

Outcomes of after-hours versus regular working hours primary percutaneous coronary intervention for acute myocardial infarction

Michelle M Graham,¹ William A Ghali,^{2,3,4} Danielle A Southern,⁴ Mouhieddin Traboulsi,^{2,5} Merril L Knudtson,^{2,5} for the APPROACH Investigators

¹Department of Medicine, University of Alberta, Edmonton, Canada

²Department of Medicine, University of Calgary, Calgary, Canada

³Department of Community Health Sciences, University of Calgary, Calgary, Canada

⁴Centre for Health and Policy Studies, University of Calgary, Calgary, Canada

⁵Libin Cardiovascular Institute, University of Calgary, Calgary, Canada

Correspondence to

Dr Michelle M Graham, Division of Cardiology, University of Alberta Hospital, 8440-112 Street, Edmonton, Alberta T6G 2R7, Canada; mmg2@ualberta.ca

APPROACH Clinical Steering Committee: Edmonton—R Tsuyuki (chair), M Graham, A Koshal; Calgary—M Curtis, WA Ghali, ML Knudtson, A Maitland, L Brent Mitchell and M Traboulsi.

Accepted 14 September 2010

Background: Primary percutaneous coronary intervention (PCI) is a proven therapy for acute ST-segment elevation myocardial infarction. However, outcomes associated with primary PCI may differ depending on time of day.

Methods and results: Using the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease, a clinical data-collection initiative capturing all cardiac catheterisation patients in Alberta, Canada, the authors described and compared crude and risk-adjusted survival for ST-segment elevation myocardial infarction patients undergoing primary PCI after-hours versus regular working hours. From 1 January 1999 to 31 March 2006, 1664 primary PCI procedures were performed (54.4% after-hours). Mortalities at 30 days were 3.6% for regular hours procedures and 5.0% for after-hours procedures ($p=0.16$). 1-year mortalities were 6.2% and 7.3% in the regular hours and after-hours groups, respectively ($p=0.35$). After adjusting for baseline risk factor differences, HRs for after-hours mortality were 1.26 (95% CI 0.78 to 2.02) for survival to 30 days and 1.08 (0.73 to 1.59) for survival to 1 year. A meta-analysis of our after-hours HR point estimate with other published risk estimates for after hours primary PCI outcomes yielded an RR of 1.23 (1.00 to 1.51) for shorter-term outcomes.

Conclusions: After-hours primary PCI was not associated with a statistically significant increase in mortality. However, a meta-analysis of this study with other published after-hours outcome studies yields an RR that leaves some questions about unexplored factors that may influence after-hours primary PCI care.

treatment,^{2–4} a particular concern after regular working hours, when facilities must be activated and staff brought in from home. Some institutions are therefore concerned that favourable outcomes may be difficult to achieve for patients presenting after hours. In a period of constrained resources, this would not lead to endorsement of routine after-hours procedures, and may in fact lead to scrutiny of how medical facilities operate at night, including more widespread adoption of night shifts.

Recent attention has also been directed towards other causes of adverse patient outcomes occurring after hours, mostly related to the effects of sleep deprivation and fatigue on healthcare provider performance, process of care and medical error.^{5–13} While none of these data are specifically related to cardiac care, one can postulate that these important factors might be at play in the provision of primary PCI.

We have developed a large, population-based, clinical registry capturing all patients undergoing cardiac catheterisation and revascularisation in Alberta, Canada, which provides a unique opportunity to evaluate outcomes in unselected patients. We sought to describe and compare crude and risk-adjusted survival for patients undergoing primary PCI for acute STEMI after-hours to those whose procedures occurred during regular working hours.

INTRODUCTION

Primary percutaneous coronary intervention (PCI) is superior to thrombolysis for acute ST-segment elevation myocardial infarction (STEMI).¹ An important factor affecting outcome in primary PCI is delays to

METHODS

Data sources

The Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) is a clinical data-collection



This paper is freely available online under the BMJ Journals unlocked scheme, see <http://qualitysafety.bmj.com/site/about/unlocked.xhtml>

initiative capturing consecutive patients undergoing cardiac catheterisation in Alberta, Canada (population 3 290 350) since 1995.¹⁴ APPROACH contains detailed information including patients' age, sex, ejection fraction and multiple comorbidities as outlined in **table 1**. It tracks therapeutic interventions (previous thrombolytic therapy, revascularisation procedures). Coronary anatomy and procedural details are also recorded. Following data entry by catheterisation laboratory staff, an enhancement procedure verifies patient comorbidities and ensures that there are no missing data fields.¹⁵ Follow-up mortality for all patients is ascertained through semiannual linkage to the Alberta Bureau of Vital Statistics. Three hospitals in two large cities (Edmonton and Calgary) provide the only revascularisation services in Alberta, and primary PCI is the preferred treatment strategy for STEMI. APPROACH and this protocol were approved by the Institutional Review boards of the University of Alberta and the University of Calgary.

The study population for this analysis consisted of STEMI patients undergoing primary PCI. Rescue PCI patients and those requiring hospital transfer were excluded. Door-to-balloon times for all patients were obtained through linkages to emergency room administrative data, and to the Calgary STEMI quality improvement data registry, which has prospectively collected time-interval data since 2004.

Timing of PCI procedures

Data in APPROACH are entered in real-time, with a database 'clock' for regular working hours (weekdays 0700–1800) or after-hours (weeknights 1800–0700, weekends and holidays). In order to measure outcomes using currently available technology and adjunctive therapy, we limited our assessment to those patients undergoing primary PCI from 1 January 1999 to 31 March 2006.

Outcome measures

Our primary goal was to determine whether after-hours procedures were associated with higher crude and adjusted mortalities at 30 days. A secondary analysis assessed survival to 1 year, though we recognise a priori that many factors can intervene over this period to potentially dilute any influence of the timing of PCI on outcomes.

Statistical analysis

Patient characteristics were compared using χ^2 tests. Kaplan–Meier plots and logrank tests were used to determine and compare crude mortalities. Multivariable Cox proportional hazards models were then used to adjust for the effects of baseline risk factors on group

Table 1 Baseline Characteristics

	After hours (n=906)	Working hours (n=758)	p Value
Clinical characteristics			
Mean age (SD), years	60.3 (13.2)	61.5 (12.7)	0.07
Sex (% female)	22.2	26.0	0.07
Ejection fraction (%)			0.08
<35	6.9	6.9	
35–50	29.9	29.2	
>50	49.9	47.2	
LV not done	10.7	14.6	
Missing	2.5	2.1	
Congestive heart failure (%)	11.9	10.6	0.38
Peripheral vascular disease (%)	4.4	4.0	0.64
Chronic pulmonary disease (%)	6.8	9.4	0.06
Cerebrovascular disease (%)	4.5	4.2	0.76
Creatinine >200 mmol/l (%)	4.0	2.5	0.09
Dialysis dependent (%)	1.0	0.5	0.29
Diabetes (%)	15.9	15.7	0.91
Hypertension (%)	50.0	47.9	0.39
Hyperlipidaemia (%)	45.8	45.4	0.86
Liver/gastrointestinal disease (%)	2.7	3.4	0.35
Malignancy (%)	3.0	2.9	0.92
Previous coronary artery bypass grafting (CABG) (%)	1.8	1.3	0.46
Previous myocardial infarction (MI) (%)	10.7	13.7	0.06
Previous percutaneous coronary intervention (PCI) (%)	3.5	3.7	0.86
Procedural characteristics			
Coronary anatomy (%)			0.79
One-vessel disease	38.5	38.9	
Two-vessel disease	31.0	29.0	
Three-vessel disease	26.6	28.4	
Left main	3.9	3.7	
Vessel intervened (%)			0.77
Right coronary	44.4	44.6	
Circumflex	12.9	14.0	
Left anterior descending	42.4	41.0	
Left mainstem	0.3	0.3	
Saphenous vein graft	0.0	0.1	
Glycoprotein IIb/IIIa inhibitor (%)	73.2	74.7	0.49
Stent use (%)	92.3	90.5	0.20
Intra-aortic balloon pump (IABP, %)	6.1	11.6	<0.0001
Inotrope use (%)	2.4	1.1	0.036
IABP+inotrope (%)	7.6	12.0	0.003

survival. The proportion hazards assumption was tested.¹⁶ The variables used for risk-adjustment analysis in these models are the baseline variables recorded in APPROACH (presented in table 1).¹⁴

Additional analysis including door-to-balloon time

The distributions of door-to-balloon times were described using simple box plots. These times were then entered as independent variables in the above-mentioned multivariable Cox proportional hazards models that included all of the baseline clinical variables, to determine whether adjustment for door-to-balloon times changed the point estimates of our adjusted HRs and were therefore a mediating factor of any potential associations of time of day with mortality. An additional sensitivity analysis using door-to-balloon time ≤ 90 min or >90 min (according to current guidelines for optimal performance of primary PCI) was performed, with door-to-balloon time first assessed as a potential confounding variable (through inclusion in the multivariable models), and then as an effect modifier (through stratification on door-to-balloon time).

We performed a meta-analysis of our study's RR for after-hours PCI along with other published studies, to place our findings in the context of what is already known about this important question. A detailed literature search identified all published manuscripts on this topic. The search strategy and study selection procedures are available from the authors upon request. Because of heterogeneity noted in the relative risks across studies (τ^2 0.051, $p=0.02$), a random effects model was chosen for pooling of results across studies.

Statistical analyses were performed using SAS Version 8.1. The meta-analysis was performed using Stata Version 8.

RESULTS

Patient characteristics

From 1 January 1999 to 31 March 2006, 1664 patients underwent primary PCI for acute MI in Alberta. Of these, 54.4% occurred after hours. Table 1 shows the baseline characteristics of regular working hours and after-hours cases. There were no significant differences between the groups in terms of cardiac risk factors, comorbidities, ejection fraction, extent of coronary

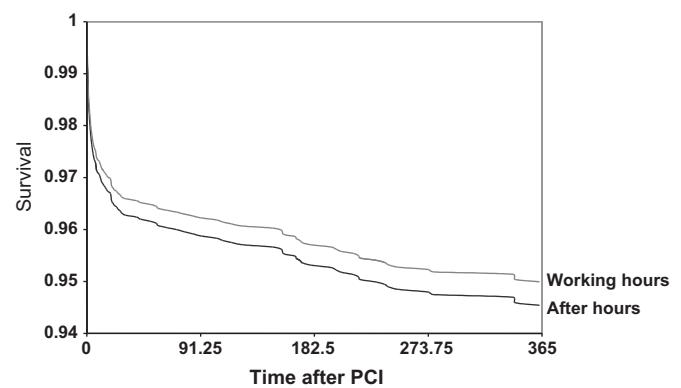


Figure 1 Kaplan–Meier survival curves to 1 year for primary percutaneous coronary intervention (PCI) performed after hours and during regular working hours.

disease or culprit vessel, with the exception of a higher use of intra-aortic balloon counterpulsation devices (alone or in combination with inotropes) during working hours, and higher use of inotropes alone after-hours.

Crude and adjusted outcomes

Mortalities at 30 days were 3.6% in the working hours group and 5.0% in the after-hours group ($p=0.16$). By 1 year, mortalities were 6.2% and 7.3% in the working hours and after-hours groups, respectively ($p=0.35$). Figure 1 shows Kaplan–Meier survival curves extending to 1 year of follow-up. After-hours patients do appear to have a poorer survival over time.

Table 2 shows the HRs and 95% CIs of 1.34 (95% CI 0.85 to 2.12) for after-hours cases relative to working hours cases for survival extending to 30 days (our primary study outcome) and 1.18 (95% CI 0.81 to 1.72) for survival extending to 1 year. After adjusting for the variables in table 1, HRs (HR-1) changed slightly to 1.26 (95% CI 0.78 to 2.02) for survival to 30 days and 1.08 (95% CI 0.73 to 1.59) for survival to 1 year.

Analysis controlling for door-to-balloon times

The median door-to-balloon time was 72.0 min in the working hours group and 80.0 min in the after-hours group ($p=0.007$), as demonstrated by the box plots in figure 2.

Table 2 also presents the HRs for survival associated with after-hours procedures, further adjusted for door-to-balloon times (HR-2, 1.23 (95% CI 0.77 to 1.99)). The

Table 2 Crude and Adjusted Hazard Ratio for survival for after-hours relative to regular hours primary PCI

	Crude HR (95% CI)	HR-1 adjusted* (95% CI)	Adjusted HR-2† (95% CI)
30-day survival	1.34 (0.85 to 2.12)	1.26 (0.78 to 2.02)	1.23 (0.77 to 1.99)
1-year survival	1.18 (0.81 to 1.72)	1.08 (0.73 to 1.59)	1.06 (0.71 to 1.56)

*HR-1 adjusted for all variables in table 1.

†HR-2 adjusted for variables in table 1 plus door-to-balloon time.

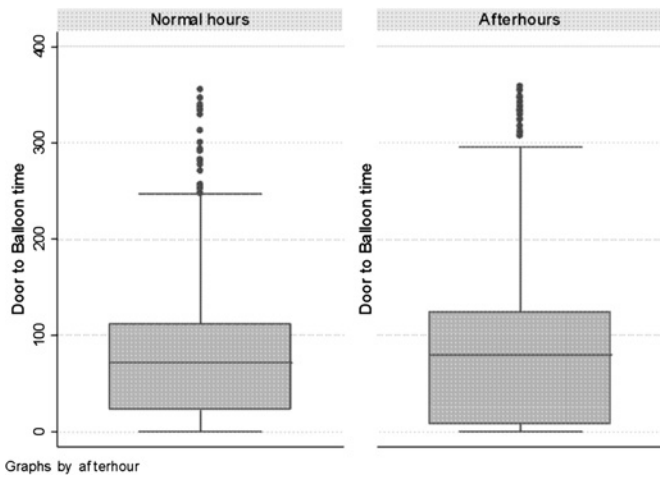
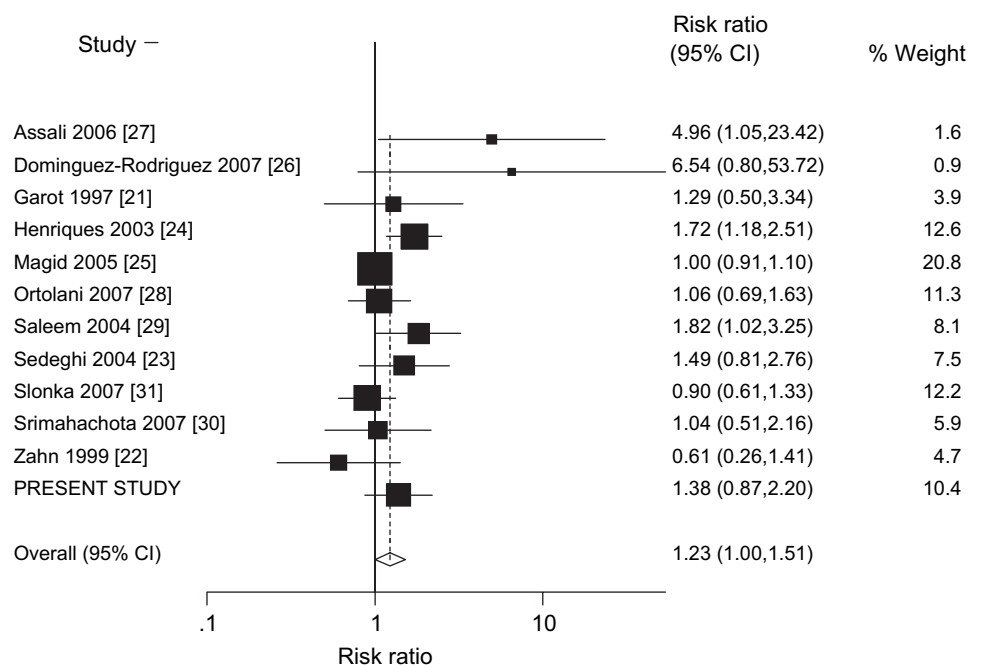


Figure 2 Boxplots illustrating door-to-balloon times for primary percutaneous coronary intervention performed after hours and during regular working hours. The median door-to-balloon time is indicated. The boundaries of the box plots refer to the 25th and 75th percentiles, with the whisker bars representing the 5th and 95th percentiles.

sequential analysis for survival to 1 year also revealed a minimal effect of this additional adjustment. The full Cox regression model can be found in [appendix 2](#). An additional sensitivity analysis performed using the door-to-balloon time cutpoints of ≤ 90 min and >90 min, treated as a confounding variable through inclusion in the multivariable models, yielded HRs that were essentially the same (30-day survival HR 1.23 (95% CI 0.77 to 1.99)). When considered as an effect modifier in stratified analyses, we found a stronger association for those with longer door-to-balloon times (≤ 90 min HR 1.23 (95% CI 0.63 to 2.42); >90 min HR 1.53 (95% CI 0.76 to 3.09)).

Figure 3 Meta-analysis of studies examining outcomes of primary percutaneous coronary intervention performed after hours and during regular working hours.



Meta-analysis

To present our study result more explicitly in the context of the existing literature, we performed a meta-analysis of studies examining outcomes in after-hours primary PCI ([figure 3](#)). The studies ranged from single centre experiences to large registries, and one clinical trial of PCI strategies (CADILLAC), conducted from 1994 to 2006. Several excluded cardiogenic shock, rescue PCI or transfer patients.^{17–21} A tabulated description of these studies is presented in [appendix 1](#). Unadjusted risk ratios ranged from 0.61 to 6.54, with an overall random-effect pooled estimate of RR of 1.23 (95% CI 1.00 to 1.52). This pooled result across 12 studies, including ours, does suggest that there may still be a need to continue exploring the possibility of an association between after-hours procedures and poorer outcomes.

DISCUSSION

Our study adds to a growing body of literature on after-hours medical care. In an unselected patient population, outcomes for after-hours PCI cases did not differ significantly from those of working-hours cases. However, the point estimate from our study suggesting a 23% increased risk for adverse events early after PCI needs to be taken in the context of other studies, some of which have shown poorer outcomes in after-hours primary PCI. Further, the 23% increase seen in this study and our meta-analysis of prior studies is hardly negligible in that it is of similar magnitude to the benefits associated with beta-blocker and thrombolytic therapy for STEMI.^{22 23}

Interest in after-hours care has heightened with increased international focus on patient safety. Such

issues have received considerable attention in relation to studies that have demonstrated increased mortality in patients with severe medical conditions admitted on weekends, as a direct result of delayed care.²⁴ Kostis and colleagues also found that weekend admissions for patients with MI were associated with a higher mortality.²⁵

With primary PCI, concerns about outcomes are most important after-hours cases where the need to bring cardiac catheterisation laboratory staff from home may result in significant treatment delays. Previous investigations show conflicting results. Garot and colleagues assessed 288 primary PCI patients and found similar door-to-balloon times and no differences in in-hospital outcome.¹⁷ However, this study was conducted in a French centre which activates the cardiac catheterisation laboratory from the ambulance and is staffed after-hours by in-house nurses. It is difficult to apply the findings of this study to areas which lack these policies. Zahn *et al* examined the outcomes of 378 patients treated during regular working hours and 113 patients treated after-hours, where mortality was lower (5.3% vs 8.7%) in the after-hours group.²⁶ However, eight facilities participated during working hours but fewer at night, raising the possibility of selection bias in after-hours cases. Data from the 2082 patients enrolled in the larger randomised CADILLAC primary PCI trial found that patients who presented after hours had similar 30-day and 1-year mortalities to those presenting during working hours.¹⁸ In contrast, in 1702 consecutive primary PCI cases, Henriques *et al* found that patients treated off-hours had a higher incidence of failed PCI and worse clinical outcomes, including increased 30-day mortality.²⁷

We noted a lack of effect of controlling for door-to-balloon times on our point estimate of RR, even when using the accepted clinical cutpoint of ≤ 90 min as a confounding variable. When treated as an effect modifier in stratified analyses, we found a stronger association of hazard for those with longer door-to-balloon times (>90 min), suggesting that the impact of the after-hours construct is even greater when treatment is delayed. These findings, and the potential signal of harm suggested by the meta-analysis presented here, require us to consider other possible contributing explanations for increased mortality in after-hours patients. One possibility is that physician fatigue could influence procedural performance, well represented in the anaesthesia literature.^{6–8} In addition, in a study of the effect of heavy night call in residents, Arnedt *et al* found that postcall impairment was at least equivalent to the ingestion of 3–4 standard alcoholic drinks.⁹ Other investigators have found that manual dexterity and surgical skills may be specifically vulnerable to sleep deprivation.^{10–12 28}

Staffing levels also tend to be lower on weekends and holidays than during working hours, despite often increased patient acuity, and are a potential contributor to suboptimal patient safety at such times.^{29–31}

Another important concern relevant to our cohort relates to the fact that all revascularisation procedures in Alberta are performed in academic tertiary care centres, and overnight care outside the cardiac catheterisation laboratory is generally provided by junior housestaff. Serious medical errors and pronounced increases in after-hours mortality have both been demonstrated in major teaching hospitals, whereas after-hours admissions to tertiary care intensive care units with on-site attending physicians are not associated with increased mortality.^{13 31–33} Thus, the combination of relatively inexperienced housestaff, low staffing and fatigue among providers may be responsible for some of the suggestion of increased hazard associated with after-hours primary PCI.

There are limitations to this study. Like other investigators studying acute MI care, we do not have any data regarding symptom onset-to-balloon time, which is difficult to characterise at night, as the perceived time of symptom onset may not reliably reflect actual ischaemic time, and patients who are at home when symptoms occur may be less likely to promptly seek medical attention. All PCI procedures were performed by experienced operators at high-volume academic centres, so our results may not be generalisable to patients in other settings, or to hospitals that do not rely upon trainees for major provision of after-hours care. Finally, our thoughts as to the other potential influences on after-hours outcomes remain speculative, as none of the above-mentioned studies are specific to cardiology.

The above notwithstanding, our findings do not support abandoning after-hours primary PCI in favour of thrombolysis. Given that the major studies of primary PCI versus thrombolysis would have included at least some after-hours patients in both treatment arms, it is unlikely that the benefit of primary PCI would be entirely negated after-hours. In addition, potential factors influencing outcomes after-hours could also apply to patients receiving thrombolysis.

In conclusion, our study findings suggest that primary PCI can be performed outside a clinical trial with acceptable short- and long-term mortalities, during working hours and after-hours. However, our findings taken in the context of other after-hours primary PCI studies, with an almost 25% increase in the risk for short-term mortality, do not provide complete reassurance; nor do they indicate complete equivalency of outcomes to working-hours procedures. This summary finding remains a concern and may be related to previously unexplored areas in after-hours care. Patient satisfaction will also need to be considered. Further research is thus still required to

determine whether processes and quality of care are influenced by understudied areas such as fatigue, staffing levels, physician experience or other factors.

Acknowledgements We would like to thank R Boone, for his thoughtful comments. We appreciate the assistance of the Calgary Health Region and the Capital Health Authority in supporting data entry by cardiac catheterisation laboratory personnel.

Funding The research and creation of this paper were supported by a grant from the Canadian Institutes of Health Research (CIHR). MLK receives partial support from the Libin Trust Fund. WAG is a Senior Health Scholar of the Alberta Heritage Foundation for Medical Research and also supported by a government of Canada Research Chair in Health Services Research and by a Health Scholar Award from the Alberta Heritage Foundation for Medical Research, Edmonton, Alberta. APPROACH was funded in 1995 by the Weston Foundation, with ongoing support from the Canadian Cardiovascular Outcomes Research Team (CCORT), a CIHR Team Grant and the Province-Wide Services Committee of Alberta Health and Wellness. The initiative has also received unrestricted support from Merck Frosst Canada, Monsanto Canada—Searle, Eli Lilly Canada, Guidant Corporation, Boston Scientific, Hoffmann-La Roche and Johnson & Johnson Inc—Cordis.

Competing interests None.

Ethics approval Ethics approval was provided by the University of Calgary and University of Alberta.

Contributors WAG participated in the study design, analysis and manuscript revision. MLK and MT participated in study design and manuscript revision. DAS participated in the analysis and manuscript revision. The members of the APPROACH steering committee mentioned in the acknowledgements section have also read and approved submission of this paper.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomized trials. *Lancet* 2003;361:13–20.
- Berger PB, Ellis SG, Holmes DR, *et al*. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction. *Circulation* 1999;100:14–20.
- Cannon CP, Gibson CM, Lambrew CT, *et al*. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA* 2000;283:2941–7.
- Zahn R, Schiele R, Gitt AK, *et al*. Impact of prehospital delay on mortality in patients with acute myocardial infarction treated with primary angioplasty and intravenous thrombolysis. *Am Heart J* 2001;142:105–11.
- Gaba DM, Howard SK. Fatigue among clinicians and the safety of patients. *N Engl J Med* 2002;347:1249–55.
- Aya AG, Mangin R, Robert C, *et al*. Increased risk of unintentional dural puncture in night-time obstetric epidural anesthesia. *Can J Anaesth* 1999;46:665–9.
- Gander PH, Merry A, Millar MM, *et al*. Hours of work and fatigue-related error: a survey of New Zealand anesthetists. *Anaesth Intensive Care* 2000;28:178–83.
- Wright MC, Phillips-Bute B, Mark JB, *et al*. Time of day effects on the incidence of anesthetic adverse events. *Qual Saf Health Care* 2006;15:258–63.
- Arnedt JT, Owens J, Crouch M, *et al*. Neurobehavioural performance of residents after heavy night call vs after alcohol ingestion. *JAMA* 2005;294:1025–33.
- Goldman LI, McDonough MT, Rosemond GP. Stresses affecting surgical performance and learning: correlation of heart rate, electrocardiogram, and operation simultaneously recorded on videotapes. *J Surg Res* 1972;12:83–6.
- Taffinder NJ, McManus IC, Gul Y, *et al*. Effect of sleep deprivation on surgeons' dexterity on laparoscopy simulator. *Lancet* 1998;352:1191.
- Grantcharov TP, Bardram L, Funch-Jensen P, *et al*. Laparoscopic performance after one night on call in a surgical department: prospective study. *BMJ* 2001;323:1222–3.
- Landrigan CP, Rothschild JM, Cronin JW, *et al*. Effect of reducing interns' work hours on serious medical errors in intensive care units. *N Engl J Med* 2004;351:1838–48.
- Ghali WA, Knudtson ML. Overview of APPROACH—the Alberta Provincial Program for Outcome Assessment in Coronary Heart Disease. *Can J Cardiol* 2000;16:1225–30.
- Norris CM, Ghali WA, Knudtson ML, *et al*. Dealing with missing data in observational health care outcome analyses. *J Clin Epidemiol* 2000;53:377–83.
- Ghali WA, Quan H, Brant R, *et al*. Comparison of 2 methods for calculating adjusted survival curves from proportional hazards models. *JAMA* 2001;286:1494–7.
- Garot P, Juliard JM, Benamer H, *et al*. Are the results of primary percutaneous transluminal coronary angioplasty for acute myocardial infarction different during the 'off' hours? *Am J Cardiol* 1997;79:1527–9.
- Sadeghi HM, Grines CL, Chandra HR, *et al*. Magnitude and impact of treatment delays on weeknights and weekends in patients undergoing primary angioplasty for acute myocardial infarction (the CADILLAC trial). *Am Heart J* 2004;94:637–40.
- Magid DJ, Wang Y, Herrin J, *et al*. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. *JAMA* 2005;294:803–12.
- Assali AR, Brosh D, Vaknin-Assa H, *et al*. The impact of circadian variation on outcomes in emergency acute anterior myocardial infarction percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2006;67:221–6.
- Ortolani P, Marzocchi A, Marzocchini C, *et al*. Clinical comparison of normal hours vs off hours percutaneous coronary interventions for ST-elevation myocardial infarction. *Am Heart J* 2007;154:366–72.
- Freemantle N, Cleland J, Young P, *et al*. Beta blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ* 1999;318:1730–7.
- Lau J, Antman EM, Jimenez-Silva J, *et al*. Cumulative meta-analysis of therapeutic trials for myocardial infarction. *N Engl J Med* 1992;327:248–54.
- Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001;345:663–8.
- Kostis WJ, Kitaw D, Marcella SW, *et al*; for the Myocardial Infarction Data Acquisition System (MIDAS 10) Study Group. Weekend versus weekday admission and mortality from myocardial infarction. *N Engl J Med* 2007;356:1099–109.
- Zahn R, Schiele R, Seidl K, *et al*. Daytime and nighttime differences in patterns of performance of primary angioplasty in the treatment of patients with acute myocardial infarction. *Am Heart J* 1999;138:1111–17.
- Henriques JP, Haasdijk AP, Zijlstra F. Outcome of primary angioplasty for acute myocardial infarction during routine duty hours versus during off-hours. *J Am Coll Cardiol* 2003;41:2138–42.
- Rothschild JM, Keohane CA, Rogers S, *et al*. Risks of complications by attending physicians after performing night-time procedures. *JAMA* 2009;302:1565–72.
- Needleman J, Buerhaus P. Nurse staffing and patient safety: current knowledge and implications for action. *Int J Qual Health Care* 2003;15:275–7.
- Pronovost PJ, Angus DC, Dorman T, *et al*. Physician staffing patterns and clinical outcomes in critically ill patients: a systematic review. *JAMA* 2002;288:2151–62.
- Tarnow-Mordi WO, Hau C, Warden A, *et al*. Hospital mortality in relation to staff workload: a 4-year study in an adult intensive care unit. *Lancet* 2000;356:185–9.
- Cram P, Hillis SL, Barnett M, *et al*. Effects of weekend admission and hospital teaching status on in-hospital mortality. *Am J Med* 2004;117:151–7.
- Arabi Y, Alshimeri A, Taher S. Weekend and weeknight admissions have the same outcome of weekday admissions to an intensive care unit with on-site intensivist coverage. *Crit Care Med* 2006;34:605–11.
- Dominguez-Rodriguez A, Garcia-Gonzalez M, Abreu-Gonzalez P. Outcome of primary angioplasty for ST-segment elevation myocardial infarction during routine duty hours versus during off-hours. Results of a single center in Spain. *Int J Cardiol* 2007;119:227–9.
- Saleem M, Kannan H, Aronow WS, *et al*. The effects of off-normal hours, age and gender for coronary angioplasty on hospital mortality in patients undergoing coronary angioplasty for acute myocardial infarction. *Am J Cardiol* 2004;93:763–4.
- Slonka G, Gasior M, Lekston A, *et al*. Comparison of results of percutaneous coronary interventions in patients with ST-segment elevation myocardial infarction during routine working hours or off-hours. *Kardiol Pol* 2007;65:1171–7.
- Srimachochota S, Boonyaratavej S, Udayachalem W, *et al*. Comparison of official hours versus non-official hours: percutaneous coronary intervention in acute ST-elevation myocardial infarction patients. *J Med Assoc Thai* 2007;90:45–51.

APPENDIX 1

Study	Overall N	Location	Inclusion criteria	Exclusion criteria	Working hours mortality	After-hours mortality	RR (95% CI)	
Dominguez-Rodriguez <i>et al</i> ³⁴	90	Spain, 2003	Consecutive primary PCI, single centre	None identified	1/51 (1.9%) in hospital	5/39 (12.8%)	6.54 (0.80 to 53.72)	
Assali <i>et al</i> ²⁰	273	Israel, 2001–2004	Consecutive primary PCI, single centre	Cardiogenic shock	2/160 (1.25%) in hospital	7/113 (6.2%)	4.96 (1.05 to 23.42)	
Ortolani <i>et al</i> ²¹	985	Italy, 2003–2005	Consecutive primary PCI, single centre	Rescue PCI, in-hospital ST-segment elevation myocardial infarction	5/160 (3.1%) at 30 days	29/382 (7.6%) in hospital	49/603 (8.1%)	1.06 (0.69 to 1.63)
Saleem <i>et al</i> ³⁵	1050	USA, 1998–2002	Consecutive primary PCI, single centre		21/656 (3.2%) in hospital	23/394 (5.8%)	1.82 (1.02 to 3.25)	
Sadeghi <i>et al</i> ¹⁸	2036	International	CADILLAC randomized controlled trial, all sites 24/7 primary PCI	Shock, bleeding, renal insufficiency	17/1047 (1.6%) at 30 days	24/989 (2.4%)	1.49 (0.81 to 2.76)	
Henriques <i>et al</i> ²⁷	1702	Netherlands, 1994–2000	Consecutive primary PCI, within 6 h, single centre	Symptom onset >6 h	17/909 (1.0%) at 30 days	33/793 (4.2%)	1.72 (1.18 to 2.51)	
Magid <i>et al</i> ¹⁹	33647	USA, 1999–2002	NRMI registry, PCI at 421 centres	Transfer patients	728/15419 (4.7%)	859/18228 (4.7%)	1.0 (0.91 to 1.10)	
Slonka <i>et al</i> ³⁶	1778	Poland, 1998–2003	Consecutive primary PCI, single centre, working hours defined as 0800–1500		33/482 (6.8%) in hospital	80/1296 (6.2%)	0.90 (0.61 to 1.33)	
Srimachochota ³⁷	256	Thailand, 1999–2003	Consecutive primary PCI, single centre		11/107 (10.3%) in hospital	16/149 (10.7%)	1.04 (0.51 to 2.16)	
Zahn <i>et al</i> ²⁶	491	Germany, 1994–1997	MITRA registry, consecutive primary PCI at eight centres during the day and three centres at night (concern for selection bias—23% of patients done after-hours)		33/378 (8.7%) in hospital	6/113 (5.3%)	0.61 (0.26 to 1.41)	
Garot <i>et al</i> ¹⁷	288	France	Consecutive primary PCI, <6 h after symptom onset, cath lab activated by cath lab staffed after hours by CCU nurses	Shock	6/113 (5.3%)	12/175 (6.9%)	1.29 (0.50 to 3.34)	
Graham	2043	Alberta, 1999–2006	Consecutive primary PCI, three centres	Transfer patients	32/896 (3.6%)	57/1147 (5.0%)	1.39	

PCI, percutaneous coronary intervention.

APPENDIX 2

Full Cox regression model (30 days and 1 year)

30-day

Model fit statistics		
Criterion	Without covariates	With covariates
–2 log L	1153.810	1050.941
AIC	1153.810	1090.941
SBC	1153.810	1138.075

Testing global null hypothesis: beta=0			
Test	χ^2	df	Pr> χ^2
Likelihood ratio	102.8685	20	<0.0001
Score	148.7902	20	<0.0001
Wald	120.9245	20	<0.0001

Analysis of maximum likelihood estimates

Parameter	df	Parameter estimate	SE	χ^2	Pr> χ^2	HR	95% CI
After hour	1	0.22990	0.24166	0.9050	0.3414	1.26	0.78 to 2.02
Age	1	0.41968	0.26344	2.5379	0.1111	1.52	0.91 to 2.55
Sex	1	-0.62751	0.24654	6.4781	0.0109	0.53	0.33 to 0.87
COPD	1	-0.05550	0.39203	0.0200	0.8874	0.95	0.44 to 2.04
CEVD	1	0.51473	0.38828	1.7574	0.1849	1.67	0.78 to 3.58
Creat	1	1.20996	0.38643	9.8038	0.0017	3.35	1.57 to 7.15
Diabetes	1	0.69557	0.26984	6.6446	0.0099	2.01	1.18 to 3.40
Dialysis	1	-0.21161	0.71513	0.0876	0.7673	0.81	0.20 to 3.29
HTN	1	-0.64629	0.25774	6.2878	0.0122	0.52	0.32 to 0.87
Lipid	1	-1.04936	0.29260	12.8618	0.0003	0.35	0.20 to 0.62
Liver/GI	1	0.25309	0.64277	0.1550	0.6938	1.29	0.37 to 4.54
Malignancy	1	-1.02538	1.02202	1.0066	0.3157	0.36	0.05 to 2.66
Old MI	1	-0.15068	0.37330	0.1629	0.6865	0.86	0.41 to 1.79
Lytic	1	-0.12468	0.72190	0.0298	0.8629	0.88	0.21 to 3.63
PVD	1	0.87345	0.36897	5.6040	0.0179	2.40	1.16 to 4.94
Ef 35	1	-0.51292	0.28934	3.1425	0.0763	0.60	0.34 to 1.06
Ef 20	1	0.09989	0.40171	0.0618	0.8036	1.11	0.50 to 2.43
Ef under20	1	1.08157	1.06411	1.0331	0.3094	2.95	0.37 to 23.74
d1	1	0.83690	0.26202	10.2018	0.0014	2.31	1.38 to 3.86
d2	1	1.39078	0.40562	11.7563	0.0006	4.02	1.81 to 8.90

Analysis of maximum likelihood estimates

Parameter	df	Parameter estimate	SE	χ^2	Pr> χ^2	HR	95% CI
After hour	1	0.07764	0.19810	0.1536	0.6951	1.08	0.73 to 1.59
Age	1	0.72647	0.21061	11.8978	0.0006	2.07	1.37 to 3.12
Sex	1	-0.49431	0.20938	5.5735	0.0182	0.61	0.41 to 0.92
COPD	1	-0.40181	0.34744	1.3375	0.2475	0.67	0.34 to 1.32
CEVD	1	0.61525	0.31582	3.7951	0.0514	1.85	1.00 to 3.44
Creat	1	1.32714	0.31433	17.8261	<0.0001	3.77	2.04 to 6.98
Diabetes	1	0.81857	0.21788	14.1147	0.0002	2.27	1.48 to 3.48
Dialysis	1	-0.49067	0.61541	0.6357	0.4253	0.61	0.18 to 2.05
HTN	1	-0.50147	0.21114	5.6409	0.0175	0.61	0.40 to 0.92
Lipid	1	-0.67676	0.22209	9.2852	0.0023	0.51	0.33 to 0.79
Liver/GI	1	0.28563	0.49074	0.3388	0.5605	1.33	0.51 to 3.48
Malignancy	1	0.43663	0.44218	0.9750	0.3234	1.55	0.65 to 3.68
Old MI	1	0.05295	0.28561	0.0344	0.8529	1.05	0.60 to 1.85
Lytic	1	-0.10150	0.59082	0.0295	0.8636	0.90	0.28 to 2.89
PVD	1	0.82531	0.31353	6.9289	0.0085	2.28	1.24 to 4.22
Ef 35	1	-0.58321	0.24534	5.6509	0.0174	0.56	0.35 to 0.90
Ef 20	1	0.08877	0.33432	0.0705	0.7906	1.09	0.57 to 2.10
Ef under20	1	0.37509	1.05195	0.1271	0.7214	1.46	0.19 to 11.44
d1	1	0.78256	0.21761	12.9322	0.0003	2.19	1.43 to 3.35
d2	1	1.44161	0.32632	19.5168	<0.0001	4.23	2.23 to 8.01

COPD – chronic pulmonary disease
 CEVD – cerebrovascular disease
 HTN – hypertension
 MI – myocardial infarction
 Lytic – thrombolytic therapy
 PVD – peripheral vascular disease
 Ef – Ejection Fraction

1-year

Model fit statistics

Criterion	Without covariates	With covariates
-2 log L	1668.884	1528.640
AIC	1668.884	1568.640
SBC	1668.884	1623.187

Testing global null hypothesis: beta=0

Test	χ^2	df	Pr> χ^2
Likelihood ratio	140.2445	20	<0.0001
Score	210.1061	20	<0.0001
Wald	166.3952	20	<0.0001