



Endotracheal intubation and outcome in high-risk patients with acute myocardial infarction undergoing primary angioplasty

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Abstract

Background: Patients with acute myocardial infarction (AMI) who undergo endotracheal intubation (ETI) are at high risk for mortality, but the outcome of those patients submitted to primary angioplasty (PCI) has not yet clearly reported.

Methods: We collected data about all consecutive patients with AMI within 12 hours who underwent primary PCI and analyzed clinical and procedural characteristics as well as in-hospital mortality of ETI compared to no-ETI patients.

Results: From September 2001 to June 2010, 1251 patients underwent primary PCI and 99 (7.9%) of them underwent ETI. ETI patients were more likely to be hypertensive (76.8% vs 67.8%, $p=0.003$), diabetic 43.4% vs 17.9%, $p<0.0001$), resuscitated by cardiac arrest (68.7% vs 0.7%, $p<0.0001$), to present with cardiogenic shock (CS) (61.6% vs 8.1%, $p<0.0001$), with a lower left ventricular ejection fraction (LVEF) ($38.9\pm 9.4\%$ vs $48.9\pm 9.2\%$, $p<0.0001$) and to be treated with intra-aortic balloon counterpulsation (IABP) (60.1% vs 15.4%, $p<0.0001$). The in-hospital mortality was higher in ETI patients (37.4% vs 4.3%, $p<0.0001$) and they were more likely to undergo stent thrombosis (3% vs 0.34%, $p=0.006$). After using the propensity score modelling. Considering the risk profile, ETI was associated to higher in hospital mortality in the patients at higher risk (39.8% vs 18.5%, $p=0.003$). Moreover, ETI was one of the most powerful predictors of in-hospital mortality at multivariate analysis (OR 37.04, 95% CI 6.0-228.45, $p=0.0001$).

Conclusions: ETI was found to be an independent predictor of mortality in high-risk AMI patients undergoing primary angioplasty. The implications for current clinical care remained undefined.

Keywords: Acute myocardial infarction, endotracheal intubation, primary percutaneous coronary intervention, primary angioplasty

Introduction

Acute myocardial infarction (AMI) represents one of the most frequent causes of lifethreatening diseases. In most industrialized countries, there is a trend toward lower mortality rates from coronary artery disease, achieved, at least in part, first by primary prevention [1] and second by the contribution of the coronary care units [2]. Despite considerable medical advances during the last decades in the management of AMI, including the early use of reperfusion strategies with primary angioplasty (PCI) with or without coronary stenting [3,4], the mortality rate remains high in high-risk settings such as cardiac arrest necessitating cardiopulmonary resuscitation, acute pulmonary edema, cardiogenic shock and reduced left ventricular ejection fraction (LVEF) ≤ 0.40 [5-7]. All these events may increase the severity and the number of failed organs, with a mortality rate reported to be as high as $\geq 60\%$ [8].

Despite aggressive management, some of these patients require endo-tracheal intubation (ETI) and invasive mechanical ventilation. Nevertheless, little is known about the prognosis of patients admitted for complicated AMI requiring ETI and mechanical ventilation undergoing primary angioplasty. The aim of this retrospective study was to assess the clinical characteristics and the in-hospital mortality of a population of patients with complicated AMI who underwent primary PCI

requiring ETI compared to the patients who did not require ETI and to evaluate the risk of ETI itself as independent predictor of mortality.

Methods

We reviewed the data of all consecutive patients with AMI admitted to our hospital between September 2001 and June 2010 and treated by primary PCI within 12 hours of symptom onset. Demographic, clinical and procedural data were collected in a dedicated database (Cardioplanet V.3.0.8, Ebit Aet S.p.A., Genoa, Italy). The study protocol was reviewed and approved by the Ethics Committee of our Institution (ASL 103, Piemonte Region, Italy).

AMI was defined as typical chest pain lasting more than 30 minutes associated with >0.1 mV ST-segment elevation in ≥ 2 contiguous electrocardiogram (ECG) leads or with new left bundle branch block. Cardiogenic shock was defined as systolic blood pressure <90 mmHg (without inotropic drugs or intra-aortic balloon pump support) secondary to severe ventricular dysfunction and associated with signs of end-organ hypoperfusion (e.g., cold and diaphoretic extremities, altered mental status, anuria). The diagnosis of acute cardiogenic pulmonary edema was disclosed when patients presented the combination of severe dyspnea on exertion, rales covering

both lung fields, and typical findings on a chest radiograph (diffuse interstitial or alveolar infiltrates).

All AMI patients who complained symptoms for ≤ 12 hours were immediately transferred to the catheterization laboratory for urgent coronary angiography. The use of abciximab, thrombus aspiration (TA), intra-aortic balloon pump (IABP) support was at the total discretion of the operator. A successful procedure was defined as a residual stenosis of treated vessels $< 40\%$ associated with a Thrombolysis In Myocardial Infarction (TIMI) 3 grade flow [9].

All patients were routinely treated with aspirin (325 mg upon arrival, and then 100 mg daily), clopidogrel (loading dose of 300 or 600 mg, and then 75 mg daily) and with an intravenous bolus of unfractionated heparin (100 U/kg body weight, or 60 U/kg body weight if also abciximab was given). Heparin therapy was stopped after the procedure, but, in case of IABP use, it was continued until its removal. When used, abciximab infusion was continued for 12 hours after the procedure. The patients undergoing ETI received the oral antiplatelet therapy through a nasogastric tube until the withdrawal of mechanical ventilation. All patients underwent an echocardiogram before coronary angiography to assess the LVEF by Simpson's rule [10] and to rule out mechanical complications (i.e., cardiac tamponade, interventricular septum or left ventricular free wall rupture, acute mitral regurgitation due to papillary muscle rupture).

Clinical end-points

The primary end point of the study was in-hospital death. Furthermore, we evaluated the occurrence of stent thrombosis and of major bleedings. Stent thrombosis was defined as definite and probable according to the Academic Research Consortium [11]; major bleedings were defined according to the Thrombolysis In Myocardial Infarction (TIMI) classification [12].

Statistical analysis

Data are reported as means (with standard deviations) or proportions. Continuous variables were compared by t-test, whereas categorical variables were compared by chi-square test. Multivariate logistic regression analysis was applied to identify independent predictors of in-hospital mortality. To this scope all variables showing p values < 0.1 at standard statistical analysis were entered into the multivariate model and included age ≥ 75 years, female gender, hypertension, diabetes, anterior location of STEMI, cardiac arrest, ETI, cardiogenic shock, LVEF $\leq 40\%$, total ischemic time (time from symptoms onset to reperfusion with PCI), multivessel disease, left main coronary artery disease, pre-PCI TIMI flow < 2 , use of IABP, lack of use of glycoprotein IIb/IIIa inhibitors, and lack of stent implantation. A p value < 0.05 was always required for statistical significance. To reduce the impact of treatment selection bias and potential confounding in an observational study, we performed rigorous adjustment for differences in

baseline characteristics of patients by the use of weighted Cox proportional hazards regression models with the inverse probability of treatment weighting (IPTW) [13]. The propensity scores were estimated without regard to outcome variables, using multiple logistic regression analysis [14].

Adjusted covariates including patient's age, sex, the presence or absence of a variety of clinical and coexisting conditions, risk factors, clinical diagnosis at the time of PCI, left ventricular function, extent of diseased vessels, infarct localization, renal failure, shock presence, cardiac arrest, TIMI flow, TA, IABP and use of abciximab were used for the generation of propensity scores and five quintiles were identified with increasing risk profile from the first to the fifth.

All model discrimination was assessed with c-statistics, and calibration was assessed with Hosmer–Lemeshow statistics.

With the Greedy 5 \rightarrow 1 digit match algorithm, we created propensity score-matched pairs without replacement (a 1:1 match) [13–14].

After all of the propensity score matches were performed, we assessed the balance in baseline covariates between the two intervention groups with the paired t test or the Wilcoxon signed rank test for continuous variables, and McNemar's test or the marginal homogeneity test for categorical variables. Comparisons were completed with Cox regression models with robust standard errors that accounted for the clustering of matched pairs. The methods mentioned above were applied to compare the clinical outcomes between the two groups. Analyses were performed using the statistical software SAS System, Version 9.1 (SAS Institute Inc., Cary, NC).

Results

Characteristics of patients

From September 2001 to June 2010, 1251 patients were admitted to our catheterization laboratory with a diagnosis of AMI and underwent primary PCI at our Centre and form the population of the present study. Patients were divided into two groups according to ETI. One group included 99 patients (7.9%) who underwent ETI whereas the other group included 1152 patients (92.1%) who did not. The clinical characteristics of the two groups are summarized in (Table 1), whereas their angiographic and procedural characteristics are shown in (Table 2). In the ETI group, 68 patients (68.7%) were intubated for cardiac arrest whereas the remaining 31 patients (31.3%) required ETI for respiratory failure associated to acute pulmonary edema with or without cardiogenic shock. Moreover, in the same group, 72 patients (72.3%) underwent ETI before their arrival in the catheterization laboratory. ETI patients were more likely to be hypertensive (76.8% vs 67.8%, $p=0.003$), diabetic 43.4% vs 17.9%, $p<0.0001$, resuscitated by cardiac arrest (68.7% vs 0.7%, $p<0.0001$), to present with cardiogenic shock (61.6% vs 8.1%, $p<0.0001$), with left main disease (16.2% vs 3.8%, $p<0.0001$), with a lower LVEF ($38.9\pm 9.4\%$ vs $48.9\pm 9.2\%$, $p<0.0001$) and to be treated with IABP (60.1% vs 15.4%, $p<0.0001$) whereas they appeared to

be less hypercholesterolemic (26.3% vs 37.8%, $p < 0.0001$). TA and stent implantation were performed less in the ETI group (38.4% vs 54.8%, $p < 0.0001$ and 80.1% vs 86.9%, $p < 0.0001$ respectively).

Table 1. Baseline Clinical Characteristics.

	All patients	ETI	No-ETI	p Value
Number of patients	1251	99 (7.9)	1152 (92.1)	--
Age	66±12	64±12	65±12	0.52
≥75 years	268 (23)	26 (26.2)	242 (21)	0.52
Females	314 (25.1)	24 (24.2)	290 (25.2)	0.93
Smoke	786 (62.8)	62 (62.3)	724 (62.8)	0.3
Hypertension	857 (68.5)	76 (76.8)	781 (67.8)	0.03
Hypercholesterolemia	460 (36.8)	26 (26.3)	434 (37.8)	<0.0001
Diabetes	250 (21.5)	43 (43.4)	207 (17.9)	<0.0001
Renal failure*	42 (3.3)	2 (2)	40 (3.5)	0.6
LVEF (%)	48.1±10	38.9±9.4	48±9.3	<0.0001
LVEF<40%	175 (15)	45 (45.4)	130 (11.3)	<0.0001
Cardiogenic Shock	155 (12.4)	61 (61.6)	94 (8.1)	<0.0001
Cardiac arrest	76 (6.1)	68 (68.7)	8 (0.7)	<0.0001
Anterior AMI	577 (46.1)	57 (57.6)	520 (45.1)	0.14
Total ischemic time (min)‡	252±204	223±214	255±203	0.13

Data are n (%) or mean±SD unless otherwise stated.

*Renal failure defined as baseline creatinine ≥2.5 mg/deciliter.

‡Time from symptoms onset to reperfusion.

Table 2. Angiographic findings and procedural details.

	All patients	ETI	No-ETI	p Value
Number of patients	1251	99 (7.9)	1152 (92.1)	--
Multivessel disease	734 (58.7)	55 (55.5)	666 (57.8)	0.16
Left main disease	60 (4.8)	16 (16.2)	44 (3.8)	<0.0001
Successful procedure*	1183 (94.6)	90 (90.1)	1093 (94.8)	0.15
IABP	237 (18.9)	60 (60.1)	177 (15.4)	<0.0001
GP IIb-IIIa inhibitors	1051 (84)	80 (80.1)	962 (83.5)	0.58
Thrombus Aspiration	669 (53.5)	38 (38.4)	669 (54.8)	<0.0001
Stent implantation	1081 (86.4)	80 (80.1)	1001 (86.9)	<0.0001

Data are n (%) unless otherwise stated.

*Successful procedure was defined as a residual stenosis of treated vessels <50% associated with a Thrombolysis In Myocardial Infarction (TIMI) 3 grade flow.

IABC=Intra-Aortic Balloon Pump.

Clinical events

In-hospital death of the whole population occurred in 87

patients (6.9%). The results of the comparisons between ETI and no-ETI patients are shown in (Table 3). The rate of in-hospital death was significantly higher in the ETI compared to no-ETI group (37.4% vs 4.3%, $p < 0.0001$), as the rate of stent thrombosis (3% vs 0.34%, $p = 0.006$). The rate of major bleedings did not significantly differ between the two groups (3% in ETI vs 2.1% in no-ETI group, $p = 0.79$). Multivariate analysis (Table 4) showed that the independent predictors of in-hospital death included age ≥75 years (odds ratio [OR] 3.96, $p = 0.0003$), LVEF ≤40% (OR 1.35, $p = 0.02$), cardiogenic shock (OR 33.4, $p < 0.0001$), anterior AMI (OR 1.82, 95% CI 1.04-3.17, $p = 0.036$) and ETI (OR 37.04, 95% CI 6.0-228.45, $p = 0.0001$). A total ischemic time ≤3 hours showed a borderline positive impact on survival (OR 0.55, $p = 0.05$), and there was also a non significant tendency of increased mortality in female,

Table 3. In-Hospital Outcomes.

	All patients	ETI	No-ETI	p Value
Number of patients	1251	99 (7.9)	1152 (92.1)	--
Death	87 (6.9)	37 (37.4)	50 (4.3)	<0.0001
Stent Thrombosis	7 (0.56)	3 (3)	4 (0.34)	0.006
Major Bleedings	27 (2.1)	3 (3)	24 (2.1)	0.79

Data are n (%) unless otherwise stated.

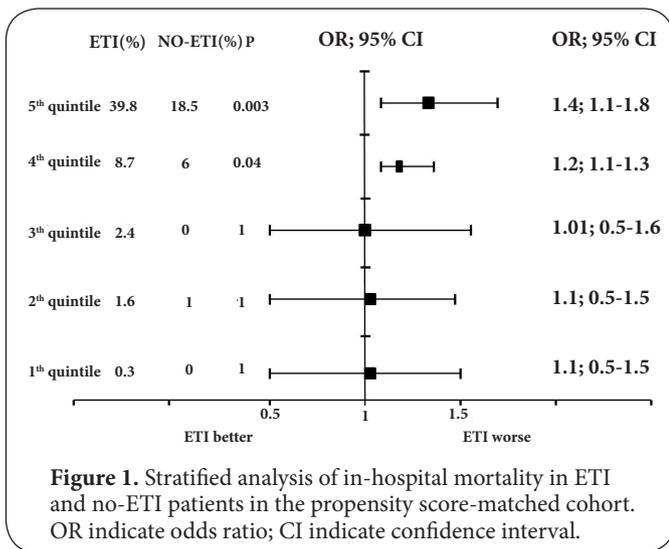
Table 4. Multivariate Analysis of In-Hospital Mortality.

	Odds Ratio	95% CI	p
Age ≥75 years	3.96	1.89-8.32	0.0003
Male Gender	0.51	0.24-1.07	0.08
Hypertension	1.31	0.71-2.40	0.38
Diabetes	0.84	0.43-1.67	0.62
LVEF ≤40%	1.35	1.05-1.72	0.02
Cardiac arrest	0.84	0.11-6.11	0.86
Cardiogenic shock	33.40	11.10-100.44	<0.0001
Endo-tracheal intubation	37.04	6.00-228.45	0.0001
IABP	1.11	0.42-2.99	0.83
Anterior location	1.82	1.04-3.17	0.036
Multivessel disease	0.87	0.49-1.53	0.62
Left main disease	1.74	0.39-7.70	0.46
GP IIb-IIIa inhibitors	1.14	0.50-2.60	0.76
TIMI flow pre-PCI ≥2	0.79	0.41-1.52	0.48
Thrombus aspiration	0.67	0.36-1.25	0.21
Stent	0.65	0.27-1.57	0.34
Total ischemic time ≤3 hours	0.55	0.30-1.01	0.05

LVEF=Left Ventricular Ejection Fraction

IABP=Intra-aortic Balloon Pump.

compared to male patients (OR 0.51, $p=0.08$). After using the propensity score modelling (Figure 1) ETI was not associated to worse outcomes in the quintiles from the first to the third (0.3% vs 0, $p=1$, in the first quintile, 1.6% vs 0, $p=1$ in the second, 2.4% vs 0, $p=1$ in the third) but it was associated to a higher death rate in the fourth and in the fifth quintiles (6% vs 8.7, $p=0.04$ and 18.5% vs 39.8%, $p=0.003$, respectively).



Discussion

The aim of the present study was to identify the clinical characteristics of the critically ill patients admitted for complicated AMI induced ETI undergoing primary PCI, compared to a similar population of patients not intubated, and to assess the role of ETI as an independent risk factor of in-hospital mortality. At our knowledge, there are few studies regarding such a population but, unlike our work, they focused on the clinical scores predictive of early mortality [15-17]. Our study confirmed that the in-hospital mortality of ETI patients was significantly higher compared to that of no-ETI patients, but it appeared to be slightly lower than those previous studies in which it ranged between 43% to 51%. Obviously the ETI patients are more critical in terms of both clinical characteristics and angiographic findings, but the propensity score analysis confirmed the significant negative impact of ETI on in-hospital mortality, at least in very high-risk patients. Furthermore, ETI was one of the most important independent predictors of mortality at multivariate analysis. The reasons of these findings are not completely clear but it could be hypothesized that an important role could be represented by the physiopathological changes induced by ETI itself, including hypotension, iatrogenic hypoxia and bradyarrhythmias [18-22] and by the major complications associated with it, like unrecognized oesophageal intubation, aspiration and pneumothorax [18,19,23]. In a series of 1954 patients received ETI, Wang and coll. found that the rate of

one or more errors occurred in 444 (22.7%) patients, including tube misplacement or dislodgement in 61 (3%), multiple ETI attempts in 62 (3%) and failed ETI in 359 (15%) [24]. Furthermore, other interventions often occur concurrently with ETI like chest compressions, electrical therapy, intravenous access, or the administration of drugs and ETI may influence patient outcome by interacting with or affecting the execution of these simultaneous therapies resulting in unintended hyperventilation, which may be deleterious in certain conditions and may increase the mortality, as shown by Davis and coll [25]. These observations contradict the assumption that aggressive airway intervention is associated with improved resuscitation outcomes [26]. Finally, last but not least, in our study the rate of stent thrombosis was significantly higher in the ETI group. This finding may be due in part to the more critical hemodynamic conditions of these patients that are associated, mainly in cardiogenic shock, with a significant reduction of the absorption of drugs from the intestine [27], in part to the difficulty to give them the needed antiplatelet therapy, mandatory after stent implantation. New intravenous antiplatelet drugs seem promising in reducing thrombotic events related to PCI [28] and then, if these data are confirmed, they could overcome these issues.

Our study has some important limitations: first, it is a retrospective analysis and is therefore subject to the limitations of such analyses. Due to its retrospective design, a weakness of our study is a deficiency in accurately collecting some history and clinical information like formal neurologic or functional severity scores [29-32] and the number of the patients who receiving mild-induced hypothermia, which has been demonstrated to have a strong beneficial impact on long-term survival and neurological status in the setting of out-of-hospital cardiac arrest [33]. Secondly, the nonrandomized nature of the comparison may have resulted into bias: for this reason, propensity score matching further enhanced the comparability of the patients. Third, the data are derived from a single center, which limits their applicability. However, this is likely to be a representative sample of the population of all-comers complicated AMI induced ETI undergone primary PCI in the real world. To our knowledge, this is the first study that can allow a significant relationship between ETI and in-hospital mortality in this population.

Conclusions

We identified that high-risk AMI patients with ETI undergoing primary PCI have significantly worse prognosis. However, we do not believe that the correct clinical interpretation is to avoid it at all. Our results most likely signal the presence of underlying problems with this procedure. Therefore, additional studies are needed to better understand the relationship between ETI and in-hospital mortality in such a population.

List of abbreviations

AMI: Acute Myocardial Infarction

PCI: Percutaneous Coronary Intervention
 LVEF: Left Ventricular Ejection Fraction
 ETI: Endotracheal Intubation
 ECG: Electrocardiogram
 TA: Thrombus Aspiration
 IABP: Intra Aortic Balloon Pump
 TIMI: Thrombolysis In Myocardial Infarction

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	FT	AG	NM	AG	MB	VI	FV
Research concept and design	✓	--	--	--	--	--	--
Collection and/or assembly of data	--	✓	✓	✓	--	✓	--
Data analysis and interpretation	--	--	--	--	✓	--	--
Writing the article	✓	--	--	--	--	--	--
Critical revision of the article	--	--	--	--	--	--	✓
Final approval of article	--	--	--	--	--	--	✓
Statistical analysis	--	--	--	--	✓	--	--

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