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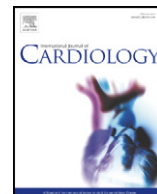
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Letter to the Editor

ST-elevation myocardial infarction with preserved ejection fraction: The impact of worsening renal failure

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Few data are available on the prognostic role of worsening renal function (WRF) in patients with ST-elevation myocardial infarction (STEMI) [1–3]. In patients with systolic dysfunction after MI (SAVE trial), WRF was associated with increased mortality in patients without renal dysfunction at baseline [4].

No data are available on the prognostic role of WRF in STEMI patients with preserved ejection fraction.

The present investigation was aimed at assessing the impact of WRF at short and long term in 681 STEMI patients with preserved ejection fraction ($\geq 45\%$, assessed by echocardiography) submitted to primary percutaneous coronary intervention (PCI) and consecutively admitted to our Intensive Cardiac Care Unit (ICCU) from 1st January 2004 to 30th June 2010.

On ICCU admission, after PCI, the following parameters were measured [5–11]: glucose (mg/dl), insulin values (mIU/l), glycated hemoglobin (HbA1c, %), troponin I (ng/ml), C-reactive protein (mg/dl) (normal values < 9), NT-pro Brain Natriuretic Peptide (NT-pro BNP) (pg/ml), erythrocyte sedimentation rate (ESR), microalbuminuria (mg/dl), uric acid (mg/dl), leukocytes ($\ast 10^3/\mu\text{l}$), fibrinogen (mg/dl). Glucose, creatinine and Tn I were measured three times a day during ICCU stay and peak values for each variable were considered. Acute insulin resistance was measured by means of homeostatic model assessment (HOMA) [5,9–12].

WRF was defined as an increased in creatinine ≥ 0.3 mg/dl [13–15].

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

Categorical data are reported as frequencies (percentages) and analyzed by means of χ^2 (or Fisher's exact test). Continuous data are reported as means \pm SD or medians (95% Confidence Interval – CI) according to their normal or not normal distribution (Kolmogorov–Smirnov one-sample normality test) and analyzed by means of Student's t-test or Mann–Whitney U-test, respectively. Study population was divided according to Worsening Renal Function in order to investigate which variables differed between the two subgroups. A univariable logistic regression analysis assessed the relationship between WRF and ICCU death. Moreover, a multivariable logistic regression analysis was carried out considering as outcome WRF. Model calibration was assessed by means of Hosmer–Lemeshow goodness-of-fit test; Nagelkerke pseudo-R square is also reported. Long time survival was explored after proportionality of risk assessment, with multivariable Cox regression analysis. In all multivariable analyses, candidate variables were chosen as those considered clinically relevant or that showed a univariate relationship with outcome; nonsignificant ones were dropped by means of backward selection. A two-tailed p value < 0.05 was considered statistically significant. (SPSS 13.0 statistical package, SPSS Inc, Chicago, IL).

In our series, 88 patients showed WRF (12.9%). Patients who showed WRF were older ($p < 0.001$), more frequently males ($p = 0.002$), smokers ($p = 0.016$) and hypertensives ($p = 0.015$). Anterior myocardial infarction was more frequent in patients with WRF ($p = 0.015$) who exhibited a higher incidence of higher Killip classes ($p < 0.001$) and a longer hospitalization ($p < 0.001$). A higher mortality rate both during ICCU and at follow-up was observed in WRF patients ($p < 0.001$).

Higher values of NT-pro BNP ($p < 0.001$), uric acid ($p < 0.001$), ESR ($p < 0.001$), fibrinogen ($p < 0.001$) and a higher incidence of hs-CRP positivity ($p = 0.002$) were observed in patients with WRF (Table 1). Ventilatory support (mechanical and non-invasive ventilation), continuous veno-venous hemodiafiltration (CVVHDF) and intra-aortic balloon pump (IABP) were more frequently used in WRF patients.

The following variables were independent predictors for the development of WRF: age (1 year step) (OR 1.05, 95%CI 1.01–1.08, $p = 0.007$), male sex (OR 0.35, 95%CI 0.16–0.76, $p = 0.008$), Killip class III–IV vs. I–II (OR 8.08, 95%CI 1.25–52.3, $p = 0.028$) and uric acid (1 mg/dl step) (OR

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Table 1
Laboratory data.

	Median (25th to 75th percentile) or frequency (%)			p
	All patients n = 681	No WRF n = 593 (87.1%)	WRF n = 88 (12.9%)	
Admission glucose (mg/dl)	125 (107 to 155)	124 (107 to 153)	130 (108 to 172)	0.130
Peak glycemia (mg/dl)	141 (120 to 177)	140 (120 to 174)	160 (124 to 206)	0.002
Insulin (mU/l)	8.7 (5.2 to 15.8)	8.7 (5.3 to 15.4)	8.9 (4.5 to 17.0)	0.972
HOMA positivity(%)	83 (12.2%)	73 (12.3%)	10 (11.1%)	0.820
Glycated Hb (%)	5.9 (5.6 to 6.3)	5.9 (5.6 to 6.4)	6.0 (5.6 to 6.3)	0.702
Admission creatinine (mg/dl)	0.90 (0.80 to 1.10)	0.90 (0.80 to 1.00)	1.00 (0.72 to 1.30)	0.006
Peak creatinine (mg/dl)	1.00 (0.87 to 1.16)	1.00 (0.80 to 1.10)	1.40 (1.10 to 1.90)	<0.001
Discharge creatinine (mg/dl)	0.90 (0.80 to 1.10)	0.90 (0.78 to 1.00)	1.20 (1.00 to 1.70)	<0.001
Microalbuminuria (mg/dl)	15.0 (6.2 to 46.5)	14.4 (6.2 to 43.6)	24.8 (6.8 to 87.0)	0.041
Peak Tn I (ng/ml)	59.0 (31.0 to 120.0)	58.4 (30.1 to 114.0)	79.0 (34.2 to 173.7)	0.053
NT-proBNP (pg/ml)	792 (326 to 1583)	673 (310 to 1452)	1854 (1030 to 7783)	<0.001
Uric acid (mg/dl)	5.6 ± 1.7	5.5 ± 1.6	6.4 ± 2.2	<0.001
ESR (mm/h)	20 (11 to 35)	19 (10 to 33)	31 (18 to 52)	<0.001
Leucocytes (*10 ³ /μl)	10.2 (8.2 to 12.6)	10.2 (8.3 to 12.6)	9.5 (7.9 to 12.6)	0.344
hs-CRP positivity (%)	284 (41.7%)	232 (39.2%)	52 (59.4%)	0.002
Fibrinogen (mg/dl)	383 (331 to 452)	380 (329 to 446)	420 (362 to 527)	<0.001

WRF: worsening renal failure; HOMA: homeostatic model assessment; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

1.25, 95%CI 1.03–1.52, $p=0.024$). Admission creatinine (1 mg/dl step) was not significantly associated (OR 0.96, 95%CI 0.91–4.19, $p=0.085$). Hosmer–Lemeshow chi-square 9.04, $p=0.339$, Nagelkerke pseudo- R^2 0.20.

WRF was associated with in-ICCU mortality [unadjusted OR 22.4 (95% CI 5.94–84.5), $p<0.001$].

At Cox regression analysis, the following variables were independently associated with long term mortality: age (1 year step) (HR 1.08, 95%CI 1.06–1.11, $p<0.001$) and discharge creatinine (1 mg/dl step) (HR 1.60, 95%CI 1.19–2.14, $p=0.002$). WRF was not an independent predictor of long term mortality.

The main finding of the present investigation, performed in consecutive STEMI patients with preserved LVEF submitted to primary PCI, is that worsening renal function is associated with increased early death, but not with a poorer survival rate at long term follow-up.

In our series, the incidence of WRF was not uncommon (12.9%), being comparable with those reported in patients with MI and systolic dysfunction (12.0%) [2] and in previous investigations enrolling STEMI patients [15,16].

We documented, for the first time, that in STEMI patients with preserved LVEF, the development of worsening renal failure identifies a subset of patients more seriously ill, being older, with more comorbidities and a higher hemodynamic derangement (as indicated by more advanced Killip classes and a higher use of devices). They also exhibited a worse in-hospital glycemic control (as inferred by peak glycemia) and a higher inflammatory activation (as indicated by higher values of hs-CRP, microalbuminuria). These factors are known to be associated with a worse prognosis at short term in STEMI patients [5,6,10–12].

Interestingly, in our series, the development of WRF was related to a more advanced hemodynamic impairment (as indicated by higher Killip class), independently of baseline renal function, thus suggesting the importance of systemic perfusion in the development of kidney injury. Similarly, Amin et al. [15] reported that left ventricular systolic dysfunction was independently associated with WRF.

In our series, WRF was not associated with increased mortality at follow-up, differently from previous studies including also STEMI patients with systolic dysfunction [15,17].

In conclusion, in a large series of STEMI patients with preserved LVEF, the development of WRF is associated with higher early mortality, since it identifies a subset of patients more seriously ill, being older, with more comorbidities and a higher hemodynamic derangement and inflammatory activation. Overall our data strongly suggest the clinical need of a close monitoring of renal function in STEMI

patients with preserved LVEF and of a more intensive treatment in those who develop WRF.

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