Title

Association of baseline and changes in health-related quality of life with mortality following myocardial infarction: Multicentre longitudinal linked cohort study

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Abstract

Background

Health related quality of life (HRQoL) for patients following myocardial infarction (MI) is frequently impaired. We investigated the association of baseline and changes in HRQoL with mortality following MI.

Methods and findings

Nationwide longitudinal study of 9,474 patients admitted to 77 hospitals in England as part of the Evaluation of the Methods and Management of Acute Coronary Events (EMMACE) study. Self-reported HRQoL was collected using EuroQol EQ-5D-3L during hospitalisation and at 1, 6 and 12-months following discharge. Data was analysed using flexible parametric and multilevel survival models. Of 9,474 individuals with MI, 2,360 (25%) were women and 2,135 (22.5%) died during the 9 years follow up period. HRQoL improved over 12 months (baseline mean, mean increase: EQ-5D 0.76, 0.003 per month; EQ-VAS 69.0, 0.5 per month). At baseline, better HRQoL was inversely associated with mortality (HR 0.55, 95% CI 0.47 to 0.63), and problems with self-care (HR 1.73, 1.56 to 1.92), mobility (1.65, 1.50 to 1.81), usual activities (1.34, 1.23 to 1.47) and pain/discomfort (1.34, 1.22 to 1.46) were associated with increased mortality. Deterioration in mobility, pain/discomfort, usual activities and self-care over 12 months were associated with increased mortality (HR 1.43, 95% CI 1.31 to 1.58; 1.21, 1.11 to 1.32; 1.20, 1.10 to 1.32; 1.44, 1.30 to 1.59, respectively).

Conclusions

After MI, poor HRQoL at baseline, its dimensions and deterioration over time are associated with increased risk of mortality. Measuring HRQoL in routine clinical practice after MI could identify at-risk groups for interventions to improve prognosis.

Trial registration

ClinicalTrials.gov NCT01808027

What is already known

- Following myocardial infarction (MI), health-related quality of life (HRQoL) is frequently impaired and often deteriorates.
- There is limited health system wide information about the association of HRQoL and mortality after MI.

What this study adds

- This prospective longitudinal linked data shows the negative impact of poor baseline HRQoL in each of the dimensions of EQ-5D on survival, and how deterioration in these dimensions is associated worse prognosis.
- The systematic measurement of HRQoL following MI may offer actionable insights for patient stratification and predicting outcomes.

Introduction

Quality of life predicts survival and rehospitalisation for a range of major health conditions including cancer, (1) pulmonary disease, (2) renal disease, (3) and organ transplantation.(4, 5) Herein, its routine measurement in clinical practice has been used to monitor disease progression, identify patients at risk of adverse outcomes, and highlight unforeseen problems due to prescribed medications,(6) thus enabling stratified care with subsequent improvements in clinical outcomes.(1, 7-9) Yet, evidence is lacking for the association of health-related quality of life (HRQoL) with prognosis for individuals admitted to hospital with myocardial infarction (MI). This is important because early death following hospitalised MI has declined, (10, 11) resulting in a much later and high burden of mortality, morbidity and healthcare utilisation.(12) Given that MI remains a common reason for hospitalisation,(12, 13) new strategies to improve latent health outcomes in this group are required.

Following MI, HRQoL is frequently impaired and often deteriorates.(14) This includes greater physical limitation and more problems with self-care, pain and mental stress.(14, 15) Poor HRQoL can persist after an initial cardiac event (14, 15) and is associated with high health resource utilisation.(16) Moreover, specific baseline patient characteristics are associated with HRQoL trajectories following MI, which form unique recovery patterns. Our earlier research found that women, those with non-ST-elevation myocardial infarction (NSTEMI), and those with long-term health conditions were less likely to show improvements in HRQoL, and that distinct multimorbidity clusters were associated with HRQoL.(14, 17) To date, however, the association between HRQoL and clinical events in patients with MI is unknown. Furthermore, the absence of systematic capture of HRQoL for individuals with MI not only precludes novel observational insights into its relationship with

prognosis, but hinders opportunities to integrate data-driven strategies based on patient perspectives to transform health provision.

The Evaluation of the Methods and Management of Acute Coronary Events, EMMACE-3 and EMMACE-4 cohorts are multicentre longitudinal studies of outcomes following MI that combine survey data with routine national health data, and include information about HRQoL.(18) There are few large-scale datasets available that combine clinical data with robust evaluation of temporal changes in HRQoL for patients with MI. We therefore used the EMMACE cohorts to extended previous research to investigate associations between HRQoL and mortality in patients hospitalised with MI.

Methods

Setting and design

The study was based on the analysis of data from 9,474 patients who participated in the EMMACE-3 and 4 nationwide longitudinal cohort studies. Details of the study have been published previously.(18) In brief, all adults aged ≥18 years admitted with ST-elevation myocardial infarction (STEMI) or NSTEMI to 77 National Health Service (NHS) hospitals in England between 1st November 2011 and 24th June 2015 were eligible to be included. The study collected data relating to medication adherence, HRQoL, co-morbidities, treatments and clinical outcomes for patients at hospitalisation and then at 1-, 6- and 12-months following hospital discharge. Records for consenting patients were linked to the United Kingdom (UK) national heart attack register (Myocardial Ischaemia National Audit Project, MINAP(19)) to gather data about past medical history, type of MI and in-hospital treatment. All-cause mortality data, with a censoring date of when the research coordinator did the mortality tracking for each participant, was collected using the NHS Spine platform and linked to the EMMACE-3 and 4 data used for this study.

Assessment of health-related quality of life

Self-reported HRQoL was quantified using EQ-5D-3L, a standardised instrument developed by the EuroQoL group and validated in post-MI patients.(20, 21) EQ-5D-3L is a descriptive classification made up of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is divided into three levels (3L): no problems, some problems, extreme problems indicating the patient's perceived level of function.(20) The EQ-5D index score ranges from −0.5 to 1, with scores less than 0 indicating states 'worse than death', 0 indicating no quality of life or 'death' and 1 indicating full health and therefore no problems in any domain. EQ-VAS is an analogue scale of 0-100

in which participants are required to indicate their own perceived health with 0 indicating 'worst imaginable health state' and 100 'best imaginable health state'.(20)

Statistical analyses

Baseline characteristics were described using frequencies and proportions for categorical data. Normally distributed continuous data were described using means and standard deviations (SD), and non-normally distributed data using medians and interquartile ranges (IQR). For descriptive analyses, baseline HRQoL scores were categorised into tertiles. Latent growth models(22) were used to describe changes in HRQoL over 12 months following MI, applying the lavaan package in R.

Flexible parametric (23) and multilevel survival models were fitted to investigate the associations of baseline and change in HRQoL with survival. Adjustment in the models was made for: diabetes mellitus, hypercholesterolaemia, hypertension, asthma/chronic obstructive pulmonary disease (COPD), cerebrovascular disease, peripheral vascular disease, smoking status, family history of coronary heart disease (CHD), age, sex, care by cardiologist, previous percutaneous coronary intervention (PCI), previous coronary artery bypass graft (CABG) surgery, previous myocardial infarction (MI), previous angina, chronic renal failure, chronic heart failure, and discharge medications (statins, aspirin, $P2Y_{12}$ inhibitors, angiotensin converting enzyme inhibitors/angiotensin receptor blockers). To investigate the association between HRQoL domains and survival, domain responses were treated as binary variables, 'some problems' and 'extreme problems' categories versus 'no problems'. The scale (proportional hazards, proportional odds or normal) and complexity (number of degrees of freedom) for flexible parametric survival models were checked on the full multivariable model. The baseline hazard on the hazard scale with five degrees of freedom produced the

optimal model through minimisation of the AIC and BIC (Supplementary Table 1). Models were fit for the primary outcome of all-cause mortality during the follow up period, and for secondary outcomes; one month, six months and one year all-cause mortality.

Multiple imputation by chained equations were used to handle missing data in variables; age and sex. Missing data in select binary treatment and medical history variables were imputed to 'no'. Details of the imputation strategy applied to handle missing data are provided in Supplementary Table 2. Rubin's rules were used to pool the results estimates of 10 number of imputations and generate 95% confidence intervals. Analyses were performed using Stata MP64 version 17 (StataCorp, www.stata.com), R version 3.1.2 and R version 4.1.0. P-values <0.05 were considered statistically significant.

Ethics

EMMACE-3 was given a favourable ethical opinion by the Leeds (Central) Research Ethics committee (REC reference: 10/H1313/74), is registered on ClinicalTrials.gov (NCT0180827) and was adopted onto the National Institute for Health Research Comprehensive Research Network portfolio (9102). EMMACE-4 was given favourable ethical opinion by the West Midlands - Black Country Research Ethics Committee (REC reference: 12/WM/0431), is registered on ClinicalTrials.gov (NCT01819103) and was adopted onto the National Institute for Health Research Comprehensive Research Network portfolio (9102). All patients included in the study have provided consent to participate and for their data to be used for research by initialling consent statements on the front of the questionnaires used for data collection.

Patient and Public Involvement

The Leeds Teaching Hospitals NHS Trust Cardiovascular Patient and Public Involvement group was involved in the project design including the setting up of the EMMACE studies. Scheduled discussions were held with the group about the study and its potential impact. Feedback was received on how to best conduct the study to ensure patient benefit.

Results

Participants characteristics

Of the 9,474 participants, mean age was 64.1 (SD 12.0) years, 2,360 (25.0%) were women, and 3,875 (40.9%) had STEMI. Overall, the comorbidity burden of the cohort was high, and many had long-term health conditions. Two thirds of patients were current or ex-smokers (6,181, 67.1%), almost half had hypertension (4,029, 44.8%), and almost a third had hypercholesterolaemia (2,911, 31.9%) (Table 1). Compared with participants in the highest tertile of HRQoL (EQVAS (> 75) and EQ-5D (=1.0)) (good HRQoL) at baseline, those in the lowest tertile (EQVAS (≤ 55) and EQ-5D (≤ 0.69)) (poor HRQoL) less frequently had a STEMI, but more frequently were women and had higher rates of cardiovascular comorbidity and asthma/COPD (Table 1).

Insert Table 1 here

HRQoL at baseline and trajectories following MI

The median EQ-5D score at baseline was 0.81 (IQR 0.59 to 1.00) and median EQ-VAS score at baseline was 70.0 (IQR 50.0 to 80.0). There was an improvement in HRQoL over 12 months following MI (baseline mean, mean increase: EQ-5D 0.76, 0.003 per month; EQ-VAS 69.0, 0.5 per month) (Supplementary Figure 1). Stratified by sex, baseline EQ-5D score mean for men was 0.74 (SD 0.28) and women 0.66 (SD 0.31). By comparison the mean EQ-5D score for an age-matched UK general population was 0.88 for men and 0.86 for women. At 12 months follow-up the mean EQ-5D scores remained below the UK age and sex matched general population mean (Supplementary Figure 2).

Changes in HRQoL by tertile

Poor HRQoL persisted for patients in the lowest baseline tertile of HRQoL during follow-up (Table 1), and these patients were more likely to report problems in all dimensions of EQ-5D, with highest frequencies observed for usual activities, mobility, pain/discomfort and anxiety/depression (Figure 1). An increase in the frequencies of patients reporting problems with mobility, pain/discomfort, anxiety/depression and usual activities was observed at 30 days for patients in the highest tertile of HRQoL at baseline (Figure 1).

Insert Figure 1 here

Mortality

Over 62,469 person-years, with a median duration of follow-up 6.9 (IQR 6.1 to 8.4) years, 2,135 (22.5%) participants died. Mortality rates at 30 days, 6 months and 12 months were 0.9% (81), 2.6% (245) and 4.2% (398), respectively. Compared with participants who were in the highest tertile of baseline HRQoL, those in the lowest tertile had higher unadjusted mortality rates (EQ-5D: 28.0 vs. 15.3% and EQ-VAS: 25.0 vs. 18.6%, $P<0.001$) and demonstrated differences in unadjusted survival (Figure 2).

Insert Figure 2 here

Association of baseline HRQoL with mortality

A 0.1 increase in baseline EQ-5D was associated with reduced mortality (adjusted HR 0.55, 95% CI 0.47 to 0.63) (Figure 3), but no statistically significant association was observed between baseline EQ-VAS score and survival. For 30-day survival, problems with mobility (HR 1.65, 1.02 to 2.68), usual activities (HR 1.73, 1.06 to 2.83) and self-care (HR 2.04, 1.26 to 3.32) were associated with increased risk of death. Pain/discomfort was also associated

with increased risk of death at six-months (HR 1.41, 1.08 to 1.85). Each of the dimensions of poor HRQoL were associated with increased risk of death at 12 months and in the longer term (Figure 3), with the exception of anxiety/depression at baseline, which was associated with increased risk of death at 12 months alone (HR 1.41, 1.15 to 1.74).

Insert Figure 3 here

Association of changes in HRQoL with mortality

Improvements in HRQoL following MI were associated with improved survival. Overall, improvement in EQ-5D during 12 months follow-up was associated with a 31% reduction in risk of death (adjusted HR 0.69, 95% CI 0.60 to 0.80) (Table 2). No statistically significant association was observed for changes in EQ-VAS and survival. Patients with a deterioration in mobility, pain/discomfort, usual activities, and self-care during the 12 months of follow-up were at increased risk of death compared with those not reporting deterioration (HR 1.43, 95% CI 1.31 to 1.58; 1.21, 1.11 to 1.32; 1.20, 1.10 to 1.32; 1.44, 1.30 to 1.59; respectively) (Table 2).

Insert Table 2 here

Discussion

Principal findings

In this national longitudinal cohort study of 9,474 patients admitted with MI to 77 hospitals in England, we found that higher HRQoL measured using EQ-5D at baseline and over time was associated with better survival. Specific dimensions of HRQoL captured by EQ-5D including problems with mobility, usual activities, and self-care have prognostic implications in the short- and long-term after MI. This study found that deterioration in mobility, usual activities, pain/discomfort and self-care, but not mental health were independently associated with adverse prognosis.

Comparison with other studies

Poor HRQoL following MI is well described.(14, 15) An observational study of 8,978 participants with MI found that almost half reported 'some' or 'severe' problems on at least one dimension of their health status.(15) This impairment in HRQoL after MI persists over time in about a third of patients.(14) Previous studies have shown that patient-reported health status measures are associated with clinical outcomes in patients with cardiovascular disease, (15, 24-26) but there is little health system wide information about the association of HRQoL and mortality. One study did find that lower EQ-5D, but not EQVAS, was associated with a higher risk of death and composite of major cardiovascular events over two years post-MI.(15) Our findings extend this by demonstrating in a large prospective study the detrimental impact of poor baseline HRQoL in each of the dimensions of EQ-5D on short and longer term outcomes, and how deterioration in these dimensions is associated with worse prognosis.

Our study did not find an association between anxiety/depression and mortality. This is in keeping with previous reports in which self-reported anxiety and depression did not predict cardiovascular outcomes.(15, 27) The findings could be attributed to improvement in management of anxiety/depression in the contemporary era, for example with prescription of antidepressants, but are in contrast to the finding that hospitalisation with neuro-psychiatric diagnoses (including anxiety and depression) following circulatory disorders are more common among patients with MI and this is associated with increased mortality compared with non-MI matched controls.(12)

Compared to a UK age- and sex-matched general population, HRQoL was lower for MI patients at hospitalisation. It improved during follow-up though remained lower than the age- and sex-matched general population average. The lower HRQoL observed in the patients could be due to impact of MI and higher comorbidity burden. In a previous study we conducted we found that reduced HRQoL in MI patients was associated with chronic renal failure, COPD, cerebrovascular disease, previous angina and previous MI,(17) all of which are highly prevalent in survivors of MI.(17)

Implications for practice

Evidence supporting the incorporation of health status in risk stratification for MI is lacking, and current efforts to systematically capture HRQoL after MI are at best minimal. Our study adds to the growing evidence that HRQoL after MI is an important variable that may be used in predicting clinical outcomes. (15, 25, 26, 28, 29) There is divergence between patients' and physicians' perceptions of patients' health status. As such, patient-reported outcome measures add a fundamental value to risk assessment and mitigation. A key finding of this study is that improvements in HRQoL are associated with favourable clinical outcomes, and

that deterioration in measurable parameters of HRQoL are associated with adverse prognosis. Assessing HRQoL routinely could help identify patients with MI who are at higher risk of premature death, allowing targeted identification of individuals who may be suitable to intervention. For example, information about HRQoL could be used to encourage enrolment into tailored programmes of cardiac rehabilitation, identify those who may be at future risk of non-adherence to medications, or schedule more frequent clinical reviews. Prospective evaluation of interventions guided by baseline and trajectory of HRQoL is required to determine the clinical and cost-effectiveness of such an approach.

Nonetheless, challenges exist in implementing HRQoL assessment following MI. First, the time and effort required to collect data pertinent to HRQoL may create burden on already overstretched healthcare systems. The establishment of quality indicators for the assessment of HRQoL after MI by professional organisations,(30) may promote healthcare regulators to develop strategies for the collection of this important aspect of MI care. Whilst the EQ-5D is a generic HRQoL questionnaire, it has been validated for MI patients and provides the ability to compare HRQoL impairment with other cardiovascular and non-cardiovascular disease. Whilst our study has shown that the EQ-5D-3L score can predict the risk of all-cause mortality in patients with MI, and that individual dimensions provide important prognostic information, it could be improved upon by data collection that captures health status dimensions specific to MI survivors (for example burden of medication and angina).

Strengths and limitations

Our study benefits from a nationwide longitudinal cohort with longer term follow-up in terms of outcomes than has been previously reported. The use of a nationwide dataset increases the generalisability of the results. However, we do acknowledge that there will have been bias in

recruitment and this will have been reflected in the findings – only those who survive to hospitals discharge could participate, and case selection will have occurred resulting in a younger and healthier cohort of people with MI. Loss of follow-up data can also introduce selection bias, which may have affected the magnitude of associations we observed. The external validity of this study could be limited by the fact that data collection for health related quality of life following MI information was conducted between November 2011 and June 2015. However, the outcome follow-up data was censored in 2020 which relates to contemporary practice.

Conclusions

This nationwide prospective cohort study found that better and improved HRQoL following MI was associated with improved survival. Patients' perspective of their own well-being is an important variable following MI, which can be incorporated into routine care to guide risk stratification, targeted identification and tailored treatment strategies.

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Competing interests declaration

I have read the journal's policy and the authors of this manuscript have the following competing interests: CPG reports study funding from Horizon 2020. CPG reports grants from Alan Turing Institute, British Heart Foundation, National Institute for Health Research, Horizon 2020, Abbott Diabetes, Bristol Myers Squibb and European Society of Cardiology. CPG reports consulting fees from AI Nexus, AstraZeneca, Amgen, Bayer, Bristol Myers Squibb, Boehrinher-Ingleheim, CardioMatics, Chiesi, Daiichi Sankyo, GPRI Research B.V., Menarini, Novartis, iRhythm, Organon and The Phoenix Group. CPG reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from AstraZeneca, Boston Scientific, Menarini, Novartis, Raisio Group, Wondr Medical and Zydus. CPG reports receiving support for attending meetings and/or travel from AstraZeneca. CPG reports participation on a Data Safety Monitoring Board or Advisory Board for DANBLCOK trial and TARGET CTCA trial. CPG reports leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid as deputy editor: EHJ Quality of Care and Clinical Outcomes, NICE Indicator Advisory Committee and Chair ESC Quality Indicator Committee. CPG reports stock or stock options with CardioMatics. CPG reports receipt of equipment, materials, drugs, medical writing, gifts or other services from Kosmos device. MH reports grants from Wellcome Trust, Alan Turing Institute and British Heart Foundation. TM reports grant from British Heart Foundation. SA reports support for attending meetings and/or travel from European Society of Cardiology. SA reports participation on a Data Safety Monitoring Board or Advisory Board for Data management and analysis group of British Cardiovascular Intervention Society. AS reports grants or contracts from European Society of Cardiology. AS reports payment or honoraria for; lectures from AstraZeneca and Gedeon Richter, for manuscript writing from Bayer and for educational events from Novartis. AS reports support for attending meetings and travel

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Contributorship:

TBD analysed the data. CPG, TM and TBD provided scientific input. CPG, BH, SA, RN, AS, MH and ASH provided expert clinical opinion and interpretation of the data. TBD, TM, MH and RMW provided expert opinion on data analyses and interpretation of the data. All authors made critical revisions and provided intellectual content to the manuscript, approved the final version to be published and agreed to be accountable for all aspects of the work. CPG is the guarantor for this study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted

Data Sharing

No additional data are available.

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494 **Table 1**: Characteristics of study participants overall and, by baseline EQVAS and EQ-5D score tertiles

Variable	Total cohort N= 9,474	EQVAS Tertile 1 (≤ 55) n= 3,200	EQVAS Tertile 2 (>55 to ≤ 75) n= 3,276	EQVAS Tertile 3 (> 75) n= 2,767	EQ-5D Tertile 1 (≤ 0.69) n=3,320	EQ-5D Tertile 2 (>0.69 to ≤ 0.88) n= 3,099	EQ-5D Tertile 3 (=1.00) n= 2,694	Missing n (%)
Age, mean (SD), yr.	64.1 (12.0)	63.6 (12.3)	64.7 (11.9)	64.0 (11.6)	64.3 (12.4)	65.0 (12.1)	62.7 (11.2)	17 (0.2)
Female, n (%)	2,360 (25.0)	983 (30.8)	775 (23.7)	542 (19.6)	1,045 (31.6)	761 (24.6)	463 (17.2)	23 (0.2)
Ex/current smoking status, n (%)	6,181 (67.1)	2,109 (67.9)	2,122 (66.6)	1,796 (66.8)	2,225 (69.1)	1,968 (65.2)	1,748 (66.7)	261 (2.8)
Family history of CHD, n (%)	3,118 (38.9)	1,004 (38.0)	1,072 (38.5)	956 (40.3)	989 (36.6)	1,005(38.4)	1,005 (42.2)	1,464 (15.5)
Comorbidities								
Previous PCI, n (%)	894 (10.0)	335 (11.2)	326 (10.5)	220 (8.3)	351 (11.4)	315 (10.7)	202 (7.8)	508 (5.4)
Previous CABG surgery, n (%)	642 (7.2)	246 (8.2)	223 (7.2)	163 (6.2)	266 (8.6)	221 (7.5)	134 (5.2)	494 (5.2)
Previous MI, n (%)	1,512 (16.8)	562 (18.7)	521 (16.7)	390 (14.8)	602 (19.4)	505 (17.2)	344 (13.2)	484 (5.1)
Previous angina, n (%)	1,778 (19.8)	702 (23.3)	603 (19.4)	432 (16.4)	741 (23.9)	602 (20.5)	366 (14.1)	491 (5.2)
Chronic renal failure, n (%)	286 (3.2)	113 (3.8)	97 (3.1)	67 (2.5)	130 (4.2)	87 (3.0)	53 (2.0)	497 (5.3)
Hypertension, n (%)	4,029 (44.8)	1,418 (47.1)	1,386 (44.6)	1,119 (42.4)	1,486 (47.9)	1,339 (45.5)	1,053 (40.5)	485 (5.1)
Chronic heart failure, n (%)	211 (2.4)	91 (3.0)	68 (2.2)	45 (1.7)	116 (3.8)	58 (2.0)	27 (1.0)	500 (5.3)
Hypercholesterolemia, n (%)	2,911 (31.9)	1,012 (33.2)	1,012 (32.0)	814 (30.3)	1,050 (33.3)	958 (32.2)	796 (30.2)	351 (3.7)
Peripheral vascular disease, n (%)	314 (3.6)	130 (4.4)	97 (3.2)	81 (3.1)	148 (4.8)	104 (3.6)	52 (2.0)	622 (6.6)
Asthma / COPD, n (%)	1,154 (12.9)	463 (15.5)	396 (12.7)	261 (9.9)	485 (15.7)	382 (13.0)	237 (9.1)	504 (5.3)
Cerebrovascular disease, n (%)	426 (4.7)	160 (5.3)	146 (4.7)	108 (4.1)	177 (5.7)	143 (4.9)	89 (3.4)	494 (5.2)
Diabetes mellitus, n (%)	1,699 (18.6)	642 (20.8)	579 (18.2)	432 (16.2)	731 (22.9)	545 (18.2)	342 (13.2)	326 (3.4)
Final diagnosis (STEMI vs. NSTEMI)	3,875 (40.9)	1,261 (39.4)	1,358 (41.5)	1,176 (42.5)	1,260 (38.0)	1,251 (40.4)	1,233 (45.8)	0 (0)
Treatments¥								

Variable	Total cohort N= 9,474	EQVAS Tertile 1 (≤ 55) n= 3,200	EQVAS Tertile 2 (>55 to ≤ 75) n= 3,276	EQVAS Tertile 3 (> 75) n= 2,767	EQ-5D Tertile 1 (≤ 0.69) n=3,320	EQ-5D Tertile 2 (>0.69 to ≤ 0.88) n= 3,099	EQ-5D Tertile 3 (=1.00) n= 2,694	Missing n (%)
Coronary intervention (PCI/CABG), n (%)	4,284 (59.5)	1,445 (59.9)	1,444 (58.0)	1,287 (60.5)	1,385 (57.2)	1,420 (60.8)	1,316 (60.3)	1,570 (17.9)
Discharge medications[¥]								
Aspirin n (%)	8,071 (99.3)	2,647 (99.2)	2,814 (99.3)	2,415 (99.5)	2,744 (99.0)	2,611 (99.4)	2,405 (99.6)	302 (3.6)
Beta blocker n (%)	7,524 (98.3)	2,457 (98.1)	2,621 (98.4)	2,271 (98.6)	2,536 (98.1)	2,441 (98.3)	2,266 (98.7)	315 (4.0)
Statins n (%)	8,065 (99.1)	2,650 (99.0)	2,805 (99.2)	2,414 (99.1)	2,756 (99.0)	2,606 (99.0)	2,396 (99.4)	311 (3.7)
ACEI/ARBs n (%)	7,535 (97.6)	2,461 (97.2)	2,602 (97.8)	2,297 (97.7)	2,543 (97.2)	2,427 (97.6)	2,281 (97.9)	342 (4.2)
$P2Y_{12}$ inhibitors n (%)	4,816 (97.3)	1,574 (97.0)	1,685 (97.5)	1,403 (97.6)	1,615 (96.8)	1,559 (97.6)	1,434 (97.9)	479 (8.8)
Cardiac rehabilitation n (%)	8,424 (97.7)	2,806 (97.0)	2,907 (97.9)	2,508 (98.3)	2,863 (97.0)	2,781 (98.0)	2,464 (98.3)	606 (6.6)
HRQoL at follow-up								
EQ-5D, median (IQR)								
Admission	0.8 (0.6 to 1.0)	0.6 (0.4 to 0.8)	0.8 (0.7 to 1.0)	0.9 (0.8 to 1.0)	0.5 (0.2 to 0.6)	0.8 (0.8 to 0.8)	1.0 (1.0 to 1.0)	361 (3.8)
30 days	0.8 (0.6 to 1.0)	0.7 (0.6 to 0.8)	0.8 (0.7 to 1.0)	0.8 (0.7 to 1.0)	0.7 (0.5 to 0.8)	0.8 (0.7 to 0.9)	0.9 (0.8 to 1.0)	2,979 (31.4)
6 months	0.8 (0.7 to 1.0)	0.8 (0.6 to 1.0)	0.8 (0.7 to 1.0)	1.0 (0.7 to 1.0)	0.7 (0.5 to 0.9)	0.8 (0.7 to 1.0)	1.0 (0.8 to 1.0)	4,031 (42.6)
12 months	0.9 (0.7 to 1.0)	0.8 (0.6 to 1.0)	0.8 (0.7 to 1.0)	1.0 (0.7 to 1.0)	0.7 (0.5 to 1.0)	0.8 (0.7 to 1.0)	1.0 (0.8 to 1.0)	4,557 (48.1)
EQVAS								
Admission	69.0 (50.0 to 80.0)	44.0 (30.0 to 50.0)	70.0 (60.0 to 70.0)	85.0 (80.0 to 90.0)	50.0 (40.0 to 70.0)	70.0 (50.0 to 80.0)	75.0 (65.0 to 86.0)	299 (3.2)
30 days	70.0 (60.0 to 80.0)	60.0 (50.0 to 75.0)	70.0 (60.0 to 80.0)	80.0 (70.0 to 90.0)	65.0 (50.0 to 75.0)	70.0 (60.0 to 80.0)	80.0 (70.0 to 90.0)	2,958 (31.2)
6 months	78.0 (62.0 to 86.0)	70.0 (50.0 to 80.0)	75.0 (65.0 to 85.0)	83.0 (75.0 to 90.0)	70.0 (50.0 to 80.0)	80.0 (65.0 to 85.0)	80.0 (70.0 to 90.0)	4,040 (42.6)
12 months	80.0 (65.0 to 90.0)	70.0 (50.0 to 80.0)	80.0 (69.0 to 86.0)	85.0 (75.0 to 90.0)	70.0 (50.0 to 80.0)	80.0 (68.0 to 87.0)	83.0 (75.0 to 90.0)	4,571 (48.3)

Abbreviations: CHD, Coronary heart disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; MI, Myocardial Infarction; COPD, chronic obstructive pulmonary disease; STEMI, ST-elevation myocardial infarction; NSTEMI, non ST-elevation myocardial infarction; HRQoL, Health related quality of life, ACEI/ARBs, angiotensin converting enzyme inhibitors /angiotensin receptor blockers, [¥]Of the eligible.

Table 2: Impact of changes in HRQoL 12 months following MI on long term survival

	Hazard ratio (95% CI)	P value
Model		
EQ 5D	0.69 (0.60 to 0.80)	<0.001
EQ VAS	0.999 (0.999 to 1.000)	0.706
EQ 5D dimensions (yes vs. no)		
Mobility problems		
No	Ref	
Yes	1.43 (1.31 to 1.58)	<0.001
Problems with usual activities		
No	Ref	
Yes	1.20 (1.10 to 1.32)	<0.001
Self-care problems		
No	Ref	
Yes	1.44 (1.30 to 1.59)	<0.001
Pain/discomfort		
No	Ref	
Yes	1.21 (1.11 to 1.32)	<0.001
Anxiety/depression		
No	Ref	
Yes	1.03 (0.94 to 1.13)	0.494

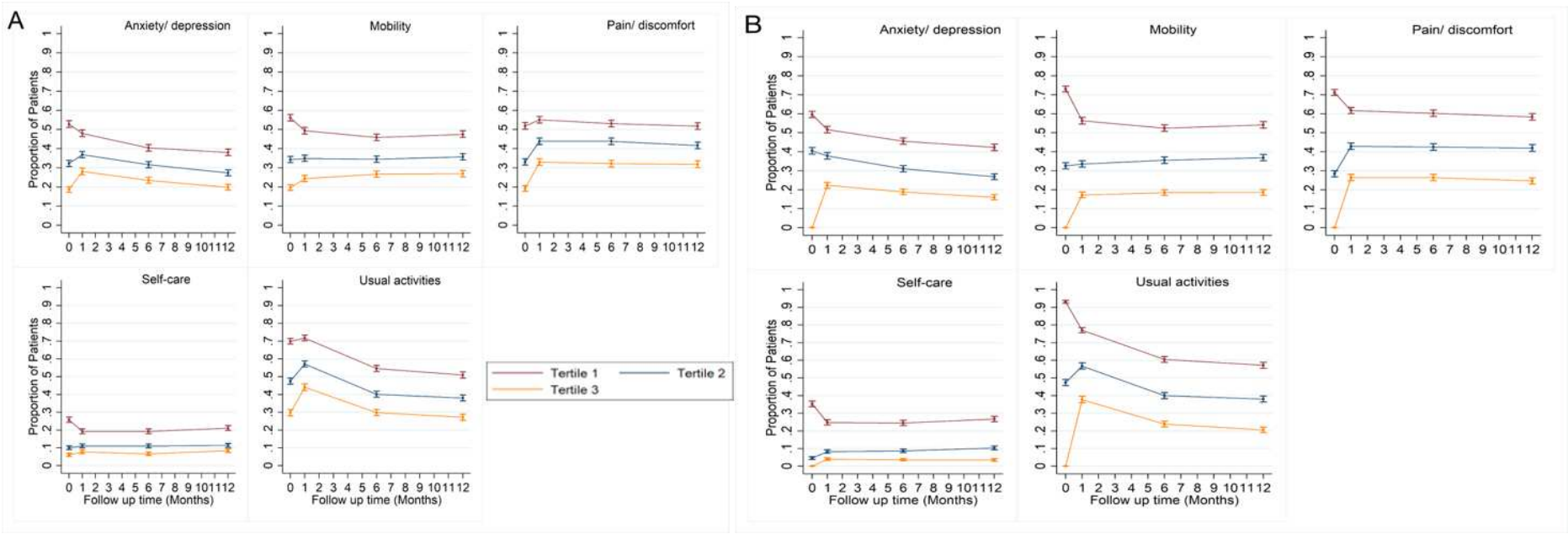
Figure legends

Figure 1: Health related quality of life domains trajectories following myocardial infarction by A) EQ5D and B) EQVAS tertiles.

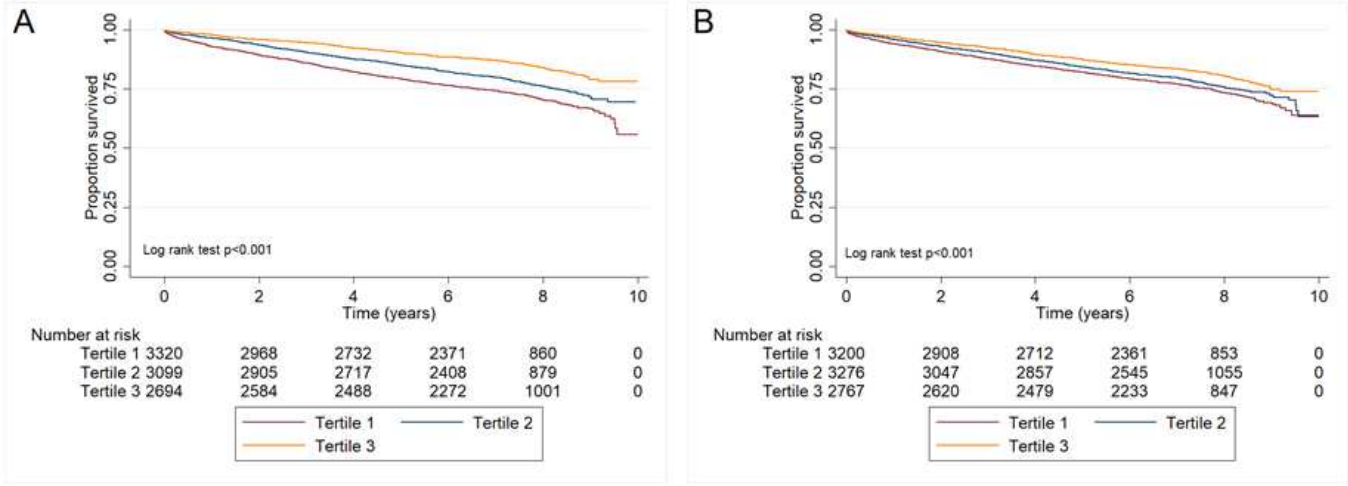
Figure 2: Unadjusted Kaplan-Meier survival estimates by HRQoL tertiles (A: by EQ5D tertiles and B: by EQVAS tertiles).

Figure 3: Impact of baseline HRQoL on survival A) 30 day, B) Six months, C) 12 months and D) long term survival.

Figure 1

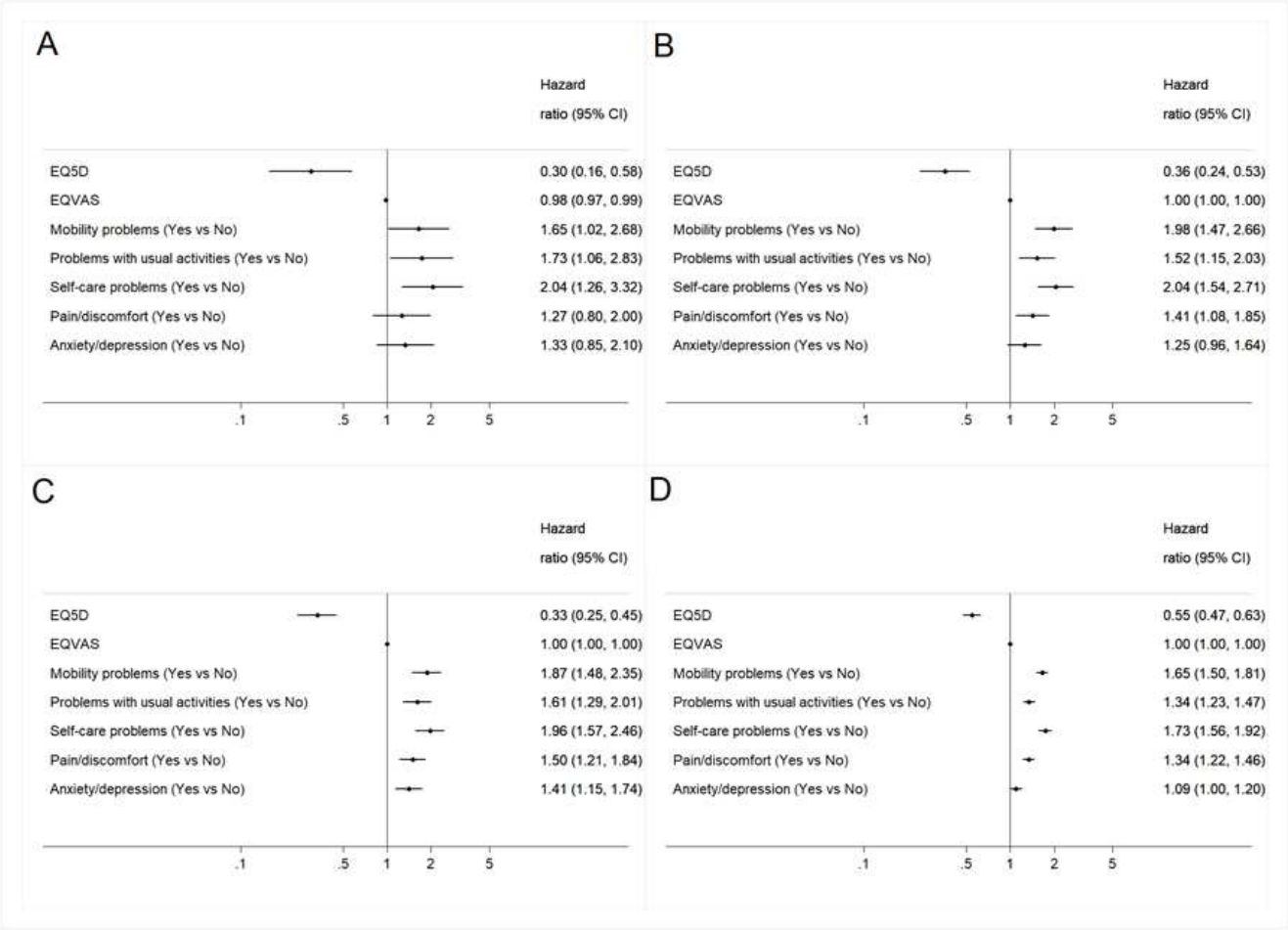

A
Anxiety/ depression
Mobility
Pain/ discomfort
Self-care
Usual activities
Proportion of Patients
Follow up time (Months)
Tertile 1
Tertile 2
Tertile 3
B
Anxiety/ depression
Mobility
Pain/ discomfort
Self-care
Usual activities
Proportion of Patients
Follow up time (Months)

519 **Figure 2**



520

Figure 3


A
Hazard ratio (95% CI)
EQ5D 0.30 (0.16, 0.58)
EQVAS 0.98 (0.97, 0.99)
Mobility problems (Yes vs No) 1.65 (1.02, 2.68)
Problems with usual activities (Yes vs No) 1.73 (1.06, 2.83)
Self-care problems (Yes vs No) 2.04 (1.26, 3.32)
Pain/discomfort (Yes vs No) 1.27 (0.80, 2.00)
Anxiety/depression (Yes vs No) 1.33 (0.85, 2.10)
.1 .5 1 2 5
B
Hazard ratio (95% CI)
EQ5D 0.36 (0.24, 0.53)
EQVAS 1.00 (1.00, 1.00)
Mobility problems (Yes vs No) 1.98 (1.47, 2.66)
Problems with usual activities (Yes vs No) 1.52 (1.15, 2.03)
Self-care problems (Yes vs No) 2.04 (1.54, 2.71)
Pain/discomfort (Yes vs No) 1.41 (1.08, 1.85)
Anxiety/depression (Yes vs No) 1.25 (0.96, 1.64)
.1 .5 1 2 5
C
Hazard ratio (95% CI)
EQ5D 0.33 (0.25, 0.45)
EQVAS 1.00 (1.00, 1.00)
Mobility problems (Yes vs No) 1.87 (1.48, 2.35)
Problems with usual activities (Yes vs No) 1.61 (1.29, 2.01)
Self-care problems (Yes vs No) 1.96 (1.57, 2.46)
Pain/discomfort (Yes vs No) 1.50 (1.21, 1.84)
Anxiety/depression (Yes vs No) 1.41 (1.15, 1.74)
.1 .5 1 2 5
D
Hazard ratio (95% CI)
EQ5D 0.55 (0.47, 0.63)
EQVAS 1.00 (1.00, 1.00)
Mobility problems (Yes vs No) 1.65 (1.50, 1.81)
Problems with usual activities (Yes vs No) 1.34 (1.23, 1.47)
Self-care problems (Yes vs No) 1.73 (1.56, 1.92)
Pain/discomfort (Yes vs No) 1.34 (1.22, 1.46)
Anxiety/depression (Yes vs No) 1.09 (1.00, 1.20)
.1 .5 1 2 5

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