

Thirst distress in outpatients with heart failure in a Mediterranean zone of Spain

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Abstract

Aims This study aimed to evaluate psychometric properties of the Spanish version of the Thirst Distress Scale for patients with Heart Failure (TDS-HF) and to describe thirst distress-associated factors in outpatients at a heart failure (HF) clinic in Spain. Thirst is common in patients with HF, but thirst distress has rarely been addressed and may significantly decrease quality of life.

Methods and results A cross-sectional study was performed assessing perceived thirst distress by patients with HF during the preceding 3 days, with the TDS-HF (scores 8 to 40). Univariable and multivariable linear regression analyses were performed to identify variables independently associated with thirst distress. Three-hundred two HF outpatients were included (age 67 ± 12 years, 74% male, HF duration 82 ± 75 months, left ventricular ejection fraction $42 \pm 14\%$). Most patients were on treatment with fluid restriction (99%), sodium restriction (99%), and diuretics (70%). The psychometric evaluation of the Spanish version of the TDS-HF showed satisfactory item-total and inter-item correlations (range from 0.77 to 0.85 and 0.60 to 0.84, respectively), and internal consistency was 0.95 (Cronbach's alpha). The majority perceived mild to moderate thirst distress, and 18% perceived it as high or severe. The mean score obtained was 16.2 ± 9.3 (median 13, Q1–Q3 8–20). Higher serum urea [beta coefficient 1.6 [95% confidence interval (CI) 0.267 to 2.92], $P = 0.019$] and lower potassium [beta coefficient -3.63 (85% CI -6.32 to -0.93), $P = 0.009$] remained significantly associated with thirst distress in the multivariable analysis, together with the dose of diuretics [beta coefficient 2.98 (95% CI 1.37 to 4.59), $P < 0.001$]. Treatment with angiotensin receptor blocker showed an independent protective effect [beta coefficient -3.62 (95% CI -6.89 to -0.345), $P = 0.03$].

Conclusions The psychometric evaluation of the Spanish version of the TDS-HF showed good psychometric properties. One in five patients experienced severe distress by thirst, but the majority had mild to moderate thirst distress. The dose of diuretics and angiotensin receptor blocker treatment influence thirst distress and could be clinically important targets to relieve thirst distress in patients with HF.

Keywords Heart failure; Thirst; Thirst distress; Quality of life; ARB; Diuretics

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Introduction

Heart failure (HF) is a major public health problem and is increasing in prevalence due to aging population and better treatment of cardiovascular diseases. Beyond crucial issues as high morbidity, with frequent hospital readmissions, and still high mortality, living with HF often means reduced

health-related quality of life and suffering a large number of symptoms, such as dyspnoea, peripheral oedema, exercise intolerance, and fatigue.^{1,2} Recent studies show that thirst is another common symptom experienced by HF patients.^{3–7}

Thirst is a physiological homeostatic response that makes one drinking water to restore the body's fluid balance.⁸ It is a subjective sensation associated with a craving for water

and a feeling of dryness in the mouth³ and without possibility to drink it causes the individual a lot of suffering. Thirst has been described as a distressing symptom in HF patients that is recognized but rarely addressed.^{5,9,10} About half of the patients in a Mediterranean population with HF experienced frequent thirst, with 33% of them experiencing thirst every day.¹¹ Moreover, the study showed that patients with frequent thirst experienced thirst more intensively and for a longer duration. This indicated that thirst can be very difficult for some patients and motivates further studies in this field.¹¹ Patients with severe HF described thirst as a source for suffering and underlined the difficulty to control and find relieve for their thirst.¹² Several factors have been suggested to promote thirst in these patients, including increased activation of neurohormonal systems, medications, and self-care practices.⁵ The treatments with the greatest association are those prescribed to control volume status, which is a core principle in HF management.¹³ The non-pharmacological treatment of fluid restriction has also been associated with increased thirst in several studies,^{7,14,15} and how to manage it could be controversial.¹⁶

Thirst as a symptom has been described by these dimensions: frequency and duration, intensity, distress, and quality.³ Thirst frequency describes how often and duration describes for how long thirst occurs. It also describes if there is a pattern of symptom occurrence. Thirst intensity can be described as the strength of the thirst, and studies examining thirst intensity in HF patients have measured it using a visual analogue scale (VAS).^{7,9} Thirst distress is a measure of to what degree a patient is bothered by thirst. Studies have examined thirst distress by quantitative measures by using scales.⁷ Finally, the quality of a symptom is what the symptom feels like and associated discomforts, as described with the patient's own words.

In 2011, the Thirst Distress Scale for patients with HF (TDS-HF) was developed. The scale has been used in Sweden, the Netherlands, and Japan and has proven to be successful to assess thirst distress in HF patients.¹⁷ The aim of the present study was to (i) evaluate psychometric properties of the Spanish version of the TDS-HF and (ii) describe thirst distress and identify factors associated with thirst distress in outpatients at an HF clinic in Spain.

Methods

The study used a cross-sectional design. The study population consists of outpatients with a scheduled visit to the HF clinic at a University Hospital in Badalona, Spain, between mid-September 2018 and early November 2018. The criteria for clinical practice referral to the HF unit have been reported elsewhere.¹⁸ The patients have routine follow-up visits at the clinic according to clinical status, consisting at least in one

visit to an HF nurse every 3 months and one visit to a physician every 6 months. Patients were included on follow-up visits to one of the two HF nurses participating in the study. Exclusion criteria were diagnosis of dementia or language barriers.

Data collection

Data were collected by a research assistant and an HF nurse. Patients scheduled to see the HF nurse were asked to fill in the questionnaire on thirst distress during their visit. Patients in need of help to read the questions or to fill in the questionnaire were assisted by the HF nurse.

Thirst Distress Scale

The Spanish version of TDS-HF (Supporting Information, *Annex S1*) was used to quantify the thirst distress perceived by the patients during the preceding 3 days. TDS-HF¹⁷ is a 5-point Likert scale that consists of eight statements about thirst. Patients were asked to rate these from 1 (strongly disagree) to 5 (strongly agree). The total TDS-HF score ranges from 8 to 40. Higher scores indicate higher thirst distress. The Spanish version of the scale was recently developed from the TDS-HF in English. This study is the first to use the translated Spanish TDS-HF in a Spanish cohort. The translation of the scale was done according to international rules.¹⁹ The English version of the scale was translated into two Spanish versions (by a professional translator with no health care education and by a Spanish cardiologist). The two translated Spanish versions were later back translated into English (US) by two professional translators. Three health care professionals compiled the final version from the two back-translated English versions (authors N. W., J. L., and T. J.; N. W. and T. J. were involved in the development of the original TDS-HF). To assess face validity and comprehensiveness, a clinician checked if the scale was easy to understand with regard to the clarity of the language. Patients with HF ($n = 3-5$) were asked to describe the relevance of the questions in the Spanish version of the TDS-HF and the usability of the scale (if the scale was clear and easy to use).²⁰

Arbitrarily, the mean total thirst distress score was divided into five categories: no distress (0–8 points), mild distress (9–16 points), moderate distress (17–24 points), high distress (25–32 points), and severe distress (33–40 points).

Demographic and clinical variables

Socio-demographic clinical characteristics, co-morbidities (including depression), and treatments were collected from interviews during the visit or from patient's medical records. To compare doses of diuretics per day, 10 mg of torsemide

were considered equivalent to 40 mg of furosemide. Patients who had changed their dose of diuretics in the last 24 h were excluded from the analysis of diuretics association with thirst distress. Medications that have been associated with an effect on fluid balance were also documented and classified (opioids, antidepressants, anti-histamines, proton pump inhibitors, and vasopressin V2 receptor blockers). Patients were also asked on amount of fluid and sodium restriction. Only blood test taken within 30 days from the visit and left ventricular ejection fraction (LVEF) measured within 1 year from the visit were included in the analyses. In addition to thirst distress by the TDS-HF, thirst intensity was measured by a VAS with rating on a line from no thirst (0 mm) to worst possible thirst (100) to be used in concurrent validity evaluation.

The HF clinic has a general informed consent and ethical approval for studies carried out at the clinic. At their baseline visit, patients are provided with and sign a written informed consent for obtaining clinical data, analytic samples, and clinical scales (such as the TDS-HF) and use them for research purposes. The study was performed in compliance with the law regarding the protection of personal data and in accordance with the international guidelines on clinical investigation of the World Medical Association's Declaration of Helsinki.

Data analysis

Continuous data showing a normal distribution are presented as the mean \pm standard deviation, and data with skewed distribution are presented as the median and interquartile range (Q1–Q3). Normal vs. skewed distribution was assessed by normal Q–Q plots. Categorical data are presented by absolute numbers and percentages. The mean value and distribution of responses for each item of TDS-HF were calculated, as well as the mean total thirst distress score.

Psychometric evaluation was conducted to assess construct validity, concurrent validity, and internal consistency. The TDS-HF has not previously been used by patients with HF who speak Spanish. It has been found that the factor structure of a scale can be inconsistent in different language versions, and therefore, an exploratory factor analysis with maximum likelihood extraction was performed.²¹ Construct validity was assessed by performing an exploratory factor analysis with maximum likelihood extraction. The Kaiser–Meyer–Olkin measure of sampling adequacy and the Bartlett test of sphericity were used to test the appropriateness of factor analysis. The concurrent validity was evaluated between the total score of TDS-HF and thirst intensity (VAS, 0–100 mm) by using the Spearman rank correlation. Internal consistency of the TDS-HF was evaluated by calculating the Cronbach's alpha. Item-total and inter-item correlations were calculated by using the Spearman correlation analysis.

Variables previously reported to be related to thirst distress or clinically considered eventually susceptible to be associated with thirst distress were included as independent co-variables in the univariable linear regression analyses in which the TDS-HF score, as continuous variable, was the dependent variable. Variables with a significant result in the univariable analyses were included in a multivariable regression analysis (backward stepwise method) in order to identify factors independently related with thirst distress. Despite no significant result in the initial univariable analyses, body mass index and age were included in the multivariable regression analysis because previous studies have shown that they can affect thirst in HF patients.⁴ A multicollinearity analysis was made to rule out collinearity between variables in the multivariable regression (using variance inflation factor range). The level of statistical significance was set at $P < 0.05$. Data analyses were performed using IBM SPSS Version 25 (Chicago, Illinois, USA).

Results

Study population

Three-hundred two patients with HF participated in the study. Another 258 patients were scheduled, but not included in the study due to a visit with one of the nurses not participating in the study. One patient was excluded due to dementia. *Table 1* shows demographics, clinical characteristics, and treatments. In summary, mean age was 67 ± 12 years, and 224 (74%) were men. Mean LVEF was $42 \pm 14\%$, with 108 patients (49%) having an LVEF under 40%. Most patients (79%) were in New York Heart Association (NYHA) class II. Median duration of HF was 4.9 (1.6–11) years. The most frequent aetiology for HF was ischaemic heart disease (42%). Nearly all patients were prescribed fluid restriction and sodium restriction (99%). Most patients (70%) were prescribed diuretics [mean dose of furosemide 61 ± 32 mg/day and median dose of torasemide 10 (5–10) mg/day]. Some of the patients were prescribed other medical therapy associated with increased thirst, such as proton pump inhibitors (47%), benzodiazepines (24%), antidepressants (19%), and opioids (2%) (*Table 1*).

Psychometric properties of the Spanish version of the Thirst Distress Scale for patients with Heart Failure

Face validity of the TDS-HF was acceptable, as assessed by a convenient number of patients with regard to the question's relevance, clarity, and easy to use. The sampling adequacy was good, as evaluated with Kaiser–Meyer–Olkin (0.92) and Bartlett's test of sphericity ($P < 0.001$).

Table 1 Demographics and clinical characteristics

Demographics		N
Age, years	67 ± 12	302
Gender, male	224 (74%)	302
Current smoking	53 (18%)	302
Living situation		
Alone	45 (15%)	302
With partner	200 (66%)	302
With others	57 (19%)	302
Educational level		
None	23 (8%)	301
Primary school	177 (59%)	301
Secondary school	74 (25%)	301
Higher education	27 (9%)	301
Clinical data		
HF duration, years	4.9 (1.6–11)	302
HF deterioration in the last 3 days	7 (2%)	302
LVEF, %	42 ± 14	220
LVEF < 40%	108 (49%)	220
BMI, kg/m ²	27 (24–30)	300
Systolic blood pressure, mmHg	126 ± 19	302
Diastolic blood pressure, mmHg	75 ± 11	302
Pulse, b.p.m.	68 (60–78)	302
HF aetiology		
Ischaemic heart disease	127 (42%)	302
Dilated cardiomyopathy	58 (19%)	302
Other	38 (13%)	302
Alcoholic cardiomyopathy	27 (9%)	302
Valve disease	27 (9%)	302
Hypertensive cardiomyopathy	16 (5%)	302
Toxic cardiomyopathy	9 (3%)	302
NYHA functional class		
NYHA class I	36 (12%)	302
NYHA class II	237 (79%)	302
NYHA class III	29 (10%)	302
NYHA class IV	0 (0%)	302
Co-morbidities		
Hypertension	201 (67%)	302
Hypercholesterolaemia	166 (55%)	302
Diabetes	119 (39%)	302
Renal failure	76 (42%)	183
Atrial fibrillation	56 (19%)	302
COPD	51 (17%)	302
Anaemia	41 (31%)	132
Peripheral vascular disease	38 (13%)	302
Depression	29 (10%)	302
Malignancy	20 (7%)	302
Stroke	11 (3%)	302
Blood tests ^a		
Urea, mmol/L	8.0 (6.0–12.5)	183
Sodium, mmol/L	138.9 ± 3.0	182
Potassium, mmol/L	4.51 ± 0.48	182
Creatinine, µmol/L	95.0 (76.0–129)	183
Hb, g/L	135 ± 19	132
NT-proBNP, pg/mL	704 (190–2894)	90
eGFR, mL/min	66.1 ± 28.1	183
Non-pharmaceutical treatments		
Fluid restriction (any)	300 (99%)	302
Fluid restriction, 1500 mL/day	277 (92%)	302
Sodium restriction (any)	300 (99%)	302
Sodium restriction, 3500 mg/day	281 (93%)	302
Cardiac resynchronization therapy	28 (9%)	302
Implantable cardioverter defibrillator	47 (16%)	302
Pharmaceutical treatment		
Diuretics	212 (70%)	302
Diuretics dose changes in the last 24 h	7 (2%)	302
Furosemide dose, mg/day	61 ± 32	92
Torsemide dose, mg/day	10 (5–10)	115

(Continues)

Table 1 (continued)

Demographics		N
ACE inhibitors	137 (45%)	302
Angiotensin receptor blockers	49 (16%)	302
Beta-blockers	285 (94%)	302
Mineralocorticoid receptor antagonists	193 (64%)	302
ARNI	59 (20%)	302
Ivabradine	47 (16%)	302
Vasopressin V2 receptor blocker	1 (0.3%)	302
Proton pump inhibitors	141 (47%)	302
Opioids	5 (2%)	302
Antidepressants	57 (19%)	302
Benzodiazepines	71 (24%)	302
Anti-histamines	0 (0%)	302
TDS-HF total score	16.2 ± 9.3	302

ACE, angiotensin-converting enzyme; ARNI, angiotensin receptor–neprilysin inhibitors; BMI, body mass index; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; Hb, haemoglobin; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; TDS-HF, Thirst Distress Scale for patients with Heart Failure.

Data are presented as *n* (%), mean ± standard deviation, or median (Q1–Q3).

^aWithin previous 30 days.

Exploratory factor analysis showed that one single factor explained 73% of the variance of the Spanish version of the TDS-HF. Concurrent validity analysis showed that the TDS-HF was significantly correlated with thirst intensity ($r = 0.59$; $P < 0.001$).

The internal consistency of the TDS-HF was 0.95 (Cronbach's alpha). Homogeneity of the items was acceptable ($r > 0.4$). The lowest item-total correlation was in Item 6 ('When I drink less water, my thirst gets worse', $r = 0.77$), and the highest was in Item 1 ('My thirst bothers me a lot', $r = 0.85$). Inter-item correlations showed the strongest correlations for Items 1 ('My thirst bothers me a lot') and 2 ('I am very uncomfortable when I am thirsty', $r = 0.84$), and 7 ('I am so thirsty I could drink water uncontrollably') and 8 ('My thirst feels difficult to overcome', $r = 0.83$). The lowest correlations were found for Items 4 ('My mouth feels dry when I am thirsty') and 8 ('My thirst feels difficult to overcome', $r = 0.60$).

Thirst distress

All patients completed the TDS-HF. Items 1, 2, 7, and 8 had the lowest mean value as many patients responded with 1 (Table 2). The lowest mean value was 1.58 ± 1.16 for Item 8 ('My thirst feels difficult to overcome'). The highest mean value occurred in Item 3 and Item 4, the highest being 2.56 ± 1.44 for Item 4 ('My mouth feels dry when I am thirsty'). The mean thirst distress score was 16.2 ± 9.3 (range 8–40). Twenty-six per cent of patients suffered no thirst distress (scores 0–8), 40% mild (9–16), 17% moderate (17–24), 9% high (25–32), and 9% severe thirst distress (33–40; Figure 1).

Factors associated with thirst distress

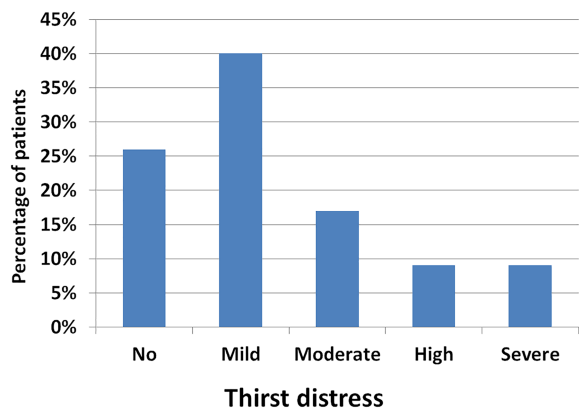
Table 3 shows univariable and multivariable regression analyses taking the thirst distress score as the dependent

Table 2 Scores of the items and item distribution

Item	Mean ± SD	Agreement for each item, <i>n</i> (%)				
		Strongly disagree			Strongly agree	
		1	2	3	4	5
1. My thirst bothers me a lot	1.87 ± 1.30	181 (60%)	45 (15%)	35 (12%)	15 (5%)	26 (8.6%)
2. I am very uncomfortable when I am thirsty	2.06 ± 1.39	161 (53%)	52 (17%)	32 (11%)	24 (7.9%)	33 (11%)
3. My mouth feels like sandpaper when I am thirsty	2.27 ± 1.40	126 (42%)	69 (23%)	46 (15%)	22 (7.3%)	39 (13%)
4. My mouth feels dry when I am thirsty	2.56 ± 1.44	92 (31%)	81 (27%)	49 (16%)	29 (9.6%)	51 (17%)
5. My saliva is very thick when I am thirsty	2.26 ± 1.43	129 (43%)	76 (25%)	26 (8.6%)	31 (10.3%)	40 (13%)
6. When I drink less water, my thirst gets worse	1.91 ± 1.36	184 (61%)	40 (13%)	31 (10%)	16 (5.3%)	31 (10%)
7. I am so thirsty I could drink water uncontrollably	1.75 ± 1.36	212 (70%)	33 (11%)	15 (5%)	6 (2%)	36 (12%)
8. My thirst feels difficult to overcome	1.58 ± 1.16	220 (73%)	38 (13%)	15 (5%)	8 (2.6%)	21 (7%)

SD, standard deviation.

Figure 1 Prevalence of the predefined categories of thirst distress. No distress (0–8 points); mild distress (9–16 points); moderate distress (17–24 points); high distress (25–32 points); and severe distress (33–40 points).



variable. No multicollinearity was found for the variables in the multivariable logistic regression (variance inflation factor range, 1.012–1.038). In the multivariable regression model that included also age, gender, body mass index, NYHA class, depression, and antidepressant treatment, only higher urea

(standardized $\beta = 0.17$; $P = 0.019$), lower potassium (standardized $\beta = -0.188$; $P = 0.009$), lack of angiotensin receptor blocker (ARB) treatment (standardized $\beta = -0.156$; $P = 0.03$), and higher dose of loop diuretics (standardized $\beta = 0.259$; $P = 0.001$) remained independently associated with thirst distress. As both depression and antidepressants can influence thirst and thirst distress and only one third of patients taking antidepressants had a diagnosis of true depression, both variables were included in the multivariable analysis. *Figure 2* shows thirst distress score (boxplots) among different doses of diuretics.

Discussion

Two main results can be derived from the present study, in which the newly developed TDS-HF in Spanish was used to measure thirst distress in a Spanish cohort of HF outpatients. First, although the majority of Spanish HF outpatients suffer mild to moderate thirst distress, almost one in five suffered moderate–severe thirst-related distress, which is not a negligible number of patients. And second, several drugs commonly used in HF patients might facilitate lower levels of thirst distress, such as ARB, in contrast to angiotensin-converting enzyme (ACE) inhibitors. A third

Table 3 Linear regression with variables associated with thirst distress

	Univariable					Multivariable				
	B coefficient		95% CI		P-value	B coefficient		95% CI		P-value
	Not standardized	Standardized	Lower	Upper		Not standardized	Standardized	Lower	Upper	
Age	0.016	0.022	-0.068	0.101	0.71	---	---	---	---	---
Gender	3.29	0.156	0.923	5.66	0.007	---	---	---	---	---
Current smoking	-0.637	-0.026	-0.397	2.123	0.65	---	---	---	---	---
BMI ^a	0.001	0.001	-0.195	0.197	0.99	---	---	---	---	---
NYHA class	4.31	0.216	2.1	6.52	<0.001	---	---	---	---	---
Diabetes mellitus	-0.209	-0.011	-2.358	1.940	0.85	---	---	---	---	---
Hypertension	1.32	0.067	-0.901	3.541	0.24	---	---	---	---	---
Renal failure ^{a,b}	2.367	0.091	-0.569	5.304	0.11	---	---	---	---	---
Anaemia ^{a,c}	1.119	0.038	-2.245	4.482	0.51	---	---	---	---	---
Depression	4.87	0.155	1.35	8.39	0.007	---	---	---	---	---
Stroke	-4.44	-0.09	-10	1.15	0.12	---	---	---	---	---
Urea ^{a,d}	1.77	0.193	0.449	3.1	0.009	1.6	0.17	0.267	2.92	0.019
Potassium ^a	-2.99	-0.156	-5.76	-0.21	0.04	-3.63	-0.188	-6.32	-0.93	0.009
Creatinine ^{a,d}	0.57	0.061	-0.78	1.91	0.41	---	---	---	---	---
Dose of diuretics ^a	3.04	0.272	1.8	4.28	<0.001	2.98	0.259	1.37	4.59	<0.001
ACEI	-0.31	-0.02	-2.42	1.80	0.77	---	---	---	---	---
ARB	-2.93	-0.117	-5.75	-0.096	0.04	-3.62	-0.156	-6.89	-0.345	0.03
Antidepressants	3.53	0.15	0.881	6.19	0.009	---	---	---	---	---

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; BMI, body mass index; CI, confidence interval; NYHA, New York Heart Association.

In the multivariable analyses, striped cells represent those variables included in the back-stepwise model but that did not remain into it (non-significant variables) while blank cells correspond to those variables not included in the analysis. Dose of diuretics: 0 = no diuretics; 1 = 1–40 mg/day; 2 = 41–80 mg/day; 3 = >80 mg/day.

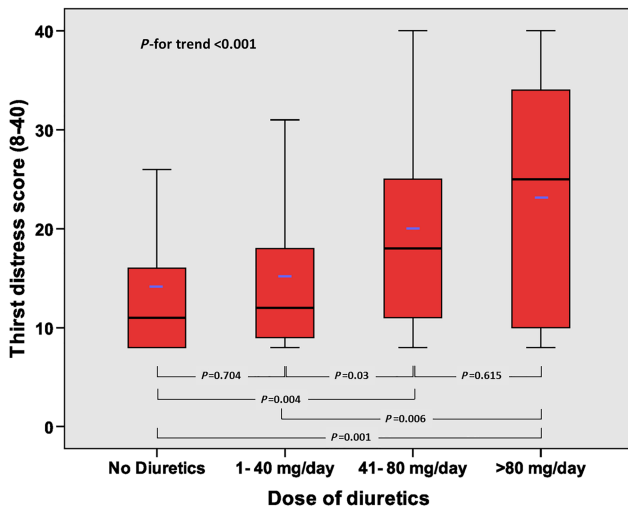
^aLess than 302 (Table 1). $N = 173$ in the multivariable analysis.

^bEstimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation) < 60 mL/min/1.73 m².

^cAccording to the World Health Organization criteria (<13 g/dL in men and <12 g/dL in women).

^dLog-transformed and per 1 SD.

Figure 2 Boxplots of thirst distress score among different doses of diuretics. The central box represents the values from the lower to the upper quartile; the middle lines represent the median; the whiskers extend to the minimum and maximum values, excluding far out values that are not displayed; and the blue dash represents mean values ($N = 205$).



interesting and novel finding was the association found between thirst distress and low blood levels of potassium.

The Spanish-language version of the TDS-HF captured the content of the original scale with relevant adaption to the cultural context. Thirst distress as measured with the TDS-HF was moderately associated with thirst intensity ($r = 0.59$), which was also seen for the original scale ($r = 0.56$).¹⁷ These results confirm that the intensity and distress of thirst are different dimensions of the same symptom and should therefore be assessed with different measurements.

The mean obtained score in this study was quite similar to the mean thirst distress score in the study by Waldr us *et al.* with data from Sweden, the Netherlands, and Japan (16.4 ± 7.8).¹⁷ Differences in total thirst distress score were quite small between that countries; the biggest difference was observed between Sweden and Japan (17.3 ± 7.6 vs. 15.4 ± 8.0). It has been suggested that thirst might differ between countries not only due to differences in demographics and treatments but also due to climate, culture, and dietary habits.¹⁷ Our study does not intend to investigate differences between countries, but maybe future research could broaden the perspective of factors that influence thirst in HF patients. An international study could also be important to get closer to determine prevalence of thirst in HF patients globally.

Factors associated with thirst distress

This is the first study to examine thirst distress in HF patients in a Spanish cohort. HF is one of the leading health issues in

Spain, causing about 3–5% of all hospital admissions.²² In the present study, increased thirst distress was associated in the univariable analysis with female gender, depression, worse NYHA class, lower serum potassium, increased levels of serum urea and creatinine, and treatments such as antidepressants and diuretics. In contrast, patients with a history of stroke and, remarkably, patients receiving ARB experienced less thirst distress.

The fact that medications can induce thirst has been previously shown.^{13,23} In our study, we found that diuretics and antidepressants increase thirst distress in HF patients while ARB seemed to decrease it. Diuretics have already been associated with thirst in HF patients.¹³

This effect has been explained by the dehydration that can be caused by the excretion of fluids from the kidneys. Interestingly, but not surprisingly, we found a clear association between the degree of thirst distress and the doses of loop diuretics, not only with loop diuretic prescription. The higher the dose, the stronger the thirst distress.

The increased sympathetic activity and the high levels of circulating angiotensin II present in HF patients can be associated with an increased activity of the thirst centre in the circumventricular organ of the hypothalamus.²⁴ Sympathetic stress causes vasoconstriction of the salivary glands with decreased salivary secretion. The decrease in saliva is detected by specific receptors in the mouth that are sensitive to changes in friction and osmosis in the mouth mucosa. These receptors will activate the thirst centre. Angiotensin II binds directly to receptors in the thirst centre and thereby causes thirst.^{24,25} In the present study, ARBs were associated with less thirst distress. ARBs are recommended to patients who experience negative side effects of ACE inhibitors,¹ in our cohort mainly due to persistent cough. ACE inhibitors and ARBs are common medications for HF patients. The mechanism for these drugs is to inhibit the effect of angiotensin II to control the neurohormonal activity in HF. In addition to the suppression of renin–angiotensin–aldosterone system, both angiotensin receptor–neprilysin inhibitors (ARNI) and ACE inhibitors have another mechanism of action by the promotion of natriuresis. ARNI prevents the degradation of natriuretic peptides through inhibition of neprilysin and ACE inhibitors by decreased degradation of the vasodilatory and natriuretic peptide bradykinin.^{26,27} This dual action with both renin–angiotensin–aldosterone system inhibition and increased natriuresis could explain both the superiority of ACE inhibitors and ARNI compared with ARB in modifying patient's prognosis and the increased thirst.¹ Studies on rats have suggested that increased levels of bradykinin are also associated with polyuria and polydipsia. The dipsogenic effect of ACE inhibitors in rats is believed to exist in humans too.²⁸

We hypothesized that patients on ARB might experience less thirst because of the change from ACE inhibitors to ARB and, in a speculative way, maybe patients who experience

severe thirst could be advised to switch medications from ACE inhibitors to ARB.

Antidepressants were also associated with increased thirst in the univariable analysis, although lost significance in the multivariable analysis. Different antidepressants have anti-cholinergic effect that modulates the regulation of the salivary glands by the autonomic nervous system. These changes include alterations in saliva composition and salivary secretion rate that can cause dry mouth.²³ Another plausible reason for increased thirst observed in patients on antidepressants is the depression itself, which was also associated with thirst in the univariable analysis. Over 20% of HF patients are estimated to suffer from depression.²⁹ Stress, anxiety, and depression have a significant effect on reducing saliva and causing dry mouth.³⁰ The high sympathetic activity seen in HF patients can be even more increased in patients experiencing psychological distress, such as depression and anxiety.³¹ The increased sympathetic activity could contribute to the increased thirst in depressive patients.²³

Low serum potassium was another factor related to increased thirst distress. This is a new finding not described previously. Beside to diet, serum potassium levels can be lowered by diuretic treatment. Remarkably, our results showed that low serum potassium increased thirst distress independently of diuretics and no collinearity was found between both variables in the regression analysis. The role of potassium in thirst in HF patients is not well elucidated, but possible mechanisms can be related to the vasodilator and natriuretic effects of potassium. Increased potassium causes endothelium-dependent vasodilatation through stimulation of Na⁺/K⁺ ATPase pump and opening of potassium channels, which hyperpolarize the vascular smooth muscle cell leading to vasodilatation³² and reducing the sensitivity to catecholamine and angiotensin II-related vasoconstriction.³³ We hypothesized that potassium can disrupt the increased sympathetic processes in HF and thereby decrease thirst in HF patients.

Our study also showed that women suffered from more thirst distress than men. This is in line with a recent study examining thirst trajectories from hospital admission to 4 weeks of follow-up.⁷ Other studies, in contrast, have shown that men with HF are thirstier than women.⁴ Studies on healthy subjects have found no difference in thirst between genders, but xerostomia (feeling of dry mouth) is more common in women.³⁴ Other explanations for the increased thirst distress in women with HF might be that they experience a greater degree of anxiety and depression.³⁵

Despite the negative impact thirst has on daily life of these patients, in current practice, there is no structural clinical evaluation of thirst in HF patients or current guidelines on how to help these patients manage their thirst. Though the absence of guidelines, there are some common strategies recommended by health care professionals. Common strategies include the use of ice chips or taking small sips of water,

but one study showed that most clinicians are unsure about the usefulness of these interventions.⁹ Introducing a screening of thirst is an important step towards helping patients who develop or suffer from thirst. This could be especially important in groups more disposed to develop thirst. Because treatments have shown to affect thirst, individual assessment of treatments could be helpful for patients experiencing thirst. As this study suggests, patients experiencing thirst might benefit from changing medication from ACE inhibitors to ARB. However, as ARBs are inferior in modifying patient prognosis in HF, our findings need to be confirmed in other studies.

If possible, the patients could benefit from lowering the dose of diuretics as well. Further studies are needed on strategies for thirst relief. Factors associated with thirst are possible target points to be included in these studies.

Limitations

The strength of this study was a large study sample including 302 patients. However, most study participants were men (74%), which limit the generalizability to all HF patients.

Also, another limitation of the generalizability is the setting at an outpatient clinic. The study population had a relatively mild to moderate HF, according to LVEF, dominating NYHA II, and moderate levels of N-terminal pro-B-type natriuretic peptide. This further limits the generalizability of the results to those taking higher doses of diuretics and in higher NYHA class (NYHA III–IV). With regard to content validity, we did not do separate analysis for the Spanish version of the TDS-HF. And this is a recommendation for future studies.³⁶

Given the cross-sectional design of this study, causality cannot be determined and confounding factors cannot be excluded. The blood samples and LVEF were not taken at time of the visit but from a medical database. To ensure that these variables were representative of the present data, only blood samples taken within 30 days and LVEF within 1 year were included. Urine sodium, which is a marker of natriuresis and might potentially modify thirst, was not measured in this study. In a previous study, the results showed that patients admitted to hospital for worsening of HF had significantly increased thirst compared with patients without HF.³⁷ The urinary sodium was significantly lower in patients with HF, which is consistent with the neurohumoral activation associated with this syndrome (70 vs. 107 mmol/L; $P < 0.006$), but there was no correlation with thirst.³⁷ Moreover, the difference in serum sodium that was measured (1.4 mmol/L) is hardly sufficient to explain the greatly increased thirst among the HF patients. A very low urinary sodium excretion (<30 mmol/L) has been associated with poor short-term prognosis, but not with thirst, in older patients with multimorbidity.³⁸ As only a few studies have investigated the relation between natriuresis and thirst in HF, it can be

advised to include such data in future studies to strengthen our knowledge of thirst in HF.

Cut-off scores used to categorize the total thirst distress score into categories were chosen arbitrarily. However, they were based on a logical reasoning based on what the mean score of each item would be if the mean total score was divided by the number of items. For this study, only data on prescribed fluid restriction were collected and no data on actual fluid intake.

Conclusions

The Spanish-language version of the TDS-HF was shown to be reliable and valid. One in five experienced severe distress by thirst, although on average the total population seemed mildly to moderately stressed. Several factors, such as depression, diuretic dose, and ARB treatment, can influence thirst distress in HF patients, and they are important targets when screening for thirst and also for thirst relief. Based on our results, treatment with ARB might have an independent protective effect on thirst distress. Evaluation of thirst in clinical practice is important. By addressing thirst as a symptom,

patients can receive the care needed that might contribute to improved quality of life.

Conflict of interest

None declared.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1. Supporting information.

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