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One-year mortality of primary angioplasty for acute myocardial infarction during regular working hours versus off-hours

Surya Dharma[1]*, MD, PhD, FIHA, FICA, FAPSIC, FESC, FSCAI; Renan Sukmawan[1], MD, PhD, FIHA; Bambang Budi Siswanto[1], MD, PhD, FIHA, FAsCC, FAPSC, FESC, FACC, FSCAI; Hananto Andriantoro[1], MD, PhD, FIHA, FICA; Iwan Dakota[1], MD, PhD, FIHA, FICA, FESC, FSCAI; Sunil V. Rao[2], MD, FSCAI

1. Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Indonesia, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia; 2. Duke University Medical Center, Durham VA Medical Center, Durham, NC, USA

KEYWORDS

- long-term mortality
- off-hours
- regular hours
- STEMI care

Abstract

Aims: We aimed to evaluate the relationship between timing of admission and long-term mortality of ST-elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (PPCI) in a tertiary care academic teaching hospital.

Methods and results: A total of 1,126 STEMI patients admitted during off-hours (week nights, weekends, holidays) and regular hours treated with PPCI between 2008-2013 were analysed. Descriptive analysis and multivariable survival analysis were used to estimate the relationship between treatment during off-hours versus regular hours and the incidence of all-cause mortality during hospitalisation and at one-year follow-up. There was a similar proportion of patients achieving door-to-device time ≤90 minutes (45.3% vs. 48%) among STEMI patients admitted during off-hours (n=857) as compared with regular hours (n=269). Aspirin and clopidogrel use within 24 hours approached 97% and 98% of patients admitted in off-hours and regular hours, respectively. Achievement of post-PPCI Thrombolysis In Myocardial Infarction flow grade 3 approached 93% and 91% in off-hours and regular hours admission, respectively (p=0.18). In-hospital mortality was similar in patients admitted during off-hours and those admitted during regular hours (5.1% vs. 5.9%; adjusted hazard ratio 0.81; 95% CI: 0.43-1.54). One-year mortality was also similar (10.5% vs. 13%; adjusted hazard ratio 0.73; 95% CI: 0.46-1.12).

Conclusions: STEMI patients who were admitted during off-hours to an academic hospital and treated with PPCI had similar survival at one year as compared with those who were admitted during regular hours. Study registration: Clinicaltrials.gov NCT02319473

**Corresponding author: Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Indonesia, National Cardiovascular Center Harapan Kita, Jl S Parman Kav 87, Slipi, Jakarta Barat, 11420, Indonesia. E-mail: drsuryadharma@yahoo.com*

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Introduction

Randomised clinical trials have shown the superiority of primary percutaneous coronary intervention (PPCI) over fibrinolysis therapy in terms of better event-free survival and clinical outcomes in patients with acute ST-elevation myocardial infarction (STEMI)[1]. However, there has been concern as to whether STEMI patients who are admitted during off-hours (week nights, weekends, and holidays) to undergo PPCI might have higher mortality than patients admitted during regular "office" hours. The mortality difference is thought to be due to the variations in door-to-device (DTD) time, door-to-ECG time, awareness of the alarm centre staff, physician performance, and the numbers of staff in the catheterisation laboratory and intensive cardiovascular care unit. On the other hand, the establishment of a STEMI network may narrow these disparities, resulting in similar outcomes regardless of the time of the patient's presentation.

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While prior studies have shown contradictory outcomes in STEMI patients who underwent PPCI during off-hours versus regular office hours[2-14], most of the studies did not evaluate the long-term outcomes[3,4,6,8,9,11-14]. Moreover, many of these studies included several centres, and results from hospitals with poor STEMI processes may offset those from leading centres (i.e., "regression to the mean"). In this context, data from a single centre may provide value by providing an example of "best practices" for PPCI if outcomes are similar between off-hours and on-hours patients. We evaluated the relationship between timing of admission of STEMI patients (off-hours versus regular hours) and long-term mortality of STEMI patients treated with PPCI in a tertiary care academic teaching hospital.

Methods

PATIENT POPULATION

Data were derived from a local registry (Jakarta Acute Coronary Syndrome [JAC] registry) in the National Cardiovascular Center Harapan Kita, Jakarta, Indonesia. The hospital is a tertiary referral and teaching hospital, serving approximately 11 million inhabitants. The hospital provides a 24/7 PPCI service and performs approximately 2,000 PCIs annually with 13 interventional cardiologists. Since 2008, all consecutive patients with acute coronary syndrome (ACS), including STEMI patients who presented within 12 hours of symptom onset and underwent PPCI in the hospital, were recorded in the database. Using the JAC registry database, we examined the characteristics of STEMI patients admitted during off-hours versus regular hours and treated with PPCI. The Jakarta Cardiovascular Care Unit Network System was developed in 2010 to provide rapid and optimal reperfusion therapy for STEMI within a regional network of 156 hospitals and 44 primary healthcare centres. The STEMI network is coordinated by the emergency department (ED) staff of our hospital and manned 24/7[15-17]. Currently, the JAC registry is the main data source for measuring the performance of the STEMI network, and this study is part of the analysis of the performance measures.

Hospital admission time (off-hours and regular hours) was the primary basis for classification used in the study cohort. Off-hours arrival time was defined as week nights (Monday to Thursday: 4 pm to 7.30 am, and Friday: 4.30 pm to 7.30 am), weekends, and holidays. Regular hours arrival was defined as weekdays/regular office hours (Monday to Thursday: 7.30 am to 4 pm, and Friday: 7.30 am to 4.30 pm).

Diagnosis of STEMI was made based on the presence of ischaemic symptoms and persistent (>20 minutes) ST-segment elevation in at least two contiguous leads, a new left bundle branch block, or a true posterior myocardial infarction confirmed by posterior leads[18]. This study has been approved by the local institutional review board committee.

STUDY SAMPLE

Between 1st January 2008 and 29th December 2013, the JAC registry database contained 15,252 ACS patients, of whom 5,237 were STEMI patients. Of these, 1,126 patients underwent PPCI and were included in the analysis. The majority of STEMI patients did not receive reperfusion therapy, mainly due to late presentation of the patient[15-17]. Patient distribution is displayed in **Figure 1**. Patients with a repeated PPCI procedure were included in the study since hospital admission time is the primary basis of the analysis.

MANAGEMENT PROTOCOL

The management of STEMI was in accordance with the European Society of Cardiology (ESC) guidelines[18]. All patients were pretreated with 160-320 mg acetylsalicylic acid and 600 mg clopidogrel orally before PPCI, followed by daily administration of 75 mg clopidogrel for six to 12 months after discharge and 80-100 mg acetylsalicylic acid indefinitely. Before PPCI, all patients received an intravenous bolus of unfractionated heparin in the catheterisation laboratory (50 IU/kg if receiving glycoprotein IIb/IIIa inhibitor [GPI] or 100 IU/kg if not receiving GPI). The use of GPI was left to the discretion of the interventional cardiologist in charge.

Vascular access site choice for PPCI was according to operator preference, and PPCI was performed based on standard techniques. In our institution, stenting only in the infarct-related coronary artery (IRA) was adopted. Technical considerations, such as direct stenting or balloon predilation were left to the operator's discretion. Manual thrombus aspiration was recommended as part of the local protocol[19].

Angiographic measurement of coronary flow using the Thrombolysis In Myocardial Infarction (TIMI) flow classification was applied to evaluate the microvascular perfusion in all patients following PPCI[20].

DATA COLLECTION AND FOLLOW-UP

Data elements consisting of demographic, clinical, procedural, angiographic and follow-up variables were collected from the JAC registry electronic database. Data quality is maintained through point-of-entry and monthly data quality checks by the principal investigator of the JAC registry (SD). In-hospital and one-year mortality were obtained from the medical records, phone calls, and/or family interviews by dedicated research staff using a standardised questionnaire.

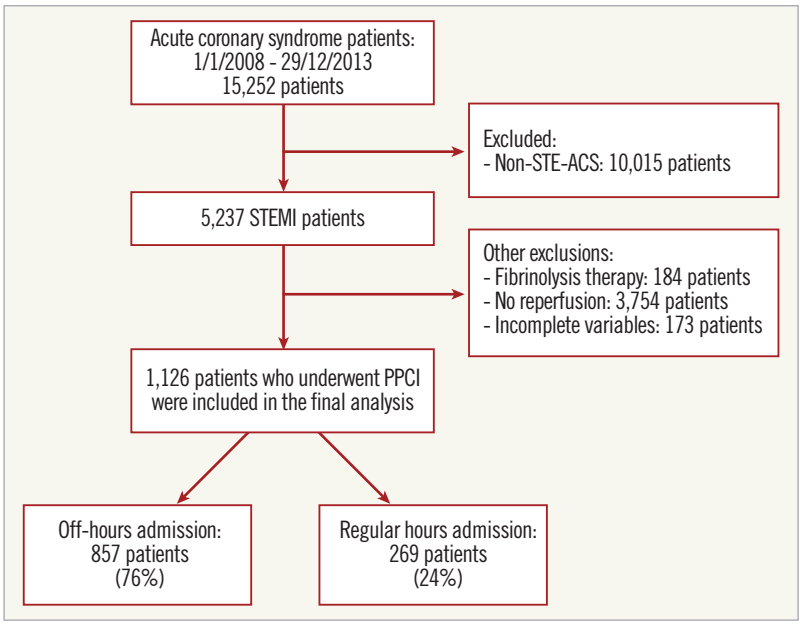

Figure 1. *Patient distribution. PPCI: primary percutaneous coronary intervention; STE-ACS: ST-elevation acute coronary syndrome; STEMI: ST-elevation myocardial infarction*

STUDY OUTCOME AND DEFINITION

The primary outcome of the study was all-cause mortality, assessed at one-year follow-up. The secondary outcomes included in-hospital mortality, proportion of patients achieving door-to-device (DTD) time ≤90 minutes, dual antiplatelet use within 24 hours and achievement of post-PPCI TIMI flow grade 3. Door-to-device time was defined as the time from patient arrival at the emergency department to the introduction of the first device, either a thrombus aspiration catheter or a balloon catheter into the IRA. Thrombolysis In Myocardial Infarction flow grade 3 was defined as a patent epicardial artery with normal flow[20].

STATISTICAL METHODS

We grouped patients according to time of admission (off-hours or regular hours). Baseline demographic, medical history, and procedural data were compared between the two groups. Data are expressed as mean±standard deviation for normally distributed continuous variables. For skewed distribution, data are expressed as median and range. Continuous variables were compared with the Student's t-test or Mann-Whitney U test and the chi-square test or Fisher's exact test was used to compare categorical variables as appropriate. Cox proportional hazard regression models were used to examine the association between treatment during off-hours versus regular hours and the incidence of all-cause mortality during hospitalisation and at one-year follow-up.

The incidence of death over time was studied with the use of the Kaplan-Meier method, and a log-rank test was applied to evaluate differences between the two groups (admission during off-hours versus regular hours). Hazard ratios (HR) (95% confidence intervals) for in-hospital and one-year mortality by off-hours and regular hours are presented, where the reference is off-hours. Several baseline clinical and procedural characteristics which are listed in **Table 1** were considered as potential confounders for the in-hospital and one-year mortality; therefore, the relevant variables were used to adjust the HRs including sex, diabetes mellitus, anterior MI, Killip class, TIMI risk score, symptom onset, thrombus aspiration and post-PPCI TIMI flow grade. The analysis was repeated in several important subgroups, including the relevant variables described.

All statistical tests were two-tailed and a p-value <0.05 was considered significant. Statistical analyses were performed with SPSS for Windows version 17.0 (SPSS Inc, Chicago, IL, USA).

Results

STUDY SAMPLE

Out of 1,126 patients presenting with STEMI who underwent PPCI in our institution, 857 (76%) presented during off-hours **(Figure 1)**.

CLINICAL CHARACTERISTICS

The majority of STEMI patients in both groups were referred from other hospitals and presented to the ED of our hospital within two to six hours after symptom onset. Aspirin and clopidogrel use within 24 hours approached 97% and 98% of patients admitted in off-hours and regular hours, respectively. Discharge treatment was similar in both groups. In general, the patient clinical characteristics were similar between off-hours and regular hours admission **(Table 1)**.

PROCEDURAL AND ANGIOGRAPHIC CHARACTERISTICS

The proportions of patients receiving DTD in ≤90 minutes and final achievement of TIMI 3 flow after PPCI were similar between the two groups. However, the use of manual thrombus aspiration during PPCI

Table 1. Clinical characteristics of STEMI patients based on timing of presentation.

		Off-hours (n=857)	Regular hours (n=269)	*p*-value
Age, years		55.44±9.73	56.4±9.94	0.15
Male gender, n (%)		753 (87%)	224 (83%)	0.052
Source of referral, n (%)	Walk-in/Ambulance	250 (29.1%)	74 (27.5%)	0.59
	Inter-hospital	580 (67.6%)	171 (63.5%)	0.21
Anterior wall MI, n (%)		484 (56.5%)	152 (56%)	0.99
Blood pressure, mmHg	Systolic BP	131 (56-220)	130 (18-240)	0.77
	Diastolic BP	80 (33-153)	77 (43-131)	0.16
Heart rate, bpm		78 (16-166)	76 (20-142)	0.23
Risk stratification, n (%)	Killip class 1	623 (72.7%)	207 (76.9%)	0.167
	Killip class 2-4	234 (27.3%)	62 (23%)	
	TIMI score >4	310 (36.2%)	88 (32.7%)	0.30
Risk factor, n (%)	Hypertension	472 (55%)	154 (57.2%)	0.53
	Diabetes mellitus	256 (29.8%)	74 (27.5%)	0.45
	Dyslipidaemia	385 (44.9%)	130 (48.3%)	0.33
	Smoker	570 (66.5%)	163 (60.6%)	0.07
	Family history	189 (22%)	57 (21.2%)	0.76
Onset of infarction, hours	2-6 hrs	463 (54%)	150 (55.7%)	0.61
	6-12 hrs	310 (36.2%)	80 (29.7%)	0.053
Antiplatelet within the first 24 hrs, n (%)	Aspirin	836 (97%)	264 (98%)	0.57
	Clopidogrel	829 (97%)	263 (98%)	0.38
Medication at discharge, n (%)	Aspirin	788 (92%)	249 (92%)	0.74
	Clopidogrel	786 (91%)	246 (91%)	0.89
	ACE inhibitor	656 (76%)	190 (71%)	0.12
	Statin	789 (92%)	240 (89%)	0.14
	Beta-blocker	646 (75%)	185 (69%)	0.08
Length of stay, days		5.86±4.63	6.45±4.91	0.07

BP: blood pressure; MI: myocardial infarction; PPCI: primary percutaneous coronary intervention; TIMI: Thrombolysis In Myocardial Infarction

was more common in the off-hours than the regular hours patients (off-hours 49.6% vs. regular hours 41.6%, p=0.009) **(Table 2)**.

MORTALITY

Survival data were complete for all patients. The cumulative incidence of all-cause mortality during the hospitalisation period was similar in STEMI patients admitted during off-hours versus regular hours (5.1% vs. 5.9%). Similarly, no statistically significant differences were found in all-cause mortality at one year (10.5% vs. 13.0%). The log-rank test of the one-year cumulative survival between the two groups was 0.21 **(Figure 2)**. Multivariable adjustment for confounders of the relation between admission timing (off-hours) showed no significant association between off-hours presentation and early or later mortality (adjusted HR for in-hospital mortality 0.81, 95% CI: 0.43-1.54; adjusted HR for one-year mortality 0.73, 95% CI: 0.46-1.12) **(Table 3)**.

Table 2. Procedural characteristics.

		Off-hours (n=857)	Regular hours (n=269)	*p*-value
Door-to-device, minutes		114±89.32	111±66.65	0.58
Door-to-device ≤90 minutes, n (%)		388 (45.3%)	129 (48%)	0.44
Manual thrombus aspiration, n (%)		425 (49.6%)	112 (41.6%)	0.009
Post-PPCI TIMI 3 flow, n (%)		801 (93%)	245 (91%)	0.18
Use of GPI, n (%)		574 (67%)	172 (64%)	0.35
Culprit vessel, n (%)	LAD	394 (46%)	117 (43.5%)	0.45
	LCX	37 (4.3%)	15 (5.6%)	0.38
	RCA	288 (33.6%)	89 (33.1%)	0.47

GPI: glycoprotein IIb/IIIa inhibitor; LAD: left anterior descending artery; LCX: left circumflex artery; PPCI: primary percutaneous coronary intervention; RCA: right coronary artery; TIMI: Thrombolysis In Myocardial Infarction

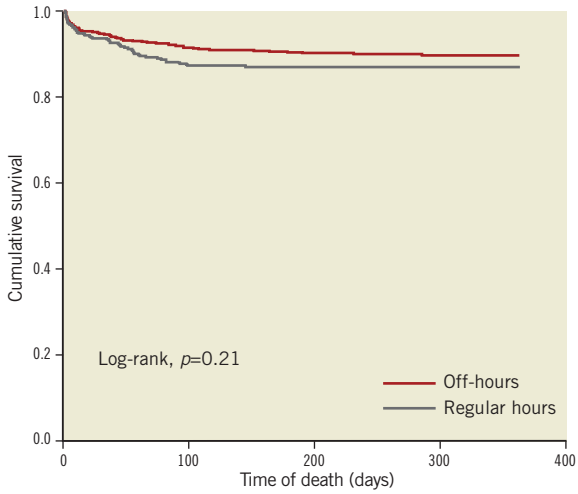

Figure 2. *The one-year cumulative survival between off-hours and regular hours admission.*

Table 3. Primary outcomes according to timing of admission.

		In-hospital			1-year		
		Number of events, n (%)	Crude HR and 95% CI	Adjusted HR and 95% CI	Number of events, n (%)	Crude HR and 95% CI	Adjusted HR and 95% CI
Death	Off-hours	44 (5.1%)	0.86 (0.48–1.52)	0.81 (0.43–1.54)	90 (10.5%)	0.77 (0.52–1.15)	0.73 (0.46–1.12)
	Regular hours	16 (5.9%)	1	1	35 (13%)	1	1

CI: confidence interval; HR: hazard ratio

SUBGROUP ANALYSIS

In the subgroup analysis involving several relevant clinical and procedural variables, we found a consistent result with respect to the similar mortality at one year between the two admission times across all subgroups **(Figure 3)**.

Discussion

In this long-term follow-up study involving 1,126 patients with STEMI undergoing PPCI at an academic hospital, we found that admission during off-hours was not associated with an increased risk of short or long-term mortality. The results are consistent in the relevant subgroups. These data suggest that, at centres with well-established STEMI processes, outcomes are not compromised even when patients present during times when full hospital operations are not available.

Prior studies have demonstrated that the disparity in quality of care may account, in part, for the differences in STEMI patients admitted during off-hours and regular hours. However, previously published data from 1999 to 2014 have shown conflicting results and demonstrated differences in reperfusion times among patients with STEMI based on the time of presentation, leading to outcome differences[2-14]. For example, previous studies showed that STEMI patients presenting during off-hours are less likely to achieve certain parameters of performance measures for STEMI care such as door-to-balloon time ≤90 minutes, door-to ECG time ≤10 minutes, and a smaller proportion of patients receiving aspirin within 24 hours than regular hours admission. Other concerns include the number and performance of physicians and hospital staff during off-hours which may differ from those encountered during regular office hours. Our study indicates that at an academic centre with an established programme for STEMI care these disparities do not exist.

There are several reasons which may explain the similar outcomes of STEMI patients admitted during off-hours and regular hours in this study. First, our hospital has similar performance for treating STEMI patients over time, as shown by the similar proportion of patients reaching a DTD time of ≤90 minutes and receiving aspirin within 24 hours between off-hours and regular hours admission. Second, the performance of the interventional cardiologist may also be similar due to the similar achievement of post-PPCI TIMI flow grade 3 of the culprit vessel in the two admission times. In addition, the higher number of thrombus aspiration procedures in the off-hours group than in the regular hours group may partly indicate that the performance of the treating interventional cardiologist in our hospital is not lacking during off-hours. Third, there are inherent structural and process characteristics of our hospital which may allow a similar quality of care during the day, at night and at weekends. For example, the catheterisation laboratory nurses on duty (two persons) stay in the hospital during the off-hours and are dedicated to support the 24 hr emergency services including PPCI. In addition, the medical residents and the cardiologist on duty also stay in the hospital during off-hours. This immediate availability of the catheterisation laboratory team is consistent with the findings from the GRACE registry that has shown higher primary PCI utilisation at academic centres[21]. The similar discharge treatment between the two groups may further explain the similar one-year mortality between the two groups. This is an important process-based performance measure and again supports the hypothesis that the system for STEMI set up at our hospital allows similar management of STEMI patients regardless of the time of day. Compared to our hospital, other hospitals in the region may have different healthcare resources and staffing patterns. Currently, only our hospital has a 24/7 service for primary PCI covered by the government healthcare insurance system and not all hospitals have an

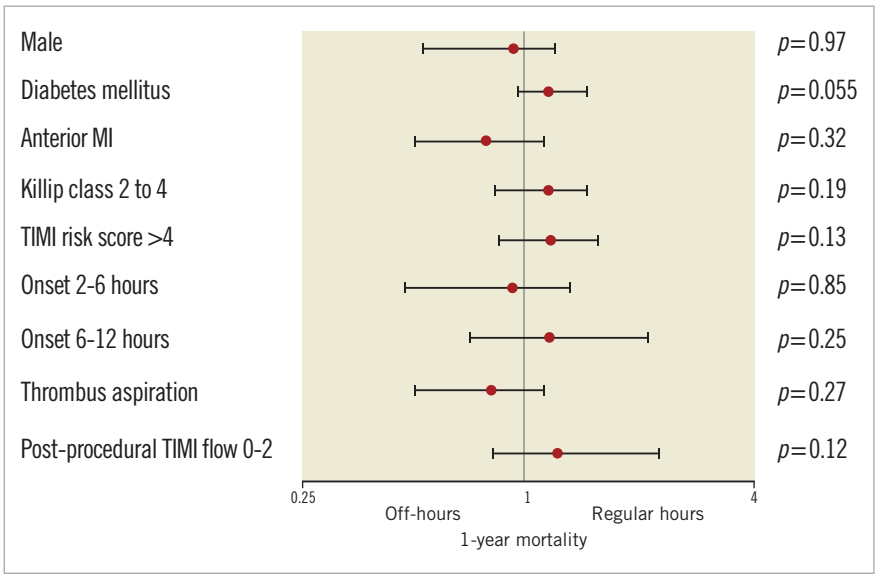

Figure 3. *Subgroup analysis of patients according to admission time and all-cause mortality at one year. Data are presented as hazard ratios and 95% confidence intervals. MI: myocardial infarction; TIMI: Thrombolysis In Myocardial Infarction*

on-site cardiologist/interventional cardiologist or catheterisation laboratory nurses during off-hours. The mean number of board-certified cardiologists per million population in Jakarta is 18.9[17]. Our study suggests that increasing this number may optimise the care of STEMI patients in the region.

Quality improvement initiatives that focus on attainment of quality measures for STEMI care at all times of presentation include: 1) additional numbers of in-house catheterisation laboratory personnel (physician and nurses) at all PPCI centres; 2) implementation of a STEMI network in the community in order to increase the awareness of STEMI among the public and reduce the symptom onset-to-door time, thus reducing the proportion of non-reperfused STEMI patients.

Limitations

The reported results are based on a single-centre experience and should not be generalised to other hospitals in the region. Furthermore, several relevant variables have not been recorded in the database, and therefore cannot be evaluated, such as revascularisation history in multivessel disease patients and medication at one-year follow-up. However, the similar outcome at one-year follow-up in both off-hours and regular hours admission might somehow explain the good balance of the relevant variables in the two admission times. Finally, our study is observational and, like all observational studies, there may be unmeasured confounders that account for our findings.

Conclusion

STEMI patients who were admitted during off-hours to an academic hospital and treated with PPCI had similar survival at one year as compared to those with regular hours admission.

Impact on daily practice

This study described the methods to assess quality of care in patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention. The hospital performance should be similar for treating patients who are admitted during off-hours and regular hours. Thus, in daily practice, the results of this study will encourage the implementation of a regional STEMI network. When such a pathway works efficiently, reperfusion times are usually within the recommended guidelines, regardless of the admission times.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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