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Mechanical ventilation in the early phase of ST elevation myocardial infarction treated with mechanical revascularization

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Abstract

Background: *So far, few data have been available on the incidence and outcome of patients with acute myocardial infarction (MI) requiring mechanical ventilation (MV). The aim of the study was to assess the clinical and prognostic impact of MV at short and long term in 106 patients with ST elevation MI (STEMI) requiring mechanical ventilation.*

Results: *The incidence of mechanical ventilation was 7.6%. Reasons for intubation were as follows: cardiogenic shock in 64 (60.4%) patients, ventricular fibrillation in 32 (30.1%) patients and acute pulmonary edema in 10 (9.5%) patients. Patients submitted to MV were older ($p = 0.016$), more frequently had a previous percutaneous coronary intervention (PCI; $p = 0.014$) and a previous MI ($p = 0.001$). A higher in-Intensive Cardiac Care Unit death was observed in MV patients (44.3% vs. 1.5%, $p < 0.001$), as well as a higher mortality at follow-up (36.7% vs. 14.8%, $p < 0.001$). MV was associated with higher mortality rates both at short and long term.*

Conclusions: *In a large series of consecutive STEMI patients submitted to MV, the need of MV is a strong prognostic indicator of mortality both at short and long term. Among mechanically ventilated STEMI patients infarct size (as inferred by TnI values) and PCI failure were independent predictors of early death, while the duration of MV was related to death at long term.* (Cardiol J 2013; 20, 6: 612–617)

Key words: ST elevation myocardial infarction, mechanical ventilation, percutaneous coronary intervention, prognosis, long term

Introduction

In critically ill patients, mechanical ventilation (MV), and its impact on outcome has been extensively studied [1–3], while so far few data have been available on the incidence and outcome of patients with acute myocardial infarction (MI) requiring MV [4–7].

The present investigation was aimed at assessing the clinical characteristics and prognosis (both at short and long term) of 106 consecutive patients with ST elevation MI (STEMI) requiring MV, all treated with primary percutaneous coronary intervention (PCI) and admitted to our Intensive Cardiac Care Unit (ICCU).

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Methods

From 1 April 2004 to 31 December 2010, 1231 consecutive patients with STEMI (within 12 h from symptoms' onset) [8] were admitted to our ICCU, which is located at a tertiary center. In our hospital, in Florence, the reperfusion strategy of STEMI patients is represented by primary PCI [9–12] (no exclusion criteria). STEMI patients are first evaluated by the Medical Emergency System staff in the pre-hospital setting and then directly admitted to the catheterization laboratory or transferred to it after a rapid stabilization in the First Aid. After primary PCI, they are admitted to our ICCU. Data were stored in a prospective registry on which a retrospective analysis had been carried out.

A successful procedure was defined as an infarct artery stenosis < 20% associated with Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow. Failure PCI was defined as resulting in TIMI grade 0 to 2 flow, regardless the residual stenosis.

The diagnosis of STEMI was based on the criteria of the American College of Cardiology/ /American Heart Association [13].

On ICCU admission, after PCI, in a fasting blood sample the following parameters were measured: sodium [mEq/L], glucose [g/L], glycated hemoglobin [Hb, %], troponin I [TnI, ng/mL], uric acid [mg/dL], NT-pro B-type natriuretic peptide [NT-proBNP, pg/mL], erythrocyte sedimentation rate (ESR), leukocytes count [$\times 10^3/\mu$L], fibrinogen [mg/dL] and hs-C-reactive protein positivity (hs--CRP). Creatinine [mg/dL] was also measured, in order to calculate glomerular filtration rate [GFR, mL/min/1.73 m^2], on admission and at discharge [14]. Glucose, TnI and creatinine were measured 3 times a day and peak values were examined. Acute insulin resistance was assessed by means of the Homeostatic Model Assessment (HOMA), as previously described [15].

Transthoracic 2-dimensional echocardiography was performed on ICCU admission in order to measure left ventricular ejection fraction (LVEF).

Ventilatory support (invasive and non-invasive ventilation), ultrafiltration (continuous-veno-venous ultrafiltration, CVVHDF) and intra-aortic balloon pump (IABP) implantation were used when needed [9, 11].

According to the policy of our center, sedoanalgesia (propofol + remifentanil) was administered to patients submitted to MV.

The primary endpoint was in-ICCU death and all-cause mortality at follow-up.

The study protocol was in accordance with the Declaration of Helsinki and approved by the local Ethics Committee. Informed consent was obtained from all the patients before enrollment.

Statistical analysis

Statistical analysis has been conducted with PASW 17.0 for Windows software (SPSS Inc, Chicago, IL). In all cases, a 2-tailed $p < 0.05$ has been considered statistically significant. After assessment of normality by means of Kolmogorov--Smirnov test for one sample, continuous variables have been reported as mean ± standard deviation or median (interquartile range: IQR); categorical variables have been depicted as frequency (percentage). For continuous variables, between-groups comparisons have been performed with Student's t-test or by means of Mann-Whitney U test. Categorical variables have been compared with χ^2 or Fisher's exact test when needed.

In the overall population predictors of death, both in-ICCU and at follow-up, have been investigated by means of logistic and Cox regression analyses, respectively. In multivariable analyses candidate variables were carefully chosen among those known to be clinically related to outcome in order to avoid model overfitting. Possible predictors for in-ICCU death were age (1 year step), admission glycemia (1 g/L step), LVEF (1% step), admission estimated GFR (eGFR; 1 mL/min/1.73 m^2 step), admission Hb (1 g/dL step) and MV; for long-term death candidate predictors were age (1 year step), nadir eGFR (1 mL/ /min/1.73 m^2 step), admission Hb (1 g/dL step), LVEF (1% step), previous acute MI and MV.

To adjust to the need of MV, a propensity analysis was carried out using a non-parsimonious logistic regression to determine the probability of a patient to receive MV. The variables included in the propensity score model were age, gender, previous PCI, previous MI, symptom-to-balloon time, PCI failure, length of ICCU stay, admission glycemia, peak TnI, history of hypertension, history of diabetes, smoking habit, location of the STEMI, heart rate and blood pressure at admission, and Killip's classification at admission. The goodness-of-fit of the propensity score model was obtained by the c-statistics.

Results

In our series, the incidence of MV was 7.6% (106/1294). In the pre-hospital setting 55 patients were intubated (51.8%), 18 patients in the Catheterization Laboratory (16.9%), 24 patients on

Table 1. Clinical characteristics.

	No MV N = 1188 (91.8%)	MV N = 106 (7.6%)	P
Age [years]	66.6 ± 12.8	69.7 ± 13.0	0.016
Males/females	883/305 (74.3%/25.7%)	72/34 (67.9%/32.1%)	0.188
Body mass index [kg/m^2]	26.3 ± 3.6	25.8 ± 3.8	0.145
History of:			
Diabetes mellitus	310 (24.0%)	33 (31.1%)	0.099
Smoking	812 (62.8%)	55 (51.9%)	0.027
COPD	117 (9.0%)	7 (6.6%)	0.396
Previous PCI	170 (13.1%)	23 (21.7%)	0.014
Previous MI	169 (13.1%)	26 (24.5%)	0.001
Hypertension	684 (52.9%)	56 (52.8%)	0.995
Symptoms-to-balloon time [min], median (IQR)	226 (150–300)	279 (180–335)	0.010
Acute MI location:			0.005
Anterior	665 (51.4%)	74 (69.8%)	
Inferior	525 (40.6%)	24 (22.6%)	
Other	104 (8.0%)	8 (7.5%)	
Coronary artery disease:			0.060
1-vessel	517 (40.0%)	30 (28.3%)	
2-vessel	430 (33.2%)	43 (40.6%)	
3 - vessel	347 (26.8%)	33 (31.1%)	
Left main coronary artery	71 (5.5%)	14 (13.2%)	0.001
CABG	31 (2.4%)	1 (0.9%)	0.508
PCI failure	66/1282 (5.1%)	20/105 (19.0%)	< 0.001
Killip class:			< 0.001
I–II	1080 (92.4%)	42 (39.6%)	
III–IV	89 (7.6%)	64 (60.4%)	
Admission LVEF [%]	42 (35–50%)	40 (35–48%)	0.025
LOS [h], median (IQR)	66 (48–90)	96 (50–168)	< 0.001
ICCU-death	19 (1.5%)	47 (44.3%)	< 0.001
Follow-up death (n = 1081)	153/1032 (14.8%)	18/49 (36.7%)	< 0.001

MV — mechanical ventilation; COPD — chronic obstructive pulmonary disease; PCI — percutaneous coronary intervention; MI — myocardial infarction; IQR — interquartile range; CABG — coronary artery bypass graft; LVEF — left ventricular ejection fraction; LOS — length of stay; ICCU — intensive cardiac care unit

hospital admission in the Emergency Department (22.6%) and the remaining 9 (8.7%) patients in ICCU. Reasons for intubation were as follows: cardiogenic shock in 64 (60.4%) patients, ventricular fibrillation in 32 (30.1%) patients and acute pulmonary edema in 10 (9.5%) patients. Non invasive ventilation was performed in 6 patients (all with acute pulmonary edema) but it was unsuccessful and they were promptly intubated. Tracheotomy was performed in 11 (10.3%) patients, in all but one percutaneously. One patient accidentally auto-extubated and was promptly re-intubated. Among patients discharged alive, MV was stopped in 37 patients (37/59, 62.7%) within the first 48 h since ICCU admission. Ventilatory associated pneumonia was observed in 23 (21.6%) patients, among whom 15 patients died.

As depicted in Table 1, patients submitted to MV were older ($p = 0.016$), more frequently had a previous PCI ($p = 0.014$) and a previous MI ($p = 0.001$). Time to symptoms-to-balloon was longer in MV patients ($p = 0.010$) who showed more frequently an anterior wall MI ($p = 0.005$), a higher incidence of PCI failure ($p < 0.001$), advance Killip class ($p < 0.001$) and a longer length of stay ($p < 0.001$). A higher in-ICCU death was observed in MV patients ($p < 0.001$), as well as a higher mortality at follow-up.

As depicted in Table 2, MV patients showed higher values of admission and peak glycemia ($p < 0.001$ and $p < 0.001$, respectively), peak TnI ($p < 0.001$), NT-proBNP ($p < 0.001$), uric acid ($p < 0.001$) and a higher incidence of HOMA

Table 2. Laboratory data.

	No MV N = 1188 (91.8%)	MV N = 106 (7.6%)	P
Admission glucose [mg/dL]	1.30 (1.09–1.60)	1.82 (1.35–2.71)	< 0.001
Peak glycemia [mg/dL]	1.48 (1.25–1.87)	2.06 (1.71–3.05)	< 0.001
Insulin [mU/L]	9.5 (5.6–16.8)	13.8 (5.2–41.8)	0.010
HOMA positivity [%]	106/757 (14.0)	25/58 (53.1)	< 0.001
Glycated hemoglobin [%]	5.9 (5.6–6.4)	6.0 (5.7–6.6)	0.448
Admission eGFR [mL/min/1.73 m^2]	85.7 ± 30.9	66.1 ± 38.8	< 0.001
Nadir eGFR [mL/min/1.73 m^2]	72.9 ± 25.6	45.2 ± 28.3	< 0.001
Microalbuminuria [mg/dL]	16.7 (6.3–53.9)	41.6 (10.6–158.0)	0.001
Peak TnI [ng/mL]	80.4 (35.5–171.5)	128.9 (59.1–384.9)	< 0.001
NT-proBNP [pg/mL]	1221 (426–3002)	3688 (1682–14356)	< 0.001
Uric acid [mg/dL]	5.6 ± 1.7	7.0 ± 2.5	< 0.001
ESR [mm/h]	22 (12–40)	33 (17–55)	0.002
Leucocytes [$\times 10^3/\mu L$]	10.7 (8.7–13.4)	13.4 (11.1–18.7)	< 0.001
hs-CRP positivity [%]	422/868 (48.6)	47/64 (73.4)	< 0.001
Fibrinogen [mg/dL]	402 (339–478)	420 (342–526)	0.066

MV — mechanical ventilation; HOMA — homeostatic model assessment; eGFR — estimated glomerular filtration rate; TnI — troponin I; NT-proBNP — NT-pro B-type natriuretic peptide; ESR — erythrocyte sedimentation rate; CRP — C-reactive protein

Table 3. Devices.

Variable	All patients	No MV	MV	P
CVVHDF	54 (4.1%)	25 (2.1%)	29 (27.4%)	< 0.001
IABP	298 (23.1%)	227 (19.1%)	71 (67.0%)	< 0.001
2 device	73 (5.6%)	21 (1.7%) IABP, CVVHDF or cPAP	52 (49.1%) MV and (IABP or CVVHDF)	< 0.001
3 device	31 (2.3%)	7 (0.6%) IABP, CVVHDF or cPAP	24 (22.6%) MV and (IABP + CVVHDF)	< 0.001

MV — mechanical ventilation; CVVHDF — continuous-venous-venous ultrafiltration; IABP — intra-aortic balloon pump; cPAP — continuous positive airway pressure ventilation

positivity ($p < 0.001$). Lower values on admission and nadir eGFR ($p < 0.001$ and $p < 0.001$, respectively) were observed in MV patients who exhibited a higher inflammatory activation, as inferred by higher values of ESR ($p = 0.02$), leukocytes ($p < 0.01$) and hs-CRP positivity ($p < 0.001$).

As shown in Table 3, MV patients were more frequently submitted to CVVHDF ($p < 0.001$) and IABP ($p < 0.001$), as well as to 2 or 3 devices simultaneously ($p < 0.001$).

At multivariable regression analysis, the following variables were independent predictors of in-ICCU death (when adjusted for admission eGFR): age (1 year step) (OR: 1.06, 95% CI 1.03–1.10, $p < 0.001$); admission glycemia (1 g/L step) (OR: 1.65, 95% CI 1.09–2.50, $p = 0.018$); LVEF (1% step) (OR: 0.96, 95% CI 0.93–1.00, $p = 0.037$); MV (OR: 6.72, 95% CI 2.93–15.38, $p < 0.001$). Hosmer-Lemeshow goodness-of-fit test χ^2 11.3, $p = 0.183$; Nagelkerke pseudo R^2 0.44.

Patients were followed-up for 37.9 (25^{th}–75^{th} percentile: 14.5–60.7) months.

At multivariable Cox regression analysis, the following variables were independent predictors of death at follow-up: age (1 year step) (HR: 1.06, 95% CI 1.05–1.08, $p < 0.001$); nadir eGFR (1 mL/min/1.73 m^2 step) (HR: 0.98, 95% CI 0.97–1.00, $p < 0.001$); LVEF (1% step) (HR: 0.98, 95% CI 0.97–1.00, $p = 0.010$); MV (OR: 1.81, 95% CI 1.08–3.05, $p = 0.026$).

Propensity score analysis

Area under the receiving operator characteristic (ROC) curve was 0.95 (95% CI 0.91–0.98), $p < 0.001$.

According to the propensity score analysis the incidence of in-ICCU mortality was higher in patients submitted to mechanical ventilation in respect to those who were not (44.3% vs. 12.3%, $p < 0.001$). At long term, the incidence of death was higher in patients who were submitted to MV, though it did not reach statistical significance (36.7 vs. 27.8, $p = 0.292$).

At multivariable regression analysis MV was an independent predictor of early death (OR: 6.72, 95% CI 2.93–15.38, $p < 0.001$).

At Cox regression analysis the following variables were independent predictors of long term mortality (when adjusted for nadir eGFR): age (1 year step) (HR: 1.08, 95% CI 1.05–1.13, $p < 0.001$); MV (HR: 1.93, 95% CI 1.02–3.65, $p = 0.044$).

Among STEMI patients submitted to mechanical ventilation

At multivariable regression analysis, the following variables were independent predictors of in-ICCU death (when adjusted for age): TnI (10 g/ /mL) (OR: 1.03, 95% CI 1.01–1.06, $p = 0.003$); PCI failure (OR: 5.97, 95% CI 1.76–20.23, $p = 0.004$).

At multivariable Cox regression analysis, the following variables were independent predictors of death at follow-up (when adjusted for discharge LVEF): age (1 year step) (HR: 1.07, 95% CI 1.02–1.12, $p = 0.005$); duration of MV (1 h/step) (HR: 1.01, 95% CI 1.00–1.02, $p = 0.001$).

Discussion

The main findings of the present investigation, performed in 106 consecutive STEMI patients requiring MV submitted to PCI, are as follows: a) MV in the early phase of STEMI is not uncommon, being detectable in the 7.6% of the entire population; b) MV patients are older and show a larger infarct size (as indicated by higher values of peak TnI and NT-proBNP), a higher inflammatory activation (as inferred by higher values of hs-CRP positivity and leukocyte count); c) MV in the early phase of STEMI is associated with an increased risk of death both at short and long term.

So far, few data have been available on the prognostic impact of MV in acute MI and results are scarcely comparable due to differences in patients' selection criteria (NSTEMI vs. STEMI) [4, 6, 16] and type of revascularization (thrombolysis vs. mechanical revascularization) [4, 7].

We reported, for the first time, the prognostic impact of MV in a large series of consecutive STEMI patients submitted to PCI. In our series the incidence of MV was higher in respect to that reported previously (7.6% vs. 1.6%) [6], but differently from Eran et al. [6] we only included STEMI patients (instead of acute coronary syndrome patients).

In accordance with previous studies [4–6, 17] we observed that MV patients exhibited a higher mortality rate (44.3%). In 2001 Lopez Messa et al. [17] reported a 65.7% mortality rate among 333 mechanically ventilated patients with acute MI in a retrospective analysis from the Spanish registry ARIAM (Analisis Retraso Infarto Agudo Miocardio). In 157 consecutive patients with acute MI requiring MV admitted to an intensive care unit and submitted to coronary reperfusion within 12 h of symptom onset in-hospital mortality rate was 50.9%. Similarly, in a subgroup of consecutive STEMI and NSTEMI patients of the German BEAT registry the overall hospital mortality rate was 48% [4] and in a small series of 51 consecutive acute MI patients who received MV for > 24 h, mortality rate was 43%. In a recent paper by Bhave et al. [5], MV was one of the predictors of the development of left ventricular dysfunction in the course of STEMI.

In our series MV is a strong independent predictor for mortality, since MV patients are older, with a larger infarct size (as indicated by peak TnI) [18–20], hemodynamic impairment (as inferred by advanced Killip class) and a higher incidence of multi-organ dysfunction (as indicated by lower eGFR and a higher use of devices, often simultaneously implanted).

Moreover, in our population, MV was associated with higher mortality rates even at follow-up. This is in accordance with previous findings by Zahger et al. [16] who described in 2005 a 30-day mortality of 29% and a 1-year mortality of 46% in a retrospective cohort of 267 consecutive patients admitted to the coronary care unit for an acute coronary syndrome requiring MV.

According to our data, among STEMI patients submitted to MV, infarct size (as inferred by TnI values) and PCI failure are independent predictors of early death, thus underscoring, even in this subgroup of STEMI patients, the impact on prognosis of a successful mechanical revascularization.

We observed, for the first time, that the duration of MV is related to death at long term in STEMI patients mechanically ventilated; this finding strongly suggests that MV should be withheld as soon as possible in these patients. However, further studies performed in larger cohorts are needed to confirm these data.

Conclusions

According to our data, among STEMI patients submitted to MV, infarct size (as inferred by TnI values) and PCI failure are independent predictors of early death, thus underscoring, even in this subgroup of STEMI patients, the impact on prognosis of a successful mechanical revascularization.

We observed, for the first time, that the duration of MV is related to death at long term in STEMI patients mechanically ventilated; this finding strongly suggest that MV should be withheld as soon as possible in these patients. However further studies performed in larger cohorts are needed to confirm these data.

Conflict of interest: none declared

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