Research Article   · Open Access ·

Clinical and prognostic implications of delirium in elderly patients with non–ST-segment elevation acute coronary syndromes

Miquel Vives-Borrás[1], Manuel Martínez-Sellés[2], Albert Ariza-Solé[3], María T. Vidán[4], Francesc Formiga[3],

Héctor Bueno[5], Juan Sanchís[6], Oriol Alegre[3], Albert Durán-Cambra[1], Ramón López-Palop[7],

Emad Abu-Assi[8], Alessandro Sionis[1], LONGEVO-SCA Investigators

[1]*Department of Cardiology, Hospital de la Santa Creu i Sant Pau, Institute of Biomedical Research IIB Sant Pau, CIBERCV, Universitat Autònoma de Barcelona, Barcelona, Spain*
[2]*Department of Cardiology, Hospital General Universitario Gregorio Marañón, CIBERCV, Universidad Complutense, Universidad Europea, Madrid, Spain*
[3]*Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*
[4]*Hospital General Universitario Gregorio Marañón, IiSGM, CIBERFES, Universidad Complutense, Madrid, Spain*
[5]*Hospital Doce de Octubre, Centro Nacional de Investigaciones Cardiovasculares, Madrid, Spain*
[6]*Hospital Clínico de Valencia, INCLIVA, Universidad de Valencia, CIBERCV, Spain*
[7]*Hospital Universitario San Juan, Alicante, Spain*
[8]*Hospital Álvaro Cunqueiro, Vigo, Spain*

Abstract

Background Elderly patients with non-ST-segment elevation acute coronary syndromes (NSTE-ACS) may present delirium but its clinical relevance is unknown. This study aimed at determining the clinical associated factors, and prognostic implications of delirium in old-aged patients admitted for NSTE-ACS. **Methods** LONGEVO-SCA is a prospective multicenter registry including unselected patients with NSTE-ACS aged ≥ 80 years. Clinical variables and a complete geriatric evaluation were assessed during hospitalization. The association between delirium and 6-month mortality was assessed by a Cox regression model weighted for a propensity score including the potential confounding variables. We also analysed its association with 6-month bleeding and cognitive or functional decline. **Results** Among 527 patients included, thirty-seven (7%) patients presented delirium during the hospitalization. Delirium was more frequent in patients with dementia or depression and in those from nursing homes (27.0% *vs.* 3.1%, 24.3% *vs.* 11.6%, and 11.1% *vs.* 2.2%, respectively; all *P* < 0.05). Delirium was significantly associated with in-hospital infections (27.0% *vs.* 5.3%, *P* < 0.001) and usage of diuretics (70.3% *vs.* 49.8%, *P* = 0.02). Patients with delirium had longer hospitalizations [median 8.5 (5.5–14) *vs.* 6.0 (4.0–10) days, *P* = 0.02] and higher incidence of 6-month bleeding and mortality (32.3% *vs.* 10.0% and 24.3% *vs.* 10.8%, respectively; both *P* < 0.05) but similar cognitive or functional decline. Delirium was independently associated with 6-month mortality (HR = 1.47, 95% CI: 1.02–2.13, *P* = 0.04) and 6-month bleeding events (OR = 2.87; 95% CI: 1.98–4.16, *P* < 0.01). **Conclusions** In-hospital delirium in elderly patients with NSTE-ACS is associated with some preventable risk factors and it is an independent predictor of 6-month mortality.

J Geriatr Cardiol 2019; 16: 121−128. doi:10.11909/j.issn.1671-5411.2019.02.008

Keywords: Acute coronary syndromes; Delirium; Prognosis; The elderly

1   Introduction

Elderly patients represent roughly one-third of all admissions for non-ST-segment elevation acute coronary syndrome (NSTE-ACS),[1,2] and an increase in this proportion is

foreseen in the coming years.[3] These patients frequently associate comorbidities such as dementia and frailty,[4] and they are known to have higher mortality,[1] and to receive less evidence-based treatments.[5] Therefore, identifying clinical predictors of worse outcomes in this specific population is mandatory.

Delirium is an acute disturbance of attention and cognitive functioning that frequently complicates hospitalization of old-aged patients.[6] Although this condition and its significance has been extensively studied in critical, medical, and even surgical care populations,[7–9] little is known about

its frequency in elderly patients admitted for NSTE-ACS and its impact on their clinical evolution. Given that risk-stratification tools for acute coronary syndrome (ACS) do not consider specific geriatric factors,[10,11] analysis of these conditions, such as delirium, may be of potential utility in clinical practice.

This study aimed to describe the clinical associated factors and the prognostic implications of delirium in a large multicenter cohort of unselected elderly patients; aged ≥ 80 years, admitted for NSTE-ACS.

2 Methods

2.1 Study population

The study population consists of 527 patients from the LONGEVO-SCA registry. The detailed study design and variables have been published previously.[12] Briefly, LONGEVO-SCA is a Spanish multicenter, prospective, observational study conducted between March 2016 and September 2016. We enrolled consecutive elderly patients admitted for NSTE-ACS in 44 tertiary and secondary hospitals. The inclusion criteria were: (1) age ≥ 80 years; (2) chest pain consistent with ACS; and (3) changes on ECG (negative T-wave or ST-segment decline) and/or elevation of myocardial damage biomarkers. The exclusion criteria were: (1) patient refusal to participate in the registry; and (2) impossibility of obtaining the geriatric tests. Patients with severe comorbidities were only excluded if symptoms of myocardial ischemia were clearly triggered only by other conditions, such as acute anemia, severe decompensated respiratory insufficiency, active infectious diseases or severe coexisting valvular disease (type 2 myocardial infarction). The inclusion in the study did not imply any change in patients' clinical management; therefore, the medical treatment, the complementary examinations including the need for coronary angiography or the choice of stents were decided by the medical team. Informed consent was obtained from the patients or their next of kin. The study was approved by the ethics committees of each center and the investigation conforms to the principles outlined in the Declaration of Helsinki. The project was supported and coordinated by the Section of Geriatric Cardiology, Spanish Society of Cardiology.

2.2 Study variables

Data were collected using specifically designed web forms (http://www.adknoma.com/LONGEVO-SCA), and quality controls were undertaken every month. We recorded the following clinical variables at study inclusion: (1) demo-graphic and previous clinical history including comorbidities; (2) case history and physical examination; (3) ECG, laboratory blood test and echocardiography at admission; (4) coronary angiography and coronary angioplasty when performed; and (5) medical treatment and clinical evolution. Standard criteria were used to define each variable. Delirium was defined as an acute and transient disorder of attention, and cognition and its diagnosis was made by the patient's medical team following the current recommendations and methods.[13,14] Bleeding events were defined as significant hemorrhages requiring surgery, hospitalization or antithrombotic therapy withdrawal. A baseline geriatric assessment was made during admission in all patients through interview with the patient, family or caregivers and referring to the patient's status prior to admission. The complete in-hospital geriatric evaluation included the Barthel index (functional capacity), the Lawton-Brody Index (instrumental activities), the Pfeiffer test (cognitive status), the FRAIL scale (frailty), the Short Physical Performance Battery (SSPB) (frailty), the Charlson Comorbidity Index and the Nutritional Assessment–Short Form.[15–21]

2.3 Follow-up

Follow-up data was obtained by telephone contact at 6-month, and from the event reports by electronic records of each hospital. The occurrence of death, major bleeding or the need of new coronary interventions was registered. Additionally, a new geriatric evaluation was also determined by assessing the Barthel and Lawton indexes and the Pfeiffer test. Cognitive decline was defined as a loss of at least one point in the 6-month Pfeifer test. Functional decline was defined as a loss of at least ten points in the 6-month Barthel score or two points in the 6-month Lawton-Brody test.[22]

2.4 Statistical analyses

Categorical variables were described by frequencies and percentages, and statistical differences were analyzed using the χ^2 test or Fisher exact test when any expected cell frequency was < 5. The continuous variables were described either by the mean and standard deviation, or by the median and interquartile range. The statistical differences among the continuous variables were analyzed using student's t test in case of a normal distribution, or the Wilcoxon rank-sum test in case of a non-normal distribution. Kaplan-Meier estimators of survival were built comparing patients who suffered delirium and those who did not. Finally, to evaluate the independent effect of delirium on 6-month mortality, a Cox regression model was implemented adjusting for propensity score weights (inverse probability of assignment weighting) including the potential confounding variables.[23] For ana-

lyzing the association between delirium and the secondary end-point (6-month bleeding events), we used a logistic regression adjusted by the previously described method. Multiple imputation using chained equations method was applied when necessary (*n* = 5) applying the "mice" package in the R Project for Statistical Computing.[24] A *P* value < 0.05 was considered significant. All analyses were performed using STATA v.13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP) and R software (R Foundation for Statistical Computing, version 3.3.2).

3 Results

3.1 Clinical characteristics

From 527 patients, 37 (7%) presented delirium during hospitalization. Table 1 summarizes the baseline clinical characteristics of the study population. Patients who developed delirium had more frequently a previous diagnosis of dementia or depression. We did not find statistically significant differences in any other main clinical characteristics between the two groups. Of note, there was a tendency towards a higher frequency of previous diagnosis of cerebrovascular disease and heart failure in those who presented delirium.

Table 2 shows the main features regarding the index hospitalization, the ACS characteristics and the procedures

performed. Patients who presented delirium were more frequently referred from nursing homes. At admission, they had a higher Killip class, higher CRUSADE score punctuation; and presented more frequently elevated troponin levels. With respect to in-hospital complications, patients who developed delirium presented a higher incidence of atrial fibrillation, infections requiring antibiotic treatment; and they were more often treated with invasive mechanical ventilation, diuretic therapy, amiodarone, and benzodiazepines. On the other hand, both groups had similar rate of invasive treatment and coronary revascularization therapy during the admission.

3.2 Geriatric evaluation

Table 3 summarizes the baseline and 6-month geriatric evaluation data. Patients who developed delirium were more comorbid, they had worse functional and instrumental capacities, and they also presented a poorer cognitive function and cognitive status. Remarkably, the prevalence of frailty (FRAIL score ≥ 3) in the entire cohort was 27%, and resulted higher in patients with delirium (44% *vs.* 26%, *P* = 0.04).

3.3 Outcome

As shown in Figure 1, patients who developed delirium had higher non-adjusted overall 6-month mortality (24.3% *vs.* 10.8%, *P* = 0.01). Table 4 describes in-hospital and

Table 1. Characteristics of the study population.

	All patients (*n* = 527)	Delirium (*n* = 37)	No delirium (*n* = 490)	*P*-value
Age, yrs	84.1 (82.1–87.1)	84.7 (82.1–87.7)	84.0 (82.1–87.0)	0.58
Female	205 (39.8%)	19 (51.4%)	186 (38.0%)	0.11
CV risk factors				
Smoker	194 (36.8%)	16 (43.2%)	178 (36.3%)	0.40
Hypertension	454 (86.2%)	33 (89.2%)	421 (85.9%)	0.58
Dyslipidemia	337 (64.0%)	21 (56.8%)	316 (64.5%)	0.35
Diabetes mellitus	210 (39.9%)	18 (48.7%)	192 (39.2%)	0.26
Medical history				
Peripheral arterial disease	71 (13.5%)	5 (13.5%)	66 (13.5%)	1.00
Cerebrovascular disease	80 (15.2%)	9 (24.3%)	71 (14.5%)	0.11
Chronic kidney disease	168 (31.9%)	14 (37.8%)	154 (31.4%)	0.42
Myocardial infarction	184 (34.9%)	12 (32.4%)	172 (35.1%)	0.74
Previous PCI	152 (28.8%)	12 (32.4%)	140 (28.6%)	0.62
Heart failure	92 (17.5%)	10 (27.0%)	82 (16.7%)	0.12
Atrial fibrillation	102 (19.4%)	5 (13.5%)	97 (19.8%)	0.35
Malignancy	89 (16.9%)	4 (10.8%)	85 (17.4%)	0.31
Dementia	25 (4.7%)	10 (27.0%)	15 (3.1%)	< 0.01
Depression	66 (12.5%)	9 (24.3%)	57 (11.6%)	0.04

Data are presented as *n* (%) or median (interquartile range). CV: cardiovascular; PCI: percutaneous coronary intervention.

Table 2. Acute coronary syndrome characteristics, care and procedures.

	All patients (*n* = 527)	Delirium (*n* = 37)	No delirium (*n* = 490)	*P*-value
Admission source				
Home	511 (97.2%)	32 (88.9%)	479 (97.8%)	0.02
Institutionalized	15 (2.9%)	4 (11.1%)	11 (2.2%)	
Admission unit				
CCU/ICU	154 (29.2%)	14 (37.8%)	140 (28.6%)	
Cardiology ward	315 (59.8%)	19 (51.3%)	296 (60.4%)	0.42
Internal medicine/Geriatrics	58 (11.0%)	4 (10.8%)	54 (11.0%)	
ACS and hospitalization characteristics				
Killip class > I	149 (28.7%)	15 (42.9%)	134 (27.7%)	0.06
GRACE score	165 ± 28	172 ± 32	165 ± 28	0.16
CRUSADE score	41 ± 13	47 ± 12	41 ± 13	0.02
Positive troponin	446 (84.6%)	36 (97.3%)	410 (83.7%)	0.03
3-vessel disease	107 (27.4%)	11 (40.7%)	96 (26.4%)	0.11
LVEF	55 (45–61)	55 (40–60)	55 (45–62)	0.42
In-hospital AF episode	52 (9.9%)	8 (21.6%)	44 (9.0%)	0.02
Infection	36 (6.8%)	10 (27.0%)	26 (5.3%)	< 0.01
Blood test parameters				
Hemoglobin, g/dL	12.8 (11.5–14.0)	12.5 (11.2–13.6)	12.8 (11.5–14.0)	0.32
Creatinine peak, mg/dL	1.1 (0.9–1.4)	1.0 (0.9–1.4)	1.1 (0.9–1.4)	0.94
Glucose peak, mg/dL	143 (113–200)	168 (132–218)	140 (112–199)	0.05
Procedures				
Coronary angiography	398 (75.5%)	27 (73.0%)	371 (75.7%)	0.71
Coronary revascularization	290 (72.7%)	20 (74.1%)	270 (72.6%)	0.87
Orotracheal intubation	9 (1.7%)	3 (8.1%)	6 (1.2%)	0.02
IABP	6 (1.1%)	1 (2.7%)	5 (1.0%)	0.35
In-hospital medical therapy				
Aspirin	503 (95.5%)	36 (97.3%)	467 (95.3%)	1.00
ADP-receptor blocker	483 (91.7%)	34 (91.9%)	449 (91.6%)	1.00
LMWH	420 (79.7%)	33 (89.2%)	387 (79.0%)	0.14
Unfractionated heparin	80 (15.8%)	8 (21.6%)	72 (14.7%)	0.26
ACEI/ARB	395 (75.0%)	25 (67.6%)	370 (75.5%)	0.28
Beta-blocker	415 (78.8%)	31 (83.8%)	384 (78.4%)	0.44
Statins	481 (91.3%)	34 (91.9%)	447 (91.2%)	0.89
Diuretic	270 (51.2%)	26 (70.3%)	244 (49.8%)	0.02
Amiodarone	28 (5.3%)	7 (18.9%)	21 (4.3%)	< 0.01
Neuroleptic	78 (14.8%)	32 (86.5%)	46 (9.4%)	< 0.01
Benzodiazepines	261 (49.5%)	23 (62.2%)	238 (48.6%)	0.11

Data are presented as means ± SD or *n* (%) or median (interquartile range). ACEI: angiotensin-converting-enzyme inhibitor; ACS: acute coronary syndrome; ADP: adenosine diphosphate; AF: atrial fibrillation; ARB: angiotensin II receptor blocker; CCU: coronary care unit; IABP: intra-aortic balloon pump; ICU: intensive care unit; LMWH: low-molecular-weight heparin; LVEF: left ventricular ejection fraction.

6-month outcomes. Patients with delirium had more frequent in-hospital and 6-month bleeding events and longer hospitalization. Our data did not reveal significant differences in the proportion of patients presenting 6-month functional decline or 6-month cognitive decline. After a Cox regression analysis with propensity score weighting including the following well balanced confounding factors: previous heart failure, depression, institutionalization, positive troponin, 3-vessel coronary artery disease, revascularization during admission, CRUSADE score, Killip class, atrial fibrillation episodes, need for mechanical ventilation, infection during hospitalization, diuretic treatment requirement, treatment with amiodarone, treatment with benzodiazepines and frailty; delirium persisted as an independent risk factor

Table 3.   In-hospital and 6-month geriatric evaluation.

	All patients (*n* = 527)	Delirium (*n* = 37)	No delirium (*n* = 490)	*P*-value
In-hospital geriatric evaluation				
Charlson (comorbidity)	2 (1–3)	3 (2–4)	2 (1–3)	0.01
Barthel (daily activities)	100 (85–100)	90 (58–100)	100 (90–100)	< 0.01
Lawton-Brody (instrumental)	6 (4–8)	4 (2–6)	6 (4–8)	< 0.01
Pfeifer (cognitive function)	1 (0–3)	4 (2–7)	1 (0–3)	< 0.01
MNA-FS (nutritional)	11 (10–13)	10 (9–11)	11 (10–13)	< 0.01
SPPB test (Frailty)	6 (2–9)	2 (1–5)	6 (3–9)	< 0.01
Frailty (FRAIL)				
No frailty (FRAIL = 0)	178 (34.2%)	8 (22.2%)	170 (35.1%)	
Pre-frailty (FRAIL 1–2)	202 (38.9%)	12 (33.3%)	190 (39.3%)	0.04
Frailty (FRAIL ≥ 3)	140 (26.9%)	16 (44.4%)	124 (25.6%)	
Frailty (SPPB < 10)	372 (81.8%)	28 (96.6%)	344 (80.8%)	0.03
6-month geriatric evaluation				
Barthel	95 (80–100)	90 (50–95)	95 (80–100)	< 0.01
Lawton-Brody	5 (3–7)	2.5 (0–4)	5 (3–7)	< 0.01
Pfeifer (cognitive function)	1 (0–3)	5 (2–9)	1 (0–2)	< 0.01

Data are presented as *n* (%) or median (interquartile range). MNA-FS: Mini Nutritional Assessment-Short Form; SPPB: short physical performance battery.
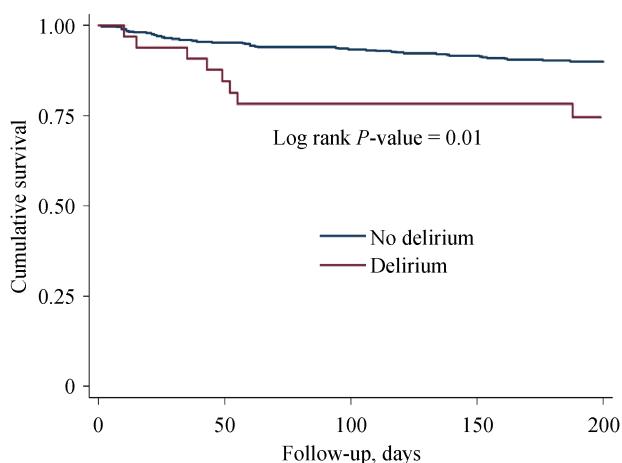

Figure 1.   Kaplan-Meier estimators of survival comparing patients who presented delirium or not. Kaplan-Meier survival curves of mortality data comparing those patients who developed delirium or not during the admission with a follow-up duration of 6 months (total *n* = 527), *P*-value is a log-rank test.

associated with 6-month mortality (HR = 1.47; 95% CI: 1.02–2.13, *P* = 0.04). Finally, a logistic regression analysis adjusted by the previously mentioned method showed that delirium was also independently associated with 6-month-bleeding events (OR = 2.87; 95% CI: 1.98–4.16, *P* < 0.01).

4   Discussion

4.1   Main findings

Our large multicenter prospective cohort provides reliable data about the frequency, clinical characteristics and prognostic implications of delirium in patients aged 80 or older admitted for NSTE-ACS. Our results show that up to 7% of octogenarians with NSTE-ACS develop delirium and that its appearance is a robust independent predictor of 6-month mortality. Additionally, delirium identified patients with higher risk of bleeding events and longer hospitalization.

Table 4.   In-hospital and 6-month outcome.

Univariate analysis	All patients (*n* = 527)	Delirium (*n* = 37)	No delirium (*n* = 490)	*P*-value
In-hospital mortality	12 (2.3%)	2 (5.4%)	10 (2.0%)	0.20
6-month mortality	62 (11.8%)	9 (24.3%)	53 (10.8%)	0.01
In-hospital bleeding	41 (7.8%)	8 (21.6%)	33 (6.7%)	< 0.01
6-month bleeding	56 (11.5%)	10 (32.3%)	46 (10.0%)	< 0.01
Length of stay, d	6 (4–10)	8.5 (5.5–14)	6 (4–10)	0.02
Cognitive decline[*]	122 (29.2%)	8 (36.4%)	114 (28.8%)	0.45
Functional decline[#]	148 (33.3%)	13 (48.2%)	135 (32.4%)	0.09

Data are presented as *n* (%) or median (interquartile range). [*]Gain of at least 1 point in the 6-month Pfeifer test; [#]Loss of at least 5 points in the 6-month Barthel score.

4.2   Delirium incidence

The incidence of delirium in hospitalized patients depends on the setting of the study population. The highest rates have been described in postoperative populations (46%),[25] and in intensive-care unit ventilated patients (82%).[7] More specifically, an incidence of 20% has been reported in patients admitted to cardiac intensive care units,[26,27] and 17% in elderly patients admitted due to acute cardiac conditions.[28] In our study, the lower observed rate could be explained by the fact that the majority of our patients were admitted to the regular ward and they were overall in better clinical condition. For example, only 25% presented heart failure. Moreover, our study is based in a very recent cohort and it could be influenced by the growing interest and interventions designed for the prevention of specific geriatric complications.[29]

4.3   Predisposing and precipitant factors for delirium

The appearance of delirium depends on the coexistence of several predisposing characteristics and the presence of distinct insults that play the role of precipitating factors.[30] We identified depression, dementia or institutionalization as baseline characteristics that may help to recognize those patients more prone to present delirium. In addition, the geriatric tests show that the comorbidity, frailty and the diminution of the functional or cognitive capacities are variables closely related to its appearance. All these findings are consistent with the previously published evidence,[31–34] and it could potentially be used to screen and identify those elderly patients admitted with NSTE-ACS, these patients need more a proactive implementation of preventive strategies for delirium. Regarding the latter, our study shows some potentially preventable precipitants, such as infections or the use of diuretics. For instance, early removal of urinary or venous catheters, and minimizing the duration of mechanical ventilation could be useful to prevent delirium.[30] Additionally, excessive depletion of these patients leading to uremia or dyselectrolytemia are known to be related with delirium, and it should be reconsidered daily.[9] Finally, non-pharmacological multicomponent approaches for prevention of delirium are effective strategies likely applicable to this specific population.[35,36]

4.4   Delirium and outcomes

Delirium has been related to higher mortality in different medical and surgical populations,[37,38] and it has also been evaluated in patients with acute cardiac conditions. Uthamalingam, *et al.*[39] observed that delirium was independently associated with higher in-hospital and 90-day mortality in patients admitted with acute heart failure in a single center retrospective cohort study. In accordance with the above, Noriega, *et al.*[28] found that delirium was associated with higher adjusted 12-month mortality in old patients admitted for acute cardiac conditions; however, only a third of them were admitted due to ACS and all patients were included in the cardiology department of a single university hospital. Finally, in critical cardiac care settings, Pauley, *et al.*[26] and Sato, *et al.*[27] reported that delirium was independently associated with in-hospital and 60-day mortality, respectively. To our knowledge, this is the first study addressing the short and long-term prognostic implications of delirium in elderly patients admitted for NSTE-ACS in a large multicenter and non-selected population. We found that delirium is a robust independent predictor of 6-month mortality and thus, this information could be useful for risk stratification in this growing and complex population. Moreover, delirium also seems to be associated with a higher risk of bleeding and longer hospitalization.

Validated risk scores are useful tools to predict outcomes in ACS,[10,11] and their use has been generalized in the last decade.[40] However, elderly NSTE-ACS patients have specific geriatric syndromes; such as frailty or delirium that may influence the prognosis,[41] and they are not considered in risk-stratification tools. In a recent cohort study in old patients admitted for ACS, frailty and comorbidity were identified as mortality predictors, and they were found to significantly reclassify risk beyond age.[42] Nonetheless, the specific impact of delirium was not studied and its potential predictive utility has not been tested. Based on our data, the appearance of delirium is related to a poorer prognosis and it should be useful when estimating the risk of death in these patients. Besides, since it is a potentially preventable and treatable cause, further research in this field would be of special interest.

Finally, our findings show a high proportion of patients presenting 6-month cognitive and functional decline, but it did not result to be significantly associated with delirium. Delirium has a transient nature,[13] and these patients have a correct recovery after the index hospitalization. Therefore, the cognitive or functional decline observed may be associated to other important factors, such as age or previous cognitive impairment.[43]

4.5   Study limitations

Our study has some limitations. This is a post-hoc analysis, and it could be influenced by the usual biases of these types of studies. Additionally, given the descriptive nature of the study, there might be residual confusion affecting the association between delirium and mortality despite the adjustment by the propensity score. Moreover, some signifi-

cant clinical variables as the presence of other geriatric syndromes, such as immobility or urinary incontinence, and data about the use of physical restraints or central vein or urinary catheters are lacking. Finally, delirium was not screened daily; thus, it possibly lead to underdetection of hypoactive delirium.

In conclusion, our study provides the first description regarding the unfavorable effect of delirium on the prognosis of elderly patients with NSTE-ACS. Our data, based on a broad and systematic geriatric assessment both on admission and 6 months after discharge, are of clinical interest and it may potentially pave the way to the addition of specific geriatric syndromes to currently existing risk scores in this population.

Acknowledgments

References

1   Rosengren A, Wallentin L, Simoons M, *et al.* Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. *Eur Heart J* 2006; 27: 789–795.

2   Alexander KP, Newby LK, Cannon CP, *et al.* Acute coronary care in the elderly, part I: non-ST-segment-elevation acute coronary syndromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation* 2007; 115: 2549–2569.

3   Dégano IR, Elosua R, Marrugat J. Epidemiology of acute coronary syndromes in Spain: estimation of the number of cases and trends from 2005 to 2049. *Rev Esp Cardiol (Engl Ed)* 2013; 66: 472–481.

4   Ekerstad N, Swahn E, Janzon M, *et al.* Frailty is independently associated with short-term outcomes for elderly patients with non-ST-segment elevation myocardial infarction. *Circulation* 2011; 124: 2397–2404.

5   Zaman MJ, Stirling S, Shepstone L, *et al.* The association between older age and receipt of care and outcomes in patients with acute coronary syndromes: a cohort study of the Myocardial Ischaemia National Audit Project (MINAP). *Eur Heart J* 2014; 35: 1551–1558.

6   Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet* 2014; 383: 911–922.

7   Ely EW, Shintani A, Truman B, *et al.* Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 2004; 29: 1753–1762.

8   Francis J, Kapoor WN. Prognosis after hospital discharge of older medical patients with delirium. *J Am Geriatr Soc* 1992; 40: 601–606.

9   Sanders RD, Pandharipande PP, Davidson AJ, *et al.* Anticipating and managing postoperative delirium and cognitive decline in adults. *BMJ* 2011; 343: d4331–d4331.

10 De Araújo Gonçalves P, Ferreira J, Aguiar C, *et al.* TIMI, PURSUIT, and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTE-ACS. *Eur Heart J* 2005; 26: 865–872.

11 Subherwal S, Bach RG, Chen AY, *et al.* Baseline risk of major bleeding in non-sT-segment- elevation myocardial infarction the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) bleeding score. *Circulation* 2009; 119: 1873–1882.

12 Alegre O, Ariza-Solé A, Vidán MT, *et al.* Impact of frailty and other geriatric syndromes on clinical management and outcomes in elderly patients with non–ST-segment elevation acute coronary syndromes: rationale and design of the LONGEVO-SCA Registry. *Clin Cardiol* 2016; 39: 373–377.

13 Inouye SK, van Dyck CH, Alessi CA, *et al.* Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990; 113: 941–948.

14 Rabe-Jabłońska J. A new draft of the mental disorders classification prepared by the American Psychiatric Association: diagnostic and statistical manual of mental disorders-IV, Options Book. *Psychiatr Pol* 1993; 27: 109–119.

15 Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. *Md State Med J* 1965; 14: 61–65.

16 Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; 9: 179–186.

17 Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *J Am Geriatr Soc* 1975; 23: 433–441.

18 Abellan van Kan G, Rolland Y, Bergman H, *et al.* The I.A.N.A Task Force on frailty assessment of older people in clinical practice. *J Nutr Health Aging* 2008; 12: 29–37.

19 Guralnik JM, Ferrucci L, Pieper CF, *et al.* Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* 2000; 55: M221–M231.

20 Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–383.

21 Rubenstein LZ, Harker JO, Salvà A, *et al.* Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci* 2001; 56: M366–M372.

22 Arnau A, Espaulella J, Serrarols M, *et al.* Risk factors for functional decline in a population aged 75 years and older without total dependence: a one-year follow-up. *Arch Geron-*

tol Geriatr 2016; 65: 239–247.

23 Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res* 2011; 46: 399–424.

24 Buuren S van, Groothuis-Oudshoorn K. Mice: multivariate imputation by chained equations in R. *J Stat Softw* 2011; 45: 1–67.

25 Saczynski JS, Marcantonio ER, Quach L, *et al*. Cognitive trajectories after postoperative delirium. *N Engl J Med* 2012; 367: 30–39.

26 Pauley E, Lishmanov A, Schumann S, *et al*. Delirium is a robust predictor of morbidity and mortality among critically ill patients treated in the cardiac intensive care unit. *Am Heart J* 2015; 170: 79–86.

27 Sato K, Kubota K, Oda H, *et al*. The impact of delirium on outcomes in acute, non-intubated cardiac patients. *Eur Hear J Acute Cardiovasc Care* 2017; 6: 553–559.

28 Noriega FJ, Vidan MT, Sánchez E, *et al*. Incidence and impact of delirium on clinical and functional outcomes in older patients hospitalized for acute cardiac diseases. *Am Heart J* 2015; 170: 938–944.

29 Buckinx F, Rolland Y, Reginster JY, *et al*. Burden of frailty in the elderly population: perspectives for a public health challenge. *Arch Public Health* 2015; 73: 19–19.

30 Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA* 1996; 275: 852–857.

31 Rudolph JL, Jones RN, Levkoff SE, *et al*. Derivation and validation of a preoperative prediction rule for delirium after cardiac surgery. *Circulation* 2009; 119: 229–236.

32 Kalisvaart KJ, Vreeswijk R, De Jonghe JF, *et al*. Risk factors and prediction of postoperative delirium in elderly hip-surgery patients: implementation and validation of a medical risk factor model. *J Am Geriatr Soc* 2006; 54: 817–822.

33 Inouye SK. Delirium in older persons. *N Engl J Med* 2006; 354: 1157–1165.

34 Marcantonio ER. Postoperative delirium a 76-year-old woman with delirium following surgery. *JAMA* 2012; 308: 73–81.

35 Inouye SK, Bogardus ST Jr, Charpentier PA, *et al*. A multicomponent intervention to prevent delirium in hospitalized older patients. *N Engl J Med* 1999; 340: 669–676.

36 Vidán MT, Sánchez E, Alonso M, *et al*. An intervention integrated into daily clinical practice reduces the incidence of delirium during hospitalization in elderly patients. *J Am Geriatr Soc* 2009; 57: 2029–2036.

37 Leslie DL, Zhang Y, Holford TR, *et al*. Premature death associated with delirium at 1-year follow-up. *Arch Intern Med* 2005; 165: 1657–1662.

38 Marcantonio ER, Flacker JM, Michaels M, *et al*. Delirium is independently associated with poor functional recovery after hip fracture. *J Am Geriatr Soc* 2000; 48: 618–624.

39 Uthamalingam S, Gurm GS, Daley M, *et al*. Usefulness of acute delirium as a predictor of adverse outcomes in patients >65 years of age with acute decompensated heart failure. *Am J Cardiol* 2011; 108: 402–408.

40 Roffi M, Patrono C, Collet JP, *et al*. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2016; 37: 267–315.

41 Sanchez E, Vidan MT, Serra JA, *et al*. Prevalence of geriatric syndromes and impact on clinical and functional outcomes in older patients with acute cardiac diseases. *Heart* 2011; 97: 1602–1606.

42 Sanchis J, Ruiz V, Bonanad C, *et al*. Prognostic value of geriatric conditions beyond age after acute coronary syndrome. *Mayo Clin Proc* 2017; 92: 934–939.

43 McCusker J, Kakuma R, Abrahamowicz M. Predictors of functional decline in hospitalized elderly patients: a systematic review. *J Gerontol A Biol Sci Med Sci* 2002; 57: M569–M577.