nutrición clínica y Dietética Hospitalaria

Artículo Original

Nutr. clín. diet. hosp. 2019; 39(1):22-31
DOI: 10.12873/391guerra

Nutritional intervention in patients with heart failure. 3 month results of a clinical trial

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Recibido: 7/octubre/2018. Aceptado: 23/marzo/2019.

ABSTRACT

Background: A variety of studies have detailed the "paradox of patients with obesity and heart failure". There exists a reverse epidemiology: obesity predisposes the development of cardiovascular diseases and heart failure, but a high body mass index improves survivability at two and at five years. Subsequently, other studies have been shifting this focus not with the body mass index, but instead with the nutritional status and unplanned weight loss. It is not clear the role of the nutritional treatment in these patients.

Aims: Evaluation of 2-part intervention (dietary recommendations + supplements) over the nutritional status, quality of life and functional capacity in heart failure patients who exhibit malnutrition or the risk thereof after 3 months treatment.

Methods: A sample of 76 chronic heart failure patients who exhibit malnutrition or the risk thereof participated in a clinical trial on an intention-to-treat basis. The intervention group received structured recommendations combined with dietary supplements for 12 weeks and control group received the standard intervention. Assessors were blinded. The nutritional status was measured with Subjective Global Assessment (SGA), QOL with Minnesota Living with Heart Failure Questionnaire and functional capacity with the 6-minute walk test.

Results: At three months, the intervention group improved four times the nutritional status measured with SGA. The control group remained similar. The intervention group improved in the same variables as the control group (except in mean total proteins) and also improved in parameters associated with energy reserves (triceps skin fold, mid-upper arm fat area and cholesterol).

Conclusion: Nutritional counseling, accompanied by normoproteic hypercaloric supplements, in patients with chronic heart failure, treated with ACEI / ARA II or beta-blockers, can improve the nutritional status at three months.

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INTRODUCTION

Heart failure can become a highly limiting disease that impairs functional capacity, nutrition, and quality of life. Considerable health care resources are consumed as a result of frequent readmissions among patients with heart failure, who are repeatedly incapacitated by dyspnea, edema, asthenia, and anorexia. Like in other chronic illness, patients with heart failure often have malnutrition, which, whether incipient or established, gradually leads to a vicious cycle[1]. Malnutrition is highly prevalent in patients hospitalized for decompensated heart failure, and approximately 30%-45% of patients could be at risk[2,3]. The association between malnutrition and increased complications, longer hospital stay[4], mortality[5], and readmission before 30 days is reasonably well documented[6]. Cardiac cachexia, malabsorption, and enteropathy are relatively common in patients with heart failure[7] and make for a poor prognosis. Cardiac cachexia is a common complication of chronic heart failure: the SOLVD study revealed a cumulative incidence of cachexia of 35% after 3 years of follow-up[8] and showed that this was a sign

of poor prognosis, irrespective of age, functional class, and left ventricular ejection fraction[9].

The association between disease and malnutrition is well documented and affects patients in many ways. In patients with advanced heart failure in particular, malnutrition acts on multiple fronts, affecting appetite, catabolism, and loss of nutrients:

- Deficient intake: Deficient intake results from dyspnea and the early sensation of satiety secondary to hepatomegaly and abdominal distension. It is also caused by an undesirable effect on appetite resulting from FNTα and from therapy with drugs such as atorvastatin, digoxin, flecainide, furosemide, hydralazine, hydrochlorothiazide, metformin, and simvastatin[10]. In addition, intake can prove deficient owing to variations in diet (eg, reduced intake of sodium), which can suppress the patient's appetite.
- Accelerated catabolism: Catabolism increases depending on the patient's symptoms and is associated with levels of catecholamines, renin, and aldosterone. Neurohormonal activation has been associated with a poorer prognosis, despite its initial benefits[11].
- Multifactorial inflammatory processes: These processes increase levels of tumor necrosis factor and other cytokines, whose action includes inhibiting appetite and reducing body fat reserves[12].
- Intestinal absorption disorders associated with congestion of intestinal veins[13,14] and with the loss of nutrients resulting from enteropathy and the subsequent loss of proteins[15].
- The unclear role of diuretics on nutrition.
- Pharmacological factors such as drug-induced xerostomia (eg, with angiotensin-converting enzyme inhibitors [ACEIs]).
- Nutrition is affected by several factors, and a clear 2-way association can be observed between disease and malnutrition, leading to cachexia and a very poor prognosis. It is difficult to know which areas can be addressed to resolve this association. At the same time, it is not clear the role of the nutritional treatment in these patients[10].

The objective of the present study is to know whether dietary recommendations and nutritional supplements can improve the nutritional status of patients with chronic heart failure who have developed frank malnutrition or are at risk of developing it.

AIMS

Determine the effect of 2-part intervention (dietary recommendations + supplements) over (1) the nutritional status, (2) quality of life and (3) functional capacity in chronic heart failure patients who exhibit malnutrition or the risk thereof after 12 weeks treatment.

MATERIAL AND METHODS

Randomized clinical trial on an intention-to-treat basis. The assessors were blinded and they were unaware the patients group. Patients were randomized 1:1 to 2 groups:

- Intervention arm: A structured educational intervention was provided to the patient and his/her main caregiver. The intervention examined dietary habits and healthy lifestyle. The patient was also given drinkable normal-protein, high-calorie dietary supplements (shakes) to be taken over a period of 12 weeks.
- Control arm: This group received standard treatment: no supplements and no structured educational intervention. The patients received information about dietary habits, from the nurse team and in the discharge report, but never in the same conditions of the intervention group (time, form and dedication)

Inclusion criteria: Patients had to be aged ≥18 years and hospitalized with a diagnosis of chronic heart failure. In addition, they had to be hemodynamically stable with acceptable control of symptoms, to the extent that they were likely to be discharged. Patients had to be in one of the following situations:

- Nonintentional loss of >5% of their body weight without fluid overload during the previous 6 months
- Risk of malnutrition calculated based on the Subjective Global Assessment (SGA)
- Risk of malnutrition according to the Mini Nutritional Assessment (MNA).

Previously we studied the concordance between SGA and MNA in heart failure patients. Our group obtained an acceptable kappa index (0,637). MNA did not show to be predictor of death[3]. The use of the MNA as a second method of nutritional assessment was to contrast the "subjective" burden of the SGA.

In addition, they had to fulfill the following conditions:

- Agree to participate in the study by giving their written informed consent
- Be receiving treatment with ACEIs, angiotensin receptor blockade (ARB), or beta blockers.

Exclusion criteria: Diagnosed active cancer, dementia or severe cognitive impairment, advanced kidney failure with renal replacement therapy, and simultaneous participation in another clinical trial.

Sample size: The sample size was calculated according to the hypothesis that when the follow-up was over, at least

40% more patients in the intervention arm would not have malnutrition than in the control arm. (They will pass from SGA ranting from B or C to A). Given the lack of sufficient evidence, the hypothesis for the calculation was agreed upon by the investigators. A loss of 25% during follow-up was estimated. Result: 33 patients per arm.

Population: Patients were recruited from the cardiology and internal medicine areas, during the in-hospital period. All of them presented compatible diagnostics with acute decompensated of chronic heart failure and presented Framingham criteria for congestive heart failure. They were interviewed, at least, on their third day of admission, most of them after intense diuretic treatment.

Randomization: A random number table was generated for 80 patients in a 1:1 ratio. Identically sized strips of paper were prepared with the word "Control" or "Intervention". The strips were folded in half, placed into opaque envelopes, which were then sealed. Numbers corresponding to the inclusion number were written on the outside of the envelope. The table generated by the randomization program was then destroyed. The envelopes were kept under lock and key.

Outcome measures: No risk of malnutrition according to the SGA and MNA; increased functional capacity measured using the 6-minute walk test; and quality of life, measured using the heart failure–specific quality of life questionnaire Minnesota Living with Heart Failure (MLHF), adapted for use in Spain[17].

Variables: In addition to the outcome measures, we collected anthropometric data (abdominal circumference, hip circumference, calf circumference, degree of swelling in the lower limbs, mid-upper arm circumference and triceps skin fold [both measured at the midpoint between the olecranon and the acromion]), sociodemographic data (educational level), clinical data (left ventricular ejection fraction, diabetes, hypertension, smoking, thyroid disease, pacemaker, New York Heart Association functional class, Charlson comorbidity index, all-cause mortality, and date of death), treatment data (AECIs, ARB, beta blockers, spironolactone, furosemide, lipid-lowering agents), and analytical data (hematocrit, hemoglobin, lymphocytes, Nt-proBNP, total proteins, albumin, creatinine, total cholesterol, LDL, HDL). We also recorded visits to the emergency department during follow-up and days of admission (all-cause) during follow-up.

Intervention: Patients were randomized to one of the groups once it was clear that they understood and agreed to participate in the study, fulfilled the inclusion criteria and none of the exclusion criteria, and gave their written informed consent.

Patients randomized to the intervention group received a 75-minute individualized training session on nutrition with their main caregiver. They were shown strategies to improve their appetite, replace salt, prepare and serve food so that it was more appetizing, perform physical exercise adapted to their functional class, remember to take medication, and to take and store their dietary supplements.

They were also given a 12-week supply of normal-protein, high-calorie nutritional supplements (1 or 2 per day depending on intake); adherence was reported by the patient him/herself or by the main caregiver. Three different beverages were provided, it depends if the patient presented diabetes, chronical kidney failure (no dialysis patients were randomized) or no this comorbidity. All of them were flavored liquid consisting of protein (milk), carbohydrate (maltodextrin and sucrose), vegetable oils (soya, sunflower and linseed oils), minerals, vitamins and trace elements. Patients were informed that the nutritional shakes did not replace but complemented their diet, especially during periods of major anorexia. A summarized composition per bottle is possible to see in Table 1. The control group followed habitual practice.

Follow-up: At 3 month, the assessor (blinded) recorded nutritional status based on SGA and MNA, the result of the 6-minute walk test, the replies to the MLHF questionnaire, anthropometric measurements, and analytical results. Assessors were formed previously in SGA and the degree of inter-observer agreement was assessed using the kappa index, it was achieved a minimum value of 0, 71 (good concordance)

Statistical analysis: Qualitative variables are presented with their frequency distribution. Quantitative variables are expressed as mean (SD). Normality was explored using the Kolmogorov-Smirnov test. Non-normally distributed variables for which the group was fewer than 35 persons were expressed using the median (IQR). The association between qualitative variables was evaluated using contingency tables and the chi-square or Fisher exact test. Quantitative variables were compared using the *t* test. Quantitative variables with

Table 1. Summarized composition per bottle of different beverages.

Co-morbidity	Kcal	Protein (gr)	Fat (gr)	Fatty acid saturated (gr)	Carbohydrate (gr)	Fibre (gr)	Osmolarity (mosmol/l)
Diabetics (D)	300	15	14	1	26.2	4	350-390
KiKidney failure(KF)	250	4.9	12.5	1.2	28.7	0	455
No D-No KF.	300	11.2	11.6	0.8-1	37.6	0.1	325-405

more than 2 categories were compared using analysis of variance. Multiple comparisons were made using a post hoc analysis with a Bonferroni correction. Statistical significance was set at $p<0.05$.

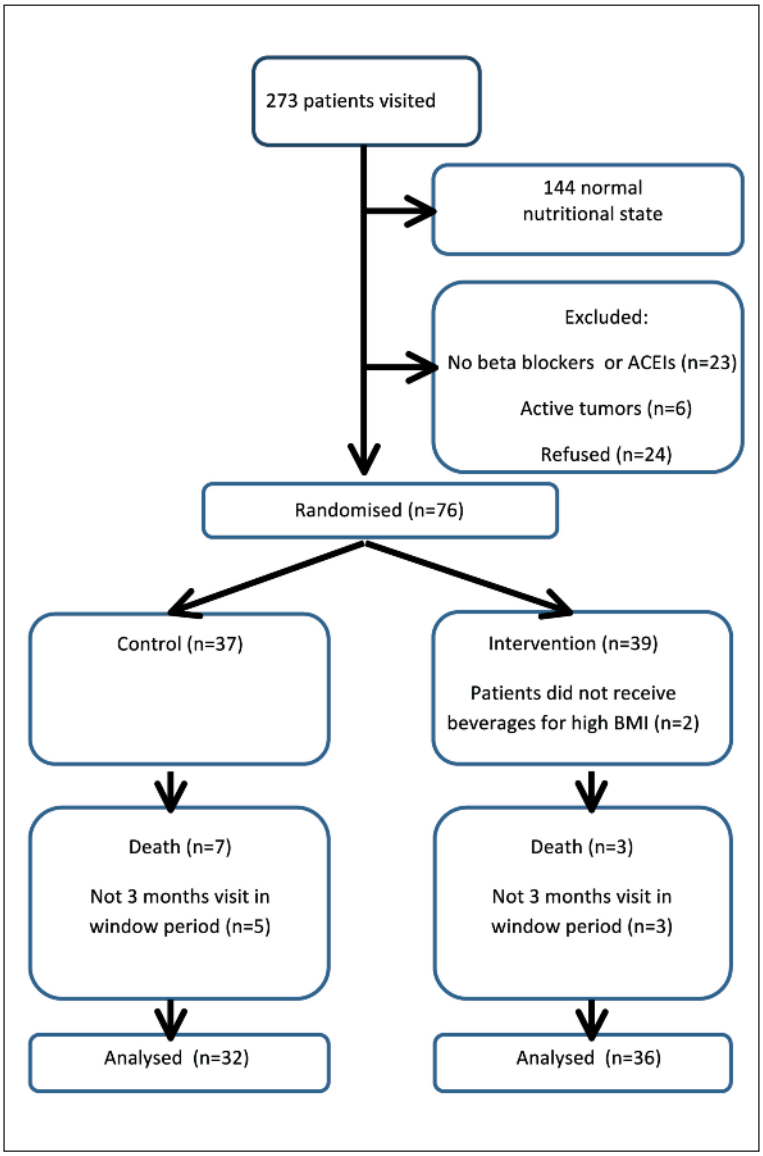
Nutritional status (MNA) and quality of life were evaluated by comparing the means for paired data. Non-normally distributed variables and cases where the groups had more than 35 members were analyzed using nonparametric tests. Significance was set at 5% for all tests of acceptance or rejection of the null hypothesis.

Data were analyzed using SPSS 21.0.

RESULTS

Patients were recruited from 273 visits to the cardiology and internal medicine units. Diagnosis was compatible with decompensated heart failure. The final study population comprised 76 patients. The progress of the 273 patients from baseline is shown in Figure 1.

Figure 1. Progress of patients from baseline.



Women accounted for 52.6% (40) of the study population, mean weight was 61.3 ± 11.4 kg, and the mean body mass index was 24.0 ± 3.7 kg/m^2.

Almost all of those patients who lived at home (69 patients, 90.8%) ate food either they or their family prepared at home. Three patients (3.9%) generally ate in municipal day centers, 2 patients (2.6%) ate food served by the municipal catering service at home, and 1 patient (1.3%) ate in a restaurant every day.

Tables 2, 3 and 4 show the characteristics of the different groups of patients.

Two well-balanced groups were formed after randomization. Differences were detected in the mean triceps skin fold (p=0.032), mid-upper arm fat area (p=0.037), and the lymphocyte count (p=0.02). The mean was lower in all cases in the intervention group. Differences were also found for educational level (p=0.016) and SGA (p=0.004). Nutritional status was more deficient in the intervention group, since it was the group in which more patients had frank malnutrition (35.9% vs 8.1%).

Comparison between the groups at month 3

Patients from both arms died during the first 3 months, and a considerable percentage were considered to have a normal nutritional status. Eight patients did not attend at three months follow-up visit in the window period (5 from the control group and 3 from the intervention group). The only differences between the groups were in abdominal circumference and hip circumference. Neither the MNA nor the SGA revealed differences in nutritional status between the groups. It is important to remember that a difference was recorded at the baseline visit, when the intervention group had poorer nutritional status.

Comparison between the baseline and 3-month visits

Analysis of the control group at baseline and at 3 months reveals increases in the mean result of the 6-minute walk test, quality of life, hemoglobin, hematocrit, total proteins, albumin, and MNA score. The only variable whose value decreased significantly was the waist-hip index, which could be interpreted as a reduction in ascites.

A similar comparison in the intervention group revealed a decrease in the values for abdominal circumference, waist-hip

Table 2. Baseline characteristics of the control and intervention groups.

		Control (n=37)		Intervention (n=39)		p Value
		N	%	N	%	
Sex	Female	20	54.10%	20	51.30%	**0.809**
Lives	Alone	5	13.50%	7	17.90%	**0.383**
	With partner	11	29.70%	7	17.90%	
	With children	20	54.10%	20	51.30%	
	With other family members	1	2.70%	3	7.70%	
	In a nursing home	0	0.00%	2	5.10%	
Hipertension	Yes	29	78.40%	23	59.00%	**0,069**
Diabetes	Yes	22	59.50%	16	41.00%	**0,108**
Smoking status	Do not know/no answer	1	2.70%	1	2.60%	**0.809**
	Ex-smoker	11	29.70%	11	28.20%	
	No	25	67.60%	26	66.70%	
	Yes	0	0.00%	1	2.60%	
Thyroid disease	Hyperthyroidism	2	5.40%	2	5.10%	**0.587**
	Hypothyroidism	8	21.60%	5	12.80%	
	Unknown	27	73.00%	32	82.10%	
Beta blockers	Yes	22	59.50%	17	43.60%	**0,167**
ACEI/ARB	Yes	29	78.40%	33	84.60%	**0,483**
Spirinolactone	Yes	18	48.60%	21	53.80%	**0,65**
Furosemide	Yes	30	81.10%	33	84.60%	**0,683**
Lipid-lowering	Yes	21	56.80%	14	35.90%	**0,068**
Educational level	Do not know/no answer	3	8.10%	2	5.10%	**0.016**
	Secondary or similar	2	5.40%	12	30.80%	
	Primary	30	81.10%	21	53.80%	
	Cannot read	0	0.00%	3	7.70%	
	University	2	5.40%	1	2.60%	
SGA	B Suspected	34	91.90%	25	64.10%	**0.004**
	C Malnutrition	3	8.10%	14	35.90%	

Table 2 continuación. Baseline characteristics of the control and intervention groups.

		Control (n=37)		Intervention (n=39)		p Value
		N	%	N	%	
NYHA class	1	1	2.70%	0	0.00%	**0.103**
	2	12	32.40%	13	33.30%	
	3	16	43.20%	24	61.50%	
	4	8	21.60%	2	5.10%	
LVEF	>50%	14	37,80%	19	48.7%	**0.200**
	35-50%	9	24,30%	8	20,50%	
	< 35%	14	37,80%	12	30,80%	
Edemas	0	12	32.40%	16	41.00%	**0.240**
	1	6	16.20%	12	30.80%	
	2	10	27.00%	4	10.30%	
	3	6	16.20%	4	10.30%	
	4	3	8.10%	3	7.70%	

index, and calf circumference. This difference can be interpreted as a reduction in edema and ascites. The variables whose values increased were triceps skin fold, mid-upper arm fatty area, 6-minute walk test, quality of life, MNA score, hemoglobin, hematocrit, albumin, lymphocytes, total cholesterol, HDL cholesterol, and LDL cholesterol. Of note, mean LDL cholesterol was 82 mg/dl, which was below the objective set for patients with ischemic heart disease.

The mortality adjusted by LVEF and by initial NYHA classification, did not demonstrate differences in survival days.

In summary:

1. The only difference in nutritional status measured using SGA was found between the baseline visit and month 3 in the intervention group, in which the patients' status improved. Nutritional status improved 2-fold in the intervention group and worsened only by only half, compared with the control group. This finding can be interpreted as a 4-fold greater magnitude of change. The improvement was statistically significant. No difference between the visits was observed for the control group (see Table 5 and figures 2 and 3).

2. Quality of life improved in both groups (statistically significant difference). The degree of difference in the means was greater in the intervention group for all the parameters except hemoglobin and hematocrit.

3. Functional capacity improved in both groups (statistically significant difference); the improvement was greater in the intervention group. In the 6-minute walk test, the intervention group increased the distance covered by 97 m compared with 85 m in the control group.

The intervention group improved in all the variables in which the control group improved—except for mean total proteins—and in parameters associated with energy reserves, namely, triceps skin fold, mid-upper arm fat area, and cholesterol.

DISCUSSION

The negative impact on nutrition in patients with heart failure is multifactorial, yet no clear approach to resolving this vicious cycle has been proposed. Evaluating a patient's nutritional status is not easy, especially in heart failure, where weight can be masked by water retention. Fluctuations in weight do not always correspond to modifications in energy reserves. In our experience, of the 2 methods of evaluating nutritional status, only SGA was associated with survival[3].

The prevalence of malnutrition —understood as a disorder of body composition characterized by excess extracellular wa-

Table 3. Measurements of quantitative variables in the different visits expressed with the mean and SD or median and interquartile range. The p value of the different possible combinations observed.

	CONTROL			INTERVENTION			P value for group	
	baseline	3 months	p value (baseline VS 3 m)	baseline	3 months	p value (baseline VS 3 m)	baseline	3 m
Age (y)	76 (8)			76 (11)			0,912	
Weight (Kg)	62,8 (11,39)	62,72 (11,49)	0,994	60,03 (11,56)	58,7 (10,16)	0,181	0,296	0,161
Height (m)	1,59 (0,08)	1,58 (0,08)	0,971	1,6 (0,08)	1,59 (0,08)	0,942	0,884	0,848
BMI (Kg/m2)	24,65 (3,41)	24,92 (3,58)	0,972	23,53 (3,92)	23,3 (3,84)	0,49	0,187	0,105
Calf circumference (cm)	32,35 (3,64)	31 (3)*	0,541	31,45 (4,04)	31 (3)*	0,009	0,313	0,098*
Abdominal circumference (cm)	99,49 (10,15)	96,52 (13,64)	0,664	95,11 (14,33)	89,81 (10,56)	0,424	0,141	0,041
Hip circumference (cm)	99,4 (9,35)	98,64 (9,02)	0,071	98,55 (12,2)	93,55 (7,72)	0,005	0,743	0,026
Waist-hip ratio	1 (0,07)	0,98 (0,1)	0,036	0,97 (0,09)	0,96 (0,08)	0,016	0,051	0,467
Triceps skin fold (cm)	25,01 (3,46)	24 (6)*	0,829*	23,63 (4,08)	23 (3)*	0,448*	0,118	0,168*
Tricipital fat(mm)	14,65 (5,14)	16 (9)*	0,821	11,85 (5,98)	11,5 (5,5)*	0,043	0,032	0,14*
Arm area (mm2)	5071 (1472)	5160 (1726)	0,218	4573 (1722)	4610 (1470)	0,051	0,183	0,200
Mid-upper arm muscle area (mm2)	3376 (985)	3438 (1140)	0,176	3261 (1091)	3195 (880)	0,363	0,634	0,366
Mid-upper arm fat area (mm2)	1694 (723)	1721 (814)	0,218	1311 (830)	1415 (826)	0,007	0,037	0,169
Nt proBNP (pg/ml)	11275 (14689)	3036 (4036)*	0,238*	7953 (11268)	2561 (2330)*	0,383*	0,298	0,611*
Hemoglobin (g/dl)	11,22 (1,78)	12,3 (1,56)	0,012	11,12 (1,72)	11,81 (1,84)	0,009	0,791	0,271
Hematocrit (%)	34,52 (5,09)	37,6 (4,78)	0,016	33,84 (5,69)	35,99 (5,58)	0,005	0,585	0,238
Proteins (g/l)	6,26 (1,27)	7,01 (0,88)	0,007	6,58 (0,76)	6,8 (0,72)	0,235	0,184	0,157
Albumin (g/l)	3,44 (0,8)	4,13 (0,43)	0,001	3,54 (0,49)	3,94 (0,55)	0,001	0,498	0,190
Lymphocytes, (x106/l)	1405 (750)	1470 (615)	0,951	1061 (481)	1270 (609)	0,022	0,020	0,210
Creatinine (mg/dl)	1,57 (0,8)	1,51 (0,89)*	0,889*	1,36 (0,66)	1,21 (0,63)*	0,584*	0,227	0,102*
Total Cholesterol (mg/dl)	131 (33)	144 (31)	0,501	132 (27)	153 (39)	0,002	0,946	0,421
HDL Cholesterol (mg/dl)	40 (16)	50(14)	0,053	45 (10)	52 (18)	0,036	0,139	0,816
LDL Cholesterol (mg/dl)	70 (27)	77 (30)	0,63	73 (23)	81 (29)	0,04	0,614	0,719
Minnesota	54,3 (12,5)	34,9 (16,5)	0,001	52,8 (15,9)	27,5 (16,2)	0,001	0,678	0,105
MNA	19,1 (2,8)	23,3 (4,8)	0,001	18,9 (4,3)	22,9 (3,4)	0,001	0,803	0,729
6 minutes walk test (m)	105,2 (112,5)	199,5 (139,4)	0,001	123,1 (92,2)	239,1 (123,9)	0,001	0,450	0,261
Charlson index	6,9 (1,7)			7,3 (2,4)			0,442	

*The marked variables not normally distributed. They are expressed with the median and interquartile range. The p value comes from nonparametric tests.

Table 4. Ranges table from baseline and 3 months follow-up.

Study group			N	Mean of ranges	Sum of ranges	Z	p Valor
Control	SGA Month 3 SGA Baseline	Negative ranges	9 a	15.33	138.00	–.389	0.697
		Positive ranges	13 b	8.85	115.00		
		Draws	10 c				
		Total	32				
Intervention	SGA Month 3 SGA Baseline	Negative ranges	4 a	15.00	60.00	–4.004	<0.001
		Positive ranges	26 b	15.58	405.00		
		Draws	6 c				
		Total	36				

a. SGA Month 3 < SGA Baseline. b. SGA Month 3 > SGA Baseline. c. SGA Month 3 = SGA Baseline.

Figure 2. Nutritional evolution intervention group.

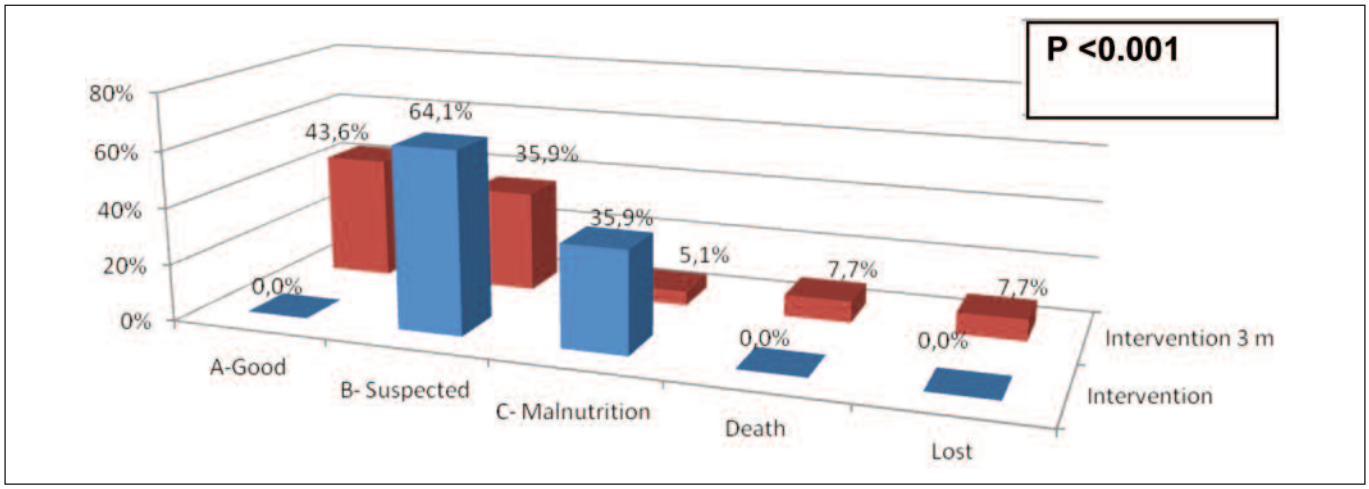
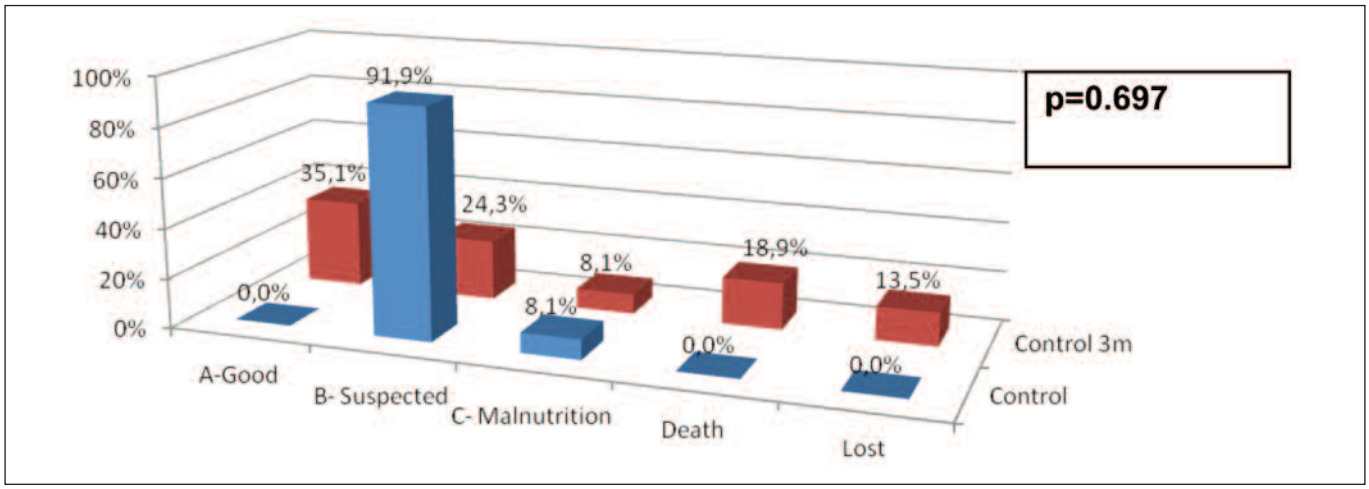


Figure 3. Nutritional evolution control group.



ter, reduced potassium, muscle mass, and fatty tissue, and an association with hypoproteinemia[18]— is high in hospitalized patients with chronic heart failure. It is necessary to perform an appropriate evaluation of nutritional status, administer appropriate pharmacologic and nutritional therapy, encourage physical exercise adapted to the patient's functional class, and ensure that the patient is closely monitored[19]. Nutritional education[20] and early nutritional interventions in critically ill patients seem to be beneficial in the case of enteral nutrition and parenteral nutrition, depending on the patient's individual condition[21]. It seems logical for approaches to this problem to be made on several levels to prove effective. In patients with malnutrition, and even more so in cases of cardiac cachexia, the oral diet should be modified in terms of energy and quality, and the option of specific dietary supplements should be considered[19]. A Cochrane review showed that double nutritional interventions (recommendations plus supplements) are more effective than either of the 2 alone or neither, especially in patients with a BMI <20 kg/m^2,[22]. The few clinical trials that evaluate energy diets in chronic heart failure reveal an increase in body weight, with variable effects on function[23]. Trying to modulate the inflammatory response alone has proven ineffective[24]. Intensification of treatment with ACEIs and beta blockers has been shown to improve the prognosis of patients with heart failure[25]. However, heart failure cannot be addressed by merely adhering to pharmacologic treatment guidelines[26]. The role of lipid-lowering drugs in patients with cardiac cachexia is controversial and should be analyzed carefully in purpose-designed studies[27].

Although groups did not differ in the global LVEF, there were differences in the distribution. The control group had fewer individuals with normal LVEF. Not in all series, the LVEF was clearly associated with nutritional status[28,3]. The right heart failure is associated with a worse nutritional status for the implications with the digestive and absorption process[29,30].

The problem of malnutrition in chronic heart failure affects the patient at multiple levels. Consequently, it seems that the only way to address this problem is through interventions aimed at several levels of nutritional status.

CONCLUSIONS

Recommendations on nutrition accompanied by normal-protein, high-calorie nutritional supplements and ACEIs/ARB or beta blockers can improve nutritional status measured using SGA in patients with heart failure at 3 months.

LIMITATIONS

Nutritional interventions could be effective for a limited period, and we do not really know up to which point it is necessary to continue monitoring and recommending supplements. Similarly, we do not know the relevance of each component: we cannot say what proportion is due to the recommendations given, the motivation a patient gains from feeling "cared for", how this can affect adherence to pharmacologic and dietary treatment, or to the nutritional supplements themselves.

Unfortunately, the peculiarities of randomization subtract value from our study, since both groups started from very different positions with respect to one of the parameters of evaluation, namely, classification of nutritional status based on SGA. We were almost unable to demonstrate differences between the groups at the visits, although we were able to demonstrate that the improvement in individuals from the intervention group was 4-fold greater than that of the control group.

It will be necessary for patients to complete the follow-up period to determine whether these effects persist over time.

FUNDING

This study was funded by the Instituto de Salud Carlos III, Ministry of Health with a grant of €11,192 (No. PI11/02428). Co-financed help by the European Regional Development Fund ERDF. "A Way of Making Europe".

ETHICS

The study was performed according to the stipulations of the Declaration of Helsinki and received the appropriate ethics committee approval. The trial is registered in ClinicalTrials.gov (NCT02599935).

In the case of the intervention group, the advice given and the nutritional supplements administered (in terms of both presentation and amount) are not subject to precedents that would lead us to envisage negative effects. In the case of the control group, no changes were made with respect to the habitual practice.

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