Original Article

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Higher in-hospital mortality during weekend admission for acute coronary syndrome: a large-scale cross-sectional Italian study

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Aims **An increased mortality risk during weekend hospital admission has been consistently observed. In the present study, we evaluated whether the current improvement in management of acute coronary syndromes (ACS) has reduced this phenomenon.**

Methods and results **We extracted data from the Italian National Healthcare System Databank of 80 391 ACS admission in the region of Lombardia between 2010 and 2014. ICD-9 codes were used to assess the diagnosis. We performed a multiple logistic regression analysis to compare the mortality rates between weekend and weekday admissions.**

Mean age of the study population was 67.6 years, 30.1% of patients were women. ST segment elevation myocardial infarction (STEMI) accounts for 42.2% of admissions. The total in-hospital mortality was 3.05% and was positively predicted by weekend admission [odds ratio (OR) 1.13, $P = 0.006$), age and female sex. The weekend effect on mortality was only significant for STEMI (OR 1.11, $P = 0.04$) in comparison to non-STEMI (NSTEMI) or unstable angina. The trend of the risk of death was found to be negatively correlated with age: the risk of death was significantly higher in all age clusters younger than 75 (OR 1.22, $P < 0.01$) and even greater in the very young subgroup under 45 years of age (OR 2.09, $P = 0.03$).

Conclusion **Our data indicate that increased mortality risk is still present during weekend admissions. This phenomenon is particularly evident in younger patients and in individuals admitted for STEMI.**

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Keywords: acute cardiac care, acute coronary syndrome, cardiac mortality, epidemiology, myocardial infarction, weekend

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Introduction

Several studies in the 1990s and early 2000s reported an excess of mortality risk for patients admitted to hospital during weekends.[1–5] The 'weekend effect' was attributed to reduced access to advance care and/or reduced hospital staffing during Saturday and Sunday and was also observed. in patients admitted for acute myocardial infarction (AMI) in spite of the consistent reduction in mortality reported in the last 20 years.[6] Other authors reported that the increase in mortality rate for AMI patients admitted during off-hours was mostly driven by lower rates of invasive strategy and increased time to reperfusion.[7]

A large-scale study focused on admission for acute coronary syndromes (ACS) in the era of primary percutaneous coronary intervention (PCI) was conducted in the United States between 2001 and 2011.[8] The authors confirmed the higher mortality in patients admitted during weekends. Another study, however, which analysed data within the same time, reported that the higher mortality rate during Saturdays and Sundays was no longer present after adjustment for differences in rates of early reperfusion strategy.[9]

Little information is instead available for European countries, especially after implementation of recent ESC guidelines for the management of patients with ST segment elevation myocardial infarction (STEMI) and NSTE-ACS, which also addressed organizational issues.[10,11]

We therefore performed a cross-sectional large-scale study of patients admitted to hospitals of the most populated Italian Northern region for ACS to evaluate whether the differences in mortality during admission in weekends versus weekdays were still present.

Materials and methods

Data source

Data were obtained upon request from the Italian National Healthcare System Databank (Banca dati SDO) for the years 2010 to 2014 and transmitted anonymously to our institution according to Italian Ministry of Health rules. This database collects every hospital admission in Italy under the National Health System. Each data record includes a patient identifier, demographic data, admission type (emergency, urgent or elective), primary and secondary diagnoses (as many as 5), length of stay and

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vital status at discharge. Each record accounts for a single hospitalization.

Study sample

ICD9 classification of diseases codes were used to assess and stratify for diagnosis of unstable angina (411.1), non-ST segment elevation myocardial infarction (NSTEMI, 410.70, 71) and STEMI (410.00, 01, 10, 11, 20, 21, 30, 31, 40, 41, 50, 51, 60, 61, 80, 81).[12] This classification was considered relevant in term of patients' management, as STEMI patients are treated with urgent revascularization and early invasive strategy for high-risk NSTE-ACS is now considered appropriate according to ESC guidelines.[13]

We limited data collection to patients discharged within 20 days from admission, to decrease the probability of including noncardiac causes of death, which, in our opinion, are more frequent among patients with longer hospital staying as a consequence of several noncardiac comorbidities.

Weekend (Saturday and Sunday) or nonweekend exposure (Monday to Friday) was categorized according to the calendar of admission.

Study variables

Demographical available variables were age, sex, length of hospital stay, ICD-9 codes for main and secondary diagnosis, day of admission and vital status at discharge.

Outcome

The main outcome of the study was in-hospital mortality among ACS patients admitted during weekends as compared to weekdays. Furthermore, differences in length of stay between weekday and weekends ACS admissions were also investigated. The mortality rate in relation to age and sex was also analysed.

Statistical analysis

Univariate logistic regression analysis was used to compare the mortality rates between weekend and weekday admissions. A separate multiple logistic model, including sex, age and weekend admission, as independent variables was built to make adjustments for available patients' demographics. A second multiple linear regression model was used to analyse the effects of day of admission, sex and age on hospital length of stay. All statistical analyses were carried out using Stata 13.0. Significance level was set as two-tailed P value less than 0.05. AQ6

Results

Patients' characteristics

Between January 2010 and December 2014, we identified 80 391 admissions with the diagnosis of ACS; 24 212 (24.9%) of them occurred during weekends. Mean age of the study population was 67.6 ± 12.5 years; 30.1% of patients were women. About 21.0% of admission were for unstable angina, 36.8% for NSTEMI and 42.2% for STEMI.

Two thousand four hundred and fifty-five patients died: the in-hospital mortality was 3.05%. One thousand seven hundred and ninety-six died after admission during the week (2.98%), whereas in-hospital death occurred in 659 patients admitted during weekend (3.29%). The mortality rate for STEMI, NSTEMI and unstable angina was 5.48, 1.69 and 0.50% during week and 5.77, 1.46 and 0.55% during weekend, respectively.

The unadjusted in-hospital mortality odds ratio (OR) for patients admitted to hospital during weekend was 1.10 [95% confidence interval (95% CI), 1.01–1.21, $P = 0.027$]. The increase in mortality for weekend admissions remained significant also when available predictors were included in the analysis (OR 1.13; 95% CI 1.03–1.24, $P = 0.006$). As expected, age was found to be positively associated with in-hospital death, with an OR of 1.06 (95% CI, 1.059–1.067, $P < 0.01$).

Patients admitted for STEMI exhibited a greater mortality than those with NSTEMI or unstable angina (see Table 1). An increased mortality was also observed in women and elderly patients.

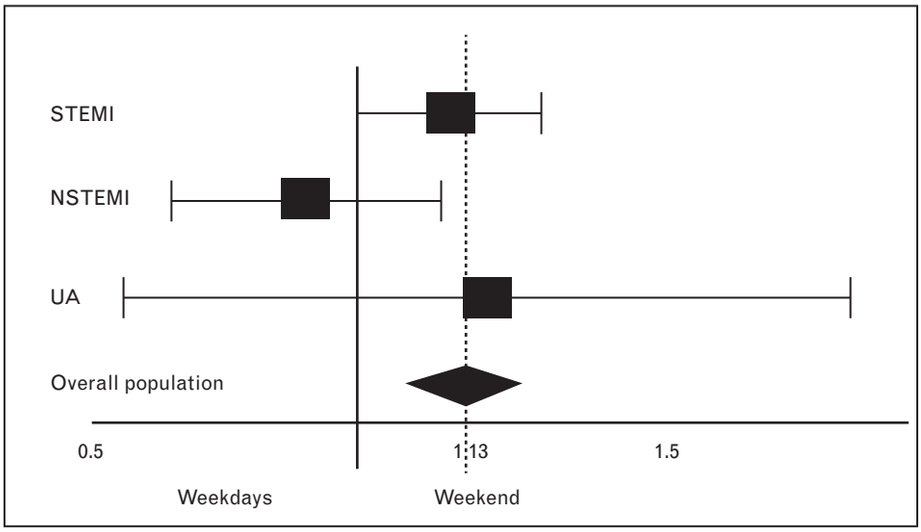
STEMI was the manifestation of ACS with the highest risk of mortality compared with NSTEMI and unstable angina, both in weekends and weekdays (Fig. 1). The weekend effect on mortality was only significant for STEMI (OR 1.11, 95% CI 1.00–1.24, $P = 0.04$) wherein

Table 1 Patients characteristics according to day of admission and vital status at discharge

Variable	Weekend admitted ($N = 20\,052$)		Weekdays admitted ($N = 60\,339$)	
In-hospital mortality	No	Yes	No	Yes
No. of admissions	19 393	659	58 543	1796
STEMI	8687 (44.79%)	532 (80.73%)	23 292 (39.79%)	1351 (75.22%)
NSTEMI	7250 (37.38%)	108 (16.39%)	21 905 (37.42%)	377 (20.99%)
UA	3456 (17.82%)	19 (2.88%)	13 346 (22.80%)	68 (3.79%)
No. of women	5691 (29.35%)	275 (41.73%)	17 481 (29.86%)	765 (42.59%)
Age	66.9 ± 12.5 y	74.5 ± 12.4 years	67.4 ± 12.4 years	75.9 ± 11.1 years
Hospital staying	8.7 ± 6.8	8.6 ± 10.3	8.4 ± 6.8	10.1 ± 9.3

Dummy variables are expressed as number (%); continuous variables are expressed as mean ± standard deviation. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; UA, unstable angina.

Fig. 1



Mortality odds ratios during admission for acute coronary syndromes and their subtypes. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; UA, unstable angina.

no differences were observed for NSTEMI (0.88, 95% CI 0.70–1.08, $P = 0.23$) or unstable angina (OR 1.04, 95% CI 0.62–1.74, $P = 0.86$).

Sex analysis

Mortality among men was lower than for women (2.5 versus 4.3%, respectively; OR 0.85, 95% CI 0.78–0.93, $P < 0.01$) (see Table 2). We also found that the risk of dying in hospital during weekend admissions among men (OR: 1.15, 95% CI 1.02–1.29) was slightly superior than that for women (OR: 1.11, 95% CI 0.96–1.28). Mean age of male patients who died in hospital was 70.7 and 73.2 years, respectively, for those admitted during weekend or weekdays. Women who died in hospital were older than men.

Age cluster analysis

To determine whether different age clusters were susceptible to the same risk of dying due to weekend admission, we performed a multiple logistic regression analysis, progressively excluding the upper age group: the effects of weekend admission on mortality was tested in patients older than 75 years and then younger than 75, 65, 55 and 45 years (see Table 3).

Mortality rate increases with age, starting from 1.2% among patients younger than 45 years, to 1.1% among younger than 55 years, 1.3% among younger than 65 years, 1.8% among younger than 75 years and 5.8% in patients older than 75 years (Fig. 2).

The risk of death attributable to weekend admission was inversely correlated with age. Patients older than 75 years

Table 2 Differences in sex subgroups

	Men ($N = 56\,179$)					Women ($N = 24\,212$)				
		Weekend admitted		Weekdays admitted			Weekend admitted		Weekdays admitted	
Variable		In-hospital death	Discharged alive	In-hospital death	Discharged alive		In-hospital death	Discharged alive	In-hospital death	Discharged alive
No. of admissions	56 179	384	13702	1031	41 062	24 212	275	5691	765	17481
No. of deaths	1415 (2.5%)	384 (100%)	0 (0%)	1031 (100%)	0 (0%)	1040 (4.3%)	275 (100%)	0 (0%)	765 (100%)	0 (0%)
STEMI	24 265 (43.2%)	307 (79.95%)	6373 (46.51%)	766 (74.30%)	16 819 (40.96%)	9597 (39.6%)	225 (81.82%)	2314 (40.66%)	585 (76.47%)	6473 (37.03%)
NSTEMI	19 919 (35.5%)	62 (16.15%)	4888 (35.67)	224 (21.73%)	14 745 (35.91%)	9721 (40.2%)	46 (16.73%)	2362 (41.50%)	153 (20.00%)	7160 (40.96)
UA	11 99[illegible] (12.[illegible]3%)	15 (3.91%)	2441 (17.81%)	41 (3.98%)	9498 (23.13%)	4894 (20.2%)	4 (1.45%)	1015 (17.84%)	27 (3.53%)	3848 (22.01%)
Age	65[illegible].2	70.7 ± 12.5	64.73 ± 12.2	73.2 ± 11.2	65.3 ± 12.1	72.6 ± 11.6	79.8 ± 10.5	72.1 ± 11.75	79.7 ± 9.6	72.3 ± 11.6
Weekend admissions	14 086 (25.07%)	384 (100%)	13 702 (100%)	0 (0%)	0 (0%)	5966 (24.6%)	275 (100%)	5691 (100%)	0 (0%)	0 (0%)
Days of admission	8.1 ± 6.7	8.4 ± 10.6	8.3 ± 6.6	10.4 ± 9.3	7.9 ± 6.4	9.5 ± 7.6	8.9 ± 10.9	9.7 ± 7.3	9.6 ± 10.1	9.5 ± 7.4

Dummy variables are expressed as number (%); continuous variables are expressed as mean ± standard deviation. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; UA, unstable angina.

Table 3 Age clusters analysis

Variable	Age > 75 years					Age < 75 years					Age < 65 years					Age < 55 years					Age < 45 years				
		Weekend		Weekdays			Weekend		Weekdays			Weekend		Weekdays			Weekend		Weekdays			Weekend		Weekdays	
		Dead	Alive	Dead	Alive		Dead	Alive	Dead	Alive		Dead	Alive	Dead	Alive		Dead	Alive	Dead	Alive		Dead	Alive	Dead	Alive
No. of admissions	24 504	359	5589	1066	17 490	53 438	277	13 233	673	39 255	31479	131	8025	290	23 033	13 575	58	3538	91	9888	3107	16	848	20	2223
No. of deaths	1425 (5.8)					950 (1.[illegible]					421 (1.3)					149 (1[illegible]					36 (1.2)				
STEMI	8855 (36.1)	271 (75.5)	1988 (35.6)	768 (72.1)	5828 (33.3)	24 170 (45.2)	240 (86.6)	6492 (49.1)	539 (80.1)	16 899 (43.1)	15 648 (49.7)	118 (90.1)	4231 (53.8)	252 (86.9)	10 957 (47.6)	7233 (53.3)	56 (96.5)	2051 (57.9)	79 (86.8)	5047 (51.0)	1768 (56.9)	16 (100)	522 (61.5)	19 (95.0)	1211 (54.5)
NSTEMI	10 739 (43.8)	74 (20.6)	2567 (45.9)	257 (24.1)	7841 (44.8)	17 891 (33.5)	32 (11.5)	4440 (33.5)	109 (16.2)	13 310 (33.9)	9744 (30.9)	10 (7.6)	2464 (30.7)	31 (10.6)	7239 (31.4)	4031 (29.7)	1 (1.7)	995 (28.1)	9 (9.9)	3026 (30.6)	887 (28.5)	0 (0)	227 (26.7)	1 (5.0)	659 (29.6)
UA	4910 (20.0)	14 (3.9)	1034 (18.5)	41 (3.8)	3821 (21.8)	11 377 (21.3)	5 (1.8)	2301 (17.4)	25 (3.7)	9046 (23.0)	6087 (19.3)	3 (2.3)	1240 (15.4)	7 (2.4)	4837 (21.0)	2311 (17.0)	1 (1.7)	492 (13.9)	3 (3.3)	1815 (18.3)	452 (14.5)	0 (0)	99 (11.6)	0 (0)	353 (15.8)
No. of women	11466 (46.8)	208 (57.9)	2610 (46.7)	497 (46.6)	8079 (46.2)	11 914 (22.3)	62 (22.4)	2892 (21.8)	182 (27.0)	8778 (22.3)	5534 (17.6)	22 (16.8)	1388 (17.3)	55 (18.9)	4069 (17.6)	2076 (15.3)	8 (13.8)	544 (15.4)	13 (14.3)	1511 (15.3)	476 (15.3)	4 (25.0)	124 (14.6)	6 (30.3)	342 (15.4)
Age	81.5 (4.2)	83.4 (4.9)	81.3 (4.1)	83.4 (4.7)	81.4 (4.1)	60.8 (9.4)	62.9 (9.7)	60.4 (9.5)	64.2 (8.2)	60.8 (9.3)	54.6 (7.2)	54.5 (7.5)	54.4 (7.3)	56.5 (6.3)	54.6 (7.1)	47.8 (5.2)	47.7 (5.9)	47.7 (5.4)	48.7 (4.6)	47.8 (5.2)	40.0 (3.9)	39.6 (4.9)	39.8 (4.0)	41.5 (2.9)	40.1 (3.9)
Weekend admissions	5948 (24.3)					13510 (25.3)					8156 (25.9)					3596 (26.5)					864 (27.8)				
Days of admission	10.5 (8.4)	9.3 (8.8)	10.6 (6.6)	10.8 (9.1)	10.5 (8.0)	7.5 (6.1)	7.6 (7.1)	7.8 (6.3)	8.7 (7.9)	7.4 (5.8)	7.0 (5.5)	7.3 (6.8)	7.3 (6.0)	7.1 (6.9)	6.9 (5.2)	6.7 (5.4)	5.1 (7.2)	7.07 (6.1)	5.3 (5.3)	6.7 (5.1)	6.7 (4.7)	1.9 (1.2)	7.0 (4.8)	4.3 (4.8)	6.7 (4.7)

Dummy variables are expressed as number (%); continuous variables are expressed as mean ± standard deviation. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; UA, unstable angina.

had a risk of dying when admitted on Saturday or Sunday similar to weekdays (OR 1.05, 95% CI 0.93–1.18, $P = 0.43$), whereas in patients younger than 75 years, the risk of death was significantly higher (OR 1.22, 95% CI 1.06–1.4, $P < 0.01$) and became even greater in younger patients' groups (OR 2.09, 95% CI 1.08–4.06, $P = 0.03$).

Length of hospital stay analysis

We found that admissions during weekend have a mean duration of 8.7 days (see Table 4), slightly higher than the duration of admissions during weekdays (8.5 days). In the multiple linear regression model, admission during weekend was a significant predictor of longer in hospital staying (β coefficient in multiple linear regression model 0.29, $P < 0.01$) together with age and female sex (β coefficient for age 0.11, $P < 0.01$; β coefficient for male sex -0.66, $P < 0.01$). These findings were coherent in terms of effect for age and sex, but differed when considering the diagnosis of admission. There was a consistent elongation of hospital stay only for unstable angina patients (β coefficient 0.44, $P < 0.01$), whereas no weekend effects on this secondary outcome was evident for STEMI and NSTEMI patients (β coefficients for STEMI 0.11, $P = 0.22$; for NSTEMI 0.07, $P = 0.39$).

Discussion

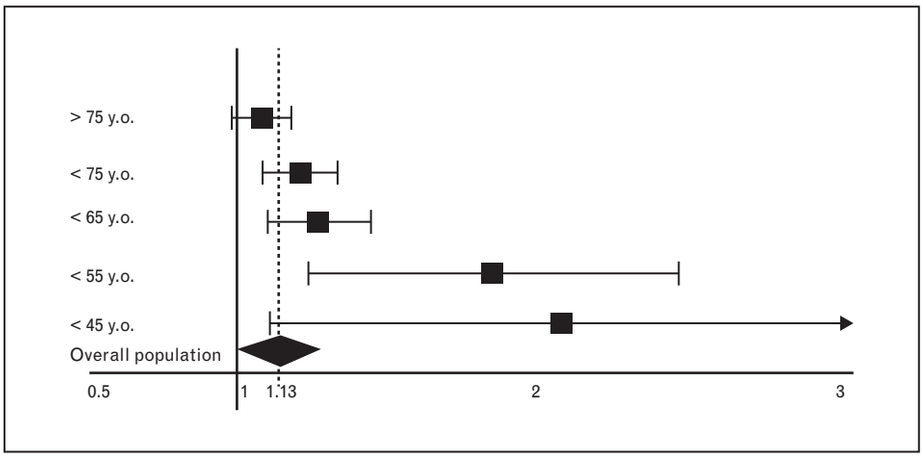
This study shows that in spite of a reduction of in-hospital mortality for ACS, which is now estimated to be 3.05%, we can still observe an increased risk of death during weekend days. The excess of mortality was particularly evident among STEMI patients than among other ACS manifestations and was more detectable in younger individuals.

These findings are in line with observations presented in the literature during the past decade, which reported a higher risk of death for patients admitted to hospital during the weekend, irrespective of age and sex.[5] We also observed that although the risk of death was consistently higher for women along the 7 days of the week, the risk of dying in hospital during weekend admission was relatively higher only for men.

The trend in excess of risk of death was found to be negatively correlated with age: in our population, the younger the patient, the higher was the risk of dying attributable to weekend admission.

Mortality from AMI has dramatically decreased during the last decades, but there are still some groups of patients, especially women and elderlies with several comorbidities who continue to have a high mortality rate.[15,1] the present study, we address a mortality risk factor not directly correlated to the severity of the disease and report that time of admission remains a critical determinant for ACS short-term outcome. Similar data were recently observed when considering the trend

Fig. 2



Mortality odds ratios during admission for acute coronary syndromes in different age groups. Mortality risk decreases as age increases. Patients younger than 45 years are at the highest risk.

in survival after in-hospital cardiac arrest in United States.[17] The Authors found that, despite an overall improvement in survival rates, there was an increased mortality during weekends and nights in comparison to on-hours. This finding was attributed to multiple factors, including changes in hospital staffing, less familiarity with patients and impact of shift work. Although the design of our study is unable to provide an explanation for the potential causes underlying the observed association between day of admission and mortality, we can speculate that longer time from symptom onset to diagnosis and treatment and hospital understaffing during weekend might play a role.[18]

The theory of understaffing was recently questioned by two recent articles by Aldridge *et al.*[19] and Hsu *et al.*[20]: these authors were unable to demonstrate a correlation between weekend staffing and mortality risk in relation to the day of admission and concluded that further investigation would have been necessary before adopting a 7-day service as a solution to the weekend effect.

When the mortality related to elective procedure and emergency admission such as those for ACS were analysed[21] in relation to the day of admission, an increased death rate was also observed during weekend. This finding, however, could not be adequately explained by variations in the number of physicians at work or by their interventional skills, thus leaving the question unresolved.

In our study cohort, we could not also analyse data on treatments and time to treatment as well as number of physicians and nurses at work. Nevertheless, a recent and coeval registry confirms that in Italy, patients suffering from an ACS are treated with high-level standards across the whole country, with optimal medical management[22] and high percentage of invasive strategy: in fact, 88% of patients underwent a coronary angiography during hospital stay.[23] A picture of the management of STEMI patients in the same area of Italy was provided by the 'LombardIMA PCI registry',[24] which enrolled a real-world population of more than 3000 patients. Unfortunately, the weekend effects were not evaluated in the above study. In addition, The National Society of Cardiologist operating in hospital together with the Organization of Italian interventionalists support a strong spread and application of local and updated protocols with the

AQ10 **Table 4 Patients characteristics**

Variable	Overall population	Weekend admitted	Weekdays admitted	
No. of admissions	80 391	20 052	60 339	
No. of deaths	2455 (3.05%)	659 (3.29%)	1796 (2.98%)	$P=0.02$
STEMI	33 862 (42.12%)	9219 (45.98%)	24 643 (40.84%)	$P<0.001$
NSTEMI	29 640 (36.8%)	7358 (36.69%)	22 282 (36.93%)	$P=0.55$
UA	16 889 (21.0%)	3475 (17.33%)	13 414 (22.23%)	$P<0.001$
No. of women	24 212 (30.2%)	5966 (29.75%)	18 246 (30.24%)	$P=0.19$
Age	67.6 ± 12.5 years	67.2 ± 12.6 years	67.7 ± 12.4 years	$P<0.001$
Weekend admissions	20 052 (24.9%)	20 052 (100%)	0 (0%)	
Hospital staying	8.5 ± 7.0	8.7 ± 7.0	8.5 ± 7.0	$P=0.001$

Dummy variables are expressed as number (%); continuous variables are expressed as mean ± standard deviation. NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; UA, unstable angina.

publication of practical statements about therapy in the field of ACS.[25]

The weekend effect on mortality was more evident in STEMI patients, whereas no significant association was found in patients admitted for NSTEMI and unstable angina: It is likely that delay to myocardial revascularization might play a critical role only in STEMI patients and affect their prognosis.

To interpret these findings, it is important to recall that whereas STEMI patients according to European guidelines are managed with prompt revascularization, coronary angiography is performed within 24–48 h from admission in NSTEMI or unstable angina if in stable conditions. To manage STEMI patients, medical and nurse staff is present in the hospital during week-days from 8 AM to 5 PM and is on call in the remaining part of the day and during all night and weekend days. Regulatory rules require the Cath-lab to be operative within 30 min from the activation call. The efficacy and respect of these rules are necessary for a centre in order to be recognized by the regional health authority. This organization is particularly effective for patients who call 112 Emergency System and have their ECG performed on site, whereas a longer delay is often experienced by patients who reach by their own the Emergency Room and are managed without a fast track protocol. The importance of delay in presentation on prognosis was also shown in a research conducted by Cerrato *et al.*,[26] who showed how late presenting myocardial infarction have a worse outcome both in terms of morbidity and mortality. This phenomenon may become more relevant during weekend days and negatively contribute to patient prognosis. This is true even among elderlies, a subgroup that benefits, such as younger patients, by invasive treatment with PCI, for an adequate early myocardial revascularization.[27]

The most important and unpredicted finding of our study, that is the increased mortality in younger ACS patients, which should therefore encourage future effort to fill this gap in standard of care between weekends and weekdays. For most of younger patients, ACS is the first manifestation of coronary artery disease and any delay in reperfusion may affect mortality. The absence of any preventive intervention, including cardiovascular therapy such as aspirin, statins and/or beta-blockers could also play a role.

Limitations of the study

Our study features some limitations that should be considered. First, the administrative database (Banca Dati SDO) does not provide information about medical history, laboratory and treatments. Thus, we were unable to assess the prognostic impact of several clinically established variables such as door-to-balloon time or Killip class. Second, given the lack of compulsivity to fill all four secondary diagnosis slots, we were unable to correctly consider the presence and role of comorbidities. Third, we arbitrary excluded admission lasting more than 20 days, to decrease the probability of including noncardiac causes of death. Thus, deaths occurring after this timeframe were not included in the study. Fourth, the study only included patients of a highly populated area in Northern Italy. Caution should therefore be adopted in extending these results to different European areas, although several and coeval studies found similar results.

Conclusion

This study shows that increased mortality-related admissions for ACS during weekends is a phenomenon that did not disappear with the overall reduction in mortality rate observed in the last years. The weekend effect on mortality was particularly evident for patients admitted for STEMI than for other ACS subtypes. The most relevant novel finding was the large effect on mortality in young patients. Further studies are required, updated and possibly in other healthcare settings, in order to establish whether the weekend effect on ACS mortality is worse among young people.

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