

Elderly Patients with Non-ST-Elevation Acute Coronary Syndrome: A Proposal to Adapt Decision Making

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Abstract

The guidelines recommend invasive treatment (coronary angiography) in elderly patients with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) with a moderate and high risk of re-infarction or death. The invasive approach has been found to be more effective in older and higher risk patients. The aim of this study was twofold: first, to determine whether the recommendations of current guidelines are followed for elderly patients with NSTEMI-ACS in our hospital; and second, to reach agreement among professionals responsible for the care of these patients (cardiologists, geriatricians, internists, specialists in emergency and critical care) on criteria that could enable the correct identification of the limitations of invasive management.

Consistent with other studies and records in Spain and in neighbouring countries we found a tendency to deprive many patients of invasive treatment due solely to their age, with no underlying functional or cognitive factors or associated disorders that warranted it; hence the importance of developing multidisciplinary consensus criteria for the adequacy of invasive treatment in elderly patients with NSTEMI-ACS. The consensus criteria expressed in this manuscript could significantly aid decision-making in these patients and serve as a communication tool between the different specialists involved in their care. The usefulness of these criteria should be tested in future studies to assess whether their application helps to reduce the variability in clinical practice and improve clinical outcomes in the elderly population, especially in very elderly individuals.

Keywords: AIMCO criteria; Invasive treatment; Acute coronary syndrome; Elderly

Introduction

The therapeutic approach to patients with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) depends on the level of risk of reinfarction or death. In low-risk individuals guidelines recommend conservative treatment, while for medium- and high-risk individuals invasive treatment (coronary angiography) is indicated [1,2]. NSTEMI-ACS is highly prevalent in the elderly [3,4]. Advanced age is a poor prognostic factor and is associated with an increased risk of death or reinfarction [1,2,5]. The scores recommended by the American (TIMI score) [1] and European guidelines (GRACE risk score) [2] consider age to be a key factor, along with the elevation of cardiac enzymes and ST elevation, for quantifying risk. Randomized trials [6-8] and a meta-analysis [9] have found strong evidence that invasive treatment is more beneficial in elderly patients with NSTEMI-ACS than younger subjects. Bach et al. [6] analysed the results of the TACTICS TIMI 18 trial by age group, concluding that the number needed to treat (NNT) to avoid one case of death or reinfarction was 250 for patients under 65 years and 9 for patients aged ≥ 75 years. A meta-analysis [9] that examined the results of the clinical trials FRISC II [7], STROKE [10] and RITA-3 [11] agrees that the greatest benefit for invasive treatment is in elderly patients; the most recent meta-analysis of Angeli et al. [12] that analyses the results of nine trials, reaches the same conclusion. However, the profile of patients who are included in clinical trials differs greatly from that of patients seen in daily clinical practice, especially in relation to elderly patients, who are often excluded from trials, particularly if they have significant comorbidity [5].

Observational studies involving patients with acute coronary syndrome without exclusions based on age or comorbidity can be a guide to therapeutic results in the real world. Several prospective [13-16] and retrospective studies [17,18] confirm that the benefits of

early invasive treatment in NSTEMI-ACS patients are greater as patient age increases, even considering the increased risk of bleeding in the elderly. Despite this evidence, several studies [14,15,19] have warned of the existence of a great variability in the treatment of NSTEMI-ACS in the elderly and the tendency to underuse invasive therapies in this population. When indicating invasive treatment in older patients with NSTEMI-ACS, guidelines recommend assessment of factors such as the risk of bleeding, life expectancy, comorbidity, quality of life and the patient's wishes [1,2]. This suggests the need for easily applied criteria to collect relevant factors to be considered in the elderly patient (functional capacity, cognitive function, comorbidity) that are not included in current risk scores and that may influence decision-making in clinical practice.

The aims of this study were: 1) to determine whether the recommendations of current guidelines are followed for elderly patients with NSTEMI-ACS in our hospital and analyse which factors in our setting are associated with not performing invasive therapies in elderly patients with NSTEMI-ACS, and 2) to propose criteria for adequacy of invasive procedures in elderly patients with NSTEMI-ACS.

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Received June 09, 2015; Accepted July 15, 2015; Published July 18, 2015

Citation: Alvarez-Fernandez B, Bernal-Lopez MR, Cabeo Inmaculada R, Martin Manuel DM, Carrillo Cristobal U, et al. (2015) Elderly Patients with Non-ST-Elevation Acute Coronary Syndrome: A Proposal to Adapt Decision Making. J Gerontol Geriatr Res 4: 227. doi:10.4172/2167-7182.1000227

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Material and Methods

Respect the first aim of this study, to determine whether the recommendations of current guidelines are followed for elderly patients with NSTEMI-ACS in our hospital and analyse which factors in our setting are associated with not performing invasive therapies in elderly patients with NSTEMI-ACS, we undertook a prospective observational study to define the variables currently associated in our setting with not performing invasive procedures. All patients aged over 65 years with NSTEMI-ACS admitted to the Regional Hospital of Malaga were included in this study and followed for 3 months (March-May 2013). Data were recorded on demographic variables (age, gender, type of residence and degree of family support), Barthel scale, vascular risk factors (diabetes, hypertension, smoking, dyslipidemia), previous diseases, previous treatment, Charlson index, GRACE score, ECG on admission, symptoms on admission, blood work on admission (blood count, renal profile, CPK-MB and troponin I on admission and peak), treatment during hospitalization, length of stay and complications during admission (bleeding, infection, and death).

Respect the second aim, to propose criteria for adequacy of invasive procedures in elderly patients with NSTEMI-ACS, we designed a qualitative study. A multidisciplinary committee (MC) was formed, composed of five experts (cardiologist, geriatrician, intensivist, internist and emergency physician), who defined and weighted the factors that can lead to improper use of invasive procedures in elderly patients with NSTEMI-ACS due to the high risk of bleeding, the presence of geriatric syndromes and/or significant comorbidities that limit life expectancy and/or quality of life. These factors were discussed in joint sessions and separately in the three clinical departments involved (Cardiology, Internal Medicine, Critical Care and Emergency), modifying them as a result of the arguments presented in these sessions. Subsequently, the agreed criteria were then sent in a personal letter to each member of the departments involved so that they could examine the criteria in detail and make any pertinent observations. The MC then reviewed the comments submitted by the various professionals and made any modifications considered appropriate. Finally, the MC reassessed the AIMCO criteria based on the results of the observational study presented here.

We continue work in this theme and the results of the next phase where AIMCO criteria will be applied prospectively will be discussed later in the time. A pre-post analysis in these patients to analyze the following variables before and after implementation of the AIMCO criteria: a) rate of invasive procedures, b) rate of invasive procedures despite having AIMCO criteria excluding such treatment, c) rate of patients in whom invasive treatment was not performed despite not having AIMCO exclusion criteria, d) rate of in-hospital bleeding complications (major and minor), f) rate of mortality and/or reinfarction at 3 months.

Statistical Analysis: The quantitative variables were expressed as the mean and standard deviation (SD) and the qualitative variables as percentages. The one-way analysis of variance (ANOVA) test was used to compare quantitative variables, and the Chi-square test and Mantel-Haenszel test were used for qualitative variables. In order to determine the factors independently associated with the performance of invasive procedures, stepwise multivariate logistic regression techniques were applied, using invasive procedure as the dependent variable, controlling for the confounding effect of other variables. The analyses were performed with Sigma Plot software (SPSS Science; Chicago, IL, USA) version 17.0.

Results

The study included 125 patients. Table 1 shows their baseline characteristics with respect to invasive treatment. In the univariate analysis, the variables associated with conservative management were: over 75 years of age, female gender, smoking, previous diuretic pretreatment, heart failure, Killip class >1, previous cognitive deterioration, hemiplegia, T wave inversion, systolic blood pressure <100 mmHg on admission, glucose >150 mg/dL, Barthel index <55 and a Charlson score >3. The AIMCO exclusion criteria were also associated with conservative therapy. Patients undergoing conservative treatment experienced higher hospital mortality than those undergoing invasive treatment (9.09% vs. 1.42%, p=0.04), with no significant differences in bleeding, infection or delirium (Table 1).

	Invasive Treatment		p
	No (n=55)	Yes (n=70)	
Age >75 years	31 (56,3)	18 (25,7)	<0.001
Age (mean)	78,4 ± 7,8	72,4 ± 5,3	<0.001
Sex			
Female (%)	30 (54,5)	22 (31,4)	<0.01
Male (%)	25 (45,5)	48 (68,6)	<0.01
Diagnostic			
Diabetes Mellitus (%)	29/55 (52,7)	33/70 (47,1)	NS
Hypertension (%)	48/55 (87,2)	59/70 (84,2)	NS
Smoker (%)	4/55 (7,2)	14/70 (20)	0.04
Dyslipidemia	33/55 (60)	43/70 (61,4)	NS
Previous treatment			
Antihypertensive	46/55 (83,6)	57/70 (81,4)	NS
Lipid Lowering	31/55 (56,3)	46/70 (65,7)	NS
Oral Antidiabetic	20/55 (36,3)	21/70 (30)	NS
Insulin	13/55 (23,6)	15/70 (21,4)	NS
Antiaggregant	40/55 (72,7)	45/70 (64,2)	NS
Anticoagulant	12/55 (21,8)	9/70 (12,8)	NS
Diuretic	37/55 (67,2)	24/70 (34,2)	<0.001
Previous pathology			
AMI	32/55 (58,1)	30/70 (42,8)	NS
HF	24/55 (43,6)	7/70 (10)	<0.001
Peripheral vascular disease	13/55 (23,6)	15/70 (21,4)	NS
Cerebral vascular disease	12/55 (21,8)	7/70 (10)	NS
Prior cognitive impairment	7/55 (12,7)	1/70 (1,4)	0.01
Dementia	3/55 (5,4)	1/70 (1,4)	NS
COPD	18/55 (32,7)	22/70 (31,4)	NS
Hemiplejia	7/55 (12,7)	2/70 (2,8)	0.03
Kidney failure	16/55 (29)	13/70 (18,5)	NS
Non-metastatic solid tumors	7/55 (12,7)	13/77 (18,5)	NS
Liver disease	0/55 (0)	2/70 (2,8)	NS
Severe bleeding in previous 3 months	2/55 (3,6)	1/70 (1,42)	NS
Electrocardiogram			
Sinus rhythm (%)	39/55 (70,9)	56/70 (80)	NS
Atrial fibriloflutter	15/55 (27,2)	12/70 (17,1)	NS
Tachycardia sinoventricular	0/55 (0)	2/70 (2,8)	NS
Left Ventricular Hypertrophy	2/55 (3,6)	2/70 (2,8)	NS
Lock Left Branch	11/55 (20)	6/70 (8,5)	NS
Lock Right Branch	8/55 (14,5)	12/70 (17,1)	NS
Hemiblock Left Atrium	5/55 (9,09)	10/70 (14,2)	NS
Atrioventricular block	7/55 (12,7)	3/70 (4,2)	NS

ST elevation	5/55 (9,09)	6/70 (8,5)	NS
ST fall	15/55 (27,2)	20/70 (28,5)	NS
Reversal of T	5/55 (9,09)	23/70 (32,8)	0.001
Symptom on admission			
Chest pain	43/55 (78,1)	63/70 (90)	NS
Dyspnea	22/55 (40)	27/70 (38,5)	NS
SBP <100	5/55 (9,09)	1/70 (1,4)	0.05
Laboratory			
Hemoglobin (mean)	12,4 ± 1,75	13,1 ± 2,18	0.05
Hemoglobin < 11	12/55 (21,8)	11/70 (15,7)	NS
Hematocrit (mean)	37,3 ± 5,02	42,2 ± 12,8	0.01
Hematocrit<40%	34/55 (61)	32/70 (45,7)	NS
Severe thrombocytopenia	1/55 (1,8)	1/70 (1,42)	NS
Glycemia (mean)	177,4 ± 70,3	142 ± 58,5	0.003
Glycemia <150 mg/dl	20/55 (36,3)	46/70 (65,7)	0.001
Creatinine (mean)	1,32 ± 0,49	3,1 ± 14,13	NS
MDRD <30 ml/min initial	9/55 (16,3)	6/70 (8,5)	NS
Sodium (mean)	139,15 ± 3,8	140,29 ± 2,6	NS
Glomerular flow (mean)	62,6 ± 76,23	65,5 ± 28,7	NS
Troponin initial	0,84 ± 2,26	1,28 ± 4,2	NS
Troponin peak	4,86 ± 11,96	4,94 ± 14,06	NS
CPK MB initial	7,38 ± 22,5	6,5 ± 20	NS
CPK MB peak	20,11 ± 56,34	30,38 ± 101,02	NS
COMPLICATIONS	17/55 (30,9)	19/70 (27,1)	NS
Bleeding	1/55 (1,8)	2/70 (2,8)	NS
Infection	10/55 (18,1)	5/70 (7,1)	NS
Delirium	2/55 (3,6)	5/70 (7,1)	NS
Exitus	5/55 (9,09)	1/70 (1,42)	0.04
Scores			
Exclusionary AIMCO	21/55 (38,1)	10/70 (14,2)	0.002
BARTHEL <55	11/55 (20)	3/70 (4,2)	0.005
Killip >1	24/55 (43,6)	16/70 (22,8)	0.01
Charlson >3	47/55 (85,4)	43/70 (61,4)	0.003
GRACE >140	33/55 (60)	36/70 (51,4)	NS

Table 1: Baseline characteristics of study population. SBP: Systolic Blood Pressure; COPD: Chronic Obstructive Pulmonary Disease eGF: estimated Glomerular Filtration rate (MDRD formula); AMI: acute Myocardial Infarction; HF: Heart Failure.

	CI 95%	P
Age >75 years	0.309 (0.127-0.754)	0.010
SBP <100 mmHg	0.086 (0.008-0.928)	0.043
Prior HF	0.194 (0.069-0.547)	0.002
Glycemia, initial >150 mg/dl	0.299 (0.123-0.728)	0.008
T-wave inversion	4.996 (1.443-17.305)	0.011

Table 2: Factors associated with invasive treatment. Multivariate analysis. SBP: Systolic Blood Pressure at admission; HF: Heart Failure.

After performing a multivariate logistic regression analysis, the variables that maintained their association with conservative treatment were: over 75 years of age, previous heart failure, systolic blood pressure on admission <100 mmHg and glucose >150 mg/dL. On the other hand, T wave inversion was associated with the performance of invasive treatment (Table 2). Regarding the consensus methodology used for the elaboration of the AIMCO criteria, 54 professionals attended clinical sessions conducted in the three departments involved (Critical Care and Emergency, Internal Medicine and Cardiology) and a subsequent joint meeting. A total of 105 letters were sent to the various participating department professionals, obtaining a response rate of 33.3%. During the sessions, observations emerged which led to the inclusion of the corresponding item as "serious systemic disease

(oncologic disease with no prospect of cure, advanced amyotrophic lateral sclerosis or other diseases with expected survival <1 year)". On the inclusion of prior heart failure in the item "prior organ failure", the majority opinion was to include only previous severe heart failure (although as a separate item), described as the presence of symptoms with significant functional impairment despite optimal treatment. The decision was made to exclude moderate heart failure because these cases could benefit from invasive treatment if the heart failure is due to underlying coronary heart disease.

Additionally, most of the participants were requested to specify the criteria to determine whether organ failure was moderate or severe and to clarify whether organ failure remained a single score or a summation if there was failure of more than one organ in the same patient. Concerning the formula used to estimate renal function, most were inclined to use the MDRD formula since it correlates better than the Cockcroft-Gault GFR for glomerular filtrate values under 60 mL/min/1.73 m² [20]. In addition, the MDRD formula does not require knowledge of the weight or height of the patient, which is an important advantage for its application in the emergency area.

Interventional cardiologists involved in the consensus argued the weighting of severe thrombocytopenia and other coagulation disorders in matching older patients for an invasive treatment. Some felt that these items were perhaps overstated, since although they may be a contraindication to stenting or surgery, knowing the anatomy by coronary angiography allows, in some cases, performance of a simple angioplasty to improve the prospects and quality of life of the patient. As a result of this discussion the weight of this item was reduced from 2 points to 1.

Discussion

Our data, in line with other studies in Spain [19] and neighbouring countries [14,15] show a tendency to perform invasive treatment of NSTEMI-ACS in patients with a lower risk and a younger age, which runs counter to the recommendations of various guidelines and the evidence available. Furthermore, there is a tendency to deprive many patients of invasive treatment solely because of their age without any associated functional or cognitive disorders to warrant this [4,21,22]. This underutilization of invasive therapy in elderly patients with NSTEMI-ACS may be because physicians consider the risk-benefit ratio of invasive procedures to be high, either because the complication rate is overestimated or because the risk of death or reinfarction in older patients is underestimated. In this regard, it is important to note that although the risk of serious complications is higher in older patients than in younger patients, comparisons must not be made between elderly versus younger patients, but between groups of the same age [23].

In the Canadian ACS Registry II, the underestimation of risk was the first reason given by treating physicians to justify the frequent exclusion of invasive treatment in patients over 75 years with NSTEMI-ACS; however, these patients had a mean GRACE score of 148, which is considered high risk [22]. Another reason contributing to exclusion may be patient refusal and/or delegation of patient decision making [24]. In many cases the information given to such fragile and vulnerable patients is not provided at the right time or in the correct form [25], which often results in the patient refusing to participate in decision-making or prevents treatment without proper information. An effective partner in some cases could be the care manager who knows the patient and can make himself take an active part in decision-making [26]. Finally, there probably exists a considerable number of patients who, due to their functional, cognitive, and comorbid conditions, would

not benefit from invasive treatment. A study conducted prospectively in patients older than 70 years who entered consecutively found that, according to the opinion of the doctors responsible, 13% had a serious disorder that contraindicated invasive treatment [24].

Decision-making in older patients is a complex process that should be based on a comprehensive assessment of the patient as a tool to weigh the risks and benefits of treatment [1,2]. Specific risk scores do not include elements that are essential for the assessment of elderly patients with heart disease. In many cases comorbidity, functional capacity and cognitive status are more determinant of patient survival and quality of life, both present and future, than the actual process to be treated. All this, together with the patient's wishes, should form the framework supporting the complex development of therapeutic decisions [27]. Therefore, in our hospital we consider it appropriate to agree on criteria for the inadequacy of invasive treatment in elderly patients with NSTEMI-ACS and a moderate or high risk of reinfarction and/or mortality. These criteria are intended to be a user-friendly application that will help reduce the variability in clinical practice of the different medical specialists who treat elderly patients with NSTEMI-ACS, as well as facilitate clinical judgment based on reasonable criteria to assess whether carrying out invasive treatment is not in fact indicated to improve the current or future prospects of the patient in terms of survival and/or quality of life. This is not a score of risk to determine the risk of an invasive treatment [28-30], only a consensus regarding in which cases it is justified not to perform invasive treatment in elderly patients with NSTEMI-ACS despite such treatment being indicated. To develop this consensus criteria, we followed qualitative methodology (surveys, clinical sessions) using a multidisciplinary approach involving emergency physicians, intensivists, cardiologists, internists and geriatricians. The results are discussed in the previous section and

Annex 1: The AIMCO criteria represent the first proposal to adapt indications for invasive treatment in elderly patients with NSTEMI-ACS. With these consensus criteria we sought specificity over sensitivity, i.e., we considered it more important that the excluded patients had inadequacy criteria than that some patients without exclusion criteria were subsequently excluded because technical or anatomical features or clinical events ruled out the invasive procedure.

Well, with respect to the first aim of our study, the results show, as we suspected, that you opt for invasive treatment in patients younger and lower risk, data consistent with other records of our country and international, and something that it goes against the recommendations of current guidelines. The second aim is, indeed, the relevant objective of the study because the first aim is little new in their results and unremarkable due the number of patients included. The relevance of this second aim is to novelty (we could not find such criteria in the literature) about that different professionals responsible for the care of these patients agree a criteria that guide to decide the non-adequacy of an invasive treatment in patients with NSTEMI-ACS of moderate and high risk although it is the treatment indicated by the guidelines. We are confident that the application of the AIMCO criteria will help contemplate elements that are frequently absent from the medical records of patients with ACS, such as previous functional and cognitive status [31], and will serve as a new communication tool between the different specialists involved in the care of these patients and be an important feature in complex decision-making in the elderly. The usefulness of these criteria should be tested in future studies (Phase 2) to evaluate whether their application helps to reduce variability in clinical practice and to improve clinical outcomes in the elderly population, especially in very elderly individuals (over 75 years old).

Competing Interests

The authors declare that they have no competing interests.

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