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SHORT COMMUNICATION

Prognostic impact of angiographic findings, procedural success, and timing of percutaneous coronary intervention in cardiogenic shock

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Abstract

Aims Urgent revascularization is the mainstay of treatment in acute coronary syndrome (ACS) related cardiogenic shock (CS). The aim was to investigate the association of angiographic results with 90-day mortality. Procedural complications of percutaneous coronary intervention (PCI) were also examined.

Methods and results This CardShock (NCT01374867) substudy included 158 patients with ACS aetiology and data on coronary angiography and complications during PCI procedure. Survival analysis was conducted with Kaplan–Meier curves and Cox regression analysis. Median age was 67 ± 11 years, and 77% were men. During 90-day follow-up, 66 (42%) patients died. Patients with one-vessel disease (n = 49) had lower mortality than patients with two-vessel (n = 59) or three-vessel (n = 50) disease (25% vs. 48% vs. 52%, P = 0.011). Successful revascularization [Thrombolysis in Myocardial Infarction (TIMI) Flow 3 post-PCI) was achieved more often in survivors than non-survivors (81% vs. 60%, P = 0.019). The median symptom-to-balloon time was 340 (196–660) minutes, with no difference between survivors and non-survivors. In multivariable mortality analysis, multivessel disease (HR 2.59, $CI_{95\%}$ 1.29–5.18) and TIMI flow <3 post-PCI (HR 2.41, $CI_{95\%}$ 1.4–4.15) were associated with 90-day mortality. Procedural PCI complications were recorded in 51 (35%) patients, arrhythmic complications being the most common (n = 32, 63%). The incidence of complications was similar between survivors and non-survivors (31% vs. 42%, P = 0.21).

Conclusions Multivessel disease is associated with worse survival in ACS-related CS. In patients undergoing PCI, arrhythmic complications were common, but not associated with excess mortality. Successful revascularization of the IRA had positive effect on outcome despite delay from symptom onset.

Keywords Cardiogenic shock; Acute coronary syndrome; Percutaneous coronary intervention

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Background

Urgent coronary angiography and revascularization are the mainstay of treatment in acute coronary syndrome (ACS) related cardiogenic shock (CS).[1] In previous studies, multivessel[2–4] and three-vessel coronary artery disease (CAD),[5–8] unsuccessful revascularization,[3–5,7–11] and left main (LM) CAD[3,5,7] have been associated with poor outcomes in ACS-related CS. However, many of these studies predate the primary percutaneous coronary intervention

(PCI) era,[5–7] were of retrospective nature[10,12] or examined registry data.[3,8,11] Furthermore, data on procedural PCI complications in ACS-related CS are scarce.

Aims

The aim of this study was to explore coronary angiographic findings in a prospective multicentre cohort of ACS-related CS. The primary objective was to investigate the association of angiographic results and 90-day mortality. In addition, procedural PCI complications were examined.

Methods

The CardShock study (NCT01374867) is a prospective multinational study on CS conducted in nine centres in eight European countries between October 2010 and December 2012. The description of the study cohort has been reported previously.[13] Briefly, consecutive patients aged over 18 years were enrolled within 6 h from detection of CS. The criteria for shock were systolic blood pressure $<$90 mmHg for 30 min despite adequate fluid therapy or need for vasoactive therapy, and $\geq$1 signs of inadequate organ perfusion: confusion or altered mental status, cool extremities, oliguria $<$0.5 mL/kg/h for the previous 6 h, or blood lactate $>$2 mmol/L.

Patients' characteristics, medical history, clinical signs, and laboratory measurements were registered. Echocardiogram was performed at study baseline. Patients were treated according to local practise. Information on angiographic findings and revascularisation procedures were collected.

This sub-study included patients with ACS aetiology and data on coronary angiography. The primary endpoint was all-cause mortality at 90 days. The vital status was confirmed by the patient or next of kin, or through hospital or population registers. The study was approved by local ethics committees and conducted in accordance with the Declaration of Helsinki.

Data are presented as means and standard deviations (SDs), medians and interquartile ranges (IQRs), or as counts and percentages. Comparisons between groups were analysed by Student's *t*-test or Mann–Whitney U-test for continuous variables and χ^2 test or Fisher's exact test for categorical variables, as appropriate.

Survival was analysed using Kaplan–Meier curves and log-rank tests. The association with 90-day mortality was assessed by univariate Cox regression for the following variables selected a priori: age, gender, comorbidities [prior myocardial infarction or coronary artery bypass grafting (CABG), diabetes, hypertension, and smoking], estimated glomerular filtration rate (eGFR), levels of lactate, high sensitivity troponin T (hs-TnT) and N-terminal pro brain natriuretic peptide (NT-proBNP) at baseline, left ventricular ejection fraction (LVEF), multivessel CAD (significant stenosis in more than one main coronary vessel or major side branch), stenosis of LM, infarct related artery (IRA), thrombolysis prior to angiography, intra-aortic balloon pump (IABP), CABG during hospital stay, PCI, symptom-to-balloon time, number of stents, drug-eluting stent, metal stent, amount of contrast agent, pre-procedural Thrombolysis in Myocardial Infarction (TIMI) grade 0/1 flow, TIMI flow $<$3 post-PCI, and PCI complications. The variables with *P* value $<$0.10 in univariate analysis were included in the multivariable analysis. The final model was built with backward stepwise method with Cox regression analysis. A two-tailed *P* value of $<$0.05 was considered statistically significant. The statistical analyses were performed using R statistical software version 3.4.3 (The "R" Foundation for Statistical Computing, Vienna, Austria).

Results

In total, 177 CardShock patients had ACS aetiology. Of these patients, 10 did not undergo angiographic evaluation, six patients did not have data on angiographic findings, and three were lost to follow-up. Finally, 158 patients were included in this study. Median age was 67 ± 11 years, and 121 (77%) were male. During the 90-day follow-up, 66 (42%) patients died. Baseline characteristics are described in Table *1*. Survivors were younger (66 ± 12 vs. 70 ± 9 years, *P* = 0.029), had fewer comorbidities, and had higher LVEF (38% ± 14 vs. 29% ± 12, *P* $<$ 0.001) than non-survivors (Table *1*).

Patients with one-vessel CAD (*n* = 49, 31%) had lower 90-day mortality than patients with two- (*n* = 59, 37%) or three- (*n* = 50, 32%) vessel CAD (25% vs. 48% vs. 52%, respectively; *P* = 0.011, Figure *1*A). Mortality was numerically higher in patients with LM or left anterior descending (LAD) as the culprit artery when compared to right coronary artery (RCA) or LCX, but the difference was not statistically significant. Successful revascularization (TIMI Flow 3 post-PCI) was achieved more often in survivors than in non-survivors (81% vs. 60%, *P* = 0.019, Table *1*, Figure *1*C), whereas there were no differences in the rate of successful revascularization between different IRAs: 72% in LM, 70% in LAD, 59% in LCX, 77% in RCA, and 80% in saphenous vein graft (SVG) (*P* = 0.67). The median symptom-to-balloon time was 340 (196-660) minutes, with no difference between groups (Table *1*). One-third of the patients (*n* = 49, 36%) developed shock only after the PCI procedure, but there was no difference in the rate of successful revascularization, if shock developed before or after the procedure (32% vs. 24%, *P* = 0.41).

In multivariable analysis, multivessel CAD (HR 2.59, $CI_{95\%}$ 1.29–5.18, *P* = 0.007), TIMI flow $<$3 post-PCI (HR 2.41, $CI_{95\%}$ 1.4–4.15, *P* = 0.001), increasing lactate (HR 1.17, $CI_{95\%}$ 1.11–

Table 1 Baseline and angiographic characteristics

	All patients (n = 158)	Survivors (n = 92)	Non-survivors (n = 66)	P
Age	67 ± 11	66 ± 12	70 ± 9	0.029
Male gender	121 (77)	75 (82)	46 (70)	0.12
ACS type: STEMI	139 (88)	80 (87)	59 (89)	0.83
Medical history				
Known coronary artery disease	49 (31)	21 (23)	28 (42)	0.014
Prior myocardial infarction	36 (23)	14 (15)	22 (33)	0.013
Prior PCI	22 (14)	10 (11)	12 (18)	0.28
CABG	9 (6)	1 (1)	8 (12)	0.009
Chronic heart failure	10 (6)	2 (2)	8 (12)	0.03
Clinical characteristics				
CardShock risk score	4 ± 2	4 ± 2	5 ± 1	<0.001
Systolic blood pressure	78 ± 14	80 ± 15	75 ± 12	0.025
LVEF	34 ± 14	38 ± 14	29 ± 12	<0.001
Laboratory tests				
Lactate (mmol/L)	3 [2-5]	2 [1-4]	4 [3-8]	<0.001
eGFR (mL/min/1.73 m^2)	63 [44-87]	71 [51-96]	49 [33-70]	<0.001
hs-TnT (ng/L)	3205 [1167-8907]	2614 909-6940]	4010 [1628-10993]	0.08
NT-proBNP (ng/L)	1751 [374-8602]	1077 [252-5029]	3769 [648-12249]	0.01
Characteristics of CAD				
Number of diseased vessels				0.011
One-vessel disease	49 (31)	37 (40)	12 (18)	
Two-vessel disease	59 (37)	31 (34)	28 (42)	
Three-vessel disease	50 (32)	24 (26)	26 (39)	
IRA				0.005
LAD	63 (40)	33 (36)	30 (47)	
LCX	21 (14)	16 (17)	5 (8)	
LM	19 (12)	9 (10)	10 (16)	
RCA	48 (31)	34 (37)	14 (22)	
SVG	5 (3)	0 (0)	5 (8)	
Treatment				
PCI	144 (91)	82 (89)	62 (94)	0.44
Thrombolysis	17 (11)	13 (14)	4 (6)	0.18
IABP	103 (65)	55 (60)	48 (73)	0.13
CABG	8 (5)	7 (8)	1 (2)	0.18

Procedural characteristics	n = 144	n = 82	n = 62	
Symptom-to-balloon time (min)	340 [196–660]	335 [210–641]	340 [190–660]	0.70
Bare metal stent	66 (46)	39 (48)	27 (44)	0.76
Multivessel PCI	38 (26)	21 (26)	17 (27)	0.96
PCI of LM	21 (15)	8 (10)	13 (21)	0.11
Total occlusion (pre-procedural TIMI 0/1)	119 (84)	65 (80)	54 (89)	0.27
Post-procedural TIMI				0.027
0/1	15 (11)	6 (7)	9 (15)	
2	25 (18)	10 (12)	15 (25)	
3	102 (72)	66 (81)	36 (60)	
Amount of contrast agent (mL)	160 [120-220]	170 [120-210]	160 [124-250]	0.66
Shock after PCI	49 (36)	33 (41)	16 (28)	0.16
Complications				
Any PCI complication	51 (35)	25 (31)	26 (42)	0.21
Ventricular tachycardia or fibrillation	27 (19)	11 (13)	16 (26)	0.10
Bradycardia	21 (15)	7 (9)	14 (23)	0.034
Dissection	8 (6)	5 (6)	3 (5)	1.00
Tamponade	1 (1)	1 (1)	0 (0)	1.00
Re-occlusion	4 (3)	1 (1)	3 (5)	0.43
Re-coronary angiography	12 (9)	10 (13)	2 (3)	0.10
Re-PCI	10 (7)	8 (10)	2 (3)	0.22

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease, CRP, C reactive protein; eGFR, estimated glomerular filtration rate; hs-TnT, high-sensitive troponin T; IABP, intra-aortic balloon pump; IRA, infarct related artery; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LM, left main coronary artery; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; NT-proBNP, N-terminal pro brain natriuretic peptide; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; SVG, saphenous vein graft; TIMI, Thrombolysis in Myocardial Infarction.
Data are presented as means ± standard deviation, medians (interquartile range) or counts (%).

1.23, $P < 0.001$), and decreasing LVEF (HR 1.03, $CI_{95\%}$ 1.01–1.06, P = 0.002) were independently associated with 90-day mortality.

Any procedural complication was recorded in 35% of the patients who underwent PCI with no difference between survivors and non-survivors (31% vs. 42%, P = 0.21, Table *1*).

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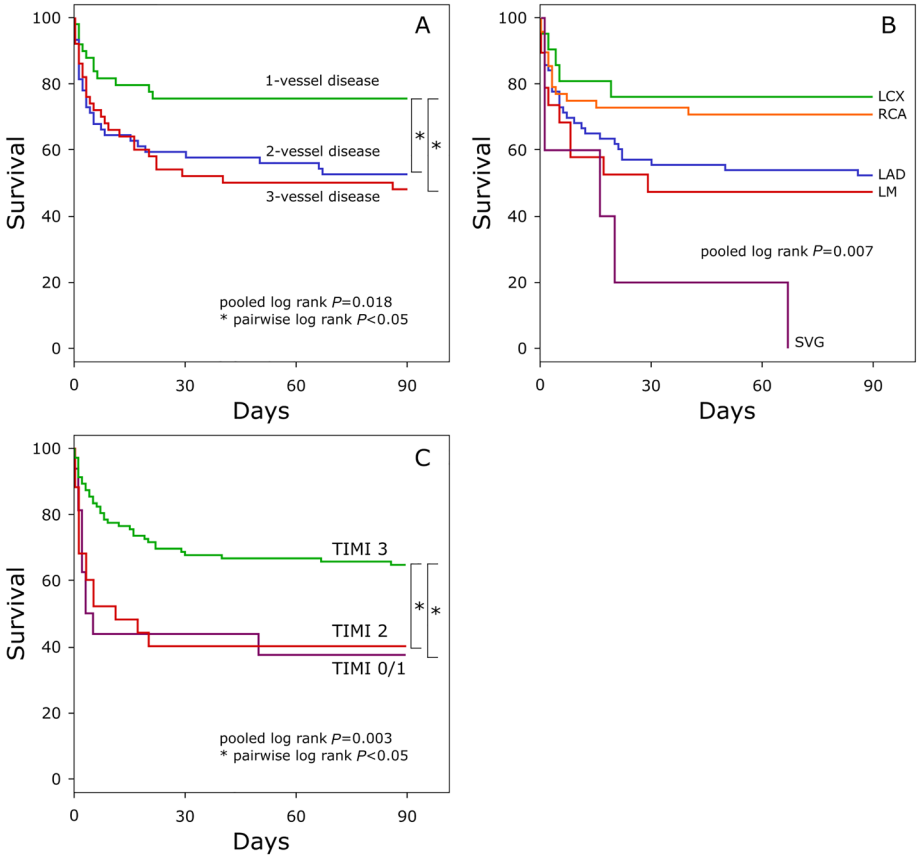
Figure 1 Kaplan–Meier 90-day survival curves in different patient groups divided by (A) severity of coronary artery disease, (B) the infarct related artery, and (C) the Thrombolysis in Myocardial Infarction flow post-percutaneous coronary intervention. (A) Patients with one-vessel disease had lower 90-day mortality rates than patients with two-vessel or three-vessel disease. (B) Patients with left anterior descending coronary artery or left main coronary artery as the infarct related artery had high mortality rates. (C) Patients with successful revascularization, i.e. TIMI Flow 3, had lower mortality rates than patients with TIMI Flows 0–2.



Arrhythmia was the most common complication: 19% had ventricular tachycardia or fibrillation, and bradycardia was recorded in 15% of patients. Bradycardia was more frequent in non-survivors than survivors (23% vs. 9%, P = 0.034), but in adjusted mortality analysis, bradycardia was not associated with the risk of 90-day death (HR 1.09, $CI_{95\%}$ 0.51–2.35, P = 0.82).

Conclusion

In this study, multivessel CAD and TIMI flow <3 post-PCI were associated with poor prognosis in ACS-related CS. Among patients undergoing PCI, arrhythmic complications were common but not associated with excess mortality.

Multivessel CAD was associated with worse survival in ACS-related CS, as previously shown.[2,3,5–8] No difference in mortality between different IRAs was discovered, similar to one previous study,[4] even though mortality rates were numerically higher in LM and LAD in comparison to RCA and LCX. In other studies, LM as the culprit artery has been associated with worse survival,[3,5,7,11] whereas RCA as the culprit artery has been associated with better prognosis.[6,12] The proportion of patients with successful revascularization was similar irrespective of the culprit artery, which suggests that high mortality rates of LM and LAD were not related to procedural failure. Indeed, the culprit vessel may only play minor role in survival in CS, especially when revascularization is successful, as mortality may be more strongly associated with haemodynamic instability and multi-organ damage.

Our study confirms that successful revascularization of the IRA is associated with good prognosis.[3,5,7–11] In our study, the median symptom-to-balloon time was suboptimal with a median delay of 6 h. Nevertheless, there was no difference in PCI timing between survivors and non-survivors. As we examined symptom-to-balloon time and not contact-to-balloon time, our results are not directly comparable to the FITT-ST-segment elevation myocardial infarction (STEMI) trial,[14] yet our results show that in CS, even delayed successful

revascularization is associated with improved prognosis. However, some factors should be taken in consideration. We did not record specific reasons for the delay in symptom-to-balloon time, such as patient-related delays to first medical contact, or transfer times. In addition, not all patients were in shock on arrival to the hospital but developed shock only after the revascularisation procedure. In patients with ACS, delayed revascularisation may predispose to later development of shock,[15] but the timing of PCI was similar between survivors and non-survivors, and there was no difference in the rate of successful revascularisation if shock developed before or after PCI. Despite prolonged symptom-to-balloon time, TIMI Flow 3 post-PCI was still associated with better outcome, indicating that successful revascularization may be a more important driver for improved prognosis than timing of the procedure.

We found no difference in survival with culprit-vessel only or multivessel PCI, in contrary to the CULPRIT-SHOCK trial.[16] The evident difference between our study and the CULPRIT-SHOCK trial is that our study was of prospective nature, which enabled the treating physician to select the most suitable patients to the multivessel PCI. In addition, some of the patients included in this study did not have CS during the PCI procedure.

The rate of procedural PCI complications was higher than reported in STEMI,[17] and slightly higher than in a registry study of ACS-related CS[11]. However, the rate of ventricular arrhythmias was similar to previously reported STEMI-related CS[10]. In this critically ill population, arrhythmic events were most likely related to the severity of the disease and not to the revascularisation procedure itself. Indeed, procedural complications did not associate with mortality, suggesting that they are transient and treatable. During PCI in CS, immediate actions, such as defibrillation and cardiac pacing, should be readily available for management of arrhythmic complications.

There are limitations to be acknowledged. Though this study is considerable for a prospective study of CS, the number of patients in some groups was low. In addition, the examination of angiograms was not centralized, but the patients were treated, and the results were reported, by experienced interventional cardiologists.

In conclusion, multivessel disease is associated with worse survival in ACS-related CS. In patients undergoing PCI, arrhythmic complications were common, but not associated with excess mortality. Successful revascularization of the IRA had a positive effect on outcome despite delay from symptom onset. Thus, in CS, even late PCI seems to be feasible.

Conflict of interest

None declared.

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