CLINICAL RESEARCH

Relationship between time of day, day of the week and in-hospital mortality in patients undergoing emergency percutaneous coronary intervention

Relation entre l’heure, les jours de semaine et la mortalité hospitalière chez les patients traités en urgence par angioplastie coronaire

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Received 16 June 2009; received in revised form 19 September 2009; accepted 25 September 2009
Available online 20 November 2009

KEYWORDS
Coronary artery disease; Percutaneous coronary intervention; Mortality; Cardiovascular events; Epidemiology

Summary
Background. — Previous studies have reported circadian variation in the rate of post-percutaneous coronary intervention (PCI) complications and mortality.
Aim. — To assess whether in-hospital outcomes during the first 48 h after admission are related to the time or the day when PCI is performed.
Methods. — Emergency PCIs (2266 total; 1396 during regular hours and 870 during off hours) performed consecutively during a 3.5-year-period (2005–2008) were evaluated. The primary endpoint was death and the secondary endpoint was a composite score based on cardiovascular complications. The association between PCI start time and in-hospital outcome was assessed using multivariable logistic regression and propensity score analysis.

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.
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doi:10.1016/j.acvd.2009.09.010
Results. — The patients’ mean age was 64.8 years and 77.3% were men. The highest death rate was for night-time PCI (3.6%), with a 5.1% occurrence rate for PCI performed between 00:00 and 03:59, and a 3.0% occurrence rate for weekend daytime PCI compared with 1.5% for weekday daytime (regular-hours) PCI. The frequency of occurrence of other clinical events did not vary significantly throughout the day. Compared with weekday daytime PCI, the odds ratio for mortality was 2.95 for night-time PCI (95% confidence interval [CI] 1.58—6.01; p = 0.0007) and 2.42 for weekend daytime PCI (95% CI 0.97—6.01; p = 0.06).

Conclusion. — Our study shows a significant time-dependent effect on in-hospital deaths in patients treated with emergency PCI. Healthcare organization and circadian variation of ischaemic processes could explain this variation in mortality.

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Introduction

ACS, including unstable angina and both STEMI and NSTEMI, require PCI in approximately 20—30% of cases [1—3]. While there is debate about whether these patients should be treated conservatively or undergo an early invasive coronary intervention [4—6], scientific societies recommend that several types of ACS undergo emergency revascularization. Thus, for NSTEMI, guidelines from the American Heart Association/American College of Cardiology and the European Society of Cardiology recommend an emergency invasive strategy in patients with refractory or recurrent angina or haemodynamic or electrical instability [7,8]. For STEMI, there is unanimous agreement that efforts must be made to shorten delays between the onset of chest pain or other symptoms and the initiation of a safe and effective reperfusion strategy [9,10]. This agreement explains why hospitals provide PCI around the clock and are confronted with emergency PCIs during both regular hours and off hours.

Previous studies have reported circadian variation in the rate of post-PCI complications and mortality [11,12], and a higher mortality rate in patients with STEMI who were treated with primary angioplasty at night than in those who were treated during the day [13—15]. Three possible explanations for this variation have been proposed. First, the baseline clinical characteristics of patients treated at night may differ from those of patients treated during the day. Second, the management of patients could be less efficient at night than during the day. Third, the efficacy of PCI may be influenced by the biological circadian rhythm.

Several questions remain. Could the circadian variation in mortality be generalized to all emergency PCIs? If the answer is yes, how do the biological circadian rhythm and the potentially less efficient night-time management of patients contribute to the increased risk of mortality after night-time emergency PCI? Finally, if less efficient night-time management of patients does exist, how does this affect other outcomes? Is the pattern identical?

We studied the relationship between the time of day or the day of the week when a PCI procedure was performed and the in-hospital outcomes for patients treated by emergency PCI. After reviewing the literature, we hypothesized that the circadian variation in mortality exists for all PCIs carried out in emergency. We then examined the potential
contributions of biological circadian rhythm and poorer night-time care to increased mortality, by comparing weekday daytime, weekend daytime and night-time treatment outcomes.

Methods

Data source and study sample

All hospitalized patients treated by PCI were registered prospectively during a 3.5-year period from 2005 to mid-2008. After the first 48 h of hospitalization, data (including patient history and clinical and procedural data) were entered into a uniform registry format. Of all procedures (n = 9099) carried out consecutively during this period, only those performed in emergency for ACS (n = 2270) were considered. Four procedures were excluded from statistical analyses because no information was available.

According to the European Society of Cardiology guidelines, ACS was defined as typical acute chest pain with persistent (>20 min) ST-segment elevation or acute chest pain without persistent ST-segment elevation [8]. The decision to use emergency PCI was based on the European Society of Cardiology guidelines [8,16]. For ST-segment elevation ACS, primary PCI was performed in patients presenting <12 h after the onset of chest pain or other symptoms not treated by thrombolysis; rescue PCI was performed if thrombolysis failed within 60 min after starting the administration [16]. For non-ST-segment elevation ACS, emergency PCI was performed in patients with refractory or recurrent angina associated with dynamic ST-segment deviation, heart failure, life-threatening arrhythmias or haemodynamic instability [8]. Senior interventional cardiologists performed all PCI procedures, during both regular hours and off hours. PCI was performed using standard balloon techniques. The administration of adjunctive medications for PCI was in agreement with the European Society of Cardiology guidelines [16].

Clinical data and measures

Patients’ records included demographic data (age, sex) and data on cardiovascular comorbidities (history of MI, history of coronary revascularization). Data for cases of coronary artery disease included the number of vessels affected and the number of vessels treated. Affected vessels were defined by the impairment of at least one major coronary trunk with >50% diameter stenosis.

In-hospital outcome records included medical events that occurred within 48 h after PCI. Post-PCI medical events included death, recurrent MI, CABG, new PCI, stroke (including stroke and transient ischaemic attack), and vascular and renal events, and were confirmed with the medical record. The primary outcome of the study was defined as death (cardiac or non-cardiac) within 48 h after PCI. The diagnosis of recurrent MI during the follow-up period was based on recurrent chest pain accompanied by re-elevation of cardiac enzymes levels and/or new ST-segment elevation on surface electrocardiography. Vascular events were defined as any vascular access site complication that required vascular surgical repair or blood transfusion. Renal events were defined as acute renal failure that required renal haemodialysis. Composite in-hospital outcomes were:

- death, recurrent MI, CABG or new PCI;
- outcome #1 and stroke;
- outcome #2 and renal or vascular events;
- recurrent MI, CABG, new PCI, stroke or renal or vascular events.

No patient was lost to follow-up.

We studied the relationship between the time of day or the day of the week that PCI was performed and the in-hospital occurrence of medical events within 48 h after PCI. In the primary analysis, the PCI period was categorized according to: six periods (00:00—03:59, 04:00—07:59, 08:00—11:59, 12:00—15:59, 16:00—19:59 and 20:00—23:59); and two periods (daytime [08:00—19:59] and night-time [20:00—07:59]). In secondary analyses, the PCI period was categorized according to: two periods (regular hours [weekdays 08:00—19:59] and off hours [weekdays 20:00—07:59 and weekends]); and three periods (weekdays [Monday–Friday], weekends [Saturday–Sunday] and nights).

Statistical analysis

Statistical analysis was performed using SAS statistical software, version 9.2 (SAS Institute Inc., Cary, NC, USA). A p-value of <0.05 was considered to be statistically significant. In a bivariate analysis, the Chi-square test was used to compare the distribution of qualitative variables. Fisher’s exact test was computed as needed. Mean values of quantitative variables were compared by Student’s t-test. The Shapiro-Wilk and Levene’s tests were used to test the normality of the distribution of the residuals and the homogeneity of variances, respectively.

Multivariable logistic regression was performed to test the independent statistical association between in-hospital outcome and time of PCI procedure. A systematic adjustment was done for age, sex, year of procedure, history of MI and coronary angioplasty, the number of vessels affected and the number of vessels treated.

In order to reduce bias caused by differences in background characteristics and to make the groups more comparable, we used a propensity score weighting method [17]. This method created a propensity score by reducing the relationship between multiple characteristics and outcomes to a single score; records belonging to each group were matched on this single score. Logistic regression was used to model the odds of being in the off-hour PCI group vs the regular-hour PCI group or the odds of being in the night-time group vs the daytime group as a function of these characteristics. A sequential matching pair between the two groups, from five to three digits of the predicted probability, was performed. This method can reduce bias in measured characteristics only.

Results

Table 1 shows the baseline characteristics of patients treated with emergency PCI procedures. Most of the patients (77.3%) were men. The patients’ mean age was 64.8 years. Nineteen per cent had a previous PCI. More than half of the patients (55.3%) had a multivessel disease (defined as
The outcomes of emergency PCI procedures are tabulated in Table 1. Stenosis) and 78.5% of patients had a single vessel treated involving of >1 major coronary trunk, with >50% diameter stenosis) and 78.5% of patients had a single vessel treated in emergency.

In-hospital death, major complications and composite outcomes of emergency PCI procedures are tabulated according to the time of the day in Table 2. Circadian variation in the mortality rate was observed (p = 0.03), peaking between midnight and 03:59 and reaching the lowest level between midday and 15:59 (5.5% vs 1.3%). The occurrence of other clinical events, including recurrent MI, CABG, PCI, stroke, and vascular and renal events, did not vary significantly across time periods. The rate of vascular and haemorrhagic complications was also similar across time periods.

Of the 2266 emergency PCIs registered, 1628 (71.8%) were done during the daytime (08:00–19:59) and 1396 (61.6%) during regular hours (daytime Monday–Friday). The basic characteristics of emergency PCI procedures performed during daytime and night-time and during regular hours and off hours are compared in Table 3. Coronary artery disease tended to be more severe (higher percentages of multivessel disease) in patients treated during the daytime and during regular hours. A history of MI was more frequent in patients treated during the daytime (7.4% vs 3.1%; p = 0.002) and during regular hours (8.2% vs 2.9%, p = 0.0001).

In-hospital deaths are tabulated according to the time of the emergency PCI procedure in Table 4. The mortality rate was significantly higher among patients who had undergone a night-time emergency PCI than among patients treated with the procedure during the daytime (3.6% vs 1.7%; p = 0.007). The occurrence of other clinical events was similar during these two-time periods. After adjustment for all covariates, the risk of in-hospital death within 48 h of PCI remained significantly higher when emergency PCI was performed at night-time than when it was performed during the daytime (odds ratio 2.52; 95% CI 1.4—4.52; p = 0.002). The adjusted risk for other clinical events was not significantly different between time periods. A greater mortality rate was also observed for emergency PCI performed during off hours than for emergency PCI performed during regular hours (3.5% vs 1.5%; p = 0.003) with an adjusted odds ratio of 2.81 (95% CI 1.56—5.06; p = 0.001).

Analyses of outcomes according to weekdays, weekends and nights are given in Table 5. Patients treated during the day on a weekday had a lower 48-h in-hospital mortality rate than patients treated during the day on a weekend or patients treated at night (1.5%, 3.0% and 3.6%, respectively, p = 0.009). There was no statistical difference between the three groups for other clinical events. After adjustment for all covariates, the odds ratio for the mortality rate was 2.95 (95% CI 1.58–6.01; p = 0.0007) for night-time vs weekday daytime treatment, and 2.42 (95% CI 0.97–6.01; p = 0.06) for weekend daytime vs weekday daytime treatment.

After propensity score matching and adjustment for all covariates, the risk of mortality remained significantly higher for emergency PCI performed at night-time than for daytime PCI, with an adjusted odds ratio of 2.89 (95% CI 1.17–7.14; p = 0.03), and for an off-hour emergency PCI procedure than for emergency PCI performed during regular hours, with an odds ratio of 3.74 (95% CI 1.56–8.96; p = 0.004) (Table 6).

Discussion

Our study reports a significant relationship between the time of a PCI procedure and the 48-h in-hospital mortality of
### Table 2  In-hospital deaths and composite outcomes of emergency PCI procedures according to time of day.

<table>
<thead>
<tr>
<th>Time of day</th>
<th>12:00—15:59</th>
<th>16:00—19:59</th>
<th>20:00—23:59</th>
<th>00:00—03:59</th>
<th>04:00—07:59</th>
<th>08:00—11:59</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST-segment and non-ST-segment elevation (n)</td>
<td>603</td>
<td>724</td>
<td>248</td>
<td>237</td>
<td>153</td>
<td>301</td>
</tr>
<tr>
<td>Death (%)</td>
<td>1.3</td>
<td>1.9</td>
<td>3.2</td>
<td>5.5</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Complications (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>0.2</td>
<td>0</td>
<td>0.4</td>
<td>0</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>0.7</td>
<td>0</td>
</tr>
<tr>
<td>Recurrent MI</td>
<td>0.8</td>
<td>1.1</td>
<td>1.2</td>
<td>2.5</td>
<td>0</td>
<td>1.3</td>
</tr>
<tr>
<td>New PCI or CABG</td>
<td>0.5</td>
<td>0.3</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>Total vascular events</td>
<td>2.2</td>
<td>1.8</td>
<td>1.2</td>
<td>1.5</td>
<td>1.3</td>
<td>2.0</td>
</tr>
<tr>
<td>Serious vascular event</td>
<td>0.2</td>
<td>0.4</td>
<td>0.4</td>
<td>0</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Non-serious vascular event</td>
<td>2.0</td>
<td>1.4</td>
<td>0.8</td>
<td>1.5</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Composite outcomes (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, recurrent MI, PCI, CABG, stroke, renal or serious vascular event</td>
<td>3.3</td>
<td>3.5</td>
<td>5.2</td>
<td>8.9</td>
<td>3.3</td>
<td>5.0</td>
</tr>
<tr>
<td>Without death</td>
<td>2.0</td>
<td>1.5</td>
<td>2.0</td>
<td>3.5</td>
<td>1.3</td>
<td>3.0</td>
</tr>
<tr>
<td>Risk of in-hospital death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>1</td>
<td>1.47</td>
<td>2.48</td>
<td>3.97</td>
<td>1.49</td>
<td>1.51</td>
</tr>
<tr>
<td>95% CI</td>
<td>(0.61—3.52)</td>
<td>(0.92—6.68)</td>
<td>(1.60—9.83)</td>
<td>(0.39—5.67)</td>
<td>(0.52—4.40)</td>
<td></td>
</tr>
<tr>
<td>Adjusteda OR</td>
<td>1</td>
<td>1.39</td>
<td>2.65</td>
<td>3.98</td>
<td>2.16</td>
<td>1.27</td>
</tr>
<tr>
<td>95% CI</td>
<td>(0.57—3.37)</td>
<td>(0.95—7.39)</td>
<td>(1.55—10.3)</td>
<td>(0.55—8.47)</td>
<td>(0.42—3.82)</td>
<td></td>
</tr>
<tr>
<td>ST-segment elevation (n)</td>
<td>416</td>
<td>509</td>
<td>229</td>
<td>201</td>
<td>133</td>
<td>220</td>
</tr>
<tr>
<td>Death (%)</td>
<td>1.9</td>
<td>2.7</td>
<td>3.5</td>
<td>6.0</td>
<td>1.5</td>
<td>2.7</td>
</tr>
<tr>
<td>Risk of in-hospital death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>1</td>
<td>1.44</td>
<td>1.85</td>
<td>3.27</td>
<td>0.78</td>
<td>1.43</td>
</tr>
<tr>
<td>95% CI</td>
<td>(0.68—3.47)</td>
<td>(0.68—4.98)</td>
<td>(1.26—8.43)</td>
<td>(0.16—3.71)</td>
<td>(0.49—4.17)</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.42</td>
<td>0.22</td>
<td>0.01</td>
<td>0.76</td>
<td>0.51</td>
<td></td>
</tr>
</tbody>
</table>
patients in need of emergency PCI. There was circadian variation in 48-h in-hospital mortality, which peaked among patients who underwent emergency PCI between midnight and 03:59.

Previous reports have found circadian variation in mortality rate after primary PCI for STEMI [13–15,18]. Contradictory evidence has been reported by Zahn et al. who found no difference in clinical events between patients with acute MI who were treated by primary PCI during the day and those who were treated at night [19]. However, only 491 patients were registered in the study by Zahn et al. and only 23% of them were treated at night. In our current investigation, 2266 patients were registered, 28.2% of whom were treated at night. We demonstrated that the suspicion of a relationship between the time a PCI procedure was performed and patient mortality was well founded for all emergency PCI procedures.

To explain this relationship, the three factors described in the introduction were considered. First, the baseline clinical characteristics of patients who presented at night and patients who presented during the day varied. Kinjo et al. reported a higher frequency of men aged <65 years, current smokers and alcohol drinkers among patients hospitalized for acute MI at night than among those hospitalized during the day [20]. Saleem et al. showed that hospital mortality for older patients with MI treated by PCI was higher during off hours than during regular hours (16.9% vs 6.9%; \( p < 0.05 \)) [21]. In our current study, patients undergoing emergency PCI who were treated during regular hours were older than those treated during off hours (66.4 ± 13.1 years vs 61.9 ± 14.2 years; \( p < 0.0001 \)); however, after propensity score matching, we demonstrated that the increased risk of mortality after emergency PCI performed at night was independent of patients’ baseline characteristics and remained statistically significant with an adjusted odds ratio of 2.89 (95% CI 1.17–7.14; \( p = 0.03 \)).

Second, the results of our current investigation could evolve from less efficient patient management during night-time hours. Several studies have reported a higher mortality rate and a lower use of invasive cardiac procedures for patients with MI who are admitted on weekends than for those admitted on weekdays [22,23], which implies poorer quality of management during off hours. Magid et al. showed that patients admitted for MI and treated with PCI during off hours (including nights and weekends) had a higher mortality rate than was observed among patients treated during regular hours [18]. In groups with similar baseline characteristics, Garot et al. found no difference in the in-hospital mortality rate between patients with STEMI who were treated with PCI during regular hours and those who were treated during off hours [24]. Their results suggest that patients’ baseline characteristics are the predominant cause of the differences observed in mortality between regular and off hours; however, their study was limited by its design, which was retrospective and included only 288 PCIs.

In our prospective study, we observed that the increased risk of mortality associated with emergency PCI performed during off hours rather than regular hours remained statistically significant after propensity score matching, with an adjusted odds ratio of 3.74 (95% CI 1.56–8.96; \( p = 0.004 \)), and was independent of patients’ baseline characteristics.
One question remains unanswered: Can the increased night-time and off-hour in-hospital mortality be attributed to a longer period of ischaemia caused by delays in management or poorer quality of PCI procedures? Magid et al. found that the period before reperfusion was longer at night than during the day, and that the adjusted mean door-to-balloon period was longer during off hours than during regular hours (116.1 min vs 94.8 min; \( p < 0.001 \)); the authors suggest that these delays may account for the higher in-hospital mortality rate after off-hour primary PCI for STEMI [18]. Sadeghi et al. reported conflicting results in a previous study. They found an identical length of time between symptom onset and hospital arrival but a longer door-to-balloon period for patients with STEMI who presented during off hours than for those who presented during regular hours (108 min vs 129 min, \( p < 0.0001 \)); however, neither presentation period nor door-to-balloon time was predictive of mortality in a multivariable analysis [25]. These results are surprising because most studies indicate that patient mortality is influenced by the length of time before reperfusion [9,10], and

### Table 3  Comparison of basic characteristics of patients undergoing emergency PCI procedures during daytime vs night-time and during regular hours vs off hours.

<table>
<thead>
<tr>
<th></th>
<th>Daytime ((n=1628))</th>
<th>Night-time ((n=638))</th>
<th>(p)</th>
<th>Regular hours ((n=1396))</th>
<th>Off hours ((n=870))</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.8 ± 13.4</td>
<td>62.2 ± 14.3</td>
<td>0.0001</td>
<td>66.6 ± 13.0</td>
<td>61.9 ± 14.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>Men</td>
<td>76.9</td>
<td>78.2</td>
<td>0.51</td>
<td>76.4</td>
<td>78.7</td>
<td>0.19</td>
</tr>
<tr>
<td>History of MI</td>
<td>7.4</td>
<td>3.1</td>
<td>0.002</td>
<td>8.2</td>
<td>2.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>History of PCI</td>
<td>21.6</td>
<td>13.6</td>
<td>0.0001</td>
<td>22.8</td>
<td>13.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>History of bypass surgery</td>
<td>4.8</td>
<td>2.4</td>
<td>0.009</td>
<td>5.0</td>
<td>2.6</td>
<td>0.006</td>
</tr>
<tr>
<td>History of renal failure</td>
<td>13.1</td>
<td>9.1</td>
<td>0.009</td>
<td>3.2</td>
<td>2.4</td>
<td>0.26</td>
</tr>
<tr>
<td>History of vascular disease</td>
<td>3.1</td>
<td>2.5</td>
<td>0.47</td>
<td>13.9</td>
<td>8.7</td>
<td>0.0002</td>
</tr>
<tr>
<td>Thrombolytic treatment</td>
<td>4.5</td>
<td>7.4</td>
<td>0.006</td>
<td>4.2</td>
<td>7.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Stent</td>
<td>89.0</td>
<td>88.2</td>
<td>0.61</td>
<td>89.3</td>
<td>87.9</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Number of vessels affected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>40.0</td>
<td>41.4</td>
<td>0.56</td>
<td>38.3</td>
<td>43.8</td>
<td>0.01</td>
</tr>
<tr>
<td>Two</td>
<td>29.8</td>
<td>29.0</td>
<td>0.71</td>
<td>30.0</td>
<td>28.8</td>
<td>0.55</td>
</tr>
<tr>
<td>Three</td>
<td>22.7</td>
<td>20.1</td>
<td>0.18</td>
<td>23.6</td>
<td>19.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Left main coronary</td>
<td>24.5</td>
<td>19.4</td>
<td>0.01</td>
<td>24.5</td>
<td>20.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Bypass graft</td>
<td>2.8</td>
<td>1.9</td>
<td>0.23</td>
<td>2.9</td>
<td>1.8</td>
<td>0.11</td>
</tr>
<tr>
<td>Not known</td>
<td>6.4</td>
<td>7.4</td>
<td>0.43</td>
<td>7.0</td>
<td>6.2</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>Number of vessels treated</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>Right coronary</td>
<td>25.4</td>
<td>32.1</td>
<td>0.007</td>
<td>24.8</td>
<td>31.2</td>
<td></td>
</tr>
<tr>
<td>Left circumflex</td>
<td>15.2</td>
<td>13.0</td>
<td></td>
<td>15.0</td>
<td>13.9</td>
<td></td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>35.6</td>
<td>36.2</td>
<td></td>
<td>34.5</td>
<td>37.8</td>
<td></td>
</tr>
<tr>
<td>Two vessels</td>
<td>14.2</td>
<td>10.5</td>
<td></td>
<td>15.3</td>
<td>9.7</td>
<td></td>
</tr>
<tr>
<td>Three vessels</td>
<td>1.8</td>
<td>1.6</td>
<td></td>
<td>2.1</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Left main coronary</td>
<td>3.0</td>
<td>1.6</td>
<td></td>
<td>3.2</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Bypass graft</td>
<td>0.9</td>
<td>1.6</td>
<td></td>
<td>1.0</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Not known</td>
<td>3.9</td>
<td>3.4</td>
<td></td>
<td>4.1</td>
<td>3.3</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation or %. MI: myocardial infarction; PCI: percutaneous coronary intervention.

### Table 4  In-hospital deaths according to time of emergency PCI procedure.

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Night-time vs daytime(^a)</td>
<td>(3.6% vs 1.7%); (p=0.007)</td>
<td>2.14(^b)</td>
<td>1.22–3.74</td>
</tr>
<tr>
<td>Off hours vs regular hours(^d)</td>
<td>(3.5% vs 1.5%); (p=0.003)</td>
<td>2.34(^b)</td>
<td>1.33–4.11</td>
</tr>
</tbody>
</table>

CI: confidence interval; OR: odds ratio; PCI: percutaneous coronary intervention.

\(^a\) Night-time: 20:00—07:59 \((n=638)\); daytime: 08:00—19:59 \((n=1628)\).

\(^b\) Unadjusted.

\(^c\) Adjusted for age, sex, history of ischaemic heart disease, year of procedure, number of vessel disease, vessels treated, thrombolytic therapy use and stent implantation.

\(^d\) Regular hours: 08:00—19:59 Monday—Friday \((n=1396)\); off hours: weekends and 20:00—07:59 Monday—Friday \((n=870)\).
Cannon et al. have suggested that door-to-balloon times in excess of 2 h increase in-hospital mortality rates by 40–60% [26]. Henriques et al. found a higher mortality rate in patients with STEMI treated by primary PCI during off hours compared with those treated during regular hours, with no difference in symptom onset, hospital-admission time and door-to-balloon time, suggesting that the duration of ischaemia is not the only factor contributing to the circadian variation in mortality rate after PCI [15]. Recently, Dominguez-Rodriguez et al. found a higher rate of PCI failures and, consequently, a higher in-hospital mortality rate in patients with MI who were treated during off hours than in those treated during regular hours [27]. Our data confirmed this higher in-hospital mortality rate in patients with STEMI treated between midnight and 03:59. Sleep deprivation could account for these results in part, because it is known to reduce performance [28] and is likely to impair the quality of PCI performed at night. In addition, if the circadian variation in mortality rate after emergency PCI depends only on the quality of care, the pattern should also be observed for other outcomes. However, we found no significant differences in the occurrence of recurrent MI, CABG, new PCI, stroke, or renal and vascular events between patients treated with emergency PCI at night and during the day (2.2% vs 2.0%; p = 0.73) or between patients treated during off hours and regular hours (2.2% vs 1.9%; p = 0.68 respectively). Our results implicate other factors in the circadian variation of mortality rate after emergency PCI.

Third, as with the circadian variation of plaque rupture [29], acute MI, and sudden cardiac death [30], it could be suggested that biological circadian rhythms may explain why the effectiveness of PCI varies depending on the time of day it is performed. Biological circadian variations have been reported for blood viscosity [31], coronary blood flow [32], platelet aggregability [33], endogenous thrombolytic activity [34], coagulation factors [35] and cortisol and catecholamine levels [36]. Several studies have revealed a circadian variation in the efficacy of thrombolytic therapy [37,38] and mortality rate after programmed PCI [6]. In our study, the comparison between weekdays, weekends and nights confirmed the influence of biological circadian rhythm in emergency PCI results. Indeed, we showed that the mortality risk for night-time PCI remained higher when compared with those for weekday daytime PCI and weekend daytime PCI (3.6% vs 1.5% vs 3%, p < 0.009, respectively). We could hypothesize that an ACS occurring at night differs from an ACS that occurs during the day and requires better treatment. One attractive strategy for improving care at night could include more rapid access to a catheterization laboratory and systematic adjunction of glycoprotein IIb/IIIa inhibitors for emergency PCI performed at night [39].

We acknowledge several limitations that restrict the interpretation of our study. Data about cardiovascular risk factors and previous treatment before PCI were not available. In particular, we were unable to assess for a potential difference in the number of rescue PCIs performed at night and during the day. Furthermore, we could not obtain data

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Risk of in-hospital death according to time of PCI procedure after propensity score matching.</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Night-time vs daytime (n = 576 pairs)</td>
<td>28</td>
</tr>
<tr>
<td>Off hours vs regular hours (n = 695 pairs)</td>
<td>33</td>
</tr>
</tbody>
</table>

*Propensity score matching (from five to three digits sequential matching pair).*

*OR: odds ratio; PCI: percutaneous coronary intervention.*

* a Adjusted for age, sex, history of ischaemic heart disease, year of procedure, number of vessel disease, vessels treated, thrombolytic therapy use and stent implantation.*
on the duration of ischaemia (pain-to-door time and door-
to-balloon time), which would have affected the prognosis
[9,10], adjunctive treatment (including glycoprotein IIb/IIIa
inhibitors), reperfusion quality after PCI or ejection frac-
tion. These factors are important as they may be used as
predictors to explain differences in cardiac prognosis. How-
ever, our analytical approach using both a propensity score
adjustment and a conventional covariate adjustment in the
logistic regression models yielded similar point estimates
and 95% confidence limits for the magnitude of association
of procedural timing and mortality risk.

This study reflects actual clinical practice and demon-
strates the existence of greater mortality risk for emergency
PCI performed at night than for daytime emergency PCI,
independent of indication and previous treatment. We show
that better management of ACS is needed and, perhaps, that
greater use of adjunctive medications should be considered
when PCI is performed at night.

Conflicts of interest

The authors have not transmitted any conflicts of interest.

Acknowledgement

We thank Mr W. Kevin Meisner, PhD, ELS for editorial support.

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