Impact of Frailty on Outcome of Older Patients With Non-ST Elevation Acute Myocardial Infarction Who Undergo Percutaneous Coronary Intervention

Marco Mele, MD[a], Ilaria Ragnatela, MD[b], Matteo Romano, MD[b], Erika Tabella, MD[b], Luciano Umberto Rossi, MD[b], Francesco Mautone, MD[b], Antonietta Mele, MD[c], Antonella Liantonio, MD[c], Paola Imbrici, MD[c], Michele Correale, MD, PhD[a], Francesco Santoro, MD, PhD[b], and Natale Daniele Brunetti, MD, PhD[b,*]

Frailty status is linked with a poorer clinical outcome, and patients with frailty are often less revascularized, even with percutaneous coronary intervention (PCI). We therefore sought to assess the impact of frailty on the clinical outcome of older patients with non-ST elevation acute myocardial infarction (NSTEMI) who underwent PCI. We prospectively enrolled 141 consecutive older patients (>75 years) admitted for NSTEMI; 104 patients underwent PCI (35 with frailty, 69 without frailty), and 37 were not revascularized (22 with frailty, 15 without). Patients with frailty were older, less frequently male, more affected by dementia and severe left ventricular dysfunction, and less treated with PCI; patients treated with PCI were younger and less affected by dementia. Thirty-day mortality rates were proportionally higher, from 3% in patients without frailty treated with PCI, to 7% in patients without frailty not treated with PCI, 17% in patients with frailty treated with PCI, and 48% in patients with frailty not treated with PCI ($p < 0.05$). Similarly, 6-month mortality rates were proportionally higher (12%, 29%, 37%, and 71%). At multivariable analysis, frail status was associated to a sixfold increased risk of mortality at 30 days; at 6 months, frail status was associated to a 3.4-fold risk of death ($p < 0.01$), but PCI was also associated to a lower risk of mortality (odds ratio 0.2, $p < 0.01$). In an observational study in older patients with NSTEMI, frail status is associated to a poorer outcome, whereas PCI is associated to a better long-term outcome. A careful selection of patient suitable for revascularization by PCI may be useful in improving outcomes of older patients with frailty with NSTEMI. **(Am J Cardiol 2024;230:41−46)**

Keywords: Elderly, Frailty, Myocardial infarction, NSTEMI, Percutaneous coronary intervention

In the last decades, the proportion of older patients presenting with acute coronary syndrome (ACS) has increased.[1] Despite a high ischemic risk, these patients carry an equally serious risk of short- and long-term complications; therefore, invasive strategy and percutaneous coronary intervention (PCI) are often avoided.[2] Given older patients are underrepresented in clinical trials,[1,3] the optimal subgroup of patients who may benefit from PCI remains a matter of debate.[4] According to current guidelines, in older patients with ACS, the risk/benefit ratio of PCI should be carefully evaluated, considering co-morbidity, ischemic versus bleeding risk, frailty and life expectancy.[2]

Frailty is an increasingly common geriatric condition characterized by great susceptibility to stress and decreased functional reserves, with consequent poor autonomy.[5] This condition is associated with great risk of death, hospitalization, cognitive impairment, falls, and disability.[5] Because a negative impact of frailty on the outcomes of older patients with ACS has been found, frailty has been proposed as a tool for the decision to refer or not to perform PCI in older patients with non-ST elevation myocardial infarction (NSTEMI).[6−8] There is contrasting evidence on the impact of frailty on the outcomes of patients with ACS who undergo PCI; that may depend on the use of different definitions of frailty used, the inclusion of patients not affected by ACS but who have type 2 myocardial infarction, and the impact of co-morbidities. Moreover, several studies investigating the impact of frailty in ACS do not specifically address the population who undergo coronary revascularization. Data concerning the impact of PCI in older patients with frailty are also conflicting.

We therefore aimed to evaluate the impact of frailty on mortality in older patients with NSTEMI who undergo PCI

[a]Cardiothoracic Department, Policlinico Riuniti Foggia, Foggia, Italy; [b]Department of Medical and Surgical Sciences, University of Foggia, Italy; and [c]Department of Pharmacy and Drug Science, Università Aldo Moro, Bari, Italy. Manuscript received August 8, 2024; revised manuscript received and accepted August 17, 2024.

This work was performed at Policlinico Riuniti Foggia—University of Foggia.

Funding: none.

See page 45 for Declaration of Competing Interest.

*Corresponding author: Tel +39 3287660350; fax: +39 0881 745424.

E-mail address: natale.brunetti@unifg.it (N.D. Brunetti).

0002-9149/

https://doi.org/10.1016/j.amjcard.2024.08.016

and the impact of PCI in older patients with frailty and with NSTEMI.

Methods

We prospectively enrolled patients with NSTEMI, GRACE score >140, age >75 years, and hospitalized in the Cardiac Care Unit of the Policlinico Riuniti University Hospital from October 1, 2022 to August 28, 2023. At admission, frailty was assessed by Clinical Frailty Scale (CFS). The level of frailty was confirmed by the relatives of the patients. For each patient, data on age, risk factors, frailty status, co-morbidity (dementia, anemia, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease), biology, echocardiography, drug therapy, and outcome (in-hospital, 30-day, and 6-month mortality) were collected. We excluded patients not able to sign the informed consent, patients with a final diagnosis of type 2 myocardial infarction, and patients treated conservatively because of a poor clinical status (e.g., cachexia) or scarce life expectancy (assessed independently by 5 cardiologists, or by the majority in 5 cardiologists in case of disagreement). CFS aims to gain information about the level of autonomy of the patient on the basis of a few simple questions.[9] The scoring scale goes from 1 to 9. Patients with frailty are defined by a score >4. Patients with score 4 are considered prefrail or patients with vulnerability, whereas scores 1 to 3 distinguish patients without frailty. Mortality was assessed by our regional administrative dataset.

All patients provided informed consent before the enrollment. Our observational study was approved by the ethics committee of Policlinico Riuniti University Hospital, according to ethical standards established by the Declaration of Helsinki.

Continuous and discrete variables were reported as mean with SD and proportions, respectively; continuous variables were compared by Student *t* test, dichotomic by chi-square test. Differences among multiple groups were tested with analysis of variance.

Multivariable forward stepwise logistic regression analysis, including only variables significant at univariable analysis, was used to calculate the odds ratio, with 95% confidence intervals and predictors of mortality. A $p < 0.05$ was considered statistically significant.

We planned a study in independent groups (older patients with NSTEMI treated with PCI or not) with 1:1 sizing. Previous data indicate that the 6-month death rate in such patients may reach 30%.[10] If the true relative mortality risk may be reduced with an odds ratio of 0.30, we would need to study 55 experimental subjects and 55 control subjects to be able to reject the null hypothesis that this relative risk equals 1 with probability (power) 0.8 and a type I error probability associated with this test of this null hypothesis of 0.05.

Results

We enrolled 141 consecutive older patients with NSTEMI; of these, 104 patients underwent PCI, 35 with frailty and 69 without frailty; 22 patients with frailty and 15 without frailty were not treated with PCI. Baseline characteristics are listed in Table 1. Patients with frailty were older (84 ± 5 vs 82 ± 5 years, p = 0.003), less likely to be male (47% vs 67%, p = 0.0222), more frequently affected by dementia (21% vs 2%, p = 0.0002) and severe left ventricular dysfunction (47% vs 30%, p = 0.0336), and less likely to be treated with PCI (61% vs 82%, p = 0.0058); N-terminal pro b-type natriuretic peptide (NT-proBNP) levels were higher (21,981 ± 30,963 vs 10,016 ± 28,970 pg/ml, p = 0.0220). Patients treated with PCI were younger (82 ± 5 vs 84 ± 6 years, p = 0.0297), less affected by dementia (7% vs 19%, p = 0.3334), and showed lower levels of NT-proBNP (8,270 ± 10,370 vs 33,576 ± 52,799 pg/ml, p <0.0001) and cardiac troponin I (5,226 ± 7,387 vs 8,433 ± 8,542 ng/L, p = 0.0313).

Thirty-day mortality rates were proportionally higher, from 3% in patients without frailty treated with PCI to 7% in patients without frailty not treated with PCI, to 17% in patients with frailty treated with PCI to 48% in patients with frailty not treated with PCI (p for trend <0.05) (Figure 1). Similarly, 6-month mortality rates were proportionally higher, from 12% in patients without frailty treated with PCI to 29% in patients without frailty not treated with PCI to 37% in patients with frailty treated with PCI to 71% in patients with frailty not treated with PCI (p for trend <0.05).

Variables significantly associated to 30-day mortality were frail status, dementia, cardiac troponin I, and NT-proBNP levels, and lower hemoglobin levels versus use of angiotensin converting enzyme inhibitors/angiotensin receptor antagonists, statins, and PCI (Table 2). At multivariable stepwise forward logistic regression analysis including such factors significant at univariable analysis, frail status was associated to a sixfold increased risk of mortality at 30 days (odds ratio [OR] 6, 95% confidence interval [CI] 1.4 to 25.9, p <0.05) (Table 3). At 6 months, frail status was associated to a 3.4-fold risk of death (OR 3.4, 95% CI 1.4 to 8.7, p <0.01), but PCI was also associated to a smaller risk of mortality (OR 0.2, 95% CI 0.1 to 0.7, p <0.01) (Table 4).

Discussion

In this observational study, we show 2 main findings: (1) frail status is associated to a poorer outcome in older subjects with NSTEMI; (2) PCI, in a nonrandomized study, is associated to a better long-term outcome, whereas in-hospital benefit of PCI is less evident.

Several studies investigated the impact of frailty on outcomes of ACS in older patients but without considering strictly the subgroup of patients who underwent PCI. According to the results of LONGEVO-SCA (Impacto de la fragiLidad y Otros síNdromes GEriátricos en el manejo y pronóstico Vital del ancianO con Síndrome Coronario Agudo sin elevación de segmento ST) registry in unselected older patients aged ≥80 years with non-ST elevation-ACS, only in approximately 2/3 of cases treated by PCI was frailty assessed by the Frail Scale, a tool similar to CFS, a predictor of 6-month mortality.[11] According to a recent meta-analysis, frailty was associated with in-hospital, short-term, and long-term mortality in patients who underwent PCI. However, the analysis encompassed studies with

Table 1
General characteristics of the population enrolled in the study

	no frail - pci		no frail - no pci		frail - pci		frail - no pci			
	N=69 Mean	SD	N=15 Mean	SD	N=35 Mean	SD	N=22 Mean	SD	frail vs no p	pci vs no p
age	82	5	82	5	83	5	86	6	0.0030	0.0297
male	68%		60%		49%		45%		0.0222	0.2828
BMI	27	3	25	2	27	4	25	4	0.8177	0.0932
hypertension	88%		93%		91%		100%		0.2581	0.1424
dyslipidemia	81%		87%		80%		68%		0.3373	0.5138
smoke	30%		33%		23%		18%		0.1962	0.6777
GFR	51	31	46	33	42	25	40	22	0.0648	0.2830
NTproBNP	6354	7993	26377	64834	11938	13204	38718	43236	0.0220	0.0000
cTnI	5042	7130	5950	6996	5589	7964	10125	9221	0.1110	0.0313
Hb	11,9	2,3	11,0	2,7	11,0	2,1	10,9	2,6	0.0545	0.1223
previous revascularization	43%		53%		46%		27%		0.4374	0.5029
dementia	3%		0%		14%		32%		0.0002	0.0334
cancer	14%		27%		11%		18%		0.6752	0.2432
anemia	48%		60%		57%		73%		0.1248	0.0821
COPD	14%		27%		26%		32%		0.1059	0.1456
diabetes	39%		73%		54%		45%		0.5140	0.1927
severe LV dysfunction	33%		13%		49%		45%		0.0336	0.5173
ACEi/ARB	81%		47%		54%		32%		0.0004	0.0002
beta-blockers	74%		87%		80%		68%		0.9502	0.9950
statins	91%		80%		91%		77%		0.5732	0.0399
MRA	43%		47%		63%		45%		0.1396	0.7119
DOACs	19%		33%		17%		18%		0.5505	0.4469
warfarin	3%		13%		3%		9%		0.9066	0.0593
DAPT	96%		20%		89%		18%		0.0066	0.0000
in-hospital mortality	3%		7%		14%		18%		0.0105	0.2069
30-day mortality	3%		7%		17%		48%		0.0000	0.0005
30-day bleeding	9%		29%		18%		11%		0.6203	0.3260

ACEi/ARB = angiotensin converting enzyme inhibitors, angiotensin receptor antagonists; BMI = body mass index; COPD = chronic obstructive pulmonary disease; cTn-I = cardiac troponin I; DAPT = dual antiplatelet therapy; DOAC = direct oral anticoagulant; GFR = glomerular filtration rate; Hb = hemoglobin; LV = left ventricular; MRA = mineralocorticoid receptor antagonists; NT-proBNP = N-terminal pro b-type natriuretic peptide; PCI = percutaneous coronary intervention.

6 different frailty assessments. Moreover, the analysis included a great proportion of patients with stable coronary artery disease.[12] Similarly, Murali-Krishnan et al[13] showed that frailty assessed by CFS was independently associated with in-hospital and 1-year mortality after PCI but including patients hospitalized for both stable coronary artery and ACS. Recently, some authors showed that frailty, assessed by CFS, was a predictor of bleeding and major adverse cardiac events at a long-term follow-up in patients who underwent PCI but with stable coronary artery disease.[14] The findings of our study confirm the negative impact of frailty on the mortality of older patients with NSTEMI who undergo PCI. Regarding the impact of PCI on patients with frailty, there are conflicting data. According to the results of the LONGEVO-SCA Registry, an invasive approach (only approximately 2/3 of patients had undergone PCI after coronary angiography) did not show a positive impact on mortality.[11] The MOSCA trial aimed to assess the effect of an invasive strategy versus a conservative strategy in older adults with frailty. The study concluded there was a lack of benefit in an invasive strategy in terms of days alive and out of hospital, and a composite end point (cardiac death, reinfarction, and revascularization after discharge)[15] In contrast, in a large retrospective study, frailty assessed by a claims-based frailty index (CFI) was associated with greater mortality, but in patients with frailty, PCI reduced in-hospital mortality in comparison with a conservative approach in patients with acute myocardial infarction.[16] CFI, even if a validated tool for the assessment of frailty, is phenotype-based and based only on administrative claims, without physical performance measures.[17] A small prospective study evaluated the impact of PCI in older patients with frailty with NSTEMI in terms of hospitalizations. The authors concluded there was a positive effect of PCI on readmissions but not on mortality.[18] This study was conducted between 2010 and 2012, and the impact of new strategies and devices could be missed (e.g., drug-coated balloon, new generation drug-eluting stents).

For the evaluation of the impact of frailty, we included only older patients with frailty who underwent PCI for 2 main reasons. First, by selecting this population, we excluded patients with NSTEMI, poor life expectancy, and quality of life, patients with the greatest risk of death and procedural complications who usually are not eligible for invasive procedures. Moreover, we reduced the probability to include patients with type 2 myocardial infarction (T2MI). In fact, this subgroup of patients often encompasses older patients and those with evidence of acute myocardial injury. An appropriate differential diagnosis between NSTEMI and T2MI is sometimes arduous, and the

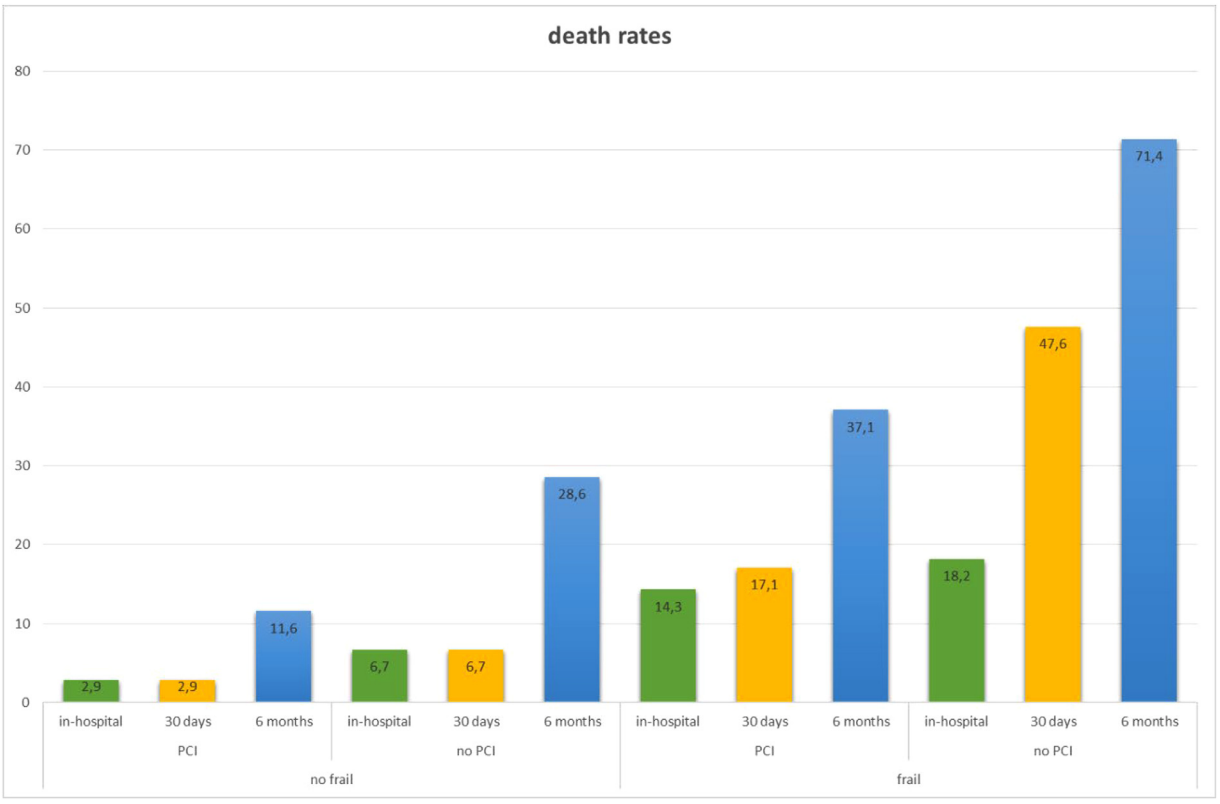

Figure 1. Mortality rates according to frail status and coronary angioplasty (PCI) during hospitalization, at 30 days and 6 months (analysis of variance p <0.05).

Table 2
Significant differences comparing patients dead at 30 days

	N=19 Dead Mean	Std.Dev.	N=122 Alive Mean	Std.Dev.	p
ACEi/ARB	11%		71%		0.0000
Frail	84%		33%		0.0000
PCI	42%		79%		0.0005
Dementia	32%		7%		0.0007
cTn-I	11291	10078	5229	7128	0.0015
Severe LV dysfunction	68%		33%		0.0024
Statins	68%		91%		0.0057
Hemoglobin	10.1	1.9	11.6	2.40	0.0116
NT-proBNP	28371	36951	12944	29000	0.0450

ACEi/ARB = angiotensin converting enzyme inhibitors angiotensin receptor antagonists; cTn-I = cardiac troponin I; LV = left ventricular; NT-proBNP = N-terminal pro b-type natriuretic peptide; PCI = percutaneous coronary intervention.

Table 3
Multivariable forward stepwise logistic regression analysis: significant predictors of 30-day mortality

	OR	95% C.I.		p
ACEi/ARB	0.076	0.015	0.386	0.002
Frail	6.064	1.421	25.873	0.015
cTn-I	1.000	1.000	1.000	0.022

ACEi/ARB = angiotensin converting enzyme inhibitors angiotensin receptor antagonists; cTn-I = cardiac troponin I; LV = left ventricular.

Table 4
Multivariable forward stepwise logistic regression analysis: significant predictors of 6-month mortality

	OR	95% C.I.		p
ACEi/ARB	0.352	0.138	0.900	0.029
Frail	3.450	1.362	8.742	0.009
PCI	0.225	0.074	0.690	0.009
Severe LV dysfunction	4.651	1.671	12.947	0.003

ACEi/ARB = angiotensin converting enzyme inhibitors angiotensin receptor antagonists; LV = left ventricular; PCI = percutaneous coronary intervention.

impact of PCI on T2MI is not so clear.[19] For these reasons, we usually do not use an invasive approach in older patients with T2MI. In other words, the population of our study can be considered a selected group of patients with great ischemic risk, who underwent PCI after a judicious evaluation of the risk/benefit ratio. We used a phenotype-based scale for the assessment of frailty as CFS for several reasons. First, it is an ease-of-use tool, performable also at bedside or through the relatives. Furthermore, it is not based only on administrative claims with the risk of inaccurate assessment as CFI. Interestingly, the impact of frailty on mortality is evident at 6 months. In-hospital and 30-day mortality could be affected by more predictive factors in the setting of hospitalization such as active bleeding, infective complications, and severe heart failure. We found a positive impact of PCI on the mortality of patients with frailty. In contrast with other studies comparing invasive (not necessarily PCI) with conservative strategy, we excluded patients with poor life expectancy and poor clinical status, selecting patients with frailty with an acceptable procedural risk, who underwent PCI. To the best of our knowledge, this is the first study showing a positive impact of PCI on the mortality of older patients with frailty who underwent PCI. New materials and devices for PCI may have contributed to this result. Further studies are warranted in a larger population and randomized to confirm such preliminary data.

In an observational study in older patients with NSTEMI, frail status is associated to a poorer outcome, whereas PCI is associated to a better long-term outcome. A careful selection of patients suitable for revascularization by PCI may be useful in improving the outcome of older patients with frailty with NSTEMI.

The main limitations of the study are its observational and monocentric nature and the relatively small number of patients enrolled.

Declaration of competing interest

The authors have no competing interests to declare.

CRediT authorship contribution statement

Marco Mele: Conceptualization, Data curation, Investigation, Methodology, Supervision, Writing – original draft, Project administration. **Ilaria Ragnatela:** Data curation, Investigation. **Matteo Romano:** Data curation, Investigation. **Erika Tabella:** Data curation, Investigation. **Luciano Umberto Rossi:** Data curation, Investigation. **Francesco Mautone:** Data curation, Investigation. **Antonietta Mele:** Investigation. **Antonella Liantonio:** Investigation. **Paola Imbrici:** Investigation. **Michele Correale:** Investigation, Methodology. **Francesco Santoro:** Investigation, Methodology. **Natale Daniele Brunetti:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – review & editing.

1. Mandelzweig L, Battler A, Boyko V, Bueno H, Danchin N, Filippatos G, Gitt A, Hasdai D, Hasin Y, Marrugat J, Van de Werf F, Wallentin L, Behar S. Euro Heart Survey Investigators. The second euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. *Eur Heart J* 2006;27:2285–2293.
2. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan GA, Dweck MR, Galbraith M, Gilard M, Hinterbuchner L, Jankowska EA, Jüni P, Kimura T, Kunadian V, Leosdottir M, Lorusso R, Pedretti RFE, Rigopoulos AG, Rubini Gimenez M, Thiele H, Vranckx P, Wassmann S, Wenger NK, Ibanez B, ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J* 2023;44:3720–3826.
3. Sinclair H, Batty JA, Qiu W, Kunadian V. Engaging older patients in cardiovascular research: observational analysis of the ICON-1 study. *Open Heart* 2016;3:e000436.
4. Mills GB, Ratcovich H, Adams-Hall J, Beska B, Kirkup E, Raharjo DE, Veerasamy M, Wilkinson C, Kunadian V. Is the contemporary care of the older persons with acute coronary syndrome evidence-based? *Eur Heart J Open* 2022;2:oeab044.
5. Vitale C, Jankowska E, Hill L, Piepoli M, Doehner W, Anker SD, Lainscak M, Jaarsma T, Ponikowski P, Rosano GMC, Seferovic P, Coats AJ. Heart Failure Association/European Society of Cardiology position paper on frailty in patients with heart failure. *Eur J Heart Fail* 2019;21:1299–1305.
6. Dou Q, Wang W, Wang H, Ma Y, Hai S, Lin X, Liu Y, Zhang X, Wu J, Dong B. Prognostic value of frailty in elderly patients with acute coronary syndrome: a systematic review and meta-analysis. *BMC Geriatr* 2019;19:222.
7. Patel A, Goodman SG, Yan AT, Alexander KP, Wong CL, Cheema AN, Udell JA, Kaul P, D'Souza M, Hyun K, Adams M, Weaver J, Chew DP, Brieger D, Bagai A. Frailty and outcomes after myocardial infarction: insights from the CONCORDANCE registry. *J Am Heart Assoc* 2018;7:e009859.
8. Ekerstad N, Javadzadeh D, Alexander KP, Bergström O, Eurenius L, Fredrikson M, Gudnadottir G, Held C, Ängerud KH, Jahjah R, Jernberg T, Mattsson E, Melander K, Mellbin L, Ohlsson M, Ravn-Fischer A, Svennberg L, Yndigegn T, Alfredsson J. Clinical Frailty Scale classes are independently associated with 6-month mortality for patients after acute myocardial infarction. *Eur Heart J Acute Cardiovasc Care* 2022;11:89–98.
9. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173:489–495.
10. Kochar A, Chen AY, Sharma PP, Pagidipati NJ, Fonarow GC, Cowper PA, Roe MT, Peterson ED, Wang TY. Long-term mortality of older patients with acute myocardial infarction treated in US clinical practice. *J Am Heart Assoc* 2018;7:e007230.
11. Llaó I, Ariza-Solé A, Sanchis J, Alegre O, López-Palop R, Formiga F, Marín F, Vidán MT, Martínez-Sellés M, Sionis A, Vives-Borrás M, Gómez-Hospital JA, Gómez-Lara J, Roura G, Díez-Villanueva P, Núñez-Gil I, Maristany J, Asmarats L, Bueno H, Abu-Assi E, Cequier À. Invasive strategy and frailty in very elderly patients with acute coronary syndromes. *EuroIntervention* 2018;14:e336–e342.
12. He YY, Chang J, Wang XJ. Frailty as a predictor of all-cause mortality in elderly patients undergoing percutaneous coronary intervention: a systematic review and meta-analysis. *Arch Gerontol Geriatr* 2022;98:104544.
13. Murali-Krishnan R, Iqbal J, Rowe R, Hatem E, Parviz Y, Richardson J, Sultan A, Gunn J. Impact of frailty on outcomes after percutaneous coronary intervention: a prospective cohort study. *Open Heart* 2015;2:e000294.
14. Shimono H, Tokushige A, Kanda D, Ohno A, Hayashi M, Fukuyado M, Akao M, Kawasoe M, Arikawa R, Otsuji H, Chaen H, Okui H, Oketani N, Ohishi M. Association of preoperative clinical frailty and clinical outcomes in elderly patients with stable coronary artery disease after percutaneous coronary intervention. *Heart Vessels* 2023;38:1205–1217.
15. Sanchis J, Bueno H, Miñana G, Guerrero C, Martí D, Martínez-Sellés M, Domínguez-Pérez L, Díez-Villanueva P, Barrabés JA, Marín F, Villa A, Sanmartín M, Llibre C, Sionís A, Carol A, García-Blas S, Calvo E, Morales Gallardo MJ, Elízaga J, Gómez-Blázquez I, Alfonso F, García Del Blanco B, Núñez J, Formiga F, Ariza-Solé A. Effect of routine invasive vs conservative strategy in older adults with frailty and non-ST-segment elevation acute myocardial infarction: a randomized clinical trial. *JAMA Intern Med* 2023;183:407–415.
16. Damluji AA, Huang J, Bandeen-Roche K, Forman DE, Gerstenblith G, Moscucci M, Resar JR, Varadhan R, Walston JD, Segal JB. Frailty

among older adults with acute myocardial infarction and outcomes from percutaneous coronary interventions. *J Am Heart Assoc* 2019;8: e013686.
17. Segal JB, Chang H-Y, Du Y, Walston JD, Carlson MC, Varadhan R. Development of a claims-based frailty indicator anchored to a well-established frailty phenotype. *Med Care* 2017;55:716–722.
18. Núñez J, Ruiz V, Bonanad C, Miñana G, García-Blas S, Valero E, Núñez E, Sanchis J. Percutaneous coronary intervention and recurrent hospitalizations in elderly patients with non ST-segment acute coronary syndrome: the role of frailty. *Int J Cardiol* 2017;228:456–458.
19. Mele M, Tricarico L, Casavecchia G, Ieva R, Iacoviello M, Di Biase M, Magnesa M, Corbo MD, Vitale E, Brunetti ND. Revascularization rates with coronary angioplasty and mortality in type 2 myocardial infarction: a meta-regression analysis. *Am J Emerg Med* 2021;47:145–148.