

Impact of Lunar Phase on Outcomes Following ST-Elevation Myocardial Infarction

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Key Words: full moon, lunar phases, STEMI, MACE, MACCE, cardiovascular outcomes.

Word Count: 2,639

Contributor statement: All authors were involved in the study design, data analysis, and revision of the manuscript. All authors read and approved the final manuscript. LS is the guarantor.

Competing interest statement: All authors declare no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work, no other relationships or activities that could appear to have influenced the submitted work.

Transparency declaration: The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate and transparent account of the study being reported; no important aspects of the study have been omitted; and any discrepancies from the study as planned have been explained.

Ethics approval: Ethics approval was obtained from the Barwon Health Human Research Ethics Committee.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1111/imj.14413](https://doi.org/10.1111/imj.14413)

Funding: The authors did not receive any funding for this study, nor do they report any conflict of interest pertaining to this research.

Patient and public involvement statement: This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

Abstract

Background: There is a long-held belief in the association between the full moon and extremes of human behaviour and adverse health consequences. Small-scale studies are conflicting, however most suggest no clear association between lunar phase and occurrence of acute coronary syndromes.

Methods: We conducted a multi-centre retrospective study from the Melbourne Intervention Group registry, including 7,570 ST-elevation myocardial infarction (STEMI) cases from 6 tertiary centres over a 12-year study period in Victoria, Australia and performed statistical analysis using Stata software.

Main outcome measures: Primary outcomes studied were the incidence of STEMI, the occurrence of major adverse cardiac and cerebrovascular events and mortality at 1 and 5 years in cases of ST-elevation myocardial infarction undergoing primary or rescue percutaneous coronary intervention during the full moon between 2005-2017 in Victoria, Australia.

Results: This study demonstrated no significant difference in STEMI incidence ($p=0.61$) nor of major adverse cardiovascular events across all lunar phases. Subgroup analysis confirmed no difference in outcomes during the full moon compared to a composite of other lunar phases. Kaplan-Meier survival estimates showed similar 30-day outcomes across lunar phases ($p=0.35$) and when comparing full moon to a composite of other lunar phases ($p=0.45$). Similarly, there was no significant difference in survival at 1 and 5 years between lunar phases ($p=0.68$) or compared to the full moon phase ($p=0.51$).

Conclusions: This study showed no significant difference in the incidence or cardiovascular outcomes and survival in patients with ST-elevation myocardial infarction undergoing primary or rescue percutaneous coronary intervention during the lunar phases.

Introduction

The influence of lunar phases, particularly the full moon phase, on extremes of health and human behaviour has been extensively studied.¹ It has been established that there is an association between the full moon phase and acute behavioural disturbance.¹ This relationship has generated interest in the possible influence of the full moon on the incidence and outcomes of adverse health conditions such as acute myocardial infarction (MI) and cardiac arrest presentations.

Recent small-scale observational studies have found no significant association between the lunar phases and incidence of acute myocardial infarction^{2,3,4} nor incidence or success of cardiopulmonary resuscitation (CPR).^{3,5,6} Many of these studies included patients with and without ST-elevation myocardial infarction (STEMI), representing a somewhat heterogeneous cohort of acute coronary syndrome (ACS) patients.^{3,4,6}

These studies did not evaluate cardiovascular outcomes in patients presenting with STEMI during the full moon phase.^{2,3,5} Understanding factors that may potentially influence cardiovascular outcomes in STEMI provides scope to implement preventive strategies to mitigate adverse outcome in this population.

The phenomenon of aberrant human behaviour during the full moon phase may influence healthcare providers and clinical outcomes of patients presenting with STEMI that proceed to primary or rescue percutaneous coronary intervention (PCI) after adjusting for traditional cardiovascular risk factors. Moreover, cases of STEMI occurring during a specific lunar phase could have unique characteristics which may influence cardiovascular outcomes.

ST-segment elevation myocardial infarction represents a unique clinical entity resulting from acute plaque rupture and the development of intraluminal coronary occlusion. Studies have extensively described potential pathophysiological mechanisms which may predispose to acute plaque rupture, however environmental mechanisms remain incompletely understood, prompting further research into the influence of temperature, humidity, diurnal, seasonal and temporal variation and circadian rhythm on the incidence of STEMI.⁷

The purpose of this study is to evaluate whether the suggested association between the full moon and adverse consequences was translatable to real-world cardiovascular outcomes. We sought to investigate the incidence of ST-elevation myocardial infarction (STEMI) during the full moon phase compared to other lunar phases using a large-scale registry in Victoria, Australia. We sought to analyze possible differences in short- and long-term cardiovascular outcomes across the lunar phases in all STEMI cases between 2005 to 2017 who proceeded to primary or rescue percutaneous coronary intervention (PCI), including mortality at 1 and 5 years.

Methods

Setting and Design

This study was a retrospective observational multi-centre study utilizing the Melbourne Intervention Group (MIG) database, a large-scale registry incorporating clinical information from hospital networks around Victoria. Data incorporated into this registry was collected prospectively from 6 healthcare services with PCI capability within Victoria, Australia.

Patient Population

The study population included 7,570 eligible patients with STEMI undergoing primary or rescue PCI who were enrolled into the registry between January 1, 2005 and June 30, 2017. Eligible patients were those patients presenting with STEMI who proceeded to primary or rescue PCI at the index presentation. STEMI was defined as ischaemic chest pain with accompanying ST segment elevation in ≥ 2 contiguous leads on electrocardiography (ECG). Primary PCI was defined as coronary angioplasty on presentation. Rescue PCI constituted cases of unsuccessful thrombolysis requiring emergent coronary angiography. Patients who did not undergo PCI were excluded from the study.

Multivessel coronary artery disease was defined by the presence of greater than or equal to 50% diameter stenosis of two or more epicardial coronary arteries.

Lunar phases were divided equally into 8 subgroups (new moon, waxing crescent moon, first quarter, waxing gibbous moon, full moon, waning gibbous moon, third quarter, waning crescent moon) based on longstanding meteorological data (duration of 3 days, 16 hours and 30 minutes per lunar phase).⁸ Cases were allocated to a particular lunar phase according to the documented date and time of symptom onset.

Outcome Measures

We sought to evaluate the association between the full-moon phase and incidence and outcomes of STEMI cases undergoing primary or rescue PCI during the 12-year study period. We further sought to assess the impact of lunar phases on short term outcomes, including early post procedure complications, in-hospital and 30-day major adverse cardiovascular and cerebrovascular events (MACCE), defined as the composite of all-cause death, myocardial infarction (MI), target vessel revascularisation (TVR), repeat revascularisation and stroke.

Long-term survival outcomes were analysed utilising national death index (NDI)-linked mortality at 1 and 5 years in this cohort. We further subdivided the data to compare outcomes during the full moon compared to a composite of all other lunar phases.

Statistical Analysis

This study compared baseline demographics, procedural characteristics and clinical outcomes across lunar phases with a subgroup analysis comparing the full moon phase to a composite of all other lunar phases.

Baseline characteristics within groups were expressed as percentages for categorical variables. Continuous data were presented as mean (SD) or median (interquartile [IQR] range) as appropriate. Comparison between groups were made using Pearson chi-squared test for categorical variables and *t* tests for continuous variables (tables 1-5).

Cox regression and Kaplan-Meier survival estimates were applied to the different lunar phases and compared by the log-rank test. All analyses were performed using Stata software, version 15.1 (StataCorp, College Station, Texas, USA).

Ethics Approval

All six hospital networks' ethics committees approved the collection of data into the MIG registry. This study was approved by Barwon Health Research Ethics Committee.

Results

Baseline demographics

Baseline characteristics were similar across all lunar phases (table 1). The average age of the cohort (n=7,570) was 62.8 ± 12.7 years, with more than half aged less than 65 years (56%). They were predominantly male (78.4%) and overweight (70.8% with BMI $\geq 25\text{kg/m}^2$).

The presence of cardiovascular risk factors was similar when comparing the full moon cohort to the remaining lunar phases (table 2). Hypertension was the most prevalent comorbidity (53.3%), followed by hypercholesterolaemia (48%), smoking (36.7%), pre-existing diabetes (16.8%), stroke (4.7%), peripheral vascular disease (3.2%), chronic kidney disease (2.5%), and obstructive sleep apnoea (2.4%). A minority had previous cardiovascular events, including myocardial infarction (12.6%) or previous cardiovascular intervention (PCI or CABG, 11.4% and 2.4%, respectively).

The cohort was subdivided into 8 subgroups based on the 8 lunar phases.

The incidence of STEMI cases undergoing primary or rescue PCI during the full moon phase (n=969) represented 12.8% of cases over the 12-year study period ($\chi^2=19.4$, $df=12$, $P=0.08$) with no significant

difference compared to all other lunar phases (n=6,601) with regard to annual or overall incidence (table 2).

Procedural Characteristics

Subgroup analysis of the full moon phase compared to all other lunar phases demonstrated a homogeneous cohort with respect to procedural characteristics (table 4).

Radial access was infrequently utilised, regardless of lunar phase (full moon vs. other lunar phases, 23.3% vs. 23.5%, p=0.90).

There was no significant difference in door-to-balloon time (DTBT) across all lunar phases (p=0.71) or during the full moon phase compared to a composite of the remaining lunar phases (median [interquartile range (IQR)], 78 minutes [49.0-118] vs. 80 minutes [51.0-118] respectively; p=0.52) In both subgroups, the majority of cases had a door-to-balloon time of less than 90 minutes (57.2% and 59.1%, respectively), that did not reach statistical significance (p=0.21).

Overall, right coronary artery (RCA) lesions were most frequent (42.4%, p=0.04), followed by left anterior descending (LAD) (41.9%), left circumflex/obtuse marginal (LCx/OM) (13.8%), left main coronary artery (LMCA) (0.9%) and ramus (0.2%). The incidence of bypass graft lesions was very low (0.85%). Subgroup analysis demonstrated no significant difference in culprit lesion during the full moon compared to a composite of other lunar phases (LAD 44.9% vs 41.4%, respectively; RCA 39.1% vs. 42.9%, respectively; p=0.075).

There was similar use of bare-metal stents (BMS) and drug-eluting stents (DES) in the subgroup analysis of full moon vs. a composite of other lunar phases (48.1% vs 44.7%, respectively; p = 0.22).

There were no differences between subgroups with respect to the mean number of stents used per case (1.2 ± 0.6 , p=0.96).

Outcomes

In-hospital adverse events

Procedural outcomes were similar across all lunar phases, including inotropic requirements (p=0.12), bleeding (p=0.12), coronary dissection (p=0.40), perforation (p=0.75) and no reflow phenomenon (p=0.19).

Subgroup analysis also demonstrated similar procedural complication rates during full moon compared to a composite of other lunar phases with respect to the no-reflow phenomenon (5.8% vs. 6.2%, p=0.21), bleeding (5.3% vs. 4.2%, p=0.11), coronary dissection (3.6% vs. 3.8%, p=0.71), stroke (0.9% vs. 0.7%, p=0.40) and coronary perforation (both 0.3%, p=1.00).

Average length of stay was similar during the full moon (5.6 ± 7.5) compared to other lunar phases (5.6 ± 5.9 , p=0.75).

Subgroup analysis demonstrated similar rates of in-hospital MACCE (full moon 9.3% vs. 9.3%, $p=0.98$), MACE (full moon 8.8% vs. 8.7%, $p=0.92$), unplanned CABG (full moon 1.6% vs. 1.4%, $p=0.70$) and stroke (full moon 0.7% vs. 0.9%, $p=0.39$).

Left ventricular (LV) dysfunction (defined as LVEF $<50\%$) was prevalent across the cohort (49.5%) and similar in STEMI cases treated during the full moon (full moon 50.9% vs. 49.3%, $p=0.39$).

In-hospital and 30-day survival

Survival to hospital discharge was high overall (93.8%; full moon 93.6% vs. 93.9%, $p=0.74$) and remained high at 30 days (93.2%; full moon 93.2% vs. 92.6%, $p=0.48$).

Short-term Major Adverse Cardiovascular Outcomes

Short-term outcomes were similar between the full moon and other lunar phases (7.4% vs. 6.8%, $p=0.48$). Specific 30-day cardiovascular outcomes during the full moon phase demonstrated similar findings, with similar rates of MI (2.2% vs. 1.9%, $p=0.49$), target vessel revascularisation (TVR) (3.5% vs. 3.4%, $p=0.85$) and stroke (1.3% vs. 0.8%, $p=0.17$).

Long-term major adverse cardiovascular outcomes

Kaplan-Meier survival analyses were conducted to assess long-term outcomes across all lunar phases (figure 2). Overall survival was 82.2% across the entire cohort at 5 years.

NDI-linkage at 1-year found 603 deaths (8.9%) overall (full moon 83 deaths, other lunar phases 520 deaths) and similar 1-year survival between the subgroups (full moon 91.2% vs. 90.5%, $p=0.49$) (figure 4).

After 5 years of follow up, there were a further 639 deaths (16.8%) overall (further 84 deaths during full moon phase, other 555 deaths across composite of other lunar phases between 1 and 5 years) with similar 5-year survival between subgroups (full moon 82.9% vs 83.2%, $p=0.86$).

Cox regression analysis demonstrated no major survival difference between the full moon cohort and remaining lunar phases when adjusted for other variables with a hazard ratio of 1.07 (95% CI, 0.89-1.29).

Study limitations

This was a large retrospective observational study. However, the outcomes of interest involved a time-dependent variable, therefore randomisation would be challenging. This analysis demonstrated no significant difference in STEMI incidence or adverse cardiovascular outcomes during the full moon phase, however the possible impact on healthcare providers is a somewhat intangible variable and was therefore not captured within the limits of this analysis.

The study consisted only of STEMI cases which continued to PCI and therefore does not encompass all STEMI presentations including coronary disease not amenable to PCI, multivessel or left main disease requiring surgical urgent surgical revascularisation, pericarditis, coronary vasospasm, Takotsubo cardiomyopathy or other aetiologies.

We elected to allocate STEMI cases to a lunar phase according to the time of symptom onset documented within the registry rather than the timing of PCI as we felt this was a more accurate reflection of the occurrence of the pathological event rather than the intervention and therefore would avoid misclassification of cases, particularly in the event of late or delayed presentation STEMI.

The nature of a retrospective analysis does not allow a power calculation and conclusions made are hypothesis-generating. While the 12-year inclusion period may provide more expansive data, contemporary STEMI management, including improvements in antiplatelet therapy, primary PCI (compared with fibrinolysis alone), radial access and STEMI pathways, have dramatically transformed over time, potentially introducing confounding bias; however, this effect would be unlikely to vary across the lunar phases. Finally, while known co-variables were considered, the influence of unknown variables remains a limitation of a cohort study.

Discussion

This is the largest study incorporating a diverse STEMI population over a 12-year study period to analyse the incidence of STEMI cases undergoing primary or rescue PCI across 8 lunar phases. The impact of lunar phase on human behaviour has been extensively documented.^{1,9} Many believe in the effect of the moon and lunar cycle on health and human behaviour.¹ More recently, studies investigating the occurrence of adverse health conditions according to lunar phases suggests a possible correlation,^{9,10,11} however this has been variable^{12,13,14} and has been more frequently linked to the new moon phase.¹⁵

This study demonstrates that STEMI presentations are not affected by the lunar cycle and in particular, the full moon phase does is not associated with a higher frequency of STEMI presentations.

The full moon phase does not appear to impact procedural complication rates nor the rate of MACCE, including all-cause death, reinfarction, repeat revascularisation or stroke.

Existing literature exploring the impact of the lunar cycle on MI incidence is sparse and conflicting.^{3,4,6} Most studies were small-scale observational analyses and included a heterogeneous group of acute coronary syndromes, including STEMI, NSTEMI and unstable angina.² These studies explored ACS frequency across different lunar phases and found no clear correlation between the full moon and incidence of acute coronary syndrome presentations.^{6,15}

In 2008, Wake *et al.* examined the association between the gravitational effect of the moon and the occurrence of MI.¹⁶ While previous studies explored the relationship between lunar phases and adverse cardiovascular events, this study explored the gravitation of the moon, describing the time taken for the moon to orbit around the earth and the distance from the centre of the moon to the centre of earth at various times along its orbit. This study found an inverse relationship, whereby the occurrence of MI presentations was highest when the gravitation of the moon was at its lowest (greater distance between the centre of the moon to the centre of earth), however the authors recognised that the mechanism behind this finding remains uncertain.

Existing studies have not evaluated any form of clinical outcomes in STEMI cases undergoing PCI according to lunar phase. Moreover, the majority of studies divided the lunar cycle into quartiles, rather than the well-recognised 8 lunar phases as outlined in this study.⁸

The present study involved a large homogeneous cohort with respect to patient and procedural characteristics, comparable door-to-balloon time, culprit lesion and extent of coronary artery disease at the time of invasive coronary angiography. This is in contrast to a previous single centre, small-scale study in 2013 which reported a statistically higher incidence of LAD culprit lesions during the full moon phase among a cohort of 452 STEMI cases.¹⁵

Procedural complication rates and survival outcomes were similar regardless of timing during the lunar cycle, and, in particular, the full moon period was not associated with worse cardiovascular outcomes or higher 1- or 5-year mortality.

Some studies suggest that circadian rhythm influences cardiovascular physiology, with diurnal variation reported in heart rate, blood pressure, vascular, endothelial and neurohormonal function.¹⁷ These processes may promote pathophysiological mechanisms involved in ACS presentations.

Moreover, seasonal variation may play a role, with a higher incidence of STEMI presentations reported during winter months, with colder weather appearing to impact on sympathetic tone, platelet function, systemic inflammation resulting in plaque destabilisation and altered fibrinolytic activity.^{18,19,20}

Despite this, the diurnal and seasonal physiological changes observed and their impact on cardiovascular events do not appear to extend to the lunar cycle. In our study, equivalent patient and procedural characteristics in a large cohort with similar cardiovascular and survival outcomes would support the position that lunar phase is not a predictor of outcomes in STEMI undergoing primary or rescue PCI.

This is consistent with previous large-scale observational studies, one of which demonstrated no significant difference in overall survival of breast cancer patients when timing of cancer surgery was stratified according to phases of the lunar cycle.²¹

Despite esoteric belief, this study strongly suggests that the full moon does not adversely impact cardiovascular outcomes in STEMI cases undergoing primary or rescue PCI and there is no correlation between the lunar cycle and incidence, outcomes or success of primary or rescue PCI in STEMI cases.

Acknowledgments

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Geelong Hospital: C Hiew, M Sebastian, T Yip, A Hutchinson, C Jaworski, M Mok, J Dyson, B McDonald, L Duff

Royal Melbourne Hospital: AE Ajani, R Warren, D Eccleston, J Lefkovits, R Iyer, R Gurvitch, W Wilson, M Brooks, LP Dawson.

Professor Duffy's work is supported by a NHMRC grant. Professor Reid is supported by a NHMRC Senior Research Fellowship (reference no. 1045862).

Disclosures

The Melbourne Interventional Group acknowledges funding from Abbott Vascular, Astra-Zeneca, BMS and Pfizer. These companies do not have access to data and do not have the right to review manuscripts or abstracts before publication.

Data sharing: The authors had full access to all of the data (including statistical reports and tables) which appear in this study. There is no additional data available.

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Table 1: Baseline characteristics in full moon cohort vs composite of other lunar phases

	Full Moon	Other lunar phases	P value
Patient characteristics			
Age, years	62.5+/-12.6	62.8+/-12.7	0.53
Gender, female (%)	21.9%	21.5%	0.80
BMI, mean (kg/m ²)	27.8 +/- 5.0	27.9 +/- 5.1	0.77
Comorbidities			
Hypertension, %	53.5%	53.2%	0.89
Diabetes, %	15.2%	17.0%	0.15
Dyslipidaemia, %	46.8%	49.4%	0.14
COPD, %	4.1%	4.3%	0.82
Smoking, %	38.5%	36.5%	0.23
OSA, %	2.2%	2.4%	0.66
PVD, %	2.9%	3.3%	0.56
Stroke, %	3.8%	4.8%	0.18
RA, %	1.9%	2.0%	0.84
CKD (eGFR <30), %	2.2%	2.6%	0.77
Previous MI, %	13.0%	12.6%	0.69
Previous PCI, %	12.9%	11.2%	0.13
Previous CABG, %	2.7%	2.4%	0.52
Heart failure, %	1.0%	1.8%	0.10

COPD=chronic obstructive pulmonary disease; OSA=obstructive sleep apnoea; PVD=peripheral vascular disease; RA=rheumatoid arthritis; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; MI=myocardial infarction; PCI=percutaneous coronary intervention; CABG=coronary artery bypass graft.

Table 2: Annual and total STEMI incidence during full moon vs composite of other lunar phases

Year	Full Moon	Other lunar phases*	P value
2005	3.7%	4.0%	0.08
2006	6.7%	6.6%	
2007	5.9%	6.9%	
2008	7.3%	6.3%	
2009	8.7%	6.5%	
2010	5.9%	7.7%	
2011	8.6%	7.4%	
2012	6.7%	8.4%	
2013	9.7%	8.6%	
2014	10.1%	10.1%	
2015	10.7%	10.9%	
2016	9.6%	10.7%	
2017	6.4%	6.0%	
Total	12.8%	87.2%	

*Other lunar phases represent a mean composite of all lunar phases excluding the lunar phase.

Table 3: Procedural characteristics in full moon cohort vs composite of other lunar phases

	Full Moon	Other lunar phases	P value
Door-to-balloon time, mins	142.6 ± 217.2	140.7 ± 216.9	0.52
Door-to-balloon <90 mins, %	57.2%	59.1%	0.26
Access, radial/brachial (%)	23.3%	23.5%	0.90
Single vessel disease, %	46.1%	46.4%	0.87
Left main disease, %	7.5%	5.8%	0.19
Lesion location			
LMCA, %	0.4%	1.0%	0.075
LAD, %	44.9%	41.4%	
LCx/OM, %	14.4%	13.7%	
RCA, %	39.1%	42.9%	
Ramus, %	0.2%	0.2%	
Bypass graft, %	1.0%	0.8%	
Stent type, DES, %	44.9%	44.6%	0.83
Stent number	1.2 ± 0.6	1.2 ± 0.6	0.97
Periprocedural complications			
Unplanned CABG, %	1.4%	1.6%	0.70
Inotrope requirements, %	10.5%	9.8%	0.57
LV dysfunction (LVEF <50%), %	50.9%	49.3%	0.39
Dissection, %	3.6%	3.8%	0.71
Perforation, %	0.3%	0.3%	0.99
Persistent no reflow, %	2.1%	1.4%	0.21
Periprocedural MI, %	1.1%	1.2%	0.80
Bleeding, %	5.3%	4.2%	0.11
Stroke, %	0.9%	0.7%	0.39

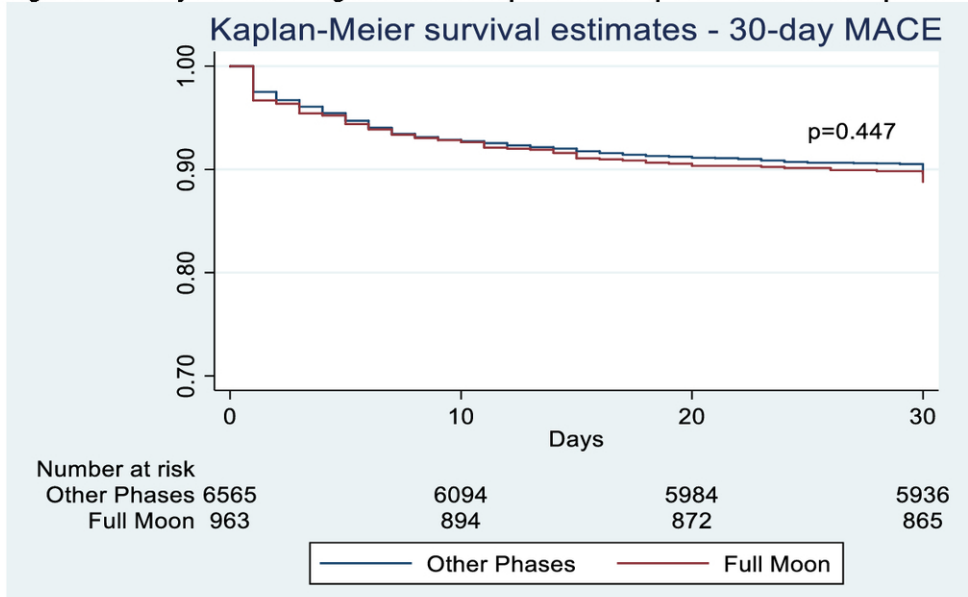
LMCA=left main coronary artery; LAD=left anterior descending; LCx/OM (left circumflex/obtuse marginal); RCA=right coronary artery; DES=drug eluting stent; LVEF=left ventricular ejection fraction.

Table 4: Outcomes during full moon phase vs composite of other lunar phases

	Full Moon	Other lunar phases	P value
LOS, days	5.64 ± 7.50	5.56 ± 5.88	0.75
In-hospital outcomes			
In-hospital MACE, %	8.7%	8.8%	0.92
In-hospital MACCE, %	9.3%	9.3%	0.98
30-day outcomes			
30-day MACE, %	11.2%	10.4%	0.44
30-day MACCE, %	11.9%	11.0%	0.39
30-day AMI, %	2.2%	1.9%	0.49
30-day TVR, %	3.5%	3.4%	0.85
30-day stroke, %	1.3%	0.8%	0.17
30-day mortality, %	7.4%	6.8%	0.48
NDI-linked mortality			
1-year mortality, %	9.5%	8.8%	0.49
5-year mortality, %	17.1%	16.8%	0.86

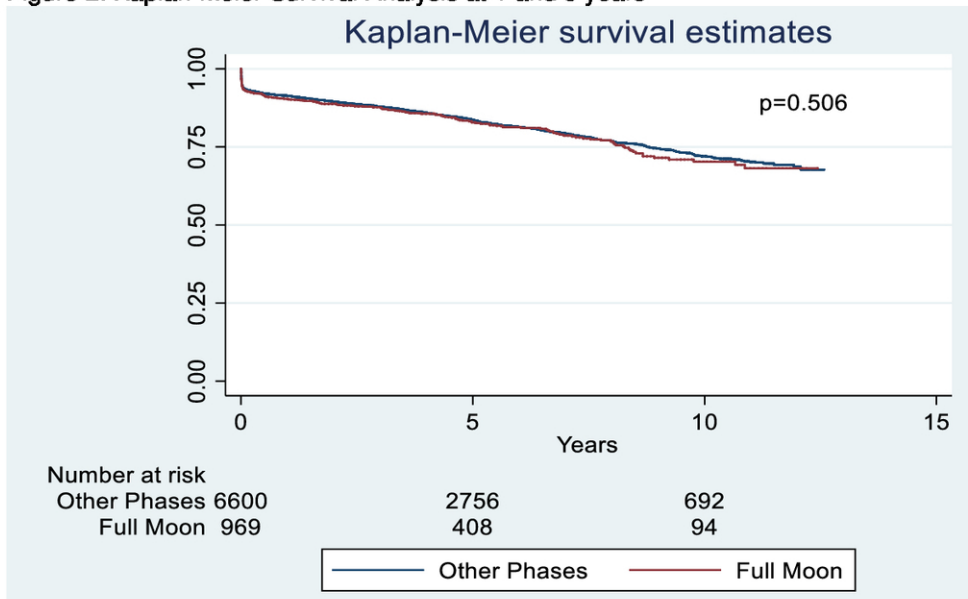
LOS=length of stay; MACE=major adverse cardiovascular events; MACCE=major adverse cardiovascular and cerebrovascular events; AMI=acute myocardial infarction; TVR=target vessel revascularisation; NDI=national death index.

Figure 1: 30-day MACE during full moon compared to composite of other lunar phases



Kaplan-Meier estimates of 30-day MACE in STEMI patients undergoing primary PCI during full moon (red line) compared to a composite of other lunar phases (blue line).

Figure 2: Kaplan-Meier Survival Analysis at 1 and 5 years



Kaplan–Meier estimates of survival in STEMI patients undergoing primary PCI during full moon (red line) compared to a composite of other lunar phases (blue line).



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Title:

Impact of lunar phase on outcomes following ST-elevation myocardial infarction

Date:

2020-03-01

Citation:

Segan, L., Brennan, A., Reid, C. M., Hiew, C., Oqueli, E., Ajani, A., Clark, D., Duffy, S. J. & Yip, T. (2020). Impact of lunar phase on outcomes following ST-elevation myocardial infarction. INTERNAL MEDICINE JOURNAL, 50 (3), pp.322-329.
<https://doi.org/10.1111/imj.14413>.

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File Description:

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