The effect of diet, lifestyle and psychological factors in the prognosis of ischemic heart failure

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1. Introduction

Heart failure (HF) is a clinical syndrome characterised by typical symptoms (such as breathlessness etc) that may be accompanied by signs (such as pulmonary crackles and peripheral oedema), caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress [1]. Coronary Artery Disease remains its commonest cause [2]. HF represents a major public health issue with increasing prevalence despite the latest therapeutic advances. Recent data shed light on the role of diet in HF pathophysiology and prognosis. In specific, the Mediterranean diet which is rich in fruit, vegetables, legumes, whole grains, fish and low-fat dairy products, with olive oil being the principal source of fat, is well-known for its beneficial effect in reducing cardiovascular disease burden [3,4].

The purpose of this prospective study was to investigate the outcomes in a group of patients presenting with ischemic heart failure with regard to their dietary, psychological and lifestyle status.

2. Materials and methods

2.1. Study population

A series of 326 consecutive patients with ischemic heart failure was prospectively enrolled in this study between June 2015 and November 2018, after approval obtained from the Hospital Ethics Committee (i.e. the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki). All subjects gave informed consent prior to enrolment.

2.2. Baseline assessment

Demographic data including previous medical history, smoking status, presence of arterial hypertension, dyslipidemia and diabetes mellitus, data on coffee, tea, beverages or alcohol consumption as well as qualitative and quantitative data regarding dietary and sleeping habits and physical activity, were recorded on a questionnaire provided to the patients. Adherence to the Mediterranean diet was assessed via a dietary questionnaire.
diet was assessed by a version of the 14-item Mediterranean Diet Adherence Screener (MEDAS), a brief questionnaire which was used in the PREDIMED trial, translated to Greek [5]. In addition, data with regard to left ventricular systolic function (eg left ventricular ejection fraction- LVEF) was quested in the patients’ medical records. BMI value, in kg/m², was calculated for every individual patient.

Assessment of anxiety and depression was performed by “The Hospital Anxiety and Depression Scale (HADS)”. [6]. HADS score, was devised 30 years ago by Zigmond and Snith and, comprising seven questions for anxiety and seven questions for depression, is frequently used in clinical practice and research, due to its simplicity, speed and ease of use [6]. A HADS questionnaire was provided to the patients and subsequently the individual score was calculated for each participant.

2.3. Follow-up and end-points

All patients were prospectively followed-up for an average of 30 months (range: 26–35 months). The study’s endpoints, recorded for every individual patient were (a) hospitalization for heart failure symptoms, (b) hospitalization for any cause and (c) death from all causes.

2.4. Statistics

All categorical variables are presented as absolute frequencies and percentages, while continuous variables are shown as means ± standard deviations. Univariate or Multivariate analysis was performed for different parameters according to the Cox regression analysis model. All tests were considered to be significant at the level of p < 0.05. SPSS statistical package, release 15.0 (SPSS Inc. Chicago, Illinois, USA) was used for all statistical analyses.

3. Results

The study patient population included 326 patients (90 females) who had a previous history of heart failure (HF) due to ischemic cardiomyopathy. New York Heart Association (NYHA) functional stage ranged between II-III. The mean age was 73.45 ± 10.9 years. Patient data are presented in Table 1. All patients were prospectively followed for an average of 30 months (range: 26–35 months).

Patient data regarding income, dietary habits, consumption of coffee, tea, beverages or alcohol, sleeping habits, physical activity and HADS score are presented in Table 2.

A total of 131 patients (40.1%) was re-hospitalized, while 29 (8.9%) died during the follow-up period. In Table 3 the demographic, clinical and socio-economic characteristics, dietary habits and psychometric measurements of the group of patients (n = 29) who manifested the study endpoint of death from all causes and those who did not are recorded (see Table 4).

In our study, patients who died were more likely to be women (eg men were 37.9% vs. 76.6% in the group of patient who remained alive, p < 0.005) and of older age (eg 82.1 ± 1.7 vs 72.3 ± 0.7 years-old in the group of patient who remained alive, p < 0.0001). On the other hand, there were no significant statistical differences between the two groups with regard to the history of arterial hypertension, diabetes mellitus or dyslipidemia, the smoking status, prior Acute Myocardial Infarction (AMI) or Coronary Artery Bypass Grafting (CABG) operation and the Left Ventricular Ejection Fraction (EF) value. In addition differences were not statistically significant, between the two groups, regarding their socio-economic characteristics (eg level of income, size of apartment/house, ownership of apartment/house).

Furthermore, there were no significant differences in the nocturnal or midday sleep duration between groups. However, in the group of patients who manifested the endpoint of death of any cause, a significantly higher amount of time was spent in watching television (3.96 ± 0.67 vs 2.89 ± 0.15 h/day, p = 0.0001).

Moreover, no significant statistical differences were revealed regarding HADS score for anxiety (7.03 ± 0.88 vs 9.21 ± 2.05, p = NS) between patients who died and those of the second group. On the contrary, patients who manifested death from any cause demonstrated a significantly increased HADS score for depression compared to those who survived during follow-up (8.62 ± 0.94 vs 6.44 ± 0.27, p < 0.05) (Fig. 1).

Table 2 Socio-economic data, dietary habits and psychometric scales of study population.

| Variable | Accommodation in owned residence | Area of residence (m²) | Personal income status/classification | Area of residence (m²) |
|----------|----------------------------------|-----------------------|--------------------------------------|-----------------------|
|          | 85.6%                            | 842 ± 2.5             | Low (1.7)                            | 46.7%                 |
|          |                                  |                       | Middle (2.0)                         | 38.7%                 |
|          |                                  |                       | High (3.0)                           | 14.6%                 |

HADS: Hospital Anxiety and Depression Scale.
Table 3
Differences in socio-economic parameters, dietary habits and psychometric scales between patients achieving study’s endpoint and patients who did not.

|                                | Alive in follow-up (n = 297) | Death in follow-up (n = 29) | P      |
|--------------------------------|-------------------------------|-----------------------------|--------|
| Male, n (%)                    | 227 (76.6)                   | 11 (37.9)                   | < 0.0001|
| Age (years)                    | 72.3 ± 0.7                   | 82.1 ± 1.7                  | 0.0001 |
| BMI (kg/m²)                    | 26.84 ± 0.97                 | 26.84 ± 4.88                | p > 0.31|
| EF (%)                         | 32.48 ± 4                    | 31.98 ± 4                   | p > 0.59|
| BP (%)                         | 47.46                        | 51.23                       | p > 0.47|
| DM (%)                         | 40.71                        | 36.41                       | p > 0.63|
| Dyslipidemia (%)               | 80.4                         | 85.7                        | p > 0.36|
| Smoking (%)                    | 57.11                        | 52.1                        | p > 0.28|
| Family History (%)             | 21.27                        | 21.60                       | p > 0.86|
| History of AMI (%)             | 18.96                        | 23.20                       | p > 0.55|
| History of CABG (%)            | 6.26                         | 6.89                        | p > 0.92|
| Private residence (YES)        | 84.6                         | 92.1                        | p > NS  |
| Area of residence (m²)         | 84.1 ± 2.7                   | 84.5 ± 7.7                  | p > NS  |
| Personal income status (%)     |                              |                             |        |
| Low                            | 46.2                         | 50.0                        |        |
| Middle                        | 39.6                         | 46.4                        |        |
| High                          | 14.3                         | 3.6                         | p > NS  |
| Nocturnal sleep (hours)        | 5.78 ± 0.10                  | 5.64 ± 0.32                 | p > NS  |
| Midday sleep/midday nap/afternoon nap (hours) | 1.15 ± 0.06 | 1.18 ± 0.17                 | p > NS  |
| Television watching (hours)    | 2.89 ± 0.15                  | 3.96 ± 0.67                 | p < 0.0001|
| HADS Anxiety Score             | 9.21 ± 2.05                  | 7.03 ± 0.88                 | p > NS  |
| HADS Depression Score          | 6.44 ± 0.27                  | 8.62 ± 0.94                 | p < 0.05|
| Bread consumption (slices/day)  | 2.18 ± 0.14                  | 2.00 ± 0.30                 | p > NS  |
| Fast-food consumption (portion/week) | 0.21 ± 0.05 | 0.24 ± 0.15                 | p > NS  |
| Dairy products consumption (portion/day) | 1.01 ± 0.06 | 1.11 ± 0.11                 | p > NS  |
| Olive oil consumption (%)      | 98.5                         | 100.0                       | p > NS  |
| Seed oil consumption (%)       | 5.6                          | 3.4                         | p > NS  |
| Butter consumption (%)         | 9.3                          | 6.3                         |        |
| Margarine consumption (%)      | 1.6                          | 3.4                         |        |
| Beverage consumption (glasses/day) | 0.32 ± 0.07 | 0.62 ± 0.28                 | p > NS  |
| Alcohol intake (glasses/day)   | 0.84 ± 0.06                  | 0.67 ± 0.13                 | p > NS  |
| White wine (%)                 | 16.2                         | 23.1                        | p > NS  |
| Red wine (%)                   | 59.9                         | 46.2                        |        |
| Whiskey (%)                    | 2.8                          | 0                           |        |
| Beer (%)                       | 3.5                          | 0                           |        |
| Ouzo (%)                       | 6.3                          | 0                           |        |
| Other(%)                       | 10.2                         | 30.8                        |        |
| Coffee drinking (cups/day)     | 1.38 ± 0.08                  | 0.64 ± 0.11                 | p < 0.0001|
| Greek coffee (%)               | 61.8                         | 58.6                        |        |
| Instant(soluble) coffee/Cappuccino (%) | 12.6       | 3.4                         |        |
| Filter coffee (%)              | 9.9                          | 3.4                         |        |
| Tea drinking (cups/day)        | 0.32 ± 0.04                  | 0.21 ± 0.07                 | p > NS  |

BMI: Body Mass Index, EF: Ejection Fraction, ABP: Arterial Blood Pressure, DM: Diabetes Mellitus, AMI: Acute Myocardial Infarction, CABG: Coronary Artery Bypass Grafting, HADS: Hospital Anxiety and Depression Scale.

Table 4
Cox proportional hazard regression for risk of death.

| Variables                     | B    | OR   | 95.0% Confidence intervals | P     |
|-------------------------------|------|------|----------------------------|-------|
| Gender (Female = 0)           | -0.68| 0.505| 0.215–1.185                 | 0.11  |
| Age                           | 0.06 | 1.06 | 1.02–1.11                  | 0.004 |
| HADS Score (HADS Score < 7 – 0) | 0.09 | 1.10 | 1.01–1.20                  | 0.03  |
| Coffee drinking (<2 cups/day – 0) | -0.41| 0.66 | 0.38–1.12                  | 0.12  |

HADS: Hospital Anxiety and Depression Scale.

Consumption of coffee was higher in the group of patients who survived during the follow-up period (1.38 ± 0.08 vs 0.64 ± 0.11 cups/day, p = 0.0001) compared to patients who died. Similar differences were not shown with regard to consumption of other drinks (eg alcohol, beverages, tea). Furthermore, there were no statistically significant differences with regard to the size of food portion, consumption of bread, dairy products and fast food, or the type of oil consumed (eg olive oil, seed oil, butter or margarine). In the univariate Cox regression analysis, consumption of ≥2 cups of coffee per day was associated with a lower risk of death from any cause during the follow up period. [OR = 0.054 (95% CI: 0.007–0.424, p = 0.005] (Fig. 2). In addition, univariate Cox regression analysis showed that a higher HADS depression score in hospitalized patients with heart failure, is associated with death from any cause. When HADS depression score was higher than 8, patients demonstrated a 104% higher risk [OR: 2.04 (95% CI: 1.23–7.92) p = 0.03] to die from any cause, compared to patients with HADS score < 4 (Fig. 3). In a multivariable Cox regression model, including age, gender, presence of depression and coffee consumption, patients with HF and depression (HADS Depression Score > 8) had worse prognosis [OR = 1.10 (95% CI: 1.01–1.20), p = 0.032] compared to HF patients free of depressive symptoms, independently of gender, age or coffee consumption. However, according to this model coffee consumption loses its prognostic
Moreover, in our study, increased alcohol consumption and adoption of a high fat/low carbohydrate diet did not have a predictive value for hospital re-admission (Fig. 4, panel A and B). Finally, it appears that eating low fat meat > 2–3 times/month is associated with a lower possibility for any cause hospital re-admission. According to our data, the possibility of hospital re-admission in this case is reduced by 21% [HR = 0.79 (95% CI: 0.64–0.98) p = 0.035] compared to patients who rarely ate meat (Fig. 4, panel C).

4. Discussion

In the present study, increased lean meat consumption, more than 2 times per month, was significantly related to a reduced risk of re-hospitalization in patients with heart failure NYHA class II-III, compared to patients who consume less meat, irrespectively of age, sex and Body Mass Index (BMI). In addition, no difference was revealed in the consumption of fish, cereals, pasta, red meat, vegetables, fruits, sweets, dairy or olive oil among patients who manifested the study’s end-points and those who did not. It is assumed that increased protein and fat intake from lean meat in addition to complying with a Mediterranean diet together with adequate intake of \( \omega-3 \)-polyunsaturated fatty acids (PUFAs) of fish origin may improve the metabolic profile, disrupt the catabolic state of the myocardium, improve systolic function, and prognosis in patients with moderate heart failure. Probably, additional clinical studies are necessary to elucidate the underlying pathophysiological mechanisms in patients with heart failure.

Previous studies demonstrated the favourable effects of the Mediterranean diet on the prognosis of heart failure, especially of ischemic cause. In patients after acute myocardial infarction followed for 4 years, adoption of a Mediterranean diet reduced the likelihood of HF, compared to patients on a Western diet [7]. On the other hand recent data suggest that following a strict Mediterranean diet, although not affecting mortality, significantly reduces hospital re-admissions during the first year after an episode of acute HF [8]. The beneficial effect of the Mediterranean diet is also reflected in the lower level of biomarkers such as natriuretic peptides and oxidized-LDL, in patients following a Mediterranean diet and an additional olive oil consumption compared to control group

Fig. 1. HADS Depression score and HADS Anxiety score comparison between patients who died and those who survived during follow-up.

Fig. 2. Univariate analysis of the effect of coffee consumption in patients’ survival (p = 0.0001).

Fig. 3. Univariate analysis of the effect of depression in patients’ survival (p < 0.05).
Furthermore, an inverse relationship between Mediterranean diet and inflammatory markers, such as IL-6 and TNFα, as well as a beneficial effect between Mediterranean diet and echocardiographic markers such as systolic and diastolic function in patients with chronic HF has also been shown [10]. Recent data suggest that the Dietary Approaches to Stop Hypertension (DASH) diet, characterised by increased consumption of fruit, vegetables, whole grains, poultry, fish, nuts and low-fat products and minimum consumption of red meat, sweet and soft drinks with a high sugar content, as well as the Mediterranean diet, are more suitable for primary and secondary prevention of HF compared to Scandinavian, Palaeolithic or Vegetarian Diets [11]. Adherence to the DASH diet results in a 16–17% reduction in overall mortality in HF patients [12], while in postmenopausal women with HF, it appears to significantly reduce mortality from HF [12].

The pathophysiological mechanisms through which dietary habits affect the prognosis of HF are mainly related to the systematic metabolism of free fatty acids (FFAs) and triglycerides, as well as to their metabolism from the cardiac myocardium [13]. Excessive free fatty acid or triglyceride intake appears to alter cardiac energy metabolism, since the myocardium uses them as energy source instead of glucose, resulting in ceramide accumulation, that consequently has a deleterious effect disrupting myocardial metabolism and resulting in systolic dysfunction [14]. In the advanced stages of HF, cardiac metabolism is shifted to glucose, since the myocardium is unable to metabolize FFAs whereas at end-stage HF, ketones are the main energy substrate, indicating the severe starvation state of the failing myocardium [15]. Also, at end-stage HF, excessive intake of fat and sugars increases insulin resistance, leading to heart failure deterioration by accelerating the catabolic state of the myocardium [16] and left ventricular remodeling [17].

Moreover, the FFA source appears to be of major importance. Recent studies highlight the favourable effect of ω3-PUFAs in HF, especially when dietary sources contain increased quantities of ω3-PUFAs to replace other FFA sources [18]. Data from GISSI-Heart Failure Trial show that administration of ω3-PUFA is associated with decreased total mortality in HF patients [19]. Moreover, short-term administration of ω3-PUFAs was revealed to improve both echocardiographic systolic markers and inflammatory and fibrosis biomarkers in these patients [20]. Finally, the importance of lipid-to-carbohydrate ratio in HF progression and prognosis has also been shown, since, according to experimental data, high fat and low-carbohydrate consumption increases the arrhythmic death risk, highlighting the need for a balanced fat and sugars intake, and avoidance of processed sugars [21].

In our study, consumption ≥ 2 cups of coffee/day significantly reduced mortality at the study population. Previous studies demonstrated that daily coffee consumption has beneficial effect on the cardiovascular system and improves prognosis with regard to both cardiovascular and overall mortality [22]. Data from the IKARIA study showed that consumption of 240 ml of coffee/day or

Fig. 4. Lack of prognostic value of alcohol consumption for any cause hospital readmission (p = ns) (A), lack of prognostic value of high fat/low carbohydrates diet for any cause hospital readmission (p = ns) (B) and favourable prognostic effect of low fat meat consumption at any cause hospital readmission (p = 0.035) (C).
consumption of 240 mL of tea/day results in improved all cause mortality [23]. In addition, in a large observation study including 185,855 participants, daily consumption of at least 1 cup of coffee was inversely associated with overall mortality, whereas increasing daily coffee consumption enhanced the beneficial effect on survival [24]. With regard to the ideal quantity of coffee, data from the ATTICA study revealed that small and moderate coffee consumption has significant favourable effects in reducing cardiovascular events [22]. Authors suggest that coffee consumption and cardiovascular prognosis follows a J-shape curve with small and moderate consumption being beneficial and excessive consumption becoming detrimental [22,25]. On the other hand, data regarding the effect of caffeine consumption particularly in patients with HF are controversial and scarce. Some authors demonstrated that coffee consumption does not enhance the presentation of newly appearing HF [26]. Furthermore, other studies failed to show mortality reductions due to congestive heart failure, related to coffee consumption [27]. However, in a meta-analysis of 5 major studies, including 140,220 patients, coffee consumption appeared to have favourable effects in reducing the incidence of HF appearance and in increasing the ability to exercise in patients with HF [28]. The strongest beneficial effect was demonstrated in patients who consumed 1–2 cups of coffee/day compared to those who did not drink coffee [29].

Moreover, in our study, tea consumption or moderate wine consumption had no effect on mortality. In contrast, data from 6973 patients participating in the GISSI-HF study, suggest that regular consumption of small amounts of wine improves vascular inflammation and was associated with improved quality of life and lower risk of depression without, however, affecting HF prognosis [30]. In addition, in experimental animal models, tea consumption appears to reverse myocardial fibrosis and dysfunction, cell apoptosis and remodeling, probably due to the effect of flavonoids such as epigallocatechin [31].

Depression is a common co-morbidity in patients with heart failure. Recent data suggest that its presence is associated with increased risk for hospital re-admission, impairment of functional capacity and increased mortality in both ischemic heart failure and dilated cardiomyopathy [32,33]. According to a registry of over 320,000 patients the manifestation of depression increases mortality by 15–20% in patients with HF compared to the general population [34]. On the other hand, the role of anxiety disorders in the progression of HF is controversial [35]. A previous study demonstrated that among elderly patients hospitalized for HF decompensation, 50% of those who suffered from major depression died during one year follow up period compared to 29% of those without major depression [36]. Moreover, symptoms of depression affect not only one-year, but also the mid-term (eg six-year) morbidity and mortality [37]. Especially people with persistent depression appear to have an even higher risk [38]. The severity of symptoms also appears to be a significant prognostic factor: In a study among patients with HF decompensation admitted to the hospital and followed-up for 6 months, 31% of patients without depression, 49% of moderate depression and 60% of those with major depression respectively experienced the combined endpoint of impairment of functional capacity or death [39]. In addition, according to data from SADHART-CHF study, improvement of depression symptoms is associated with a reduction in the likelihood of re-hospitalization [40]. In the present study, we showed that depression, but not anxiety, is an independent, unfavourable prognostic factor for moderate HF. This finding highlights the necessity for early diagnosis and individualized both behavioural and pharmaceutical treatment of depression.

Individualized and multifactor treatment of depression is very important both for improving the prognosis of the disease and for symptom relief, especially in end-stage HF patients [41]. Data from large randomized trials with regard to medical treatment in these cases are controversial. Recent clinical trials demonstrate that the use of escitalopram does not reduce the risk of re-hospitalization or mortality compared to the placebo [42]. In contrast, benzodiazepines may be cardioprotective, while fluoxetine may have a deleterious effect [43]. Sertraline, on the other hand failed to improve prognosis of HF [44], while a beneficial effect of venlafaxine was documented when co-administrated with aripiprazole in patients with end-stage HF [45]. Finally, in a study of 259 patients with HF and depression, antidepressants were not associated with improved prognosis, despite improvement in symptoms [46]. In addition to medical treatment, the implementation of standardized programs for the treatment of depression, such as the PROCIDE model, is shown to significantly improve symptoms of depression, quality of life, self-control and self-monitoring of patients [47]. Patients should be encouraged to take part in self-management and self-monitoring programs, in order to receive proper information on the HF symptoms and to be trained when to seek medical attention [48].

In addition, in our study, we showed that patients who manifested the endpoints of the study were characterised by a sedentary lifestyle. Sedentary lifestyle, defined as reduced physical activity and/or watching television for several hours, is considered as an independent risk factor for cardiovascular disease [49]. In addition, recent studies showed a strong relationship between reduced physical activity and increased BMI, and HF manifestation [50]. A recent meta-analysis of 25,000 patients also showed that reduced physical activity is associated with a higher prevalence of depressive symptoms in HF patients [51]. Moreover, in HF, sedentary lifestyle appears to be an independent and unfavourable prognostic indicator for morbidity and mortality whereas increasing physical activity improves prognosis [52]. Additionally, it appears that low rather than high-intensity exercise is most beneficial [53].

In conclusion, dietary advice needs to be carefully individualized to meet the needs of the patient. In general, approaches based on the Mediterranean or DASH diet should be considered. Previous studies and recommendations highlight the importance of a plant-based diet including plenty of vegetables, fruits, legumes, nuts and seeds. Red meat amounts should be limited with a shift to white meat and fish. Based on our data we would recommend eating low fat meat at least 1–2 times/week. Alcohol consumption should be moderate. In addition, according to our findings, consumption of ≥2 cups of coffee per day is desirable. Physical activity is encouraged, according to individual exercise tolerance whereas sedentary lifestyle should be avoided (eg reduce the time spent in watching television). Finally, depression should be diagnosed in early stages and effectively treated by means of both medical and non pharmacological measures.

5. Limitations

This study was conducted at just one site in an urban area in Greece. Patient habits, lifestyle, and priorities may vary in other regions. In addition, the sample of this study is relatively small. Probably due to the small number of patients, this study was unable to demonstrate a clear benefit of Mediterranean diet in the prognosis of patients with heart failure. Moreover, the study included mainly men (eg women represented approximately 27% of the study population), the mean age was relatively low and the majority was Caucasian. Thus, caution is needed to generalize the findings of this study to older patients, women, and other ethnicities. Finally, data regarding diet and lifestyle are based on self-reporting and thus may suffer from measurement error.
6. Conclusion

Our data demonstrate that consumption of two or more cups of coffee per day is related to lower mortality rates in patients with ischemic heart failure. In addition, a higher HADS score for depression, but not for anxiety, is inversely associated with prognosis. Moreover, sedentary lifestyle is related to worst outcomes. Finally, in our study, a low fat meat diet (>2–3 times/month), compared to patients who rarely ate meat, was associated with lower possibility for hospital re-admission.

On the other hand no significant statistical differences were revealed among patients with better outcomes compared to those with worst outcomes with regard to consumption of fish, cereals, pasta, red meat, vegetables, fruits, sweets, dairy, olive oil, alcohol, beverages and tea, or with regard to their socio-economic characteristics or sleep duration.

Conflicts of interest

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