Gender Differences in Health-Related Quality of Life in Patients with Congestive Heart Failure and Past Coronary Artery Bypass Graft Surgery

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Nare Vardanyan, MD, MPH (c)

Advising team: Lusine Abrahamyan, MD, MPH, PhD

Michael E. Thompson, MS, DrPH

Yeva Sahakyan, MD, MPH, MSc

Turpanjian School of Public Health

American University of Armenia

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ABSTRACT

Background: Heart failure (HF) causes a large health and economic burden to society. Despite significant advances in treatment over the past twenty years, the incidence, prevalence, hospitalizations, and mortality from HF continue to increase. HF patients endure diminished health-related quality of life (HRQoL). In this study I evaluated gender differences in HRQoL in patients with HF who had had coronary artery bypass graft surgery (CABG) at Nork Marash Medical Center (NMMC) in Yerevan, Armenia.

Methods: The study utilized a retrospective cohort design with a cross-sectional telephone survey. The study population included all patients who had had CABG between January 1, 2016 and December 31, 2018 and were diagnosed with HF at the time of CABG or during the follow-up period (end of follow-up: March 31, 2019). HRQoL was evaluated by using the Minnesota Living with Heart Failure Questionnaire (MLHFQ). Multivariable linear regression analysis identified independent predictors of HRQoL in HF patients.

Results: Overall, 86% (n=80) of 93 patients included in the final analysis were men. Women were somewhat older (66.69 vs. 61.23, p=0.017). All participants had at least one comorbid disease. The mean MLHFQ score for women was higher (66.8 vs. 59.9, p =0.354) but not statistically significant. Patients with HF functional class (NYHA) II/III/IV had MLHFQ scores 10.13 (2.73 to 17.54) points higher (i.e., worse HRQoL) than patients in HF class I. Similarly, employed patients had 16.97 (95% CI: 7.43 to 26.5) points lower MLHFQ scores (i.e., better HRQoL).

Conclusions: This study found no statistically significant gender difference in disease-specific HRQoL. Class I functional status of HF (NYHA) and being employed were associated with

better HRQoL. We would recommend to evaluate the impact of complications after surgery, adherence to treatment, and HF-related readmissions on HRQoL in these patients in future research.

1. INTRODUCTION

Heart failure (HF) is the complex, chronic and progressive condition characterized by impaired function of heart to pump or fill with blood, resulting shortness of breath, orthopnea, sudden dyspnea, ankle swelling, tiredness, fatigue, and reduced exercise tolerance.[1,2] HF causes a significant burden to patients, caregivers, and society and is considered a major cause of morbidity and mortality worldwide.[3]

The New York Heart Association (NYHA) categorizes HF into functional classes I-IV considering the severity of symptoms and tolerance to physical activity.[2] Historically, based on the measurement of the left ventricle ejection fraction (LVEF), we can classify HF as normal or preserved (HFpEF: LVEF>50%), mid-range (HFmrEF: LVEF 40-49%, a "grey area"), and reduced (HFrEF: LVEF < 40%).[2]

1.1 Global burden of heart failure

An estimated 26 million people worldwide have HF.[1] HF prevalence is increasing both in the US and in Europe.[4] In the US, it affects 5.7 million with an anticipated 46% increase in prevalence by 2030.[1] The number of people living with HF is 6.5 million in Europe and 2.5 million in Japan.[5] The annual incidence of HF is 950,000 in the US and is greater among adults aged ≥65 years (1 per 100 population).[1,5] The prevalence of HF ranges from 1.4% to 1.8% and the incidence rate from 1.3 to 4.4 cases per 1000 population in European countries.[1] The prevalence of HF is 1.3% in China and 1% in Japan.[1]

The costs of HF treatment are high and are projected to increase both in the US and in Europe.[4] The global annual economic burden of HF was $108 billion in 2012.[6] HF costs have both high direct (~$65 billion for hospital service, medical treatment, physician visits, primary healthcare, and follow-up costs) and indirect costs (~$43 billion for loss of earning potential, unpaid care morbidity and premature mortality).[6] In high-income countries, direct costs were the main cost drivers while indirect costs were the drivers in low to middle-income countries.[6] In 2012, the estimated indirect cost of HF was $6 million in Armenia.[6]

1.2. Etiology of HF

The European Society of Cardiology guidelines on HF management identified myocardial diseases, abnormal loading diseases and arrhythmias as the main causes of HF.[2] Most patients with HF have coronary artery disease (CAD), including those with a history of myocardial infarction and/or revascularization.[2,7,8,9] Other reasons for developing HF are diseases with abnormal loading conditions such as hypertension, valve and myocardium structural defects, pericardial and endo-myocardial pathologies, high output status, volume, arrhythmias, toxic damage of the heart, immune-mediated or inflammatory damage, infiltration, metabolic damage, and genetic disorders.[2]

Though the etiology of HF is similar for both in men and women (ischaemic heart disease, hypertension, diabetes mellitus), the prevalence of these factors varies. As such hypertension, and heart valve disease are more frequent in women with HF in women than in men.[10] A systematic review on gender differences in etiology of HF showed that CAD was more prevalent in men than in women while DM was equally prevalent in both genders.[11]

1.3. Prognosis of HF

HF is one of the most known causes of preventable hospitalizations. About 50% of patients with chronic HF are re-hospitalized within the first year after hospital discharge .[12, 13] According to the studies, HF-related hospitalizations increase reaching to 1 million per year both in the US and in Europe.[4]

The long-term prognosis for patients with HF is poor, despite the significant changes in the treatment of HF during 20 past years.[1,2,4] The study based on the ESC-HF registry which includes 21 European and Mediterranean countries reported that among 2,440 patients with congestive heart failure (CHF) at 1-year follow-up: (i) the re-hospitalization rate was 9.9%, (ii) the all-cause mortality rate pooled for all the participant countries was 14.5%, and (iii) there were significant differences between different countries both in the clinical characteristics and outcomes.[4] Results from the heart function assessment registry trial in Saudi Arabia (HEARTS-chronic) showed at 1 year the all-cause mortality rate was 9% (93.7% of which were cardiac-related), the all-cause hospitalization rate was 39%, and the survival rate was 91% in patients with HF.[14]

The NYHA functional class of HF is a strong predictor of HF-related mortality. Studies reported that the mortality rate for patients with NYHA class IV is 44% at 6 months, while for patients with NYHA class II and III it is 15-20% at 1 year.[12] LVEF also have a significant role in predicting early and late outcomes of HF.[15] ESC-HF-long-term registry prospective study showed that re-hospitalization rates "for HF in the HFrEF, HFmrEF, and HFpEF groups were 14.6%, 8.7%, and 9.7%, respectively" and the mortality rates were 8.8%, 7.6%, and 6.3% respectively at 1 year of follow-up.[15] The report from the CHART II study showed that women with HFpEF had higher risks of cardiovascular death than men.[9]

1.4. HF management

The important objectives of HF treatment are improvements in clinical and functional status and health-related quality of life (HRQoL), and reduction of hospital readmission rates and mortality.[2] The main groups of evidence-based medications for treating HFrEF (NYHA class II-IV), include angiotensin-converting enzyme inhibitors (ACEIs), mineralocorticoides/aldosterone receptor antagonists (MRAs), and beta-blockers (BB).[2]

ACEIs showed decreased mortality in men with HFpEF but not in women, while BBs improved mortality in women with EF<40% but not in men.[9]

HF patients generally have multiple comorbidities and, therefore, require multidisciplinary care. For patients with HF and CAD, CAD management can directly affect HF symptoms and outcomes. Compared with medical treatment, coronary revascularization through percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG) are superior for patients who have CAD and HF.[16] Both PCI and CABG led to significant decrease in mortality rates compared with medical therapy alone in patients with CAD and LVEF < 40%, but survival after CABG was higher than after PCI in these patients.[17] A prospective study with 4,616 patients with multi-vessel CAD and HFrEF reported similar survival with PCI and CABG (mean follow-up was 3 years) with CABG patients having higher risk for stroke after surgery than those after PCI, and PCI patients had higher risks of MI and repeated revascularizations.[18] A US-based study showed an improvement in LVEF after CABG in patients with LVEF 25%-46%, while patients who had LVEF<25% experienced no significant change in LVEF.[19]

1.5. Health-related quality of life in HF patients

HF is a chronic, progressive condition with negative effects on the physical and emotional functions of patients.[20] Predictors of health-related quality of life (HRQoL) in HF patients had been investigated in many studies. One of the important predictors is the NYHA class with lower functional classes predicting lower HRQoL.[21] Another important factor of HRQoL for patients with HF is the depression which is prevalent in 11% to 25% of patients.[13,21] Depression has an independent effect both on the physical and psychological dimensions of HRQoL.[21] Other factors associated with poor HRQoL include existing comorbidities such as hypertension, diabetes, chronic obstructive pulmonary disease, chronic kidney disease[5] and readmission rate.[13]

Many studies in the past assessed gender differences in HRQoL for patients with HF. A study in Sweden among HFpEF patients reported similar HRQoL using a disease-specific questionnaire (Minnesota Living with Heart Failure Questionnaire= MLHFQ), while the general HRQoL was better in men compared to women.[22] A study conducted in Greece using MLHFQ also found no difference in HRQoL in men and women with HF (NYHA class II-IV).[5] A Korean study among 114 patients with HF showed that better HRQoL was associated with male sex as well as older age, fewer comorbidities, and better physical and economic status.[8] Study conducted in Brazil showed worse HRQoL in young and female patients comparing to older and male patients though the differences were not significant.[23] The 12-month evaluation of HF outcomes in multidisciplinary clinics in Quebec showed better survival in women with higher functional class of HF (NYHA) and LVEF while the HRQoL score was overall higher in men.[24] A recent large study in the US with 12,058 men and 3,357 women with HF reported that although women with HFrEF live longer, had fewer comorbidities, and lower readmissions than men their HRQoL was poorer comparing to men.[25]

1.6. Study rationale

Nork Marash Medical Center (NMMC) is one of the leading cardiac surgery centers in the Caucasus region with about 25 years of history. Each year, more than 200 CABG surgeries are performed in the center. The follow-up of patients after heart surgeries continues in NMMC's outpatient Adult Cardiology Clinic. Studies conducted over the past 10 years at NMMC have focused mostly on clinical outcomes of coronary artery disease interventions such as PCI and CABG.[26] However, no study assessed patient-reported outcomes in patients with HF. The HRQoL of patients with HF is significantly lower comparing to the HRQoL of general population or to patients with other chronic conditions.[8] Knowledge about HRQoL will provide valuable information about targeted care interventions after CABG in patients with HF.

1.7. Study aim and specific objectives

This study aimed to investigate HRQoL and predictors of HRQoL in patients with HF who had CABG in the past. The primary objective of the study was to evaluate gender differences in HRQoL of patients with HF who had CABG in the past.

Secondary objectives were to:

1. Explore the association between LVEF and HRQoL,

2. Investigate the effect of HF NYHA class on HRQoL.

2. METHODS

2.1. Study Design

The study design consisted of a retrospective chart abstraction and a cross-sectional telephone survey of patients who had a clinical diagnosis of HF during their last visit to the outpatient clinic in NMMC between January 1 2016, and December 31 2018, and had a CABG in the past. This sampling frame was chosen because NMMC has the highest volume of CABG surgery in Armenia and has electronic databases and structured medical records available for research purposes.

2.2. Study Population

The study target population included all patients who had HF at the time and/or after CABG in Armenia. The study sample population included patients who had physician-established diagnosis of HF during their last visit to the outpatient clinic of NMMC between January 1, 2016 and December 31, 2018 and the CABG in the past.

Inclusion criteria for this study were:

- patients who were ≥18 years (at the time of surgery) and had CABG in the past,
- speaking Armenian and living in Armenia.

Exclusion criteria were patients who had valve surgeries with CABG and patients who had another major disease at the time of last follow-up (e.g., cancer).

2.3. Data Sources and collection methods

The sources of the information about the patients with HF after CABG were medical records and the electronic database (which also contains surgical discharge documents) of NMMC. First, the list of the patients who underwent CABG and had diagnosis of HF between January 1st 2016, and December 31st 2018, obtained from the electronic database of NMMC. Then, the outpatient medical records of these patients had retrieved. Patients who had HF during their last visit to NMMC and met the eligibility criteria were selected. The contact information of these patients was extracted from their medical records. Then patients had contacted by telephone (see Appendix 1 for Journal form) for the oral consent (Appendices 2A and 2B) to participate in the phone survey, for agreement to access their medical records, and extract information pertinent to this research study.

2.4. Study Survey Instrument

A recent systematic review identified 19 questionnaires available for HRQoL assessment of patients with HF.[27] The most commonly used questionnaires for assessment HRQoL of patients with HF were Kansas City Cardiomyopathy Questionnaire (KCCQ) and Minnesota Living with HF (MLHFQ).[27] For this study I used MLHFQ instrument (see Appendix 3). The MLHFQ is a disease-specific HRQoL tool that has 21 items rated on six-point Likert scales, reflecting different degrees of impact of HF on HRQoL, from 0 (none) to 5 (very much). It has two dimensions: physical (8 items, score range 0-40) and emotional (5 items, range 0–25). The remaining 8 items are used only for the calculation of total score. The total score ranges from 0 (best) to 105 (worst).[28] MLHFQ has a certified Armenian translation which was used for this study.

I used the EQ-5D-5L questionnaire to assess general HRQoL.[29] It includes five dimensions ("mobility, self-care, usual activities, pain/discomfort, and anxiety/depression"), each of them has three levels of response ("no problems, slight problems, moderate problems, severe problems and extreme problems"). The index-based score of 1 represents the best possible health and 0 represents dead, with some health conditions valued as being worse than dead (<0). EQ-5D-5L also contains a visual analogue scale (VAS), which enables patients to evaluate their current health status on the range from 0 (worst imaginable health state) to 100 (the best imaginable health state).[29] The English and Armenian versions of survey instrument are presented in the Appendices 3A and 3B, respectively.

2.5. Chart abstraction

I developed a chart abstraction form to obtain information about variables used in the data analysis (Appendix 4). The demographic data (age, gender), clinical information (clinical symptoms of HF), echocardiographic data (LVEF), HF class NYHA were obtained from the outpatient medical cards. Medical cards were also used to extract information about the prescribed medicines, and concomitant diseases, such as myocardial infarction (MI), hypertension (AH), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and others.

2.6. Variables

The dependent variable was the MLHFQ HRQoL score (continuous). The main independent variable of interest was gender (dichotomous). Other independent variables of interest included:

age (continuous), LVEF (categorical), NYHA class (categorical), myocardial infarction
(dichotomous), diabetes mellitus (dichotomous), hypertension (dichotomous), chronic
obstructive pulmonary disease (dichotomous), chronic kidney disease (dichotomous), smoking
status (dichotomous), ACE/ARB use (dichotomous), BB use (dichotomous), MRAs
(dichotomous) (Appendix 5).

Sample size calculation

Given continuous outcome variable, we did sample size calculation based on the comparison of
two sample means formula:

$$n = \frac{2\sigma^2 [Z_{1-\alpha/2} + Z_{1-\beta}]^2}{(\mu_1 - \mu_2)^2}$$

where,

$\sigma =$ Estimated standard deviation (assumed to be equal for each group)

$\mu_1 =$ Estimated mean HRQoL score for women

$\mu_2 =$ Estimated mean HRQoL score for men

I based the calculation on the assumption that the number of males will be twice that of females.
Therefore, the resultant sample size was further multiplied with the following coefficient:

$$\frac{n[k-1]^2}{4k}$$

where the k is the men-to- women ratio (i.e. 2) and n is the sample size computed assuming equal
allocation. I used Stata software to calculate the sample size (Appendix 6). In a study by
Pelegrino et al, the reported QoL score was 39.3 for females and 31.8 for males (pooled sd =

24.6) measured using MLHFQ.[23] The required sample to detect a 7.5-unit difference, with 80% power and a two-sided significance level of .05, is 381 (female= 127 and male= 254).[23]

Taking account the fact that the number of patients who had HF during their last visit to the outpatient clinic of NMMC and had CABG from January 1, 2016 to December 31, 2018, can be less than estimated sample size I conducted a telephone survey with all the eligible patients who gave consent to participate in the study.

2.8. Data analysis

Data were single entered. The student investigator performed data cleaning and performed range check for outliers and missing values. If the variable had more than 10% missing values, it was excluded from the analysis. Continuous variables were reported as means and standard deviations and were compared using Student t-test. Categorical variables were presented as counts and frequencies and were compared using Chi-square or Fisher-exact (for variables with counts≤5) tests. Predictors of HRQoL were analyzed using unadjusted and adjusted linear regression analysis. To assess the independent effect of gender on HRQoL a multivariable linear regression analysis was performed. All variables were included in the univariable linear regression analysis. Those variables who had p-values<0.25 were included in the multivariable linear regression analysis. Adjustment for confounding factors was done. Results with a p-value less than 0.05 were considered as statistically significant. SPSS software was used for the data analysis.

2.9. Ethical considerations

The study protocol was approved by the Institutional Review Board of American University of Armenia. NMMC approved the conduct of the study and accessing the necessary medical records. I obtained oral consent from participants (Appendices 2A and 2B). The evaluation posed no more than minimal risk for the patients. Patients we reassured that their care at NMMC would not be affected if they refused to participate. If during the phone call a patient was identified as deceased, the interviewer expressed condolence to the relative of the patient and discontinued the interview respectfully. Participants had no direct benefits from participating in the study.

3. RESULTS

3.1 Administrative Data

Of 540 patients who underwent CABG in NMMC from January 1, 2016, to December 31, 2018, 160 patients were eligible for the study. Of them, 93 completed the phone survey, 2 participants agreed to participate but did not complete the interview, 17 refused to participate in the survey, mostly citing lack of time, 29 phone numbers were impossible to reach after 4 attempts (either invalid numbers or non-response), 16 patients were abroad, and 3 participants had hearing problems and could not participate. The survey response rate was 58% (93/160). Data from 93 patients were included in the final analysis.

3.2. Baseline characteristics of the patients

A description of patient baseline characteristics is presented in Table 1. The majority of participants were men (n =80 or 86%). The mean age of participants was 62.0 (standard

deviation =7.7). Men were younger than women (mean age: 61.23 vs. 66.69, p=0.017). At least one concomitant disease was found in 74 men (92.5%) and in 13 women (100%). Men and women did not differ in their history of myocardial infarction (77.5% and 76.9% respectively, p =0.963) and arrhythmia (7.5% and 7.7% respectively, p-value=0.981). Women had higher prevalence of hypertension and diabetes mellitus (92.3% and 75%, p-value=0.185, 53.8% and 32.5%, p =0.136 respectively). More men than women had HF at perioperative stage (21.3% vs 7.7%, p=0.251). The prescription of ACEIs, BBs and other medications was similar between genders during the last visit to the NMMC outpatient clinic. Unemployment was higher for women than men (76.9% vs 47.5% p = 0.05). Majority of participants were married 78 (83.9%); the rate was significantly higher for men than for women (78.8% vs 53.8%, p < 0.001).

3.3 Health-related Quality of life

The mean HRQoL score for the full sample using the disease-specific MLHFQ was 60.8 (24.8). Men and women reported similar HRQoL scores (59.9 (24.4) and 66.8 (26.9), p =0.354 (Table 2).

The HRQoL responses based on EQ-5D were analyzed by item (Table 3). Men were less likely to report mobility problems (no problem were reported by 44, 55% vs. n=6, 46.2%), though the difference failed to reach statistical significance (p =0.232). Similarly, men and women reported similar disability rates related to self-care (no problems were reported by 66.3% of men and 61.5% women, p = 0.929), usual activities (no problems were reported by 66.3% of men and 53.8% of women, p = 0.680), pain/discomfort (no problems were reported by 73.8% of men and 84.6% of women, p = 0.751), and anxiety/depression (no problems were reported by 75% of men and 69.2% of women, p = 0.695). Health status on the day interviewed showed no statistically

significant differences between genders: for the total sample the mean VAS score was 62.2 (18), for men the mean VAS score was 62.52 (18.82), and for the women the mean VAS score was 60 (12.42), p-value=0.641.

3.4 Univariable predictors of QoL

Univariable linear regression analysis was used to identify predictors of HRQoL of patients with heart failure who had CABG in the past. Characteristics such as NYHA classes and employment status were significant predictors of HRQoL in patients with HF who had CABG in the past (Table 4). Patients with NYHA class II/III/IV had by 11.66 (95 % CI: 1.45 to 21.86) points higher MLHFQ score (i.e., worse HRQoL) compared to patients with NYHA class I. Similarly, patients who were employed reported to have by 16.81 (95% CI: 7.05 to 26.58) points lower score (i.e., better HRQoL) than unemployed patients.

3.5. Multivariable regression analysis

The variables with p-values < 0.25 such as MI, DM, NYHA class during the last visit, employment status and LVEF were considered for the stepwise elimination procedure for the model selection. The final multivariable model included gender, employment status and NYHA class as independent predictors HRQoL for patients with HF who had CABG in the past (Table 5). Adjusted for employment status and NYHA class, gender have no effect on HRQoL (0.33; 95% CI: -13.80 to 14.47, p =0.354). Unemployment and lower functional classes (NYHA II/III/IV) were associated with higher score (i.e., lower disease-specific HRQoL). After adjusting for gender and employment status, patients with NYHA classes II/III/IV had 10.13 (2.73 to

17.54) points higher MLHFQ score (i.e., worse HRQoL) compared to patients with NYHA class I. After adjusting for gender and NYHA class, employed patients had by 16.97 (95% CI: 7.43 to 26.5) points lower MLHFQ score (i.e., better HRQoL) than unemployed patients.

4. DISCUSSION

This study sought to evaluate gender differences in HRQoL of patients with HF who had CABG in the past. A phone survey was paired with the retrospective chart abstraction of patients who had CABG in NMMC from January 1, 2016, to December 31, 2018, and had physician-diagnosed HF during their last follow-up visit to the outpatient clinic. Men and women reported similar overall disease-specific HRQoL scores.

Different studies in the past evaluated gender differences in HRQoL in patients with HF (Table 7). In the current study, most participants were men. This finding is explained by the ischaemic etiology of HF, which is more frequent in men than in women. Men in this study were significantly younger than the women. Participants in similar international studies tended to be older, such as in a Korean study which evaluated gender differences using MLHFQ (the mean age of participants was > 65 years old) and in a Swedish study where the mean age of participants was more than 75 years.[8,22] The earlier manifestation of HF in our patients compared to patients in other countries reflect the shorter life expectancy in Armenia. Men and women in this study experienced similar MI prevalence. This finding contrasts with other studies as the literatures suggests CAD is less likely in women than in men.[10, 22, 24] A retrospective study conducted in Bulgaria showed no significant difference in prevalence of hypertension and DM in women and in men with HF, although women had slightly higher incidences of these diseases.[30] In this study, comorbidities such as AH and DM were higher in women. This finding can be

explained by more severe manifestation of clinical symptoms of these diseases in women. In contrast to this study, several studies reported no gender difference in prevalence of these comorbidities[5, 22] or in prescribed medications (ACEIs, BBs and others).[22] Men and women in this study were not different in prescribed medications, in contrast to a study conducted in Saudi Arabia which reported that BBs were under-prescribed in women while men were under-prescribed ACEIs.[31]

The proportion of employed men were twice as higher as the proportion of employed women in this study, which contrasts to other similar studies where most HF patients were unemployed,[23,32,33] perhaps reflective of the slightly younger patient population. The proportion of married participants was higher than the proportion of unmarried participants in the current study, while in the similar study by Fotos et al., the proportion of married and unmarried participants were similar.[5] Smokers in our study were predominantly men, consistent with the gender gap in smoking prevalence in Armenia.[34]

According to the literature, disease-specific HRQoL scores run higher in men.[8,22,24,25] In the current analysis, men and women had similar HRQoL composite scores. This finding aligns with the study conducted in Brazil which evaluated demographic and clinical determinants of HRQoL in HF patients in the outpatient clinic.[23] Women in this study population reported better general health, which contrasts with the study conducted in Sweden using EQ-5D-3L questionnaire.[22] The EQ-VAS score was similar in men and women in our study, in contrast to the Swedish study where women's EQ-VAS score was worse than men's.[22]

The results of univariable analysis showed that MI, HF lower functional classes (NYHA), and employment status are significant predictors of HRQoL of participants. Multiple regression

analysis showed that the lower classes (II-IV) of HF and being unemployed negatively impact HRQoL in patients with HF who had CABG in the past.

The current study had both strengths and limitations. One of the strengths of this study that it was first to evaluate HRQoL of patients with HF who had CABG in the past in Armenia. Previous studies conducted in NMMC investigated outcomes related to the CAD.[26] One of the major strengths of our study was the use of the certified Armenian version of the validated disease-specific MLHFQ for the first time.

The study was conducted in one center which limits the generalizability of findings, even though NMMC is the oldest and largest cardiac surgery center in Armenia and patients can be representative of the country population. Another source of bias can be inaccuracies in the medical records: inconsistence in reporting heart failure status of the patient or misinterpretation of some other variables. About one-fifth of phone numbers were invalid. Because of time constraints, I was unable to obtain surgical discharge documents, which might have provided information on hospital admission, discharge and time spent at ICU. These variables may be considered as predictors of HRQoL of patients after CABG.

Conclusions and recommendations

The current study aimed to evaluate gender differences in HRQoL of patients who diagnosed HF during their last visit to the outpatient clinic of NMMC and had CABG from January 1 2016, to December 31 2018. The study found no significant gender differences in total score of MLHF disease-specific questionnaire. Results of multiple linear regression analysis showed that unemployment and lower classes (II-IV) of HF (NYHA) were associated with lower HRQoL of

HF patients who had CABG in the past. General health measured by EQ-5D-5L questionnaire showed that in 3 dimensions from 5, men reported worse results than women though the VAS scale results were not different.

Further studies need to assess HRQoL of patients who had CABG before 2016. It would be useful to evaluate HRQoL before and after CABG surgery of those patients who had HF by the time of surgery in order to assess the impact of surgery on HRQoL of these patients. It would be important to include more surgical data in the future research: complications during and after the surgery, hours spent at ICU. Compliance to the medical treatment after surgery, readmissions because of HF, any re-do CABG surgeries will be an important predictors of HRQoL of HF patients who had CABG surgeries before which will be valuable to evaluate.

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Tables

Table 1. Baseline characteristics of patients

Patient characteristics	Total n=93	Men n=80	Women n=13	p-value
Risk factors and comorbidities				
Age (years), mean (SD)*	62.0 (7.7)	61.2 (7.4)	66.7 (7.9)	0.017
Current smoker, n (%)*	11 (11.8)	11 (13.8)	0	0.154
Concomitant disease, n (%)	87 (93.5)	74 (92.5)	13 (100)	0.307
Myocardial infarction, n (%)	72 (77.4)	62 (77.5)	10 (76.9)	0.963
Hypertension, n (%)	72 (77.4)	60 (75)	12 (92.3)	0.185
Diabetes mellitus, n (%)	33 (35.5)	26 (32.5)	7 (53.8)	0.136
Arrhythmia, n (%)	7 (7.5)	6 (7.5)	1 (7.7)	0.981
Chronic obstructive pulmonary disease, n (%)	3 (3.2)	3 (3.8)	0	0.633
Chronic kidney disease, n (%)	3 (3.2)	3 (3.8)	0	0.633
Heart failure at perioperative stage, n (%)	18 (19.4)	17 (21.3)	1 (7.7)	0.251
Other disease, n (%)	34 (36.6)	28 (35)	6 (46.2)	0.439
LVEF at the last clinic visit				
>40%, n (%)	56 (60.2)	43 (53.8)	13 (100)	0.264
<40%, n (%)	37 (39.8)	37 (46.3)		
NYHA class at the last clinic visit				
I, n (%)	43 (46.2)	39 (48.8)	4 (30.8)	0.205
II, III, or IV, n (%)	49 (52.7)	40 (50)	9 (69.2)	
Medications at the last clinic visit ACEIs, n (%)	83 (89.2)	72 (90)	11 (84.6)	0.561
BBs, n (%)	92 (98.9)	80 (100)	12 (92.3)	0.981
Other medication, n (%)	92 (98.9)	80 (100)	12 (92.3)	0.013
Employment status*				
Employed, n (%)	45 (48.4)	42 (52.5)	3 (23.1)	0.050
Unemployed, n (%)	48 (51.6)	38 (47.5)	10 (76.9)	
Marital status *				
Married, n (%)	78 (83.9)	71 (78.8)	7 (53.8)	0.001
Single/widowed/divorced, n (%)	15 (16.1)	9 (11.3)	6 (46.2)	
Monthly family spending *				
Less than 50.000AMD, n (%)	1 (1.1)	1 (1.3)	0	0.373
51.000-100.000 AMD, n (%)	7 (7.5)	7 (8.8)	0	
101.000-200.000 AMD, n (%)	32 (34.4)	27 (33.8)	5 (38.5)	
201.000-300.000 AMD, n (%)	25 (26.9)	22 (27.5)	3 (23.1)	
More than 300.000AMD, n (%)	1 (1.1)	1 (1.3)	0	
Don't know/Refuse to answer, n (%)	27 (29)	22 (27.5)	5 (38.5)	

*At the time of the survey.

AMD = Armenian dram; ACEI =; BB =Betta blockers;

Table 2. Minnesota HF questionnaire items by gender

Item	Total n=93	Men n=80	Women n=13	p-value
Q1. Ankle swelling				
Score = 0, n (%)	65 (69.9)	59 (73.8)	6 (46.2)	0.141
Score = 1 to 3, n (%)	9 (9.7)	6 (7.5)	3 (23.1)	
Score = 4 to 5, n (%)	19 (20.5)	15 (18.8)	4 (30.8)	
Q2. sit or lie down to rest during the day				
Score = 0, n (%)	31 (33.3)	28 (35)	3 (23.1)	0.338
Score = 1 to 3, n (%)	11 (1.9)	9 (11.4)	2 (15.4)	
Score = 4 to 5, n (%)	51 (54.9)	43 (53.8)	8 (61.6)	
Q3. walking about or climbing stairs difficult				
Score = 0, n (%)	22 (23.7)	20 (25)	2 (15.4)	0.653
Score = 1 to 3, n (%)	14 (15.1)	10 (13.6)	4 (30.8)	
Score = 4 to 5, n (%)	57 (61.3)	50 (62.5)	7 (53.9)	
Q4. working around the house or yard difficult				
Score = 0, n (%)	42 (45.2)	40 (50)	2 (15.4)	0.026
Score = 1 to 3, n (%)	12 (13)	10 (12.6)	2 (15.4)	
Score = 4 to 5, n (%)	48 (40.9)	29 (36.3)	9 (69.3)	
Q5. going places away from home difficult				
Score = 0, n (%)	51 (54.8)	45 (56.3)	6 (46.2)	0.216
Score = 1 to 3, n (%)	14 (15.1)	13 (16.3)	1 (7.7)	
Score = 4 to 5, n (%)	28 (30.2)	22 (27.6)	6 (46.2)	
Q6. sleeping well at night difficult				
Score = 0, n (%)	32 (34.4)	29 (36.3)	3 (23.1)	0.381
Score = 1 to 3, n (%)	12 (12.9)	10 (12.6)	2 (15.4)	
Score = 4 to 5, n (%)	49 (52.7)	41 (51.3)	8 (61.6)	
Q7. relating to or doing things with friends or family difficult				
Score = 0, n (%)	66 (71)	56 (70)	10 (76.9)	0.696
Score = 1 to 3, n (%)	11 (11.8)	10 (12.6)	1 (7.7)	
Score = 4 to 5, n (%)	15 (16.2)	13 (16.3)	2 (15.4)	
Q8. working to earn a living difficult				
Score = 0, n (%)	53 (57)	43 (53.8)	10 (76.9)	0.140
Score = 1 to 3, n (%)	7 (7.6)	6 (7.5)	1 (7.7)	
Score = 4 to 5, n (%)	33 (35.5)	31 (38.8)	2 (15.4)	
Q9. recreational pastimes, sports or hobbies difficult				
Score = 0, n (%)	43 (46.2)	38 (47.5)	5 (38.5)	0.543
Score = 1 to 3, n (%)	7 (7.6)	6 (7.6)	1 (7.7)	
Score = 4 to 5, n (%)	43 (46.2)	36 (45)	7 (53.8)	

Q10. sexual activities difficult

Score = 0, n (%)	47 (50.5)	35 (43.8)	12 (92.3)	0.002
Score = 1 to 3, n (%)	7 (7.6)	7 (8.9)	0	
Score = 4 to 5, n (%)	39 (41.9)	38 (47.5)	1 (7.7)	

Q11. eat less of the foods like

Score = 0, n (%)	40 (43)	38 (47.5)	2 (15.4)	0.141
Score = 1 to 3, n (%)	23 (34.8)	18 (22.5)	5 (38.5)	
Score = 4 to 5, n (%)	30 (32.3)	24 (30)	6 (46)	

Q12. short of breath

Score = 0, n (%)	45 (48.4)	41 (51.3)	4 (30.8)	0.264
Score = 1 to 3, n (%)	20 (21.5)	17 (21.3)	3 (23.1)	
Score = 4 to 5, n (%)	28 (30.1)	22 (27.6)	4 (46.2)	

Q13. tired, fatigued, or low on energy

Score = 0, n (%)	24 (25.8)	23 (28.8)	1 (7.7)	0.062
Score = 1 to 3, n (%)	6 (6.5)	6 (7.5)	0	
Score = 4 to 5, n (%)	63 (67.8)	51 (63.8)	12 (92.3)	

Q14. stay in a hospital

Score = 0, n (%)	64 (68.8)	58 (72.5)	6 (46.2)	0.026
Score = 1 to 3, n (%)	25 (26.9)	19 (23.8)	6 (46.2)	
Score = 4 to 5, n (%)	4 (4.3)	3 (3.8)	1 (7.7)	

Q15. costing money for medical care

Score = 0, n (%)	13 (14)	13 (16.3)	1 (7.7)	0.084
Score = 1 to 3, n (%)	10 (10.8)	9 (11.3)	1 (7.7)	
Score = 4 to 5, n (%)	70 (75.3)	58 (72.6)	11 (84.6)	

Q16. giving you side effects from treatments

Score = 0, n (%)	64 (67.7)	59 (73.8)	4 (30.8)	0.014
Score = 1 to 3, n (%)	11 (11.9)	7 (8.8)	4 (30.8)	
Score = 4 to 5, n (%)	19 (20.4)	14 (17.5)	5 (38.5)	

Q17. feel a burden to your family or friends

Score = 0, n (%)	71 (76.3)	62 (77.5)	9 (69.2)	0.613
Score = 1 to 3, n (%)	6 (6.5)	4 (5.1)	2 (15.4)	
Score = 4 to 5, n (%)	16 (17.2)	14 (17.6)	2 (15.4)	

Q18. feel a loss of self-control in your life

Score = 0, n (%)	35 (37.6)	31 (38.8)	4 (30.8)	0.657
Score = 1 to 3, n (%)	6 (6.5)	6 (7.6)	0	
Score = 4 to 5, n (%)	52 (55.9)	43 (53.8)	9 (69.3)	

Q19. making you worry

Score = 0, n (%)	49 (52.7)	45 (56.3)	4 (30.8)	0.063
Score = 1 to 3, n (%)	13 (11)	8 (12.5)	3 (23.1)	
Score = 4 to 5, n (%)	30 (32.3)	24 (30.1)	6 (46.2)	

Q20. difficult for you to concentrate or remember things

Score=0, n (%)	31 (33.3)	27 (33.8)	4 (30.8)	0.815
Score = 1 to 3, n (%)	12 (12.9)	10 (12.6)	2 (15.4)	

Score = 4 to 5, n (%)	45 (48.4)	39 (48.8)	6 (46.2)	
Q21. feel depressed				
Score = 0, n (%)	55 (59.1)	51 (63.8)	4 (30.8)	0.032
Score = 1 to 3, n (%)	7 (7.6)	4 (5.1)	3 (23.1)	
Score = 4 to 5, n (%)	31 (33.4)	25 (31.3)	6 (46.2)	
Composite score, mean (SD)	60.8 (24.8)	59.9 (24.4)	66.8 (26.9)	0.354

Note: Higher the Minnesota questionnaire score the worse is the quality of life

Table 3. Health related quality of life using EQ-5D questionnaire

Items	Total n=93, %	Men n=80, %	Women n=13, %	p-value
Mobility/Walking about				
No problems	50 (53.8)	44 (55.0)	6 (46.2)	0.232
Slight problems	23 (24.7)	20 (25.0)	3 (23.1)	
Moderate problems	15 (16.1)	13 (16.3)	2 (15.4)	
Severe problems	2 (2.2)	1 (1.3)	1 (7.7)	
Unable to walk	3 (3.2)	2 (2.5)	1 (7.7)	
Self-Care/Washing or dressing yourself				
No problems	61 (65.6)	53 (66.3)	8 (61.5)	0.929
Slight problems	17 (18.3)	14 (17.5)	3 (23.1)	
Moderate problems	10 (10.8)	8 (10.0)	2 (15.4)	
Severe problems	5 (5.4)	5 (6.3)	0	
Unable to wash or dress	0	0	0	
Doing usual activities				
No problems	60 (64.5)	53 (66.3)	7 (53.8)	0.680
Slight problems	20 (21.5)	16 (20.0)	4 (30.8)	
Moderate problems	11 (11.8)	9 (11.3)	2 (15.4)	
Severe problems	1 (1.1)	1 (1.3)	0	
Unable to do	1 (1.1)	1 (1.3)	0	
Pain/Discomfort				
No problems	70 (75.3)	59 (73.8)	11 (84.6)	0.751
Slight problems	13 (14.0)	13 (16.3)	2 (15.4)	
Moderate problems	9 (9.7)	7 (8.8)	0	
Severe problems	1 (1.1)	1 (1.3)	0	
Extreme problems	0	0	0	
Anxiety/Depression				
No problems	69 (74.2)	60 (75)	9 (69.2)	0.695
Slight problems	19 (20.4)	16 (20.0)	3 (23.1)	
Moderate problems	4 (4.3)	3 (3.8)	1 (7.7)	
Severe problems	1 (1.1)	1 (1.3)	0	
Extreme problems	0	0	0	
Current health status mean VAS, (SD)	62.2(18.0)	62.52(18.82)	60(12.42)	0.641

VAS_Visual analogue scale

Table 4. Univariable linear regression analysis of predictors of HRQoL

Variables	Regression coefficient (95% CI)	p-value
Gender		
Men	-6.91 (-21.65 to 7.83)	0.354
Women (reference)		
Age (years)	-0.07 (-0.75 to 0.59)	0.817
Current smoking status		
Yes	3.07 (-12.82 to 18.96)	0.702
No (reference)		
Concomitant disease		
Yes	-3.73 (-24.61 to 17.14)	0.723
No (reference)		
Myocardial infarction		
Yes	-7.93 (-20.13 to 4.25)	0.199
No (reference)		
Arterial hypertension		
Yes	2.98 (-9.83 to 15.80)	0.645
No (reference)		
Diabetes mellitus		
Yes	8.18 (-2.46 to18.82)	0.130
No (reference)		
Arrhythmia		
Yes	-5.71 (-13.70 to 25.13)	0.560
No (reference)		
Chronic obstructive pulmonary disease		
Yes	14.63 (-14.24 to 43.51)	0.317
No (reference)		
Chronic kidney disease		
Yes	5.33 (-23.69 to 34.35)	0.351
No (reference)		
Heart failure at perioperative stage		
Yes	-2.99 (-15.99 to 10.00)	0.648
No (reference)		
Other disease		
Yes	4.2 (-6.39 to 14.96)	0.428
No (reference)		
LVEF during the last visit		
< 40%	5.26 (-5.88 to 15.81)	0.324
≥ 40% (reference)		
HF class (NYHA) during the last visit	11.66 (1.45 to 21.86)	
II/III/IV		0.026
I (reference)		

Employment status		
Employed	-16.81 (-26.58 to -7.05)	0.001
Unemployed (reference)		
Marital status		
Married	5.48 (-8.445 to 19.41)	0.436
Not married (reference)		
Monthly family spending n (%)		
Less than 50.000AMD	reference	0.505
51.000-100.000 AMD	11.48 (-11.14 to 33.44)	
101.000-200.000 AMD	8.38 (-4.52 to 21.29)	
201.000-300.000 AMD	12.23 (-1.62 to 26.09)	
More than 300.000 AMD	30.48 (-19.82 to 80.79)	
Don't know/Refuse to answer	7.48 (-42.82 to 57.79)	

Table 5. Multivariable regression analyses of predictors of HRQoL

Predictors	Regression coefficient (CI 95%)	p-value
Men Women (reference)	0.33 (-13.80 to 14.47)	0.962
Employed	-16.97 (-26.5 to -7.43)	0.001
NYHA II/ III/ IV classes NYHA I class (reference)	10.13 (2.73 to 17.54)	0.008

Appendices

Appendix 1. Journal form

Patient ID	Telephone number	Interview date (MM/DD/YY)	Interview option codes

Interview option codes

1. Agreed to participate, completed the interview

2. Agreed to participate, did not complete the interview

3. Refused to participate

4. Non-response (invalid contact)

5. Died

6. Other

American University of Armenia

Turpanjian School of Public Health

Institutional Review Board #1

Consent form (English)

Title of the project: **Gender Differences in Health-Related Quality of Life in Patients with Congestive Heart Failure and Past Coronary Artery Bypass Graft Surgery**

Hello. My name is Nare Vardanyan. I am a cardiologist and the second-year student at the Master of Public Health program in the American University of Armenia (AUA). Within the scope of my master thesis project, I am investigating predictors of health-related quality of life (HRQoL) of patients with Heart Failure (HF) after Coronary Artery Bypass Grafting surgery (CABG).

Nork Marash Medical Center (NMMC) provided your contact information as someone of 300 patients who underwent CABG at (NMMC) and is currently diagnosed with HF during the last visit to NMMC from January 1st 2016 to 31 December 2018. Your contact information was taken from your NMMC card with the knowledge and agreement from the NMMC staff. If you agree, I would like to ask you several questions about your health-related quality of life after the CABG.

Your participation in this study is voluntary. The interview will last about 10 minutes and will take place only once at the most convenient time for you. Participating involves no risk for you.

You can stop the interview at any time point and you can skip over any question you do not want to answer. Some information will be used from Your NMMC medical card with Your permission for the study purposes. Your choice to participate or not will not affect your further medical care at NMMC or penalize you in any way. You will not directly benefit from participating in this study. However, the information you will provide will be useful for research and for the other patients.

Everything you tell us will remain confidential. All the information you will provide will be grouped with the information of the other participants and will not contain any person identifiable data about you. The information you will provide will be used for research purposes only. Your contact information will be available for the researchers only, and will be destroyed after the end of the study. Do you agree to participate?

If you have more questions about this study you can contact to dean of School of Public Health Varduhi Petrosyan via following number (37460) 61 25 92. If you think that you have not been treated properly or you have been hurt by participating in this survey you can contact Varduhi Hayrumyan, the Human Protections Administrator of the American University of Armenia (37460) 61 25 61.

Thank you!

Հայաստանի Ամերիկյան Համալսարան

Թրպանճեան Հանրային առողջապահության բաժին

Գիտահետազոտական էթիկայի թիվ 1 հանձնաժողով

Իրազեկ համաձայնության ձև

Հետազոտության անվանումը: **Առողջությամբ պայմանավորված կյանքի որակի**

սեռային տարբերությունը՝ սրտային անբավարարությամբ հիվանդների մոտ՝

առտոկորոնար շունտավորման վիրահատությունից հետո:

Իմ անունը Նարե Վարդանյան է: Ես սրտաբան եմ և Հայաստանի ամերիկյան

համալսարանի (ՀԱՀ) Թրպանճեան Հանրային առողջապահության ֆակուլտետի

ուսանող եմ: Իմ մագիստրական թեզի շրջանակներում՝ ես կատարում եմ հարցում

Նորք Մարաշ բժշկական կենտրոնի (ՆՄԲԿ) հիվանդների շրջանում՝ պարզելու

համար առողջության հետ կապված կյանքի որակը սրտային անբավարարություն

(ՍԱ) ունեցող հիվանդների շրջանում առտոկորոնար շունտավորման (ԱԿՇ)

վիրահատությունից հետո:

Դուք ընտրվել եք որպես մեկն այն 300 հիվանդներից, ով ենթարկվել է ԱԿՇ

վիրահատության ՆՄԲԿ-ում և ում մոտ ախտորոշվել է ՍԱ՝ վերջին այցի ժամանակ՝

հունվար 1-ից 2016թ. մինչև դեկտեմբերի 31 2018թ. ընկած ժամանակահատվածում: Ձեր կոնտակտային տվյալները վերցվել են ՆՄԲԿ-ի Ձեր քարտից՝ տնօրինության թույլտվությամբ: Եթե Դուք համաձայն եք, Ձեզ հարցեր կուղղեմ՝ առողջության հետ կապված Ձեր կյանքի որակի մասին՝ ԱԿՇ վիրահատությունից հետո:

 Հարցմանը մասնակցելը կամավորական սկզբունքով է: Հարցումը կտևի մոտավորապես 10 րոպե և մեկ անգամ՝ Ձեզ հարմար ժամանակ: Դուք իրավունք ունեք չպատասխանել ցանկացած հարցի կամ ընդհատել հարցումը ցանկացած պահի: Ձեր թույլտվությամբ՝ ՆՄԲԿ-ի Ձեր բժշկական քարտից որոշ տվյալներ կօգտագործվեն հետազոտության նպատակով: Հարցմանը չմասնակցելը չի ազդի ՆՄԲԿ Ձեր հետագա այցելությունների վրա և չի ունենա բացասական հետևանքներ: Հարցմանը մասնակցելու դեպքում որևէ դրամական խրախուսանք նախատեսված չէ: Այնուամենայնիվ, Ձեր տրամադրած տվյալները կարևոր կլինեն գիտահետազոտական տեսանկյունից և այլ հիվանդների համար:

Ձեր կողմից տրամադրված տվյալները կպահվեն գաղտնի և կօգտագործվեն միայն հետազոտական նպատակներով: Ձեր տրամադրած տեղեկատվությունը խմբավորվելու է այլ մասնակիցների տրամադրած տեղեկատվության հետ և չի պարունակելու անձր բացահայտող որևէ տվյալ: Ձեր կոնտակտային տվյալները

հասանելի կլինեն միայն հետազոտություն իրականացնող անձանց և կցնշացվեն հետազոտությունից անմիջապես հետո: Համաձայն՞ եք մասնակցել հարցմանը:

Հետազոտության հետ կապված հետազա հարցերի համար կարող եք զանգահարել Հանրային առողջապահության ֆակուլտետի դեկան Վարդուհի Պետրոսյանին հետևյալ հեռախոսահամարով (37460) 612592: Եթե դուք կարծում եք, որ այս հարցման ընթացքում Ձեզ հետ ճիշտ չեն վարվել, Դուք կարող եք դիմել Հայաստանի ամերիկյան համալսարանի գիտական էթիկայի հանձնաժողովի համակարգող` Վարդուհի Հայրումյանին (37460) 612561:

Շնորհակալություն:

MINNESOTA LIVING WITH HEART FAILURE QUESTIONNAIRE

The following questions ask how much your heart failure (heart condition) affected your life during the past month (4 weeks). After each question, circle the 0, 1, 2, 3, 4 or 5 to show how much your life was affected. If a question does not apply to you, circle the 0 after that question.

Did your heart failure prevent

you from living as you wanted during the past month (4 weeks) by -	No	Very Little				Very Much
1. causing swelling in your ankles or legs?	0	1	2	3	4	5
2. making you sit or lie down to rest during the day?	0	1	2	3	4	5
3. making your walking about or climbing stairs difficult?	0	1	2	3	4	5
4. making your working around the house or yard difficult?	0	1	2	3	4	5
5. making your going places away from home difficult?	0	1	2	3	4	5

6. making your sleeping well at night

    difficult?   **0   1   2   3   4   5**

7. making your relating to or doing things

    with your friends or family difficult?   **0   1   2   3   4   5**

8. making your working to earn a living

    difficult?   **0   1   2   3   4   5**

9. making your recreational pastimes, sports

    or hobbies difficult?   **0   1   2   3   4   5**

10. making your sexual activities difficult?   **0   1   2   3   4   5**

11. making you eat less of the foods you

    like?   **0   1   2   3   4   5**

12. making you short of breath?   **0   1   2   3   4   5**

13. making you tired, fatigued, or low on

    energy?   **0   1   2   3   4   5**

14. making you stay in a hospital?   **0   1   2   3   4   5**

15. costing you money for medical care?   **0   1   2   3   4   5**

16. giving you side effects from treatments?   **0   1   2   3   4   5**

17. making you feel you are a burden to your

family or friends?	**0**	**1**	**2**	**3**	**4**	**5**

18. making you feel a loss of self-control

in your life?	**0**	**1**	**2**	**3**	**4**	**5**
19. making you worry?	**0**	**1**	**2**	**3**	**4**	**5**

20. making it difficult for you to concentrate

or remember things?	**0**	**1**	**2**	**3**	**4**	**5**
21. making you feel depressed?	**0**	**1**	**2**	**3**	**4**	**5**

EQ-5D-5L

1. **Mobility**

   - **I have no problems in walking about** ☐

   - **I have slight problems in walking about** ☐

   - **I have moderate problems in walking about** ☐

   - **I have moderate problems in walking about** ☐

   - **I am confined to bed** ☐

2. **Self-Care**

   - **I have no problems with self-care** ☐

   - **I have slight problems washing and dressing myself** ☐

   - **I have moderate problems washing and dressing myself** ☐

   - **I have severe problems washing and dressing myself** ☐

   - **I am unable to wash and dress myself** ☐

3. **Usual Activities (e.g. work, study, housework, family or leisure activities)**

   - **I have no problems with performing my usual activities** ☐

   - **I have slight problems with performing my usual activities** ☐

   - **I h I have some problems with performing my usual activities** ☐

   - **I have severe problems with performing my usual activities** ☐

   - **I am unable to perform my usual activities** ☐

4. Pain/Discomfort

- **I have no pain or discomfort** □

- **I have slight pain or discomfort** □

- **I have moderate pain or discomfort** □

- **I have moderate pain or discomfort** □

- **I have extreme pain or discomfort** □

5. Anxiety/Depression

- **I am not anxious or depressed** □

- **I am slightly anxious or depressed** □

- **I am moderately anxious or depressed** □

- **I am severely anxious or depressed** □

- **I am extremely anxious or depressed** □

Imagine the scale is numbered from 0 to 100, where 100 means the best health you can imagine, 0 means the worst health you can imagine. Now, please tell the number you will mark your health on the scale today.

—	100
—	95
—	90
—	85
—	80
—	75
—	70
—	65
—	60
—	55
—	50
—	45
—	40
—	35
—	30
—	25
—	20
—	15
—	10
—	5
—	0
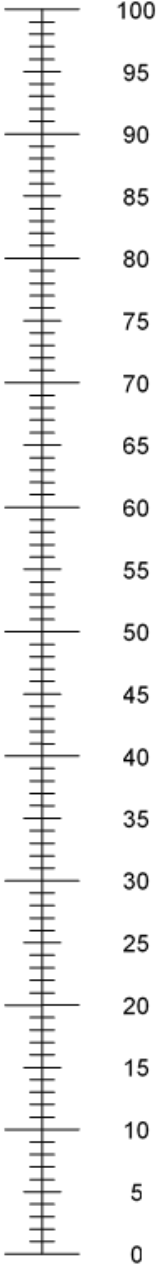
Demographic data

1. Gender 1. Male 2. Female

2. Can you tell your age, please? 1._____ 2. Refuse to answer

3. What is your highest level of education? 1. School < 10years

           2. School 10 years

           3. Professional technical

           4. Institute/University

4. Are you currently employed (Including self-employment, farming, and seasonal/migrant work)?   1. Yes

      2. No

5. What is your marital status? (choose one option) 1. Single

      2. Married

      3. Widowed

      4. Divorced

      5. Refuse to answer

6. On average, what is your household income per month?

  1) Less than 50,000 drams

  2) From 50,000 - 100,000 drams

  3) From 100,001 - 200,000 drams

  4) From 200,001 - 300,000 drams

  5) Above 300,000 drams

  6) Don't know/Refuse to answer

7. Have you ever smoke? 1.Yes, (go to the next question)

                                 2. No.

8. Do you smoke currently? 1. Yes (go to the next question) 2. No

9. How many cigarettes do you smoke daily? 1. Less than 10

                                 2. 11-20

                                 3. More than 21

ՄԻՆՆԵՍՈԹԱՅԻ LIVING WITH HEART FAILURE®

(ՍՐՏԱՅԻՆ ԱՆԲԱՎԱՐԱՐՈՒԹՅԱՄԲ ԱՊՐԵԼԸ) ՀԱՐՑԱՐԱՆ

Հետևյալ հարցերը տրվում են՝ պարզելու համար, թե վերջին ամսվա (4 շաբաթների) ընթացքում որքան է Ձեր սրտային անբավարարությունեն (արտի վիճակը) ազդել Ձեր կյանքի վրա: Յուրաքանչյուր հարցից հետո շրջանակի մեջ վերցրեք 0, 1, 2, 3, 4 կամ 5 թվերից մեկը՝ ցույց տալու համար, թե որքան է դաազդել Ձեր կյանքի վրա: Եթե հարցը Ձեզ չի վերաբերում, ապա այդ հարցից հետո շրջանակի մեջ վերցրեք 0-ն:

Ձեր սրտային անբավարարությունը վերջին ամսվա (4 շաբաթների) ընթացքում

խանգարե՞լ է Ձեզ ապրել այնպես, ինչպես որ կցանկանայիք, քանի որ՝

    Ոչ   Շատ քիչ   Չափազանց շատ

1.   պատճառ է հանդիսացել, որ Ձեր ոտնաթաթերը կամ ոտքերն այտուցվեն: 0   1   2   3   4   5

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2.   օրվա ընթացքում ստիպել է Ձեզ հանգստանալ ու նպատակով նստել կամ պառկել : 0   1   2   3   4   5

3.   Ձեզ համար դժվարացրել է քայլելը կամ աստիճաններով բարձրանալը: 0   1   2   3   4   5

4.   Ձեզ համար դժվարացրել է տանը կամ բակում գործ անելը:
        0   1   2   3   4   5

5.   Ձեզ համար դժվարացրել է տանից հեռու տեղեր գնալը: 0
        1   2   3   4   5

6.   Ձեզ համար դժվարացրել է գիշերային լավ քուն առնելը:
        0   1   2   3   4   5

7.   Ձեզ համար դժվարացրել է Ձեր ընկերների կամ ընտանիքի անդամների հետ շփումը կամ նրանց հետ տարբեր գործեր անելը:
        0   1   2   3   4   5

8.   Ձեզ համար դժվարացրել է ապրուստն ապահովելու համար աշխատելը: 0   1   2   3   4   5

9.   Ձեզ համար դժվարացրել է ժամանցը, սպորտով կամ նախասիրություններով զբաղվելը: 0   1   2   3   4
        5

10.   Ձեզ համար դժվարացրել է Ձեր սեռական կյանքը: 0   1
        2   3   4   5

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11. Ձեզ ստիպել է ավելի քիչ ունել Ձեր սիրած ունելիքները:

0   1   2   3   4   5

12. Ձեզ մոտ եղել է շնչարգելություն: 0   1   2   3

4   5

13. Ձեզ մոտ եղել է հոգնածություն, ու ժառապություն կամ էներգիայի պակաս: 0   1   2   3   4   5

14. Ձեզ ստիպել է զանվել հիվանդանցում: 0   1   2

3   4   5

15. Ձեզ ստիպել է ավել ացել առողջություն պահպանման համար Ձեր ծախսերը: 0   1   2   3   4   5

16. Ձեզ մոտ ուժման հետևանքով կողմնակի

ազդեցություններ են առաջացել: 0   1   2   3   4   5

17. Ձեզ մոտ առաջացրել է Ձեր ընտանիքի անդամների կամ ընկերների համար բեռ դառնալու զգացողություն: 0   1

2   3   4   5

18. Ձեզ մոտ առաջացրել է զգացողություն, որ այլես Դուք չեք կարողանում տնօրինել Ձեր սեփական կյանքն այն չափով, որքան կցանկանայիք:0   1   2   3   4   5

19. Ձեզ ստիպել է անհանգստանալ: 0   1   2   3   4

5

20. Ձեզ համար դժվարացրե՞լ է կենտրոնանալը կամ ինչ-որ բան վերհիշելը: 0 1 2 3 4 5

21. Ձեզ ստիպե՞լ է ընկճված զգալ: 0 1 2 3 4 5

Յուրաքանչյուր հարցում, խնդրում ենք նշեք, արդյոք ունեք որևէ խնդիրներ կապված նշված առողջազրծողությունների հետ, նշելով այն պատասխանը որը լավագույնս նկարագրում է Ձեր առողջական վիճակն այսօր:					
#		Ոչ մի դժվա- րություն են	Թեթև դժվա- րություն են	Միջին դժվա- րություն են	Մեծ դժվա- րություն են	Ի վիճակի չեմ կատարել
1	Քայլել	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
2	Լվացվել կամ հագնվել	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
3	Կատարել առօրյա գործեր (աշխատանքի, ուսման, տան կամ ժամանցի հետ կապված)	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
#		Ոչ մի	Թեթև	Միջին	Ուժեղ	Ծայրահեղ

4	Ցավ կամ անհարմարավետություն	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
5	Տագնապ կամ ընկճվածություն	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

Խնդրում եմ պատկերացրեք ջերմաչափի սանդղակ համարակալված 0-ից 100 թվերով, որտեղ 100-ը նշանակում է լավագույն առողջական վիճակը՝ Ձեր պատկերացմամբ, իսկ 0-ն նշանակում է վատագույն առողջական վիճակը՝ Ձեր պատկերացմամբ: Որ թիվը կբնութագրի Ձեր առողջական վիճակն այսօր:
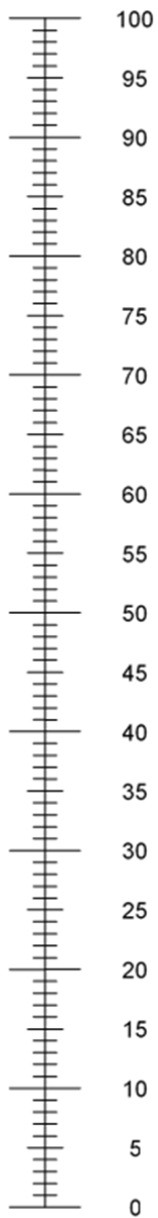
Դեմոգրաֆիկ տվյալներ

1. Սեռ (չ կարդալ) 1. Արական 2. Իգական

2. Տարիքը 1. ____ 2. Հրաժարվում է պատասխանել

3. Ինչ՞ կրթություն ունեք: 1. Միջնակարգ (քիչ քան 10 տարի)

2. Միջնակարգ (10 տարի)

3. Միջին մասնագիտական

4. Ինստիտուտ/Համալսարան

4. Ներկայումս աշխատու՞մ եք (Ներառյալ ինքնազբաղվածությունը, գյուղատնտեսությունը և սեզոնային ին/միգրացիոն աշխատանքը): 1. Այո

2. Ոչ

5. Ինչ պիսի՞ են է Ձեր ամուսնական կարգավիճակը (Ընտրեք մեկ տարբերակ):

1. Չամուսնացած

2. Ամուսնացած

3. Այրի

4. Ամուսնալուծված

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5. Հրաժարվում է

պատասխանել

6. Որքա՞ն է Ձեր ընտանիքի միջին ամսական եկամուտը:

1) 50,000 դրամից քիչ

2) 50,000 - 100,000 դրամ

3) 101,000 - 200,000 դրամ

4) 201,000 - 300,000 դրամ

5) Ավելի քան 300,000 դրամ

6) Չգիտեմ/Հրաժարվում եմ պատասխանել

7. Դուք երբևէ ծխել եք՞ : **1.** Այո (անցնել հաջորդ հարցին) **2.** Ոչ

8. Դուք ներկայումս ծխում եք՞ : **1.** Այո (անցնել հաջորդ հարցին)

2. Ոչ

9. Ներկայումս օրեկան քանի՞ ծխախոտ եք օգտագործում: **1. 10-
ից քիչ**

2. 11-20

3. 21-ից չ ատ

Medical record data extraction form

Demographic data
1. #ID   /phone number/
2. Date of birth __ /__ /__ (MM/DD/YY)
3. Gender □ 1.male □ 2. female
Perioperative data
4. CABG date __ /__ /__ (day/ month/year)
5. Concomitant disease at the time of surgery □ a. yes □ b. no

If yes: □ 1. MI □ 2. AH, □ 3. DM, □ 4. Arrhythmia, □ 5. COPD, □ 6. CKD
    □ 7. Other
    7a. Specify other_____

Clinical information at last clinic visit
6. Date of the last follow-up visit __ /__/ __ (MM/DD/YY)
7. Clinical symptoms of HF (during the last visit)   □ 1. Shortness of breath □ 2. Orthopnea □ 2. Dyspnea (nocturnal) □ 3. Ankle swelling □ 4.Tiredness □ 5. Fatigue □ 6. Exercise tolerance reduction □ 7. No complains   □ 8. Other complains
8. Heart Failure class (NYHA) at the last visit □ 1. I □ 2. II □ 3. III □ 4. IV
9. Ejection fraction at the last visit □ 1. >50% □ 2. 40-49% □ 3. <40%
10. Prescribed medications during the last visit □ 1. ACEIs/ARBs, □ 2. MRAs, □ 3. BBs, □ 4. Others

Appendix 5. List of variables

Variable name	Variable type	Variable measure	Source of the Variable
Dependent variables			
MLHFQ HRQoL score	continuous	0-105	Telephone survey
EQ-5D-5L	continuous	0-25	Telephone survey
Perioperative Independent variables			
Age	continuous	18 and above	Medical record
Gender	dichotomous	Male/female	Medical record
CABG date	date	Mm/dd/yyyy	Medical record
Concomitant disease	dichotomous	Yes/ no	Medical record
Myocardial infarction	dichotomous	Yes/no	Medical record
Hypertension	dichotomous	Yes/no	Medical record
Diabetes mellitus	dichotomous	Yes/no	Medical record
Arrhythmia	dichotomous	Yes/no	Medical record
Chronic obstructive pulmonary disease	dichotomous	Yes/no	Medical record
Chronic kidney disease	dichotomous	Yes/no	Medical record
Heart failure	dichotomous	Yes/no	Medical record
Other disease	dichotomous	Yes/no	Medical record
Other specify	string	Arthrosis (example)	Medical record
Independent variables during the last visit			
The last follow-up visit	date	Mm/dd/yyyy	Medical record
Clinical symptoms	dichotomous	Yes/no	Medical record
Shortness of breath	dichotomous	Yes/no	Medical record
Orthopnea	dichotomous	Yes/no	Medical record
Dyspnea at night	dichotomous	Yes/no	Medical record
Ankle swelling	dichotomous	Yes/no	Medical record
Tiredness	dichotomous	Yes/no	Medical record
Fatigue	dichotomous	Yes/no	Medical record
Exercise tolerance reduction	dichotomous	Yes/no	
No complains	dichotomous	Yes/no	Medical record
Other complains	dichotomous	Yes/no	Medical record
LVEF	continuous	>40%, <40%	Medical record
HF class (NYHA)	ordinal	I, II, III, IV	Medical record
Smoking status	dichotomous	Yes/no	Telephone survey
Prescribed drugs	dichotomous	Yes/no	Medical record

ACEIs/ARBs	dichotomous	Yes/no	Medical record
MRAs	dichotomous	Yes/no	Medical record
BBs	dichotomous	Yes/no	Medical record
Other medication	dichotomous	Yes/no	Medical record

Appendix 6. Sample size calculation

	Pelegrino et. Al, 2011	Fotos et al., 2012	Faxen U. et al, 2018	Chu Sang Hui et al., 2014	Feldman et al., 2011
M SD	M1=39.3 M2=31.8 SD=24.6	M1=63.8 M2=62.2 SD=20.3	M1=31 M2=29 SD=21	M1=39.1 M2=29.5 SD=22.3	M1=28.77 M2=27.85 SD=22.7
Alpha=0.05 Power=80% (assuming 1:1 ratio)	N=153 each group	N=2453 in each group	N=1731 in each group	N=83 in each group	N=9557 in each group
Response rate=80% (assuming 1:1 ratio)	153/0.8=184	2453/0.8=3066	1731/0.8=2163	83/0.8=103	9557/0.8=11946
Alpha=0.05 Power=80% (assuming 2:1 ratio)	N1 = 127 N2=254	N1=2044 N2=4088	N1=1154 N2=2308	N1=55 N2=110	N1=6371 N2=12742
Response rate=80% (assuming (2:1 ratio)	N1 = 160 N2=320	N1=2555 N2=5110	N1=1442 N3=2885	N1=69 N2=138	N1=7964 N2=15928

Two sided t-test

sampsi 39.3 31.8, p(0.8) r(2) sd1(24.6) sd2(24.6) a(0.05)
Estimated sample size for two-sample comparison of means
Test Ho: m1 = m2, where m1 is the mean in population 1
           and m2 is the mean in population 2
Assumptions:
     alpha =   0.0500 (two-sided)
     power =   0.8000
        m1 =   39.3
        m2 =   31.8
       sd1 =   24.6
       sd2 =   24.6
     n2/n1 =   2.00
Estimated required sample sizes:

        n1 =   127
        n2 =   254

Appendix 7. Review of articles in gender differences of HRQoL in HF patients

Author, Country	Study Population	HQoL instrument	Predictors	HQoL score (SD)
Fotos et al., 2012, Greece	A total of 199 patients (participation rate 67.9%)	Minnesota living with heart failure	Severe HF, Diabetes Mellitus, Arterial Hypertension, Chronic renal failure, Chronic respiratory failure, Cancer, Low physical capacity	Male 62.2 (20.5) 0.6 Female 63.8 (20.2) p-value 0.6
Kraai I. et al, 2013, Sweden	100 patients (mean age 70+9 years; 71% male)	Minnesota living with heart failure, EQ-5D	61% attach more weight to quality of life over longevity; while 9% and 14% were willing to trade 6 and 12 months, respectively, for perfect health and attach more weight to quality of life	Total score 26 (0–87) p-value=0.15 Emotional component 4.5 (0–25) p-value=0.23 Physical component 12 (0–40) p-value=0.36
Pelegrino M. et al, 2011 Brazil	130 patients average age was 55.1 (SD= 14.9), male (n=77, 59.2%)	Minnesota living with heart failure, SF-36 Portuguese version (for mental health)	NYHA class (II, III, IV) severity and psychological factors, such as mood, depression, anxiety associated with the lower HQoL	Female 39.3 (23.3) Male 31.8 (25.4) p-value 0.092
Faxen U. et al., 2018, Sweden	378 patients were studied: 212 were women (57%).	Minnesota living with heart failure, EQ-5D-3L (general health)	Disease-specific HQoL was similar both in male and female with LVpEF, Women had worse general health measure, Poor QoL associated with on the severe HF in both sexes and	Men 31 (21), Women 29 (21) p = 0.269.

			adverse outcomes in males	
CHU Sang Hui et al., 2014, Korea	114 patients (male 55), the mean age of the participants was 65.8 (12.4) years	Minnesota living with heart failure, Generic measure: WHOQOL-BREF	A lower MLHFQ score associated older age, male sex, better functional status, better economic status, fewer comorbid conditions	QoL score: Men = 29.5 (22.9) Women = 39.1 (21.8) Regress coeff: Beta= 0.198
Feldman et al., 2011, Canada	531 patients (mean age 66 years), 26% women	MLHFQ, 6-minute walk test (6MWT), a measure of submaximal exercise capacity	Predictor for mortality is older age, Better survival associated with female gender, non-ischaemic etiology, lower HF NYHA class, higher EF, women have lower HQOoL comparing to men	Entry to clinic Men 43.83 (23.98) Women 50.36 (23.50) After 12 months Men 27.85 (23.09) Women 28.77 (22.32) p-value< 0.001
Hoekstra et al., 2012, the Netherlands	661 patients (62% male), age 71 years	Cantril's Ladder of Life (global well-being), RAND36, MLHFQ	QoL independent predictor of HF 3 year mortality, lower HQoL associated with older age, female gender, HF long-term diagnosis, co-morbidities. NYHA class (III–IV), low eGFRs, no prescription of beta-blockers.	The mean score in total group MLHFQ was 44 (21)

Kozhekenova et al., 2014, Kazakhstan	285 patients (mean age 60.8) 204 women, 81 men,	MLHFQ	Hypertension, DM, CKD associated with the worse HQoL	Total score 34.7 (13.8)