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PII: S0735-1097(16)35036-7

DOI: [10.1016/j.jacc.2016.08.023](https://doi.org/10.1016/j.jacc.2016.08.023)

Reference: JAC 22901

To appear in: *Journal of the American College of Cardiology*

Received Date: 24 July 2016

Revised Date: 15 August 2016

Accepted Date: 22 August 2016

Please cite this article as: Selvaraj S, Bhatt DL, Stone GW, Gibson CM, Steg PG, Hamm CW, Price MJ, Deliargyris EN, Prats J, Mahaffey KW, White HD, Harrington RA, for the CHAMPION PHOENIX Investigators, “Off-Hours” Versus “On-Hours” Presentation in ST-Segment Elevation Myocardial Infarction: Findings from CHAMPION PHOENIX, *Journal of the American College of Cardiology* (2016), doi: 10.1016/j.jacc.2016.08.023.

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Running title: Off Hours Effect in STEMI

Funding: CHAMPION PHOENIX was sponsored by the Medicines Company.

ACKNOWLEDGEMENTS: We thank Steven E. Elkin, MS and Debra Bernstein, PhD of The Medicines Company for their statistical support, along with Yuyin Liu, MS of the Harvard Clinical Research Institute for independent verification of the analyses. The Harvard Clinical Research Institute received funding from The Medicines Company and Chiesi for these analyses.

DISCLOSURES: Dr. Deepak L. Bhatt discloses the following relationships - Advisory Board: Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Duke Clinical Research Institute, Harvard Clinical Research Institute, Mayo Clinic, Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), Harvard Clinical Research Institute (clinical trial steering committee), HMP Communications (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), Population Health Research Institute (clinical trial steering committee), Slack Publications (Chief Medical Editor, Cardiology Today’s Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Vice-Chair), VA CART Research and Publications Committee (Chair); Research Funding: Amarin, Amgen,

AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemix, Medtronic, Pfizer, Roche, Sanofi Aventis, The Medicines Company (including for his role as co-chair of the CHAMPION trials); Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Co-Investigator: Biotronik, Boston Scientific, St. Jude Medical; Trustee: American College of Cardiology; Unfunded Research: FlowCo, PLx Pharma, Takeda. Dr. Ph. Gabriel Steg has received research grants from Merck, Sanofi, and Servier; speaking or consulting fees from Amarin, AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers-Squibb, CSL-Behring, Daiichi-Sankyo, GlaxoSmithKline, Janssen, Lilly, Merck Novartis, Pfizer, Regeneron, Sanofi, Servier, and The Medicines Company. Dr. Harvey D. White discloses the following relationships – Honoraria: AstraZeneca; Research Funding: Sanofi-Aventis, Eli Lilly, National Health Institute, Glaxo Smith Kline, Merck Sharpe & Dohme, AstraZeneca, Omthera Pharmaceuticals, Pfizer New Zealand, Intarcia Therapeutics, Elsal Inc, DalGen Products and Services, Daiichi Sankyo Pharma Development.

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Timely percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) is a cornerstone of therapy. Several analyses have demonstrated worse outcomes for patients presenting with STEMI during off-hours compared with during the workday (1). The etiology of this difference is likely multifactorial, including changes in staffing, delays in intervention, and higher procedural complications (2). The majority of available data derive from registries with retrospective collection of clinical characteristics and outcomes, while little is available from prospective, randomized trials (1,3). There continues to be debate regarding whether this effect exists in the contemporary era (1-3). Finally, comprehensive delineation of relevant outcomes, including stent thrombosis (ST), is rarely available from registry data. Such information is crucial to understanding differences in care. We sought to determine if such differences existed in a large, contemporary, international trial.

We dichotomized the subgroup of patients with recent STEMI from CHAMPION PHOENIX according to time of presentation (4). Off-hour PCI was defined by intervention performed during weekdays from 7PM-7AM, weekends, and holidays. Continuous data are presented as mean $\pm$ standard deviation. Categorical variables are presented as a count and percentage. Endpoints were evaluated at 48 hours and 30 days. The primary efficacy outcome was a combined endpoint of all-cause death, MI, stent thrombosis, or ischemia-driven revascularization at 48 hours. The primary safety outcome for this analysis was GUSTO-defined moderate or severe bleeding, while ACUITY-defined major or minor bleeding was also examined.

T-tests were used to compare normally distributed continuous variables (or non-parametric equivalent when appropriate). Chi-squared tests (or Fisher's exact test when appropriate) were used to compare categorical variables. Because timing of PCI was not

randomized, we used logistic multivariate regression with propensity score analysis to determine the risk of all outcomes. Propensity scores were constructed using age, randomization arm, enrollment site (United States vs. non-United States), previous MI, previous PCI, history of diabetes, clopidogrel loading dose, type of anticoagulant, and type of stent. All study participants provided written informed consent. A 2-sided p-value <0.05 was considered statistically significant.

In the STEMI cohort of CHAMPION PHOENIX (1,992/10,942), the mean age was 61 ± 12 years, 26% were female, and 10% were enrolled from the United States (**Table**). Most participants underwent angiography through femoral access (79%). On-hours participants were more likely to be enrolled from the United States, have diabetes mellitus, have a prior PCI, and receive a higher dose clopidogrel load, low molecular weight heparin, bivalirudin, or a drug-eluting stent ($p < 0.05$ for all comparisons). Bailout therapy with GP IIb/IIIa inhibitors was similar in the groups. Off-hours participants underwent PCI more rapidly from symptom onset (median: 5.00 vs. 5.98 hours, $P < 0.0001$).

The risk of the primary efficacy outcome was not significantly different for on-hours presentation on unadjusted analysis (RR, 1.11 [95% CI 0.68, 1.83], $p = 0.67$) or after multivariate propensity score adjustment (RR, 1.00 [95% CI 0.57, 1.74], $p = 0.99$). There was no significant difference in risk of ST with on-hours PCI (adjusted RR 0.57 [95% CI 0.27, 1.21], $p = 0.15$) or in the primary safety outcome ($p = 0.22$). Cangrelor showed consistent benefits regardless of time of PCI for all outcomes ($p > 0.05$ for interaction). Additionally, no interaction was observed by site of enrollment ($p > 0.05$ for all outcomes).

In this randomized trial, we showed that in contrast to findings from several prior studies, time of PCI did not affect STEMI efficacy or safety outcomes. These findings are reassuring and

suggest that outcomes for STEMI revascularization are not dependent upon time of presentation. Such information is important given that previous studies suggesting a difference in efficacy were retrospective with un-adjudicated outcomes. The additional collection of ST and ischemia-driven revascularization are important endpoints in PCI that are not widely available in previous studies.

The present study question was not pre-specified and thus not specifically powered for these analyses. As such, we caution interpretation and cannot rule out potential harm associated with off-hours presentation. Also, because CHAMPION PHOENIX was not a primary STEMI trial, door-to-balloon time was not specifically collected. Therefore, time from admission to PCI is presented, which acknowledges the potential heterogeneity of defining admission time in the trial. Additionally, though several clinical characteristics of our participants were similar to those observed in large registries, there was a lower rate of prior coronary procedures, and therefore the studied population may be lower risk (3,5). Finally, the times to treatment were shorter for off-hours participants, and therefore the similar efficacy and safety outcomes findings observed in this clinical trial may not apply to all STEMI programs.

In conclusion, previous hazards identified with off-hours presentation in STEMI were not seen in a large, international, contemporary trial with prospective data collection and adjudication of efficacy outcomes. Such data are reassuring and may reflect global quality improvement measures in STEMI care.

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Table. Baseline Demographic and Clinical Characteristics According to Time of Presentation

Characteristics	On-hours Presentation (N=1206)	Off-hours Presentation (N=786)	Absolute Rate Difference (95% CI)	Adjusted Odds Ratio (95% CI)	P- value
Randomization to cangrelor, n	569 (47.2)	393 (50.0)	-	-	0.21
Age, y	61 ± 12	60 ± 12	-	-	0.06
Female, n (%)	315 (26.1)	199 (25.3)	-	-	0.69
48-hour efficacy outcomes, n (%)					
Primary endpoint*	41 (3.4)	24 (3.1)	0.4 (-1.2, 1.9)	1.00 (0.57, 1.74) [^]	0.99 [^]
Stent thrombosis	15 (1.2)	17 (2.2)	-0.9 (-2.1, 0.3)	0.57 (0.27, 1.21) [^]	0.15 [^]
Death from any cause	11 (0.9)	9 (1.1)	-0.2 (-1.2, 0.7)	0.89 (0.34, 2.34) [^]	0.81 [^]
Myocardial infarction	15 (1.2)	3 (0.4)	0.9 (0.1, 1.6)	2.57 (0.70, 9.44) [^]	0.16 [^]
Ischemia-driven revascularization	6 (0.5)	6 (0.8)	-0.3 (-1.0, 0.5)	0.52 (0.15, 1.76) [^]	0.29 [^]
30-day efficacy outcomes, n					
Primary endpoint*	69 (5.7)	41 (5.2)	0.5 (-1.5, 2.6)	0.95 (0.62, 1.47) [^]	0.83 [^]
Stent thrombosis	24 (2.0)	25 (3.2)	-1.2 (-2.6, 0.3)	0.56 (0.30, 1.03) [^]	0.06 [^]
Death from any cause	32 (2.7)	21 (2.7)	0.0 (-1.5, 1.4)	1.00 (0.55, 1.83) [^]	0.99 [^]
Myocardial infarction	19 (1.6)	9 (1.1)	0.5 (-0.6, 1.5)	1.04 (0.44, 2.45) [^]	0.93 [^]
Ischemia-driven	13 (1.1)	10 (1.3)	-0.2 (-1.2, 0.8)	0.61 (0.25, 1.51) [^]	0.29 [^]
48-hour adverse outcome, n					
GUSTO-defined moderate or severe bleeding	10 (0.8)	9 (1.1)	-0.3 (-1.2, 0.6)	0.51 (0.18, 1.48) [^]	0.22 [^]
ACUITY-defined major or minor bleeding	178 (14.3)	125 (15.1)	-0.8 (-4.0, 2.3)	0.91 (0.69, 1.20) [^]	0.49 [^]

ACUITY, Acute Catheterization and Urgent Intervention Triage Strategy; CABG, coronary artery bypass graft; CI, confidence interval; GP, glycoprotein; GUSTO, Global Use of Strategies to Open Occluded Coronary Arteries; LAD, left anterior descending; PCI, percutaneous coronary intervention.

*Primary endpoint: death from any cause, myocardial infarction, ischemia-driven revascularization, or stent thrombosis.

[^]Odds ratio adjusted for age, randomization arm, enrollment site, previous myocardial infarction, previous PCI, history of diabetes, clopidogrel loading dose, type of anticoagulant, and type of stent. P-value is shown for adjusted odds ratio.

#Data presented as median (25th, 75th percentile)