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Original Research

Long-term impact of frailty on mortality and quality of life in mechanically ventilated acute myocardial infarction patients undergoing percutaneous coronary intervention

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ABSTRACT

Background: Frailty is a recognized predictor of adverse outcomes after percutaneous coronary intervention (PCI), but its long-term association with mortality and health-related quality of life (HRQoL) remains uncertain. This study evaluated the three-year association between discharge frailty and subsequent frailty, mortality, and HRQoL in post-PCI patients.

Methods: This retrospective cohort study included patients with acute myocardial infarction (AMI) who underwent PCI, required ICU/CICU admission with mechanical ventilation and/or advanced life support, and remained alive at routine 6-month follow-up. Frailty was assessed at discharge and reassessed after three years. HRQoL was assessed using the EQ-5D-3 L descriptive system and summarised using a study-specific level-sum impairment score; this was not a preference-weighted EQ-5D utility index.

Results: Among 164 patients, 131 (79.9%) were frail at discharge. During three-year follow-up, 51 patients (31.1%) died. Crude mortality did not differ significantly between frail and non-frail patients (32.1%vs. 27.3%; p = 0.595). In adjusted logistic regression, moderate-to-severe discharge frailty was independently associated with death during the follow-up interval (adjusted OR 2.55; 95% CI 1.06–6.11; p = 0.036). Among survivors, 43 (38.1%) remained frail at follow-up. Moderate-to-severe discharge frailty was associated with moderate-to-severe frailty at three-year follow-up (adjusted OR 12.75; 95% CI 1.84–88.35; p = 0.010), although the wide confidence interval indicates limited precision and supports an exploratory interpretation. Poor HRQoL, defined as an EQ-5D-3 L level-sum score ≥8, was present in 33 survivors. Neither age >60 years (adjusted OR 1.56; 95% CI 0.44–5.53; p = 0.492) nor discharge frailty was independently associated with poor HRQoL.

Conclusion: Among mechanically ventilated AMI patients undergoing PCI who survived to routine 6-month follow-up, moderate-to-severe frailty at hospital discharge was independently associated with death during the three-year follow-up interval. It was also associated with moderate-to-severe frailty at follow-up, although this estimate was imprecise and should be interpreted as hypothesis-generating. Discharge frailty was not independently associated with poor long-term HRQoL.

1. Introduction

Frailty is a multidimensional syndrome characterised by reduced physiological reserve and increased vulnerability to stressors, predisposing individuals to adverse clinical outcomes [1]. In patients with cardiovascular disease, frailty has been consistently associated with higher rates of mortality, rehospitalisation, functional decline, and prolonged recovery [2]. Patients undergoing percutaneous coronary intervention (PCI) often present with multiple comorbidities and significant cardiovascular burden, making frailty assessment particularly relevant in this population.

Survivors of cardiovascular interventions may experience persistent physical limitations, psychological distress, and reduced quality of life, which may be influenced by frailty status at hospital discharge [3].

Although frailty has consistently been associated with short-term adverse outcomes following cardiac intensive care unit (CICU)

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discharge [4], uncertainty remains regarding its long-term impact on survival, persistent frailty, and health-related quality of life after PCI [5]. Existing studies have largely focused on elderly populations, short follow-up durations, or mortality alone, with limited data evaluating the combined trajectory of frailty, survival, and quality of life after PCI. Furthermore, evidence from low- and middle-income countries remains scarce.

Although frailty is a well-established marker of early adverse outcomes after PCI and cardiac critical illness, an important uncertainty remains among patients who survive the initial high-risk period: whether frailty at hospital discharge represents only transient peri-procedural vulnerability or whether it identifies a persistent biological-risk phenotype associated with late mortality, ongoing frailty, and impaired health-related quality of life. This uncertainty is particularly relevant in high-risk AMI/ACS patients requiring mechanical ventilation and/or advanced life support after PCI, in whom survival beyond discharge and the early follow-up period may not necessarily translate into complete functional recovery.

This study therefore examined a two-stage survivor cohort from a low- and middle-income country, including post-PCI patients who survived hospital discharge and remained alive at routine 6-month follow-up, with structured reassessment at approximately three years. This setting and follow-up window allowed us to evaluate long-term outcomes beyond the early post-PCI mortality phase and to assess whether discharge frailty predicts later mortality, persistent frailty, and HRQoL among survivors.

We tested three primary hypotheses: first, that moderate-to-severe frailty at hospital discharge would be independently associated with death during the three-year follow-up interval; second, that moderate-to-severe frailty at discharge would be associated with persistent or progressive frailty at long-term follow-up; and third, that the relationship between discharge frailty and long-term HRQoL may differ from its relationship with mortality and persistent frailty. The HRQoL analysis was therefore considered exploratory, recognising that perceived quality of life may be influenced by factors beyond discharge frailty severity alone.

Therefore, the aim of this study was to determine the association between discharge frailty severity and death during the three-year follow-up interval, frailty persistence or progression, and study-specific EQ-5D-3 L impairment among high-risk mechanically ventilated AMI patients undergoing PCI who survived to routine six-month follow-up.

2. Methods

2.1. Study design and setting

This was a retrospective cohort with structured three-year follow-up conducted at the National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan. The study was based on a previously published cohort of post-PCI acute myocardial infarction patients who required ICU/CICU admission with mechanical ventilation and/or advanced life support. The present analysis was restricted to patients from that cohort who survived hospital discharge and remained alive at routine 6-month follow-up; therefore, the three-year outcomes should be interpreted as survivor-conditioned outcomes among six-month survivors.

2.2. Ethical considerations

The study was approved by the institutional ethics review board (IRB-62/2025). Informed consent was obtained in the original cohort, and verbal consent was obtained during follow-up contact. All data were anonymised to maintain confidentiality.

2.3. Study population

The source population was derived from patients with acute myocardial infarction who underwent PCI between August 2021 and January 2022 and required mechanical ventilation and/or advanced life support during ICU/CICU admission. As shown in Fig. 1, among 6036 patients with acute myocardial infarction, 419 required mechanical ventilation, and 312 patients were included in the original audit/cohort after applying eligibility criteria. During routine short-term follow-up, 98 patients died before or by the 6-month assessment, leaving 214 patients eligible for the present three-year follow-up. Of these, 50 were lost to follow-up, and 164 patients were included in the final analysis.

The present study therefore represents a two-stage follow-up design. The first stage comprised the original cohort and routine follow-up to 6 months. The second stage comprised structured three-year follow-up among patients who remained alive at routine 6-month follow-up. Accordingly, all three-year outcomes in the current analysis are conditional on survival to routine 6-month follow-up and should not be interpreted as outcomes for all post-PCI patients or for the entire original mechanically ventilated AMI PCI cohort.

2.4. Participants

Eligible participants included adult patients (≥ 18 years) who were

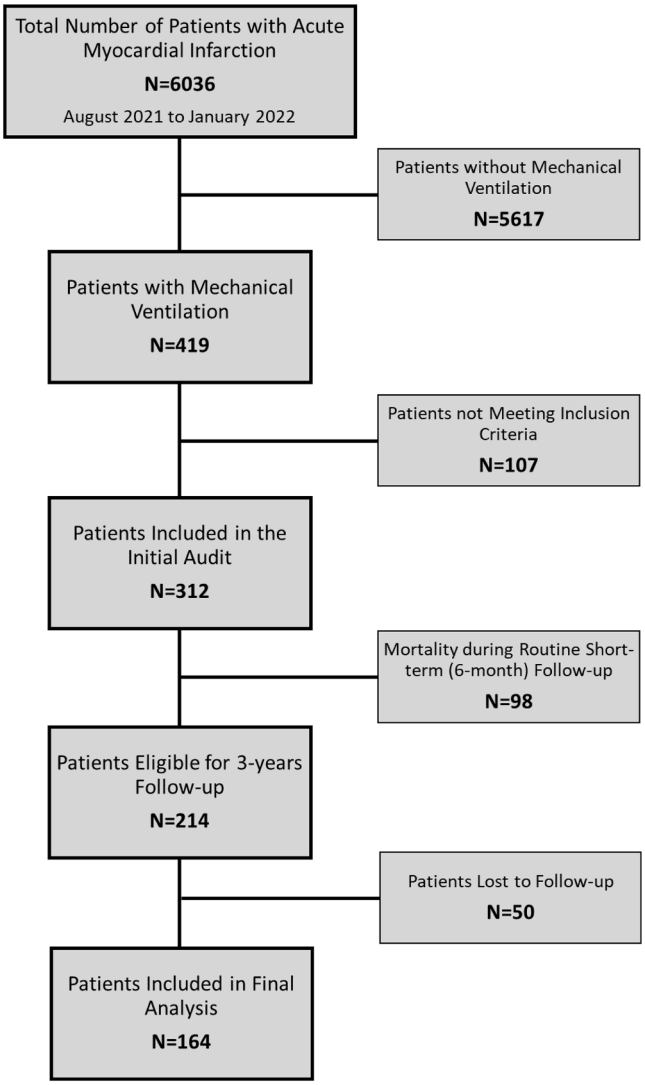

Fig. 1. Patient flow diagram showing the two-stage cohort selection process.

enrolled in the original frailty cohort and had a documented frailty score at the time of discharge following PCI. Patients with significant cognitive impairment that prevented reliable communication or informed consent were excluded. Details regarding the study population and baseline frailty assessment are presented elsewhere [5]. Participants were contacted via telephone for follow-up assessment three years post-discharge on their registered contact number (self as well as attendant). Three contact attempts were made (on different weekdays and different day parts (time) before classifying a participant as lost to follow-up. Because patients who died before routine 6-month follow-up were not eligible for the current three-year assessment, the analysed cohort represents a survivor-conditioned subset of the original mechanically ventilated AMI PCI cohort.

2.5. Variables

The primary outcomes were all-cause mortality and HRQoL at three years. Secondary outcomes included frailty status at follow-up and progression to moderate-to-severe frailty. The main exposure variable was frailty status at discharge (non-frail or frail). The primary exposure was discharge frailty severity measured using the modified ACTION Registry Frailty Score [25]. For descriptive analyses, frailty was categorised as non-frail, mild frailty, and moderate-to-severe frailty. For the primary regression analyses, moderate-to-severe frailty at discharge was analysed as a binary exposure, defined as frailty score $\geq$3 versus frailty score 0–2. Secondary outcomes included frailty status at three-year follow-up, moderate-to-severe frailty at follow-up, and poor HRQoL. Covariates included age, sex, hypertension, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, smoking status, type of PCI, medication adherence, physical activity, and participation in cardiac rehabilitation. Mortality was analysed as a binary outcome over the structured follow-up interval using logistic regression; thus, the reported odds ratios reflect associations with death during follow-up and should not be interpreted as hazard ratios from a time-to-event survival analysis survivor-conditioned mortality outcome.

2.6. Data sources and measurement

Baseline data were extracted from the original cohort database [5]. Frailty was assessed using a modified ACTION Registry Frailty Score, adapted from Dodson et al. [6] and applied in our previously published cohort. The score includes three clinically assessed domains: walking or motor function, cognition, and activities of daily living. Each domain was scored from 0 to 2, giving a total score ranging from 0 to 6. Walking or motor function was scored as 0 for unassisted walking or lower-limb motor power 4–5/5, 1 for assisted walking or lower-limb motor power 2–3/5, and 2 for non-ambulatory status or lower-limb motor power 0–1/5. Cognition was scored as 0 for normal cognition, 1 for mildly impaired cognition, and 2 for moderately or severely impaired cognition. Activities of daily living were scored as 0 for independence in activities of daily living, 1 for partial assistance in at least one activity of daily living, and 2 for full assistance in at least one activity of daily living.

Total frailty scores were categorised as follows: non-frail = 0, mild frailty = 1–2, and moderate-to-severe frailty = 3–6. The same scoring approach and thresholds were used at hospital discharge and at three-year follow-up. Persistent frailty was defined as any frailty at follow-up, corresponding to a frailty score $\geq$ 1 among survivors. Moderate-to-severe frailty at follow-up was defined as a frailty score $\geq$ 3.

HRQoL was assessed using the EQ-5D-3 L descriptive system and summarised using a study-specific level-sum impairment score; this was not a preference-weighted EQ-5D utility index. The EQ-5D-3 L includes five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain has three response levels, scored as 1, 2, or 3, where 1 indicates no problems and 3 indicates severe or extreme problems [7,8]. In this study, an EQ-5D-3 L level-sum score was calculated by summing the five domain scores. The possible score range was therefore 5 to 15, with higher scores indicating worse HRQoL. This was not a preference-weighted EQ-5D utility index. For descriptive reporting, HRQoL level-sum scores were categorised a priori as no problems = 5, mild impairment = 6–7, moderate impairment = 8–10, and severe impairment = 11–15. For regression analyses, poor HRQoL was defined as moderate or severe impairment, corresponding to an EQ-5D-3 L level-sum score $\geq$ 8 [8]. Mortality data were obtained from hospital records or family contact.

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2.7. Bias

To minimise information bias, standardised questionnaires were used for follow-up assessment. The same frailty instrument was applied at discharge and follow-up to ensure comparability. Multiple attempts were made to contact participants to reduce loss to follow-up bias.

2.8. Study size

All patients from the original frailty cohort who met the inclusion criteria were included in this follow-up study. No additional sampling was performed [5].

2.9. Quantitative variables

Continuous variables such as age and EQ-5D-3 L level-sum score were analysed as numerical variables and summarised using mean $\pm$ standard deviation or median with interquartile range, as appropriate. Frailty was analysed using predefined categories based on the modified ACTION Registry Frailty Score: non-frail = 0, mild frailty = 1–2, and moderate-to-severe frailty = 3–6. For regression analysis, discharge moderate-to-severe frailty was defined as frailty score $\geq$ 3, and poor HRQoL was defined as EQ-5D-3 L level-sum score $\geq$ 8. Age was additionally categorised as $>$ 60 years for regression analysis.

2.10. Statistical methods

Categorical variables were summarised as frequencies and percentages, and continuous variables were summarised using mean $\pm$ standard deviation or median with interquartile range, as appropriate. Logistic regression analyses were performed to identify factors associated with three outcomes: all-cause mortality, moderate-to-severe frailty at three-year follow-up, and poor HRQoL. Although mortality is a time-to-event outcome, the present analysis evaluated death as a binary outcome over the structured three-year follow-up interval among patients alive at routine 6-month follow-up. Cox proportional hazards modelling was not performed because the study was not designed as a formal time-to-event survivor-conditioned mortality outcome. Therefore, mortality estimates are reported as odds ratios reflecting association with death during the follow-up interval rather than hazard ratios.

Univariable logistic regression was first performed for candidate predictors, including age, sex, hypertension, diabetes mellitus, smoking/drug addiction, chronic kidney disease, chronic obstructive pulmonary disease, discharge frailty severity, medication adherence, physical activity, and cardiac rehabilitation, depending on outcome availability.

To reduce overfitting in this modest-sized cohort, variables with $p < 0.20$ in univariable analysis were entered into the corresponding multivariable model. The final mortality model included chronic kidney disease and moderate-to-severe frailty at discharge. The final model for moderate-to-severe frailty at follow-up included moderate-to-severe frailty at discharge and medication non-adherence. The final poor HRQoL model included age $>$ 60 years and smoking/drug addiction. Adjusted odds ratios with 95% confidence intervals were reported.

Events-per-variable were calculated for the final adjusted models.

The mortality model included 51 events and two predictors, and the poor HRQoL model included 33 events and two predictors. The model for moderate-to-severe frailty at follow-up included 18 events and two predictors, giving an events-per-variable ratio of approximately 9; therefore, this model was interpreted cautiously as exploratory. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 164 mechanically ventilated AMI patients who underwent PCI, survived hospital discharge, remained alive at routine 6-month follow-up, and completed three-year follow-up assessment were included in the final analysis. Of these, 125 patients (76.2%) were male, and the mean age was 58.6 ± 10.3 years. At hospital discharge, using the modified ACTION Registry Frailty Score, 33 patients (20.1%) were non-frail, and 131 patients (79.9%) had some degree of frailty. Among frail patients, 102 (77.9%) had mild frailty, defined as a score of 1–2, and 29 (22.1%) had moderate-to-severe frailty, defined as a score of 3–6 (Table 1).

3.2. Follow-up and clinical outcomes

The median follow-up duration was 1146 [766.5 - 1231] days. The all-cause mortality rate was 31.1% (51). Among three-year survivors, 43 patients (38.1%) were frail at follow-up. Among frail survivors with available severity classification, 25 had mild frailty and 18 had moderate-to-severe frailty.

The mean EQ-5D-3 L level-sum score was 6.5 ± 2.3. Using the study-specific impairment categories, 28 survivors (24.8%) had moderate impairment and 5 survivors (4.4%) had severe impairment.

There were no statistically significant differences in the baseline characteristics and follow-up outcomes in relation to the discharge frailty status (Table 1).

3.3. Factors associated with mortality

In univariable analysis, chronic kidney disease and moderate-to-severe frailty at discharge met the prespecified threshold for multivariable modelling. In the final adjusted logistic regression model, moderate-to-severe frailty at discharge was independently associated with death during the follow-up interval (adjusted OR 2.55; 95% CI 1.06–6.11; p = 0.036). This estimate reflects the odds of death over the observed follow-up period and should not be interpreted as a hazard ratio from a survival model.

In univariable analysis, chronic kidney disease and moderate-to-severe frailty at discharge met the prespecified threshold for multivariable modelling. In the final adjusted logistic regression model, moderate-to-severe frailty at discharge was independently associated with death during the three-year follow-up interval (adjusted OR 2.55; 95% CI 1.06–6.11; p = 0.036). Chronic kidney disease was not statistically significant after adjustment (adjusted OR 4.05; 95% CI 0.68–24.24; p = 0.125). These estimates should be interpreted as odds ratios for death during follow-up, not as hazard ratios from a time-to-event model. Tables 2, 3, 4

3.4. Factors associated with moderate-to-severe frailty

In the model evaluating moderate-to-severe frailty at three-year follow-up, moderate-to-severe frailty at discharge and medication non-adherence met the prespecified threshold for multivariable modelling. Moderate-to-severe frailty at discharge was associated with moderate-to-severe frailty at follow-up (adjusted OR 12.75; 95% CI 1.84–88.35; p = 0.010). However, the confidence interval was wide, indicating limited precision and sparse outcome events; therefore, this association

Table 1
Baseline characteristics and follow-up outcomes of post-PCI patients stratified by frailty status at discharge.

	Overall	Discharge Frailty		P-value
		Non Frail	Frail	
Total (N)	**164**	**33 (20.1%)**	**131 (79.9%)**	-
Sex				
Male	125 (76.2%)	29 (87.9%)	96 (73.3%)	0.078
Female	39 (23.8%)	4 (12.1%)	35 (26.7%)	
Age (yrs)	58.6 ± 10.3	56.4 ± 11.6	59.1 ± 9.9	0.184
18 to 50 yrs	41 (25%)	6 (18.2%)	35 (26.7%)	0.385
51 to 65 yrs	87 (53%)	21 (63.6%)	66 (50.4%)	
>65 yrs	36 (22%)	6 (18.2%)	30 (22.9%)	
Type of PCI				
Stent	155 (94.5%)	33 (100%)	122 (93.1%)	0.121
POBA	9 (5.5%)	0 (0%)	9 (6.9%)	
Co-morbid condition				
Hypertension	142 (86.6%)	32 (97%)	110 (84%)	0.050
Diabetes	56 (34.1%)	8 (24.2%)	48 (36.6%)	0.179
Smoking/drug addictions	43 (26.2%)	12 (36.4%)	31 (23.7%)	0.138
Chronic kidney disease	7 (4.3%)	1 (3%)	6 (4.6%)	0.694
Chronic obstructive pulmonary disease	4 (2.4%)	0 (0%)	4 (3.1%)	0.309
Discharge Frailty Level				
Mild frailty	102 (77.9%)	-	102 (77.9%)	-
Moderate-to-severe frailty	29 (22.1%)	-	29 (22.1%)	
Follow-up				
Mortality	51 (31.1%)	9 (27.3%)	42 (32.1%)	0.595
Cardiopulmonary Arrest	37 (72.5%)	6 (66.7%)	31 (73.8%)	0.904
Cardiovascular Event	9 (17.6%)	2 (22.2%)	7 (16.7%)	
Respiratory Failure	5 (9.8%)	1 (11.1%)	4 (9.5%)	
Duration of follow-up/death (days)	1146 [766.5–1231]	1129 [875–1214]	1152 [748–1233]	0.573
Follow-up Frailty				
Non Frail	70 (61.9%)	19 (79.2%)	51 (57.3%)	0.050
Frail	43 (38.1%)	5 (20.8%)	38 (42.7%)	
Follow-up Frailty Level				
Mild frailty	25 (58.1%)	3 (60%)	22 (57.9%)	0.929
Moderate-to-severe frailty	18 (41.9%)	2 (40%)	16 (42.1%)	
Quality of Life				
HRQOL Assessment	6.5 ± 2.3	5.9 ± 1.9	6.6 ± 2.3	0.110
No problems (5)	72 (63.7%)	19 (79.2%)	53 (59.6%)	0.339
Mild (6–7)	8 (7.1%)	1 (4.2%)	7 (7.9%)	
Moderate (8–10)	28 (24.8%)	3 (12.5%)	25 (28.1%)	
Severe (11–15)	5 (4.4%)	1 (4.2%)	4 (4.5%)	
Mobility				
No problems	88 (77.9%)	20 (83.3%)	68 (76.4%)	0.762
Some problems	18 (15.9%)	3 (12.5%)	15 (16.9%)	
Unable to walk	7 (6.2%)	1 (4.2%)	6 (6.7%)	
Self-care				
No problems	84 (74.3%)	21 (87.5%)	63 (70.8%)	0.242
Some problems	28 (24.8%)	3 (12.5%)	25 (28.1%)	
Unable to care for self	1 (0.9%)	0 (0%)	1 (1.1%)	
Usual activities				
No problems	75 (66.4%)	19 (79.2%)	56 (62.9%)	0.260
Some problems	34 (30.1%)	5 (20.8%)	29 (32.6%)	
Unable to perform usual activities	4 (3.5%)	0 (0%)	4 (4.5%)	
Pain and discomfort				
No pain	85 (75.2%)	20 (83.3%)	65 (73%)	0.512
Moderate pain	26 (23%)	4 (16.7%)	22 (24.7%)	
Severe pain	2 (1.8%)	0 (0%)	2 (2.2%)	
Anxiety and depression				
Not anxious/depressed	83 (73.5%)	20 (83.3%)	63 (70.8%)	0.441
Moderate anxiety/depression	29 (25.7%)	4 (16.7%)	25 (28.1%)	
Severe anxiety/depression	1 (0.9%)	0 (0%)	1 (1.1%)	
Medication Adherence				
Fully adherent	13 (11.5%)	2 (8.3%)	11 (12.4%)	0.815
Somewhat adherent	6 (5.3%)	1 (4.2%)	5 (5.6%)	

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Table 1 (*continued*)

	Overall	Discharge Frailty		P-value
		Non Frail	Frail	
Non-adherent	94 (83.2%)	21 (87.5%)	73 (82%)	
Physical Activity				
Regular physical activity	47 (41.6%)	11 (45.8%)	36 (40.4%)	0.477
Limited physical activity	61 (54%)	13 (54.2%)	48 (53.9%)	
Sedentary lifestyle	5 (4.4%)	0 (0%)	5 (5.6%)	
Cardiac Rehabilitation	72 (63.7%)	17 (70.8%)	55 (61.8%)	0.414

PCI: percutaneous coronary intervention, POBA: plain old balloon angioplasty, HRQOL: health related quality of life.
Frailty was assessed using the modified ACTION Registry Frailty Score. Total scores were categorised as non-frail = 0, mild frailty = 1–2, and moderate-to-severe frailty = 3–6. HRQoL was assessed using the EQ-5D-3 L level-sum score, calculated by summing the five domain scores; possible range 5–15, with higher scores indicating worse HRQoL.

Table 2
Factors associated with mortality at three-year follow-up among post-PCI patients.

Factors	Unadjusted		Adjusted	
	OR [95% CI]	P-value	OR [95% CI]	P-value
Female	0.98 [0.45 - 2.13]	0.960	-	-
Age > 60 yrs	1.03 [0.53 - 2.01]	0.919	-	-
Hypertension	0.96 [0.37 - 2.53]	0.937	-	-
Diabetes	1.56 [0.79 - 3.10]	0.204	-	-
Smoking/drug addictions	0.95 [0.44 - 2.01]	0.887	-	-
Chronic kidney disease	6.03 [1.13 - 32.22]	0.036	4.05 [0.68 - 24.24]	0.125
Moderate-to-severe frailty at discharge	2.76 [1.17 - 6.52]	0.02	2.55 [1.06 - 6.11]	0.036

OR: odds ratio, CI: confidence interval.
Moderate-to-severe frailty at discharge was defined as modified ACTION Registry Frailty Score ≥3 and was compared with frailty score 0–2.

Table 3
Factors associated with moderate-to-severe frailty at three-year follow-up among post-PCI patients.

Factors	Unadjusted		Adjusted	
	OR [95% CI]	P-value	OR [95% CI]	P-value
Female	0.69 [0.17 - 2.86]	0.613	-	-
Age > 60 yrs	1.57 [0.45 - 5.43]	0.475	-	-
Hypertension	3.40 [0.35 - 33.4]	0.294	-	-
Diabetes	0.50 [0.14 - 1.77]	0.283	-	-
Smoking/drug addictions	1.35 [0.08 - 23.2]	0.835	-	-
Moderate-to-severe frailty at discharge	5.70 [0.97 - 33.6]	0.054	12.75 [1.84 - 88.35]	0.01
Medication non-adherence	0.18 [0.03 - 1.04]	0.056	0.08 [0.01 - 0.54]	0.01
No Cardiac Rehabilitation	1.50 [0.39 - 5.77]	0.555	-	-

OR: odds ratio, CI: confidence interval.
Moderate-to-severe frailty was defined as modified ACTION Registry Frailty Score ≥3. The reference category was frailty score 0–2.

Table 4
Factors associated with poor HRQoL at three-year follow-up.

Factors	Unadjusted		Adjusted	
	OR [95% CI]	P-value	OR [95% CI]	P-value
Female	1.29 [0.51 - 3.27]	0.589	-	-
Age > 60 yrs	1.80 [0.79 - 4.08]	0.159	1.56 [0.44 - 5.53]	0.492
Hypertension	1.76 [0.46 - 6.71]	0.405	-	-
Diabetes	1.71 [0.73 - 4.02]	0.216	-	-
Smoking/drug addictions	0.05 [0.01 - 0.42]	0.005	1.10 [0.06 - 20.01]	0.949
Moderate-to-severe frailty at discharge	1.48 [0.47 - 4.64]	0.503	-	-
Medication non-adherence	0.66 [0.23 - 1.85]	0.424	-	-
No Cardiac Rehabilitation	0.69 [0.29 - 1.64]	0.397	-	-

OR: odds ratio, CI: confidence interval.
Poor HRQoL was defined as an EQ-5D-3 L level-sum score ≥8, corresponding to moderate or severe impairment. The EQ-5D-3 L level-sum score was calculated by summing the five domain scores and was not a preference-weighted EQ-5D utility index.

should be interpreted as exploratory and hypothesis-generating rather than definitive. Medication non-adherence was also retained in the adjusted model (adjusted OR 0.08; 95% CI 0.01–0.54; p = 0.010), but because of the unexpected direction of association and sparse events, this finding should be interpreted cautiously and not as evidence of a protective effect.

3.5. Factors associated with poor quality of life

In the model evaluating poor HRQoL, defined operationally as an EQ-5D-3 L level-sum score ≥ 8, age > 60 years and smoking/drug addiction met the prespecified threshold for multivariable modelling Neither variable remained independently associated with poor HRQoL after adjustment. Age > 60 years had an adjusted OR of 1.56 (95% CI 0.44–5.53; p = 0.492), and smoking/drug addiction had an adjusted OR of 1.10 (95% CI 0.06–20.01; p = 0.949). Moderate-to-severe frailty at discharge was not associated with poor HRQoL in univariable analysis and was not retained in the final adjusted model.

The principal findings were: (1) approximately one-third of this survivor-conditioned cohort died during the three-year follow-up interval; (2) moderate-to-severe frailty at discharge was independently associated with death during follow-up; (3) moderate-to-severe frailty at discharge was associated with moderate-to-severe frailty at follow-up, but the wide confidence interval indicates limited precision and supports an exploratory interpretation; and (4) discharge frailty was not independently associated with poor HRQoL, and no robust independent predictor of poor HRQoL was identified in the final adjusted model.

4. Discussion

This survivor-conditioned three-year follow-up study evaluated long-term outcomes among a high-risk cohort of mechanically ventilated AMI patients who underwent PCI, required ICU/CICU admission with advanced life support, and remained alive at routine 6-month follow-up. Importantly, the present analysis was restricted to six-month survivors and therefore reflects outcomes among early survivors rather than the entire post-PCI population. Consequently, the reported three-year outcomes should be interpreted as survivor-conditioned outcomes among patients alive at routine 6-month follow-up, rather than as outcomes for all patients initially treated with PCI and advanced life support.Within this survivor-conditioned cohort,

approximately one-third of patients died during subsequent long-term follow-up, and moderate-to-severe frailty at hospital discharge was independently associated with long-term mortality and moderate-to-severe frailty at follow-up. These findings suggest that discharge frailty in this population is not merely a transient marker of acute illness severity but may identify a persistent vulnerability phenotype associated with adverse long-term outcomes. In contrast, discharge frailty was not independently associated with poor long-term HRQoL, and age $>$ 60 years was not statistically significant after adjustment.

These findings suggest that mortality, persistent frailty, and perceived quality of life may not follow identical long-term pathways after post-PCI critical illness.

In this study, frailty and HRQoL were operationalised using simple, reproducible clinical constructs. Frailty was measured using a modified ACTION Registry Frailty Score based on walking or motor function, cognition, and activities of daily living. The use of the same frailty score at discharge and follow-up allowed longitudinal comparison of frailty categories. HRQoL was assessed using the EQ-5D-3 L descriptive system; however, because a preference-weighted EQ-5D utility index was not calculated, our HRQoL outcome should be interpreted as a level-sum measure of reported functional and symptom burden rather than as a formal utility value.

A key finding was the difference between broad frailty status and frailty severity. Crude mortality was similar when patients were classified simply as frail or non-frail at discharge. However, when frailty severity was considered, moderate-to-severe frailty at discharge was independently associated with death during the three-year follow-up interval. This suggests that the presence of any frailty may be too broad a construct in this high-risk cohort, particularly because mild frailty was common after critical illness and PCI. Moderate-to-severe frailty may better capture a deeper loss of physiological reserve, functional dependence, and vulnerability to subsequent cardiovascular or non-cardiovascular stressors. Therefore, discharge frailty assessment may be most clinically useful when severity is reported rather than when frailty is treated only as a binary variable.

The high long-term mortality observed in this study is notable because the present analysis was conditional on survival to six months. Patients who died before routine six-month follow-up were not included in the current three-year analysis. Therefore, the observed mortality does not represent total mortality from the original AMI PCI cohort; rather, it reflects residual long-term risk among early survivors of post-PCI critical illness. This distinction is important. Survival beyond hospital discharge and early follow-up does not necessarily indicate biological recovery. In patients who required mechanical ventilation or advanced life support, discharge frailty may identify ongoing vulnerability that persists beyond the apparent resolution of the acute cardiovascular event.

Frailty has been linked with adverse outcomes in cardiovascular patients. In a previous study of elderly patients undergoing PCI, frailty has been associated with a threefold increase in-hospital death and a two-fold rise in all-cause mortality [9]. A meta-analysis of fourteen studies evaluating frailty among patients undergoing coronary bypass grafting showed higher 30-day and one-year mortality among frail individuals compared to non-frail patients [10]. An observational study from South Korea documented a mortality rate 29.4% over ten years among frail cardiovascular patients [11]. Another study showed that frail older patients with AMI undergoing PCI had a significantly higher all-cause mortality compared with non-frail patients [12]. In a previous study conducted in our setup, the majority of patients (67.3%) were classified as having moderate-to-severe frailty at hospital discharge, indicating that frailty was an independent predictor of long-term mortality with nearly a threefold higher risk even after adjustment for age, sex, and comorbidities [5].

A key consideration in interpreting the present findings is survivorship bias introduced by the two-stage design. In the original cohort from our centre, a much larger proportion of patients were classified as having moderate-to-severe frailty at discharge. In contrast, among the six-month survivors included in the present analysis, only 22.1% of frail patients had moderate-to-severe frailty at discharge. This difference is likely explained, at least in part, by early mortality among the most severely frail patients before the 6-month structured three-year follow-up among six-month survivors. Consequently, the current cohort may represent a relatively healthier subset of the original mechanically ventilated AMI PCI population. This survivor selection may attenuate the observed association between frailty and later HRQoL, underestimate the total burden of frailty progression in the original cohort, and means that the reported three-year outcomes should be interpreted as conditional outcomes among six-month survivors rather than as outcomes for all patients initially treated with PCI and advanced life support.

A meta-analysis in patients with COVID-19 showed that frailty individually predicts mortality, supporting its role in detecting high-risk individuals and helping clinical decision-making [13]. Similarly, another study showed that frailty in patients with acute coronary syndromes was associated with increased adverse events, higher in-hospital mortality and prolonged hospital stay [14]. These findings highlight the significance of incorporating frailty assessment into the clinical evaluation of cardiovascular patients. By identifying high-risk individuals, physicians or clinicians may better be able to take treatment decisions, optimise post-procedural monitoring, and implement targeted supportive interventions.

The association between discharge frailty and moderate-to-severe frailty at follow-up supports the concept that frailty in this population is not merely a transient peri-procedural state. Patients with moderate-to-severe frailty at discharge were more likely to have moderate-to-severe frailty at three years. However, this estimate had a wide confidence interval, indicating limited precision and sparse outcome events. Therefore, this finding should be interpreted as hypothesis-generating rather than definitive. It nevertheless raises an important clinical question: whether frailty identified at discharge represents a modifiable trajectory that could be altered through structured rehabilitation, nutritional support, medication optimisation, and closer multidisciplinary follow-up. This observation is consistent with a longitudinal cohort showing that frailty often increases as time goes on, with nearly 30% of prefrail individuals eventually becoming frail [15]. Similarly, Hirokazu Shimono and colleagues reported that frail patients who underwent successful percutaneous intervention and had stable coronary artery disease, receiving optimal medical therapy, experienced worse clinical outcomes [16]. Another study showed that more than one-quarter of patients aged $\geq$ 80 years with acute myocardial infarction who underwent PCI were frail, and the frequency of frailty increased during hospitalisation [17].

The association between discharge moderate-to-severe frailty and moderate-to-severe frailty at follow-up suggests that frailty in this population may not be only a transient peri-procedural state. However, because the adjusted estimate had a wide confidence interval, this finding should be interpreted as hypothesis-generating. Future studies should test whether frailty identified at discharge represents a modifiable trajectory that can be altered through structured rehabilitation, nutritional support, medication optimisation, and closer multidisciplinary follow-up.

In hospitalised patients, frailty often coexists with malnutrition and has been linked to poor outcomes, including higher readmission rates, longer hospital stays and increased mortality [18]. Our study extends these findings by demonstrating that frailty at discharge also predicts adverse long-term outcomes, particularly persistent frailty and increased mortality over a three-year follow-up period.

Although moderate-to-severe frailty at discharge was associated with death during follow-up and with moderate-to-severe frailty at three years, it was not independently associated with poor long-term HRQoL. This finding differs from much of the previous literature, where frailty has often been associated with worse quality of life. In the present study,

moderate-to-severe frailty at discharge was not associated with poor HRQoL, and age > 60 years did not remain statistically significant after adjustment. Therefore, we did not identify a robust independent predictor of poor HRQoL in this cohort. Cross-sectional analyses have shown that frail individuals experience significantly poorer HRQoL in comparison to non-frail individuals [19]. Frailty has been reported in approximately 43% of patients with type 2 diabetes and has been associated with considerable reductions in quality-of-life measures [20]. A recent study showed that older adults with frailty receiving acute healthcare had poor health-related quality of life, with HRQoL declining progressively as the severity of frailty increased, and confirmed that the EQ-5D is a reliable tool for assessing quality of life in this population [21].

In the present study, neither age > 60 years nor discharge frailty was independently associated with poor HRQoL in the corrected adjusted model. Because HRQoL was operationalised using an EQ-5D-3 L level-sum impairment score rather than a preference-weighted EQ-5D utility index, these findings should be interpreted as study-specific impairment results and may not be directly comparable with studies reporting standard EQ-5D index values or other validated HRQoL summary measures. Therefore, we did not identify a robust independent predictor of poor HRQoL in this cohort. This may reflect survivor selection, limited statistical power, the multidimensional nature of quality of life, and the use of an EQ-5D level-sum measure rather than a preference-weighted utility index. In the corrected adjusted model, age > 60 years was not independently associated with poor HRQoL, and discharge frailty was not associated with poor HRQoL. This suggests that the determinants of perceived long-term quality of life in this survivor cohort may differ from those of mortality and persistent frailty.

In contrast, frailty did not independently predict poor HRQoL. Several explanations are possible, including survivor bias, limited statistical power, and the multidimensional nature of quality of life. Patients surviving to long-term follow-up may represent a healthier subgroup, reducing the apparent influence of discharge frailty on HRQoL outcomes.

Uchmanowicz B. et al. demonstrated a strong link between frailty syndrome and reduced quality of life in elderly hypertensive patients [22]. Previous studies done in this context show that patients with coronary heart disease have shown that frailty commonly coexists with ageing and is associated with poorer quality of life [23]. In a study of 508 hospitalised elderly patients with coronary heart disease, multidimensional frailty was identified in more than half of the participants (53.15%), underscoring the considerable burden of frailty in this population [24].

Medication non-adherence was very common, affecting 83.2% of patients with follow-up assessment. Although medication adherence was not the primary focus of this study, this finding is clinically important. In a post-PCI population, long-term adherence to antiplatelet therapy, statins, beta-blockers, renin–angiotensin system inhibitors, and other secondary prevention therapies may strongly influence recurrent cardiovascular events, functional recovery, and survival. The high non-adherence rate may reflect structural barriers relevant to LMIC settings, including medication cost, fragmented follow-up, limited rehabilitation access, low health literacy, and competing socioeconomic pressures. Future studies should evaluate whether discharge frailty combined with medication non-adherence identifies a particularly vulnerable subgroup requiring intensified follow-up.

An additional observation in this study was the unanticipated association between smoking status and HRQoL. Previous studies consistently reported an adverse impact of smoking on health-related quality of life, with patients who smoked showing considerably lower EQ-5D-5 L and EQ-VAS scores across different age groups [25]. Smoking/drug addiction showed an association with poor HRQoL in univariable analysis but was not significant after adjustment. Given the small number of events, wide confidence interval, and potential for residual confounding or sparse-data instability, this finding should not be interpreted as evidence of a protective or causal association.

These findings have practical implications. First, frailty assessment at hospital discharge should be considered in high-risk AMI PCI patients who require ICU/CICU admission and advanced life support, but severity should be documented rather than simply recording frail versus non-frail status. Second, future interventional studies should test whether integrating frailty assessment into discharge planning can improve outcomes. A feasible intervention in similar LMIC cohorts could combine structured cardiac rehabilitation, nutritional optimisation, medication-adherence counselling, early outpatient review, and multidisciplinary follow-up targeted specifically to patients with moderate-to-severe discharge frailty.

4.1. Limitations

This study has several limitations. First, it was conducted at a single tertiary cardiovascular centre in an LMIC setting, which may limit external validity. The cohort consisted of mechanically ventilated AMI patients who underwent PCI and required ICU/CICU admission with advanced life support; therefore, the findings should not be assumed to apply to elective PCI patients, non-ventilated PCI populations, lower-risk ACS patients, or healthcare systems with substantially different follow-up, rehabilitation, and secondary prevention structures.

Second, the sample size was modest, and several outcome models had limited numbers of events. This was particularly relevant for the model evaluating moderate-to-severe frailty at three-year follow-up, where the adjusted estimate for discharge moderate-to-severe frailty had a wide confidence interval. These findings should therefore be interpreted as hypothesis-generating rather than definitive.

Third, the study population was not an unselected PCI cohort but a high-risk group of AMI patients requiring mechanical ventilation and/or advanced life support after PCI. Moreover, because the current analysis included only patients who survived to routine 6-month follow-up, the results are most applicable to post-PCI critical illness survivors rather than to all AMI PCI patients. This distinction is important because early deaths among the most severely frail patients may modify the apparent relationship between discharge frailty, long-term frailty trajectories, mortality, and HRQoL.

Fourth, outcome assessment was performed by structured telephone follow-up, which may have introduced recall bias, reporting bias, and potential misclassification of frailty, medication adherence, physical activity, cardiac rehabilitation participation, and HRQoL. Although the same frailty instrument was used at discharge and follow-up, telephone-based reassessment may not fully capture functional status compared with direct clinical evaluation.

The HRQoL outcome was based on a study-specific EQ-5D-3 L level-sum impairment score rather than a preference-weighted EQ-5D utility index. Although this approach provided a simple operational measure of impairment across EQ-5D-3 L domains, it may limit comparability with studies using standard EQ-5D utility values or other validated HRQoL summary scores. This measurement choice may partly explain the absence of a robust independent association between discharge frailty and poor HRQoL in the present cohort.

Fifth, loss to follow-up may have introduced additional selection bias. Patients who could not be contacted may have differed systematically from those included in the final analysis with respect to socioeconomic status, access to care, medication adherence, functional recovery, recurrent cardiovascular events, or survival.

Finally, residual confounding cannot be excluded. Important variables such as socioeconomic status, nutritional status, rehabilitation intensity, medication affordability, detailed functional capacity, recurrent hospitalisations, and long-term treatment adherence were not fully captured. Therefore, the observed associations, particularly those with wide confidence intervals, should be interpreted cautiously and require validation in larger multicentre cohorts.

Mortality was analysed as a binary outcome using logistic regression

rather than as a time-to-event outcome using Cox proportional hazards modelling. Therefore, the mortality findings describe associations with death over the follow-up interval among six-month survivors and do not provide hazard-based estimates of survival over time. Future studies with larger sample sizes, precise event dates, and longer prospective follow-up should use time-to-event methods to better characterise the timing and dynamics of post-PCI mortality.

5. Conclusion

In this survivor-conditioned three-year follow-up study of mechanically ventilated AMI patients undergoing PCI who remained alive at routine 6-month follow-up, moderate-to-severe frailty at hospital discharge was independently associated with death during the follow-up interval. Moderate-to-severe discharge frailty was also associated with moderate-to-severe frailty at follow-up, but the wide confidence interval indicates limited precision and supports a hypothesis-generating interpretation. Discharge frailty was not independently associated with poor long-term HRQoL, and no robust independent predictor of poor HRQoL was identified in the final adjusted model. These findings require validation in larger multicentre cohorts before they can inform routine practice recommendations.

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Declaration of the use of AI

AI-assisted technologies were used solely for linguistic editing of the manuscript. No scientific content, data, figures, images, or other substantive material was generated using AI-assisted technologies.

Ethical statement

This study was approval by the ethical review board (IRB) of the National Institute of Cardiovascular Diseases (NICVD), Karachi.

Studies on human and/or animal statement

This observational study involving human participants was conducted in accordance with Declaration of Helsinki.

Informed consent

Verbal informed consent was obtained during follow-up contact from all the patients regarding their participation in the study and publication of data while maintaining confidentiality and anonymity. Due to observational nature of the study, IRB waived the written consent and verbal consent were approved by the IRB.

Approval ± registration number

IRB-62/2025

CRediT authorship contribution statement

Sadaf Shaikh: Visualization, Validation, Supervision, Data curation, Conceptualization. **Muhammad Sohaib Arif:** Software, Project administration, Methodology, Data curation. **Madiha Masroor:** Data curation. **Ahras Adeeb Ansari:** Validation, Supervision, Data curation, Conceptualization. **Muhammad Imran Ansari:** Writing – original draft, Validation, Supervision, Software, Resources, Project administration, Data curation, Conceptualization. **Aziz Ur Rehman Memon:** Conceptualization. **Musa Karim:** Writing – review & editing, Project administration, Formal analysis, Conceptualization. **Jawed Abubaker:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data and material will be available upon request.

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