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Outcomes of early invasive treatment strategy in elderly patients with non-ST elevation acute coronary syndromes

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Background **As benefits of revascularization in non-ST elevation acute coronary syndromes (NSTEACSs) in the elderly are still unproven, we sought to assess the association between invasive or conservative management of NSTEACS and short-, mid- and long-term mortality or composite outcome of all-cause mortality and myocardial infarction in a cohort of consecutive elderly patients.**

Methods and Results **Consecutive NSTEACS patients older than 75 years discharged between 2006 and 2010 from a single intensive cardiac care unit, and managed with invasive or conservative strategy according to available guidelines were retrospectively surveyed. By multivariate regression and sensitivity analysis, crude and adjusted mortality and composite outcome were estimated at prespecified time points of short-term (in-hospital or 30 days mortality), mid-term (T1: 31 days to 6 months), and long-term (T2: 31 days to 12 months). A total of 453 patients (median age 80 years, 47% men) were evaluated; 301 (66.5%) underwent invasive treatment. Invasive was associated with significantly lower risk of short- [odds ratio (OR) 0.28, 95% confidence interval (CI) 0.12–0.67, $P = 0.004$], mid- (OR 0.33, 95% CI 0.16–0.67, $P = 0.003$) and long-term mortality (OR 0.34, 95% CI 0.20–0.58, $P < .0001$). Invasive strategy was also associated with nonsignificant lower short- (OR 0.55, 95% CI 0.28–1.07, $P = 0.077$), and highly significant lower mid- (OR 0.52, 95% CI 0.34–0.81, $P = 0.003$) and long-term adjusted cumulative composite outcome rate (OR 0.68, 95% CI 0.46–0.98, $P = 0.004$).**

Conclusion **In NSTEACS elderly patients, invasive strategy is independently associated with lower short-, mid- and long-term mortality and composite outcome.**

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Introduction

In recent years, the incidence of elderly patients admitted to intensive coronary care units (ICCUs) has globally increased because of the improved life expectancy and the decline in mortality. Acute coronary syndromes (ACS) are the leading cause of death in both men and women older than 65 years.[1–3] Elderly patients diagnosed with ACS represent a high-risk population and on this basis they should be treated more aggressively. However, elderly patients are often underrepresented in clinical trials and consistent evidence of the benefit of coronary revascularization in this class of age is not so conclusive.[4]

Large international registries indicated that many elderly patients with non-ST elevation acute coronary syndromes (NSTEACS) do not receive evidence-based therapies, even though myocardial revascularization, when performed, was associated with significant benefit in terms of mortality and morbidity.[5,6] Moreover, a multicentric randomized ad hoc designed trial showed that invasive strategy yields better survival free from a composite of all-cause mortality, nonfatal myocardial infarction (MI), disabling stroke and repeat hospitalizations, mainly driven by recurrent MI.[7,8] Conversely, a 10-year follow-up of real-world data of 2002–2004 years[9] points toward higher event rate and lower potential benefit from percutaneous revascularization in elderly as compared with young people. In addition a recent reanalysis of CRUSADE cohort indicates that even though older patients treated at academic hospitals are more likely to receive in-hospital revascularization than their counterparts admitted at nonacademic hospitals, they get only a modestly lower risk-adjusted 30-day and not improved risk-adjusted 1-year mortality.[10]

Our study aims to retrospectively assess the association between invasive or conservative management of NSTEACS and short-, mid- and long-term mortality or composite outcome of all-cause mortality and MI in a cohort of consecutive elderly patients.

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Methods

We conducted a retrospective analysis of a monocentric cohort of patients 75 years or older with NSTEACS admitted to our ICCU across years 2006–2010. Patients' data retrieved from clinical charts, and imaging storing systems, were analyzed by multivariate regression analysis.

All admitted patients hereby consented to retrospective anonymized participation into clinical surveys, as approved and validated by an ethics committee and complying to Helsinki declaration.

Study population

Consecutive patients aged at least 75 years at admission with a diagnosis of NSTEACS were selected. Chronic renal failure (clearance less than 30 ml/min), acute anemia (according to WHO definition), previous or current oncologic or cerebrovascular history were not considered exclusion criteria. Either type 1 or type 2 NSTEACS were included.

Treatment strategy

Invasive strategy was defined as angiography at the index admission, including emergency, urgent or delayed percutaneous coronary intervention (PCI) or surgery (coronary artery bypass graft surgery, CABG), according to coronary anatomy, physician and patient preference. Conservative treatment was defined as a medical only treatment during the index admission, with drug therapies recommended by current guidelines.[11] During the study enrolment period comprised between 2006 and 2010, considerable variations in ACS treatment protocols and pharmaceutics were not adopted, with consistent patterns of care across time, so that a uniform referral pattern to conservative or invasive strategy was adopted by the same physicians for all patients involved.

Outcome measures

Primary endpoint was defined as all-cause mortality at the prespecified time points. We considered as prespecified time points: short-term – the index admission (in-hospital or 30-day mortality); mid-term – T1 (T1), defined as the time between 31 days to 6 months; and long-term – T2 (T2), defined as the time between 31 days to 12 months. To avoid the impact of the events that occurred in the ACS acute phase, we excluded the first 30 days following the index event from the analysis of mid- and long-term outcome.

Major bleedings were defined as a drop in hemoglobin of at least 3 g/dl and/or need for transfusion.

Secondary endpoint was defined as the cumulative rate of the composite outcome of all-cause mortality and MI at short-term (30 days), mid-term (6 months) and long-term (12 months). The first occurring event was the censored event.

Statistics

Crude and adjusted mortality and cumulative composite outcome rates were calculated. Multivariate regression analysis was used to assess the effect of strategy on mortality and composite outcome, adjusting for factors (age, sex and comorbidities) that could affect study outcomes. Risk factors potentially associated with outcomes were chosen among the conditions identified in the literature and from clinical judgment. Among those factors, age and sex were considered *a priori* risk factors; the others were selected by a stepwise bootstrap procedure to assign an importance rank for predictors in regression. The variables introduced into the models were age, sex, admission creatinine clearance, ejection fraction (EF), hemoglobin and Killip classes, admission heart rate, blood pressure and cardiac arrest, ST deviation, peak troponin level, time from admission to PCI, albumin serum levels (albumin serum levels <3 g/dl were considered as a surrogate marker of frailty).

To estimate the odds ratios (ORs) of mortality and composite outcome at 30 days by strategy, a multivariate logistic regression was applied. Conversely, to evaluate mortality at T1 and T2 time intervals, and cumulative event rate of composite outcome at 6 and 12 months, Cox proportional hazard models were calculated by taking into account the amount of time for which an experimental unit contributed to the study, after verification of the proportionality assumption.

Effect modification by age classes, and specific conditions identified in the literature and from clinical judgment, was also tested, including categorization into spontaneous atherothrombotic or secondary to ischemic imbalance infarction as advised by current guidelines.[11]

A sensitivity analysis using genetic matching was performed to evaluate the robustness of our results: OR obtained from risk adjustment techniques were compared with those obtained after genetic matching. Genetic matching, a generalization of propensity score matching, is a method of multivariate matching, which uses a search algorithm to determine the weight of each covariate, improving balance among the individual covariates by searching over the space of distance metrics to find the best metric for optimizing covariate balance.

Sample size

Sample power of our study population was verified by comparing the patients treated with invasive ($n=301$) and conservative ($n=152$) strategies, whereas the ratio between the rates of the two groups was about 1–3 for the outcomes of mortality and 1–2 for the composite endpoints, using an alpha of 0.05. It resulted always higher than 95%, except for the composite outcome at short-term, where it was found to be 61%.

All statistical analyses were performed by using SAS Version 9.2 and R 2.15.1.

Table 1 Patients' clinical characteristics by adopted strategy

	Total $n=453$	Invasive strategy 301 (66.5)	Conservative strategy 152 (33.5)	*P*
Demographic characteristics				
Age tertile (*n*, %)				
74–79 years	204	164 (54.5)	40 (26.3)	<0.0001
80–84 years	150	100 (33.2)	50 (32.9)	
85+ years	99	37 (12.3)	62 (40.8)	
Men (*n*, %)	213	159 (52.8)	52 (34.2)	0.001
Body mass index kg/m^2 (mean ± SD)	453	26.7 ± 4.7	25.6 ± 5.1	0.028
Risk factors				
Smoking (*n*, %)	46	12 (7.9)	34 (11.3)	0.015
Dyslipidemia (*n*, %)	220	161 (53.5)	59 (38.8)	0.003
Hypertension (*n*, %)	414	276 (91.7)	138 (90.8)	0.749
Diabetes (*n*, %)	188	124 (41.2)	64 (42.1)	0.853
Biochemical risk profile				
CKMB I peak value ng/ml (mean ± SD)	453	33.0 ± 54.5	39.8 ± 82.1	0.353
Troponin I peak value ng/ml (mean ± SD)	453	15.3 ± 62.8	14.1 ± 35.9	0.782
Troponin I admission value ng/ml (mean ± SD)	453	3.5 ± 11.7	4.5 ± 13.4	0.424
NT-proBNP (mean ± SD)	453	6402 ± 9878	14524 ± 16409	<0.0001
Total cholesterol mg/dl (mean ± SD)	453	166 ± 43	163 ± 39	0.386
HDL cholesterol (mean ± SD)	453	43 ± 13	43 ± 13	0.999
Triglycerides (mean ± SD)	453	119 ± 53	125 ± 68	0.329
Admission glycemia mg/dl (mean ± SD)	453	139 ± 68	165 ± 85	0.001
Admission albumin mg/dl (mean ± SD)	453	3.4 ± 0.46	3.2 ± 0.56	0.002
Admission creatinine clearance classes				
>60 ml/min (*n*, %)	98	80 (26.6)	18 (11.8)	<0.0001
30–60 ml/min (*n*, %)	247	168 (55.8)	79 (52.0)	
<30 ml/min (*n*, %)	99	49 (16.3)	50 (32.9)	
Admission hemoglobin quartiles				
1 (5.7–11.1 g/dl) (n,%)	129	59 (19.6)	70 (46.1)	<0.0001
2 (11.2–12.45 g/dl) (*n*, %)	120	85 (28.2)	35 (23.0)	
3 (12.45–13.9) (*n*, %)	103	81 (26.9)	22 (14.5)	
4 (13.9–21) (*n*, %)	101	76 (25.3)	25 (16.5)	
Clinical risk profile				
Admission SBP mmHg (mean ± SD) (PAS)	453	145 ± 32	143 ± 31	0.518
Admission heart rate bpm (mean ± SD)	453	85 ± 24	92 ± 23	0.005
Aspirin prescription in the previous 7 days (*n*, %)		138 (45.8)	72 (47.4)	0.759
PCI in the previous 30 days (*n*, %)	4	2 (0.7)	2 (1.3)	0.484
CABG in the previous 30 days (*n*, %)	0	–	–	–
Admission GRACE risk score classes				
≤150 (*n*, %)	54	42 (14.0)	12 (7.9)	0.123
150–170 (*n*, %)	56	39 (13.0)	17 (11.2)	
≥170 (*n*, %)	343	220 (73.1)	123 (80.9)	
Killip class				
1 (*n*, %)	215	160 (53.2)	55 (36.2)	0.002
2 (*n*, %)	181	112 (37.2)	69 (45.4)	
3 (*n*, %)	56	29 (9.6)	27 (17.8)	
4 (*n*, %)	1	0	1 (0.7)	
Cardiac arrest at admission (*n*, %)	5	4 (1.3)	1 (0.7)	0.629
Max ST segment deviation	453	85 ± 24	92 ± 23	
Ejection fraction classes				0.406
>50% (*n*, %)	157	106 (35.2)	51 (33.6)	0.161
30–50% (*n*, %)	227	156 (51.8)	71 (46.7)	
<30% (*n*, %)	69	39 (13.0)	30 (19.7)	
Valvular heart disease[a] (≥moderate) (*n*, %)	240	149 (49.5)	91 (59.9)	0.037
Presentation symptoms				
Chest pain (*n*, %)	331	246 (81.7)	85 (55.9)	<0.0001
Dyspnea (*n*, %)	242	144 (47.8)	98 (64.5)	0.001
Syncope (*n*, %)	30	16 (5.3)	14 (9.2)	0.116

CABG, coronary artery bypass graft surgery; CKMB, creatine kinase myocardial band; HDL, high-density lipoprotein; NT-proBNP, NT-pro Brain Natriuretic Peptide; PCI, percutaneous coronary intervention.

Results

Baseline characteristics

A total of 453 white patients (median age: 80 years, 47% men) with NSTEACS were evaluated. Of these, 301 (66.5%) were treated with an invasive strategy, whereas in 152 (33.5%) a conservative strategy was adopted. In the invasive group, 178 (59.1%) patients underwent PCI and 14 (4.7%) patients were treated with CABG. The remaining 109 patients (36.2%) did not undergo revascularization because coronary lesions were considered nonsignificant ($n=51$, 46.8%) or not amenable by either percutaneous or surgical procedure ($n=50$, 45.9%). In eight patients (7.3%) periprocedural risk was judged excessive and unacceptable. Major bleeding and/or need for transfusions occurred in 29 of patients who underwent invasive strategy: 14 out of 178 (7.8%)

Table 2 Patients' outcome according to invasive or conservative strategy

	Invasive *n* (%) 301 (66.5)	Conservative *n* (%) 152 (33.6)	*P*
Study endpoint			
Mortality			
In-hospital	8 (2.7)	14 (9.2)	0.002
30-Day cumulative	11 (3.7)	21 (13.8)	<0.0001
T1 time point	17 (5.9)	23 (17.6)	<0.0001
T2 time point	29 (10.4)	36 (27.5)	<0.0001
12-Month cumulative	40 (13.3)	57 (37.5)	<0.0001
Cumulative composite outcome			
30-Day	25 (8.3)	24 (15.8)	0.016
6-Month	52 (17.3)	56 (36.8)	<0.0001
12-Month	74 (24.6)	64 (42.1)	<0.0001
AMI/ACS			
30-Day AMI/ACS	14 (4.7)	4 (2.6)	0.299
6-Month AMI/ACS	27 (9.0)	15 (9.9)	0.756
12-Month AMI/ACS	39 (13.0)	16 (10.5)	0.455
Adverse clinical events during hospitalization			
Cardiac arrhythmia	64 (21.3)	28 (18.5)	0.498
Major bleeding/transfusion	29 (9.6)	36 (23.7)	<0.0001
Sepsis/infections	20 (6.6)	30 (19.7)	<0.0001
AKI, whichever defined	11 (3.7)	12 (8.0)	0.050

AKI, acute kidney injury; AMI/ACS, acute myocardial infarction/acute coronary syndromes; T1, 31 days to 6 months; T2, 31 days to 12 months.

patients treated with PCI, 10 out of 14 patients (71.4%) in the CABG group and finally 4 out of 109 patients (3.6%) who had only coronary angiography.

Clinical and biochemical characteristics of invasive and conservative patients are reported in Table 1. Invasive patients were more commonly men and younger than conservative patients ($P = 0.001$ and $P < 0.0001$, respectively). Median time from admission to procedure was low, equal to 1 day (interquantile range 0–3 days), consistently with an early invasive strategy. Comorbidity profile was less severe in invasive patients than in conservative patients, as proved by the higher creatinine clearance and hemoglobin values (Table 1). Compared with conservative patients, invasive patients presented more often with classical ACS symptoms as chest pain (81.7 vs. 55.9%, $P < 0.001$), while they had dyspnea or other symptoms less frequently (47.8 vs. 64.5%, $P = 0.001$). Finally, invasive patients had lower Killip classes than conservative patients (class 1–2: 90.4 vs. 81.6%, class 3–4: 9.6 vs. 18.5%, $P = 0.002$, respectively) (Table 1).

Outcome

Mortality

A total of 40 (13.3%) invasive patients and 57 (37.5%) conservative patients died during 1-year follow-up ($P < 0.0001$). Mortality rates at the prespecified time points are reported in Table 2.

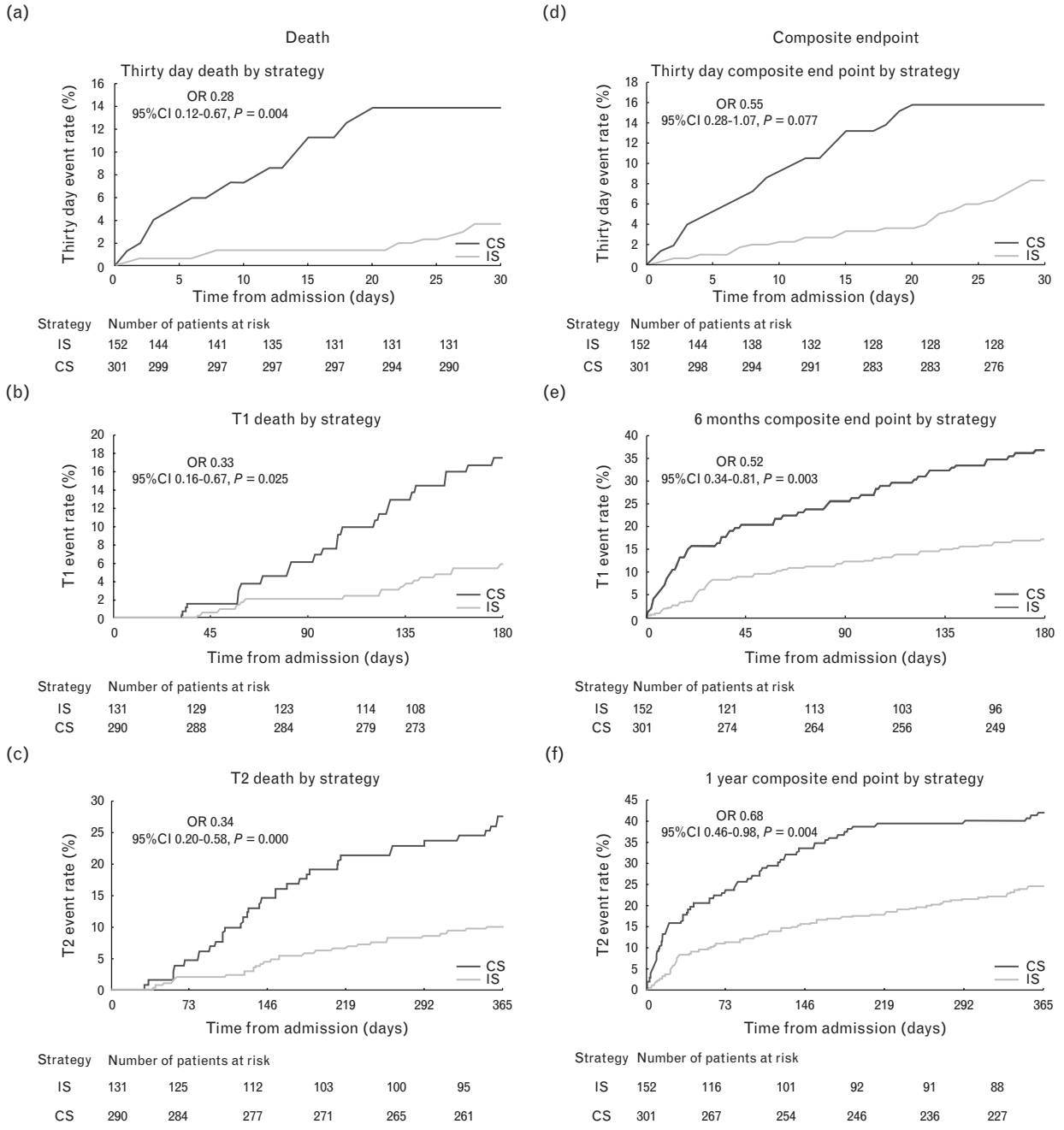
Crude and adjusted ORs to estimate the risk of mortality between strategies are reported in Table 3. Comparing adjusted short-term mortality in invasive to conservative group, a statistically significant reduction in 30-day mortality was observed in the invasive group [OR 0.28, 95% confidence interval (CI) 0.12–0.67, $P = 0.004$]. This reduction was confirmed throughout the mid- and long-term follow-up at T1 (OR 0.33, 95% CI 0.16–0.67, $P = 0.003$) and T2 periods (OR 0.34, 95% CI 0.20–0.58, $P < .0001$) (Fig. 1 A–C; Table 3). No interaction between the three defined age classes of young old, old,

Table 3 Death predictors at the prespecified time points by univariate and multivariate analysis

Mortality	OR univariate	95% CI	*P*	OR multivariate	95% CI	*P*
In-hospital						
Invasive strategy[a]	0.27	0.11–0.66	0.004	0.37	0.22–1.68	0.060
Admission creatinine clearance 30–60 ml/min	4.09	0.52–32.41	0.182	4.21	0.51–35.05	0.183
Admission creatinine clearance <30 ml/min[b]	10.90	1.37–86.87	0.024	7.75	0.87–68.62	0.066
Killip class 2[c]	4.13	1.12–15.25	0.033	3.26	0.86–12.32	0.082
Killip class 3[c]	13.25	3.46–50.79	0.000	8.40	2.03–34.80	0.003
30-Day						
Invasive strategy[a]	0.24	0.11–0.51	0.000	0.28	0.12–0.67	0.004
Ejection fraction 30–50%[d]	1.85	0.64–5.29	0.253	1.13	0.36–3.60	0.830
Ejection fraction ≤30%[d]	7.74	2.66–22.48	0.000	3.40	1.00–11.58	0.051
Admission Killip class 2[e]	2.92	1.10–7.76	0.032	1.90	0.66–5.45	0.233
Admission Killip class 3[e]	9.29	3.31–26.06	<.0001	4.64	1.45–14.88	0.010
T1 Time Point						
Invasive strategy[a]	0.31	0.17–0.58	0.000	0.33	0.16–0.67	0.003
Admission albumin level >3 g/dl	0.26	0.14–0.50	<.0001	0.37	0.19–0.73	0.004
Admission systolic blood pressure (mmHg)	0.99	0.98–1.00	0.016	0.99	0.97–1.00	0.011
Admission Killip class 2[c]	3.62	1.61–8.14	0.002	4.61	1.79–11.87	0.002
Admission Killip class 3[c]	6.17	2.44–15.64	0.000	10.05	3.36–30.08	<.0001
Admission cardiac arrest episode	4.87	0.67–35.49	0.118	11.14	1.29–96.51	0.029
T2 Time Point						
Invasive strategy[a]	0.33	0.20–0.53	<0.0001	0.34	0.20–0.58	<.0001
Admission albumin level > 3 g/dl	0.37	0.22–0.60	<0.0001	0.46	0.27–0.78	0.004
Admission systolic blood pressure (mmHg)	0.99	0.98–1.00	0.017	0.99	0.98–1.00	0.013
Diabetes	2.04	1.26–3.37	0.004	1.77	1.05–2.99	0.031
Admission Killip class 2[c]	2.29	1.30–4.00	0.004	2.11	1.15–3.85	0.002
Admission Killip class 3[c]	3.90	1.96–7.88	0.000	3.96	1.86–8.44	<0.0001

CI, confidence interval; OR, odds ratio. [a] Conservative strategy as ref. [b] >60 ml/min as ref. [c] Killip 1 as ref. [d] EF >50% as ref. [e] Killip 1 as ref.

Fig. 1



Time to all-cause mortality according to conservative or invasive strategy at 30 days (a), T1 (b) and T2 (c). Time to composite endpoint according to conservative or invasive at 30 days (d), 6 months (e) and 1 year (f).

and very old NSTEACS patients (75–79, 80–84, older than 85 years, Table 1) and the invasive strategy effect on mortality was found at any time. Advanced Killip class was the factor with the strongest effect on in-hospital (OR 8.40, 95% CI 2.03–34.80, $P = 0.003$) and 30-day mortality (OR 4.64, 95% CI 1.45–14.88, $P = 0.010$) and influenced significantly also the mid- (OR 10.05, 95% CI 3.36–30.08, $P < 0.0001$) and the long-term outcome (OR 3.96, 95% CI 1.86–8.44, $P < 0.0001$). Albumin values greater than 3 g/dl have been found protective in mid-term and long-term follow-up and were significantly associated with decreased T1 ($P = 0.004$) and T2 mortality ($P = 0.004$) (Table 3). Of interest, the benefits of an invasive strategy at 1 year were higher in patients with albumin levels of 3 g/dl or less, with interaction between albumin and invasive strategy effect on mortality showing

Table 4 Composite endpoint predictors at the prespecified time points by univariate and multivariate analysis

Cumulative composite endpoint	OR univariate	95% CI	*P*	OR multivariate	95% CI	*P*
30-Day						
Invasive strategy[a]	0.48	0.27–0.88	0.017	0.55	0.28–1.07	0.077
Ejection fraction 30–50%[b]	2.04	0.92–4.49	0.078	1.96	0.87–4.41	0.102
Ejection fraction ≤30%[b]	4.57	1.89–11.05	0.001	3.91	1.56–9.80	0.004
6-Month						
Invasive strategy[a]	0.41	0.28–0.60	<0.0001	0.52	0.34–0.81	0.003
Admission albumin level >3 g/dl	0.55	0.37–0.82	0.004	0.57	0.38–0.87	0.010
Diabetes	1.93	1.32–2.82	0.001	1.74	1.16–2.63	0.008
Admission Killip class 3[c]	4.21	2.48–7.15	<0.0001	3.36	1.89–5.90	<0.0001
Admission Killip class 4[c]	24.14	3.22–180.76	0.002	17.05	2.12–137.14	0.008
12-Month						
Invasive strategy[a]	0.47	0.36–0.69	<0.0001	0.68	0.46–0.98	0.004
Admission systolic blood pressure (mmHg)	0.99	0.99–1.00	0.018	0.99	0.99–1.00	0.031
Diabetes	1.77	1.27–2.48	0.001	1.60	1.12–2.28	0.010
Admission creatinine clearance 30–60 ml/min[d]	1.72	1.01–2.93	0.045	1.49	0.86–2.58	0.152
Admission creatinine clearance <30 ml/min[d]	3.41	1.96–5.94	<.0001	2.09	1.14–3.82	0.017
Admission Killip class 3[e]	3.30	2.06–5.28	<.0001	2.73	1.65–4.52	<0.0001

CI, confidence interval; OR, odds ratio. [a] Conservative strategy as ref. [b] EF >50% as ref. [c] Killip 1 as ref. [d] >60 ml/min as ref. [e] Killip 1 as ref.

a reinforcement of invasive strategy benefit with albumin levels lower than 3 g/dl (*P* for interaction 0.037).

Composite outcome

The composite outcome of all-cause mortality and MI occurred in 74 (24.6%) invasive patients and in 64 (42.1%) conservative patients during 1-year follow-up ($P < 0.0001$). At 30 days, 6 and 12 months, MIs rates did not differ significantly between the two adopted strategies. Cumulative composite outcome rates at the prespecified time points are reported in Table 2.

Crude and adjusted association between strategy and cumulative composite outcome rate are reported in Table 4. No significant association between strategy and 30-day composite outcome was found. However, invasive patients had lower composite outcome rate at 6 (OR 0.52, 95% CI 0.34–0.81, $P = 0.003$) and 12 months (OR 0.68, 95% CI 0.46–0.98, $P = 0.004$) (Fig. 1 E–F and Table 4). No interaction between the three defined age classes of young old, old and very old NSTEACS patients and invasive strategy effect on composite outcome was found at any time.

Ejection fraction less than 30%, Killip class, diabetes and advanced kidney disease (creatinine clearance <30 ml/min) were all associated with higher composite outcome rates with statistical significance varying according to follow-up duration (Table 4). Albumin values greater than 3 g/dl were associated with significantly lower composite outcome ($P = 0.010$) at 6 months (Table 4). A nonsignificant interaction ($P = 0.075$) was found between albumin and effect of invasive strategy, with early revascularization achieving the most significant reduction of composite outcome at 1 year in patients with albumin 3 g/dl or less. Similar results were found using genetic matching approach. No interaction between strategy and age or the specific conditions considered was found.

Discussion

The present large monocentric study of a consecutive academic cohort of elderly patients with NSTEACS indicates that an invasive strategy provides a consistent reduction in all-cause mortality and composite outcome (all-cause mortality and MI) at the different prespecified time points. Multivariate and propensity score analyses show that in the elderly cohort, an invasive strategy is associated with a three-fold decrease in all-cause mortality, and a two-fold lower rate of composite outcome at short-, mid- or long-term follow-up. In addition, advanced Killip class and a left ventricular ejection fraction lower than 30% resulted as the main predictors of short-term outcome.

Our study is representative of the high-risk elderly patients admitted with diagnosis of NSTEACS in a contemporary ICCU. About 70% of our patients were characterized by a GRACE risk score higher than 170, approximately 15% presenting with advanced Killip class and more than 60% with a left ventricular EF lower than 50%. Two-thirds of the overall patients were managed invasively. In European and US registries, the reported proportion of elderly patients assigned to an invasive strategy is slightly lower and declines from 50 to 33% in patients aged beyond 70 and 80 years, respectively.[12–15]

Data from the present study indicate that the invasively managed patients were characterized by lower age, a typical clinical presentation, a less severe clinical profile, with lower prevalence of advanced Killip class, and higher hemoglobin and creatinine clearance values, as compared with conservative. Nonetheless, despite these differences, the statistical post-hoc adjustment method adopted in our study allowed the balancing of baseline characteristics between the invasive and conservative groups by matching each invasive patient to a conservative one who has the nearest conditional probability of receiving the same treatment, given his/her measured baseline characteristics.

Treatment strategy and outcome

Our results show a lower invasive-related mortality and composite outcome risk at either short-, mid- and long-term follow-up, with a sizeable reduction in both endpoints by about two- or three-fold. The mortality benefit of an aggressive strategy has been previously demonstrated in non-ad-hoc designed randomized trials and in large registries, in particular in high-risk elderly patients with ACSs.[12–22] However, a recent trial, enrolling elderly high-risk NSTEACS patients treated invasively from January 2008 to May 2010, did not face a reduced mortality, but experienced significantly better survival free from the composite of all-cause mortality, nonfatal MI, disabling stroke and repeat hospitalization for cardiovascular causes or bleeding.[8]

In our study, the benefit of an early invasive strategy persists across all age groups, including the old (older than 75 years) and very old (85 years or older), in agreement with the Myocardial Ischemia National Audit Project (MINAP) registry data.[23] In addition, the troponin positivity status at admission did not affect the mortality benefit of the invasive strategy contrary to what observed by Savonitto *et al.*[7]

Other predictors of outcome

Hemodynamic conditions such as a presentation with advanced Killip classes and severely impaired left ventricular EF were the main predictors of the in-hospital phase and short-term outcome. These data appear consistent with those previously published, and individuate hemodynamic instability, as the most relevant predictor of outcome in the elderly patients with NSTEACS during the acute phase of illness.[24,25]

Moreover, normal serum albumin had a protective effect in the mid- and long-term with regard to both mortality and composite outcome. Albumin is considered as a surrogate marker of frailty.[26] Interestingly, no interaction was found between serum albumin levels and the choice of the treatment strategy and the long-term benefit of invasive management appeared strengthened in patients with low levels of albumin. These data may suggest that frailty should not represent a reason for not referring elderly to invasive treatment. However, the management decision for elderly patients with NSTEACS is actually complex and it should be 'patient centered', as reported in recent guidelines, considering patient preferences, goal, comorbidities, functional and cognitive status and life expectancy.[27]

Limitations

The present data represent a real-world monocentric registry of elderly NSTEACS treatment at an academic hospital. Individual decisions on patient management such as reasons for not offering an early invasive treatment were not recorded. Hence the issue of residual selection bias leading to confounding cannot be fully excluded despite propensity adjustment and homogeneity of hospital treatment protocols and staffing organization across the years of enrollment. Nevertheless the sample size is adequate to show difference in outcome between the two adopted strategies, and reported data are consistent with that coming from other published studies, both observational[20] and randomized.[21] Finally, a prospective evaluation of frailty assessment with measurements of daily living activities was not collected and computed.

Conclusion

An invasive revascularization strategy offered to elderly patients with NSTEACS was associated with about three-fold improved mortality and composite outcome at either short-, mid- or long-term, in both frail and nonfrail patients. An advanced Killip class and hemodynamic status appear to be the major determinants of outcome during in-hospital phase of NSTEACS. Elderly patients with NSTEACS exhibit a high ischemic risk profile and should be more often offered evidence-based medical therapies and early revascularization.

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