) were male. The study included 4, 7 and 9 patients in NYHA functional classes I-III, respectively. Although the study protocol was designed to include class IV patients, their frailty, and the effects of the COVID-19 pandemic in the patients' self-caring strategies, hindered the participation of any patients in this class. Twelve patients were being treated at the Bellvitge University Hospital and 8 patients were being treated at the Puerta del Hierro University Hospital.

Understanding of QoL by patients with HF

During the in-depth interviews, the participants described how living with HFrEF impacted their lives, including how they experienced the symptoms of HF and their effects on daily routines (summarized in Table 3). Their responses provided relevant insights on what QoL meant to them. For many patients, QoL was "being able to do what they did before" and missed being independent, their everyday life and maintaining an active lifestyle.

Patients tended to self-limit and isolate to limit symptomatology due to progression-related fears or even fear to a sudden death, despite a more sedentary lifestyle being detrimental to the recovery and to their own QoL.

Impact of demographic factors in perception of QoL

Attitudes and perceptions towards HFrEF seemed to strongly depend on age and education. Young patients tend to be more informed about the disease and challenge the healthcare practitioners' opinions.

In contrast, older patients had a difficult time differentiating between HFrEF symptoms and those associated with the normal process of ageing. Often caregivers had to help them understand the information provided by healthcare workers.

The interviews also revealed that male patients showed more dependency towards caregivers than their female counterparts. Female caregivers tended to strongly challenge male patients' perception of QoL. In one case, the wife of a 63-year old NYHA III patient was very critical of her husband's attitude and thought that part of his evolution strongly depended on his will, and asked him to exercise more, read, get on the computer, and go out for a ride on the motorcycle. They even consulted with a psychologist friend to help them handle the situation.

PROMs and health status

The results of the EQ-5D-5L and KCCQ showed a high correlation with the NYHA functional classes, and also between the two PROMs (Table 2). No differences were observed in scores with respect to gender, or between the patients from the two hospitals.

Some patients with lower NYHAs, despite having visible constraints in health status, indicated high scores in the EQ-5D-5L VAS score. For example, a 76-year-old female with major comorbidities [patient 1-10] with NYHA I indicated a EQ-5D-5L VAS score of 90 and emphasized that her QoL was good. This contrasted with the views expressed by her caregiver.

Regardless of the NYHA, some patients seemed to minimize and relativize the impact of HFrEF on their QoL. Caregivers, in contrast, could emphasize the limitations imposed by HFrEF. For example, the wife and caregiver of a 79-year-old, NYHA II male patient [1-11] indicated that in the consultation with the cardiologist the patient usually underestimated his condition. In another case, the wife of a 74-year-old NYHA III male patient commented that she must be “present with the doctors, because when they ask him something, he usually answers that he is fine and does not really say what is wrong with him.”

Patients with advanced NYHAs, who experienced one or several hospital admissions, compared their current experience with the disease to those acute periods of fear and greater uncertainty. Patients showed a limited portrait of their QoL due to the required reference to the last 2-weeks in the questionnaire. For example, a NYHA III male patient [2-8] had doubts when filling out the questionnaires since he related his mobility limitations to a problem with his legs (a consequence of an aortic dissection) but he did not relate it to HF. Also, he mentioned that his physical and emotional situation was much better now compared to the initial moments where he was more affected. He had a hard time taking the prior two weeks as a reference point, therefore his responses showed a feeling of improvement compared to the most critical moments.

Another NYHA III patient [2-6] had doubts when filling the questionnaires, since his symptoms varied from day to day and between morning, afternoon and night. He also had moments of crises where he considered his symptoms to be worse, so limiting to the last two weeks seemed difficult. Likewise, he stated that shortness of breath or air was something he thought he got from lying down for a long time and not that it was a symptom of HFrEF.

Caregivers could overestimate and present a dramatic view of the patient's day-to-day life with HFrEF. Family caregivers showed more distress when discussing their relatives with HFrEF compared to that showed by remunerated caregivers:

> *“she is concerned about his low spirits and his anguish. She says that the symptoms she develops from anxiety can "mask" the symptoms of HF,*

> *such as pressure and pain in the chest, agitation, a feeling of suffocation."* [caregiver of patient 1-8, NYHA III]

> *"As cardiologists told us that little can be done to improve his condition, we live these years 'as a gift'."* [caregiver of patient 1-6]

Caregivers' roles and needs

In this study, only five patients were able to live without a caregiver. Generally, strong family bonds were apparent and important for the patient. Caregivers were often in charge of organizing visits to the healthcare providers, keeping track of parameters such as weight and blood pressure, and administering medication. Caregivers acted also as interpreters of the disease status on behalf of their patients.

Relationships with healthcare providers

The interactions between patients and caregivers with healthcare workers at hospitals were investigated by the social scientists by accompanying them to a medical appointment. The study showed that patients are usually highly positive about their experience with cardiologists and nurses. A 58-year-old male patient [1-9] explained that the nurse called him weekly to ask about how he was coping, and to discuss data such as weight and blood pressure changes. He generally felt very accompanied by the hospital staff, both cardiologists and nurses. Other patients also expressed a high opinion of the healthcare personnel. Often patients highly value their relationship with the nurse, as they probably feel more confident to express their experiences to his/her.

DISCUSSION

In this study we used ethnographic methods with HFrEF patients and their caregivers, complemented with general and disease-specific health status assessments, to obtain insights regarding patients' disease perception and attitudes towards their disease. Ethnographic methods adopt a phenomenological perspective, aiming to understand individuals' life experiences to acquire relevant knowledge. The results of this study suggest that the patient's perspectives of their QoL were dependent on their memories of what they could do before, and often were better than reality. Caregivers, in contrast, offered a distinct view of the patient's status and QoL, often substantially worse and emphasizing the severity of their life-limiting condition.

As healthcare systems aim to become more 'patient-centered', there is a recognized need to capture accurately the patient's experience of the disease, in an effort to improve it. The use of various forms of PREMs and PROMs have therefore become common in assessing current treatments and new therapies and medical interventions, although their application in clinical practice is still very limited. Despite their widespread use by cardiologists, an awareness of the limitations of PROMs when evaluating the experience of the patient with HF is critical for their interpretation. For example, the effects of comorbid conditions could add confounding factors to the evaluation of HF through a single PROM instrument. Likewise, patients often relate their overall QoL experience to the moments of crisis, such as hospitalizations, 'anchoring' all subsequent experiences to those events and distorting their responses in the questionnaires.

In the general population the understanding of HF and its outcome is low, contributing to anxiety about the evolution of the disease in both patients and caregivers. In contrast, other life-limiting diseases, such as cancer, often have better-defined pathways of care and psychosocial support.[31] In this regard, patient associations and support groups could play a role by helping the patient understand

the disease, the treatments, and the expectations. Patient associations promote social integration and help patient share their experiences, providing the necessary encouragement to cope with their disease and go on with daily activities. Also, as reflected in some of the interviews described in this study, it is important for the patient to feel that he/she can have rapid access to medical services. In this regard, the study reflected that that while some patients were reluctant to discuss aspects of daily life or to express their feelings and fears to the cardiologist, they were more open and felt closer to the nurse, a relationship that was highly valued by many patients. Generally, an efficient and fluid communication with all the healthcare providers involved in the treatment is essential.[12,30]

The study revealed that the fear to losing independence and the uncertainty about the progress of their disease could be factors that motivate some HF patients to downplay their limitations. Conversely, caregivers could overemphasize the poor QoL of the patients, also motivated by concerns of the progress of the disease, its unpredictable trajectory, and lack of proper knowledge and training. Also, it is possible that, since these caregivers were very often family members, their views could be overstated due to emotional attachment to the patient. In any case, these results suggest that instruments should be developed to help caregivers in their daily work with patients with HF, so that they are better informed on the course of the disease and expectations.[26] In this regard, numerous recent studies have highlighted challenges experienced by caregivers of patients with HF.[35–38] Some initiatives along these lines, such caregiver-specific QoL questionnaires,[39] and video coaching,[40,41] are currently being developed and tested.

The results of our study suggest recommendations for future PROM design or questionnaire selection. In patients with HF the PROM instruments should aim to truly mirror patients' experience, using language that the patient associates with their cultural views of QoL. To provide insights on relevant changes in QoL, the PROMs should be constructed to capture specific timepoints related to the patient experience

(e.g., healthcare status before the diagnosis, and before and after hospitalizations). In this way, reference points in the patient's lives could be established that favored meaningful QoL before/after comparations. Instruments should allow an alternative stratification based on these clinical events and patients' perceived QoL along them. Also, as self-care behaviors can greatly affect symptoms in patients with HF,[42] the patient's self-caring strategies, perception of autonomy, level of empowerment, and the perception of past and present experiences with the disease should be taken into consideration when developing and introducing future PRO instruments.[43] Finally, additional instruments should be developed to evaluate the key aspects of the patient' support system, and explore caregivers' needs.

Given the lack of studies assessing the patient's and caregiver's perspective on the HFrEF pathway in Spain, this study aimed to fill this gap to better understand possible cultural differences. The ethnographic approach, which involved in-depth interviews with patients at their homes and with their caregivers, made it possible to collect relevant data not normally discussed or shared in healthcare facilities. Both patients and caregivers could talk freely and explain the aspects of the disease that they considered under control and those where change was deemed necessary. However, a limitation of this study is that the small sample size, although not unusual in qualitative research that requires extensive and detailed analysis of each patient, may not fully represent the diversity of people with HFrEF in Spain. Also, as it is the case in other ethnographic studies, interviewing patients and caregivers together may have resulted in individual perspectives being altered or withheld. Finally, since this study was carried out during the COVID-19 pandemic, it is possible that the disruption imposed by the social restrictions could have some effect in the results described here.

In conclusion, this study analyzed, by the use of PROMs and in-depth interviews, the complexity of the actual experiences of the patients with HFrEF. The lack of knowledge about the disease generates confusion and anxiety about symptoms, and patients could tend to minimize the impact of HF in QoL. Patients tend

to maintain a closer relationship with their nurses, compared with the cardiologist, favoring a more open discussion of feelings and experiences related to the disease with them. In order to provide personalized care to HFrEF patients, QoL could be assessed by comparing two points in time, thus helping the healthcare practitioner understand the patient's point of view of specific interventions. Since QoL is a multidimensional, subjective concept that is affected by a variety of factors, its evaluation should be carefully designed to capture specific moments and changes in the trajectory of the disease. The study suggests that tools and training should be made available to caregivers to alleviate the burden of care and anxiety derived from uncertainty in the progression of the disease. Further work is needed to fully integrate the use of well-designed and useful PROMs and PREMs into clinical practice.

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Contributors

RR, LV,SCC, JCC and BP conceived and designed the study. JCC, EC, EH, ECB, PGC, NJ, MRM, CE, SY, SJM, LAT, AGM, PMB, LYF, JSC, SVL, and MSG contributed to patient recruitment and data collection. JCC, JSC, BP, LV, SCC, MFE, and RR compiled and analyzed the data. JCC, BP, LV, SCC, and RR drafted the manuscript, which was revised by the other authors. All authors read and approved the final manuscript.

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Competing interests

JCC received fees from AstraZeneca for the coordination and oversight of the study. RR, MFE, and SCC received research funding from AstraZeneca. RFdlF, BP, and LV are employees of AstraZeneca. All other authors report no competing interests.

Patient and public involvement

CardioAlianza, a Spanish association of patients with cardiovascular disease and their caregivers, was involved in designing, providing feedback for interpretation of data, and in the dissemination of this research.

Patient consent for publication

Informed consent for participation in the study and publication of the results were obtained from each patient prior to study initiation.

Ethics approval

This study was approved by the Ethics Review Board of the Bellvitge University Hospital on March 12th, 2020 with number PR062/20.

Data availability statement

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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TABLES

Table 1. Demographic and clinical characteristics of the patients.

Variable	N=20
Age, years, mean (SD)	72.5 (11.4)
Range (minimum-maximum)	38-85
Gender, male, N (%)	13 (65.0)
Time since diagnosis, years, mean (SD)	2.35 (2.9)
Recent diagnosis (less than 2 months), N (%)	2 (10.0)
NYHA, N (%)	
I	4 (20.0)
II	7 (35.0)
III	9 (45.0)
LVEF, %, mean (SD)	31.1 (6.0)
Diabetes, type 2, N (%)	9 (45.0)

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation.

Table 2. Evaluation of health status by PROMs. Scores for EQ-5D-5L and KCCQ.

	NYHA I-II (N=11)	NYHA III (N=9)	All NYHA (N=20)
EQ-5D-5L, patients reporting any limitation[1], N (%)			
Mobility	5 (40.5)	9 (100)	14 (70.0)
Self-care	0	7 (77.8)	7 (35.0)
Usual activities	4 (36.4)	8 (88.9)	12 (60.0)
Pain/Discomfort	4 (36.4)	6 (66.7)	10 (50.0)
Anxiety/Depression	4 (36.4)	8 (88.9)	12 (60.0)
EQ-5D-5L, patients reporting severe or extreme limitations[2], N (%)			
Mobility	0	5 (55.6)	5 (25.0)
Self-care	0	2 (22.2)	2 (10.0)
Usual activities	0	3 (33.3)	3 (15.0)
Pain/Discomfort	1 (9.1)	2 (22.2)	3 (15.0)
Anxiety/Depression	0	2 (22.2)	2 (10.0)
EQ-5D-5L global, mean (SD)			
Index value	0.85 (0.17)	0.37 (0.36)	0.64 (0.36)
VAS score	74.55 (23.50)	45.56 (14.46)	61.50 (24.45)
KCCQ, mean (SD)			
Physical limitation	81.06 (19.04)	39.72 (26.59)	62.46 (30.56)
Symptom stability	59.10 (12.61)	66.67 (30.62)	62.50 (22.21)
Symptom frequency	84.66 (17.14)	57.64 (27.14)	72.50 (25.59)
Symptom burden	91.67 (11.18)	61.11 (24.30)	77.92 (23.61)
Self-efficacy	94.32 (10.25)	85.94 (18.22)	90.79 (14.34)
Quality of life	82.58 (13.15)	33.33 (20.83)	60.42 (30.09)
Social limitation	85.61 (14.02)	31.94 (26.62)	61.46 (33.94)
KCCQ global scores, mean (SD)			
Overall summary	82.69 (9.81)	41.09 (20.55)	63.97 (26.06)
Clinical summary	81.30 (10.82)	49.55 (22.31)	67.01 (23.10)
Total symptom	81.54 (10.85)	59.37 (23.50)	71.56 (20.55)

[1] Any score but 1 (no problems).

[2] Only patients scoring 4 or 5 in each domain.

EQ-5D-5L, EuroQoL 5D-5L questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; PRO, patient-reported outcome; SD, standard deviation; VAS, visual analogue scale.

Table 3. Domains and main perceptions among HFrEF patients.

Domains	**Patients and caregivers' quotes**
Domain 1. Meanings related to QoL	
Attachment to previous routines	"This has split my old age in two, having many things to do and not being able to do them because you get very tired. I miss that freedom that I had. Now I feel tied." [1-1]
	"What I have missed the most is driving, I spent 20 years as a taxi driver." [2-1]
	"For me quality of life means to go wherever you want, to do strange things." [2-4]
	"I have always solved the problems that arised, but now I feel impotence because I can't do this anymore." [2-8]
Fears of progression	"The symptoms depend on the day, they are not permanent, some days you are tired, others not." [2-2]
	"Before I went out to the country with my dog, and I liked to go out with the bike but I can't anymore, I have to depend on a cane." [2-4]
	"I was in a good, well-paid job and I liked it, but when this happened, I completely disconnected." [2-8]
Impact of demographic factors	"It has been tough. Especially emotionally when you listen to the doctor who gives you a serious diagnosis and you do not know what you are facing, you think what my life expectancy will be or how you are going to live from now on. This news is not the same for an 86-year-old than for a 38-year-old." [2-6, 38-year-old woman]
	"They have always been clear about what is happening to me, the question is why, since I am not a patient with a family history of disease." [2-5, female, age 62 years]
Domain 2. Caregivers' roles	
Tracking at home	"I keep track of pressure, weight, urine. Every day. I have it written down here in the notebook and I also send it through the hospital's APP. But I really don't know if it is of much use. When I had to call the ambulance everything seemed normal, I kept a similar record in recent days." [caregiver of 78-year-old, NYHA III patient 1-6]
Medical appointments	"When we go to the hospital the doctors ask him if he sleeps well or if he is drowning and he always answers that he is fine, but he is not. The last time he had been sleeping on the couch because he couldn't sleep in bed even with 3 pillows. That's why I always go to the controls with him." [caregiver of 74-year-old NYHA III patient 2-4]
Domain 3. Relationships with healthcare providers	
Commitment	"I come to the very dedicated medical consultations and with the certainty that I am more closely watched than a Ferrari" [2-5, female, age 62 years]
Trustworthiness	"I sit in a consultation where they take their time, and they answer all my doubts. The big difference is that now I feel more secure, I know that I must deal with weight, urine, food. Having the possibility of calling them 24 hours a day gives you more peace of mind." [2-6, female, age 38 years]
	"The nurse is better than any cardiologist, everyone loves her." [2-5, female, age 62 years]
	"The nurse is very close, I think they have chosen a person with a character and attitude that is just what a patient needs." [2-6]

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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

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Original research

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

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ABSTRACT

Objectives: To gather insights on the disease experience of patients with heart failure with reduced ejection fraction (HFrEF), and assess how patients' experiences and narratives related to the disease complement data collected through standardized patient-reported outcome measures (PROMs). Also, to explore new ways of evaluating the burden experienced by patients and caregivers.

Design: Observational, descriptive, multicenter, cross-sectional, qualitative study.

Setting: Secondary care, patient's homes.

Participants: Twenty patients with HFrEF (NYHAs I-III) aged 38-85 years.

Measures: PROMs EuroQoL 5D-5L and Kansas City Cardiomyopathy Questionnaire and patient interview and observation.

Results: A total of 20 patients with HFrEF participated in the study. The patients' mean (SD) age was 72.5 (11.4) years, 65% were male, and were classified in NYHA functional classes I (N=4), II (N=7) and III (N=9). The study showed a strong impact of HF in the patients' quality of life (QoL) and disease experience, as revealed by the standardized PROMs (EQ-5D-5L global index=0.64 [0.36]; KCCQ total symptom score=71.56 [20.55]) and the in-depth interviews. Patients and caregivers often disagreed describing and evaluating perceived QoL, as patients downplayed their limitations and caregivers overemphasized the poor QoL of the patients. Patients related current QoL to distant life experiences or to critical moments in their disease, such as hospitalizations. Anxiety over the disease progression is apparent in both patients and caregivers, suggesting that caregiver-specific tools should be developed.

Conclusions: PROMs are an effective way of assessing symptoms over the most recent time period. However, especially in chronic diseases such as HFrEF, PROM scores could be complemented with additional tools to gain a better understanding of the patient's status. New PROMs designed to evaluate and compare specific points in the life of the patient could be clinically more useful to assess changes in health status.

Strengths and limitations of this study

- This study followed an ethnographic approach to collect data on patient's experiences and narratives related to heart failure, a type of study not before carried out in Spain and with scarce reports worldwide.
- Both patients and caregivers could discuss freely and explain in detail the aspects of the disease that they considered under control and those where change was deemed necessary.
- The often-contrasting views of patients and caregivers highlighted the difficulties in obtaining accurate and objective evaluations of quality of life.
- Although the selection of patients aimed for inclusiveness and diversity, the limited number of HFrEF patients selected for in-depth analysis may not be fully representative of the population of HFrEF patients in Spain.
- The ethnographic interviews took place in the context of the COVID-19 pandemic, which transformed the daily routines of patients and caregivers and may have to a certain extent altered their perspective of living with HFrEF.

INTRODUCTION

Despite advances in treatment, heart failure (HF) remains one of the leading causes of hospitalization and readmissions, death and disability worldwide.[1,2] The economic burden of HF, mainly driven by recurrent hospitalizations, consumes an estimated 1-2% of healthcare budgets.[3,4] The progressive aging of the population in some Western countries, such as Spain, and increasing HF prevalence, have positioned this disease as a major public health problem.[5–7]

Clinically, HF can be classified based on the left ventricular ejection fraction (LVEF) into HF with reduced ejection fraction (HFrEF), defined as an EF ≤40%, mildly-reduced ejection fraction (HFmrEF), defined as EF >40% and <50%, and HF with preserved ejection fraction (HFpEF), defined as an ejection fraction ≥50%.[8] Patients in these subgroups often have distinct underlying etiologies, demographics, co-morbidities and response to therapies.[9,10] Additionally, the presence and severity of symptoms and exercise intolerance of patients with HF is usually categorized following the New York Heart Association (NYHA) classification into four functional classes (I-IV), being class IV the worst.[11]

HF can severely affect the quality of life (QoL) of the patient by reducing their independence and ability to undertake daily living activities, and can also disturb their mental health and psychosocial well-being.[12,13] Prior studies have shown that patients with HF had an even higher incidence of limitations than patients with chronic diseases such as diabetes, cancer, or Alzheimer's disease.[13] Several patient-reported outcome measures (PROMs) have been used to quantify health status in patients with HF, such as the generic EuroQoL 5D-5L (EQ-5D-5L) and the disease-specific Kansas City Cardiomyopathy Questionnaire (KCCQ).[13–17] PROMs such as the KCCQ have a good correlation with prognosis and their use has been encouraged by the American Heart Association in both routine clinical practice and clinical trials of new therapies.[18,19] However, although these PROMs can be useful indicators of health status and how HF

impacts patients' QoL within a 2-week recall period, they have not been designed to reflect some of the patient's and caregiver's perspectives on living with HF, including aspects such as the importance of interactions with family or healthcare providers, feelings related to the course of their disease, or barriers to accessing healthcare resources.[20] These unique aspects of culture, preferences, customs, values and attitudes, could have an impact on treatment effectiveness and outcomes. Complementary to PROMs, in-depth interviews with patients and caregivers are useful to evaluate quality of patient care and the interaction between the patient and the healthcare system.[21] However, neglecting the limitations PROMs could hinder our understanding of the patient's attitudes and real-life disease experiences.

Ethnographic qualitative studies involve observation of the patients and caregivers in their real-world settings to determine how they behave in specific contexts. Ethnographic research collects comprehensive information from multiple sources such as interviews, caregiver perspectives, non-participant observation of healthcare visits and home tours, among others, and has previously been carried out to investigate QoL in patients with HF.[12,22–27] Previous ethnographic studies conducted in patients from the United Kingdom identified barriers to interventions for HF and critical points on disease pathways which resulted in an increase in the risk of admission.[28–30]

Little is known about the patient's and caregiver's perspective of living with HF in Spain, and previous studies did not evaluate patients by LVEF.[31] The objective of this study was to gather insights on the disease experiences of patients with HFrEF and their caregivers, and the impact on their everyday life. 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.[32,33] The goal was to improve awareness of healthcare professionals, service providers, policy makers and educators on the factors that can potentially influence treatment effectiveness, and the existence of aspects of the patient's experience that are not covered by existing tools. In turn, this may encourage firstly, a more active participation of healthcare providers, patients and caregivers in clinical decisions considering not only the disease state, but also cultural factors and individual values and attitudes, and secondly, the development of instruments for the evaluation of healthcare interventions.

METHODS

We conducted an observational, cross-sectional, descriptive, multicenter, and mixed methods study to obtain insights regarding HFrEF patients' perception and attitudes towards their disease. The patients in the study were recruited at the Departments of Cardiology of 2 large tertiary-level hospitals, namely, the Puerta del Hierro University Hospital (Majadahonda, Madrid, Spain) and the Bellvitge University Hospital (Hospitalet de Llobregat, Barcelona, Spain). The patient populations attended by these hospitals were socioeconomically very distinct, as the Puerta del Hierro University Hospital is located at a high-income district of Madrid, and the Bellvitge University Hospital covers a suburban area of mostly low or very low-income patients. Due to the qualitative and observational design of the study, there was no masking or randomization. Clinical management of the patients followed routine clinical practice, with no changes in treatment or additional clinical assessments specific for this study. All decisions related to disease management were made at the discretion of the treating physician without interference by the sponsor. Informed consent was obtained from each patient prior to study initiation. The patients authorized the interview with their main caregiver as part of the informed consent process. The study protocol was approved by the Ethics Review Board of the Bellvitge University Hospital on March 12th, 2020 with number PR062/20.

Patient selection

Patients were assessed for eligibility by local clinical staff according to selection criteria at each participating center. Patients were classified by NYHA class and could be belong to any of the 4 classes I to IV. The inclusion criteria were ≥18 years at the time of consent, established documented diagnosis of HFrEF (LVEF ≤40%), and signed consent to participate. Patients unable to complete the PROMs because of any psychological or physical condition and patients hospitalized at inclusion were excluded.

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.

Data collection

The patient's demographic information and medical history were collected from medical records at the selection visit. On the day of the home visit the patients first completed two health status questionnaires and then two female senior researchers (SCC, MFE) with >5 years of experience in medical sociology and medical anthropology conducted a semi-structured interview following a topic guide (See Supplementary Materials). There was no prior relationship between the interviewer and the patient, who was informed about the research goals prior to starting the interview. The interview conducted at the patient's home lasted approximately 90 minutes. In some instances, with the consent of the patient, his/her closest caregivers were interviewed at the patient's home on the same day for about 30 min. The interview with the caregivers aimed at understanding their perception of the patient's status and evaluating their social and emotional relationship with the patient.

In order to gather observational data to complement participants' accounts of their medical experience, 6 out of 20 patients (two per NYHA class) consented that the same researcher carrying out the interview would observe their first healthcare appointment after the home interview. Direct observation allowed researchers to gather information regarding patients' objective and subjective experiences during medical encounters, about how patients and caregivers conveyed concerns and needs, and provided clues about incongruent behaviour. A single appointed researcher observed the initial and main focus of conversations with healthcare providers, questions by patients and caregivers, and patients' use of verbal and non-verbal communication (e.g., behaviour that suggested passive, nervous, impatient, caring, or expectant attitudes). Immediately after the appointment, patients and caregivers, if present, were asked to evaluate the medical visit (clinical encounters last 20 minutes on average). Researchers took field notes and added reflexive comments about the encounter and about participants' experience.

The in-depth interview aimed to capture the patients' experience with the disease from their own point of view, whereas the non-participant observation during the medical visits allowed to investigate the relationship with the healthcare practitioners for both of patients and family members.

Data from in-depth interviews were collected by audio recording and field notes, whereas data from direct observation of medical encounters were collected by field notes only, taking into consideration all aspects of the patient's life and in all cases protecting the patient's data privacy.

Quantitative outcomes and analyses

Secondary variables assessed included PROMs by using the EQ-5D-5L and KCCQ. The EQ-5D-5L is a self-reported questionnaire used to derive a standardized measure of health status, also referred to as a utility score.[34] The KCCQ is a self-administered HF-specific instrument and has shown to be a valid, reliable and responsive measure for patients with HF.[14] Spanish validated versions of these questionnaires were used.[35,36] For the EQ-5D-5L, the number and percentage of patients reporting any type of limitation for each questionnaire dimension, the number and percentage of patients reporting “severe” or “extreme” responses for each questionnaire dimension, as well as the index value and the visual analogue scale (VAS, where 100 equals the best health HF patients can imagine), were assessed; for the KCCQ, the score for each domain/subdomain, and a summary score for the total symptom score, clinical symptom score and overall summary score were assessed (scores range from 0 to 100; were higher scores indicate a better health status). The PROMs were analyzed descriptively.

Qualitative outcomes and analyses

The following primary variables were assessed: the patient’s profile; the patient’s emotional perception (values, attitude, frustration, fear) during the HFrEF journey, including the role of the caregiver; key relationships and communication processes during the patient HFrEF journey (patient-doctor, patient-carer/family); main barriers to accessing healthcare services experienced by patients during the HFrEF journey; and the patient’s unmet needs (cognitive, emotional and functional) associated with HF. Observational data, interviews and documentary materials were analyzed at three levels: individual patient cases, across cases within research centers, and across research centers to synthesis.

Thematic content analysis was used to analyse the data gathered from interviews and direct observation of clinical encounters. The analysis was carried out by field researchers in six steps: 1) read and re-read of interview and medical encounters’ fieldnotes; 2) identification of main topics per interview domain; 3) text codification to identify current and new domains; 4) review of PROM scores per interviewer and NYHA class; 5) comparison of PROM scores and fieldwork data; and 6) and synthesis of repetitive patterns.

Subsequently, data triangulation was used to integrate quantitative and qualitative information by the researchers, individually and in joint sessions. Three types of triangulation were used: investigator, data and methodological triangulation. Two investigators were involved in the data collection and analysis. Findings from each investigator were compared to develop a deeper understanding of how the different investigators view the issue. Preliminary conclusions were discussed with the broader team of authors in further analysis sessions. Regarding data triangulation, investigators compared the answers from patients and caregivers (information sources) separately to identify areas of agreement and disagreement over the main topics. Regarding methodological triangulation, findings from interviews, direct observations of medical appointments, and PROM scores were compared to identify incongruences and disparities in patients' responses (e.g., patients reporting mild limitations in PROMs but highlighting severe limitations during the interview and/or medical appointment).

The analytical process aimed to reach theoretical saturation where no new dimensions emerged during joint sessions.

RESULTS

Patient characteristics

A total of 20 patients with HFrEF participated in the study (Table 1). The mean (SD) age of the patients was 72.5 (11.4) years (range, 38-85 years), and 13 (65.0%) were male. The study included 4, 7 and 9 patients in NYHA functional classes I-III, respectively. Although the study protocol was designed to include class IV patients, their frailty, and the effects of the COVID-19 pandemic in the patients' self-caring strategies, hindered the participation of any patients in this class. Twelve patients were being treated at the Bellvitge University Hospital and 8 patients were being treated at the Puerta del Hierro University Hospital.

Understanding of QoL by patients with HF

During the in-depth interviews, the participants described how living with HFrEF impacted their lives, including how they experienced the symptoms of HF and their effects on daily routines (summarized in Table 2). Their responses provided relevant insights on what QoL meant to them. For many patients, QoL was "being able to do what they did before” and missed being independent, their everyday life and maintaining an active lifestyle.

Patients tended to self-limit and isolate to limit symptomatology due to progression-related fears or even fear to a sudden death, despite a more sedentary lifestyle being detrimental to the recovery and to their own QoL.

Impact of demographic factors in perception of QoL

Attitudes and perceptions towards HFrEF seemed to strongly depend on age and education. Young patients tend to be more informed about the disease and challenge the healthcare practitioners’ opinions.

In contrast, older patients had a difficult time differentiating between HFrEF symptoms and those associated with the normal process of ageing. Often caregivers had to help them understand the information provided by healthcare workers.

The interviews also revealed that male patients showed more dependency towards caregivers than their female counterparts. Female caregivers tended to strongly challenge male patients’ perception of QoL. In one case, the wife of a NYHA III patient was very critical of her husband’s attitude and thought that part of his evolution strongly depended on his will, and asked him to exercise more, read, get on the computer, and go out for a ride on the motorcycle. They even consulted with a psychologist friend to help them handle the situation.

PROMs and health status

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 3). 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). No differences were observed in scores with respect to gender, or between the patients from the two hospitals.

Some patients with lower NYHAs, despite having visible constraints in health status, indicated high scores in the EQ-5D-5L VAS score. For example, a patient with major comorbidities [1-10] with NYHA I indicated a EQ-5D-5L VAS score of 90 and emphasized that her QoL was good. This contrasted with the views expressed by her caregiver (Table 2).

Regardless of the NYHA, some patients seemed to minimize and relativize the impact of HFrEF on their QoL. Caregivers, in contrast, could emphasize the limitations imposed by HFrEF. For example, the wife and caregiver of a NYHA II patient [1-11] indicated that in the consultation with the cardiologist the patient usually underestimated his condition. In another case, the wife of a NYHA III patient commented that she must be “present with the doctors, because when they ask him something, he usually answers that he is fine and does not really say what is wrong with him.”

Patients with advanced NYHAs, who experienced one or several hospital admissions, compared their current experience with the disease to those acute periods of fear and greater uncertainty. Patients showed a limited portrait of their QoL due to the required reference to the last 2-weeks in the questionnaire. For example, a NYHA III patient [2-8] had doubts when filling out the questionnaires since he related his mobility limitations to a problem with his legs (a consequence of an aortic dissection) but he did not relate it to HF. Also, he mentioned that his physical and emotional situation was much better now compared to the initial moments where he was more affected. He had a hard time taking the prior two weeks as a reference point, therefore his responses showed a feeling of improvement compared to the most critical moments.

Another NYHA III patient [2-6] had doubts when filling the questionnaires, since his symptoms varied from day to day and between morning, afternoon and night. He also had moments of crises where he considered his symptoms to be worse, so limiting to the last two weeks seemed difficult. Likewise, he stated that shortness of breath or air was something he thought he got from lying down for a long time and not that it was a symptom of HFrEF.

Caregivers could overestimate and present a dramatic view of the patient's day-to-day life with HFrEF. Family caregivers showed more distress when discussing their relatives with HFrEF compared to that showed by remunerated caregivers:

> *“she is concerned about his low spirits and his anguish. She says that the symptoms she develops from anxiety can "mask" the symptoms of HF, such as pressure and pain in the chest, agitation, a feeling of suffocation.”* [caregiver of patient 1-8, NYHA III]

> *“As cardiologists told us that little can be done to improve his condition, we live these years ‘as a gift’.”* [caregiver of patient 1-6]

Caregivers’ roles and needs

In this study, only five patients were able to live without a caregiver. Generally, strong family bonds were apparent and important for the patient. Caregivers were often in charge of organizing visits to the healthcare providers, keeping track of parameters such as weight and blood pressure, and administering medication (Table 2). Caregivers acted also as interpreters of the disease status on behalf of their patients.

Relationships with healthcare providers

The interactions between patients and caregivers with healthcare workers at hospitals were investigated by the social scientists by accompanying them to a medical appointment. The study showed that patients are usually highly positive about their experience with cardiologists and nurses (Table 2). A patient [1-9] explained that the nurse called him weekly to ask about how he was coping, and to discuss data such as weight and blood pressure changes. He generally felt very accompanied by the hospital staff, both cardiologists and nurses. Other patients also expressed a high opinion of the healthcare personnel. Often patients highly value their relationship with the nurse, as they probably feel more confident to express their experiences to his/her.

DISCUSSION

In this study we used ethnographic methods with HFrEF patients and their caregivers, complemented with general and disease-specific health status assessments, to obtain insights regarding patients' disease perception and attitudes towards their disease. Ethnographic methods adopt a phenomenological perspective, aiming to understand individuals' life experiences to acquire relevant knowledge. The results of this study suggest that the patient's perspectives of their QoL were dependent on their memories of what they could do before, and often were better than reality. Caregivers, in contrast, offered a distinct view of the patient's status and QoL, often substantially worse and emphasizing the severity of their life-limiting condition.

As healthcare systems aim to become more 'patient-centered', there is a recognized need to capture accurately the patient's experience of the disease, in an effort to improve it. The use of PROMs have therefore become common in assessing current treatments and new therapies and medical interventions, although their application in clinical practice is still very limited. Despite their widespread use by cardiologists, an awareness of the limitations of PROMs when evaluating the experience of the patient with HF is critical for their interpretation. For example, the effects of comorbid conditions could add confounding factors to the evaluation of HF through a single PROM instrument. Likewise, patients often relate their overall QoL experience to the moments of crisis, such as hospitalizations, 'anchoring' all subsequent experiences to those events and distorting their responses in the questionnaires.

In the general population the understanding of HF and its outcome is low, contributing to anxiety about the evolution of the disease in both patients and caregivers. In contrast, other life-limiting diseases, such as cancer, often have better-defined pathways of care and psychosocial support.[30] In this regard, patient associations and support groups could play a role by helping the patient understand

the disease, the treatments, and the expectations. Patient associations promote social integration and help patient share their experiences, providing the necessary encouragement to cope with their disease and go on with daily activities. Also, as reflected in some of the interviews described in this study, it is important for the patient to feel that he/she can have rapid access to medical services. In this regard, the study reflected that that while some patients were reluctant to discuss aspects of daily life or to express their feelings and fears to the cardiologist, they were more open and felt closer to the nurse, a relationship that was highly valued by many patients. Generally, an efficient and fluid communication with all the healthcare providers involved in the treatment is essential.[12,29]

The study revealed that the fear to losing independence and the uncertainty about the progress of their disease could be factors that motivate some HF patients to downplay their limitations. Conversely, caregivers could overemphasize the poor QoL of the patients, also motivated by concerns of the progress of the disease, its unpredictable trajectory, and lack of proper knowledge and training. Also, it is possible that, since these caregivers were very often family members, their views could be overstated due to emotional attachment to the patient. In any case, these results suggest that instruments should be developed to help caregivers in their daily work with patients with HF, so that they are better informed on the course of the disease and expectations.[25] In this regard, numerous recent studies have highlighted challenges experienced by caregivers of patients with HF.[37–40] Some initiatives along these lines, such caregiver-specific QoL questionnaires,[41] and video coaching,[42,43] are currently being developed and tested.

The results of our study suggest recommendations for future PROM design or questionnaire selection. In patients with HF the PROM instruments should aim to truly mirror patients' experience, using language that the patient associates with their cultural views of QoL. To provide insights on relevant changes in QoL, the PROMs should be constructed to capture specific timepoints related to the patient experience

(e.g., healthcare status before the diagnosis, and before and after hospitalizations). In this way, reference points in the patient's lives could be established that favored meaningful QoL before/after comparations. Instruments should allow an alternative stratification based on these clinical events and patients' perceived QoL along them. Also, as self-care behaviors can greatly affect symptoms in patients with HF,[44] the patient's self-caring strategies, perception of autonomy, level of empowerment, and the perception of past and present experiences with the disease should be taken into consideration when developing and introducing future PROM instruments.[45] Finally, additional instruments should be developed to evaluate the key aspects of the patient' support system, and explore caregivers' needs.

Given the lack of studies assessing the patient's and caregiver's perspective on the HFrEF pathway in Spain, this study aimed to fill this gap to better understand possible cultural differences. The ethnographic approach, which involved in-depth interviews with patients at their homes and with their caregivers, made it possible to collect relevant data not normally discussed or shared in healthcare facilities. Both patients and caregivers could talk freely and explain the aspects of the disease that they considered under control and those where change was deemed necessary. However, a limitation of this study is that the small sample size, although not unusual in qualitative research that requires extensive and detailed analysis of each patient, may not fully represent the diversity of people with HFrEF in Spain. Also, as it is the case in other ethnographic studies, interviewing patients and caregivers together may have resulted in individual perspectives being altered or withheld. Finally, since this study was carried out during the COVID-19 pandemic, it is possible that the disruption imposed by the social restrictions could have some effect in the results described here.

In conclusion, this study analyzed, by the use of PROMs and in-depth interviews, the complexity of the actual experiences of the patients with HFrEF. The lack of knowledge about the disease generates confusion and anxiety about symptoms, and patients could tend to minimize the impact of HF in QoL. Patients tend

to maintain a closer relationship with their nurses, compared with the cardiologist, favoring a more open discussion of feelings and experiences related to the disease with them. In order to provide personalized care to HFrEF patients, QoL could be assessed by comparing two points in time, thus helping the healthcare practitioner understand the patient's point of view of specific interventions. Since QoL is a multidimensional, subjective concept that is affected by a variety of factors, its evaluation should be carefully designed to capture specific moments and changes in the trajectory of the disease. The study suggests that tools and training should be made available to caregivers to alleviate the burden of care and anxiety derived from uncertainty in the progression of the disease. Further work is needed to fully integrate the use of well-designed and useful PROMs into clinical practice.

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Contributors

RR, LV, SCC, JCC and BP conceived and designed the study. JCC, EC, EH, ECB, PGC, NJ, MRM, CE, SY, SJM, LAT, AGM, PMB, LYF, JSC, SVL, and MSG contributed to patient recruitment and data collection. JCC, JSC, BP, LV, SCC, MFE, and RR compiled and analyzed the data. JCC, BP, LV, SCC, and RR drafted the manuscript, which was revised by the other authors. All authors read and approved the final manuscript.

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Competing interests

JCC received fees from AstraZeneca for the coordination and oversight of the study. RR, MFE, and SCC received research funding from AstraZeneca. RFdIF, BP, and LV are employees of AstraZeneca. All other authors report no competing interests.

Patient and public involvement

CardioAlianza, a Spanish association of patients with cardiovascular disease and their caregivers, was involved in designing, providing feedback for interpretation of data, and in the dissemination of this research.

Patient consent for publication

Informed consent for participation in the study and publication of the results were obtained from each patient prior to study initiation.

Ethics approval

This study was approved by the Ethics Review Board of the Bellvitge University Hospital on March 12th, 2020 with number PR062/20.

Data availability statement

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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TABLES

Table 1. Demographic and clinical characteristics of the patients.

Variable	N=20
Age, years, mean (SD)	72.5 (11.4)
Range (minimum-maximum)	38-85
Gender, male, N (%)	13 (65.0)
Time since diagnosis, years, mean (SD)	2.35 (2.9)
Recent diagnosis (less than 2 months), N (%)	2 (10.0)
NYHA, N (%)	
I	4 (20.0)
II	7 (35.0)
III	9 (45.0)
LVEF, %, mean (SD)	31.1 (6.0)
Diabetes, type 2, N (%)	9 (45.0)

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation.

Table 2. Domains and main perceptions among HFrEF patients.

Domains	**Patients and caregivers' quotes**
Domain 1. Meanings related to QoL	
Attachment to previous routines	"This has split my old age in two, having many things to do and not being able to do them because you get very tired. I miss that freedom that I had. Now I feel tied." [1-1]
	"What I have missed the most is driving, I spent 20 years as a taxi driver." [2-1]
	"For me quality of life means to go wherever you want, to do strange things." [2-4]
	"I have always solved the problems that arised, but now I feel impotence because I can't do this anymore." [2-8]
Fears of progression	"The symptoms depend on the day, they are not permanent, some days you are tired, others not." [2-2]
	"Before I went out to the country with my dog, and I liked to go out with the bike but I can't anymore, I have to depend on a cane." [2-4]
	"I was in a good, well-paid job and I liked it, but when this happened, I completely disconnected." [2-8]
Filling out PROM questionnaires	"Are you sure of the answer? You barely can walk without taking a break after a few minutes… Are you sure about "rarely"? You feel down quite often" [caregiver of NYHA III patient 2-4].
	"I will help you, mom, you must answer within the suggested scale, from mild to severe… Mild is not what you have here, you have moderate problems to get up or go for a long walk… this other one is not mild either, I've noticed that you frequently feel anxious and sadder than before… Are you sure about this number on the scale? Why do you say 80 out of 100? You are not that OK, mom; I wish you would be that OK" [caregiver of NYHA I patient 1-10]
Domain 2. Caregivers' roles	
Tracking at home	"I keep track of pressure, weight, urine. Every day. I have it written down here in the notebook and I also send it through the hospital's APP. But I really don't know if it is of much use. When I had to call the ambulance everything seemed normal, I kept a similar record in recent days." [caregiver of NYHA III patient 1-6]
Medical appointments	"When we go to the hospital the doctors ask him if he sleeps well or if he is drowning and he always answers that he is fine, but he is not. The last time he had been sleeping on the couch because he couldn't sleep in bed even with 3 pillows. That's why I always go to the controls with him." [caregiver of NYHA III patient 2-4]
	"Doctor, he says that he feels OK, but I noticed that he is more anxious, more obsessed about how many times he goes to pee per day. Most days he gets up and cannot sleep worrying about his condition" [caregiver of NYHA III patient 1-6]
Domain 3. Relationships with healthcare providers	
Commitment	"I come to the very dedicated medical consultations and with the certainty that I am more closely watched than a Ferrari" [2-5]
Trustworthiness	"I sit in a consultation where they take their time, and they answer all my doubts. The big difference is that now I feel more secure, I know that I must deal with weight, urine, food. Having the possibility of calling them 24 hours a day gives you more peace of mind." [2-6]
	"The nurse is better than any cardiologist, everyone loves her." [2-5]
	"The nurse is very close, I think they have chosen a person with a character and attitude that is just what a patient needs." [2-6]

Table 3. Evaluation of health status by PROMs. Scores for EQ-5D-5L and KCCQ.

	NYHA I-II (N=11)	NYHA III (N=9)	All NYHA (N=20)
EQ-5D-5L, patients reporting any limitation[1], N (%)			
Mobility	5 (40.5)	9 (100)	14 (70.0)
Self-care	0	7 (77.8)	7 (35.0)
Usual activities	4 (36.4)	8 (88.9)	12 (60.0)
Pain/Discomfort	4 (36.4)	6 (66.7)	10 (50.0)
Anxiety/Depression	4 (36.4)	8 (88.9)	12 (60.0)
EQ-5D-5L, patients reporting severe or extreme limitations[2], N (%)			
Mobility	0	5 (55.6)	5 (25.0)
Self-care	0	2 (22.2)	2 (10.0)
Usual activities	0	3 (33.3)	3 (15.0)
Pain/Discomfort	1 (9.1)	2 (22.2)	3 (15.0)
Anxiety/Depression	0	2 (22.2)	2 (10.0)
EQ-5D-5L global, mean (SD)			
Index value	0.85 (0.17)	0.37 (0.36)	0.64 (0.36)
VAS score	74.55 (23.50)	45.56 (14.46)	61.50 (24.45)
KCCQ, mean (SD)			
Physical limitation	81.06 (19.04)	39.72 (26.59)	62.46 (30.56)
Symptom stability	59.10 (12.61)	66.67 (30.62)	62.50 (22.21)
Symptom frequency	84.66 (17.14)	57.64 (27.14)	72.50 (25.59)
Symptom burden	91.67 (11.18)	61.11 (24.30)	77.92 (23.61)
Self-efficacy	94.32 (10.25)	85.94 (18.22)	90.79 (14.34)
Quality of life	82.58 (13.15)	33.33 (20.83)	60.42 (30.09)
Social limitation	85.61 (14.02)	31.94 (26.62)	61.46 (33.94)
KCCQ global scores, mean (SD)			
Overall summary	82.69 (9.81)	41.09 (20.55)	63.97 (26.06)
Clinical summary	81.30 (10.82)	49.55 (22.31)	67.01 (23.10)
Total symptom	81.54 (10.85)	59.37 (23.50)	71.56 (20.55)

[1] Any score but 1 (no problems).

[2] Only patients scoring 4 or 5 in each domain.

EQ-5D-5L, EuroQoL 5D-5L questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; PRO, patient-reported outcome; SD, standard deviation; VAS, visual analogue scale.

SUPPLEMENTARY MATERIALS

for

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

by Raül Rubio et al.

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1. SEMI-STRUCTURED INTERVIEW GUIDELINE [Notes for RESEARCHER in blue].

Presentation

Thank you for taking part in this interview.

Please note that:

- Your responses are confidential and anonymous. Under no circumstances will your personal data be shared when the results are published. All answers will be treated in aggregate form.
- A Piece of Pie complies with all European and North American data protection laws and complies with the guidelines set by the EphMRA (European Pharmaceutical Market Research Association) codes of conduct for market research.
- You may discontinue your participation in this research at any time and, as well as the right not to answer any questions you do not wish to answer.

With your permission, we will audio record your responses to facilitate our analysis.

[RESEARCHER: Start recording audio.]

I will now introduce myself. My name is [XXX], I work for A Piece of Pie, an innovation consulting firm.

We are currently conducting a study on behalf of a pharmaceutical company, which would like to better understand the experience of patients suffering from Heart Failure.

We would be very grateful if you could share with us your personal experience and help us identify areas for improvement throughout your experience, from the moment of the first symptoms to the present.

Please note that there are no right or wrong answers, as we are interested in your opinions and your personal experience with the condition.

The interview (90 min.)

RESEARCHER: Tailor the questions to the way the patient refers to the disease and use the term provided by the patient to make him/her feel more comfortable. Whenever you believe that the caregiver could provide us with additional information on any of the topics discussed, please direct questions to him/her as well. If, on the other hand, you have the impression that it will be more valuable to ask certain questions only to the caregiver, do so after the interview with the patient. Always ask the patient for permission before talking to the caregiver.

Exploration area	**1. KNOW THE PATIENT (15 min)**
Goals	• **Generate a relationship with the patient** • **Better understand the person and their context** • **Understand your daily habits and routines**
Ethnographic explanation	*To begin with, I would like to get to know you as a person and familiarize myself with your personal situation...*

1. **Person:** I would like you to introduce yourself and explain to me:
    a) How old are you? Who do you live with?
    b) Tell me a little more about yourself, what do you like to do? What are your hobbies? What do you do? What do you value most now in your life? Why?
2. **Self-description:** If you were to describe yourself, what 3 words would you use? What comes to mind when you think of yourself?
3. **The patient's day-to-day life:** Tell me what a "typical" day looks like. What do you do from the time you wake up until you go to sleep? Differentiate weekday from weekends (i.e., hobbies). *RESEARCHER: be sure they explain their day to day routines to be able to refer to them later when exploring the impact of the disease. Write down on post-its moments with the greatest impact.*
    a) What time of day would you say you like best? When do you feel most at ease? Why?
    b) And what moment do you like the least? Why?
    c) What things do you have the hardest time doing?
    d) Is there anything you've had to give up in recent times? What do you miss?
4. **Outside view:** What do you think a good friend of yours or family member would say to me if I asked them what [patient's name] is like?
5. **Values:** If you were to tell a young family member what is most important in life, what would you say to them? Do you have any kind of personal "maxim"? Why do you think it's important? *[RESEARCHER: If health-related issues arise, ask when it became important to have a healthy life in your family and/or social environment]*

Exploration area	**2. MEANING OF QUALITY OF LIFE (15 min)**
Goals	• **Understand what they associate to quality of life** • **Understand the impact of different HF symptoms on their quality of life**
Ethnographic explanation	*Now I would like us to talk about those things that for you represent quality of life.*

6. **Quality of Life.** Definition: Now that you have completed this map, how would you define quality of life?
   a) What things allow you to have quality of life? How do you feel about them?
   b) What other things keep you from having a better quality of life? How do you feel about them?
7. **Current feeling:** How do you feel at this moment in your life? Do you have any small rituals that help you in your day to day? *RESEARCHER: Ask about eating habits, physical activity, cultural activities, etc.*
   a) Is there anything that particularly bothers you? Could you give me an example?
   b) What makes you happy?
   c) If you could improve 3 things from your day to day, what things would you choose? What would you give up?

Exploration area	**3. HEART FAILURE (15 min)**
Goals	• **Understand the impact of HF on the patient's life** • **Understand the patient's perception of HF**
Ethnographic explanation	*Now I would like you to tell me specifically about the disease you suffer...*

8. **HF:** I would like you to explain to me in your own words how do you see heart failure.

9. **Explanation of the disease**: Do you remember how they explained to you what HF was? What words did they use? Who did so? Could it have been done better? What did they miss?

10. **Living with HF:** What is it like to live with HF? When do you feel it becomes more "uphill"? What helps you overcome it?

11. **Other diagnoses:** Are you diagnosed with other diseases? Were they prior to HF? Are they related in any way?

Exploration area	4. LIFE JOURNEY (15 min)
Goals	• Understand the impact of HF on the patient's life • Understand the patient's perception of HF
Ethnographic explanation	*To continue I would like us to briefly talk about the most important moments with the disease ...*

12. **Significant moments with the disease:** Now I would like you to think about 5-6 significant moments since you were diagnosed with the disease. *RESEARCHER: Write down every moment in a post-it. Pay attention to whether hospitalization, transplant or heart attack arise spontaneously and if not, ask if you have experienced any of these moments and if so write them down next to the other moments.*
    a) Why have you precisely chosen these moments?
    b) How did you experience each of these moments?
    c) Which one of them was the best moment for you? *RESEARCHER: Ask what "the best" means to this patient*
    d) Which one of them was the worst moment for you? *RESEARCHER: Ask what "the worst" means and, if it is related to the patient's illness, ask:* → Is there anything that could have better helped you cope during those times?
    e) Which of these moments changed your life the most? Why?

13. **Life before HF**: What was your life like before you were diagnosed with HF? What things have changed the most? What do you miss?
    c) Since you were diagnosed… how has your lifestyle changed? How do you feel about it? What could help you?
    d) At the beginning of the interview, you explained to me what a day in your life looks like. How would this change if life were the way it used to be?
    e) Could you specify how you think the disease changed your life? *[RESEARCHER: dig into issues such as new interpretations of reality, changes in values, etc.]*

Exploration area	5. CARE AND EMOTIONAL PROCESS (20 min.)
Goals	**Understand the HF Patient Journey** **Identify unmet needs** **Understand the perception of the different treatments that the patient has gone through**
Ethnographic explanation	*Now I would like us to delve into the journey you have followed since the beginning of the risk factors until now…*

Let's assume that you meet a person who has just been diagnosed with heart failure and does not know what it means to suffer from this condition. If you asked him to tell you about your experience, from the first symptoms until today

14. **Life without the disease**: What was your life like before the disease? If you look back, what do you miss the most?
15. **Previous diseases:** What diseases have you been diagnosed with? Who diagnosed you?
    a) Were you warned of the risk of developing heart failure?
    b) What did they explain to you?
    c) Were you advised to make lifestyle changes? *RESEARCHER, ask about exercise, diet, tobacco, or alcohol consumption…*
    d) Were you given any preventive treatment?
16. **First symptoms:**
    a) What changes did you experience that made you think something was wrong? For how long?
    b) What did you think might be going on?
17. **Diagnosis:**
    a) Do you remember what was explained to you?
    b) What tests have you done? Was the process burdensome?
    c) What doubts did you have?
    d) What did you think was going to happen at the time?
    e) Did you search for information on the internet?
    f) Did you contact any patient associations?
    g) Have you met anyone with this condition during the process? How has it affected you?
18. **First treatment:**
    a) Do you remember the name of your treatment?
    b) How was the first medication taken?
    c) Did you have any routines to do so?
    d) Did you stop taking the treatment at some point?
19. **Follow-up visits:**
    a) What were the routines of the visits like?

b) Was it hard for you to make them? Currently, how do you feel when you must go to the doctor?

20. **Evolution of the disease:**
    a) How did you find out that the disease was changing? Were there any significant moments?

21. **Hospital admission** (if applies)**:**
    a) What was the process like? How many days last the hospital admission?
    b) How was the experience in the emergency room?
    c) Have you had more than one hospital admission?

22. **Surgery** (if applies)**:**
    a) What kind of device was implanted? Would you be able to explain how it works?
    b) What things does it allow you to do that you couldn't do before? How does this make you feel?
    c) What things can't you do now? How does this make you feel?

23. **Experience PROM questionnaires:** before the interview you answered a set of questionnaires about your symptoms and quality of life.
    a) From what we talked about during the interview, what things do you think should be included in these questionnaires?
    b) What things should your cardiologist know to make decisions?

Exploration area	6. HOME TOUR (10 min.)
Goals	**• Complement and contrast the information obtained during the interview with the patient's environment.** **• Understand the immediate context in which patients live (routines, rituals, and concessions to the HF)**
Ethnographic explanation	*For us it would be very useful to be able to understand how the disease affects your day to day. If you could show us your house, please, I'm sure it would help us understand...*

RESEARCHER: The home visit should be made at the appropriate time during the interview. It should be done naturally as a continuation of the conversation: asking for places and things inside the house (medicines, refrigerator, sofa, bedroom) that are important in terms of the impact that HF has on your life be shown.

For instance, ask whether there has been any home reform since they have had HF diagnosed. As you walk around, ask the patient about their daily routines and their life under treatment. Try to understand how the patient has adapted his/her life to the disease and his/her level of activity.

If the participant does not mention anything spontaneously, focus on:

- *Evidence that signals his/her 'lifestyle', hobbies.*
- *Written information about HF.*
- *Evidence of contact with HCPs.*

- *Rooms where she/he takes treatment or workout.*
- *Rooms where medicines are stored.*

Please, contrast the information mentioned during the interview with what you observe in the house. If allowed by the participant, take pictures of everything the patient deems relevant to treatment and their life with HF.

With this we would conclude the interview. Thank you very much for your time and participation. Do you have any comments or questions you want to share?

[END RECORDING]

2. OBSERVATION GUIDE OF MEDICAL APPOINTMENTS WITH HCPS

This guide is intended to guide the observation before, during and after the medical visit of selected patients. During the appointment, neither the patient nor the doctor will be asked questions by the researcher.

The objectives of the visit are:

1. Observe whether which topics are discussed during the medical appointment, and whether any of them is directly related to quality of life with the condition.
2. Understand the language that is used by both parties when talking about the condition.

RESEARCHER, prior to the visit, make sure that the patient understands the purpose of the observation within the study.

I – PRE-VISIT: Observation of the hospital environment

RESEARCHER, indicate the center, scheduled time of the visit and the start time of the observation.

Begin by observing the ***hospitals environment.*** *What surprises you the most? Why?*
Focus on:

- Occupancy of the center: number of patients in the waiting room, number of health workers.
- Space: design, decoration, lighting, colors, atmosphere.
- Organization: Allocation and ease of access.

Observe the ***interviewee.*** *What does he/she look like? (For example, tired, relaxed, irritated, etc.) Is there anything that stands out? Inquire about your expectations before the visit.*
Focus on:

- Arrival time, ease of access, companions (if applies).
- Body posture and non-verbal signs (facial expression, comfort level with the accompanying situation).
- Preparation for the visit: if the patient brings documents, medical tests, notebooks or tracking applications.
- Waiting times for the visit.
- If applies: Interaction with other health agents (residents, reception, nursing).

II – DURING THE VISIT: Observation of the patient medical interaction

RESEARCHER: Describe the physical space, organization, and arrangement of furniture. Also write down the ***exact time of the start of the visit.***
Focus on:

- Initial time of the visit.
- Initial greeting, use of gestures and non-verbal cues.
- Initial conversation. How general are they? How specific?
    - Questions from the doctor, order, and type.

        - On quality of life and/or impact of HF on a day-to-day basis.
        - Type of assessment and use of questionnaires.
        - Types of recommendations (functional, social, quality of life).
        - How the patient responds.
    - Questions from the patient, order, and type.
        - On quality of life and/or impact of HF on a day-to-day basis.
        - How your doctor responds
- Central conversation:
    - Topics of conversation that arouse greater patient attention (e.g., quality of life, impact on daily activity).
    - Topics of conversation that arouse greater attention from the doctor (e.g., clinical, psychological, or social, quality of life or other aspects).
    - Dominant language; use of colloquial language vs medical language.
- Body posture, proxemics and physical distance from the patient and the doctor during the visit.
- Use of silences and non-verbal gestures (gestures of approval, doubt, or confusion).
- Closing of the visit
    - Time and language used for the closing of the visit.
    - Approach of next steps by the doctor and the patient.
    - Farewell, use of gestures and non-verbal cues.
- If applies: interaction with other health agents (residents, receptionist, nursing).

III – AFTER THE VISIT: Observation of the patient

RESEARCHER: Write down the exact ***time of the end*** *of the visit. Accompany the patient at the exit of the visit and / or another instance of contact related to the visit (reception desks). If possible, know your perception about the results of the visit.*

Focus on:

- End time/duration of the visit.
- The patient's body posture and non-verbal gestures.
- Language used to assess the visit.
- If applies: interaction with other health agents (residents, reception, nursing).

End of observation.***

ETHNOQOL – COREQ CHECKLIST
5 October 2021

No.	Item	Description	Section #
Domain 1: Research team and reflexivity			
Personal characteristics			
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group? SCC MFE	Line 201
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD* *SCC, PhD* *MFE, BA*	NA
3.	Occupation	What was their occupation at the time of the study? Senior researchers	Line 201
4.	Gender	Was the researcher male or female? Female	Line 201
5.	Experience and training	What experience or training did the researcher have? >5 years of experience in medical sociology and medical anthropology	Line 202
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement? No.	Line 204
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? *E.g. Personal goals, reasons for doing the research* *Research goals*	Line 205
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? *E.g. Bias, assumptions, reasons and interests in the research topic* *None.*	NA
Domain 2: Study design			
Theoretical framework			
9.	Methodological orientation and theory	What methodological orientation was stated to underpin the study? *E.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis* *Thematic analysis* *Phenomenological perspective*	Lines 150-161, and section on Methods
Participant selection			
10.	Sampling	How were participants selected? *E.g. purposive, convenience, consecutive, snowball* *Purposeful*	Line 194
11.	Method of approach	How were participants approached? *E.g. face-to-face, telephone, mail, email*	Lines 186-196

		face-to-face	
12.	Sample size	How many participants were in the study? 20	Line 194 and 287
13.	Non-participation	How many people refused to participate or dropped out? What were the reasons for this? None	Lines 186-294
Setting			
14.	Setting of data collection	Where was the data collected? *E.g. home, clinic, Workplace* *Patients' home*	Lines 198-232
15.	Presence of non-participants	Was anyone else present besides the participants and researchers? No.	Lines 198-232
16.	Description of sample	What are the important characteristics of the sample? *E.g. demographic data, date* *demographic data and clinic characteristics*	Lines 286-294 and Table 1
Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested? Yes. No pilot tested.	See Supplementary Materials
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many? No.	NA
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data? Yes, audio recording.	Lines 229-232
20.	Field notes	Were field notes made during and/or after the interview or focus group? During interviews and after direct observations of medical appointments.	Lines 229-232
21.	Duration	What was the duration of the interviews or focus group? 90 min for interviews and 20 min for clinical encounters.	Line 206, 222
22.	Data saturation	Was data saturation discussed? Yes, in joint analysis sessions with authors.	Line 280
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction? No.	NA
Domain 3: analysis and findings			
Data analysis			
24.	Number of data coders	How many data coders coded the data? The two field researchers	Line 270
25.	Description of the coding tree	Did authors provide a description of the coding tree? Authors provided the description of domains, no coding tree.	Lines 267-279
26.	Derivation of themes	Were themes identified in advance or derived from the data? Derived from data.	Lines 267-279

27.	Software	What software, if applicable, was used to manage the data? No.	NA
28.	Participant checking	Did participants provide feedback on the findings? No.	NA
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? *E.g. Participant number* *Yes.*	Table 2
30.	Data and findings consistent	Was there consistency between the data presented and the findings? Yes, in joint analysis sessions.	Lines 267-279
31.	Clarity of major themes	Were major themes clearly presented in the findings? Yes, in joint analysis sessions.	See Results section
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes? Yes.	Yes, Table 2 and Results section

BMJ Open

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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Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Research methods, Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, QUALITATIVE RESEARCH

Original research

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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ABSTRACT

Objectives: To gather insights on the disease experience of patients with heart failure with reduced ejection fraction (HFrEF), and assess how patients' experiences and narratives related to the disease complement data collected through standardized patient-reported outcome measures (PROMs). Also, to explore new ways of evaluating the burden experienced by patients and caregivers.

Design: Observational, descriptive, multicenter, cross-sectional, mixed-methods study.

Setting: Secondary care, patient's homes.

Participants: Twenty patients with HFrEF (NYHAs I-III) aged 38-85 years.

Measures: PROMs EuroQoL 5D-5L and Kansas City Cardiomyopathy Questionnaire and patient interview and observation.

Results: A total of 20 patients with HFrEF participated in the study. The patients' mean (SD) age was 72.5 (11.4) years, 65% were male, and were classified in NYHA functional classes I (N=4), II (N=7) and III (N=9). The study showed a strong impact of HF in the patients' quality of life (QoL) and disease experience, as revealed by the standardized PROMs (EQ-5D-5L global index=0.64 [0.36]; KCCQ total symptom score=71.56 [20.55]) and the in-depth interviews. Patients and caregivers often disagreed describing and evaluating perceived QoL, as patients downplayed their limitations and caregivers overemphasized the poor QoL of the patients. Patients related current QoL to distant life experiences or to critical moments in their disease, such as hospitalizations. Anxiety over the disease progression is apparent in both patients and caregivers, suggesting that caregiver-specific tools should be developed.

Conclusions: PROMs are an effective way of assessing symptoms over the most recent time period. However, especially in chronic diseases such as HFrEF, PROM scores could be complemented with additional tools to gain a better understanding of the patient's status. New PROMs designed to evaluate and compare specific points in the life of the patient could be clinically more useful to assess changes in health status.

Strengths and limitations of this study

- This study followed an ethnographic approach to collect data on patient's experiences and narratives related to heart failure, a type of study not before carried out in Spain and with scarce reports worldwide.
- Both patients and caregivers could discuss freely and explain in detail the aspects of the disease that they considered under control and those where change was deemed necessary.
- The often-contrasting views of patients and caregivers highlighted the difficulties in obtaining accurate and objective evaluations of quality of life.
- Although the selection of patients aimed for inclusiveness and diversity, the limited number of HFrEF patients selected for in-depth analysis may not be fully representative of the population of HFrEF patients in Spain.
- The ethnographic interviews took place in the context of the COVID-19 pandemic, which transformed the daily routines of patients and caregivers and may have to a certain extent altered their perspective of living with HFrEF.

INTRODUCTION

Despite advances in treatment, heart failure (HF) remains one of the leading causes of hospitalization and readmissions, death and disability worldwide.[1,2] The economic burden of HF, mainly driven by recurrent hospitalizations, consumes an estimated 1-2% of healthcare budgets.[3,4] The progressive aging of the population in some Western countries, such as Spain, and increasing HF prevalence, have positioned this disease as a major public health problem.[5–7]

Clinically, HF can be classified based on the left ventricular ejection fraction (LVEF) into HF with reduced ejection fraction (HFrEF), defined as an EF ≤40%, mildly-reduced ejection fraction (HFmrEF), defined as EF >40% and <50%, and HF with preserved ejection fraction (HFpEF), defined as an ejection fraction ≥50%.[8] Patients in these subgroups often have distinct underlying etiologies, demographics, co-morbidities and response to therapies.[9,10] Additionally, the presence and severity of symptoms and exercise intolerance of patients with HF is usually categorized following the New York Heart Association (NYHA) classification into four functional classes (I-IV), being class IV the worst.[11]

HF can severely affect the quality of life (QoL) of the patient by reducing their independence and ability to undertake daily living activities, and can also disturb their mental health and psychosocial well-being.[12,13] Prior studies have shown that patients with HF had an even higher incidence of limitations than patients with chronic diseases such as diabetes, cancer, or Alzheimer's disease.[13] Several patient-reported outcome measures (PROMs) have been used to quantify health status in patients with HF, such as the generic EuroQoL 5D-5L (EQ-5D-5L) and the disease-specific Kansas City Cardiomyopathy Questionnaire (KCCQ).[13–17] PROMs such as the KCCQ have a good correlation with prognosis and their use has been encouraged by the American Heart Association in both routine clinical practice and clinical trials of new therapies.[18,19] However, although these PROMs can be useful indicators of health status and how HF

impacts patients' QoL within a 2-week recall period, they have not been designed to reflect some of the patient's and caregiver's perspectives on living with HF, including aspects such as the importance of interactions with family or healthcare providers, feelings related to the course of their disease, or barriers to accessing healthcare resources.[20] These unique aspects of culture, preferences, customs, values and attitudes, could have an impact on treatment effectiveness and outcomes. Complementary to PROMs, in-depth interviews with patients and caregivers are useful to evaluate quality of patient care and the interaction between the patient and the healthcare system.[21] However, neglecting the limitations PROMs could hinder our understanding of the patient's attitudes and real-life disease experiences.

Ethnographic qualitative studies involve observation of the patients and caregivers in their real-world settings to determine how they behave in specific contexts. Ethnographic research collects comprehensive information from multiple sources such as interviews, caregiver perspectives, non-participant observation of healthcare visits and home tours, among others, and has previously been carried out to investigate QoL in patients with HF.[12,22–27] Previous ethnographic studies conducted in patients from the United Kingdom identified barriers to interventions for HF and critical points on disease pathways which resulted in an increase in the risk of admission.[28–30]

Little is known about the patient's and caregiver's perspective of living with HF in Spain, and previous studies did not evaluate patients by LVEF.[31] The objective of this study was to gather insights on the disease experiences of patients with HFrEF and their caregivers, and the impact on their everyday life. 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.[32,33] The goal was to improve awareness of healthcare professionals, service providers, policy makers and educators on the factors that can potentially influence treatment effectiveness, and the existence of aspects of the patient's experience that are not covered by existing tools. In turn, this may encourage firstly, a more active participation of healthcare providers, patients and caregivers in clinical decisions considering not only the disease state, but also cultural factors and individual values and attitudes, and secondly, the development of instruments for the evaluation of healthcare interventions.

METHODS

We conducted an observational, cross-sectional, descriptive, multicenter, and mixed methods study to obtain insights regarding HFrEF patients' perception and attitudes towards their disease. The patients in the study were recruited at the Departments of Cardiology of 2 large tertiary-level hospitals, namely, the Puerta del Hierro University Hospital (Majadahonda, Madrid, Spain) and the Bellvitge University Hospital (Hospitalet de Llobregat, Barcelona, Spain). The patient populations attended by these hospitals were socioeconomically very distinct, as the Puerta del Hierro University Hospital is located at a high-income district of Madrid, and the Bellvitge University Hospital covers a suburban area of mostly low or very low-income patients. Due to the qualitative and observational design of the study, there was no masking or randomization. Clinical management of the patients followed routine clinical practice, with no changes in treatment or additional clinical assessments specific for this study. All decisions related to disease management were made at the discretion of the treating physician without interference by the sponsor. Informed consent was obtained from each patient prior to study initiation. The patients authorized the interview with their main caregiver as part of the informed consent process. The study protocol was approved by the Ethics Review Board of the Bellvitge University Hospital on March 12th, 2020 with number PR062/20.

Patient selection

Patients were assessed for eligibility by local clinical staff according to selection criteria at each participating center. Patients were classified by NYHA class and could be belong to any of the 4 classes I to IV. The inclusion criteria were ≥18 years at the time of consent, established documented diagnosis of HFrEF (LVEF ≤40%), and signed consent to participate. Patients unable to complete the PROMs because of any psychological or physical condition and patients hospitalized at inclusion were excluded.

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.

Data collection

The patient's demographic information and medical history were collected from medical records at the selection visit. On the day of the home visit the patients first completed two health status questionnaires and then two female senior researchers (SCC, MFE) with >5 years of experience in medical sociology and medical anthropology conducted a semi-structured interview following a topic guide (See Supplementary Materials). There was no prior relationship between the interviewer and the patient, who was informed about the research goals prior to starting the interview. The interview conducted at the patient's home lasted approximately 90 minutes. In some instances, with the consent of the patient, his/her closest caregivers were interviewed at the patient's home on the same day for about 30 min. The interview with the caregivers aimed at understanding their perception of the patient's status and evaluating their social and emotional relationship with the patient.

In order to gather observational data to complement participants' accounts of their medical experience, 6 out of 20 patients (two per NYHA class) consented that the same researcher carrying out the interview would observe their first healthcare appointment after the home interview. Direct observation allowed researchers to gather information regarding patients' objective and subjective experiences during medical encounters, about how patients and caregivers conveyed concerns and needs, and provided clues about incongruent behaviour. A single appointed researcher observed the initial and main focus of conversations with healthcare providers, questions by patients and caregivers, and patients' use of verbal and non-verbal communication (e.g., behaviour that suggested passive, nervous, impatient, caring, or expectant attitudes). Immediately after the appointment, patients and caregivers, if present, were asked to evaluate the medical visit (clinical encounters last 20 minutes on average). Researchers took field notes and added reflexive comments about the encounter and about participants' experience.

The in-depth interview aimed to capture the patients' experience with the disease from their own point of view, whereas the non-participant observation during the medical visits allowed to investigate the relationship with the healthcare practitioners for both of patients and family members.

Data from in-depth interviews were collected by audio recording and field notes, whereas data from direct observation of medical encounters were collected by field notes only, taking into consideration all aspects of the patient's life and in all cases protecting the patient's data privacy.

Quantitative outcomes and analyses

Secondary variables assessed included PROMs by using the EQ-5D-5L and KCCQ. The EQ-5D-5L is a self-reported questionnaire used to derive a standardized measure of health status, also referred to as a utility score.[34] The KCCQ is a self-administered HF-specific instrument and has shown to be a valid, reliable and responsive measure for patients with HF.[14] Spanish validated versions of these questionnaires were used.[35,36] For the EQ-5D-5L, the number and percentage of patients reporting any type of limitation for each questionnaire dimension, the number and percentage of patients reporting “severe” or “extreme” responses for each questionnaire dimension, as well as the index value and the visual analogue scale (VAS, where 100 equals the best health HF patients can imagine), were assessed; for the KCCQ, the score for each domain/subdomain, and a summary score for the total symptom score, clinical symptom score and overall summary score were assessed (scores range from 0 to 100; were higher scores indicate a better health status). The PROMs were analyzed descriptively.

Qualitative outcomes and analyses

The following primary variables were assessed: the patient’s profile; the patient’s emotional perception (values, attitude, frustration, fear) during the HFrEF journey, including the role of the caregiver; key relationships and communication processes during the patient HFrEF journey (patient-doctor, patient-carer/family); main barriers to accessing healthcare services experienced by patients during the HFrEF journey; and the patient’s unmet needs (cognitive, emotional and functional) associated with HF. Observational data, interviews and documentary materials were analyzed at three levels: individual patient cases, across cases within research centers, and across research centers to synthesis.

Thematic content analysis was used to analyse the data gathered from interviews and direct observation of clinical encounters. The analysis was carried out by field researchers in six steps: 1) read and re-read of interview and medical encounters’ fieldnotes; 2) identification of main topics per interview domain; 3) text codification to identify current and new domains; 4) review of PROM scores per interviewer and NYHA class; 5) comparison of PROM scores and fieldwork data; and 6) and synthesis of repetitive patterns.

Subsequently, data triangulation was used to integrate quantitative and qualitative information by the researchers, individually and in joint sessions. Three types of triangulation were used: investigator, data and methodological triangulation. Two investigators were involved in the data collection and analysis. Findings from each investigator were compared to develop a deeper understanding of how the different investigators view the issue. Preliminary conclusions were discussed with the broader team of authors in further analysis sessions. Regarding data triangulation, investigators compared the answers from patients and caregivers (information sources) separately to identify areas of agreement and disagreement over the main topics. Regarding methodological triangulation, findings from interviews, direct observations of medical appointments, and PROM scores were compared to identify incongruences and disparities in patients' responses (e.g., patients reporting mild limitations in PROMs but highlighting severe limitations during the interview and/or medical appointment).

The analytical process aimed to reach theoretical saturation where no new dimensions emerged during joint sessions.

RESULTS

Patient characteristics

A total of 20 patients with HFrEF participated in the study (Table 1). The mean (SD) age of the patients was 72.5 (11.4) years (range, 38-85 years), and 13 (65.0%) were male. The study included 4, 7 and 9 patients in NYHA functional classes I-III, respectively. Although the study protocol was designed to include class IV patients, their frailty, and the effects of the COVID-19 pandemic in the patients' self-caring strategies, hindered the participation of any patients in this class. Twelve patients were being treated at the Bellvitge University Hospital and 8 patients were being treated at the Puerta del Hierro University Hospital.

Understanding of QoL by patients with HF

During the in-depth interviews, the participants described how living with HFrEF impacted their lives, including how they experienced the symptoms of HF and their effects on daily routines (summarized in Table 2). Their responses provided relevant insights on what QoL meant to them. For many patients, QoL was "being able to do what they did before" and missed being independent, their everyday life and maintaining an active lifestyle.

Patients tended to self-limit and isolate to limit symptomatology due to progression-related fears or even fear to a sudden death, despite a more sedentary lifestyle being detrimental to the recovery and to their own QoL.

Impact of demographic factors in perception of QoL

Attitudes and perceptions towards HFrEF seemed to strongly depend on age and education. Young patients tend to be more informed about the disease and challenge the healthcare practitioners' opinions.

In contrast, older patients had a difficult time differentiating between HFrEF symptoms and those associated with the normal process of ageing. Often caregivers had to help them understand the information provided by healthcare workers.

The interviews also revealed that male patients showed more dependency towards caregivers than their female counterparts. Female caregivers tended to strongly challenge male patients' perception of QoL. In one case, the wife of a NYHA III patient was very critical of her husband's attitude and thought that part of his evolution strongly depended on his will, and asked him to exercise more, read, get on the computer, and go out for a ride on the motorcycle. They even consulted with a psychologist friend to help them handle the situation.

PROMs and health status

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 3). 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). No differences were observed in scores with respect to gender, or between the patients from the two hospitals.

Some patients with lower NYHAs, despite having visible constraints in health status, indicated high scores in the EQ-5D-5L VAS score. For example, a patient with major comorbidities [1-10] with NYHA I indicated a EQ-5D-5L VAS score of 90 and emphasized that her QoL was good. This contrasted with the views expressed by her caregiver (Table 2).

Regardless of the NYHA, some patients seemed to minimize and relativize the impact of HFrEF on their QoL. Caregivers, in contrast, could emphasize the limitations imposed by HFrEF. For example, the wife and caregiver of a NYHA II patient [1-11] indicated that in the consultation with the cardiologist the patient usually underestimated his condition. In another case, the wife of a NYHA III patient commented that she must be “present with the doctors, because when they ask him something, he usually answers that he is fine and does not really say what is wrong with him.”

Patients with advanced NYHAs, who experienced one or several hospital admissions, compared their current experience with the disease to those acute periods of fear and greater uncertainty. Patients showed a limited portrait of their QoL due to the required reference to the last 2-weeks in the questionnaire. For example, a NYHA III patient [2-8] had doubts when filling out the questionnaires since he related his mobility limitations to a problem with his legs (a consequence of an aortic dissection) but he did not relate it to HF. Also, he mentioned that his physical and emotional situation was much better now compared to the initial moments where he was more affected. He had a hard time taking the prior two weeks as a reference point, therefore his responses showed a feeling of improvement compared to the most critical moments.

Another NYHA III patient [2-6] had doubts when filling the questionnaires, since his symptoms varied from day to day and between morning, afternoon and night. He also had moments of crises where he considered his symptoms to be worse, so limiting to the last two weeks seemed difficult. Likewise, he stated that shortness of breath or air was something he thought he got from lying down for a long time and not that it was a symptom of HFrEF.

Caregivers could overestimate and present a dramatic view of the patient's day-to-day life with HFrEF. Family caregivers showed more distress when discussing their relatives with HFrEF compared to that showed by remunerated caregivers:

> *“she is concerned about his low spirits and his anguish. She says that the symptoms she develops from anxiety can "mask" the symptoms of HF, such as pressure and pain in the chest, agitation, a feeling of suffocation.”* [caregiver of patient 1-8, NYHA III]

> *“As cardiologists told us that little can be done to improve his condition, we live these years ‘as a gift’.”* [caregiver of patient 1-6]

Caregivers’ roles and needs

In this study, only five patients were able to live without a caregiver. Generally, strong family bonds were apparent and important for the patient. Caregivers were often in charge of organizing visits to the healthcare providers, keeping track of parameters such as weight and blood pressure, and administering medication (Table 2). Caregivers acted also as interpreters of the disease status on behalf of their patients.

Relationships with healthcare providers

The interactions between patients and caregivers with healthcare workers at hospitals were investigated by the social scientists by accompanying them to a medical appointment. The study showed that patients are usually highly positive about their experience with cardiologists and nurses (Table 2). A patient [1-9] explained that the nurse called him weekly to ask about how he was coping, and to discuss data such as weight and blood pressure changes. He generally felt very accompanied by the hospital staff, both cardiologists and nurses. Other patients also expressed a high opinion of the healthcare personnel. Often patients highly value their relationship with the nurse, as they probably feel more confident to express their experiences to his/her.

DISCUSSION

In this study we used ethnographic methods with HFrEF patients and their caregivers, complemented with general and disease-specific health status assessments, to obtain insights regarding patients' disease perception and attitudes towards their disease. Ethnographic methods adopt a phenomenological perspective, aiming to understand individuals' life experiences to acquire relevant knowledge. The results of this study suggest that the patient's perspectives of their QoL were dependent on their memories of what they could do before, and often were better than reality. Caregivers, in contrast, offered a distinct view of the patient's status and QoL, often substantially worse and emphasizing the severity of their life-limiting condition.

As healthcare systems aim to become more 'patient-centered', there is a recognized need to capture accurately the patient's experience of the disease, in an effort to improve it. The use of PROMs have therefore become common in assessing current treatments and new therapies and medical interventions, although their application in clinical practice is still very limited. Despite their widespread use by cardiologists, an awareness of the limitations of PROMs when evaluating the experience of the patient with HF is critical for their interpretation. For example, the effects of comorbid conditions could add confounding factors to the evaluation of HF through a single PROM instrument. Likewise, patients often relate their overall QoL experience to the moments of crisis, such as hospitalizations, 'anchoring' all subsequent experiences to those events and distorting their responses in the questionnaires.

In the general population the understanding of HF and its outcome is low, contributing to anxiety about the evolution of the disease in both patients and caregivers. In contrast, other life-limiting diseases, such as cancer, often have better-defined pathways of care and psychosocial support.[30] In this regard, patient associations and support groups could play a role by helping the patient understand

the disease, the treatments, and the expectations. Patient associations promote social integration and help patient share their experiences, providing the necessary encouragement to cope with their disease and go on with daily activities. Also, as reflected in some of the interviews described in this study, it is important for the patient to feel that he/she can have rapid access to medical services. In this regard, the study reflected that that while some patients were reluctant to discuss aspects of daily life or to express their feelings and fears to the cardiologist, they were more open and felt closer to the nurse, a relationship that was highly valued by many patients. Generally, an efficient and fluid communication with all the healthcare providers involved in the treatment is essential.[12,29]

The study revealed that the fear to losing independence and the uncertainty about the progress of their disease could be factors that motivate some HF patients to downplay their limitations. Conversely, caregivers could overemphasize the poor QoL of the patients, also motivated by concerns of the progress of the disease, its unpredictable trajectory, and lack of proper knowledge and training. Also, it is possible that, since these caregivers were very often family members, their views could be overstated due to emotional attachment to the patient. In any case, these results suggest that instruments should be developed to help caregivers in their daily work with patients with HF, so that they are better informed on the course of the disease and expectations.[25] In this regard, numerous recent studies have highlighted challenges experienced by caregivers of patients with HF.[37–40] Some initiatives along these lines, such caregiver-specific QoL questionnaires,[41] and video coaching,[42,43] are currently being developed and tested.

The results of our study suggest recommendations for future PROM design or questionnaire selection. In patients with HF the PROM instruments should aim to truly mirror patients' experience, using language that the patient associates with their cultural views of QoL. To provide insights on relevant changes in QoL, the PROMs should be constructed to capture specific timepoints related to the patient experience

(e.g., healthcare status before the diagnosis, and before and after hospitalizations). In this way, reference points in the patient's lives could be established that favored meaningful QoL before/after comparations. Instruments should allow an alternative stratification based on these clinical events and patients' perceived QoL along them. Also, as self-care behaviors can greatly affect symptoms in patients with HF,[44] the patient's self-caring strategies, perception of autonomy, level of empowerment, and the perception of past and present experiences with the disease should be taken into consideration when developing and introducing future PROM instruments.[45] Finally, additional instruments should be developed to evaluate the key aspects of the patient' support system, and explore caregivers' needs.

Given the lack of studies assessing the patient's and caregiver's perspective on the HFrEF pathway in Spain, this study aimed to fill this gap to better understand possible cultural differences. The ethnographic approach, which involved in-depth interviews with patients at their homes and with their caregivers, made it possible to collect relevant data not normally discussed or shared in healthcare facilities. Both patients and caregivers could talk freely and explain the aspects of the disease that they considered under control and those where change was deemed necessary. However, a limitation of this study is that the small sample size, although not unusual in qualitative research that requires extensive and detailed analysis of each patient, may not fully represent the diversity of people with HFrEF in Spain. Also, as it is the case in other ethnographic studies, interviewing patients and caregivers together may have resulted in individual perspectives being altered or withheld. Finally, since this study was carried out during the COVID-19 pandemic, it is possible that the disruption imposed by the social restrictions could have some effect in the results described here.

In conclusion, this study analyzed, by the use of PROMs and in-depth interviews, the complexity of the actual experiences of the patients with HFrEF. The lack of knowledge about the disease generates confusion and anxiety about symptoms, and patients could tend to minimize the impact of HF in QoL. Patients tend

to maintain a closer relationship with their nurses, compared with the cardiologist, favoring a more open discussion of feelings and experiences related to the disease with them. In order to provide personalized care to HFrEF patients, QoL could be assessed by comparing two points in time, thus helping the healthcare practitioner understand the patient's point of view of specific interventions. Since QoL is a multidimensional, subjective concept that is affected by a variety of factors, its evaluation should be carefully designed to capture specific moments and changes in the trajectory of the disease. The study suggests that tools and training should be made available to caregivers to alleviate the burden of care and anxiety derived from uncertainty in the progression of the disease. Further work is needed to fully integrate the use of well-designed and useful PROMs into clinical practice.

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Contributors

RR, BP, LV, SCC, and JCC conceived and designed the study. EC, NJ, MRM, SY, SJM, LA, AG, PM, LSF, MTSG, EH, CE, ECM, JVLI, JSC, and JCC contributed to patient recruitment and data collection. SCC and MFE conducted the interviews and collected qualitative data. RR, BP, LV, SCC, MFE, JSC, JCC compiled and analyzed the data. RF, YR and MSS contributed to data interpretation in coordination with patient support organizations. RR, BP, LV, SCC, and JCC drafted the manuscript, which was revised by the other authors. PG provided a critical revision of an earliest version and contributed to the interpretation of the results. All authors read and approved the final manuscript.

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Competing interests

JCC received fees from AstraZeneca for the coordination and oversight of the study. RR, MFE, and SCC received research funding from AstraZeneca. RFdlF, BP, and LV are employees of AstraZeneca. All other authors report no competing interests.

Patient and public involvement

CardioAlianza, a Spanish association of patients with cardiovascular disease and their caregivers, was involved in designing, providing feedback for interpretation of data, and in the dissemination of this research.

Patient consent for publication

Informed consent for participation in the study and publication of the results were obtained from each patient prior to study initiation.

Ethics approval

This study was approved by the Ethics Review Board of the Bellvitge University Hospital on March 12th, 2020 with number PR062/20.

Data availability statement

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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TABLES

Table 1. Demographic and clinical characteristics of the patients.

Variable	N=20
Age, years, mean (SD)	72.5 (11.4)
Range (minimum-maximum)	38-85
Gender, male, N (%)	13 (65.0)
Time since diagnosis, years, mean (SD)	2.35 (2.9)
Recent diagnosis (less than 2 months), N (%)	2 (10.0)
NYHA, N (%)	
I	4 (20.0)
II	7 (35.0)
III	9 (45.0)
LVEF, %, mean (SD)	31.1 (6.0)
Diabetes, type 2, N (%)	9 (45.0)

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation.

696 **Table 2.** Domains and main perceptions among HFrEF patients.

Domains	**Patients and caregivers' quotes**
Domain 1. Meanings related to QoL	
Attachment to previous routines	"This has split my old age in two, having many things to do and not being able to do them because you get very tired. I miss that freedom that I had. Now I feel tied." [1-1]
	"What I have missed the most is driving, I spent 20 years as a taxi driver." [2-1]
	"For me quality of life means to go wherever you want, to do strange things." [2-4]
	"I have always solved the problems that arised, but now I feel impotence because I can't do this anymore." [2-8]
Fears of progression	"The symptoms depend on the day, they are not permanent, some days you are tired, others not." [2-2]
	"Before I went out to the country with my dog, and I liked to go out with the bike but I can't anymore, I have to depend on a cane." [2-4]
	"I was in a good, well-paid job and I liked it, but when this happened, I completely disconnected." [2-8]
Filling out PROM questionnaires	"Are you sure of the answer? You barely can walk without taking a break after a few minutes… Are you sure about "rarely"? You feel down quite often" [caregiver of NYHA III patient 2-4].
	"Not sure how to stick to the last 15 days when I answer these questions. Some days I feel better than others and I cannot possible say how I have been doing only in the past 15 days. I notice a lot of variation". "It is hard to put a number here… And it is even harder because I can only think about a very a low number… I am not ok right now. It is very sad to realise how low I am, how bad is my health now (referring to the VAS score in the EQ-5D-5L questionnaire)". [2-6]
	"I will help you, mom, you must answer within the suggested scale, from mild to severe… Mild is not what you have here, you have moderate problems to get up or go for a long walk… this other one is not mild either, I've noticed that you frequently feel anxious and sadder than before… Are you sure about this number on the scale? Why do you say 80 out of 100? You are not that OK, mom; I wish you would be that OK" [caregiver of NYHA I patient 1-10]
Domain 2. Caregivers' roles	
Tracking at home	"I keep track of pressure, weight, urine. Every day. I have it written down here in the notebook and I also send it through the hospital's APP. But I really don't know if it is of much use. When I had to call the ambulance everything seemed normal, I kept a similar record in recent days." [caregiver of NYHA III patient 1-6]
Medical appointments	"When we go to the hospital the doctors ask him if he sleeps well or if he is drowning and he always answers that he is fine, but he is not. The last time he had been sleeping on the couch because he couldn't sleep in bed even with 3 pillows. That's why I always go to the controls with him." [caregiver of NYHA III patient 2-4]
	"Doctor, he says that he feels OK, but I noticed that he is more anxious, more obsessed about how many times he goes to pee per day. Most days he gets up and cannot sleep worrying about his condition" [caregiver of NYHA III patient 1-6]
Domain 3. Relationships with healthcare providers	
Commitment	"I come to the very dedicated medical consultations and with the certainty that I am more closely watched than a Ferrari" [2-5]
Trustworthiness	"I sit in a consultation where they take their time, and they answer all my doubts. The big difference is that now I feel

	more secure, I know that I must deal with weight, urine, food. Having the possibility of calling them 24 hours a day gives you more peace of mind." [2-6]
	"The nurse is better than any cardiologist, everyone loves her." [2-5]
	"The nurse is very close, I think they have chosen a person with a character and attitude that is just what a patient needs." [2-6]

Table 3. Evaluation of health status by PROMs. Scores for EQ-5D-5L and KCCQ.

	NYHA I-II (N=11)	NYHA III (N=9)	All NYHA (N=20)
EQ-5D-5L, patients reporting any limitation[1], N (%)			
Mobility	5 (40.5)	9 (100)	14 (70.0)
Self-care	0	7 (77.8)	7 (35.0)
Usual activities	4 (36.4)	8 (88.9)	12 (60.0)
Pain/Discomfort	4 (36.4)	6 (66.7)	10 (50.0)
Anxiety/Depression	4 (36.4)	8 (88.9)	12 (60.0)
EQ-5D-5L, patients reporting severe or extreme limitations[2], N (%)			
Mobility	0	5 (55.6)	5 (25.0)
Self-care	0	2 (22.2)	2 (10.0)
Usual activities	0	3 (33.3)	3 (15.0)
Pain/Discomfort	1 (9.1)	2 (22.2)	3 (15.0)
Anxiety/Depression	0	2 (22.2)	2 (10.0)
EQ-5D-5L global, mean (SD)			
Index value	0.85 (0.17)	0.37 (0.36)	0.64 (0.36)
VAS score	74.55 (23.50)	45.56 (14.46)	61.50 (24.45)
KCCQ, mean (SD)			
Physical limitation	81.06 (19.04)	39.72 (26.59)	62.46 (30.56)
Symptom stability	59.10 (12.61)	66.67 (30.62)	62.50 (22.21)
Symptom frequency	84.66 (17.14)	57.64 (27.14)	72.50 (25.59)
Symptom burden	91.67 (11.18)	61.11 (24.30)	77.92 (23.61)
Self-efficacy	94.32 (10.25)	85.94 (18.22)	90.79 (14.34)
Quality of life	82.58 (13.15)	33.33 (20.83)	60.42 (30.09)
Social limitation	85.61 (14.02)	31.94 (26.62)	61.46 (33.94)
KCCQ global scores, mean (SD)			
Overall summary	82.69 (9.81)	41.09 (20.55)	63.97 (26.06)
Clinical summary	81.30 (10.82)	49.55 (22.31)	67.01 (23.10)
Total symptom	81.54 (10.85)	59.37 (23.50)	71.56 (20.55)

[1] Any score but 1 (no problems).

[2] Only patients scoring 4 or 5 in each domain.

EQ-5D-5L, EuroQoL 5D-5L questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; PRO, patient-reported outcome; SD, standard deviation; VAS, visual analogue scale.

SUPPLEMENTARY MATERIALS

for

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

by Raül Rubio et al.

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1. SEMI-STRUCTURED INTERVIEW GUIDELINE [Notes for RESEARCHER in blue].

Presentation

Thank you for taking part in this interview.

Please note that:

- Your responses are confidential and anonymous. Under no circumstances will your personal data be shared when the results are published. All answers will be treated in aggregate form.
- A Piece of Pie complies with all European and North American data protection laws and complies with the guidelines set by the EphMRA (European Pharmaceutical Market Research Association) codes of conduct for market research.
- You may discontinue your participation in this research at any time and, as well as the right not to answer any questions you do not wish to answer.

With your permission, we will audio record your responses to facilitate our analysis.

[RESEARCHER: Start recording audio.]

I will now introduce myself. My name is [XXX], I work for A Piece of Pie, an innovation consulting firm.

We are currently conducting a study on behalf of a pharmaceutical company, which would like to better understand the experience of patients suffering from Heart Failure.

We would be very grateful if you could share with us your personal experience and help us identify areas for improvement throughout your experience, from the moment of the first symptoms to the present.

Please note that there are no right or wrong answers, as we are interested in your opinions and your personal experience with the condition.

The interview (90 min.)

RESEARCHER: Tailor the questions to the way the patient refers to the disease and use the term provided by the patient to make him/her feel more comfortable. Whenever you believe that the caregiver could provide us with additional information on any of the topics discussed, please direct questions to him/her as well. If, on the other hand, you have the impression that it will be more valuable to ask certain questions only to the caregiver, do so after the interview with the patient. Always ask the patient for permission before talking to the caregiver.

Exploration area	**1. KNOW THE PATIENT (15 min)**
Goals	• **Generate a relationship with the patient** • **Better understand the person and their context** • **Understand your daily habits and routines**
Ethnographic explanation	*To begin with, I would like to get to know you as a person and familiarize myself with your personal situation...*

1. **Person:** I would like you to introduce yourself and explain to me:
    a) How old are you? Who do you live with?
    b) Tell me a little more about yourself, what do you like to do? What are your hobbies? What do you do? What do you value most now in your life? Why?
2. **Self-description:** If you were to describe yourself, what 3 words would you use? What comes to mind when you think of yourself?
3. **The patient's day-to-day life:** Tell me what a "typical" day looks like. What do you do from the time you wake up until you go to sleep? Differentiate weekday from weekends (i.e., hobbies). *RESEARCHER: be sure they explain their day to day routines to be able to refer to them later when exploring the impact of the disease. Write down on post-its moments with the greatest impact.*
    a) What time of day would you say you like best? When do you feel most at ease? Why?
    b) And what moment do you like the least? Why?
    c) What things do you have the hardest time doing?
    d) Is there anything you've had to give up in recent times? What do you miss?
4. **Outside view:** What do you think a good friend of yours or family member would say to me if I asked them what [patient's name] is like?
5. **Values:** If you were to tell a young family member what is most important in life, what would you say to them? Do you have any kind of personal "maxim"? Why do you think it's important? *[RESEARCHER: If health-related issues arise, ask when it became important to have a healthy life in your family and/or social environment]*

Exploration area	2. MEANING OF QUALITY OF LIFE (15 min)
Goals	• Understand what they associate to quality of life • Understand the impact of different HF symptoms on their quality of life
Ethnographic explanation	*Now I would like us to talk about those things that for you represent quality of life.*

6. **Quality of Life.** Definition: Now that you have completed this map, how would you define quality of life?
    a) What things allow you to have quality of life? How do you feel about them?
    b) What other things keep you from having a better quality of life? How do you feel about them?
7. **Current feeling:** How do you feel at this moment in your life? Do you have any small rituals that help you in your day to day? *RESEARCHER: Ask about eating habits, physical activity, cultural activities, etc.*
    a) Is there anything that particularly bothers you? Could you give me an example?
    b) What makes you happy?
    c) If you could improve 3 things from your day to day, what things would you choose? What would you give up?

Exploration area	3. HEART FAILURE (15 min)
Goals	• Understand the impact of HF on the patient's life • Understand the patient's perception of HF
Ethnographic explanation	*Now I would like you to tell me specifically about the disease you suffer...*

8. **HF:** I would like you to explain to me in your own words how do you see heart failure.

9. **Explanation of the disease**: Do you remember how they explained to you what HF was? What words did they use? Who did so? Could it have been done better? What did they miss?

10. **Living with HF:** What is it like to live with HF? When do you feel it becomes more "uphill"? What helps you overcome it?

11. **Other diagnoses:** Are you diagnosed with other diseases? Were they prior to HF? Are they related in any way?

Exploration area	**4. LIFE JOURNEY (15 min)**
Goals	- **Understand the impact of HF on the patient's life** - **Understand the patient's perception of HF**
Ethnographic explanation	*To continue I would like us to briefly talk about the most important moments with the disease ...*

12. **Significant moments with the disease:** Now I would like you to think about 5-6 significant moments since you were diagnosed with the disease. *RESEARCHER: Write down every moment in a post-it. Pay attention to whether hospitalization, transplant or heart attack arise spontaneously and if not, ask if you have experienced any of these moments and if so write them down next to the other moments.*

    a) Why have you precisely chosen these moments?

    b) How did you experience each of these moments?

    c) Which one of them was the best moment for you? *RESEARCHER: Ask what "the best" means to this patient*

    d) Which one of them was the worst moment for you? *RESEARCHER: Ask what "the worst" means and, if it is related to the patient's illness, ask:* → Is there anything that could have better helped you cope during those times?

    e) Which of these moments changed your life the most? Why?

13. **Life before HF**: What was your life like before you were diagnosed with HF? What things have changed the most? What do you miss?
    c) Since you were diagnosed… how has your lifestyle changed? How do you feel about it? What could help you?
    d) At the beginning of the interview, you explained to me what a day in your life looks like. How would this change if life were the way it used to be?
    e) Could you specify how you think the disease changed your life? *[RESEARCHER: dig into issues such as new interpretations of reality, changes in values, etc.]*

Exploration area	5. CARE AND EMOTIONAL PROCESS (20 min.)
Goals	• **Understand the HF Patient Journey** • **Identify unmet needs** • **Understand the perception of the different treatments that the patient has gone through**
Ethnographic explanation	*Now I would like us to delve into the journey you have followed since the beginning of the risk factors until now...*

Let's assume that you meet a person who has just been diagnosed with heart failure and does not know what it means to suffer from this condition. If you asked him to tell you about your experience, from the first symptoms until today

14. **Life without the disease**: What was your life like before the disease? If you look back, what do you miss the most?
15. **Previous diseases:** What diseases have you been diagnosed with? Who diagnosed you?
    a) Were you warned of the risk of developing heart failure?
    b) What did they explain to you?
    c) Were you advised to make lifestyle changes? *RESEARCHER, ask about exercise, diet, tobacco, or alcohol consumption...*
    d) Were you given any preventive treatment?
16. **First symptoms:**
    a) What changes did you experience that made you think something was wrong? For how long?
    b) What did you think might be going on?
17. **Diagnosis:**
    a) Do you remember what was explained to you?
    b) What tests have you done? Was the process burdensome?
    c) What doubts did you have?
    d) What did you think was going to happen at the time?
    e) Did you search for information on the internet?
    f) Did you contact any patient associations?
    g) Have you met anyone with this condition during the process? How has it affected you?
18. **First treatment:**
    a) Do you remember the name of your treatment?
    b) How was the first medication taken?
    c) Did you have any routines to do so?
    d) Did you stop taking the treatment at some point?
19. **Follow-up visits:**
    a) What were the routines of the visits like?

  b) Was it hard for you to make them? Currently, how do you feel when you must go to the doctor?

20. **Evolution of the disease:**
  a) How did you find out that the disease was changing? Were there any significant moments?

21. **Hospital admission** (if applies)**:**
  a) What was the process like? How many days last the hospital admission?
  b) How was the experience in the emergency room?
  c) Have you had more than one hospital admission?

22. **Surgery** (if applies)**:**
  a) What kind of device was implanted? Would you be able to explain how it works?
  b) What things does it allow you to do that you couldn't do before? How does this make you feel?
  c) What things can't you do now? How does this make you feel?

23. **Experience PROM questionnaires:** before the interview you answered a set of questionnaires about your symptoms and quality of life.
  a) From what we talked about during the interview, what things do you think should be included in these questionnaires?
  b) What things should your cardiologist know to make decisions?

Exploration area	**6. HOME TOUR (10 min.)**
Goals	• **Complement and contrast the information obtained during the interview with the patient's environment.** • **Understand the immediate context in which patients live (routines, rituals, and concessions to the HF)**
Ethnographic explanation	*For us it would be very useful to be able to understand how the disease affects your day to day. If you could show us your house, please, I'm sure it would help us understand...*

RESEARCHER: The home visit should be made at the appropriate time during the interview. It should be done naturally as a continuation of the conversation: asking for places and things inside the house (medicines, refrigerator, sofa, bedroom) that are important in terms of the impact that HF has on your life be shown.

For instance, ask whether there has been any home reform since they have had HF diagnosed. As you walk around, ask the patient about their daily routines and their life under treatment. Try to understand how the patient has adapted his/her life to the disease and his/her level of activity.

If the participant does not mention anything spontaneously, focus on:

- *Evidence that signals his/her 'lifestyle', hobbies.*
- *Written information about HF.*
- *Evidence of contact with HCPs.*

- *Rooms where she/he takes treatment or workout.*
- *Rooms where medicines are stored.*

Please, contrast the information mentioned during the interview with what you observe in the house. If allowed by the participant, take pictures of everything the patient deems relevant to treatment and their life with HF.

With this we would conclude the interview. Thank you very much for your time and participation. Do you have any comments or questions you want to share?

[END RECORDING]

2. OBSERVATION GUIDE OF MEDICAL APPOINTMENTS WITH HCPS

This guide is intended to guide the observation before, during and after the medical visit of selected patients. During the appointment, neither the patient nor the doctor will be asked questions by the researcher.

The objectives of the visit are:

1. Observe whether which topics are discussed during the medical appointment, and whether any of them is directly related to quality of life with the condition.
2. Understand the language that is used by both parties when talking about the condition.

RESEARCHER, prior to the visit, make sure that the patient understands the purpose of the observation within the study.

I – PRE-VISIT: Observation of the hospital environment

RESEARCHER, indicate the center, scheduled time of the visit and the start time of the observation.

Begin by observing the ***hospitals environment.*** *What surprises you the most? Why?*
Focus on:

- Occupancy of the center: number of patients in the waiting room, number of health workers.
- Space: design, decoration, lighting, colors, atmosphere.
- Organization: Allocation and ease of access.

Observe the ***interviewee.*** *What does he/she look like? (For example, tired, relaxed, irritated, etc.) Is there anything that stands out? Inquire about your expectations before the visit.*
Focus on:

- Arrival time, ease of access, companions (if applies).
- Body posture and non-verbal signs (facial expression, comfort level with the accompanying situation).
- Preparation for the visit: if the patient brings documents, medical tests, notebooks or tracking applications.
- Waiting times for the visit.
- If applies: Interaction with other health agents (residents, reception, nursing).

II – DURING THE VISIT: Observation of the patient medical interaction

RESEARCHER: Describe the physical space, organization, and arrangement of furniture. Also write down the ***exact time of the start of the visit.***
Focus on:

- Initial time of the visit.
- Initial greeting, use of gestures and non-verbal cues.
- Initial conversation. How general are they? How specific?
    - Questions from the doctor, order, and type.

        - On quality of life and/or impact of HF on a day-to-day basis.
        - Type of assessment and use of questionnaires.
        - Types of recommendations (functional, social, quality of life).
        - How the patient responds.
    - Questions from the patient, order, and type.
        - On quality of life and/or impact of HF on a day-to-day basis.
        - How your doctor responds
- Central conversation:
    - Topics of conversation that arouse greater patient attention (e.g., quality of life, impact on daily activity).
    - Topics of conversation that arouse greater attention from the doctor (e.g., clinical, psychological, or social, quality of life or other aspects).
    - Dominant language; use of colloquial language vs medical language.
- Body posture, proxemics and physical distance from the patient and the doctor during the visit.
- Use of silences and non-verbal gestures (gestures of approval, doubt, or confusion).
- Closing of the visit
    - Time and language used for the closing of the visit.
    - Approach of next steps by the doctor and the patient.
    - Farewell, use of gestures and non-verbal cues.
- If applies: interaction with other health agents (residents, receptionist, nursing).

III – AFTER THE VISIT: Observation of the patient

RESEARCHER: Write down the exact ***time of the end*** *of the visit. Accompany the patient at the exit of the visit and / or another instance of contact related to the visit (reception desks). If possible, know your perception about the results of the visit.*

Focus on:

- End time/duration of the visit.
- The patient's body posture and non-verbal gestures.
- Language used to assess the visit.
- If applies: interaction with other health agents (residents, reception, nursing).

End of observation.***

ETHNOQOL – COREQ CHECKLIST
5 October 2021

No.	Item	Description	Section #
Domain 1: Research team and reflexivity			
Personal characteristics			
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group? SCC MFE	Line 201
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD* *SCC, PhD* *MFE, BA*	NA
3.	Occupation	What was their occupation at the time of the study? Senior researchers	Line 201
4.	Gender	Was the researcher male or female? Female	Line 201
5.	Experience and training	What experience or training did the researcher have? >5 years of experience in medical sociology and medical anthropology	Line 202
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement? No.	Line 204
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? *E.g. Personal goals, reasons for doing the research* *Research goals*	Line 205
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? *E.g. Bias, assumptions, reasons and interests in the research topic* *None.*	NA
Domain 2: Study design			
Theoretical framework			
9.	Methodological orientation and theory	What methodological orientation was stated to underpin the study? *E.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis* *Thematic analysis* *Phenomenological perspective*	Lines 150-161, and section on Methods
Participant selection			
10.	Sampling	How were participants selected? *E.g. purposive, convenience, consecutive, snowball* *Purposeful*	Line 194
11.	Method of approach	How were participants approached? *E.g. face-to-face, telephone, mail, email*	Lines 186-196

		face-to-face	
12.	Sample size	How many participants were in the study? 20	Line 194 and 287
13.	Non-participation	How many people refused to participate or dropped out? What were the reasons for this? None	Lines 186-294
Setting			
14.	Setting of data collection	Where was the data collected? *E.g. home, clinic, Workplace* *Patients' home*	Lines 198-232
15.	Presence of non-participants	Was anyone else present besides the participants and researchers? No.	Lines 198-232
16.	Description of sample	What are the important characteristics of the sample? *E.g. demographic data, date* *demographic data and clinic characteristics*	Lines 286-294 and Table 1
Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested? Yes. No pilot tested.	See Supplementary Materials
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many? No.	NA
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data? Yes, audio recording.	Lines 229-232
20.	Field notes	Were field notes made during and/or after the interview or focus group? During interviews and after direct observations of medical appointments.	Lines 229-232
21.	Duration	What was the duration of the interviews or focus group? 90 min for interviews and 20 min for clinical encounters.	Line 206, 222
22.	Data saturation	Was data saturation discussed? Yes, in joint analysis sessions with authors.	Line 280
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction? No.	NA
Domain 3: analysis and findings			
Data analysis			
24.	Number of data coders	How many data coders coded the data? The two field researchers	Line 270
25.	Description of the coding tree	Did authors provide a description of the coding tree? Authors provided the description of domains, no coding tree.	Lines 267-279
26.	Derivation of themes	Were themes identified in advance or derived from the data? Derived from data.	Lines 267-279

27.	Software	What software, if applicable, was used to manage the data? No.	NA
28.	Participant checking	Did participants provide feedback on the findings? No.	NA
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? *E.g. Participant number* *Yes.*	Table 2
30.	Data and findings consistent	Was there consistency between the data presented and the findings? Yes, in joint analysis sessions.	Lines 267-279
31.	Clarity of major themes	Were major themes clearly presented in the findings? Yes, in joint analysis sessions.	See Results section
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes? Yes.	Yes, Table 2 and Results section