Invasive mechanical ventilation in acute coronary syndromes in the era of percutaneous coronary intervention

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Albert Ariza Solé, Joel Salazar-Mendiguchía, Victòria Lorente-Tordera, José C Sánchez-Salado, José González-Costello, Pedro Moliner-Borja, Joan A Gómez-Hospital, Nicolás Manito-Lorite, Ángel Cequier-Fillat

Abstract

Background: Percutaneous coronary intervention (PCI) improves prognosis in patients with acute coronary syndromes (ACS) reducing ischaemic complications and the development of heart failure, thus potentially changing invasive mechanical ventilation (IMV) requirements. Little information exists about patients with ACS requiring IMV in the current era. We aimed to analyze IMV requirements and characteristics of ACS patients treated under current recommendations (including a high rate of PCI).

Methods: Baseline characteristics, indications for IMV, management and in-hospital and mid-term clinical course were analyzed prospectively in a consecutive series of patients with ACS admitted to a tertiary care hospital.

Results: We included 1821 patients, of which 106 (5.8%) required IMV. Mean follow-up was 347 days. PCI was performed in 84% of cases. Patients with IMV had more comorbidities, worse left ventricular function and more unstable hemodynamic parameters on admission. In-hospital mortality in patients requiring IMV was 29%. These patients also had higher mid-term mortality (hazard ratio (HR) 6.58; 95% confidence interval (CI) 4.49–9.64; p 0.001). The most common indication for IMV was cardiopulmonary arrest (CA) (65; 61%), followed by pulmonary oedema (27; 26%) and shock (14; 13.2%). Patients with CA were younger, with better hemodynamic parameters at admission, more favourable coronary anatomy and higher rates of PCI. There were no significant differences in overall mortality between the three groups. The main cause of death in CA patients was persistent vegetative state.

Conclusions: Mortality in patients with ACS requiring IMV remained high despite a high rate of PCI. Baseline characteristics, management and clinical course were different according to the reason for IMV. The most common cause for IMV requirement was CA.

Keywords

Acute coronary syndromes, percutaneous coronary, intervention, invasive mechanical ventilation, prognosis, mortality

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Percutaneous coronary intervention (PCI) has emerged during the last decades as one of the most important therapeutic tools in patients with acute coronary syndromes (ACS).¹ PCI improves the prognosis of patients with ACS,^{2,3} reducing the incidence of ischaemic complications and heart failure,⁴ especially in those patients at higher risk,^{5–7} thus potentially changing the need for invasive mechanical ventilation (IMV) in this clinical scenario. Little information is available regarding the profile of patients with ACS requiring IMV in the current era. Most of the few published articles regarding this subject come from an era when PCI was

not a widespread practice,^{8–12} had different methodologies and analyzed quite different populations.^{13–15}

Our objective was to better define the characteristics of ACS patients requiring IMV, the relative frequency of each of the indications for IMV, their in-hospital management

Bellvitge University Hospital, Spain

Corresponding author:

Albert A Solé, Cardiology Department, Bellvitge University Hospital, Feixa Llarga s/n 08907, L'Hospitalet de Llobregat, Barcelona, Spain.

Email address: aariza@bellvitgehospital.cat

and in-hospital and mid term clinical course in a consecutive series of ACS treated under current recommendations.

Methods

Study design and population

All consecutive patients admitted to the Coronary Care Unit (CCU) of our center with a diagnosis of ACS between October 2009 and April 2012 were prospectively included.

Definitions

ACS without ST segment elevation was defined as the presence of chest pain during the previous 48 h with ST segment changes on electrocardiography indicating ischemia or a positive troponin test. ACS with ST segment elevation was defined as the presence of chest pain with persistent ST-segment elevation of at least 0.1 mV in at least two contiguous leads or a new left bundle-branch block. Major bleeding was defined by the TIMI bleeding definition.¹⁶

Indications for IMV were divided in three groups: cardiac arrest, shock and pulmonary oedema. Cardiac arrest was defined as a cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation.¹⁷ Shock was defined as the presence of severe hypotension (systolic arterial blood pressure <90 mm Hg (or a systolic arterial blood pressure decrease of 40 mm Hg for patients with chronic underlying hypertension) leading to severe hypoperfusion of vital organs (including cyanosis, cold extremities, change in mental status, persistent oliguria, worsening of renal and/or hepatic function).^{18,19} Pulmonary oedema was defined as signs of lung congestion (the combination of severe dyspnea, rales covering both lung fields, and typical findings on a chest radiograph (diffuse interstitial or alveolar infiltrates) and severe respiratory insufficiency without fulfilling criteria for shock.^{19,20}

CCU treatment protocol

Criteria for CCU admission: ACS patients were considered suitable for CCU admission if they had an ACS with ST segment elevation or non-ST elevation myocardial infarction (NSTEMI) of intermediate-high risk, requiring ST segment changes suggesting ongoing ischemia or a positive troponin test. Patients with a life expectancy of less than one year, especially those with severely impaired quality of life, and patients considered not suitable to achieve relevant clinical benefit with invasive treatments because of their comorbidities were considered not suitable for CCU admission.

Criteria for IMV were (a) deterioration of consciousness with an inability to protect the airway and to maintain sufficient oxygen supply; (b) acute respiratory failure (arterial PO_2 <60 mm Hg; arterial PCO_2 >60 mm Hg; respiratory

rate >40 respirations/min, or a clinical course clearly leading to such conditions); or (c) cardiac arrest.

The main ventilation method after intubation as well as for the main period of ventilation was assisted volume control ventilation (95%) followed by pressure support ventilation (PSV) with positive end-expiratory pressure (PEEP) in the rest of patients.

The therapeutic hypothermia program was initiated at our center in March 2010. Therapeutic hypothermia was administered according to guidelines^{21,22} as soon as possible upon arrival to the CCU. Hypothermia was induced by infusion of 30 ml/kg of 4°C Ringer's solution and surface cooling using an external cooling system, the Arctic Sun® 2000 gel pads system (Bard, Covington, Georgia, USA). Target core temperature was 33–34°C and was maintained for 24 h with subsequent active rewarming of 0.25°C per hour until normothermia (37°C) was achieved.

The indications for therapeutic hypothermia were coma status following resuscitation from CA due to ventricular fibrillation (VF) or non-VF (including asystole) without initial response to reversal of sedation with flumazenil and naloxone. Patients with hemodynamic instability were considered not suitable for hypothermia. Neurological outcome was assessed using the five-item scale Cerebral Performance Category (CPC).²³ CPC was assessed at discharge from hospital. Brain death was assessed by clinical neurologic exploration in combination with trans-cranial Doppler examination.

Data collection

The data was collected prospectively on site by trained physicians using a standardized case report form. Baseline characteristics, medical history, biochemical and electrocardiographic findings, treatments administered during hospitalization, echocardiograms, coronary angiography results, IMV requirements, indications for IMV, other invasive procedures (e.g. intra-aortic counterpulsation), incidence of in-hospital complications (major bleeding and infection requiring antibiotics) and mortality were collected.

Creatinine clearance was calculated at admission using the Cockcroft-Gault formula.²⁴ Heart rate, systolic blood pressure and Killip class were measured on admission to the CCU. Monitor-measured heart rate was used and systolic blood pressure was measured by invasive monitoring or non-invasively in cases without invasive pressure line. For heart rate and systolic blood pressure values we used the mean from the first three measures in the first 30 minutes.

Follow-up criteria

Mid-term overall mortality was also assessed. Information on deaths was obtained from hospital records, death certificates or telephone contact with relatives of the patient or

referring physician. When there was more than one underlying cause of death, the assignment was made taking into consideration the most clinically relevant cause.

Baseline characteristics, procedures performed, treatments and clinical course were analyzed separately according to requirements and indications for IMV.

Statistical analysis

Variables were analyzed for normal distribution using the Shapiro-Wilk test. Quantitative variables are expressed as mean and standard deviation. Non-normally distributed variables are expressed as median and interquartile range. Categorical variables are expressed as numbers and percentages.

The relationship between quantitative variables that followed a normal distribution was analyzed with the Student's *t* test. Due to the small sample size, comparisons of quantitative variables according to the indications for IMV were performed using the non-parametric Kruskal-Wallis test. For the same reason, comparison of quantitative variables among ventilated patients who died and those who survived were performed using the non-parametric Mann Whitney U test. The relationship between categorical variables was analyzed with the Chi-square test, with the correction of continuity when indicated.

Baseline characteristics, treatments and procedures performed were compared between IMV patients who survived and IMV patients who died using Cox regression univariate regression analysis.

Survival analysis was performed using Kaplan Meier curves and differences between groups were evaluated using the log rank test. The PASW Statistics 18 (Chicago, Illinois, USA) was used for all analysis and a value of $p < 0.05$ was considered statistically significant.

Results

A total of 1821 patients were admitted to our CCU for an ACS during this period, of whom 106 (5.8%) required IMV. Baseline and clinical characteristics comparing both groups (IMV vs no IMV) are summarized in Table 1. In-hospital procedures and clinical course are summarized in Table 2. Patients requiring IMV had a higher prevalence of comorbidities, ST elevation myocardial infarction (STEMI), poorer left ventricular function, more unstable haemodynamic parameters (higher heart rate and lower systolic blood pressure) and higher Killip class on admission, requiring more often invasive procedures (pulmonary artery catheter, intra-aortic balloon counterpulsation). On the other hand, this group underwent less coronary angiographies, with a similar percentage of PCI and worse TIMI flow of the culprit lesion after PCI. Seventy-two of the 106 patients (68%) were intubated in the pre-hospital setting.

We obtained follow-up data in 1711 patients (94%). Mean follow up was 347 days. Patients needing IMV had a significantly higher mid-term mortality (hazard ratio (HR) 6.58; 95% confidence interval (CI) 4.49–9.64; $p < 0.001$). Sixteen out of 38 deaths (42%) in IMV patients were of non-cardiac origin. Cumulative survival in both groups is shown in Figure 1.

Table 1 also shows baseline characteristics regarding indications for IMV. Table 2 shows management and clinical course regarding the indications for IMV. The most common indication for IMV was CA ($n=65$, 61%). In general terms, patients with CA were younger, more frequently male and with less cardiovascular risk factors (except for smoking) and other comorbidities. CA patients had a higher incidence of STEMI, with higher rates of acute reperfusion (specially primary PCI). The lowest rate of acute reperfusion in STEMI was observed in patients intubated for shock. CA patients were in a more stable hemodynamic status on admission (higher systolic blood pressure and lower heart rate), with lower Killip class as compared to the rest of patients. They also had a more favorable coronary anatomy and a greater percentage of coronary angiograms and PCI. In addition, the rates of successful PCI were also higher than in patients with pulmonary edema or shock.

We also observed some differences regarding invasive procedures requirements and in-hospital course. In contrast to the rest, most of the CA patients were intubated in the pre-hospital setting. Their requirements of invasive procedures (Swan-Ganz catheter, intra-aortic balloon counterpulsation, dialysis) were lower. Patients with pulmonary edema or shock had higher rates of in-hospital major bleeding and need for transfusion than CA patients. Significant differences regarding infectious complications or in-hospital mortality between the three subgroups were not observed. The group with higher frequency of non-cardiac mortality was the CA group, mainly related to neurological sequelae of CA. Their discharge neurologic status was as follows: CPC 1: 47 (72.3%); CPC 2: 6 (9.2%); CPC 3: 1 (1.5%); CPC 4: 7 (10.8%); and CPC 5: 4 (6.2%). Twenty-four CA patients received mild therapeutic hypothermia. Their discharge neurologic status was as follows: CPC 1: 13 (54.2%); CPC 2: 4 (16.7%); CPC 3: 1 (4.2%); CPC 4: 4 (16.7%); and CPC 5: 2 (8.3%).

Two of the four patients who suffered brain death were organ donors. The remaining two patients were considered unsuitable for organ donation because of their comorbidities.

We did not observe significant differences in mid-term mortality regarding indications for IMV. However, we observed different timings of mortality according to the indication for IMV (Figure 2). Deaths occurred earlier in CA and shock patients than in pulmonary edema patients. Median duration of survival was 4.1 days in patients who died with shock, 4.4 days in patients who died with CA and 37 days in patients who died with pulmonary edema. In addition, deaths

Table 1. Baseline, clinical characteristics and angiographic data according to invasive mechanical ventilation requirements and indications.

	IMV requirements			IMV indications			
Baseline and clinical characteristics							
	IMV (n=106)	No IMV (n=1715)	p	Heart failure (n=27)	Shock (n=14)	Cardiac arrest (n=65)	p
Sex (male)	80 (76)	1330 (78)	0.631	15 (56)	10 (71)	55 (85)	0.012
Age (years)	62±11.6	62±13.0	0.941	68±8.4	69±9.0	58±11.8	0.000
Diabetes mellitus	36 (34)	476 (28)	0.168	16 (59)	6 (43)	14 (22)	0.002
Hypertension	64 (60)	983 (57)	0.536	22 (82)	12 (86)	30 (46)	0.001
Dyslipidemia	66 (62)	969 (57)	0.245	19 (70)	8 (57)	39 (60)	0.622
Active smoker	51 (48)	733 (43)	0.364	7 (26)	3 (21)	41 (63)	0.001
PAV	15 (14.2)	175 (10.2)	0.197	8 (30)	3 (21)	4 (6.2)	0.007
Previous MI	14 (13.2)	225 (13.1)	0.979	7 (26)	2 (14.3)	5 (7.7)	0.062
Renal failure	55 (57)	376 (23)	0.001	19 (76)	12 (86)	24 (42)	0.001
COPD	19 (17.9)	258 (15.0)	0.405	9 (33)	1 (7.1)	9 (13.8)	0.068
STEMI	85 (84)	1307 (78)	0.123	15 (58)	12 (86)	58 (95)	0.000
Anterior MI	57 (54)	724 (42)	0.179	14 (52)	7 (50)	36 (55)	0.924
Troponin +	106 (100)	1671 (97)	0.166	27 (100)	14 (100)	65 (100)	–
LVEF (%)	43 (12.9)	52 (10.8)	0.000	47 (15.3)	39 (12.3)	42 (11.1)	0.140
Killip class			0.001				0.000
I	54 (53)	1372 (82)		7 (27)	2 (16.7)	45 (71)	
II	7 (6.9)	221 (13.1)		2 (7.7)	1 (8.3)	4 (6.3)	
III	17 (16.8)	65 (3.9)		12 (46)	1 (8.3)	4 (6.3)	
IV	23 (23)	24 (1.4)		5 (19.2)	8 (67)	10 (15.9)	
STEMI management							
Reperfusion			0.078				0.009
Primary PCI	68 (74)	1099 (82)		13 (72)	6 (50)	49 (79)	
Lysis	14 (15.2)	55 (4.1)		1 (5.6)	2 (16.7)	11 (17.7)	
No acute reperfusion	10 (10.9)	136 (10.1)		3 (16.7)	4 (33)	3 (4.8)	
Ischemia time	255 (175–332)	224 (165–330)	0.345	292 (192–371)	258 (168–266)	255 (171–338)	0.573
Angiographic data							
Coronary angiogram	94 (89)	1662 (97)	0.001	23 (85)	10 (71)	61 (94)	0.045
PCI	85 (80)	1436 (84)	0.345	19 (70)	8 (57)	58 (89)	0.008
N affected vessels	1.8 (0.8)	1.6 (0.8)	0.089	2.4 (1.1)	2.1 (1.3)	1.5 (0.7)	0.000
Left main disease	8 (8.5)	83 (5.0)	0.135	4 (17.4)	2 (20)	2 (3.3)	0.046
Post-PCI 3 TIMI flow in culprit	75 (88)	1363 (95)	0.002	16 (84)	5 (63)	54 (93)	0.025

COPD: chronic pulmonary obstructive disease; IMV: invasive mechanical ventilation; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PAV: peripheral artery vasculopathy; PCI: percutaneous coronary intervention; STEMI: ST segment elevation myocardial infarction; TIMI: thrombolysis in myocardial infarction.

Data are presented as number (%) in qualitative variables and mean±standard deviation in quantitative variables. Renal failure is defined as a glomerular filtration rate < 60 ml/min; COPD is defined as previous clinical diagnosis of chronic obstructive pulmonary disease requiring chronic bronchodilator treatment; Ischemia time: Time from onset of symptoms to PCI. Ischemia time is expressed as median and interquartile range (25–75%).

occurred more often during the hospitalization period in patients with shock (100%) or CA (90%), in comparison to patients with pulmonary oedema (55%).

Table 3 shows baseline characteristics and invasive procedures in intubated patients who died and intubated patients who survived. Patients who died were more frequently male, diabetic, with chronic obstructive pulmonary disease (COPD), and renal failure. Interestingly, these patients had a tendency to undergo less coronary angiographies and PCI, with a higher number of invasive non-coronary procedures, longer duration of intubation and more

frequency of in-hospital intubation. Significant differences regarding the indication for IMV were not observed. Patients who died had significantly poorer left ventricular function and a more unstable hemodynamic parameters at admission.

Discussion

The main findings of our study were (a) ACS patients who required IMV had a worse prognosis, irrespective of their indication for IMV, (b) clinical characteristics,

Table 2. In-hospital invasive procedures and clinical course according to invasive mechanical ventilation requirements and indications.

	IMV requirements			IMV indications			
In-hospital procedures performed	IMV (n=106)	No IMV (n=1715)	p	Heart failure (n=27)	Shock (n=14)	Cardiac arrest (n=65)	p
In-hospital IMV	34 (32)	—		17 (63)	7 (54)	10 (15.9)	0.001
Duration IMV (days)	2 (1–6)	—		2 (1–6)	2 (1–8)	2 (1–5)	0.264
Tracheostomy	8 (7.5)	—		3 (11.1)	0	5 (7.7)	0.574
Non-invasive ventilation	12 (11.3)	11 (0.6)	0.001	9 (33)	0	3 (4.6)	0.001
Swan-Ganz catheter	24 (22)	21 (1.2)	0.001	10 (37)	5 (36)	9 (13.8)	0.024
Intra-aortic balloon	32 (30)	77 (4.5)	0.001	15 (56)	7 (50)	10 (15.4)	0.001
Renal replacement therapies	7 (6.6)	14 (0.8)	0.001	4 (14.8)	2 (14.3)	1 (1.5)	0.030
Therapeutic hypothermia	25 (24)	—		1 (3.7)	0	24 (37)	0.001
Clinical Course							
Major bleeding	9 (8.5)	9 (0.5)	0.001	3 (11.1)	4 (29)	2 (3.1)	0.006
Transfusion	19 (17.9)	26 (1.5)	0.001	7 (26)	5 (36)	7 (10.8)	0.032
Infections	48 (45)	43 (2.5)	0.001	13 (48)	6 (43)	29 (45)	0.960
In-hospital mortality	31 (29)	34 (2.0)	0.001	6 (22)	6 (43)	19 (29)	0.483
Overall mortality	38 (35)	79 (8.9)	0.001	11 (41)	6 (43)	21 (33)	0.480
Non-cardiac mortality	16 (15.1)	21 (1.2)	0.001	4 (36)	1 (16.7)	11 (52)	0.260

Data are presented as number (%) in qualitative variables and mean±standard deviation in quantitative variables. IMV: invasive mechanical ventilation. Duration of IMV is expressed as median and interquartile range (25–75%). Major bleeding was defined by the TIMI classification. Infections were defined as infectious complications requiring antibiotics.

Figure 1. Cumulative survival according to the need for invasive mechanical ventilation.

management and clinical course were different according to the reason for IMV and (c) the most common indication for IMV in our patients was CA.

PCI improves the prognosis of patients with ACS,^{2,3,5} reducing the ischemic complications and the development of heart failure.^{4,6,7} The advent of generalized

primary PCI in the management of these patients¹ and the early response of the emergency medical services may have contributed to the change in profile of patients admitted to CCUs during the last years.²⁵ Little information is available regarding IMV requirements in patients with ACS.

Figure 2. Overall survival according to indications for invasive mechanical ventilation.

Few previous studies have addressed this issue in different ways. Most of these studies analyzed patients who were admitted more than 10 years ago and with much lower rates of PCI:^{8–12} therefore management and prognosis of these patients was quite different to our series.

There are some more recent series with more updated management and higher rates of PCI.^{13–15} However, the selective inclusion criteria of these series, makes it difficult to establish the relative importance of each of the indications for IMV in the entire spectrum of ACS in the current era. Some authors included only ventilated patients for more than 24¹³ or 72 hours¹¹, others included only reperfused STEMI patients¹² and others included STEMI patients requiring CPR.^{14,15} Reflecting these inclusion criteria, their populations and rates of in-hospital mortality are also quite heterogeneous, but in general higher than in our series.

The information regarding the indications for intubation is quite contradictory. Some series do not include this information.^{9,11} In the rest, the relative frequency of each of the indications for IMV is as different as the populations analyzed. While in certain series, as in ours, cardiac arrest seems to be the most common indication for IMV,^{10,14,15} in others the findings are quite different. Lesage et al.¹² analyzed retrospectively a series of 157 patients with myocardial infarction subjected to reperfusion therapy in the first 12 hours and requiring IMV. The main indication for IMV

was cardiogenic shock (51%), followed by heart failure (45%). Patients from this series were admitted between 1996–2001. Around 20% of them were reperfused with fibrinolytics. In addition, the incidence of failed reperfusion was high (more than 20% of cases). These differences could have contributed to the higher incidence of cardiogenic shock in this population. Otherwise we cannot exclude some differences in inclusion criteria (patients in the series of Lesage et al were included if they were considered suitable to obtain benefit of PCI in the first 12 hours of admission) to justify differences observed in indications for IMV. Table 4 summarizes the main characteristics of these studies.

Our work describes, in a prospective fashion, a series of consecutive ACS patients requiring IMV and who received up-to-date management, including early PCI. Including all consecutive ACS patients allows us, in contrast to previous studies, to reflect the nature of the entire spectrum of ACS patients requiring IMV and to assess the relative importance of each of the indications for IMV in the current era.

Thus, the description of three groups according to the indication for IMV, with different risk profile, comorbidities and clinical course is one of the most interesting contributions of the present work.

The most numerous group involved patients with CA, who were younger, had less comorbidities and a higher incidence of STEMI and acute reperfusion than the rest of

Table 3. Baseline characteristics and procedures performed according to vital status.

	Death with IMV (n=38)	Alive with IMV (n=57)	p
Age (years)	64±10.8	62±12.5	0.425
Male sex	32 (84)	39 (68)	0.083
Diabetes mellitus	15 (40)	19 (33)	0.663
Active smoker	19 (50)	27 (47)	0.836
Previous MI	5 (13.2)	7 (12.3)	0.568
COPD	9 (24)	9 (15.8)	0.425
Renal failure	24 (75)	24 (45)	0.007
STEMI	30 (86)	47 (86)	0.973
LVEF (%)	38±15.2	46±11.1	0.028
Coronary angiogram	31 (82)	53 (93)	0.089
PCI	28 (74)	48 (84)	0.295
Ischemia time (min)	264 (171–442)	248 (189–340)	0.442
Number of vessels affected	1.77 (1.1)	1.74 (0.9)	0.349
Killip class			0.042
I	16 (43)	35 (65)	
II	5 (13.5)	2 (3.7)	
III	4 (10.8)	9 (16.7)	
IV	12 (32)	8 (14.8)	
Systolic blood pressure	103±24	126±31	0.001
Heart rate	102±20	94±20	0.068
Indication for IMV			
Pulmonary edema	11 (29)	13 (23)	0.535
Shock	6 (15.8)	6 (10.5)	
CA	21 (55)	38 (67)	
In-hospital IMV	17 (47)	15 (25)	0.028
Duration of IMV (days)	5 (1.7–7.2)	1 (1–3.5)	0.013
Intra-aortic balloon	15 (40)	12 (21)	0.051
Swan-Ganz catheter	12 (31)	9 (15.8)	0.069
Renal replacement therapies	5 (13.2)	2 (3.5)	0.078

COPD: chronic pulmonary obstructive pulmonary disease; IMV: invasive mechanical ventilation; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention. STEMI: ST segment elevation myocardial infarction.

Data are presented as number (%) in qualitative variables and mean±standard deviation in quantitative variables. Ischemia time (time from onset of symptoms to PCI in STEMI patients) and duration of IMV are presented as median and interquartile range (25–75%). COPD is defined as previous clinical diagnosis of chronic obstructive pulmonary disease requiring chronic bronchodilator treatment; Renal failure is defined as glomerular filtration <60 ml/min.

IMV patients. Their more stable hemodynamic status on admission lead to less invasive procedures. This group showed the highest proportion of non-cardiac related deaths, mainly due to neurological consequences of post-anoxic encephalopathy. Patients with CA who survived the initial hospitalization period had a low rate of post-discharge mortality.

The data in our series showed an elevated mortality, although less than previously reported. The lower incidence of cardiogenic shock in our patients, as compared to previous data, may be justified in part by an updated management and higher rate of PCI in this clinical scenario, thus leading to a better clinical outcome.

On the other hand, we included all consecutive ACS patients admitted to our CCU. As mentioned before, different inclusion criteria in other series may probably contribute to select higher risk populations than ours, thus making

it difficult to compare clinical outcomes between these quite different populations.

Patients requiring IMV had a greater need for invasive procedures compared with the rest, possibly due to the greater overall severity of their clinical scenario. Paradoxically, coronary angiography was performed less frequently in this group. This apparent paradox has been previously described¹⁰ and can be explained by a probable selection bias derived from the severity of the patients and complications of the disease that yielded them to be considered as not suitable candidates for certain interventions.

The use of noninvasive ventilation (NIV), while not a specific objective of this study, requires a special comment. Its low utilization in our series is due in part to the high frequency of prehospital intubation, which precluded the use of NIV before IMV. On the other hand, the high frequency of CA and shock, in which the use of NIV is

Table 4. Main characteristics of previous studies regarding endotracheal intubation in acute coronary syndromes.

Authors	Period of inclusion	n	Population	Design	% PCI	Mortality	Indications for IMV
Lopez Mesa	1999	335	MI and MV	R	NA	65.7% I-H	Not specified (60% CS)
Kouraki	2001–2002	458	MI and IMV	P	39	48% I-H	48% VT/ VF CA 39% HF
Zahger	1998–2002	267	ACS, IMV>72 h	R	51	29% (I-H) 45% (1-year)	Not specified
Lesage	1996–2001	157	MI reperfusion <12 h and IMV	R	All	51% (28 d)	51% CS 45 % PE 35% CA
Ernan	2006–2008	51	MI IMV>24 h	P	67	43% I-H	Not specified (55% CR)
Koeth	2003–2004	190	STEMI and pre-hospital CR	P	55	37% in-hospital	CR (80% VF)
Speiser	1978–1981	112	MI and IMV	–	–	75% I-H	50% arrhythmias 50% HF
Peels	2004–2005	38	STEMI primary PCI successful CR	P	All	50% I-H	CA

ACS: acute coronary syndromes; CA: cardiac arrest; CR: cardiac resuscitation; CS: cardiogenic shock; HF: heart failure; I-H: in-hospital; IMV: invasive mechanical ventilation; MI: myocardial infarction; MV: mechanical ventilation; NA: not assessed; PCI: percutaneous coronary intervention; PE: pulmonary edema; R: retrospective; P: prospective; STEMI: ST segment elevation myocardial infarction; VF: ventricular fibrillation; VT: ventricular tachycardia.

discouraged, also explains the low frequency of NIV. In patients with in-hospital intubation due to pulmonary oedema, NIV was used in approximately 50% of cases.

The low rate of hypothermia in our series (less than a half of CA patients) is due to several reasons. Our hypothermia program was started a few months later after the initiation of our study. Otherwise, we did not apply hypothermia in patients showing good neurologic response on admission using sedation antagonists such as flumazenil and naloxone. This possible selection bias might also be an explanation for the worse neurologic outcome observed in patients treated with therapeutic hypothermia.

Our study has several limitations. It is a single-center study with a relatively small number of intubated patients. As it is an observational study, the indication leading to IMV was taken under each physician's clinical criteria, possibly leading to certain bias. In addition, it is a quite recent series with short follow-up periods in some of our patients. The sample is a heterogeneous one, with most of the patients having STEMI and around 20% non-ST elevation ACS. Finally, our inclusion criteria were different to the previous studies, making it difficult to compare the outcomes of these quite different populations.

Our hypothesis was that the current management of ACS could have contributed to a change in the incidence of the indications for IMV of patients admitted to CCUs. In spite of the limitations of our study, we believe that the finding of CA as the main indication for IMV in our series, in contrast to previous data,^{4,5,8} might support this hypothesis.

We also believe that the heterogeneity of our population is in turn one of the strengths of our work. The prospective inclusion of consecutive ACS patients in our series reflects the reality of IMV requirements in this

clinical scenario in the current era. The description of different groups of patients according to the indications for IMV with different risk profile, management requirements and outcomes has not been properly described in this clinical scenario.

Conclusions

Mortality in patients with ACS requiring IMV remains high regardless of the advances in the management, including early PCI in an elevated number of patients. The baseline characteristics, management and clinical course were different according to the reason for IMV. The most common indication for IMV in our series was CA.

Conflict of interest

The authors declare that there are no conflicts of interest.

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