International Journal of Cardiology 245 (2017) 35–42

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Patients with non-ST segment elevation acute coronary syndromes managed without coronary revascularization: A population needing treatment improvement

Alberto Menozzi [a,*], Stefano De Servi [b], Roberta Rossini [c], Marco Ferlini [d], Daniela Lina [a], Maurizio Giuseppe Abrignani [e], Piera Capranzano [f], Nazario Carrabba [g], Marcello Galvani [h], Alfredo Marchese [i], Gianfranco Mazzotta [j], Luciano Moretti [k], Nicola Signore [l], Massimo Uguccioni [m], Zoran Olivari [n], Leonardo De Luca [o]

[a] Division of Cardiology, Azienda Ospedaliero-Universitaria, Parma, Italy
[b] Division of Cardiology, IRCCS Multimedica, Sesto San Giovanni, Milan, Italy
[c] Division of Cardiology, ASST Papa Giovanni XXIII, Bergamo, Italy
[d] Division of Cardiology, Policlinico San Matteo, Pavia, Italy
[e] Division of Cardiology, Ospedale S. Antonio Abate, Trapani, Italy
[f] Division of Cardiology, Ospedale Ferrarotto, Catania, Italy
[g] Division of Cardiology, Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy
[h] Division of Cardiology, Ospedale Morgagni-Pierantoni, Forlì, Italy
[i] Interventional Cardiology Unit, Anthea Hospital, Bari, Italy
[j] Division of Cardiology, Ospedale S. Andrea, La Spezia, Italy
[k] Division of Cardiology, Ospedale Mazzoni, Ascoli Piceno, Italy
[l] Division of Cardiology, Azienda Ospedaliero-Universitaria Policlinico di Bari, Italy
[m] Division of Cardiology, Azienda Ospedaliera San Camillo Forlanini, Rome, Italy
[n] Division of Cardiology, Ospedale Ca' Foncello, Treviso, Italy
[o] Division of Cardiology, San Giovanni Evangelista Hospital, Tivoli, Rome, Italy

ARTICLE INFO

Article history:
Received 12 February 2017
Received in revised form 7 May 2017
Accepted 16 May 2017

Keywords:
NSTE-ACS
DAPT
Ticagrelor
Conservative management
Coronary revascularization

ABSTRACT

NSTE-ACS patients are a heterogeneous population, with different clinical features and prognosis. A large proportion of them is medically managed, without any revascularization. In the EYSHOT and FAST-MI registries such patients were 40% and 35%, respectively.

These patients are at higher risk of adverse cardiovascular events and have a worse prognosis compared with those receiving revascularization.

Medically managed NSTE-ACS patients consist of different subgroups: those not undergoing coronary angiography, those without significant coronary artery disease, and those with coronary stenoses not referred to revascularization.

Patients with NSTE-ACS for whom a conservative strategy without coronary angiogram is planned must be very carefully selected. In patients with comorbidities, frailty, or advanced age, a careful balance between benefits and risks is needed to choice the management strategy (perform or not coronary angiography and/or revascularization), as evidence-based medicine data are lacking in the setting of frailty and comorbidities. In this decisional process, it should be also taken into consideration the role of coronary anatomy in risk stratification and treatment guidance.

NSTE-ACS patients managed without revascularization less frequently receive guideline-recommended pharmacological treatment. Dual antiplatelet therapy (DAPT) is recommended for 12 months also in medically managed patients, after careful balancing of ischemic and bleeding risk. In these patients it is mandatory to optimize pharmacological treatment, including antiplatelet therapy, to improve outcome. In NSTE-ACS medically managed, the proportion of patients discharged with DAPT should be increased in comparison with current practice, and the use of ticagrelor in place of clopidogrel should be considered in selected patients.

Abbreviations: NSTE-ACS, acute coronary syndrome/syndromes without persistent ST-segment elevation; ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; DAPT, dual antiplatelet therapy; NO, nitric oxide.

* Corresponding author at: Division of Cardiology, Azienda Ospedaliero-Universitaria di Parma, Via Gramsci 14, 43125, Parma, Italy.
E-mail address: almenozzi@ao.pr.it (A. Menozzi).

http://dx.doi.org/10.1016/j.ijcard.2017.05.066
0167-5273/

1. Introduction

Cardiovascular disease is the leading cause of death in developed countries and NSTE-ACS represent one of the most common clinical presentations of ischemic heart disease [1].

The availability of high-sensitive cardiac markers has led to a significant increase in the number of patients diagnosed with non-ST-elevation ACS. Today, NSTE-ACS patients are a heterogeneous population with very different clinical features and prognosis.

Although significant advances in the treatment of NSTE-ACS patients have been made over the last few decades, further improvement of both short- and long-term prognosis of these patients is needed because recurring events are still frequent after a NSTE-ACS and long-term mortality is even higher than that of ST-segment elevation myocardial infarction [2]. This concept is particularly true for NSTE-ACS patients managed with a conservative strategy.

Based on recent randomized trials [3] current guidelines recommend an early invasive strategy defined as coronary angiography performed within 24–72 h since diagnosis of NSTE-ACS in high- and intermediate-risk patients followed by coronary revascularization when appropriate [4]. However, in real-world clinical practice a significant proportion of patients with NSTE-ACS are managed with a conservative strategy. NSTE-ACS patients not undergoing coronary revascularization are at higher risk of adverse cardiovascular events and may have a worse prognosis, including short- and long-term mortality, compared with those receiving revascularization [5,6].

2. Epidemiology

In every-day clinical practice a significant proportion of NSTE-ACS patients does not undergo diagnostic angiography and a further proportion does not undergo revascularization procedures during the initial hospitalization after coronary angiography [7,8] [Table 1]. In the Italian EYSHOT and French FAST-MI registries, patients medically managed were 40% and 35%, respectively [9,10].

In the last years, the awareness of the benefits associated with coronary revascularization in NSTE-ACS patients has led to a significant increase in the number of NSTE-ACS patients undergoing coronary angiography. The GRACE registry published in 2006 showed that up to 40% of patients did not undergo coronary angiography [11], whereas the more recent FAST-MI (2010) and the EYESHOT (2015) registries reported rates ranging from 10 to 13% of patients, respectively [9,10]. These data are consistent with those of randomized clinical trials. In the CURE trial, published in 2001, 62.5% of patients were medically managed, 21% underwent PCI, and 16.5% had CABG [12], whereas in the PLATO trial, published in 2009, only 26% of patients did not undergo coronary revascularization, 64% underwent PCI and 10% CABG [13].

Many variables, including clinical, demographical, institutional and economic factors affect the decision about managing patients with an invasive or a conservative strategy [7].

3. Ischemic and bleeding risks in patients not undergoing coronary revascularization

In the GUSTO IV-ACS trial a 50% reduction in 1-year mortality was shown in patients undergoing revascularization within 30 days after hospital admission compared with patients managed without revascularization [14] and in a sub-analysis of the ICTUS trial in-hospital revascularization was found to be independently associated with a reduction in 4-year mortality (about 40% relative risk reduction) and 3-year event rate of death or spontaneous myocardial infarction (about 55% relative risk reduction) as compared with a medically management strategy [15]. More recently, in a Swedish registry, including >20,000 NSTE-ACS patients [16], hospital readmission rates for ACS at 6 and 12 months were similar in elderly undergoing revascularization or not but 6-month and 2-year mortality was significantly higher in non-revascularized patients than in patients receiving PCI or CABG [17].

Usually, NSTE-ACS patients managed without coronary revascularization who experience the poorest prognosis are those expected to be at higher risk of events based on the GRACE risk score. Interestingly, an inverse relationship between predicted risk of adverse outcomes and the use of cardiac catheterization has been described in NSTE-ACS because the use of invasive cardiac procedures is often concentrated in the lowest-risk group of patients regardless of geographic region, availability of cardiac catheterization and revascularization facilities, or overall utilization patterns of invasive procedures at individual institutions. It is also well established that clinical characteristics associated with high risk of ischemic events, such as advanced age, renal failure and history of prior coronary revascularization, frequently occur in patients with NSTE-ACS intended for a conservative strategy [5,18,19,20,21].

Often, medically managed patients have also a high bleeding risk and the perceived high bleeding risk is usually the main reason leading to a conservative strategy rather than an invasive one, as it is well known that bleeding events negatively affect prognosis, also in terms of mortality [22].

Therefore balancing risks and benefits of coronary revascularization in complex NSTE-ACS patients may be difficult because many clinical factors have been associated with both ischemic and bleeding risk.

In conclusion, the prognosis of patients excluded from an invasive strategy is often influenced in first instance by the concomitant characteristics of the subjects themselves, as they tend to be older, have more severe comorbidities and are often frail. However, the decision to avoid coronary angiography may not only mean missing the detection (and therefore the treatment) of high risk conditions such as severe/extensive coronary artery disease but it may also negatively impact on the choice of pharmacological therapy as coronary anatomy remains unknown. For this reason, efforts to improve adherence to currents guidelines recommendations are needed in NSTE-ACS patients.

4. Subgroups of NSTE-ACS patients medically managed

Patients with NSTE-ACS managed with a conservative strategy are a heterogeneous population which includes patients at very high risk of

Table 1
Management strategies in NSTE-ACS patients in four contemporary European registries.

Registry (enrollment period)	Patients with NSTE-ACS (n)	Patients undergoing coronary angiography (%)	Patients not undergoing coronary angiography (%)	Patients undergoing PCI (%)	Patients undergoing CABG (%)	Patients not undergoing revascularization (after coronary angiography) (%)
BLITZ 4[24] (2009–2010)	5786	4923 (85.0)	863 (14.9)	2898 (66.8)[a]	583[b] (13.4)	855 (19.8)
MANTRA[8] (2009–2010)	3563	2758 (77.4)	805 (22.6)	1505 (55)	NA	NA
FAST-MI[10] (2010)	1306	1185 (90.8)	121 (9.2)	859 (72)	66 (6)	260 (22)
EYESHOT[9] (2013)	1519	1258 (82.8)	261 (17.2)	831 (66)	140 (11)	287 (23)

NA: data not available.
[a] Of 4336 patients with available data.
[b] During hospital admission for ACS or planned during hospitalization.