Research Article

Patients' perception of health status and ischaemic burden in stable coronary artery disease

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Abstract

Background: Angina pectoris, the main manifestation of coronary artery disease has an unfavorable impact on quality of life. The aim of this study was to assess Health-Related Quality Of Life (HRQoL) in patients with Stable Coronary Artery Disease (SCAD) and to explore possible relationships between HRQoL and the risk factors for ischaemic heart disease, the Canadian Cardiovascular Society (CCS) angina severity class, and the extent of myocardial ischaemia on Single Photon Emission Computed Tomography Myocardial Perfusion Imaging (SPECT-MPI).

Methods: HRQoL was assessed with the use of two generic questionnaires, EQ-5D-3L and SF-36v2 in one hundred consecutive patients with SCAD.

Results: Most of the patients presented problems on the dimensions of mobility, pain/discomfort, and anxiety/depression of the EQ-5D questionnaire. The EQ-VAS score was 61.96 ± 20.99, and the mean EQ-5D index value was 0.54 ± 0.31. The mean scores of the Physical Component Summary and the Mental Component Summary of the SF-36 questionnaire were 43.49 and 41.01 respectively. Higher CCS angina class, female gender and poor physical activity were significantly correlated with worse HRQoL. No statistically significant association was detected between HRQoL and the extent of ischaemia on myocardial perfusion imaging.

Conclusions: Patients with SCAD have an impaired HRQoL, which can be reliably assessed by generic HRQoL questionnaires. Angina severity could be used as a surrogate of HRQoL, but individual perception of health status should be measured independently of the amount of ischaemiaon cardiac perfusion scintigraphy.

Introduction

Coronary Artery Disease (CAD) is a major cause of mortality, morbidity and disability, and imposes a significant economic burden on global health systems [1,2]. The majority of patients with CAD suffer from chronic stable angina, which has a significant impact on quality of life. The need to assess the effect of treatment and interventions on quality of life is increasingly being recognized by clinicians [3], however only few of them are familiar with quality of life assessment tools or formally use them in their daily practice [4]. Health-related quality of life (HRQoL) refers to the impact that health conditions and their manifestations have on an individual's quality of life. HRQoL can be assessed by "generic"questionnaires, which address general issues of health and multiple features of quality of life, or "disease-specific", which focus on specific aspects of a particular disease [5]. The quality of life of Greek patients suffering from CAD has recently been acknowledged as an important determinant of long-term outcome [6-8], but has not been thoroughly studied. In addition, little is known about the association between HRQoL of patients with Stable Coronary Artery Disease (SCAD) and the extent of ischaemia on Single Photon Emission Computed Tomographymyocardial Perfusion Imaging (SPECT-MPI), a widely used non-invasive diagnostic tool [9]. Only one study has previously examined the association between two scales of the SF-36 questionnaire, namely physical functioning and general health, and the results obtained by SPECT-MPI. The study showed that myocardial perfusion imaging results predicted only a small percentage of the variation in scores of the two SF-36 scales [10].

The purpose of our study was to assess HRQoL in patients with SCAD and its relationship to known risk factors for ischaemic heart disease, the Canadian Cardiovascular Society (CCS) angina severity class, and the extent of ischaemia on SPECT-MPI. We hypothesized that the extent of ischaemia on perfusion imaging could be a surrogate marker for HRQoL.

Materials and methods

Study design and patient population

Prospective single-centre study including one hundred consecutive patients (76% male; mean age 65 years) with CAD referred for a SPECT-MPI study at the Department of Nuclear Medicine of AHEPA University Hospital, Greece. Inclusion criteria were known history of SCAD according to the 2013 European Society of Cardiology (ESC) criteria [11]; age ≥18 years; ability to understand and complete the questionnaires. Exclusion criteria were recent acute coronary event (within previous month); recent history of life-threatening arrhythmias (within three months); severe arterial hypertension (systolic blood pressure ≥ 200 mmHg and/or diastolic blood pressure ≥110 mmHg); physical disability; history of mental disorder; dementia; pregnancy. Patients with absolute and relative contraindications to exercise testing underwent vasodilator stress testing and vice versa [12]. Ethical approval for the study was granted by the Scientific Council and the Administrative Council of AHEPA University Hospital and all patients provided written consent.

SPECT-MPI studies

The patients underwent treadmill exercise or pharmacologi-cal stress testing with intravenous infusion of adenosine 140 μgr/kg/min for 5 min or dipyridamole 140 μgr/kg/min for 4 min. 250 MBq ^{99m}Technetium-Sestamibi, 250 MBq ^{99m}Technetium-Tetrofosmin (MYOVIEW), or ^{201}Thallium were administered at maximum level of exercise on the treadmill, on the third minute of adenosine infusion, or three minutes after the end of dipyridamole infusion. When technetium was used, a second dose of 750 MBq was administered at rest. Images were obtained after the stress test and 2 hours later, at rest. Patients were divided into 4 groups according to the amount of ischaemia on their SPECT-MPI studies: i) no ischaemia; ii) small amount of ischaemia (<5%); iii) moderate ischaemia (5-15%); iv) severe ischaemia (>15%).

HRQoL assessment

HRQoL was assessed using the Greek version of two generic questionnaires EQ-5D-3L and SF-36v2 which are reliable and sensitive tools for the assessment of quality of life of patients with ischaemic heart disease [13-15] and have been validated for the Greek population [16,17]. The EQ-5D-3L questionnaire consists of a descriptive system and a Visual Analogue Scale (EQ VAS). The descriptive system has five quality of life dimensions that define health: mobility; self-care; usual activities; pain or discomfort; anxiety or depression. Each dimension has three levels, indicating no problems, some or moderate problems or extreme problems. The EQ VAS asks responders to self-rate their health on a "thermometer" visual analogue scale, with "best imaginable health state" set at 100 and "worst imaginable health state" set at 0. The responses from the descriptive part of the questionnaire can be converted into a single health index utility score, the EQ-5D index [18,19]. The mean EQ-5D index value was calculated using the York A1 Tariff algorithm. SF-36v2 is a brief, short-form health survey with 36 questions which yield 8 health domain scales: Physical Functioning (PF); Role-Physical (RP); Bodily Pain (BP); General Health (GH); Vitality (VT); Social Functioning (SF); Role-Emotional (RE); Mental Health (MH). The eight scales form two summary measures, the Physical and Mental Component Summary (PCS and MCS) Measures [20]. SF-36 scores were calculated using the Quality Metric Health Outcomes(tm) Scoring Software 4.5. Patients filled in the HRQoL questionnaires and a questionnaire about demographic data, medical history, CCS angina class and treatment for CAD immediately before their SPECT-MPI study.

Statistical analysis

The analysis was undertaken using the Statistical Package for the Social Sciences (SPSS) version 21 for Windows. The association of patient demographic characteristics, past medical history, smoking, alcohol consumption, aerobic exercise duration, CSS angina class and of SPECT-MPI results with HRQoL was tested using the bivariate analysis. The continuous dependent variables, the EQ-5D index and the EQ VAS were compared with the above categoric independent variables by Student's t-test. Associations between the results of SPECT-MPI studies and the parameters of the two questionnaires were performed with the Fisher's exact test, one way ANOVA for the four categories of ischaemia, and Pearson chi-square test when the results were merged into two groups of ischaemia. A P value of <0.05 was considered statistically significant. The Pearson correlation coefficient was used to evaluate the strength of the linear rela-

tion between CCS class, myocardial perfusion imaging results and SF-36 scores, EQ-5D answers on dimensions, EQ VAS (visual analogue scale) scores and EQ-5D index results.

Results

Patient characteristics

Patient characteristics are shown in Table 1. Most patients were male (76%), older than 60 years (63%) and non-smokers (69%). Sixty-three percent of the patients suffered from previous myocardial infarction. Percutaneous Coronary Intervention (PCI) was performed in 60% of the patients, Coronary Artery Bypass Grafting (CABG) in 17%, while 23% of patients were on pharmacological treatment alone. Most of the patients had hypertension and dyslipidemia (82% and 87% respectively), 36% suffered from diabetes mellitus and 26% from heart failure.

Table 1: Demographic patient characteristics and history of CAD.

Males, (n = %)	76.0
Average age, (years) Age range, (years)	65.0 37.0 - 84.0
BMI, (kg/m²)	29.2 ± 5.2
Current smokers, (n = %)	31.0
Exercise level Less than 1.5 hours per week, (n = %) More than 1.5 hours per week, (n = %)	 64.0 36.0
Time of CAD diagnosis During the previous year, (n = %) More than 1 year ago, (n = %)	 24.0 76.0
History of acute myocardial infarction, (n = %)	63.0

Treatment for CAD
     PCI, (n = %)
     CABG, (n = %)
     Medical management, (n = %)
	
	 60.0
	 17.0
	 23.0

BMI: Body Mass Index; CABG: Coronary Artery Bypass Grafting; CAD: Coronary Artery Disease; PCI: Percutaneous Coronary Intervention.

CCS angina class and SPECT-MPI findings

The majority of the patients were in CCS angina class II (42%) or III (21%). Only 12% of the patients were in class IV, while 13% were in class I and 12% reported having no angina or equivalent symptoms. A sizeable proportion of the patients (44%) had a small extent of ischaemia on SPECT-MPI, and 30% showed no inducible ischaemia. Moderate and extensive ischaemia was detected in 24% and 2% of the patients, respectively. Approximately one third of the patients (33%) had a myocardial scar and 14% had evidence of myocardial dysfunction.

HRQoL findings

Patients' responses are shown in Table 2. The EQ-VAS mean score was 61.96 ± 20.99, and the mean EQ-5D index value was 0.54 ± 0.31. The mean scores of the SF-36 PCS and MCS measures were 43.49 and 41.01 respectively. Patients reported the lowest scores on the GH and VT scales. Most patients had problems with mobility and suffered from moderate pain/discomfort. Anxiety/depression of moderate or high intensity was also a common problem. Furthermore, patients reported limited social functioning.

Table 2: SF-36 and EQ-5D-3L questionnaire results.

SF-36 scale	Mean value	Standard deviation	Minimum	Maximum
PF	54.21	27.99	0.00	100.00
RP	55.38	30.27	0.00	100.00
BP	58.76	29.79	0.00	100.00
GH	47.20	25.45	0.00	100.00
VT	49.00	28.05	0.00	100.00
SF	63.00	31.13	0.00	100.00
RE	65.50	27.17	0.00	100.00
MH	52.15	25.86	0.00	100.00
PCS	43.49	9.48	19.90	64.31
MCS	41.01	13.58	12.46	65.38
EQ-5D-3LDimension	**N = %**			
Mobility No problems Some/moderate problems Confined to bed	 30.0 70.0 0			
Self-care No problems Some/moderate problems Unable to wash or dress	 86.0 14.0 0			
Usual activities No problems Some/moderate problems Unable to perform usual activities	 53.0 43.0 4.0			
Pain/discomfort No pain/discomfort Moderate Extreme	 33.0 58.0 9.0			
Anxiety/depression Not anxious/depressed Moderately anxious/depressed Extremely anxious/depressed	 17.0 53.0 30.0			
EQ-VAS index	61.96 (± 20.99)			
EQ-5D Index (York A1 Tariff)	0.54 (±0.31)			

Patients' responses on SF-36 and EQ-5D HRQoL questionnaire. BP: Bodily Pain; GH: General Health; MCS: Mental Component Summary; MH: Mental Health; PCS: Physical Component Summary; PF: Physical Functioning; RE: Role-Emotional; RP: Role-Physical; SF: Social Functioning; VT: Vitality.

Correlation between HRQoL and patient characteristics

Men were found to have statistically significantly better results than women on the dimension of pain/discomfort (p=0.030) of the EQ-5D questionnaire and on the scales of PF (p=0.002), RP (p=0,004), BP (p=0.002), GH (p=0.04), SF (p=0.008) and PCS (p=0.001) of the SF-36 questionnaire. Patients over 60 years-old scored better on the MSC (p=0.004).

Patients who used to exercise for more than 1.5 hours per week had higher scores on the scales of PF (p=0.000), RP (p=0.013), BP (p=0.001), GH (p=0.039), VT (p=0.001), SF (p=0.032) and the PCS (p=0.000) of the SF-36 questionnaire. They also reported higher scores on the dimensions of mobility (p=0.001), usual activities (p=0.003), and pain/discomfort (p=0.012) of the EQ-5D questionnaire, and had higher EQ-

5DVAS score (67.67 vs. 58.75, p=0.041) and EQ-5Dindex (0.962 vs. 0.905, p=0.032). No significant correlation was found between HRQoL and smoking status, BMI, or history of previous myocardial infarction. Patients with a previous CABG had lower EQ-5DVAS scores (48.35).

Correlation between HRQoL, angina severity class and SPECT-MPI results

There was a negative correlation between CCS class and all scales of SF-36 questionnaire, the EQ-5DVAS score (r=-0.367, p=0.000) and the EQ-5D index (r=-0.558, p=0.000), and a highly statistically significant positive correlation with all the dimensions of the EQ-5D questionnaire. Patients with more severe angina reported lower scores on all scales of the SF-36 and all dimensions of the EQ-5D questionnaire.

The extent of ischaemia on SPECT MPI showed a mild but statistically significant inverse association with the SF scale (r=-0.203, p=0.043) and the MCS (r=-0.201, p=0.045) of the SF-36

questionnaire. No significant correlation was detected with any of the dimensions of EQ-5D questionnaire, EQ-5D index or EQ-5D VAS. Patients were subsequently classified into two groups according to the severity of ischaemia, namely those with negative SPECT MPI results or a small amount of ischaemia, and those with moderate or severe ischaemia. Similarly, no significant correlation was observed between the severity of ischaemia and the scales of the SF-36 questionnaire, the dimensions of the EQ-5D questionnaire, the EQ-5D index or the EQ-5D VAS.

Furthermore, the extent of ischaemia on myocardial perfusion imaging was not found to be a significant determinant of HRQoL on multiple regression analysis. More specifically, this showed that only the CCS angina class was associated with all the dimensions of the EQ-5D and the scales of the SF-36 questionnaire, while some dimensions and scales were associated with gender, age, exercise duration and type of treatment for CAD (Table 3) (Figure 1).

Table 3: Multivariate linear regression models on HRQoL using the EQ-5D and the SF-36 instruments.

Variable	Outcomes											
	EQ-5D VAS			EQ-5D Index			SF-36 PCS			SF-36 MCS		
	Coef	St.er	p	Coef	St.er	p	Coef	St.er	p	Coef	St.er	p
CCS class	-15.17	4.905	0.003	-0.332	0.066	0.000	-7.171	1.896	0.000	-12.674	2.882	0.000
SPECT-MPI	-2.218	4.717	0.639	-0.076	0.063	0.232	-0.756	1.824	0.680	-4.759	2.772	0.089
Age	3.708	4.854	0.447	0.073	0.065	0.263	3.068	1.877	0.106	7.675	2.851	0.009
Gender	1.620	5.495	0.769	-0.127	0.074	0.088	-6.330	2.124	0.004	-3.280	3.228	0.312
Exercise duration	3.641	4.652	0.436	0.027	0.062	0.667	4.370	1.799	0.017	-0.470	2.733	0.864
Type of treatment	-5.545	5.582	0.323	-0.159	0.075	0.036	-4.577	2.158	0.037	-3.481	3.280	0.291
BMI	-0.584	5.796	0.920	0.023	0.078	0.765	1.037	2.241	0.645	3.687	3.405	0.282
Smoking	-4.132	4.999	0.411	-0.073	0.067	0.281	-1.842	1.933	0.343	-1.715	2.937	0.561
Family status	-4.856	5.640	0.392	0.001	0.075	0.985	-0.684	2.181	0.755	-4.738	3.314	0.156
Education	-0.081	4.391	0.985	-0.064	0.059	0.278	0.780	1.698	0.647	-1.341	2.580	0.605
Previous acute MI	-4.107	4.663	0.381	0.047	0.066	0.475	0.043	1.893	0.982	0.452	2.877	0.876

Multiple linear regression analysis results of the relationship between angina severity, ischaemia, and demographic characteristics with HRQoL. BMI: Body Mass Index; CCS: Canadian Cardiovascular Society; MI: Myocardial Infarction; SPECT-MPI: Single Photon Emission Computed Tomography – Myocardial Perfusion Imaging.
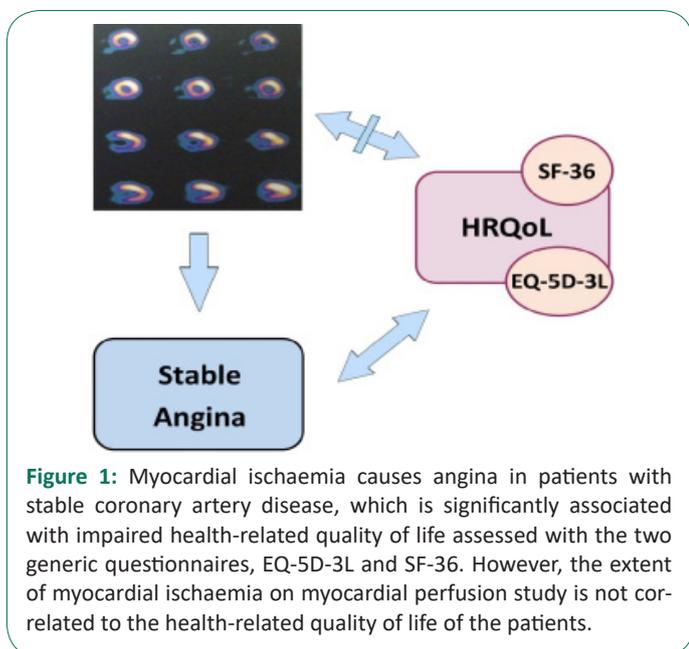

Figure 1: Myocardial ischaemia causes angina in patients with stable coronary artery disease, which is significantly associated with impaired health-related quality of life assessed with the two generic questionnaires, EQ-5D-3L and SF-36. However, the extent of myocardial ischaemia on myocardial perfusion study is not correlated to the health-related quality of life of the patients.

Discussion

Assessment of HRQoL has become an integral part of the management of patients with CAD, as it is not only considered as important as life expectancy by the patients but can also predict adverse health outcomes [21]. Patients with CAD have worse cognitive, physical and psychological states compared to age-matched controls [22]. The estimated EQ-5D index and the mean values of the SF-36 PCS and MCS measures in the present study are similar to those reported in previous studies of patients with CAD [23,24] and lower than those measured in representative samples of the Greek general population [16,17]. Compared to patients with SCAD in the United States of America, patients in the present study had similar EQ-5D VAS mean score (61.96 compared to 63.4) and comparable PCS and MCS mean scores (43.49 compared to 48.9 and 41.01 compared to 36.9, respectively) but had lower mean EQ-5D index (0.54 compared to 0.73) [25]. On the contrary, EQ-5D VAS mean score was lower than the one reported in patients with ischaemic heart disease from 22 European countries (61.96 versus 66.42) [26]

and compared to patients with SCAD and moderate or severe ischemia included in the ISCHEMIA trial (68.8 and 69.2 in the two patient groups) [27]. Compared to Greek patients evaluated a month post-hospitalisation for CAD, patients in the present study had lower mean EQ-5D VAS score and EQ-5D index but scored higher on most of the scales of the SF-36 questionnaire [8].

Patients with chronic stable angina report lower HRQoL in multiple domains [28]. Our findings are consistent with previous studies showing significant inverse association of angina severity to HRQoL [29,30]. Furthermore, similar to previous studies female gender and lack of exercise were associated with lower HRQoL indices [26,31,32]. The impaired HRQoL in women may be explained by a greater frequency of angina attacks, less aggressive treatment for CAD, physical inactivity, and difficulties in the management of risk factors for CAD [30].

Most of the patients had no or mild ischaemia on SPECT-MPI, while the proportion of patients with moderate or severe myocardial ischaemia was low, in keeping with previous studies in patients with SCAD [33]. Overall, there was no significant correlation between HRQoL as assessed with the two generic questionnaires and myocardial ischaemia on cardiac scintigraphy. Although the extent of ischaemia on SPECT MPI showed a mild statistically significant inverse association with the SF scale and the MCS component of the SF-36 questionnaire, this significance was lost on multiple regression analysis. A previous study in 195 patients with known or suspected CAD also showed no statistically significant correlation of the SF-36 PF and GH scales to the extent of ischaemia on SPECT-MPI [10]. Moreover, in a recent study in 3003 patients with angina (23% with known CAD) HRQoL as assessed with the Seattle Angina Questionnaire had no association with the perfusion defect on SPECT-MPI or Positron Emission Tomography (PET) scans [34]. In the ORBITA study, although patients with myocardial ischaemia on stress echocardiography reported less angina after percutaneous coronary intervention, there was no statistically significant interaction with HRQoL [35]. On the contrary, in the ISCHEMIA trial patients with moderate or severe ischaemia and baseline angina had improvements in HRQoL when treated with revascularisation, suggesting an association of the extent of ischaemia with HRQoL [27].

The results of the present and previous studies may be explained by the mysterious nature of angina. Angina is the transient chest discomfort caused by oxygen supply and demand mismatch in the myocardium [11]. It is an unpleasant sensory and emotional experience with not entirely clear pathophysiological mechanisms. It has long been recognised that there are wide variations in the perception of angina among individuals but also in the same individual. Subsequently, there is no strong connection between stimulus intensity (extent of myocardial ischaemia) and the subjective intensity of anginal pain [36].

The present study has several limitations. First, it included patients only from one centre and there was a small representation of females, thus the results may not entirely represent the population of patients with SCAD. Furthermore, HRQoL was measured using two generic questionnaires which have been proven reliable and sensitive for the assessment of quality of life of patients with ischaemic heart disease and have been widely used in large populations of patients with CAD [26]. Although disease-specific questionnaires like the Seattle Angina Questionnaire also assess some general aspects of health, they are designed primarily to assess the functional status of pa-

tients and its association with symptoms [5]. However, disease-specific instruments may have been more sensitive in detecting differences in quality of life of patients with CAD and possible associations with the extent of ischaemia on SPECT-MPI studies. Finally, the study may have been underpowered to detect small differences in HRQoL as the proportion of patients with severe myocardial ischaemia was low. The strengths of the study are that it included patients which represented all the spectrum of SCAD according to the recently published ESC criteria, and patients undergoing either exercise or pharmacological stress SPECT MPI. Moreover, HRQoL questionnaires were filled in immediately before testing to avoid any bias from the test results or the patients' perception of how well they performed. Finally, all the individual questionnaire scales, dimensions, as well as the summary measures were included in the statistical analysis.

Conclusion

Patients' perception of health status is associated with the subjective pain they experience in daily life as stable angina, but it is not correlated to the extent of myocardial ischaemia (Figure 1). The results of the study underscore the need for comprehensive assessment of physical and emotional health and functionality in all patients with CAD irrespective of the objectively measured amount of ischaemia on imaging studies.

Declarations

Author Contributions: Conceptualization and methodology, C.N.; formal analysis, C.N.; investigation, C.N., G.G., and E.M.; visualization, C.N., and M.R; writing—original draft preparation, C.N.; writing—review and editing, M.R., D.N., E.M., and T.D.K.

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Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study.

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