

Article

Use of Cangrelor in Patients Undergoing Percutaneous Coronary Intervention: Insights and Outcomes from District General Hospital

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Abstract

Background/Objectives: Cangrelor, an intravenous P2Y₁₂ inhibitor, is increasingly used during percutaneous coronary intervention (PCI) for rapid and reversible platelet inhibition in patients unable to take oral antiplatelet agents, particularly in emergencies such as ST-elevation myocardial infarction (STEMI), cardiac arrest, or cardiogenic shock. This single-centre study evaluates cangrelor and outcomes in a non-surgical centre. **Methods:** Between June 2017 and December 2021, all the patients for whom cangrelor was used at a district general hospital (DGH) in the UK were included in this study. Data collection included baseline characteristics, admission, procedural details, and patient outcomes. The primary outcome was a composite of all-cause mortality, bleeding, and cardiovascular events, including myocardial infarction, stent thrombosis, and stroke, within 48 h. Secondary outcomes included predictors of the composite outcome at 48 h. **Results:** During the study period, cangrelor was administered peri-procedurally to 93 patients. Males comprised 85% of the patients; the mean age was 65.5 ± 10.6 years. A total of 1 patient (1.1%) had a cardiovascular event within 48 h of cangrelor administration, whereas all-cause mortality occurred in 17 patients (18%) within 48 h. No major bleeding events were noted at 48 h following cangrelor administration. Regression analysis did not find predictors of composite outcomes at 48 h. **Conclusions:** Cangrelor offers a potential alternative to oral P2Y₁₂ inhibitors in specific high-risk scenarios. Further research is needed to validate its role in broader populations.

Keywords: cangrelor; P2Y₁₂ inhibitor; PCI; cardiac arrest; ST-elevation myocardial infarction



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1. Introduction

Cardiovascular disease is increasing in prevalence and becoming a healthcare challenge especially in the developing world [1–9], especially with the recent COVID-19 and

other outbreaks [10,11]. Dual antiplatelet therapy, involving an oral P2Y₁₂ receptor antagonist alongside aspirin, is the established standard of care during percutaneous coronary intervention (PCI) [12]. Clopidogrel, one of the most frequently prescribed P2Y₁₂ receptor antagonists, can occasionally exhibit variable antiplatelet effects, leading to high platelet reactivity and an increased risk of adverse thrombotic events in some patients [13]. Newer antiplatelet agents, such as ticagrelor and prasugrel, provide faster, more potent, and more consistent P2Y₁₂ antagonism than clopidogrel, enhancing ischaemic outcomes in clinical studies. However, they are also linked to a higher risk of bleeding and have been reported to have an occasional delayed onset of antiplatelet action [14–16]. Moreover, oral antiplatelet agents typically exhibit a relatively slow onset and offset of activity, which could pose challenges in emergencies. Consequently, there has been growing interest in developing a potent P2Y₁₂ receptor antagonist that can be administered intravenously (IV) with a rapid onset and offset of action. Cangrelor's short half-life may have reduced bleeding risks in this population. Risk stratification tools, including PRECISE-HBR and ICARUS, indicate that this cohort, with a median age of 65 and 12% having chronic kidney disease, was at intermediate bleeding risk [17,18]. Cangrelor is a reversible P2Y₁₂ receptor antagonist that is not a thienopyridine but an adenosine triphosphate analogue. It is given as an IV bolus followed by an infusion, rapidly reaching the peak concentration within 2 min and maintaining its concentration consistently throughout the infusion. It significantly inhibits adenosine diphosphate-induced platelet aggregation for the duration of the infusion. Upon the discontinuation of the infusion, its effect reverses quickly, with platelet function returning to normal within 60 min [8]. Cangrelor was approved based on its superior efficacy in reducing thrombotic complications compared to clopidogrel in patients undergoing PCI [9]. Consequently, its use in real-world settings has increased [10]. While its clinical efficacy compared to potent oral P2Y₁₂ inhibitors has not been thoroughly examined, pharmacodynamic research has demonstrated that cangrelor mitigates the limitations of oral therapies by achieving rapid and potent platelet inhibition [19–21]. Furthermore, studies have refined the optimal approach to transitioning from cangrelor to oral P2Y₁₂ inhibiting therapy. This study aims to present the outcomes of cangrelor use in a district general hospital (DGH) with a heart attack centre (HAC).

2. Materials and Methods

This was a single-centre, retrospective analysis of the use of cangrelor at Royal Derby Hospital (RDH), United Kingdom (UK). This study included consecutive PCI cases where cangrelor was administered between June 2017 and December 2021 (55 months). RDH is a DGH with 24/7 access to invasive coronary angiography and PCI. It has two cardiac catheterisation laboratories and no on-site cardiac surgery service. All the PCIs performed during the above period were screened for the use of cangrelor, and all the cases where cangrelor was used were included in this study. The decision to use cangrelor was at the discretion of the treating physician. No standardised protocol for cangrelor use was in place during the study period. The standard administration of cangrelor comprised an intravenous bolus dose of 30 µg/kg, followed by a 4 µg/kg/min intravenous infusion over two hours. When transitioning patients to oral ticagrelor, the 180 mg ticagrelor bolus dose was given as early as possible during the cangrelor infusion; for patients transitioning to oral clopidogrel or prasugrel, 600 mg of clopidogrel or a 60 mg prasugrel bolus dose was administered during the last half hour of the cangrelor infusion. There was no control group in this study. Only the first treatment was included in this report if a patient received cangrelor treatment more than once during the study period. The research reported in this article adheres to the Declaration of Helsinki. This study was conducted as part of an approved hospital audit (reference: UHDBM259; approval date: 1 November 2024) using

anonymised, retrospective data. Ethics committee review was deemed unnecessary as no new interventions were introduced. The need for consent was waived. This study was designed and reported in accordance with the STROBE checklist [22].

2.1. Variables and Data Source

Our institution's electronic files were reviewed to determine the number of patients who received cangrelor among those undergoing PCI during the specified period. Detailed data collection was undertaken for these patients, including the collection of information on demographics and outcomes.

2.2. Outcomes

Primary efficacy outcomes included cardiovascular events such as myocardial infarction, stent thrombosis, and stroke within 48 h. Primary safety outcomes included all-cause mortality and bleeding, as defined by the Bleeding Academic Research Consortium BARC criteria (Supplementary Table S1). Major bleeding was considered BARC type 3 or above [15]. Secondary outcomes included predictors of the composite outcome at 48 h.

2.3. Statistical Analysis

Continuous variables are expressed as the mean and standard deviation (SD). Categorical variables are expressed as numbers and percentages (%). Student's *t*-tests and Kruskal–Wallis tests were used to compare continuous variables between the groups, depending on the normality of the distribution. A logistic regression model was used to explore the predictors of composite outcomes at 48 h following the cangrelor dose. Cox regression models investigated the relationship between composite outcomes and variables at 48 h. A 2-sided *p*-value < 0.05 was considered statistically significant. All *p*-values are two-sided and are presented without adjustment for multiple testing. Statistical analysis was performed using GraphPad Prism V10.3 for Mac (San Diego, CA, USA; www.graphpad.com). Accessed on 1 June 2024.

3. Results

3.1. Baseline Characteristics

During the study period, 93 patients took cangrelor peri-procedurally. Patient characteristics are shown in Table 1. The mean age was 65.5 ± 10.6 years, and 85% were males. The most common comorbidity was hypercholesterolaemia in 42% of patients, followed by hypertension in 33%. The most common presenting diagnosis was ST-elevation myocardial infarction (STEMI) in 62 patients (67%), followed by cardiac arrest in 25 patients (27%) and angina or non-ST-elevation myocardial infarction in 6 patients (6%). A transthoracic echocardiogram (TTE) was conducted in 78 patients (84%) before cangrelor administration, of which 27 (35%) showed a left ventricular ejection fraction (LVEF) < 40%, 27 (35%) had an LVEF of 40–50%, and 24 (30%) had an LVEF > 50%. The mean door-to-balloon time was 32 min. No patients received pre-treatment with oral P2Y12 inhibitors. All patients had either an oral or per-rectal loading dose of aspirin of 300 mg along with cangrelor. The mean SYNTAX score was 26 ± 8.5 , consistent with high-risk PCI patients. Post-cangrelor, 64 patients transitioned to ticagrelor, 23 to clopidogrel, and 6 to prasugrel.

Table 1. Baseline characteristics of patients, according to study population.

	Total (<i>n</i> = 93)	48 h Survival (<i>n</i> = 76)	48 h Mortality (<i>n</i> = 17)	<i>p</i> -Value
Demographics, <i>n</i> (%) or median (IQR)				
Male	78 (85%)	65 (86%)	14 (82%)	0.07
Age (years)	65.5 ± 10.6	68 ± 10	66 ± 11	0.47
Chronic kidney disease	20 (22%)	7 (9%)	2 (12%)	0.99
Smoker	29 (31%)	25 (33%)	4 (24%)	0.12
Hypertension	31 (33%)	25 (33%)	6 (35%)	0.37
Hypercholesterolaemia	39 (42%)	31 (41%)	8 (47%)	0.45
Diabetes mellitus	9 (10%)	3 (8%)	6 (11%)	0.89
Procedure details, <i>n</i> (%) or mean ± standard deviation				
Radial artery access	73 (78%)	60 (79%)	13 (76%)	0.82
Procedure time	44 ± 13	47 ± 10	41 ± 14	0.08
Complex PCI (multivessel or bifurcation stenting)	44 (47%)	36 (47%)	8 (47%)	0.89
Presentation, <i>n</i> (%)				
Angina/NSTEMI	6 (6%)	6 (8%)	0 (0%)	0.34
Cardiac arrest	25 (27%)	21 (28%)	4 (24%)	0.74
STEMI without cardiac arrest on presentation	62 (67%)	49 (64%)	13 (76%)	0.12
LVEF, <i>n</i> (%) *				
LVEF > 50%	24 (30%)	20 (30%)	4 (33%)	0.89
LVEF 40–50%	27 (35%)	23 (35%)	4 (33%)	0.21
LVEF < 40%	27 (35%)	23 (35%)	4 (33%)	0.21

STEMI: ST-elevation myocardial infarction. NSTEMI: non-ST-elevation myocardial infarction. LVEF: left ventricular ejection fraction. PCI: percutaneous coronary intervention. * An echocardiogram was performed on 78 patients, of which 66 showed 48 h survival, and 12 showed 48 h mortality.

3.2. Clinical Outcomes

3.2.1. Efficacy Outcomes

Only one patient (1.1%) had a cardiovascular event that was identified as stent thrombosis within 48 h of cangrelor administration, and this patient was admitted with STEMI and underwent primary PCI. No strokes were reported.

3.2.2. Safety Outcomes

There were no bleeding events at 48. No major bleeding or allergic reactions were reported following cangrelor administration. All-cause mortality occurred in 17 patients (18%) within 48 h. The causes of death included cardiogenic shock (10 patients), multi-organ failure (4 patients), and refractory cardiac arrest (3 patients). Among the 17 patients who died within 48 h, Killip class and shock index were available in 14 cases. Of these, 11 patients (79%) were classified as Killip class III or IV, and the median shock index was 1.17 (interquartile range [IQR]: 1.07–1.23), consistent with significant haemodynamic compromise at presentation. These severity markers are summarised in Supplementary Table S2.

Regarding secondary outcomes, the logistic regression model in Table 2 did not show any predictive factor of the primary composite outcome at 48 h after cangrelor administration.

Table 2. Logistic regression of predictors of composite outcomes at 48 h post-cangrelor administration.

Univariable Analysis *		
Variable	OR (95% CI)	p-Value
Mechanical ventilation	5.2 (1.5–24)	0.02
Age (for every 10-year increase)	0.98 (0.97–1)	0.16
Males (versus females)	0.79 (0.21–3.8)	0.74
LVEF < 40% (LVEF versus >40%)	4.6 (0.55–95)	0.16
Hypertension (yes versus no)	0.7 (0.3–1.6)	0.44
Diabetes mellitus (yes versus no)	1.3 (0.4–6.1)	0.75
Chronic kidney disease (yes versus no)	0.9 (0.35–2.2)	0.91
Hypercholesterolaemia (yes versus no)	0.76 (0.4–1.6)	0.44
Smoker (yes versus no)	0.45 (0.2–1)	0.11
Cardiac arrest presentation (versus STEMI presentation)	0.76 (0.2–2.4)	0.65

* Multivariable analysis was not conducted due to the lack of multiple statistically significant variables. OR: odds ratio. CI: confidence interval. LVEF: left ventricle ejection fraction. STEMI: ST-elevation myocardial infarction.

4. Discussion

Although the use of cangrelor and its outcomes have been studied in tertiary care settings [23], to our knowledge, this is the first study to investigate these factors in non-surgical centres. This study contributes to the literature by providing real-world insights into cangrelor use in a DGH setting, where resource availability and patient acuity differ from those in tertiary centres. Our findings align with existing studies demonstrating cangrelor's efficacy in high-risk PCI scenarios. The low bleeding rates in our cohort are consistent with CHAMPION Phoenix, while the higher all-cause mortality reflects the acuity of our population [24,25]. Our decision to use cangrelor in the primary PCI setting is primarily based on its safety in the CHAMPION studies and its pharmacological properties, which offer rapid onset, effective P2Y₁₂ inhibition, and the potential for rapid offset, if necessary, in acute situations [26,27]. Cangrelor is currently the only intravenous platelet P2Y₁₂ inhibitor for clinical use [20]. It provides prompt, potent, and reliable antiplatelet effects. Such pharmacological properties help overcome the limitations of oral P2Y₁₂ inhibitors, which are characterised by an inevitable delay in their onset of action, exacerbated in high-risk, short-term settings where gastrointestinal absorption is further compromised [28].

Our 48 h composite outcomes were greater than those of the CHAMPION PHOENIX trial (17.1% versus 3.8%) [26]. Our cohort comprised more STEMI cases and fewer angina/non-ST-elevation myocardial infarction (NSTEMI) cases than the CHAMPION PHOENIX trial (71% versus 17.6% and 8% versus 82.4%, respectively) [9]. This difference may account for the disparity in outcomes between the two studies. Major bleeding events were minimal in both our cohort and the CHAMPION PHOENIX trial (0% and 0.16%, respectively). Meta-analyses of the CHAMPION trials have demonstrated that cangrelor effectively reduces peri-procedural thrombotic events without significantly increasing the risk of major bleeding [17]. The low bleeding risk associated with cangrelor is attributed to its short half-life, rapid clearance from the body, and reversible action. These characteristics enable platelet function to recover swiftly after the drug is discontinued, thus minimising the potential duration of bleeding risk. This is particularly advantageous for high-risk bleeding patients undergoing PCI. The findings from the CHAMPION PHOENIX trial and related studies support this notion [26], having demonstrated minimal bleeding complications peri-procedurally, which ensures a generally safe profile for the drug at the 48 h mark. The higher mortality observed in our study likely reflects differences in population acuity, including more STEMI and cardiac arrest cases. Methodological differences, such as event ascertainment, further complicate comparisons.

Besides reducing the ischaemic complications of PCI in previous studies [26], cangrelor may also be beneficial in clinical situations where adenosine diphosphate (ADP) receptor blockade is required but a short-acting intravenous agent is preferred. An example would be patients awaiting open-heart surgery, where lower doses of cangrelor have consistently been shown to inhibit platelets without causing a significant increase in bleeding [29]. Our cohort's absence of major bleeding events (BARC type ≥ 3) supports cangrelor's favourable safety profile in the acute setting, consistent with the CHAMPION trials and other real-world studies. The high 48 h mortality rate (18%) is best understood in the context of significant baseline haemodynamic instability. Among those who died, the majority presented with Killip class III/IV, and the median shock index exceeded 1.1. These objective markers are consistent with severe cardiac dysfunction and support the interpretation that early mortality was largely driven by clinical acuity, rather than adverse events related to cangrelor use.

Cangrelor, therefore, represents an ideal agent overall for reducing the risk of thrombotic complications in patients undergoing PCI who have not been pre-treated with an oral P2Y₁₂ inhibitor and especially in contexts where the absorption of an oral agent is impeded or impaired (e.g., haemodynamically unstable or intubated patients unable to swallow or those who may not fully absorb an oral antiplatelet agent due to STEMI or cardiogenic shock) [20]. The introduction of cangrelor into clinical practice has expanded its applications and differed from how it was investigated in registration trials. Our observations, alongside those of previous studies, highlight the need for further prospective evaluations of cangrelor in various care settings, which will yield insights into its efficacy in real-world clinical practice. The limited sample size restricts our ability to draw definitive conclusions. Future multicentre studies are needed to validate the safety and effectiveness of cangrelor in broader populations. This study emphasises the utility of cangrelor in high-risk scenarios, particularly STEMI and cardiac arrest, where oral antiplatelets are impractical. However, individual assessments of bleeding and ischaemic risk should guide its adoption in similar settings. The strength of this study lies in reporting the outcomes of patients treated with cangrelor in real-world clinical practice. However, akin to previous reports, a notable limitation is the absence of a control group for outcome comparison. Without such a comparison, it is challenging to estimate the actual benefits and risks of cangrelor treatment in these critically ill patients, who are primarily acute coronary syndrome patients at high risk of both ischaemic and bleeding events. Balancing these risks to optimise patient outcomes remains a clinical challenge. This study is retrospective and limited to a single centre and is thus subject to the standard limitations of retrospective studies. Consequently, our findings are hypothesis-generating and necessitate confirmation in randomised controlled trials. Certain procedural details, such as stent type and pre-treatment regimens, were not consistently documented, which restricts our ability to evaluate their impact on outcomes. Moreover, our analysis did not encompass information on the types of wires, balloons, and stents utilised during PCI. Furthermore, data regarding medical treatments prior to PCI, which may have influenced the risk of composite outcomes, was unavailable. Additionally, information on peri-procedural myocardial infarction was also lacking. Nevertheless, mortality is more pertinent than this specific complication, and overall, mortality is a more significant outcome. The absence of a control group limits direct comparison with oral P2Y₁₂ inhibitors. However, cangrelor was predominantly administered in high-acuity, emergent cases in which oral antiplatelet therapy was contraindicated or infeasible. Consequently, patients receiving oral agents represent a distinct clinical population, precluding valid comparison. This real-world observational design aimed to describe outcomes in such high-risk patients, rather than to establish comparative efficacy. This study was observational and did not include a formal control group. Although com-

parisons with oral P2Y12-treated patients are clinically relevant, our high-acuity cangrelor population differed significantly in baseline characteristics (e.g., higher STEMI and Killip class III/IV prevalence). These differences would confound direct comparisons. Future studies should employ propensity score matching or multivariable adjustment to account for such differences.

5. Conclusions

Cangrelor offers potential as an alternative to oral P2Y12 inhibitors in specific high-risk scenarios in different care settings. Further research is needed to validate its role in broader populations.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/hearts6030016/s1>, Table S1: Bleeding definitions based on the Bleeding Academic Research Consortium (BARC) criteria and events observed in the cohort. Table S2: Objective baseline severity markers in 48 h mortality cases.

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Informed Consent Statement: This project was conducted as part of an audit approved by the hospital board and involved a prospective analysis of retrospectively collected anonymised data (reference: UHDBM259). Therefore, the hospital board waived the need for consent.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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Abbreviations

The following abbreviations are used in this manuscript:

ADP	Adenosine Diphosphate
BARC	Bleeding Academic Research Consortium
CI	Confidence Interval
DGH	District General Hospital
HAC	Heart Attack Centre
HBR	High Bleeding Risk
ICARUS	Identification of Coronary Artery disease Risk Using a Systematic score
IQR	Interquartile Range
IV	Intravenous
LVEF	Left Ventricular Ejection Fraction
MDPI	Multidisciplinary Digital Publishing Institute
NSTEMI	Non-ST-Elevation Myocardial Infarction
OR	Odds Ratio
PCI	Percutaneous Coronary Intervention

SD	Standard Deviation
STEMI	ST-Elevation Myocardial Infarction
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
SYNTAX	Synergy Between PCI With Taxus and Cardiac Surgery
TLA	Three-Letter Acronym
TTE	Transthoracic Echocardiogram
UK	United Kingdom
RDH	Royal Derby Hospital

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