

The Relationship Between Biochemical Variables and the Quality of Life in Patients with Chronic Heart Failure

CARMEN ELENA PLESOIANU^{1,2}, GABRIELA ANDRIESCU², DELIA SALARU^{1,2*}, CATALINA ARSENESCU GEORGESCU^{1,2}

¹ Institute of Cardiovascular Diseases George I. M. Georgescu, 50 Carol I Blvd., 700503, Iasi, Romania

² Grigore T. Popa University of Medicine and Pharmacy, 16 Universitatii Str., 700115, Iasi, Romania

The aims of this paper were to assess the quality of life with the use of the SF36 Questionnaire in patients with chronic heart failure and to establish the relationship between specific biochemical variables and the various aspects of the quality of life. The scores for various components of the quality of life were significantly affected by hemoglobin levels, creatinine clearance, fibrinogen levels and gamma-glutamyl-transferase levels, while lipid fractions and liver enzymes did not prove to have a significant impact on the quality of life.

Keywords: biochemical variables, quality of life, heart failure

Health-related quality of life (HRQL) assessment has increasingly come to the attention of medical researchers during the past 4 decades, as it reflects the multi-dimensional impact of the disease, its treatment, and other variables on patient's lives [1]. If during the 50s and 60s it was considered that the quality of life was mainly linked to the severity of the disease and the effectiveness of pharmacological treatment, it has been recently proved that the patient's subjective perspective of well-being is a significantly better predictor of morbidity and mortality than the evaluation of physiological variables [2]. As the objective measures focus on cells, organs, and organ systems, the assessment of symptom status is a humanistic and holistic approach. Improving the quality of life holds particular appeal as a target for interventions in chronic heart conditions, such as chronic heart failure [3, 4]. The cardinal importance of the disease results from its bad prognosis and increasing occurrence due to the aging of population. Chronic heart failure also involves high economic costs as it is the most common cause of hospital admissions for older adults [5]. Patients with heart failure experience various physical and emotional symptoms such as dyspnea, fatigue, edema, depression, sleeping difficulties and chest pain [6, 7]. These symptoms have an important impact on daily physical and social activities and result in poor QOL. Poor QOL is related to high hospitalization and mortality rates [8, 9].

Experimental part

A number of 55 female patients, admitted and investigated for chronic heart failure in the Cardiovascular Diseases Institute George I. M. Georgescu during month June 2017 participated in this prospective study. Inclusion criteria were a diagnosis of confirmed heart failure, New York Heart Association functional classes (NYHA) I to IV, and ability to speak Romanian. Exclusion criterion was severe psychiatric or cognitive problems. The diagnosis of heart failure was confirmed by medical record reviews. We obtained the informed consent for participation in this study from all patients after explanation of the purpose and procedure of the study.

The patients aged between 42 and 86 years. To assess quality of life, we used the Short-Form Health Survey (SF-36). This instrument was developed in 1992 by Ware and Sherbourne and validated in Brazil by Ciconelli et al [10]. The results were calculated by attributing scores to each

question, which were then transformed into a scale ranging from 0 to 100, where 0 corresponds to the worst quality of life and 100 to the best. Each dimension was analysed separately. The questionnaire measures 8 health domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health.

The statistical data was processed with SPSS 18.0. The results are presented as percentage or mean \pm SD. For the continuous variables, we used Student's unpaired t-test to compare two groups, and ANOVA to compare more than two groups. Whenever the ANOVA test result was significant, we then compared the groups two by two. Pearson's correlation test was employed to correlate two variables from the same group. The Kruskal-Wallis test is used for comparing ordinal variables for more than two groups. Statistical significance was set at $p < 0.05$.

Results and discussions

Glomerular filtration rate (GFR) was estimated by the creatinine clearance according to the Cockcroft and Gault [10] formula, using the serum creatinine measurement available for each patient. The stages of CKD were classified as suggested by the Kidney Disease Outcomes Quality Initiative and are presented in table 1.

When assessing the quality of life, according to the domains of the SF-36, we found a statistically significant effect of the creatinine clearance on the scores of the SF-36 questionnaire on the items physical functioning ($p=0.001$), role physical ($p=0.01$), vitality ($p=0.02$), bodily pain ($p=0.005$) and general health ($p=0.017$).

The Role Emotional component of the SF-36 questionnaire recorded the lowest scores, with an average of 8.33 for the patients with a creatinine clearance ranging from 30-15 mL/min. Patients with creatinine clearance above 90 mL / min were found to have average physical activity values four times higher than the mean values for patients with creatinine clearance between 30-15 mL / min. The highest values were recorded for the score evaluating the social functioning both in patients with creatinine clearance above 90 mL / min (median 81.25) and in patients with creatinine clearance between 30- 15 mL / min (averaging 53.13). A study by Alan S. Go et al on 59,772 adults followed for 2 years, demonstrated a predictive value of chronic renal disease for cardiovascular mortality in patients with chronic heart failure [11] (table 2, fig. 1).

* email: deliasalaru@gmail.com, Phone: (+40)759161971

Stage of CKD	Glomerular filtration rate (ml/min)	Description
1	≥ 90	Kidney damage with normal renal function
		Presence of proteinuria
2	60–89	Kidney damage with small decrease in GFR
3	30–59	Kidney damage with moderate decrease in GFR
4	15–29	Kidney damage with large decrease in GFR
5	<15	Kidney failure, end-stage renal disease

Table 1
STAGES OF CHRONIC KIDNEY DISEASE

Quality of life domains	Creatinine Clearance						FANOVA test (p)
	> 90	60-90	45-60	30-45	15-30	< 15	
Physical function	60.00	57.74	32.00	69.67	13.75	-	0.001
Role physical	37.50	48.390	33.33	33.33	18.75	-	0.106
Role emotional	16.67	44.07	13.33	22.22	8.33	-	0.010
Vitality	47.50	47.90	32.67	36.67	17.50	-	0.020
Mental health	60.00	53.77	46.67	42.67	27.00	-	0.155
Social functioning	81.25	69.35	61.67	79.17	53.13	-	0.612
Bodily pain	56.25	59.29	32.17	27.50	35.00	-	0.005
General health	52.50	54.58	36.00	28.33	35.00	-	0.017

Table 2
THE RELATIONSHIP BETWEEN CREATININE CLEARANCE AND QUALITY OF LIFE

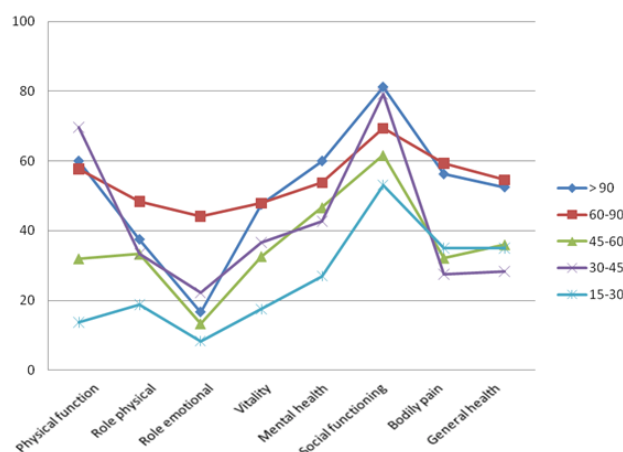


Fig.1. The relationship between quality of life scores and the Creatinine Clearance

AST and quality of life

27.3% of patients had individual values above the baseline (5-40 U/l).

The SF36 scores did not differ significantly according to levels of AST enzyme (fig. 2, table 3).

ALT and quality of life

The relationships between the ALT levels and various domains on the SF-36 questionnaire are summarized in table 4. ALT levels were grouped into two categories (<40 U/mL and >40 U/mL). The values have been adjusted

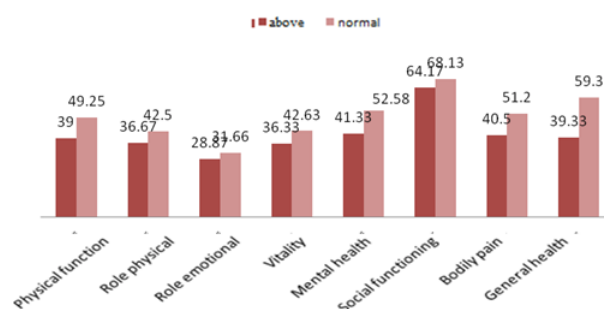


Fig. 2. Mean Values for QoL scores according to AST levels

for age, gender and race. 9.1% of the patients had individual values above the reference interval. (7-56 U/l). The correlation between the high level of ALT and the quality of life was not statistically significant ($p > 0.05$) (table 4, fig. 3)

Gamma-glutamyl-transferase (GGT)

49.1% of the patients had individual values of GGT above the reference interval (7-32 U/l). The relationship between high levels of GGT enzyme and quality of life was statistically significant regarding the following items: role functioning (34.26 vs 47.32; $p=0.05$) and bodily pain (39.93 vs 56.34; $p=0.021$) (table 5, fig.4).

Quality of Life domains	High values (n=15)	Normal values (n=40)	t-Student (p)
Physical function	39.00±27.27	49.25±23.58	0.175
Role physical	36.67±31.15	42.50±22.79	0.449
Role emotional	28.87± 30.51	31.66± 32.86	0.777
Vitality	36.33±22.16	42.63±20.60	0.327
Mental health	41.33±22.86	52.58±20.52	0.085
Social functioning	64.17±27.09	68.13±29.00	0.648
Bodily pain	40.50±31.72	51.20±24.25	0.187
General health	39.33±20.86	59.30±21.47	0.128

Table 3
THE RELATIONSHIP BETWEEN AST AND QOL SCORES

Quality of life domains	High values (n=5)	Normal values (n=50)	t-Student (p)
Physical function	39.99± 27.10	48.25 ± 23.33	0.486
Role physical	36.98±21.01	42.50 ± 22.20	0.587
Role emotional	38.87 ± 30.51	31.66 ± 32.86	0.759
Vitality	40.10± 22.16	42.64±20.01	0.749
Mental health	41.13± 22.88	52.58 ± 20.00	0.305
Social functioning	66.37 ±20.09	68.13 ± 29.13	0.710
Bodily pain	49.52±24.72	51.20 ± 24.25	0.370
General health	47.22±18.86	59.30 ± 21.47	0.782

Table 4
THE RELATIONSHIP BETWEEN ALT AND
QOL SCORES

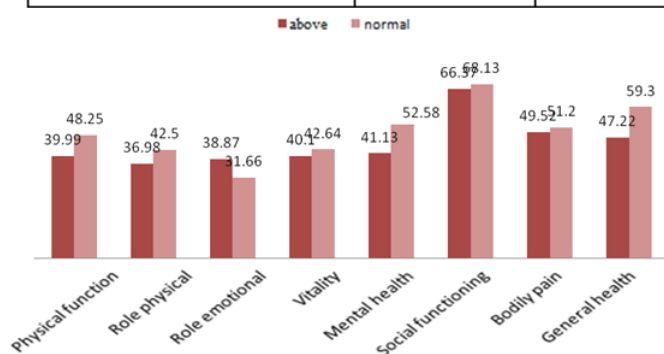


Fig. 3. Mean scores of QoL components associated with ALT levels

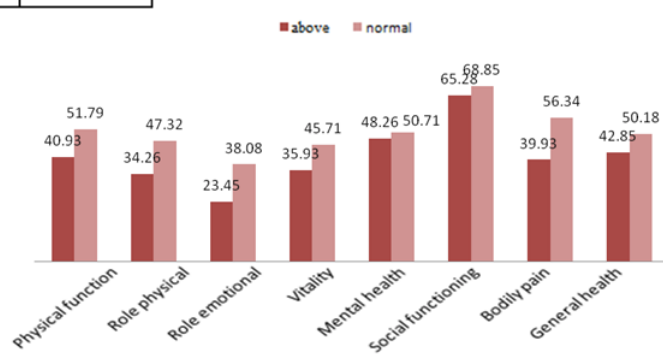


Fig. 4. The relationship between GGT and the scores for quality of life items

Lipidic Profile

Triglycerides and the quality of life

27.3% of the patients had individual values above the baseline (< 150 mg/dL). The SF36 scores did not differ significantly according to levels of triglycerides ($p>0.05$) (table 6, fig 5).

LDL-cholesterol and the quality of life

70.9% of the patients had individual values above the baseline (< 70 mg/dL). The association between high levels of LDL-cholesterol and the quality of life was not statistically significant ($p>0.05$) (fig. 6, table 7).

HDL-cholesterol and the quality of life

HDL-cholesterol levels were grouped into two categories (<46 mg/dL and >46mg/dL). 52.7% of the patients had individual values under the baseline (>46 mg/dL). The SF36 scores did not differ significantly according to HDL-cholesterol levels($p>0.05$) (fig. 7, table 8).

Less than half of the patients with chronic heart failure achieved the target for LDL cholesterol and HDL -cholesterol. Hyperlipidemia is a well-documented adjustable risk-factor in patients with heart failure. The increased risk is associated with high levels of LDL-cholesterol(>70mg/dL) correlated with low levels of HDL-cholesterol (less than 40mg/dL) [12-14]. The relationship

Quality of life domains	High levels (n=27)	Normal levels (n=28)	t-Student (p)
Physical function	40.93±26.61	51.79±24.24	0.105
Role physical	34.26±20.97	47.32±27.50	0.050
Role emotional	23.45± 30.51	38.08±34.79	0.090
Vitality	35.93±20.24	45.71± 20.98	0.084
Mental health	48.26± 22.63	50.71±20.83	0.677
Social functioning	65.28±29.28	68.85±27.74	0.653
Bodily pain	39.93±21.48	56.34±28.92	0.021
General health	42.85±20.51	50.18±2.34	0.211

Table 5
RELATIONSHIP BETWEEN GGT AND QUALITY OF LIFE

Table 6
RELATIONSHIP BETWEEN TRIGLYCERIDES AND QUALITY OF LIFE

High values (n=15)	Normal values(n=40)	t-Student (p)
51.00 ± 20.89	44.75 ± 26.16	0.410
40.00 ± 29.58	41.25 ± 23.72	0.871
28.88 ± 30.51	31.66 ± 32.86	0.777
43.33 ± 21.10	40.00 ±21.18	0.605
48.53 ± 19.06	49.88 ± 22.65	0.839
67.67 ± 23.08	63.44 ± 29.47	0.124
47.67 ± 28.64	48.51 ± 26.21	0.918
49.67 ± 23.18	45.43 ± 21.14	0.521

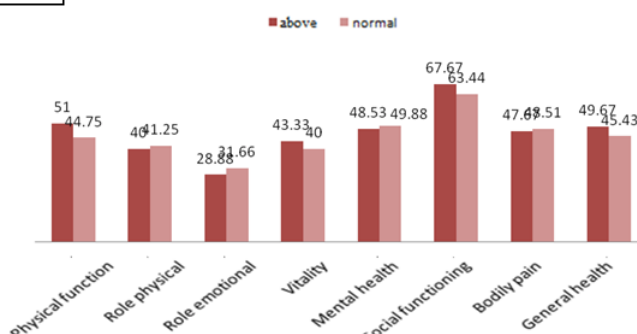


Fig. 5. Mean SF-36 scores according to triglycerides levels

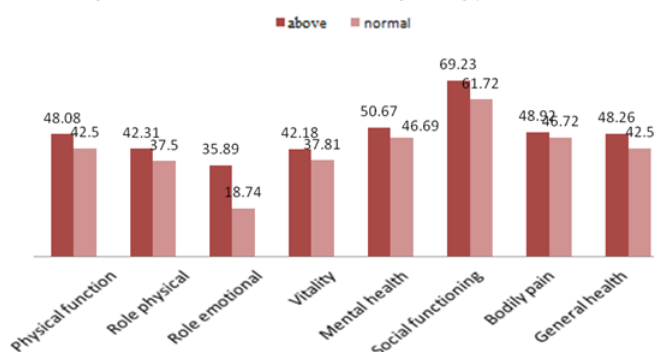


Fig. 6. Mean values for SF-36 scores according to LDL-cholesterol levels

Quality of life domains	High levels (n=39)	Normal values (n=16)	t-Student (p)
Physical function	48.08 ± 26.72	42.50 ± 19.58	0.454
Role physical	42.31 ± 26.99	37.50 ± 20.41	0.525
Role emotional	35.89 ± 33.67	18.74 ±14.24	0.071
Vitality	42.18 ± 21.61	37.81 ± 19.83	0.489
Mental health	50.67 ± 20.71	46.69 ± 24.00	0.539
Social functioning	69.23 ± 28.08	61.72 ± 29.04	0.376
Bodily pain	48.92 ± 25.59	46.72 ± 29.82	0.783
General health	48.26 ± 21.54	42.50 ± 21.83	0.374

Table 7
RELATIONSHIP BETWEEN QUALITY OF LIFE AND LDL-CHOLESTEROL

Quality of life domains	Reduced values (n=29)	Normal values (n=26)	t-Student (p)
Physical function	40.86 ± 24.64	52.69 ± 23.93	0.454
Role physical	36.21 ± 24.63	46.15 ± 25.19	0.525
Role emotional	29.87 ± 32.54	32.04 ± 31.94	0.071
Vitality	38.79 ± 20.02	43.27 ± 22.22	0.489
Mental health	47.86 ± 20.77	51.35 ± 22.69	0.539
Social functioning	62.07 ± 30.34	75.60 ± 25.25	0.376
Bodily pain	43.19 ± 27.44	53.96 ± 24.98	0.783
General health	41.28 ± 21.14	52.50 ± 20.89	0.374

Table 8
THE RELATIONSHIP BETWEEN HDL-CHOLESTEROL
AND THE QUALITY OF LIFE

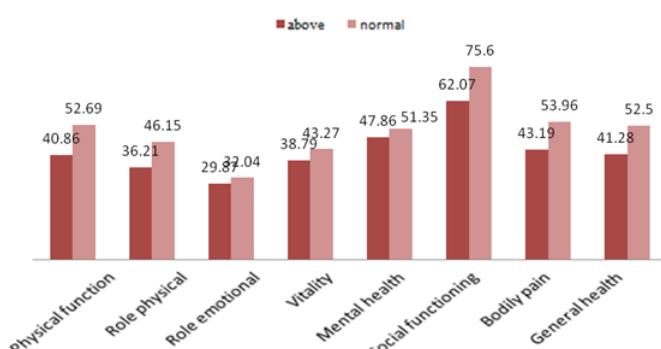


Fig. 7. Mean SF-36 scores according to HDL-cholesterol levels

between the two lipidic fractions and the quality of life was not statistically significant.

Hemoglobin and the Quality of life

Anemia is an important co-morbidity in patients with chronic heart failure, with a prevalence of appropriately 30% among these patients [15,16]. Anemia can lead to a variety of symptoms similar to those of heart failure, such as vertigo, tachycardia or dyspnea. BC Kraai et al demonstrate in a recently published study that anemia is an important factor influencing the quality of life in patients

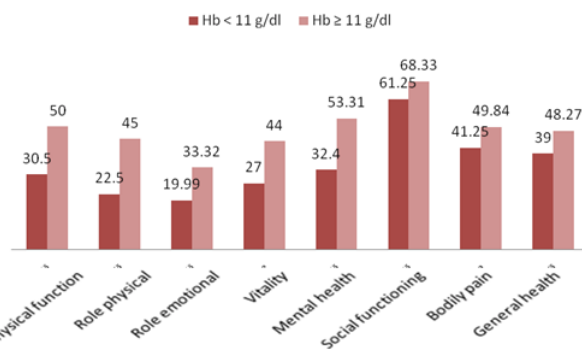


Fig. 8. Mean values for quality of life scores according to Hb levels

hospitalized for heart failure, with a particularly significant impact on social functioning and general health status [13]. Nearly one fifth of the patients included in our study had anemia.

The relationships between the Hgb levels and various domains on the SF-36 questionnaire are summarized in table 9. Hgb levels were grouped into two categories (<11 g% and ≥11 g%). The values have been adjusted for age, gender and race, and there are no significant differences between the two groups, regarding these variables. A significant association was identified between

Quality of life domains	Hb < 11 g/dl (n=10)	Hb ≥ 11 g/dl (n=45)	t-Student (p)
Physical function	30.50 ± 21.40	50.00 ± 24.31	0.023
Role physical	22.50 ± 18.45	45.00 ± 24.77	0.009
Role emotional	19.99 ± 7.36	33.32 ± 4.97	0.037
Vitality	27.00 ± 115.31	44.00 ± 20.99	0.019
Mental health	32.40 ± 18.52	53.31 ± 20.48	0.005
Social functioning	61.25 ± 33.05	68.33 ± 27.39	0.479
Bodily pain	41.25 ± 12.54	49.84 ± 28.71	0.361
General health	39.00 ± 19.26	48.27 ± 21.90	0.050

Table 9
THE RELATIONSHIP BETWEEN HEMOGLOBIN
AND THE QUALITY OF LIFE

Quality of life domains	Above (n=30)	Normal (n=25)	t-Student (p)
Physical function	44.50 ± 23.83	48.80 ± 26.23	0.527
Role physical	39.17 ± 26.00	43.00 ± 24.45	0.579
Role emotional	24.44 ± 30.23	38.65 ± 32.88	0.101
Vitality	40.50 ± 18.07	41.40 ± 24.47	0.876
Mental health	49.97 ± 20.99	48.96 ± 22.67	0.865
Social functioning	69.58 ± 29.30	64.00 ± 27.32	0.471
Bodily pain	46.33 ± 24.85	50.62 ± 28.95	0.557
General health	44.23 ± 21.31	49.40 ± 22.00	0.382

Table 10
THE RELATIONSHIP BETWEEN ESR VALUES
AND THE QoL

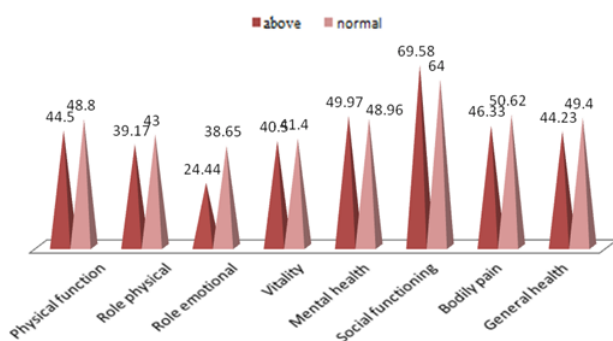


Fig. 9. Mean QoL scores correlated with the ESR values

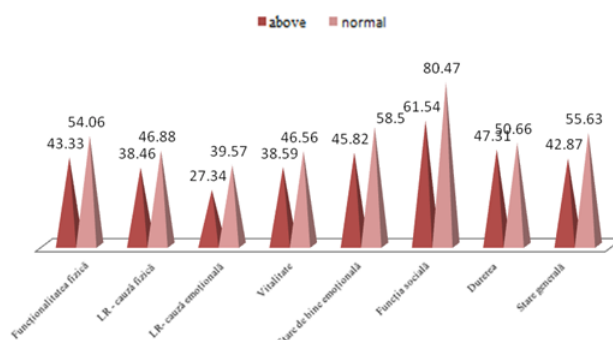


Fig. 10. Mean QoL scores correlated with the ESR values

Quality of life domains	Above (n=39)	Normal (n=16)	t-Student (p)
Physical function	43.33 ± 24.74	54.06 ± 24.03	0.147
Role physical	38.46 ± 22.83	46.88 ± 30.10	0.264
Role emotional	27.34 ± 29.48	39.57 ± 36.95	0.200
Vitality	38.59 ± 20.96	46.56 ± 20.71	0.204
Mental health	45.82 ± 21.77	58.50 ± 18.76	0.047
Social functioning	61.54 ± 30.13	80.47 ± 17.66	0.023
Bodily pain	47.31 ± 25.59	50.66 ± 29.73	0.676
General health	42.87 ± 20.56	55.63 ± 21.98	0.045

Table 11
THE RELATIONSHIP BETWEEN FIBRINOGEN VALUES
AND THE QOL

Hgb levels and the following components of the SF-36: physical functioning (30.50 vs 50; $p=0.023$), role physical (22.50 vs 45; $p=0.009$), role emotional (19.99 vs 33.32; $p=0.037$), vitality (27 vs 44; $p=0.019$), mental health (32.40 vs 53.31; $p=0.005$) and general health (39 vs 48.27; $p=0.05$) (fig. 8).

The relationship between erythrocyte sedimentation rate (ESR) and the quality of life

The relationship between the ESR levels and the domains of the quality of life are summarized in table 10.

ESR levels were grouped into two categories ($<13\text{mm/h}$ and $>13\text{mm/h}$). 54.5% patients presented individual values above the baseline. There was no significant association between ESR values and the quality of life ($p>0.05$) (fig. 9).

Association between fibrinogen values and the quality of life

Fibrinogen levels were grouped into two categories ($<400\text{mg/dL}$ and $>400\text{mg/dL}$). 70.9% had individual values above the reference interval (200-400 mg/dL). A

significant association was identified between fibrinogen levels and the following components of the SF-36: mental health (45.82 vs 58.50; $p=0.047$); social functioning (61.54 vs 80.47; $p=0.023$); general health (42.87 vs 55.63; $p=0.045$).

In figure 10 and table 11 is shown the relationship between the high level of fibrinogen and the quality of life.

Conclusions

There are statistically significant differences for certain components of the quality of life in anemic patients versus those without anemia. Anemic patients have significantly lower scores for almost all components of quality of life, without adversely affecting the social functioning and bodily pain.

There are statistically significant differences in certain components of the quality of life score based on creatinine clearance. Patients with creatinine clearance below 15 ml/min have lower values for the following items of quality of life: physical functioning, role emotional, vitality, bodily pain, general health.

There are no significant differences in quality of life between patients with elevated values of liver enzymes and those with normal values.

Our study did not show a better quality of life in patients with levels of lipid fractions within the reference range compared to those outside the reference range.

Regarding the inflammatory syndrome, patients with fibrinogen levels above the reference interval associated significantly lower scores for the following components of the QoL: mental health, social functioning and general health.

References

1. ***Post MW. Definitions of quality of life: what has happened and how to move on. Topics in spinal cord injury rehabilitation. 2014;20(3):167-80.
2. PENNACCHINI M, BERTOLASO M, ELVIRA MM, DE MARINIS MG. A brief history of the Quality of Life: its use in medicine and in philosophy. Clin Ter. 2011;162(3):e99-e103.
3. JUENGER J, SCHELLBERG D, KRAEMER S, et al. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. Heart 2002;87(3):235-241.
4. HOEKSTRA T, JAARSMA T, VAN VELDHUISEN DJ, HILLEGE HL, SANDERMAN R, LESMAN-LEEGTE I. Quality of life and survival in patients with heart failure. European Journal of Heart Failure 2013 Jan;15(1):94-102.

5. KONSTAM V, SALEM D, POULEUR H, KOSTIS J, GORKIN L, SHUMAKER S, MOTTARD I, WOODS P, KONSTAM MA, YUSUF S. Baseline quality of life as a predictor of mortality and hospitalisation in 5,025 patients with congestive heart failure. American Journal of Cardiology 1996;78:890-895.
6. NORDGREN L, SORENSEN S. Symptoms experienced in the last six months of life in patients with end-stage heart failure. Eur J Cardiovasc Nurs. 2003 Sep;2(3):213-217. [PubMed]
7. ZAMBROSKI CH, MOSER DK, BHAT G, ZIEGLER C. Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. Eur J Cardiovasc Nurs. 2005 Sep;4(3):198-206.
8. ALLA F, BRIANCON S, GUILLEMIN F, JUILLIERE Y, MERTES PM, VILLEMOT JP, ZANNAD F. Self-rating of quality of life provides additional prognostic information in heart failure. Insights into the EPICAL study. Eur J Heart Fail. 2002 Jun;4(3):337-343. [PubMed]
9. KONSTAM V, SALEM D, POULEUR H, KOSTIS J, GORKIN L, SHUMAKER S, MOTTARD I, WOODS P, KONSTAM MA, YUSUF S. Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. SOLVD Investigations. Studies of Left Ventricular Dysfunction Investigators. Am J Cardiol. 1996 Oct 15;78(8):890-895.
10. CICONELLI RM, FERRA MB, SANTOS W, MEINAO I, QUARESMA MR. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36) Rev Bras Reumatol. 1999;39(3):143-150.
11. GO AS, YANG J, ACKERSON LM, LEPPER K, ROBBINS S, MASSIE BM, SHLIPAK MG. Hemoglobin level, chronic kidney disease, and the risks of death and hospitalization in adults with chronic heart failure: the Anemia in Chronic Heart Failure: Outcomes and Resource Utilization (ANCHOR) Study. Circulation. 2006 Jun 13;113(23):2713-23.
12. NELSON RH. Hyperlipidemia as a Risk Factor for Cardiovascular Disease. Primary care 2013;40(1):195-211.
13. OUATU A, TANASE DM, FLORIA M, IONESCU SD, AMBARUS V, ARSENESCU-GEORGESCU C. Chronic kidney disease: Prognostic marker of nonfatal pulmonary thromboembolism. Anatol J Cardiol. 2015 Nov;15(11):938-43. doi: 10.5152/akd.2014.5739.
14. MACOVEI L, PRESURA RM, ARSENESCU GEORGESCU C. Systemic or local thrombolysis in high-risk pulmonary embolism. Cardiol J. 2015;22(4):467-74.
15. KRAAI IH, LUTTIK ML, JOHANSSON P, DE JONG RM, VAN VELDHUISEN DJ, HILLEGE HL, JAARSMA T. Health related quality of life and anemia in hospitalized patients with heart failure. International Journal of Cardiology 2012 Nov 29;161(3):151-5.
16. GRECU M, FLORIA M, GEORGESCU CA. Abnormal atrioventricular node conduction and atrioventricular nodal reentrant tachycardia in patients older versus younger than 65 years of age. Pacing Clin Electrophysiol. 2009 Mar;32 Suppl 1:S98-100.

Manuscript received: 5.04.2017