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Clinical paper

Cangrelor in cardiogenic shock and after cardiopulmonary resuscitation: A global, multicenter, matched pair analysis with oral $P2Y_{12}$ inhibition from the IABP-SHOCK II trial

Michal Droppa[a,1], *Muthiah Vaduganathan*[b,1], *Ramkumar V. Venkateswaran*[b], *Abhayjit Singh*[b], *Paul M. Szumita*[c], *Russel J. Roberts*[d], *Arman Qamar*[c], *Luis Hack*[a], *Dominik Rath*[a], *Meinrad Gawaz*[a], *Georg Fuernau*[e], *Suzanne de Waha-Thiele*[e], *Steffen Desch*[h], *Steffen Schneider*[f], *Taoufik Ouarrak*[f], *Farouc A. Jaffer*[g], *Uwe Zeymer*[f], *Holger Thiele*[h], *Deepak L. Bhatt*[b,2], *Tobias Geisler*[a,*,2]

[a] *Department of Cardiology and Cardiovascular Medicine, University Hospital of Tübingen, Germany*
[b] *Brigham and Women's Hospital Heart & Vascular Center and Harvard Medical School, Boston, MA, USA*
[c] *Department of Pharmacy, Brigham and Women's Hospital, Boston, MA, USA*
[d] *Department of Pharmacy, Massachusetts General Hospital, Boston, MA, USA*
[e] *Medical Clinic II, (Cardiology/Angiology/Intensive Care Medicine), University Heart Center Lübeck, University Hospital Schleswig-Holstein, University of Lübeck, Lübeck, Germany*
[f] *Institut für Herzinfarktforschung, Ludwigshafen, Germany*
[g] *Department of Medicine, Cardiology Division, Massachusetts General Hospital, Boston, MA, USA*
[h] *Heart Center Leipzig at University of Leipzig, Leipzig, Germany*

Abstract

Aims: Cangrelor has a potentially favorable pharmacodynamic profile in cardiogenic shock (CS). We aimed to evaluate the clinical course of CS patients undergoing percutaneous coronary intervention (PCI) treated with cangrelor.

Methods and results: We retrospectively identified 136 CS patients treated with cangrelor. Patients were 1:1 matched to CS patients from the IABP-SHOCK II trial not receiving cangrelor by age, sex, cardiac arrest, type of myocardial infarction, culprit lesion, glycoprotein IIb/IIIa inhibitor, and oral $P2Y_{12}$-receptor inhibitor and followed-up for 12 months. The study cohort consisted of 88 matched pairs. Thirty-day and 12-month mortality was 29.5% and 34.1% in cangrelor-treated patients and 36.4% and 47.1% in control group (P = 0.34 and P = 0.08, respectively). The rate of definite acute stent thrombosis was 2.3% in both groups. Moderate and severe bleeding events occurred in 21.6% in the cangrelor and 19.3% in the control group (P = 0.71). Patients treated with cangrelor more frequently experienced ≥1 TIMI flow grade improvement during PCI (92.9% vs. 81.2%, P = 0.02).

* Corresponding author at: Department of Cardiology and Cardiovascular Medicine, University Hospital of Tübingen, Otfried-Müller-Straße 10, 72076 Tübingen, Germany.
E-mail address: tobias.geisler@med.uni-tuebingen.de (T. Geisler).
[1] Both authors contributed equally to this manuscript.
[2] Both senior authors contributed equally to this manuscript.

https://doi.org/10.1016/j.resuscitation.2019.02.008
Received 2 December 2018; Received in revised form 1 February 2019; Accepted 11 February 2019

Conclusion: Cangrelor treatment was associated with similar bleeding risk and significantly better TIMI flow improvement compared with oral $P2Y_{12}$ inhibitors in CS patients undergoing PCI. The use of cangrelor in CS offers a potentially safe and effective antiplatelet option and should be evaluated in randomized trials.

Keywords: ACS/NSTE-ACS, Cardiogenic shock, Cardiopulmonary resuscitation, Adjunctive pharmacotherapy

Introduction

Cardiogenic shock (CS) and cardiopulmonary resuscitation in patients with acute coronary syndrome are associated with high mortality and risk of adverse cardiovascular events despite optimal interventional therapy.[1,2] Antithrombotic therapy during percutaneous coronary intervention (PCI) and stent implantation reduce thrombotic complications such as stent thrombosis and recurrent myocardial infarction. Antiplatelet effects of oral $P2Y_{12}$-receptor inhibitors are delayed in CS patients due to slower absorption and metabolism, and challenges with adequate enteral access in intubated patients.[3] The intravenous $P2Y_{12}$-receptor inhibitor, cangrelor, may overcome these complexities due to its excellent bioavailability, fast-acting properties, and safety in renal impairment.[4,5] Cangrelor has been demonstrated to safely reduce ischemic events, including stent thrombosis, in large randomized clinical trials compared with oral clopidogrel in patients undergoing PCI.[6–9] However, CS was an exclusion criterion in these landmark clinical trials, and few, single-center experiences have evaluated the impact of intravenous $P2Y_{12}$-receptor inhibition in high-risk patients with cardiopulmonary resuscitation or CS, especially compared with use of newer oral $P2Y_{12}$-receptor inhibitors, prasugrel and ticagrelor.[10–17] Thus, we aimed to evaluate the clinical course of patients in CS undergoing PCI treated with cangrelor or oral $P2Y_{12}$-receptor inhibitors in this global, multicenter observational study.

Methods

We retrospectively reviewed all patients with acute coronary syndrome complicated by CS treated with cangrelor in 3 tertiary centers (University Hospital of Tübingen, Germany; Brigham and Women's Hospital, Boston, MA, USA; and Massachusetts General Hospital, Boston, MA, USA). All patients underwent PCI and the decision to use cangrelor was left to the treating physician. Cangrelor was administrated during the PCI as a bolus of 30 μg/kg followed by infusion of 4 μg/kg/min (or 0.75 μg/kg/min without a bolus in case of bridging) for at least 2 h. Oral $P2Y_{12}$-receptor inhibitors were loaded after the completion of infusion in case of clopidogrel and prasugrel or before, during, or after cangrelor infusion in the case of ticagrelor.[10] Exclusion criteria were prolonged pre-procedural resuscitation and age older than 90 years. Baseline and procedural characteristics, ischemic and bleeding complications, and mortality were extracted from review of the electronic health record. A control cohort of patients was identified from the large randomized Intra-aortic Balloon Pump in Cardiogenic Shock (IABP-SHOCK) II trial[1] treated with oral $P2Y_{12}$-receptor inhibitors. The study design and the eligibility criteria have been described elsewhere.[1] Patients were matched according to age, sex, cardiac arrest, type of myocardial infarction (ST-segment elevation myocardial infarction – STEMI vs. non-ST-segment elevation

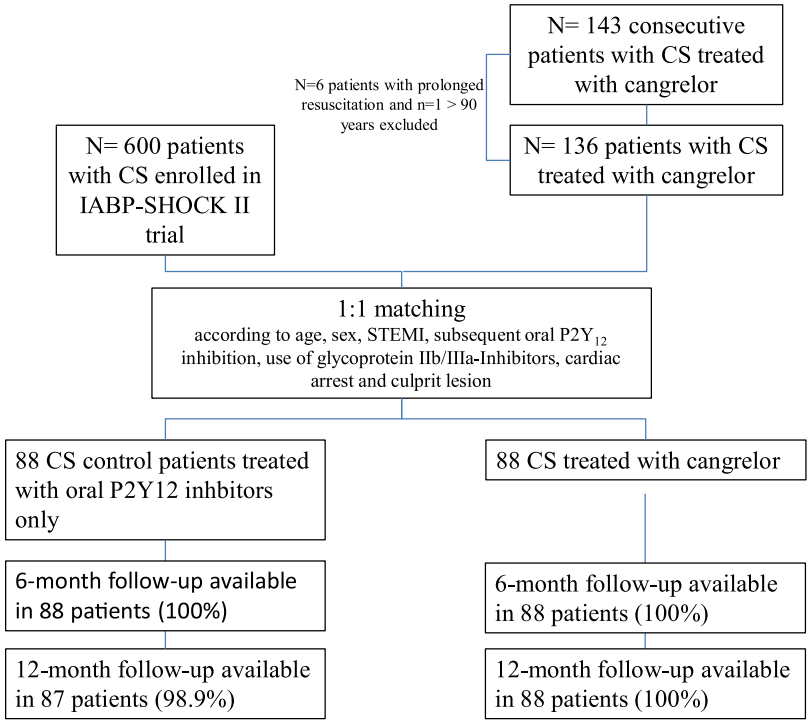

Fig. 1 – Flow chart and patient selection. CS — cardiogenic shock, STEMI — ST-segment elevation myocardial infarction.

Table 1 – Baseline, procedural characteristics, and key clinical outcomes of the global cangrelor cohort and the IABP-SHOCK II randomized trial cohort.

	IABP-SHOCK II cohort (n = 600)	Multicenter cangrelor-treated patients (n = 136)
Age in years, median (IQR)	70 (58; 77)	68 (59; 77)
Sex female/male	187 / 413 (31.2% / 68.8%)	39 / 97 (28.7% / 71.3%)
NSTE-ACS n (%)	182/600 (30.3%)	50 (37.8%)
STEMI	418/600 (69.7%)	82/132 (62.1%)
- LAD or LM culprit	308/600 (51.3%)	56/120 (46.7%)
- Non-LAD or LM culprit	292/600 (48.7%)	64/120 (53.3%)
Diabetes mellitus	195/596 (32.7%)	42/132 (31.8%)
Chronic kidney disease	124/598 (20.7%)	17/131 (13.0%)
Cardiopulmonary resuscitation	270/600 (45.0%)	62/135 (45.9%)
Therapeutic hypothermia	197/600 (32.8%)	25/135 (18.5%)
Mechanical circulatory support	310(600) (51.7%)	59/136 (43.4%)
Glycoprotein IIb/IIIa inhibitor use	281/598 (47.0%)	14/127 (11.0%)
$P2Y_{12}$-receptor blocker		
- Ticagrelor/prasugrel	111/512 (21.7%)	90/136 (66.2%)
- Clopidogrel	401/512 (78.3%)	46/136 (33.8%)
Cangrelor full dose	–	113/136 (83.1%)
Cangrelor bridging dose	–	30/136 (22.1%)
Unfractionated heparin	550/598 (92.0%)	129/135 (95.6%)
Bivalirudin	65/598 (10.9%)	7/129 (5.4%)
Aspirin	546/598 (91.3%)	52/53 (98.1%)
PCI	575/600 (95.8%)	114/134 (85.1%)
Type of stent		
DES	249/538 (46.3%)	105/114 (92.1%)
BMS	305/538 (56.7%)	5/14 (4.4%)
Mechanical thrombectomy	162/600 (27.0%)	18/128 (14.1%)
Key clinical outcomes of unmatched cohorts		
30-day mortality	244/599 (40.7%)	40/136 (29.4%)
12-month mortality	307/595 (51.6%)	48/136 (35.3%)
In-hospital GUSTO moderate and severe bleeding	123/600 (20.5%)	33/136 (24.3%)
Definite acute stent thrombosis	7/600 (1.2%)	2/131 (1.5%)
Renal replacement therapy	110/600 (18.3%)	22/133 (16.5%)

BMS — bare metal stent, CI — confidence interval, CKD — chronic kidney disease (glomerular filtration rate <30 ml/min), DES — drug-eluting stent, IQR — interquartile range, LAD — left anterior descending artery, LM — left main coronary artery, NSTE-ACS — non-ST-segment elevation acute coronary syndrome, PCI — percutaneous coronary intervention, RR — relative risk, STEMI — ST-segment elevation myocardial infarction, GUSTO — Global Use of Strategies to Open Occluded Coronary Arteries.

myocardial infarction – NSTEMI), culprit lesion localization (anterior vs. non-anterior myocardial infarction), glycoprotein IIb/IIIa inhibitor (GPI) use, and oral antiplatelet therapy (clopidogrel vs. prasugrel/ticagrelor either as initial therapy or after switching from cangrelor to oral $P2Y_{12}$ inhibition). Periprocedural, in-hospital events, and mortality at 30 days and 1 year were compared between 1:1 matched groups. Bleeding events were recorded according to Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) criteria.[18] Acute stent thrombosis was defined as definite stent thrombosis according to the Academic Research Consortium criteria[19] occurring within 24 h after PCI. Thrombolysis in Myocardial Infarction (TIMI) flow was assessed from angiographic scene of the target vessel before and after the PCI.[20]

Categorical variables were presented as counts and percentages and were compared by χ^2 tests. Continuous variables were presented as median and interquartile range (IQR) or mean and standard deviation and were compared by Mann-Whitney-Wilcoxon test. Of the 600 patients enrolled in IABP-SHOCK II trial and 136 patients in CS treated with cangrelor across the 3 institutions, 88 matched pairs (1:1 matching) were identified (Fig. 1). Post-PCI survival curves were constructed by the Kaplan-Meier method and were compared between matched groups using log-rank tests. All P-values were 2-tailed and <0.05 was considered statistically significant. All analyses were performed using SAS statistical package version 9.3 (Cary, North Carolina, USA).

The study was approved by the institutional ethics committees at the University Hospital Tübingen (553/2017BO2), Partners HealthCare (2016P001952/PHS), and University of Leipzig (202-2006) and complies with the Declaration of Helsinki and good clinical practice guidelines. Given the use of anonymized data already collected as part of routine diagnosis and treatment, written informed consent was not required. In the IABP-SHOCK II trial, all patients or their legally authorized representatives provided written informed consent.

Results

From November 2015 to August 2017, 143 patients with CS and treated with cangrelor were screened at the 3 institutions; 7 patients were excluded because of prolonged resuscitation and older age (>90 years) (Fig. 1). Patient characteristics of the cangrelor and the control cohort from IABP-SHOCK II trial are shown in Table 1. Administration of GPI was more frequent in the IABP-SHOCK II trial compared with the cangrelor CS cohort (47.0% versus 11.0%). In the IABP-SHOCK II trial, 21.7% of patients were treated with newer $P2Y_{12}$-inhibitors and 78.3%

with clopidogrel, whereas in the cangrelor CS cohort 66.2% of patients were treated with newer $P2Y_{12}$-inhibitors and 33.8% with clopidogrel after end of cangrelor infusion. Mortality rates were 40.7% and 29.4% at 30-days and 51.6% and 35.3% at 12 months in patients in the IABP-SHOCK II trial cohort and in cangrelor-treated patients, respectively. The unadjusted relative risk was 0.72 (95% confidence interval 0.55–0.95) for 30-day mortality and 0.68 (95% confidence interval 0.54–0.87) for 12-month mortality in the cangrelor group compared with the IABP-SHOCK II trial cohort (Table 1).

After 1:1 matching according to predefined criteria, 88 matched pairs were identified.

Baseline and procedural characteristics of the matched cohorts are shown in Table 2.

Patients were approximately 70 years old, 71.6% patients were male, 70.5% patients had STEMI, whereas 29.5% had NSTEMI, 47.7% had anterior myocardial infarction, 46.6% patients undergone cardiopulmonary resuscitation, 13.6% patients were treated with intravenous GPI, 56.8% received prasugrel or ticagrelor, and 43.2% were treated with clopidogrel after PCI. Median resuscitation time in matched cohort was 12.5 (IQR 6.0–22.0) min. In the cangrelor group, more patients received drug-eluting stents compared with the control group, and mechanical thrombectomy was used less frequently. Mostly unfractionated heparin was used as an anticoagulant during PCI, whereas more patients received bivalirudin in the control group.

A total of 89.9% of patients received cangrelor as initial infusion only, similar to the Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition (CHAMPION) trial, and 17% of patients received cangrelor for a prolonged time using a lower dosing strategy similar to the BRIDGE study protocol.[21]

Median follow-up in the cangrelor group was 360 (IQR 198–571) days. In the matched cohorts, all-cause mortality at 30 days was 29.5% vs. 36.4% (P = 0.34) and at 1 year was 34.1% vs. 47.1% (P = 0.08) in the cangrelor group and IABP-SHOCK II matched control group, respectively. Cangrelor-treated patients experienced numerically lower mortality compared with CS patients not treated with cangrelor up to 1-year, but these differences did not reach statistical significance (log-rank P = 0.15; Fig. 2). Moderate or severe GUSTO bleeding occurred in 21.6% of cangrelor-treated patients and 19.3% of the control group (P = 0.71). There were 2 cases of acute stent thrombosis (2.3%) in both matched groups. Patients treated with cangrelor showed improved TIMI flow rates compared with patients treated with oral $P2Y_{12}$-receptor inhibitors only ($\geq$1 TIMI flow grade improvement 92.9% vs. 81.2%, P = 0.02, Table 3).

Discussion

In this global, multicenter, observational study, cangrelor was associated with similar bleeding risk, improved TIMI flow grade,

Table 2 – Baseline and procedural characteristics of cangrelor treated and matched control patients.

	IABP-SHOCK II matched cohort treated with oral $P2Y_{12}$ inhibitors (n = 88)	Multicenter cangrelor-treated patients (n = 88)	P
Age in years, median (IQR)	70.5 (59.0; 77.0)	68.5 (58.5; 77.0)	0.94
Sex female /male	25 / 63/ (28.4 / 71.6%)	25 / 63 (28.4/71.6%)	1.00
NSTE-ACS n (%)	26/88 (29.5%)	26/88 (29.5%)	1.00
STEMI	62/88 (70.5%)	62/88 (70.5%)	1.00
- LAD or LM culprit	42/88 (47.7 %)	42/88 (47.7 %)	1.0
- Non-LAD or LM culprit	44/88 (53.3%)	44/88 (53.3%)	1.0
Diabetes mellitus	21/88 (23.9 %)	26/88 (29.5 %)	0.39
Chronic kidney disease	58.6 (43.9; 71.1)	57.7 (37.7; 73.2)	0.81
Cardiopulmonary resuscitation	41/88 (46.6 %)	41/88 (46.6 %)	1.0
Therapeutic hypothermia	25/88 (28.4 %)	21/88 (23.9 %)	0.49
Mechanical circulatory support	41/88 (46.6 %)	36/88 (40.9 %)	0.45
Glycoprotein IIb/IIIa inhibitor use	12/88 (13.6 %)	12/88 (13.6 %)	1.00
Aspirin	81/88 (92.0 %)	40/41 (97.6 %)	0.23
$P2Y_{12}$-receptor blocker			
- Ticagrelor/prasugrel	60/88 (56.8%)	60/88 (56.8%)	1.00
- Clopidogrel	38/88 (43.2%)	38/88 (43.2 %)	1.00
Cangrelor full dose		79/88 (89.9 %)	
Cangrelor bridging dose		15/88 (17.0 %)	
Unfractionated heparin	74/88 (84.1 %)	84/88 (95.5 %)	0.013
Bivalirudin	15/88 (17.0 %)	6/88 (6.8 %)	0.036
PCI	85/88 (96.6 %)	77/86 (89.5 %)	0.066
Type of stent			
DES	44/79 (55.7 %)	71/77 (92.2 %)	< 0.001
BMS	36/79 (45.6 %)	3/77 (3.9 %)	< 0.001
Mechanical thrombectomy	27/88 (30.7 %)	16/88 (18.2 %)	0.054

BMS — bare metal stent, CKD — chronic kidney disease (glomerular filtration rate <30 ml/min), DES — drug-eluting stent, IQR — interquartile range, LAD — left anterior descending artery, LM — left main coronary artery, NSTE-ACS — non-ST-segment elevation acute coronary syndrome, PCI — percutaneous coronary intervention, STEMI — ST-segment elevation myocardial infarction.

and a numerically lower 1-year mortality compared with oral $P2Y_{12}$ inhibitors in CS patients undergoing PCI.

Potent antiplatelet therapies are a cornerstone part of the management in patients undergoing PCI, reducing risks of stent thrombosis and ischemic events.[22,23] In a recent registry of 5833 consecutive patients undergoing PCI, CS was the strongest predictor of stent thrombosis.[24] In addition, CS patients, especially those requiring mechanical circulatory support, are at high risk for major bleeding. Taken together, highly effective, fast-acting, and controllable platelet inhibition is desired to prevent early thrombotic events and to reverse platelet inhibition in case of serious bleeding. Despite progress in interventional treatment and adoption of mechanical circulatory support strategies, mortality remains high in patients with CS,[1,2] necessitating a search for new therapeutic strategies. Bioavailability of oral $P2Y_{12}$-receptor inhibitors is often limited in patients with CS. Organ hypoperfusion in CS can impair gastrointestinal absorption of all oral $P2Y_{12}$-receptor inhibitors and influence efficiency of bioactivation of prodrugs of clopidogrel and prasugrel to pharmacologically active metabolites.[25] Therapeutic hypothermia used after cardiopulmonary resuscitation[26,27] and morphine further delay antiplatelet effects, even with newer $P2Y_{12}$ inhibitors.[28–30] Mechanical ventilation necessitating gastric tube placement can complicate immediate oral administration of $P2Y_{12}$-receptor inhibitors, especially in the emergency setting.

Cangrelor is a parenteral $P2Y_{12}$-receptor inhibitor which can overcome these issues. It has favorable pharmacokinetics with almost immediate onset of platelet inhibition and very short plasma half-life allowing fast platelet recovery.[31] We have previously shown that cangrelor allows better periprocedural platelet inhibition in patients with acute coronary syndromes treated with PCI compared

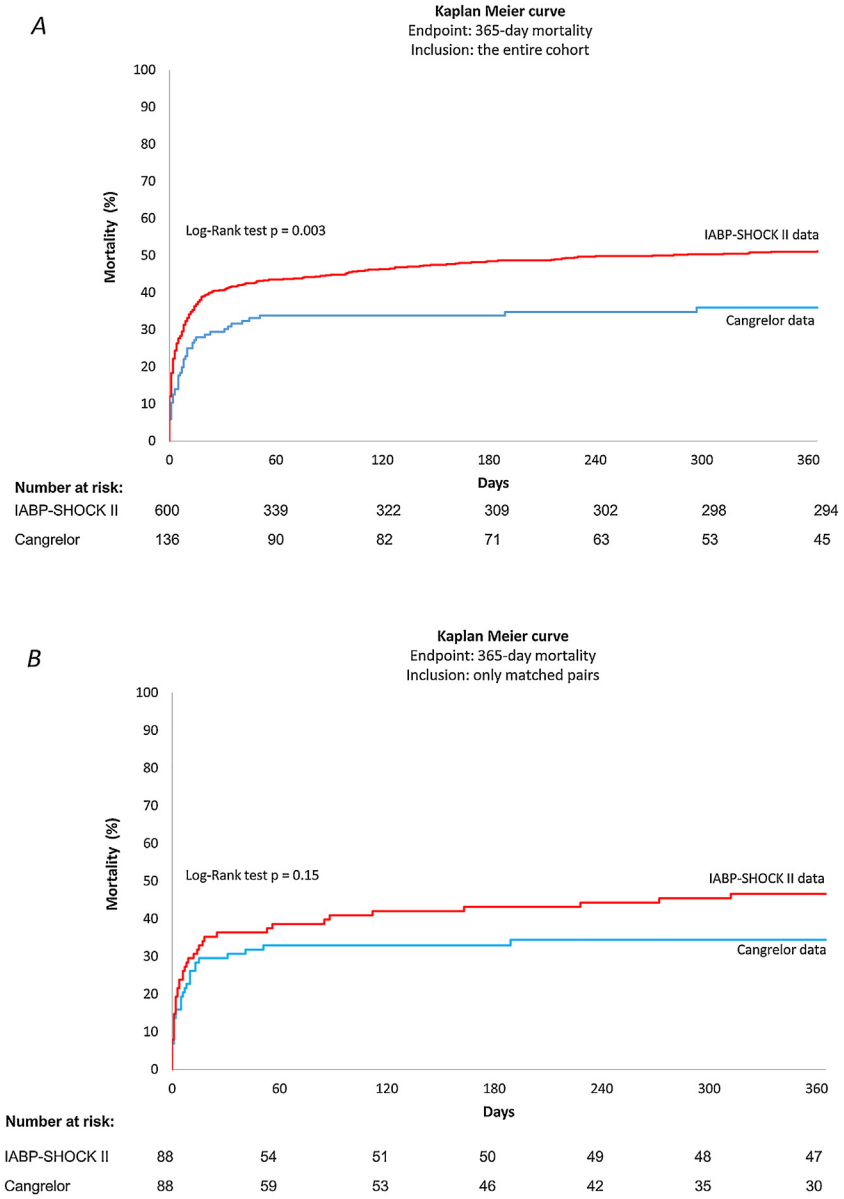

Fig. 2 – Kaplan-Meier survival curves comparing 12-month mortality rates between cangrelor- and oral $P2Y_{12}$-receptor inhibitor only-treated patients in cardiogenic shock undergoing PCI. A — entire cohort, B — matched pair comparison. Event curves were compared using the log-rank test.

Table 3 – In-hospital complications and post-PCI mortality.

	Matched control cohort (n = 88)	Cangrelor (n = 88)	P-Value
TIMI flow before PCI			0.67
0	58/85 (68.2%)	49/84 (58.3%)	
1	5/85 (5.9%)	21/84 (25%)	
2	10/85 (11.8%)	10/84 (11.9%)	
3	12/85 (14.1%)	4/84 (4.8%)	
TIMI flow after PCI			0.27
0	4/84 (4.7%)	2/84 (2.4%)	
1	2/85 (2.4%)	0/84 (0.0%)	
2	3/85 (3.5%)	3/84 (3.6%)	
3	76/85 (89.4%)	79/84 (94.0%)	
TIMI flow improvement			
- At least 1 grade	69/85 (81.2 %)	78/84 (92.9 %)	0.02
- At least 2 grades	57/85 (67.1 %)	68/84 (81.0 %)	0.04
Definite acute stent thrombosis	2/88 (2.3 %)	2/88 (2.3 %)	1.00
Renal replacement therapy	16/88 (18.2 %)	13/87 (14.9 %)	0.56
Sepsis	17/88 (19.3 %)	8/41 (19.5 %)	0.98
12-month stroke	1/88 (1.1 %)	2/41 (4.9 %)	0.19
30-day mortality	32/88 (36.4%)	26/88 (29.5%)	0.34
12-month mortality	41/87 (47.1 %)	30/88 (34.1 %)	0.079
In-hospital GUSTO moderate and severe bleeding	17/88 (19.3 %)	19/88 (21.6 %)	0.71

GUSTO — Global Use of Strategies to Open Occluded Coronary Arteries, TIMI — thrombolysis in myocardial infarction.

with oral $P2Y_{12}$-receptor inhibitors.[10] There are limited data evaluating the clinical profile of cangrelor in the context of CS and cardiopulmonary resuscitation, primarily from case series and single-center reports.[11–14,17]

Data on the use of GPI in CS patients are also limited. Routine upfront GPI with abciximab did not improve outcome in CS patients in the PRimary Angioplasty for patients with acute myocardial infarction, transported from the General non-PCI hospitals to catheterization Units with or without Emergency thrombolysis (PRAGUE)-7 trial.[32] A single center registry from Cleveland Clinic suggested better TIMI flow and lower long-term mortality with abciximab in PCI patients with CS.[33] Previous analyses from pooled, patient-level data from the 3 CHAMPION trial cohorts suggest that cangrelor might be as effective and associated with less bleeding events as clopidogrel and routine GPI.[34,35]

Background anticoagulant choice may modify the safety and efficacy profile of selected antiplatelet agents. In our study, patients in the control group were more often treated with bivalirudin for periprocedural anticoagulation. Use of bivalirudin did not affect bleeding rates compared with unfractionated heparin in patients with acute coronary syndromes in a recent large registry-based randomized trial[36] and in a smaller study of patients in CS.[37]

Of note, we observed a high number of CS patients in the cangrelor group who experienced improved TIMI flow during PCI and the rate was higher compared with patients in the control group who received oral $P2Y_{12}$ inhibitors only. Cangrelor has been shown to reduce clot size and to promote clot stability in animal *in vivo* thrombosis models and patients with heart failure.[38] In addition, cangrelor has been shown effective to reduce intraprocedural stent thrombosis in PCI patients compared with oral $P2Y_{12}$ inhibition.[39] As such, cangrelor presents an attractive option in preventing clot growth and distal embolization in CS. Further mechanistic data, including with intracoronary imaging, may help to better understand the acute effects of cangrelor in this setting.

The present study is subject to a number of limitations. Although mortality was high, the study was not powered to detect differences between groups. Given the non-randomized design and potential for selection bias, these findings should be regarded as hypothesis-generating. Despite matching, there were differences in stent types in both populations, which could possibly have impact on medium/long-term outcome. However in a separate analysis from IABP-SHOCK II trial, there was no effect of BMS versus DES on outcome after adjustment for other risk factors.[40] We therefore do not believe that the use of BMS in the control group would have impacted the overall results. It was not possible to adjust for variation in subsequent one year treatment *i.e.* regarding drug or device based heart failure therapy and therefore treatment differences might have influenced results. Timing of $P2Y_{12}$ receptor blockade was highly variable in both cohorts. We believe that the variability of timing reflects the clinical reality where pretreatment in CS is heterogeneous. In a recent analysis of STEMI patients pre-treated with ticagrelor, cangrelor provided additional antiplatelet effects when given adjunctively during PCI.[41] Despite thorough matching of both cohorts based on established risk factors that are known to influence mortality in CS, there may be known or unknown factors that remained unbalanced between these groups.

Conclusions

Cangrelor offers an attractive antiplatelet strategy in patients in CS undergoing PCI. Cangrelor-treated patients in CS in this multicenter observational study experienced similar rates of bleeding, improved TIMI flow, and numerically lower mortality compared with matched controls treated with oral $P2Y_{12}$ inhibitors. These results are hypothesis-generating and should be further explored in randomized clinical trials in this setting.

Conflicts of interest

MD received travel honoraria by Medtronic.

TG reports personal fees from Astra Zeneca, grants and personal fees from Bayer Healthcare, personal fees from Boehringer Ingelheim, grants and personal fees from Bristol Myers Squibb, personal fees from Pfizer, grants and personal fees from Daiichi Sankyo, grants and personal fees from Eli Lilly, grants and personal fees from Medicines Company, personal fees from MSD, grants from Siemens Healthcare, grants from Spartan Bioscience, outside the submitted work

MV is supported by the KL2/Catalyst Medical Research Investigator Training award from Harvard Catalyst (NIH/NCATS Award UL 1TR002541), serves on advisory boards for Amgen, AstraZeneca, Bayer AG, and Baxter Healthcare, and participates in clinical endpoints committees for studies supported by Novartis and the NIH.

AQ is supported by the NHLBI T32 postdoctoral training grant (T32HL007604).

FAJ has sponsored research grants from Siemens, and Canon, has a consulting agreement with Boston Scientific, Abbott Vascular and Siemens. Massachusetts General Hospital has a patent licensing arrangement with Canon Corporation, and Dr. Jaffer has the right to receive licensing royalties.

UZ discloses the following relationships - Speaker's honoraria and consulting fees from Bayer, Bristol-Myers Squibb/Pfizer, Daiichi-Sankyo, Boehringer Ingelheim, Trommsdorf, Ferrer.

DLB 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, TobeSoft; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine, Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), Population Health Research Institute (COMPASS clinical trial steering committee funded by Bayer), 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 (Chair), VA CART Research and Publications Committee (Chair); Research Funding: Abbott, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi (including for his role as co-Chair of the CHAMPION PHOENIX trial), Eisai, Ethicon, Forest Laboratories, Idorsia, Ironwood, Ischemix, Lilly, Medtronic, PhaseBio, Pfizer, Regeneron, Roche, Sanofi Aventis, Synaptic, 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 (now Abbott), Svelte; Trustee: American College of Cardiology; Unfunded Research: FlowCo, Merck, PLx Pharma, Takeda.

All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Acknowledgements

This study was in part funded by the DFG (German Research Foundation) – Project 374031971 – TRR 240.

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