

World Journal of *Cardiology*

World J Cardiol 2020 November 26; 12(11): 513-598



ORIGINAL ARTICLE

Retrospective Study

- 513 Effectiveness and safety of antithrombotic strategies in elderly patients with acute myocardial infarction
Rondano E, Bertolazzi M, Galluzzo A, Maltese L, Caccianotti P, Macchiò S, Mazza S, Di Ruocco MV, Favretto S, Occhetta E, Rametta F

Clinical Trials Study

- 526 Endothelial progenitor cells mobilization after maximal exercise according to heart failure severity
Kourek C, Karatzanos E, Psarra K, Georgiopoulos G, Delis D, Linardatou V, Gavrielatos G, Papadopoulos C, Nanas S, Dimopoulos S

SYSTEMATIC REVIEWS

- 540 Rapid right ventricular pacing for balloon valvuloplasty in congenital aortic stenosis: A systematic review
Mylonas KS, Ziogas IA, Mylona CS, Avgerinos DV, Bakoyiannis C, Mitropoulos F, Tzifa A

META-ANALYSIS

- 550 Effects of left ventricular assist device on pulmonary functions and pulmonary hemodynamics: A meta-analysis
Ullah W, Meizinger C, Ali Z, Panchal A, Saeed R, Haas DC, Rame E
- 559 Medical therapy *vs* early revascularization in diabetics with chronic total occlusions: A meta-analysis and systematic review
Khan MS, Sami FA, Singh H, Ullah W, Al-Dabbas M, Changal KH, Mir T, Ali Z, Kabour A
- 571 Transradial *vs* transfemoral secondary access outcomes in transcatheter aortic valve implantation: A systematic review and meta-analysis
Radhakrishnan SL, Ho KKL
- 584 Cardiac adverse events of immune checkpoint inhibitors in oncology patients: A systematic review and meta-analysis
Nso N, Antwi-Amoabeng D, Beutler BD, Ulanja MB, Ghuman J, Hanfy A, Nimo-Boampong J, Atanga S, Doshi R, Enoru S, Gullapalli N

ABOUT COVER

Editorial board member of *World Journal of Cardiology*, Dr. Alexander Kharlamov, MD, FESC (2018), FACC (2019), FEACVI (2019), has 24 years of clinical experience in general cardiology (since 1996; Consultant Physician since 2007; Board-Certified Cardiologist since 2010), 19 years of translational research experience in nanomedicine and biomedical engineering (since 2001), and about 13 years of bench-to-bedside study experience in interventional cardiology (a leader of the research group since 2007), including investigations into advanced imaging, vascular biology, and pathology, RTD of cardiovascular imaging software and medical devices (bioresorbable scaffolds and stents). He is an author of more than 60 articles and grant proposals for the European Commission, and has received various national and international awards for his research work. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of *World Journal of Cardiology* (*WJC*, *World J Cardiol*) is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJC mainly publishes articles reporting research results and findings obtained in the field of cardiology and covering a wide range of topics including acute coronary syndromes, aneurysm, angina, arrhythmias, atherosclerosis, atrial fibrillation, cardiomyopathy, congenital heart disease, coronary artery disease, heart failure, hypertension, imaging, infection, myocardial infarction, pathology, peripheral vessels, public health, Raynaud's syndrome, stroke, thrombosis, and valvular disease.

INDEXING/ABSTRACTING

The *WJC* is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Scopus, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Jia-Hui Li; Production Department Director: Xiang Li; Editorial Office Director: Jia-Ping Yan.

NAME OF JOURNAL

World Journal of Cardiology

ISSN

ISSN 1949-8462 (online)

LAUNCH DATE

December 31, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Ramdas G Pai, Dimitrios Tousoulis, Marco Matteo Ciccone

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1949-8462/editorialboard.htm>

PUBLICATION DATE

November 26, 2020

COPYRIGHT

© 2020 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Retrospective Study

Effectiveness and safety of antithrombotic strategies in elderly patients with acute myocardial infarction

Elisa Rondano, Marzia Bertolazzi, Alessandro Galluzzo, Ludovica Maltese, Paolo Caccianotti, Sergio Macciò, Stefano Mazza, Maria Virginia Di Ruocco, Serena Favretto, Eraldo Occhetta, Francesco Rametta

ORCID number: Elisa Rondano 0000-0002-1252-9257; Marzia Bertolazzi 0000-0001-8797-1923; Alessandro Galluzzo 0000-0003-2803-6761; Ludovica Maltese 0000-0003-3085-1642; Paolo Caccianotti 0000-0001-5814-0493; Sergio Macciò 0000-0002-6669-029X; Stefano Mazza 0000-0002-6537-819X; Maria Virginia Di Ruocco 0000-0003-2503-3661; Serena Favretto 0000-0002-7001-3224; Eraldo Occhetta 0000-0002-1663-3561; Francesco Rametta 0000-0002-1599-1084.

Author contributions: Rondano E, Bertolazzi M, Rametta F designed the research; Occhetta E approved the research, Rondano E, Bertolazzi M, Galluzzo A, Maltese L, Caccianotti P, Macciò S, Mazza S, Di Ruocco MV, Favretto S performed the research and contributed to data acquisition; Rondano E, Bertolazzi M, Galluzzo A, Occhetta E, Maltese L analyzed the data; Rondano E, Bertolazzi M, Galluzzo A, Maltese L wrote the paper; Occhetta E and Rametta F revised the paper; and all authors approved the final version of the article.

Institutional review board

statement: The study was reviewed and approved for publication by our Institutional Reviewer.

Elisa Rondano, Marzia Bertolazzi, Alessandro Galluzzo, Ludovica Maltese, Paolo Caccianotti, Sergio Macciò, Stefano Mazza, Maria Virginia Di Ruocco, Serena Favretto, Eraldo Occhetta, Francesco Rametta, Cardiology Department, St. Andrea Hospital, Vercelli 13100, Italy

Corresponding author: Alessandro Galluzzo, MD, Doctor, Cardiology Department, St. Andrea Hospital, Corso Mario Abbiate 21, Vercelli 13100, Italy. alessandro.galluzzo@unito.it

Abstract

BACKGROUND

Elderly patients represent a rapidly growing part of the population more susceptible to acute coronary syndromes and their complications. However, literature evidence is lacking in this clinical setting.

AIM

To describe the clinical features, in-hospital management and outcomes of “elderly” patients with myocardial infarction treated with antiplatelet and/or anticoagulation therapy.

METHODS

This study was a retrospective analysis of all consecutive patients older than 80 years admitted to the Division of Cardiology of St. Andrea Hospital of Vercelli from January 2018 to December 2018 due to ST-elevation myocardial infarction (STEMI) or non-ST elevation myocardial infarction (NSTEMI). Clinical and laboratory data were collected for each patient, as well as the prevalence of previous or in-hospital atrial fibrillation (AF). In-hospital management, consisting of an invasive or conservative strategy, and the anti-thrombotic therapy used are described. Outcomes evaluated at 1 year follow-up included an efficacy ischemic endpoint and a safety bleeding endpoint.

RESULTS

Of the 105 patients enrolled (mean age 83.9 ± 3.6 years, 52.3% males), 68 (64.8%) were admitted due to NSTEMI and 37 (35.2%) due to STEMI. Among the STEMI patients, 34 (91.9%) underwent coronary angiography and all of them were treated with percutaneous coronary intervention (PCI); among the NSTEMI patients, 42 (61.8%) were assigned to an invasive strategy and 16 (38.1%) of them underwent a PCI. No significant difference between the groups was found

Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: All the authors have no conflict of interest related to the manuscript.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Specialty type: Cardiac and cardiovascular systems

Country/Territory of origin: Italy

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: April 13, 2020

Peer-review started: April 13, 2020

First decision: April 26, 2020

Revised: July 28, 2020

Accepted: October 12, 2020

Article in press: October 12, 2020

Published online: November 26, 2020

P-Reviewer: Tung TH

S-Editor: Wang JL

L-Editor: Webster JR

P-Editor: Li JH

concerning the prevalence of previous or in-hospital de-novo AF. 10.5% of the whole population received triple antithrombotic therapy and 9.5% single antiplatelet therapy plus oral anticoagulation (OAC), with no significant difference between the subgroups, although a higher number of STEMI patients received dual antiplatelet therapy without OAC as compared with NSTEMI patients. A low rate of in-hospital death (5.7%) and 1-year cardiovascular death (3.3%) was registered. Seven (7.8%) patients experienced major adverse cardiovascular events, while the rate of minor and major bleeding at 1-year follow-up was 10% and 2.2%, respectively, with no difference between NSTEMI and STEMI patients.

CONCLUSION

In this real-world study, a tailored evaluation of an invasive strategy and antithrombotic therapy resulted in a low rate of adverse events in elderly patients hospitalized with acute myocardial infarction.

Key Words: Antiplatelet therapy; Anticoagulant therapy; Elderly patients; Safety; Acute myocardial infarction

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: This real-world study focuses on the difficult but common scenario of elderly patients admitted with acute myocardial infarction (AMI), for which literature evidence is lacking. We retrospectively identified 105 patients older than 80 years admitted for AMI. An invasive revascularization strategy was weighed considering the ischemic/hemorrhagic risk and was more common in ST-elevation myocardial infarction than in non-ST-elevation myocardial infarction patients. Despite the significant prevalence of atrial fibrillation and concomitant treatment with oral anticoagulation, the rates of in-hospital and 1-year cardiovascular death, ischemic and bleeding events were lower than those described previously, underlying the importance of a tailored therapeutic approach in this population.

Citation: Rondano E, Bertolazzi M, Galluzzo A, Maltese L, Caccianotti P, Macciò S, Mazza S, Di Ruocco MV, Favretto S, Occhetta E, Rametta F. Effectiveness and safety of antithrombotic strategies in elderly patients with acute myocardial infarction. *World J Cardiol* 2020; 12(11): 513-525

URL: <https://www.wjgnet.com/1949-8462/full/v12/i11/513.htm>

DOI: <https://dx.doi.org/10.4330/wjc.v12.i11.513>

INTRODUCTION

Elderly patients, with an increased average lifespan, represent a rapidly growing part of the population who are more susceptible both to acute coronary syndromes (ACS) and to their complications as well as complications related to antithrombotic treatment^[1,2]. These patients are poorly represented in clinical studies and are more likely to have multiple comorbidities^[3,4].

There is no universally accepted definition of an “elderly” patient. The most commonly used cut-off in the literature is 75 years as a significant worsening of outcome after an acute coronary event has been shown by this age^[5], but a cut-off of 80 years might be more significant and correspond to clinical practice^[6]. As these patients more frequently present with atypical symptoms, the diagnosis of myocardial infarction (MI) may be delayed or missed. Irrespective of age, an early invasive strategy should be considered in ACS, although increasing age is known to be an important predictor of worse outcomes^[6-8]. Furthermore, the need to start antiplatelet therapy and eventually anticoagulant therapy, if atrial fibrillation (AF) is associated, increases the risk of morbidity and mortality in this frail population. For all these reasons and due to the paucity of specific evidence, the management of these patients still represents a challenge^[9].

In the present real-world study on a population of “elderly” patients hospitalized



due to an acute myocardial infarction, we aimed to investigate our practice during in-hospital time and outcomes during the first year of follow-up, including the safety of antithrombotic therapy^[10].

MATERIALS AND METHODS

All consecutive patients older than 80 years admitted to the Division of Cardiology of St. Andrea Hospital of Vercelli from January 2018 to December 2018 for ST-elevation myocardial infarction (STEMI) or non-ST elevation myocardial infarction (NSTEMI) were retrospectively evaluated. The diagnosis was based on the European Society of Cardiology guidelines for the management of acute myocardial infarction in patients presenting with and without ST-segment elevation^[3,4].

For each patient, we evaluated cardiovascular risk factors (hypertension, hyperlipidemia, diabetes, overweight defined as body mass index > 25, smoking, family history of coronary artery disease), creatinine and hemoglobin levels at admission and discharge. An evaluation of the global hemorrhagic risk for each patient was performed a posteriori by calculating the PRECISE-DAPT score^[11]. We also reported the prevalence of previous paroxysmal, persistent/permanent AF or its in-hospital de-novo incidence.

In-hospital management, consisting of coronary angiography and percutaneous coronary angioplasty or conservative strategy is described, as well as the following medical therapy for each patient, in particular treatment with single or dual antiplatelet therapy (DAPT) started during hospitalization and, when necessary, anticoagulant therapy [vitamin K inhibitors (VKAs) or direct oral anticoagulants (DOACs)].

The 1-year follow-up data were collected through ambulatory visits or telephone interviews and were focused on the efficacy endpoint consisting of major adverse cardiovascular events (MACEs, including CV death, stroke and myocardial infarction) and the safety endpoint including minor and major bleeding, classified according to the modified thrombolysis in myocardial infarction trial definitions^[12]: A bleeding event was defined as major if it was intracranial or if red blood cell transfusion was clinically indicated in association with a significant drop in hemoglobin level. One-year global death is also reported.

A comparison between STEMI and NSTEMI patients was performed concerning clinical features, invasive and medical management and subsequent follow-up.

Statistical analysis

Data are shown as median (interquartile range) for continuous variables, and number (percentage) for categorical data. Student's *t*-test, Mann-Whitney *U* test, Fisher's exact test, and χ^2 test were used, as appropriate. A *P* value < 0.05 was considered statistically significant. Survival curves including the log-rank test for STEMI and NSTEMI patients were built. Statistical analyses were performed with SPSS Statistics Version 23 (IBM, United States). The statistical methods used in this study were reviewed by our expert Biostatistician Eraldo Occhetta.

RESULTS

Baseline patients' characteristics are shown in Table 1. Of the 105 patients enrolled, 68 (64.8%) were admitted for NSTEMI and 37 (35.2%) for STEMI (Figure 1). The mean age of these patients was 83.9 ± 3.6 years.

Patients presenting with STEMI were more likely to receive an invasive treatment: 34 (91.9%) underwent coronary angiography and all of them were treated with percutaneous revascularization; among the NSTEMI patients, 42 (61.8%) underwent coronary angiography and 16 (38.1%) of them had a percutaneous angioplasty performed (Table 2 and Figure 2). The most common reasons for revascularization not being performed in this subgroup of patients were non-obstructive coronary artery disease, small target vessels inappropriate for intervention, extensive three vessel disease without a "culprit lesion" identified and associated severe valvular disease. The most common reason for coronary angiography not being performed in 38.2% of patients, instead, was the perception of the absence of a net clinical benefit by the treating physicians considering the global risk/benefit ratio.

Twenty-five patients (23.8%) had AF either before or as new onset during the index

Table 1 Baseline patients' characteristics, *n* (%)

Parameters	All (<i>n</i> = 105)	Pathology		<i>P</i> value
		STEMI (<i>n</i> = 37)	NSTEMI (<i>n</i> = 68)	
Age (yr)	83.9 ± 3.6	83.6 ± 3.9	84.0 ± 3.5	0.592
Males	55 (52.3)	16 (43.2)	39 (57.3)	0.239
BMI (kg/m ²)	25.9 ± 5.4	25.7 ± 3.8	26 ± 6.1	0.787
LVEF (%)	45 ± 11.1	43 ± 12.2	46 ± 10.5	0.190
History of AF	15 (14.3)	5 (13.5)	10 (14.7)	0.900
Paroxysmal	7 (7.7)	3 (8.1)	4 (5.9)	-
Persistent/Permanent	8 (7.6)	2 (5.4)	6 (8.8)	-
New onset AF	10 (9.5)	3 (8.1)	7 (10.2)	0.999
Hypertension	75 (71.4)	23 (62.2)	52 (76.5)	0.186
Dyslipidemia	36 (34.3)	10 (27)	26 (38.2)	0.347
Diabetes	34 (32.4)	13 (35.1)	21 (30.9)	0.821
Overweight	20 (19)	5 (13.5)	15 (22.1)	0.421
Smoking active or previous	21 (20)	5 (13.5)	16 (23.5)	0.332
Family history of CAD	9 (8.6)	4 (10.8)	5 (7.4)	0.789
Creatinine at admission (mg/dL)	1.15 ± 0.4	1.0 ± 0.4	1.2 ± 0.5	0.039
Creatinine at discharge (mg/dL)	1.31 ± 0.6	1.3 ± 0.5	1.3 ± 0.7	0.999
Hemoglobin at admission (g/dL)	12.6 ± 2.1	13.2 ± 2.0	12.3 ± 2.1	0.035
Hemoglobin at discharge (g/dL)	12.3 ± 1.9	12.4 ± 1.7	12.2 ± 1.9	0.594

Continuous variables are presented as mean value ± SD or median value (IQR). STEMI: ST-elevation myocardial infarction; NSTEMI: Non-ST-elevation myocardial infarction; BMI: Body mass index; LVEF: Left ventricular ejection fraction; AF: Atrial fibrillation; CAD: Coronary artery disease.

Table 2 Acute management and antithrombotic therapy, *n* (%)

Treatment strategy	All (<i>n</i> = 105)	Pathology		<i>P</i> value
		STEMI (<i>n</i> = 37)	NSTEMI (<i>n</i> = 68)	
Acute management				
Coronary angiography	76 (72.4)	34 (91.9)	42 (61.8)	0.001
Coronary revascularization	60 (57.1)	34 (91.9)	26 (38.2)	< 0.001
Elective medical therapy	29 (27.6)	3 (8.1)	26 (38.2)	0.001
Antithrombotic therapy				
SAPT	18 (17.1)	3 (8.1)	15 (22)	0.115
DAPT	66 (62.9)	28 (75.7)	38 (55.9)	0.072
SAPT + OAC	10 (9.5)	3 (8.1)	7 (10.3)	0.999
Triple therapy	11 (10.5)	3 (8.1)	8 (11.8)	0.823

STEMI: ST-elevation myocardial infarction; NSTEMI: Non-ST-elevation myocardial infarction; SAPT: Single antiplatelet therapy; DAPT: Double antiplatelet therapy; OAC: Oral anticoagulation.

hospitalization that required specific treatment with oral anticoagulation. No significant difference was found between NSTEMI and STEMI patients concerning the history or new onset of AF.

With regard to antithrombotic medications: 8.1% of STEMI patients and 22% of NSTEMI patients received a single antiplatelet therapy; 75.7% of STEMI patients and

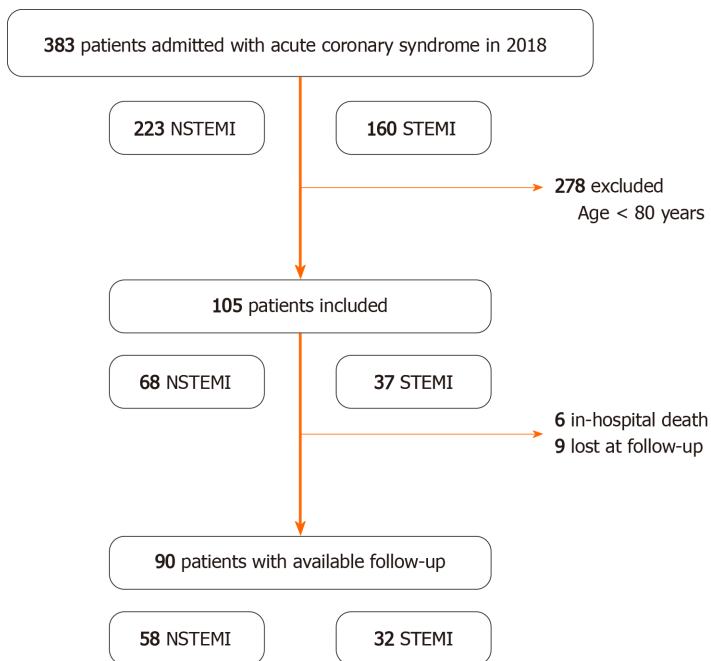


Figure 1 Study flow-chart. This figure shows the patients selected and followed-up in our study. NSTEMI: Non-ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction.

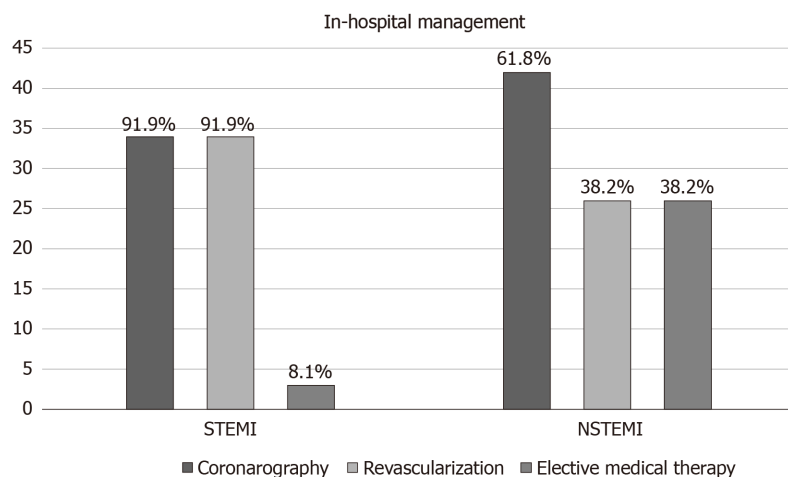


Figure 2 In-hospital patient management. This figure shows the in-hospital management of patients. Percentages refer to the single non-ST-elevation myocardial infarction and ST-elevation myocardial infarction population, respectively. NSTEMI: Non-ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction.

55.9% of NSTEMI patients were treated with DAPT; 8.1% of STEMI and 10.3% of NSTEMI were treated with single antiplatelet therapy plus antithrombotic therapy (VKAs or DOACs); 8.1% of the STEMI group and 11.8% of the NSTEMI group were treated with DAPT plus anticoagulant therapy (VKAs or DOACs) (Table 2). Following statistical analyses, STEMI patients, as compared with NSTEMI patients, showed a trend towards a higher rate of DAPT administration.

Values of serum creatinine varied significantly from admission to discharge, in STEMI but not in NSTEMI patients, while a trend towards significance was found for hemoglobin; these differences may likely reflect the higher percentage of the invasive strategy in the former group.

During hospitalization, 6 (5.7%) patients (3 in the NSTEMI and 3 in the STEMI group) died, all due to cardiovascular causes. One major bleeding complication (hematoma at the femoral access site) and 2 minor bleeding complications occurred.

After hospital discharge, 9 patients were lost to follow-up. For the remaining 90 patients, the mean follow-up was 11.1 ± 7.2 mo. Table 3 summarizes the main outcomes.

Table 3 Clinical outcomes, *n* (%)

Clinical outcomes	All	Pathology		P value
		STEMI	NSTEMI	
Efficacy endpoint				
In-hospital mortality	6/105 (5.7)	3/37 (8.1)	3/68 (4.4)	0.702
1-year MACEs ¹	7/90 (7.8)	4/32 (12.5)	3/58 (5.2)	0.457
Ischemic stroke	1/90 (1.1)	0/32	1/58 (1.7)	-
Cardiovascular death	3/90 (3.3)	2/32 (6.3)	1/58 (1.7)	-
Myocardial infarction	3/90 (3.3)	2/32 (6.3)	1/58 (1.7)	-
1-year non-cardiovascular death	11/90 (12.2)	6/32 (18.8)	5/58 (8.6)	0.369
Safety endpoint				
In-hospital minor bleeding	2/105 (1.9)	0/37	2/68 (2.9)	0.834
In-hospital major bleeding	1/105 (1.0)	0/37	1/68 (1.5)	0.999
Minor bleeding after discharge ¹	9/90 (10)	3/32 (9.4)	6/58 (10.3)	0.999
Major bleeding after discharge ¹	2/90 (2.2)	0/32	2/58 (3.4)	0.846

¹1-year MACE and after-discharge bleeding events percentages refer to 90 patients (9 patients were lost to follow-up and 6 patients died during hospitalization). STEMI: ST-elevation myocardial infarction; NSTEMI: Non-ST-elevation myocardial infarction; MACEs: Major adverse cardiovascular events.

MACEs were recorded in 7 patients (7.8%). Only 3 patients (3.3%) experienced cardiovascular death, while 11 patients (12.2%) died of non-cardiovascular causes, mainly due to malignancy, pneumonia or sepsis. No deaths attributable to bleeding complications were recorded.

No significant difference was found between NSTEMI and STEMI patients concerning the incidence of all-cause death or any event during hospitalization or follow-up (Figure 3 and Table 3).

Concerning the safety endpoint, 2 patients experienced a major non-fatal spontaneous bleeding event at follow-up: One of them was on DAPT, the other was on triple antithrombotic therapy. Minor bleeding was reported in 9 patients (10%). Even if no specific antithrombotic strategy significantly correlated with the safety endpoints, all patients who experienced bleeding were taking DAPT or dual/triple antithrombotic therapy. The hemorrhagic risk estimated through the PRECISE-DAPT score [median value 35 (IQR 29-40)] did not correlate with the incidence of minor or major bleeding events ($P = 0.602$); however, as specified, this score was retrospectively calculated and was not used to determine the duration of DAPT.

DISCUSSION

In this retrospective registry of elderly patients admitted to our division due to myocardial infarction, we describe our in-hospital management of this population, and report a low incidence of complications in the short and medium-term follow-up.

Available data to guide the management of elderly patients are limited, both because they are underrepresented in Acute Coronary Syndrome registries (27%–34%) and randomized controlled trials (RCTs) (13%–15%)^[13–15], and because, due to a selection bias, RCTs may not be representative of the population treated in everyday clinical practice^[1,2]. It is known that the atypical clinical and ECG presentation and the lower specificity of troponin assays may delay the diagnosis^[16,17]. In registries, elderly patients are less likely to receive evidence-based therapies and undergo an invasive strategy compared with younger patients^[13]. Therefore, focusing on this subgroup is of particular interest for two main reasons. Firstly, with the aging of the population, the elderly represent a growing number of patients presenting with myocardial infarction. Moreover, age is a very important prognostic factor: Patients over 75 years account for 60% of the entire mortality due to cardiovascular diseases and they are often more subject to infarct-related complications such as heart failure and pulmonary edema,

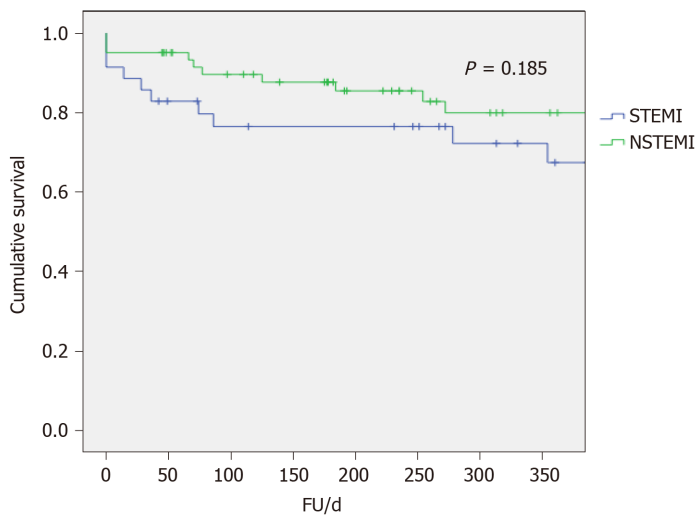


Figure 3 Kaplan-Meier curves of all-cause death. This figure shows the 1-year survival curves. *P* value refers to the Log-rank test. NSTEMI: Non-ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction; FU: Follow-up.

which occur in more than half of patients over 75 years and in 65% of patients over the age of 85; shock occurs in more than 10% of patients over 75 years and is mainly due to rupture of the left ventricular free wall or papillary muscles or to advanced ventricular dysfunction^[2,18].

In our real-world cohort, the mean age was 83 years, higher than that reported in previous studies^[19,20]. A tailored therapeutic approach based on a comprehensive evaluation of the patient's status and comorbidities proved successful as we report a rate of adverse events at follow-up lower than previous studies^[21,22] (Table 4). Since the available evidence differs between NSTEMI and STEMI elderly patients, we differentiated these populations, reporting data for each subgroup.

Revascularization in NSTEMI

European clinical practice guidelines on non-ST elevation acute coronary syndrome (NSTEMI-ACS) state that elderly patients should be considered for an invasive strategy and emphasize the need for a detailed clinical evaluation including comorbidities, life expectancy, quality of life, frailty and patient preferences, in order to individualize the risks and benefits^[3]. However, no specific recommendation is available to guide therapeutic decisions based on these parameters.

With regard to NSTEMI in the GRACE registry, coronary angiography was performed in 67% of patients < 70 years of age compared with 33% in patients over 80 years^[21,22]. Similar percentages were observed in the CRUSADE experience (coronary revascularization performed in 40.1% of patients 75–89 years of age *vs* 12.6% in those ≥ 90 years)^[23,24], in the SWEDEHEART experience^[25] and in the Euroheart ACS survey^[13]. In our experience, the percentages were higher than those reported in previous studies. In fact, 61.8% of NSTEMI patients greater than 80 years underwent coronary angiography and of these 61.9% underwent percutaneous revascularization. Nagata *et al*^[19] adopted an invasive strategy in 94% of NSTEMI but reported high rates of in-hospital mortality (8.5%) in patients > 80 years of age.

Whether acute revascularization is the best strategy for these patients is still a matter of debate. In the FRISC II-ICTUS-RITA-3 study, the invasive therapeutic strategy performed better in elderly NSTEMI-ACS patients than in younger patients^[26]. On the contrary, Sanchis *et al*^[27] and García-Blas *et al*^[28] showed that invasive management did not modify long-term outcome in comorbid elderly patients with NSTEMI. The Italian-ACS trial included 313 NSTEMI-ACS patients over 75 years and found no significant benefit of the routine invasive strategy in a composite primary endpoint including ischemic and bleeding events, when compared to selective invasive strategy^[6]. On the other hand, the After Eighty trial (457 NSTEMI-ACS patients ≥ 80 years) showed a significant benefit of the routine invasive strategy in the composite primary ischemic endpoint compared to the conservative strategy^[29], although only 457 patients were included out of 4187 screened and the included population may not reflect the whole spectrum of elderly patients. In a meta-analysis of four RCTs comparing routine invasive strategy with a selective invasive strategy, including 1887 patients (mean age 79 years) no significant difference in all-cause death, cardiovascular

Table 4 Comparison of observational studies including elderly patients with acute coronary syndrome

Ref.	Cohort	Mean age (yr)	Invasive strategy (%)	In-hospital mortality (%)	Major bleeding (%)	MACEs (%)
Rosengren <i>et al</i> ^[13] , 2006	NSTE-ACS, STE-ACS	N/A; 25% of patients > 75 yr	34.6	4.7; 9.7 in patients > 75 yr	N/A	N/A
Devlin <i>et al</i> ^[22] , 2008	NSTE-ACS	66	38	5.8	2.4	9.2
Nagata <i>et al</i> ^[19] , 2017	NSTE-ACS (Elderly group > 80 yr)	73	79	8.5	0	9.9
Toleva <i>et al</i> ^[32] , 2015	STE-ACS (Elderly group > 75 yr)	82.2	70.1	14.2	13	27.6

NSTE-ACS: Non ST-elevation acute coronary syndrome; STE-ACS: ST-elevation acute coronary syndrome; MACEs: Major adverse cardiovascular events; N/A: Not available.

death or major bleeding was found between both strategies at a median 36-mo follow-up^[30].

The prognostic impact of revascularization in our patients would be difficult to assess due to the retrospective nature of the study design. Within this context, evidence from the literature and clinical practice shows that a routine early invasive strategy is not always the most favorable, because similar results may be obtained with a medical conservative strategy.

Revascularization in STEMI

Despite the lower rate of revascularization in the elderly, its benefit appears to be maintained at an older age in this context^[7]. There is no upper age limit with respect to reperfusion, especially with primary percutaneous coronary intervention (PCI)^[31]. Observational studies have shown that coronary reperfusion therapy (thrombolysis or PCI) also during STEMI is little used in older age, with a trend directly correlated to age (64.8% between 65 and 69 years, 60.1% between 70 and 74 years, 50.4% between 75 and 79 years, 35.4% between 80 and 84 years, 20.4% > 85 years)^[32]. A possible explanation for this is the paucity of data on reperfusion in the elderly with STEMI, the presence of atypical symptoms and the related diagnostic and therapeutic delay and comorbidities^[18]. In our hospital 91.9% of STEMI patients underwent coronary angiography and primary PCI.

Antithrombotic therapy

The optimal therapy after STEMI and NSTEMI acute treatment is well codified by the actual ESC guidelines^[33]. In addition, anticoagulant therapy association in AF patients (triple therapy) has recently been confirmed in a Joint European Consensus^[34]. One of the reasons for suboptimal administration of evidence-based medications in the elderly is that patients may more frequently have contraindications to medications or pharmacodynamic characteristics (absorption, metabolism, distribution and excretion of drugs) that make them prone to medication side effects^[1,2]. In particular, they have an augmented bleeding risk due to aging, impaired renal function and comorbidities. Observational studies have shown frequent excess dosing of antithrombotic therapies in elderly patients: In this context, lower doses of DOACs could avoid these risks^[35,36]. Moreover, personalized therapeutic choices between dual and triple antithrombotic therapy for concomitant AF may improve benefits and reduce risks in frail and elderly patients^[37,38]. Our population presented a high hemorrhagic risk as shown by the median values of the PRECISE-DAPT score; however, with a tailored therapeutic approach we found a low rate of significant bleeding even in those treated invasively.

In conclusion, the authors of this article acknowledge that specific guidelines on the management of elderly patients with ACS are lacking, yet these patients tend to present with various comorbidities, often associated, and exploring every specific scenario in order to standardize clinical management would be impractical.

Trials necessarily restrict enrollment criteria and tend to exclude extreme ages or patients with comorbidities due to the heterogeneity of their clinical presentation.

We therefore present a small cohort of patients showing what is likely to be a common scenario in a cardiology ward. We do believe that, in such a complex context, the approach to treatment should be tailored to the patient: Even if a thorough knowledge of the scientific evidence is essential, physicians need to draw on

experience and common sense.

Limitations of the study

Our study has some limitations. First of all, due to the limited sample size studied, our comparison between STEMI and NSTEMI patients does not have adequate statistical power (90%) for all the results reported (though keeping in mind the limits of a post-hoc power analysis), which therefore need to be interpreted with caution.

Moreover, the retrospective design of the study did not allow a more comprehensive evaluation of patients through a “frailty” assessment that may be useful in the context studied. Moreover, as the PRECISE-DAPT score values were retrospectively calculated, we could not assess its impact in guiding DAPT duration in order to reduce bleeding events. Observational studies, despite their methodological limitations, may reflect evidence closer to the real-life population. Indeed, our study was conceived to describe our real-world practice in elderly patients with acute myocardial infarction and provide information on the management and outcome of this disease in the aging society.

CONCLUSION

In this observational study, we describe data from a real-world setting of elderly patients hospitalized with acute myocardial infarction, and report low in-hospital mortality and a low rate of medium-term ischemic and hemorrhagic complications.

Although the available evidence does not allow us to establish firm recommendations in this subgroup of patients, we report that an invasive strategy in selected cases and an adequate antithrombotic therapy, even in this critical context, can be safely performed. Measures to reduce complication rates in this population include an accurate selection of patients suitable for an invasive strategy, evaluating the presence of comorbidities, a radial access whenever possible and correct dosing of antithrombotic drugs.

Larger registry cohorts with a higher number of patients enrolled are mandatory to study the setting of elderly patients with acute coronary syndromes.

ARTICLE HIGHLIGHTS

Research background

Despite the aging of the population, which makes the clinical presentation of elderly patients with acute myocardial infarction more common, there are no specific guidelines on the management of this subgroup and data are generally extrapolated from trials in which elderly patients represent a minority of the cohort studied. Indeed, controversy exists both on the need for an invasive strategy, especially in frailer patients, and on the optimal medical management.

Research motivation

Exploring and describing the setting of elderly patients with myocardial infarction is particularly useful to identify aspects that need to be improved and sources of mistakes in everyday clinical practice.

Research objectives

In the present real-world study on a population of elderly patients hospitalized due to an acute myocardial infarction, we aimed to investigate our practice during in-hospital time and outcomes during the first year of follow-up.

Research methods

We retrospectively analyzed all consecutive patients older than 80 years admitted to the Division of Cardiology of our center in 2018 for acute myocardial infarction. Clinical and laboratory data were collected. In-hospital management, consisting of an invasive or conservative strategy, and the anti-thrombotic therapy used were described. Outcomes evaluated at 1 year follow-up included an efficacy ischemic endpoint and a safety bleeding endpoint.

Research results

We enrolled a total of 105 patients with a mean age was 83.9 ± 3.6 years. Patients presenting with ST-elevation myocardial infarction (STEMI) (35%) received an invasive treatment in more than 90% of cases, while the number of patients with non-ST-elevation myocardial infarction (NSTEMI) (65%), who underwent coronary angiography and percutaneous angioplasty was lower (38%). Coronary angiography was not performed when the absence of a net clinical benefit was perceived by the treating physicians considering the global risk/benefit ratio, while coronary angioplasty was not performed mainly due to the absence of an obstructive coronary artery disease or technical reasons. Atrial fibrillation, either before or as new onset during the index hospitalization, was found in 24% of patients. With regard to antithrombotic medications, 10.5% of the whole population received triple antithrombotic therapy and 9.5% single antiplatelet therapy plus oral anticoagulation (OAC), with no significant difference between the subgroups, although a higher number of STEMI patients received dual antiplatelet therapy without OAC as compared with NSTEMI patients. A low rate of in-hospital death (5.7%) and 1-year cardiovascular death (3.3%) was registered. Major adverse cardiovascular events were recorded in 7 patients (7.8%). Interestingly, 11 of 14 deaths at one-year follow-up were the result of non-cardiovascular causes, mainly due to malignancy, pneumonia or sepsis. No deaths attributable to bleeding complications were recorded, while only 2 patients experienced a major non-fatal spontaneous bleeding event at follow-up.

Research conclusions

The authors of this article acknowledge that specific guidelines on the management of elderly patients with acute coronary syndrome are lacking, yet these patients tend to present with various comorbidities, often associated, and exploring every specific scenario in order to standardize clinical management would be impractical. Trials necessarily restrict enrollment criteria and tend to exclude extreme ages or patients with comorbidities due to the heterogeneity of their clinical presentation. We therefore present a small cohort of patients showing what is likely to be a common scenario in a cardiology ward. We do believe that, in such a complex context, the approach to treatment should be tailored to the patient: Even if a thorough knowledge of the scientific evidence is essential, physicians need to draw on experience and common sense. Through this approach, the rate of complications and death was relatively low in our population. The main limitation of this study, namely its retrospective nature, is somehow a point of strength, as it avoids selection biases which characterize previous studies.

Research perspectives

Future studies on the elderly population should be based on a registry design. Larger studies with a higher number of patients enrolled are mandatory.

REFERENCES

- 1 **Alexander KP**, Newby LK, Cannon CP, Armstrong PW, Gibler WB, Rich MW, Van de Werf F, White HD, Weaver WD, Naylor MD, Gore JM, Krumholz HM, Ohman EM; American Heart Association Council on Clinical Cardiology; Society of Geriatric Cardiology. 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 [PMID: [17502590](#) DOI: [10.1161/circulationaha.107.182615](#)]
- 2 **Alexander KP**, Newby LK, Armstrong PW, Cannon CP, Gibler WB, Rich MW, Van de Werf F, White HD, Weaver WD, Naylor MD, Gore JM, Krumholz HM, Ohman EM; American Heart Association Council on Clinical Cardiology; Society of Geriatric Cardiology. Acute coronary care in the elderly, part II: ST-segment-elevation myocardial infarction: 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**: 2570-2589 [PMID: [17502591](#) DOI: [10.1161/circulationaha.107.182616](#)]
- 3 **Roffi M**, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen S, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S; ESC Scientific Document Group. 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 [PMID: [26320110](#) DOI: [10.1093/eurheartj/ehv320](#)]
- 4 **Ibanez B**, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P; ESC Scientific Document Group. 2017 ESC Guidelines for the

- management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018; **39**: 119-177 [PMID: 28886621 DOI: 10.1093/eurheartj/ehx393]
- 5 **Malkin CJ**, Prakash R, Chew DP. The impact of increased age on outcome from a strategy of early invasive management and revascularisation in patients with acute coronary syndromes: retrospective analysis study from the ACACIA registry. *BMJ Open* 2012; **2**: e000540 [PMID: 22344538 DOI: 10.1136/bmjopen-2011-000540]
 - 6 **Savonitto S**, Cavallini C, Petronio AS, Murena E, Antonicelli R, Sacco A, Steffenino G, Bonechi F, Mossuti E, Manari A, Tolaro S, Toso A, Daniotti A, Piscione F, Morici N, Cesana BM, Jori MC, De Servi S; Italian Elderly ACS Trial Investigators. Early aggressive vs initially conservative treatment in elderly patients with non-ST-segment elevation acute coronary syndrome: a randomized controlled trial. *JACC Cardiovasc Interv* 2012; **5**: 906-916 [PMID: 22995877 DOI: 10.1016/j.jcin.2012.06.008]
 - 7 **Bach RG**, Cannon CP, Weintraub WS, DiBattiste PM, Demopoulos LA, Anderson HV, DeLuca PT, Mahoney EM, Murphy SA, Braunwald E. The effect of routine, early invasive management on outcome for elderly patients with non-ST-segment elevation acute coronary syndromes. *Ann Intern Med* 2004; **141**: 186-195 [PMID: 15289215 DOI: 10.7326/0003-4819-141-3-200408030-00007]
 - 8 **Bauer T**, Koeth O, Jünger C, Heer T, Wienbergen H, Gitt A, Zahn R, Senges J, Zeymer U; Acute Coronary Syndromes Registry (ACOS) Investigators. Effect of an invasive strategy on in-hospital outcome in elderly patients with non-ST-elevation myocardial infarction. *Eur Heart J* 2007; **28**: 2873-2878 [PMID: 17982163 DOI: 10.1093/eurheartj/ehm464]
 - 9 **Madhavan MV**, Gersh BJ, Alexander KP, Granger CB, Stone GW. Coronary Artery Disease in Patients ≥ 80 Years of Age. *J Am Coll Cardiol* 2018; **71**: 2015-2040 [PMID: 29724356 DOI: 10.1016/j.jacc.2017.12.068]
 - 10 **Lip GYH**, Collet JP, Haude M, Byrne R, Chung EH, Fauchier L, Halvorsen S, Lau D, Lopez-Cabanillas N, Lettino M, Marin F, Obel I, Rubboli A, Storey RF, Valgimigli M, Huber K; ESC Scientific Document Group. 2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a joint consensus document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA). *Europace* 2019; **21**: 192-193 [PMID: 30052888 DOI: 10.1093/europace/euy174]
 - 11 **Costa F**, van Klaveren D, James S, Heg D, Räber L, Feres F, Pilgrim T, Hong MK, Kim HS, Colombo A, Steg PG, Zanchin T, Palmerini T, Wallentin L, Bhatt DL, Stone GW, Windecker S, Steyerberg EW, Valgimigli M; PRECISE-DAPT Study Investigators. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. *Lancet* 2017; **389**: 1025-1034 [PMID: 28290994 DOI: 10.1016/S0140-6736(17)30397-5]
 - 12 **Mehran R**, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, Serebruany V, Valgimigli M, Vranckx P, Taggart D, Sabik JF, Cutlip DE, Krucoff MW, Ohman EM, Steg PG, White H. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation* 2011; **123**: 2736-2747 [PMID: 21670242 DOI: 10.1161/CIRCULATIONAHA.110.009449]
 - 13 **Rosengren A**, Wallentin L, Simoons M, Gitt AK, Behar S, Battler A, Hasdai D. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. *Eur Heart J* 2006; **27**: 789-795 [PMID: 16464911 DOI: 10.1093/eurheartj/ehi774]
 - 14 **Wiviott SD**, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson CM, Antman EM; TRITON-TIMI 38 Investigators. Prasugrel vs clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2007; **357**: 2001-2015 [PMID: 17982182 DOI: 10.1056/nejmoa0706482]
 - 15 **Wallentin L**, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA; PLATO Investigators; Freij A; Thorsén M. Ticagrelor vs clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2009; **361**: 1045-1057 [PMID: 19717846 DOI: 10.1056/NEJMoa0904327]
 - 16 **Brieger D**, Eagle KA, Goodman SG, Steg PG, Budaj A, White K, Montalescot G; GRACE Investigators. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. *Chest* 2004; **126**: 461-469 [PMID: 15302732 DOI: 10.1378/chest.126.2.461]
 - 17 **Reiter M**, Twerenbold R, Reichlin T, Haaf P, Peter F, Meissner J, Hochholzer W, Stelzig C, Freese M, Heinisch C, Breidhardt T, Freidank H, Winkler K, Campodarve I, Gea J, Mueller C. Early diagnosis of acute myocardial infarction in the elderly using more sensitive cardiac troponin assays. *Eur Heart J* 2011; **32**: 1379-1389 [PMID: 21362702 DOI: 10.1093/eurheartj/ehr033]
 - 18 **White HD**, Braunwald E, Murphy SA, Jacob AJ, Gotcheva N, Polonetsky L, Antman EM. Enoxaparin vs. unfractionated heparin with fibrinolysis for ST-elevation myocardial infarction in elderly and younger patients: results from ExTRACT-TIMI 25. *Eur Heart J* 2007; **28**: 1066-1071 [PMID: 17456482 DOI: 10.1093/eurheartj/ehm081]
 - 19 **Nagata T**, Hyakuna Y, Miyata K, Mohri M. Contemporary practice and outcomes of an elderly cohort of Japanese patients with non-ST-elevation acute coronary syndrome in the era of routine early invasive strategy. *Int J Cardiol* 2017; **240**: 49-54 [PMID: 28416248 DOI: 10.1016/j.ijcard.2017.03.118]
 - 20 **Steg PG**, Goldberg RJ, Gore JM, Fox KA, Eagle KA, Flather MD, Sadiq I, Kasper R, Rushton-Mellor SK, Anderson FA; GRACE Investigators. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol* 2002; **90**: 358-363 [PMID: 12161222 DOI: 10.1016/S0002-8506(02)00000-0]

- 10.1016/s0002-9149(02)02489-x]
- 21 **Fox KA**, Eagle KA, Gore JM, Steg PG, Anderson FA; GRACE and GRACE2 Investigators. The Global Registry of Acute Coronary Events, 1999 to 2009--GRACE. *Heart* 2010; **96**: 1095-1101 [PMID: 20511625 DOI: 10.1136/hrt.2009.190827]
- 22 **Devlin G**, Gore JM, Elliott J, Wijesinghe N, Eagle KA, Avezum A, Huang W, Brieger D; GRACE Investigators. Management and 6-month outcomes in elderly and very elderly patients with high-risk non-ST-elevation acute coronary syndromes: The Global Registry of Acute Coronary Events. *Eur Heart J* 2008; **29**: 1275-1282 [PMID: 18387940 DOI: 10.1093/eurheartj/ehn124]
- 23 **Skolnick AH**, Alexander KP, Chen AY, Roe MT, Pollack CV Jr, Ohman EM, Rumsfeld JS, Gibler WB, Peterson ED, Cohen DJ. Characteristics, management, and outcomes of 5,557 patients age > or =90 years with acute coronary syndromes: results from the CRUSADE Initiative. *J Am Coll Cardiol* 2007; **49**: 1790-1797 [PMID: 17466230 DOI: 10.1016/j.jacc.2007.01.066]
- 24 **Alexander KP**, Chen AY, Roe MT, Newby LK, Gibson CM, Allen-LaPointe NM, Pollack C, Gibler WB, Ohman EM, Peterson ED; CRUSADE Investigators. Excess dosing of antiplatelet and antithrombin agents in the treatment of non-ST-segment elevation acute coronary syndromes. *JAMA* 2005; **294**: 3108-3116 [PMID: 16380591 DOI: 10.1001/jama.294.24.3108]
- 25 **Damman P**, Jernberg T, Lindahl B, de Winter RJ, Jeppsson A, Johanson P, Held C, James SK. Invasive strategies and outcomes for non-ST-segment elevation acute coronary syndromes: a twelve-year experience from SWEDEHEART. *EuroIntervention* 2016; **12**: 1108-1116 [PMID: 26573973 DOI: 10.4244/EIJY15M11_05]
- 26 **Damman P**, Clayton T, Wallentin L, Lagerqvist B, Fox KA, Hirsch A, Windhausen F, Swahn E, Pocock SJ, Tijssen JG, de Winter RJ. Effects of age on long-term outcomes after a routine invasive or selective invasive strategy in patients presenting with non-ST segment elevation acute coronary syndromes: a collaborative analysis of individual data from the FRISC II - ICTUS - RITA-3 (FIR) trials. *Heart* 2012; **98**: 207-213 [PMID: 21930723 DOI: 10.1136/heartjnl-2011-300453]
- 27 **Sanchis J**, Núñez E, Barrabés JA, Marín F, Consuegra-Sánchez L, Ventura S, Valero E, Roqué M, Bayés-Genís A, Del Blanco BG, Dégano I, Núñez J. Randomized comparison between the invasive and conservative strategies in comorbid elderly patients with non-ST elevation myocardial infarction. *Eur J Intern Med* 2016; **35**: 89-94 [PMID: 27423981 DOI: 10.1016/j.ejim.2016.07.003]
- 28 **García-Blas S**, Bonanad C, Sanchis J. Invasive strategy in elderly patients with acute coronary syndrome in 2018: close to the truth? *J Geriatr Cardiol* 2019; **16**: 114-120 [PMID: 30923542 DOI: 10.11909/j.issn.1671-5411.2019.02.004]
- 29 **Tegn N**, Abdelnoor M, Aaberge L, Endresen K, Smith P, Aakhus S, Gjertsen E, Dahl-Hofseth O, Ranhoff AH, Gullestad L, Bendz B; After Eighty study investigators. Invasive vs conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomised controlled trial. *Lancet* 2016; **387**: 1057-1065 [PMID: 26794722 DOI: 10.1016/S0140-6736(15)01166-6]
- 30 **Garg A**, Garg L, Agarwal M, Rout A, Raheja H, Agrawal S, Rao SV, Cohen M. Routine Invasive Versus Selective Invasive Strategy in Elderly Patients Older Than 75 Years With Non-ST-Segment Elevation Acute Coronary Syndrome: A Systematic Review and Meta-Analysis. *Mayo Clin Proc* 2018; **93**: 436-444 [PMID: 29439831 DOI: 10.1016/j.mayocp.2017.11.022]
- 31 **Bueno H**, Betriu A, Heras M, Alonso JJ, Cequier A, García EJ, López-Sendón JL, Macaya C, Hernández-Antolín R; TRIANA Investigators. Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) randomized trial and pooled analysis with previous studies. *Eur Heart J* 2011; **32**: 51-60 [PMID: 20971744 DOI: 10.1093/eurheartj/ehq375]
- 32 **Toleva O**, Ibrahim Q, Brass N, Sookram S, Welsh R. Treatment choices in elderly patients with ST: elevation myocardial infarction-insights from the Vital Heart Response registry. *Open Heart* 2015; **2**: e000235 [PMID: 26196017 DOI: 10.1136/openhrt-2014-000235]
- 33 **Valgimigli M**, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, Jüni P, Kastrati A, Kolh P, Mauri L, Montalescot G, Neumann FJ, Petricevic M, Roffi M, Steg PG, Windecker S, Zamorano JL, Levine GN; ESC Scientific Document Group; ESC Committee for Practice Guidelines (CPG); ESC National Cardiac Societies. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2018; **39**: 213-260 [PMID: 28886622 DOI: 10.1093/eurheartj/ehx419]
- 34 **Andreotti F**, Rocca B, Husted S, Ajjan RA, ten Berg J, Cattaneo M, Collet JP, De Caterina R, Fox KA, Halvorsen S, Huber K, Hylek EM, Lip GY, Montalescot G, Morais J, Patrono C, Verheugt FW, Wallentin L, Weiss TW, Storey RF; ESC Thrombosis Working Group. Antithrombotic therapy in the elderly: expert position paper of the European Society of Cardiology Working Group on Thrombosis. *Eur Heart J* 2015; **36**: 3238-3249 [PMID: 26163482 DOI: 10.1093/eurheartj/ehv304]
- 35 **Lauw MN**, Eikelboom JW, Coppens M, Wallentin L, Yusuf S, Ezekowitz M, Oldgren J, Nakamya J, Wang J, Connolly SJ. Effects of dabigatran according to age in atrial fibrillation. *Heart* 2017; **103**: 1015-1023 [PMID: 28213368 DOI: 10.1136/heartjnl-2016-310358]
- 36 **Avgil-Tsadok M**, Jackevicius CA, Essebag V, Eisenberg MJ, Rahme E, Behloul H, Pilote L. Dabigatran use in elderly patients with atrial fibrillation. *Thromb Haemost* 2016; **115**: 152-160 [PMID: 26354766 DOI: 10.1160/TH15-03-0247]
- 37 **Golwala HB**, Cannon CP, Steg PG, Doros G, Qamar A, Ellis SG, Oldgren J, Ten Berg JM, Kimura T, Hohnloser SH, Lip GYH, Bhatt DL. Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials. *Eur Heart J* 2018; **39**: 1726-1735a [PMID: 29668889 DOI: 10.1093/eurheartj/ehy162]
- 38 **Gragnano F**, Calabrò P, Valgimigli M. Is triple antithrombotic therapy, or rather its duration and composition, the true culprit for the excess of bleeding events observed in patients with atrial fibrillation

undergoing coronary intervention? *Eur Heart J* 2019; **40**: 216-217 [PMID: [30395219](#) DOI: [10.1093/eurheartj/ehy675](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

