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Health-related quality of life at 30-days among Indian patients with acute myocardial infarction: results from the ACS QUIK trial

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Abstract

Background: Despite a high cardiovascular disease burden, data on patient-reported health status outcomes among individuals with cardiovascular disease in India are limited.

Methods and Results: Between November 2014 and November 2016, we collected health-related quality of life data among 1,261 participants in the Acute Coronary Syndrome Quality

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Improvement in Kerala (ACS QUIK) trial. We used a translated, validated version of the Seattle Angina Questionnaire administered 30 days after discharge for acute myocardial infarction, wherein higher scores represent better health status. We compared results across sex, myocardial infarction type, and randomization status using regression models that account for clustering and temporal trends.

Mean (SD) age was 60.8 (13.7) years, 62% were men, and 63% presented with STEMI. More than two out of five respondents (44%) experienced angina 30 days after hospitalization, but most (68% of respondents with angina; 27% of the total sample) experienced it <1/week (SAQ angina frequency score 60). Respondents rated high median (IQR) scores for angina frequency (100.0 [80.0, 100.0]) overall with similar unadjusted scores by sex, but between-hospitality variability was high. Median (IQR) physical limitation scale response was 58.3 (41.7, 77.8), which is consistent with limitations in moderate- and high-intensity activities at 30-day follow-up. Older respondents had more angina frequency and physical limitations and lower treatment satisfaction and quality of life. Women had greater physical limitations (median [IQR] = 52.8 [38.9, 72.2] for women versus median [IQR] = 61.1 [44.4, 80.6] for men, $p<0.01$). Overall treatment satisfaction was high with median (IQR) score = 81.3 (75.0, 93.8), but overall quality of life was lower with median (IQR) score = 66.7 (50.0, 83.3). Allocation to the quality improvement intervention group had the strongest direct association with higher quality of life (difference=4.2, $p=0.03$), but overall effects were modest.

Conclusions: This study represents the largest report of quality of life among myocardial infarction survivors in India with variability across age, sex, and quality improvement intervention status. Wide variability demonstrated across hospitals warrants further study.

Keywords

health-related quality of life; acute myocardial infarction; Asian Indian; global health

Background

India has among the world's highest burden of heart disease. In 2015 alone, an estimated 7.3 million individuals died from acute myocardial infarction.¹ Potentially contributing to this high mortality is the marked heterogeneity in presentation and management of patients with acute coronary syndrome, as documented in the Kerala ACS Registry.^{2,3} Overall, patients in Kerala are younger, more likely to present with ST-segment elevation myocardial infarction, and less likely to receive reperfusion compared with patients in the United States.⁴

Inpatient and short-term mortality are important outcomes in ACS, but it is also important to understand the health status (symptoms, function, and quality of life) of survivors after hospital discharge because these outcomes can be improved with medical therapy and revascularization. Patients often care as much or more about the quality of life than their survival. Data on patient-reported health status outcomes among acute myocardial infarction survivors in India are limited and are important to understand, given the growing prevalence of heart disease in India.

The objective of this study was to evaluate health-related quality of life among Indian patients who have survived acute myocardial infarction at 30 days as a descriptive study within the Acute Coronary Syndrome Quality Improvement in Kerala (ACS QUIK) trial. We were also interested in evaluating differences across age, sex, type of myocardial infarction, hospital type, and randomization status and to evaluate potential covariates associated with health-related quality of life to identify groups or targets for future intervention.

Methods

Anonymized data and materials are in the process of being made publicly available through the national Heart, Lung, and Blood Institute's Biologic Specimen and Data Repository Information Coordinating Center.

ACS QUIK trial

The methods and primary outcome of the Acute Coronary Syndrome Quality Improvement in Kerala (ACS QUIK) cluster randomized, stepped wedge trial have been published.^{5,6} In brief, the study's primary aim was to evaluate the effect of an evidence-based, locally adapted quality improvement toolkit on the primary outcome of 30-day major adverse cardiovascular events, defined as all-cause mortality, reinfarction, stroke, and major GUSTO bleeding. The quality improvement toolkit included 1) an audit and feedback reporting mechanism, 2) training on the interpretation of these reports for informing quality improvement team meetings, 3) standardized admission and discharge order sets, 4) translated and culturally adapted patient education materials related to tobacco cessation, dietary advice, and physical activity, and 5) linkage to emergency cardiovascular care training. The study recruited 21,374 eligible participants (76% men) with acute myocardial infarction based on the Third Universal Definition of Acute Myocardial Infarction⁷ across 63 hospitals (67% private, 14% government, 19% non-profit) in Kerala, India between November 2014 and November 2016. The follow-up rate was 99% at 30-days. In ACS QUIK, the primary outcome rate of major adverse cardiovascular events at 30 days was 5.3% in the intervention group and 6.4% in the control group (unadjusted odds ratio = 0.82 [95% CI: 0.73, 0.91]). However, after adjusting for clustering effects and temporal trends, this effect was no longer demonstrated (OR=0.98 [95% CI: 0.80, 1.21]).

Sampling frame and data collection

Among a sub-sample of 1,261 eligible participants, we also evaluated health-related quality of life at 30 day follow-up as a secondary objective of the trial using a translated, validated version of the Seattle Angina Questionnaire in Malayalam, the local language in Kerala (courtesy of CV Outcomes, Inc.).⁸ The Seattle Angina Questionnaire is a 19-item instrument that evaluates patient-reported health status across 5 domains: physical limitations, angina stability, angina frequency, treatment satisfaction, and how the respondent perceives their coronary disease to impact their quality of life. Scores range from 0 to 100 for each domain, with higher scores representing better health status. A mean difference of 5 points or greater is considered clinically significant.

To oversample underrepresented groups, including younger women, we used a stratified random sampling frame based on age tertiles (<50 years, 50–69 years, 70 years and above) and sex. We sought to evaluate the prevalence and distribution of health related quality of life among acute myocardial infarction survivors across age- and sex-groups in the ACS QUIK trial. We stratified age by <50, 51–70, and >70 years. A sample of 2,400 participants provided 80% power with a two-sided alpha of 0.05 to detect differences between age- and sex-groups based on an anticipated Seattle Angina Questionnaire score at 30-days of 60 for 369 participants in each strata, assuming ~10% missingness. During the recruitment period, we had slow recruitment in this sub-study in the underrepresented groups and, after consultation with the trial's Data and Safety Monitoring Board, expanded recruitment to include individuals in both the intervention and control groups in November 2015.

The Seattle Angina Questionnaire is designed as a self-administered survey, but our formative research suggested that participants would not be likely to complete this survey without support from each site's research staff. Therefore, sites used research staff to administer the survey by in-person or telephonic interview. We excluded individuals who had missing SAQ data.

Statistical analysis

We report unadjusted demographic, laboratory, and clinical outcome data using summary statistics, including mean and standard deviation for normally distributed continuous variables and median with interquartile ranges for skewed, continuous variables overall and by sex and type of myocardial infarction (STEMI versus NSTEMI), which we compared using Student's *t* test or Wilcoxon rank sum as appropriate. We also compared unadjusted frequencies for categorical variables overall and by strata using Chi-square tests. We compared results from SAQ across sex, type of myocardial infarction, and randomization status using mixed effect linear, logistic or quantile regression models that account for within-hospital clustering and temporal trends. We also report data by participating hospital. We adjusted for variables from the Global Registry of Acute Coronary Events (GRACE) risk score,⁹ including age, sex, type of myocardial infarction, systolic blood pressure, heart rate, acute heart failure, cardiogenic shock, and resuscitated cardiac arrest to evaluate the relationship between exposures of interest (age, sex, type of myocardial infarction, and randomization status) and individual responses to the Seattle Angina Questionnaire. We excluded serum creatinine in the models due to the high degree of missingness of this covariate.

We used Stata version 14 (College Station, TX: StataCorp LP), SAS version 9.4 (Cary, NC: SAS), and R version 3.3.0 (Vienna, Austria: R Foundation) for our statistical analyses.

Ethical considerations

The study received ethics board approval from local, national, and international bodies and was approved by the Indian Health Ministry Screening Committee. All participants or their proxies provided written informed consent to participate.

Results

For this sub-study, the participant flow is reported in Supplemental Figure 1. We recruited 1,356 participants from the main trial (overall ACS QUIK trial n=21,374 participants) and arrived at a final sample of 1,261 participants for this sub-study after excluding incomplete and duplicate surveys or ineligible participants. The primary reason for exclusion was not meeting criteria for a myocardial infarction either due to missing or normal biomarker results, transfer patients without further interventions, or admission outside the study period. The median (interquartile range, IQR) number of days from discharge to survey completion at follow-up (IQR) was 31 (29, 34) days.

Table 1 presents unadjusted and adjusted demographic, clinical, and laboratory data, overall and stratified by sex. The mean (standard deviation, SD) age of the respondents was 60.8 (13.7) years, which was similar to the overall trial population (Supplemental Table 1). Most respondents were men (62% compared with 76% in the overall trial because of the stratified random sampling frame in this study), and most presented with ST-segment elevation myocardial infarction (63%, compared with 65% in the overall trial). The median (IQR) time from symptom onset to arrival was 261 (120, 885) minutes. Women were older (mean [SD] age = 64.0 [13.1] years versus 58.8 [13.6] years, adjusted $p<0.01$) and were less likely to present with ST-segment elevation myocardial infarction (56% versus 68%, adjusted $p<0.01$) than men.

Table 2 displays the overall summary results from the Seattle Angina Questionnaire overall and by sex, and Supplemental Table 2 displays the results within the sub-scale of each domain. More than two out of every five respondents (44%) experienced some angina during the month after hospitalization, but most of these (68% of respondents with angina; 27% of the total sample) had episodes of angina less than once a week. On the other hand, one out of every 10 respondents (10.6%) had weekly angina, and less than 1% of respondents had daily angina. Women had higher rates of weekly or daily angina compared with men (unadjusted angina frequency prevalence: 12.2% versus 9.9%, adjusted $p<0.01$). Supplemental Tables 3 and 4 demonstrate unadjusted and adjusted results stratified by type of myocardial infarction and randomization status, which were largely similar. The respondents rated high median (IQR) scores for angina frequency (100.0 [80.0, 100.0]), indicating minimal impact on quality of life, with similar unadjusted scores by sex. The median (IQR) physical limitation scale response was 58.3 (41.7, 77.8), indicating limitations with moderate and high-intensity activity levels at 30-day follow-up. Women experienced greater physical limitations than men (median [IQR] = 52.8 [38.9, 72.2] for women versus 61.1 [44.4, 80.6] for men, $p<0.01$). Figure 1 demonstrates physical limitation score results by subscale of the Seattle Angina Questionnaire across a range of activity levels. Treatment satisfaction was also high with a median (IQR) score of 81.3 (75.0, 93.8), whereas overall quality of life was lower with a median (IQR) score of 66.7 (50.0, 83.3). Both treatment satisfaction and overall quality of life scores were similar for men and women.

Figure 2 demonstrates variability of physical limitation (panel A), angina frequency (panel B), treatment satisfaction (panel C), and quality of life (panel D) scores by center, which

demonstrates wide variability overall, with the largest variability seen in physical limitation and overall quality of life domains.

Supplemental Table 5 displays univariable association of baseline demographics (including age and sex), presentation (including type of myocardial infarction), and randomized group allocation with SAQ scores, and Table 3 demonstrates these data adjusted for the GRACE risk score covariates. After adjustment, older decade of age was associated with more physical limitations (difference = -4.1 per decade, $p < 0.01$), greater angina frequency (difference = -0.9 score per decade, $p < 0.01$), lower treatment satisfaction (difference = -0.7 per decade, $p = 0.01$), and lower quality of life scores (difference = -0.7 per decade, $p = 0.05$). Compared with women, men had less physical limitations (difference = 3.1 , $p = 0.01$) and less frequent angina (difference = 2.0 , $p = 0.01$). Patients who were transferred had lower levels of treatment satisfaction (difference = -1.7 , $p = 0.03$), and those randomized to the intervention group was associated with had better quality of life (difference = 4.2 , $p = 0.03$) but lower treatment satisfaction (difference = -2.9 , $p = 0.05$).

Discussion

This study represents the largest report of health-related quality of life among myocardial infarction survivors in India. Our results demonstrate that more than two out of every five respondents (44%) in Kerala experience angina in the month following hospital discharge for acute myocardial infarction, although most have infrequent angina occurring less than once per week. Older individuals report greater physical limitations, greater angina frequency, and lower treatment satisfaction and overall quality of life. Women had greater physical limitations and angina frequency than men, whereas quality of life outcomes were similar across types of myocardial infarction. Most importantly, we identified wide variability in responses to the Seattle Angina Questionnaire across the participating hospitals, particularly related to physical limitations and overall quality of life. This observation represents an opportunity to learn from participating hospitals about strategies used to optimize health-related quality of life following acute myocardial infarction.

Differences in physical functioning between men and women may be related to differences in baseline characteristics, treatment, or a combination thereof. We tried to account for these differences in our multivariable models but residual confounding may remain. However, we have previously demonstrated similar treatment and in-hospital clinical outcomes between men and women in Kerala, including death, reinfarction, stroke, heart failure, or cardiogenic shock, after adjustment for baseline differences in comorbidities and presentation.¹⁰

Individuals allocated to the ACS QUIK quality improvement intervention group had higher quality of life scores. We have previously demonstrated higher treatment rates, including reperfusion and anti-angina medications at discharge, in the intervention group compared with the control group.⁶ While the intervention did not target health-related quality of life, these findings may be true but may also be related to risk of recruitment bias, residual confounding between the groups, imprecision, or chance. It seems unlikely that increased treatment led to worse treatment satisfaction, but this question merits further research.

Previous studies evaluating health-related quality of life in India have included fewer than 100 participants each, and no study had more than 25 women.^{11–14} Three of these studies that evaluated quality of life were among military veterans after revascularization (2 studies) and patients with coronary artery disease and panic disorder treated at a north Indian government hospital (1 study), and they demonstrated more angina, lower quality of life and lower treatment satisfaction than in participants in our study.^{12–14} On the other hand, our results were similar to baseline health-related quality of life estimates from a 2017 Indian trial evaluating the effect of ranolazine among individuals with microvascular dysfunction.¹¹

Data from the 2003–2004 Prospective Registry Evaluating Myocardial Infarction: Events and Recovery (PREMIER, n= 1,815 participants) in the United States demonstrated that 27% and 24% of post-myocardial infarction patients had angina at 1- and 6-month follow-up, respectively,¹⁵ which were lower than angina rates from ACS QUIK. In the PREMIER study, individuals with persistent angina were three times more likely to report low treatment satisfaction, even after multivariable adjustment. Among participants in the 2005–2008 Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) registry (n=2,915 participants), 29% of post-myocardial infarction survivors reported angina at 1-month follow-up (12% new angina; 17% persistent angina),¹⁶ which was again lower than results from ACS QUIK. Patients with angina in the TRIUMPH study were more likely to be younger, non-white, and uninsured than individuals without angina. The presence of angina at 1-month follow-up was also associated with increased risk for all-cause rehospitalization (persistent angina hazard ratio [HR]=1.35, 95% CI: 1.06, 1.71 or new angina at 30 days HR=1.40, 95% CI: 1.08, 1.82) and angina (persistent angina HR=3.55, 95% CI: 3.05, 4.13 or new angina HR=3.38, 95% CI: 2.59, 4.42) at 1 year follow-up.¹⁶ Whether or not a similar, longitudinal relationship exists between post-discharge angina and longer-term rehospitalization and angina among patients in Kerala is uncertain but seems plausible. In a subsample of the 2008–2012 Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study with pre-enrollment coronary artery disease (n=3,501 total participants [67% women]; n=672 [65% women] with coronary artery disease), women demonstrated more physical limitations, more angina, less treatment satisfaction, and poorer quality of life than men.¹⁷ Among ACS QUIK participants, women had greater physical limitations and more angina than men, but other domains were similar between sexes.

Strengths and limitations

Our study has several strengths, including being the largest study of health-related quality of life among survivors of acute myocardial infarction in India, particularly women, and using a translated, validated instrument designed for patients with coronary artery disease. However, our study also has limitations. First, our study was restricted to hospitals in Kerala and thus may not be representative of all of India, including states with lower per capita income. Second, we did not capture baseline health status and were thus not able to measure changes in health status over time. Third, we did not achieve our target sample due to low recruitment of underrepresented age-sex groups and expanding our sampling frame during the trial to include individuals in the intervention group. However, because the differences between the intervention and control groups were modest and because we were able to

adjust for group allocation, the influence of this change is likely minimal. Fourth, the trial in which this sub-study was embedded randomized on the cluster level yet recruited participants on the individual level, which raises the possibility of recruitment bias that may have influenced our results.

Conclusions

Angina is common following hospital discharge for patients with recent acute myocardial infarction in Kerala and warrants post-discharge follow-up for evaluation and management, though most individuals experience mild, infrequent angina. While the rate of angina may be higher than previously reported in high-income country settings, the overall quality of life scores among ACS QUIK was similar to, if not higher than, previous studies though variability across hospitals is wide. However, older individuals and women have lower quality of life outcomes. The ACS QUIK quality improvement intervention improved health-related quality of life, though this comparison was not made across randomized groups. Additional research is needed to help explain the variability in quality of life across age, sex, and hospitals, in particular. Future research will help better understand the underlying reasons and translatable factors why some hospitals attain better health status outcomes in their patients. This research will help toward achieving the goal of improving the quality of life of patients following acute myocardial infarction in Kerala, India, and other low- and middle-income country settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

StatTag²⁵ (v3.0, Chicago, IL) was used for the preparation of results in this manuscript. StatTag facilitates reproducible research by embedding output from statistical programs (Stata, SAS, and R) in Microsoft Word documents. Code files used for generation of results can be downloaded at: <https://github.com/abigailbaldrige/ACS-QUIK>. Author Contributions: Drs. Huffman, Kondal, and Zhao, and Ms. Baldrige and Mr. Ali had full access to all study data and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Appendix A.

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WHAT IS KNOWN:

- In 2015, 7.3 million individuals died from acute myocardial infarction in India.
- Little is known about symptoms, function, and quality of life of acute myocardial infarction survivors in India.

WHAT THIS STUDY ADDS:

- This study collected data on health-related quality of life among 1,261 Indian patients who have survived acute myocardial infarction at 30 days within the Acute Coronary Syndrome Quality Improvement in Kerala (ACS QUIK) trial.
- More than 2 out of every 5 patients (44%) experienced angina at 30 days with wide between-hospital heterogeneity.
- The ACS QUIK quality improvement intervention improved health-related quality of life, though this comparison was not made across randomized groups.

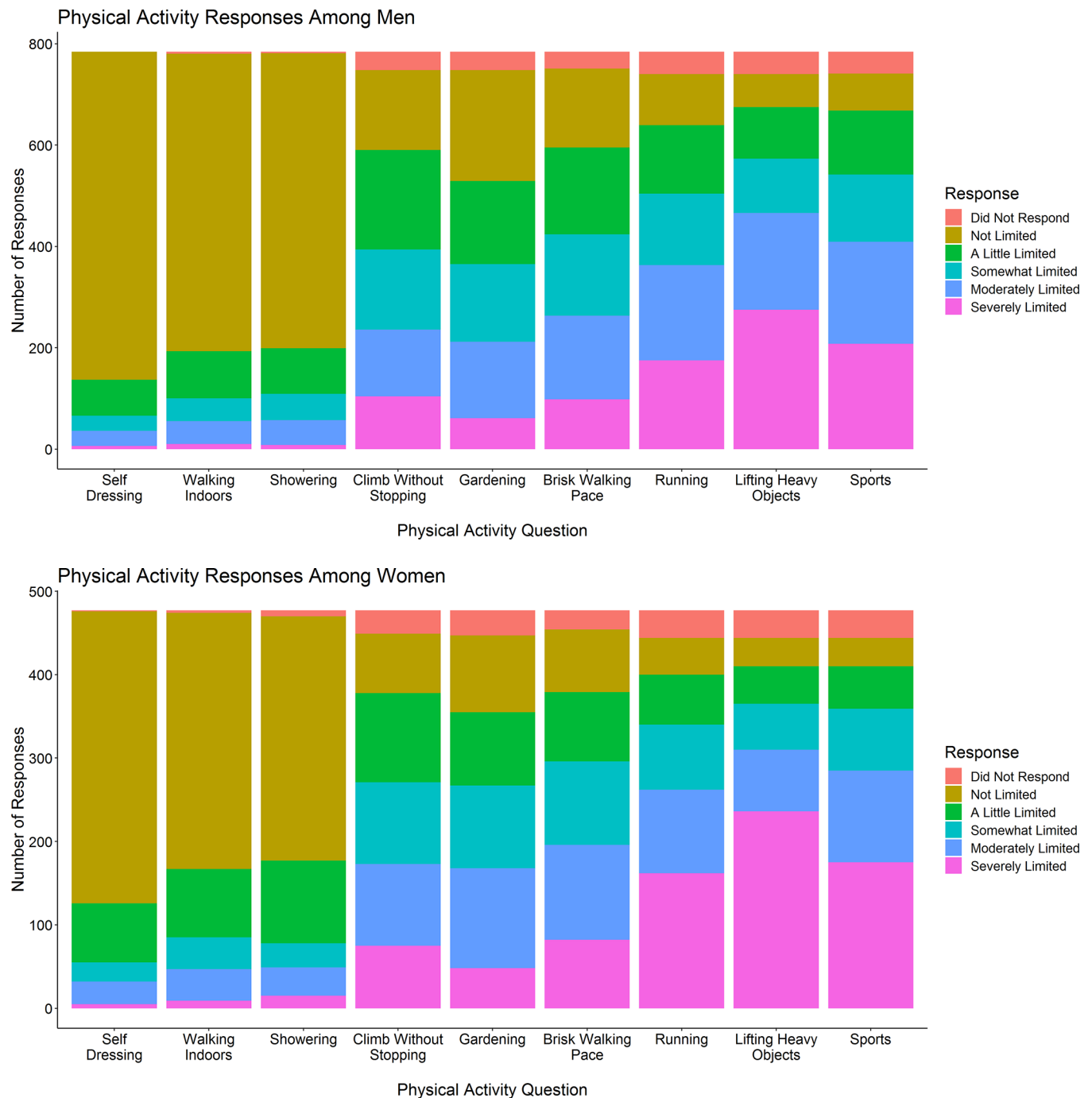


Figure 1. Stacked bar chart of physical limitation scores by subscale of the Seattle Angina Questionnaire among A) 784 men and B) 477 women from the Acute Coronary Syndrome Quality Improvement in Kerala trial.

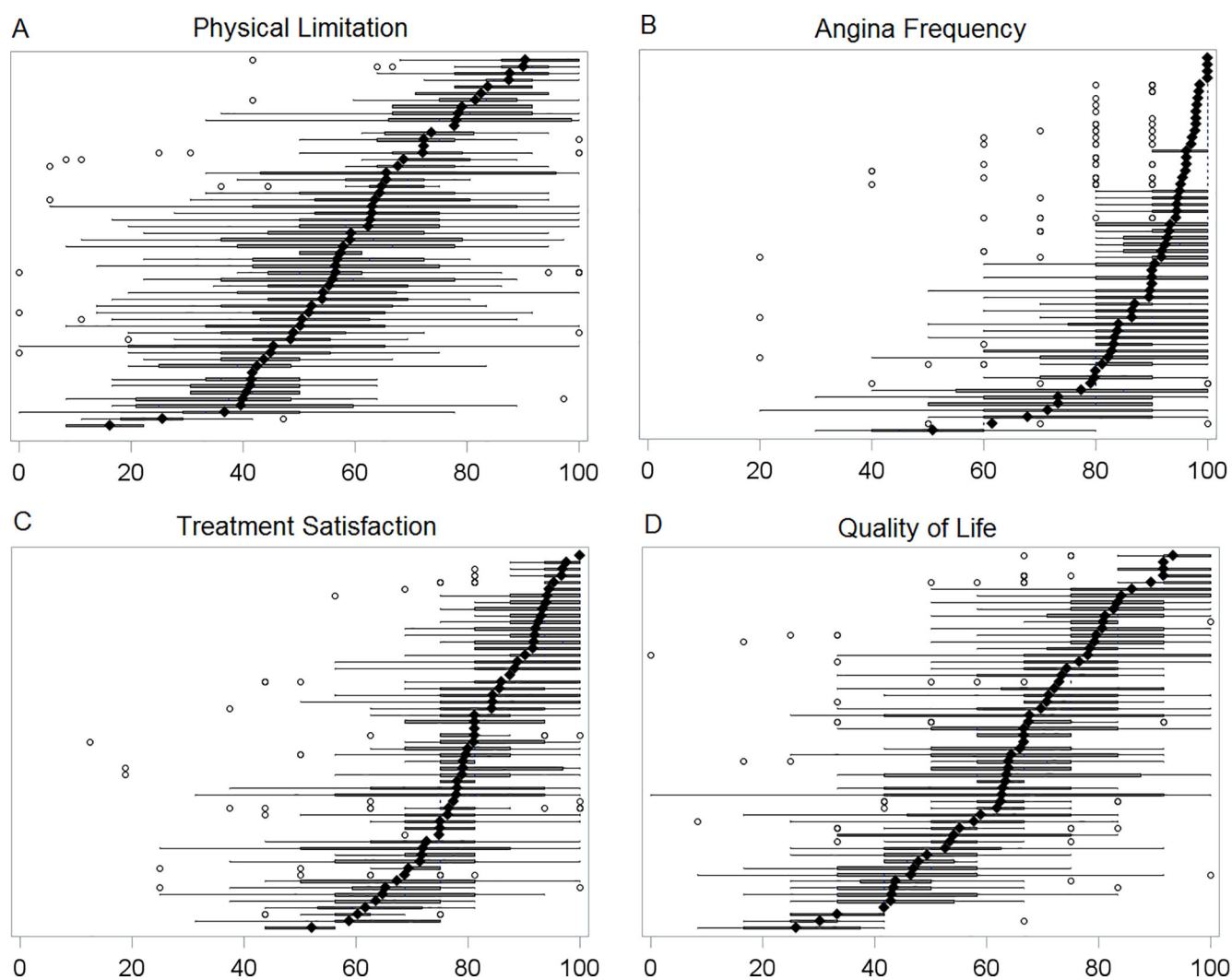


Figure 2. Boxplot of mean scores by center for physical limitation (panel A), angina frequency (panel B), treatment satisfaction (panel C) and quality of life (D).

Table 1.

Demographics, clinical presentation, and laboratory data from 1,261 ACS QUIK respondents who completed Seattle Angina Questionnaires, with unadjusted p-value for differences by sex and adjusted for within-hospital clustering and temporal trends.

Characteristics	N	Overall n=1261	Men n=784	Women n=477	P-Value	
					Unadjusted*	Adjusted†
Age, mean (SD), years	1261	60.8 ± 13.7	58.8 ± 13.6	64.0 ± 13.1	<.01	<.01
History of tobacco use, n (%)	1261	360 (28.5)	335 (42.7)	25 (5.2)	<.01	<.01
History of diabetes, n (%)	1261	581 (46.1)	318 (40.6)	263 (55.1)	<.01	<.01
Transferred from another facility, n (%)	1261	530 (42.0)	349 (44.5)	181 (37.9)	0.02	0.01
No insurance, n (%)	1261	953 (75.6)	581 (74.1)	372 (78.0)	0.12	0.09
ST-elevation myocardial infarction, n (%)	1261	800 (63.4)	535 (68.2)	265 (55.6)	<.01	<.01
Symptom-to-door time, median (IQR), min	1214	261 (120–885)	240 (115–840)	313 (135–960)	0.02	<.01
Body weight, mean (SD), kg	1261	62.9 ± 10.7	65.9 ± 10.0	57.9 ± 10.1	<.01	<.01
Systolic blood pressure, mean (SD), mmHg	1261	141.2 ± 29.1	139.0 ± 27.9	144.8 ± 30.7	<.01	<.01
Heart rate, mean (SD), beats per min	1261	81.8 ± 21.0	79.7 ± 21.2	85.3 ± 20.1	<.01	<.01
Initial troponin, median (IQR), ng/ml	671	1.23 (0.30–6.71)	1.65 (0.34–10.00)	0.88 (0.25–3.17)	<.01	0.03
Low-density lipoprotein cholesterol, mean (SD), mg/dl	959	125.1 ± 42.5	122.1 ± 42.5	129.6 ± 42.2	<.01	0.03
Triglycerides, median (IQR), mg/dl	959	115 (84–160)	117 (82–170)	113 (88–152)	0.57	0.87
Serum creatinine, median (IQR), mg/dl	380	1.0 (0.9–1.3)	1.1 (0.9–1.3)	1.0 (0.8–1.2)	<.01	<.01
Fasting glucose, median (IQR), mg/dl	807	135 (106–189)	129 (104–180)	143 (110–206)	<.01	0.02
Hemoglobin, mean (SD), mg/dl	1236	13.1 ± 2.2	13.8 ± 2.0	11.9 ± 1.8	<.01	<.01
Intervention, n (%)	1261	328 (26)	175 (22)	153 (32)	<.01	Nonestimable

Abbreviation: IQR, interquartile range.

*Two sample t-test, chi-squared test, or Mann Whitney U test

†Linear, quantile, or logistic regression with adjustment for time (step) and random cluster effect.

Table 2.

Seattle Angina Questionnaire results evaluating differences in 30-day health-related quality of life among ACS QUIK trial respondents, unadjusted p-value for differences by sex and adjusted for within-hospital clustering and temporal trends using multinomial logistic regression with cluster and step (outcomes 0 = none, 1 = monthly, 2 = weekly, 3 = daily for angina frequency).

Seattle Angina Questionnaire Component	N	Overall n=1261	Men n=784	Women n=477	P-Value	
					Unadjusted*	Adjusted†
Any angina, n (%)	1261	560 (44.4)	338 (43.1)	222 (46.5)	0.23	0.07
Angina frequency scale, median (IQR)	1261	100.0 (80.0–100.0)	100.0 (80.0–100.0)	100.0 (80.0–100.0)	0.11	0.51
Angina frequency	1261				<.01	<.01
Daily		7 (0.6)	0 (0.0)	7 (1.5)		
Weekly		134 (10.6)	78 (9.9)	56 (11.7)		
Monthly		419 (33.2)	260 (33.2)	159 (33.3)		
None		701 (55.6)	446 (56.9)	255 (53.5)		
Physical limitation scale, median (IQR) ‡	1184	58.3 (41.7–77.8)	61.1 (44.4–80.6)	52.8 (38.9–72.2)	<.01	<.01
Treatment satisfaction scale, median (IQR)	1261	81.3 (75.0–93.8)	81.3 (75.0–93.8)	81.3 (75.0–93.8)	0.67	1.00
Overall quality of life scale, median (IQR)	1261	66.7 (50.0–83.3)	66.7 (50.0–83.3)	66.7 (50.0–83.3)	0.46	1.00

Abbreviation: IQR, interquartile range.

* Chi-squared test, or Mann Whitney U test

† Quantile, or logistic regression with adjustment for time (step) and random cluster effect.

‡ Per SAQ scoring instructions if the responses to any of the questions within the physical limitation score are “6 = Limited for other reasons or did not do the activity” then the response is set to missing. The scoring uses a modified imputation to fill in the missing values based on the other responses to physical activity questions. If more than 4 items are missing then the score for physical activity cannot be accurately calculated

Table 3.

Association among baseline demographics, presentation, and randomized group allocation with Seattle Angina Questionnaire scores, adjusted for GRACE risk score covariates (age, sex, type of myocardial infarction, systolic blood pressure, heart rate, acute heart failure, cardiogenic shock, and resuscitated cardiac arrest), cluster, and temporal trends.

Characteristics	Beta Coefficient (P-value) *			
	Physical Limitation	Angina Frequency	Treatment Satisfaction	Quality of Life
Demographics and presentation				
Age, years	-0.41 (<.01)	-0.09 (<.01)	-0.07 (0.01)	-0.07 (0.05)
Male	3.07 (0.01)	2.00 (0.01)	0.62 (0.44)	0.98 (0.33)
History of tobacco use	0.30 (0.82)	0.14 (0.87)	0.23 (0.80)	0.30 (0.80)
History of diabetes	-0.93 (0.38)	-0.95 (0.18)	-0.99 (0.18)	-0.36 (0.70)
Transferred from another facility	1.03 (0.38)	0.07 (0.93)	-1.71 (0.03)	-0.07 (0.95)
No insurance	0.40 (0.78)	0.36 (0.71)	0.09 (0.93)	1.96 (0.13)
ST-elevation myocardial infarction	2.69 (0.03)	-0.44 (0.59)	1.42 (0.09)	0.87 (0.42)
Symptom-to-door time, hours	0.02 (0.45)	-0.02 (0.40)	0.01 (0.70)	-0.05 (0.02)
Body weight, kg	-0.04 (0.49)	0.10 (0.01)	0.04 (0.25)	0.11 (0.03)
Systolic blood pressure, mmHg	0.01 (0.54)	0.01 (0.46)	-0.02 (0.17)	-0.02 (0.21)
Heart rate, beats per min	-0.07 (0.01)	-0.01 (0.44)	-0.003 (0.86)	-0.01 (0.72)
Laboratory				
Initial troponin, mg/dl	0.01 (0.82)	-0.04 (0.07)	0.01 (0.47)	-0.04 (0.11)
Low-density lipoprotein cholesterol, mg/dl	-0.01 (0.33)	0.004 (0.65)	0.01 (0.29)	-0.01 (0.62)
Triglycerides, mg/dl	0.02 (0.06)	0.0002 (0.97)	0.0001 (0.99)	0.01 (0.16)
Serum creatinine, mg/dl	-1.45 (0.40)	-0.15 (0.88)	-1.84 (0.05)	-0.26 (0.85)
Fasting glucose, mg/dl	-0.02 (0.09)	0.0003 (0.95)	-0.005 (0.48)	-0.01 (0.47)
Hemoglobin, g/dl	0.45 (0.12)	0.25 (0.19)	0.25 (0.22)	-0.07 (0.79)
Intervention	-0.32 (0.88)	-1.57 (0.27)	-2.92 (0.05)	4.15 (0.03)

* Linear model in the form of outcome = Seattle Angina Questionnaire domain, adjusted for step, random cluster, age, male, ST-elevation myocardial infarction, systolic blood pressure, heart rate, incident heart failure, incident shock, and incident cardiac arrest.