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Post-resuscitation myocardial dysfunction in out-of-hospital cardiac arrest patients randomized to immediate coronary angiography versus standard of care

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ABSTRACT

Background: Immediate coronary angiography with subsequent percutaneous coronary intervention (PCI) has the potential to reduce post-resuscitation myocardial dysfunction in out-of-hospital cardiac arrest (OHCA) patients. The aim of this study was to see if immediate coronary angiography, with potential PCI, in patients without ST-elevation on the ECG, influenced post-resuscitation myocardial function and cardiac biomarkers.

Methods: A secondary analysis of the Direct or Subacute Coronary Angiography in Out-of-Hospital Cardiac Arrest (DISCO) trial (ClinicalTrials.gov ID: NCT02309151). Patients with bystander-witnessed OHCA, without ST-elevations on the ECG were randomly assigned to immediate coronary angiography within two hours of cardiac arrest (n = 38) versus standard-of-care with deferred angiography (n = 40). Outcome measures included left ventricle ejection fraction (LVEF) at 24 h, peak Troponin T levels, lactate clearance and NT-proBNP at 72 h.

Results: In the immediate-angiography group, median LVEF at 24 h was 47% (Q1-Q3; 30–55) vs. 46% (Q1-Q3; 35–55) in the standard-of-care group. Peak Troponin-T levels during the first 24 h were 362 ng/L (Q1-Q3; 174–2020) in the immediate angiography group and 377 ng/L (Q1-Q3; 205–1078) in the standard-of-care group. NT-proBNP levels at 72 h were 931 ng/L (Q1-Q3; 396–2845) in the immediate-angiography group and 1913 ng/L (Q1-Q3; 489–3140) in the standard-of-care group.

Conclusion: In this analysis of OHCA patients without ST-elevation on the ECG randomized to immediate coronary angiography or standard-of-care, no differences in post-resuscitation myocardial dysfunction parameters between the two groups were found. This finding was consistent also in patients randomized to immediate coronary angiography where PCI was performed compared to those where PCI was not performed.

1. Introduction

Post-resuscitation myocardial dysfunction (PRMD) occurs in a substantial proportion of patients after successful return of spontaneous circulation (ROSC) [1,2] in cases of out-of-hospital cardiac arrest (OHCA). PRMD has been defined as impairment of left-ventricle systolic function, high serum concentrations of cardiac biomarkers and a need of vasoactive drugs. The PRMD is often transient and reversible [3,4]. If PRMD is persistent after 72 h, it is associated with worse prognosis [5]. The severity and the reversibility of PRMD is affected by the underlying cause of the cardiac arrest, for example coronary occlusion with subsequent myocardial injury. PRMD with myocardial stunning can occur without evidence of coronary occlusion and might be the result of global ischemia occurring during resuscitation [6]. Thus, measurements of myocardial function and of cardiac biomarkers during the post-resuscitation period may provide important diagnostic and prognostic information [7].

Immediate coronary angiography with subsequent percutaneous coronary intervention (PCI) has the potential to reduce the myocardial infarction area, improve left-ventricle ejection fraction

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(LVEF) and hemodynamic performance in the initial phase of the post-resuscitation period.

We have recently published results concerning the initial phase of the Direct or Subacute Coronary Angiography in Out-of-Hospital Cardiac Arrest (DISCO) trial (ClinicalTrials.gov ID: NCT02309151), where 78 patients with bystander-witnessed OHCA, and without ST-elevations on the ECG were randomly assigned to immediate coronary angiography versus standard of care [8].

The aim of this secondary analysis was to study if immediate coronary angiography with potential PCI influences markers of PRMD such as left-ventricular ejection fraction, biomarkers and lactate clearance in OHCA patients compared with those admitted to an intensive care unit (ICU) without receiving immediate coronary angiography.

2. Methods

This is a predefined secondary analysis of the initial phase of the DISCO study, of which the trial design [9] and results [8] have been published previously. The initial phase of the DISCO study was a multicenter, randomized clinical trial investigating feasibility and safety aspects in OHCA patients without ST-elevation when randomized to either immediate coronary angiography within two hours of the cardiac arrest or standard of care in the ICU with a potential coronary angiography performed at a later stage (i.e. after three days).

LVEF was measured 24 h after hospital arrival. Other measurements were Troponin levels at hospital admission and peak Troponin levels, NT-proBNP levels at ICU admission and 72 h after the cardiac arrest, and lactate clearance at six hours and 24 h after hospital arrival.

In a subgroup of patients randomized to immediate angiography, we compared outcome measures between those that underwent PCI versus no PCI.

An additional 39 patients were followed in the observational ST-elevation non-randomized group (see supplementary Tables). This observational group was also compared as regards outcome measures between those that underwent PCI versus no PCI.

The DISCO study was approved by the regional ethics committee in Stockholm, Sweden (Identification Number 2014/1139-31/2) and is registered at ClinicalTrials.gov (NCT02309151).

2.1. Patients

Witnessed-OHCA patients over 18 years of age with ROSC admitted alive to hospital were screened by means of 12-lead ECG as early as possible. Patients without ST-segment elevation or presumed new left-bundle branch block were eligible for randomization. Exclusion criteria included obvious non-cardiac causes, terminally ill patients with a life expectancy less than one year, expected time to coronary angiography more than 120 min, known pregnancy and patients not unconscious (Glasgow coma scale > 8).

2.2. Data collection

Data collection was performed according to a prespecified clinical report form (CRF). Coronary angiography and PCI data were collected from the Swedish Coronary Angiography and Angioplasty Register (SCAAR). Fluid administration, vasopressor and inotrope support was given at the discretion of the treating physician at each hospital, guided by standard procedures for hemodynamic support. No prespecified targets of blood pressure or heart rate were given as a result of the pragmatic design of the study. The need of vasopressors and inotropes was recorded for the first seven days unless the patient died before that.

3. Outcome measurements

3.1. LVEF at 24 h

Transthoracic echocardiography was performed by an echocardiographic-certified cardiologist in the intensive care unit to evaluate cardiac function at 24 h after the cardiac arrest. The echocardiographic examination was performed as close as possible to 24 h after the cardiac arrest and if this time-point occurred during the night it was permitted to perform the examination in the morning. Regional wall motion abnormalities of the left ventricle were analyzed, and the ejection fraction was calculated using the modified Simpson's method.

3.2. Peak level of high-sensitivity cardiac troponin T (hs-cTnT)

Hs-cTn is a biomarker of myocardial injury mainly used for diagnosing myocardial infarction. Concetrations of hs-cTn were measured in the first blood sample in the emergency room immediately after ROSC and further at 6 h, 12 h and 24 h. The Elecsys hs-cTnT assays (Roche Diagnostics, Basel, Switzerland) were used for evaluation.

3.3. N-terminal pro-B-type natriuretic peptide (NT-proBNP) at ICU admission and at 72 h

NT-proBNP is expressed in the heart and brain and is used as a biomarker when evaluating and diagnosing heart failure. NT-proBNP was collected at admission to the ICU and at 72 h if the patient was still alive. The Elecsys NT-pro BNP assays (Roche Diagnostics, Basel, Switzerland) were used for evaluation.

3.4. Lactate clearance at 6 h and 24 h

Arterial lactate levels were measured in the emergency room and every four hours in the ICU. Lactate clearance was calculated as lactate 6-hour lactate clearance (%), i.e. 100 × (initial lactate – 6-hour lactate) / initial lactate. Lactate clearance was also examined at 24 h. Lactate blood-gas analyzers were not standardized across the participating hospitals.

3.5. Statistics

Categorical variables are presented as numbers and percentages. Continuous variables are presented as medians and interquartile ranges (IQRs). Differences between the randomized groups were analyzed using the Chi-square test for categorical variables and the Mann-Whitney U test for continuous variables. All statistical analyses were performed using STATA software (StataCorp).

4. Results

A total of 78 patients were randomized from January 1, 2015 to October 15, 2017 of which 38 to the immediate-angiography group and 40 in the standard-of-care group (Fig. 1). No major differences in baseline characteristics between the groups were found. Previous myocardial infarction, previous PCI and diabetes were numerically more frequent in the standard-of-care group. Known heart failure, previous stroke, and previous cancer were numerically somewhat more frequent in the immediate-angiography group (see Table 1). The median time from randomization to coronary

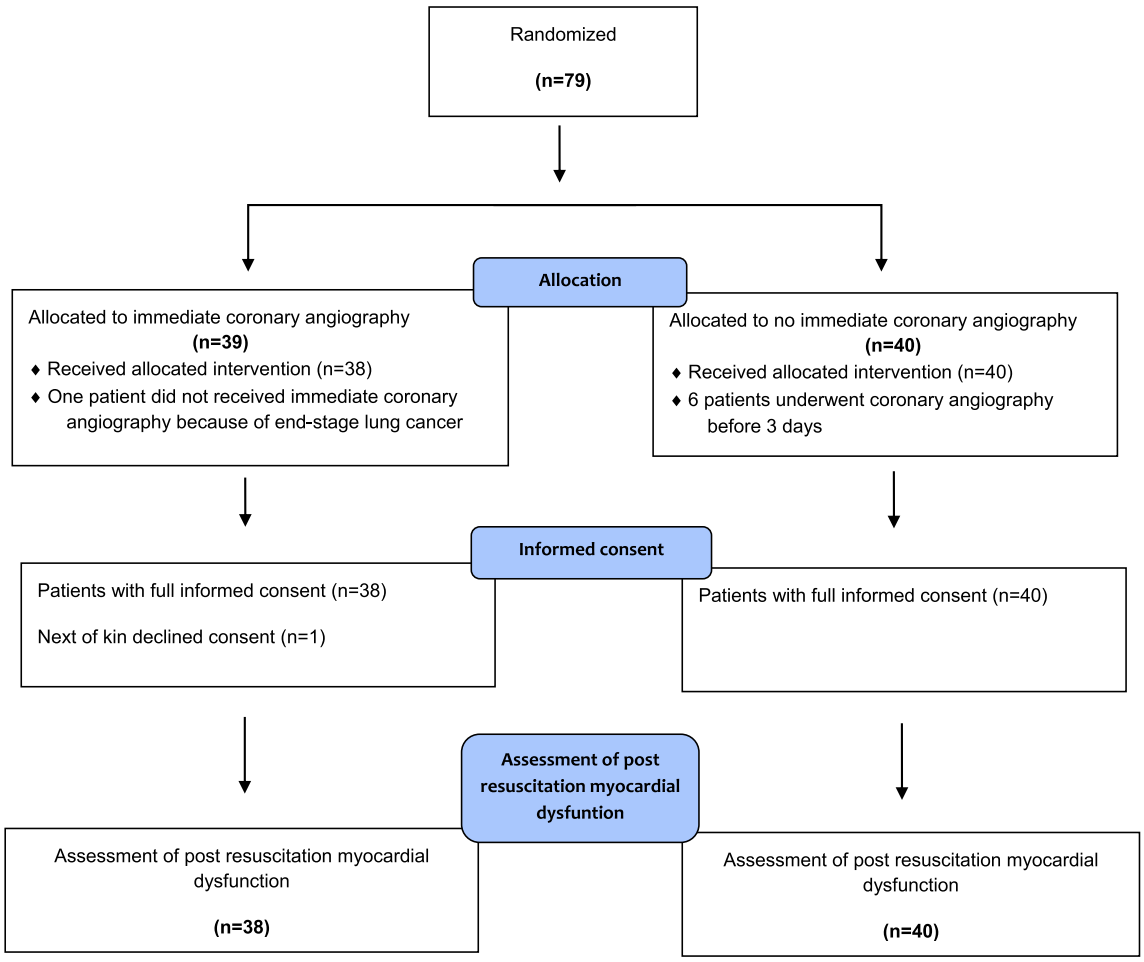

Fig. 1.

angiography was 69 min (IQR; 42–94 min) in the immediate angiography group. Two patients with ECG results classified as normal ECG were included and randomized to immediate coronary angiography but after a second interpretation of the ECG the patients were found to have ST-elevation. There was no difference between the groups regarding the need for vasopressors and inotropes (see Supplementary appendix Table 2).

Baseline data for the observational, non-randomized, ST-elevation patients are also presented in the Supplementary Appendix, Table 1.

4.1. Left Ventricular ejection fraction

There was no significant difference between the groups in LVEF observed 24 h after the cardiac arrest, with a mean LVEF of 47% (Q1-Q3; 30–55%) in the immediate-angiography group compared with 46% (Q1-Q3; 35–55) in the standard-of-care group (Table 2).

Within the subgroup of patients randomized to immediate angiography (n = 38) when comparing those that underwent PCI (n = 15) vs. no PCI (n = 23), the median LVEF at 24 h was 50% in the revascularized patients vs. LVEF 45% in those with immediate angiography where PCI was not performed (Table 3).

4.2. High-sensitivity cardiac Troponin

In the immediate-angiography group, the median peak hs-cTnT level was 362 ng/L (Q1-Q3; 174–2020), compared with 377 ng/L (Q1-Q3; 205–1078) in the standard-of-care group. There was no difference in the hospital-admission hs-cTnT levels when comparing the two groups (Table 2).

In the subgroup of patients randomized to immediate angiography (n = 38), when comparing those that underwent PCI (n = 15) vs. those that did not (n = 23), the median hospital-admission Hs-cTn level was 102 ng/L (Q1-Q3; 29–789) in patients that underwent PCI vs. 49 ng/L (Q1-Q3; 23–127) in patients that did not. Peak levels were 1395 ng/L vs. 227 ng/L (Table 3).

4.3. NT-proBNP

Median NT-proBNP levels at ICU admission were 931 ng/L (Q1-Q3; 396–2845) in the immediate- angiography group and 1431 ng/L (Q1-Q3; 160–2390) in the standard-of-care group. After 72 h, the NT-proBNP levels were 931 ng/L (Q1-Q3; 396–2845) in the immediate-angiography group vs. 1913 ng/L (Q1-Q3; 489–3140) in the standard-of-care group (Table 2).

In the subgroup of patients randomized to immediate angiography, when comparing those that underwent PCI vs. no PCI, NT-proBNP levels were 1260 ng/L (Q1-Q3; 773–3200) at 72 h (PCI) vs 939 ng/L (Q1-Q3; 400–4030) in the group without PCI (Table 3).

4.4. Lactate clearance

In the immediate-angiography group, lactate clearance at six hours was 70.7% (Q1-Q3; 56.0–79.5) compared with 75.2% (Q1-

Table 1
Baseline characteristics.

Group of characteristics	Characteristics	No ST elevation	
		Immediate CAG n = 38	Standard care n = 40
	Age years median (Q1-Q3)	71 (62–78)	70 (61–77)
	Male	22 (57.9%)	31 (77.5%)
Pre-hospital characteristics	*Location of arrest-Home*	22 (57.9%)	25 (62.5%)
	Bystander CPR	28 (73.7%)	30 (75.0%)
	Initial rhythm VT/VF	20 (52.6%)	22 (55.0%)
	Initial rhythm asystole	8 (21.1%)	4 (10.0%)
	Initial rhythm PEA	7 (18.4%)	13 (32.5%)
	Initial rhythm unknown	3 (7.9%)	1 (2.5%)
Medical history	*Ischemic heart disease*	9 (23.7%)	10 (25.0%)
	Previous myocardial infarction	6 (15.8%)	8 (20.0%)
	Previous PCI	4 (10.5%)	7 (17.5%)
	Previous CABG	3 (7.9%)	3 (7.5%)
	Heart failure	7 (18.4%)	6 (15.0%)
	COPD	7 (18.4%)	7 (17.5%)
	Previous Stroke	6 (15.8%)	4 (10.0%)
	Cancer	7 (18.4%)	6 (15.0%)
	Diabetes	6 (15.8%)	10 (25.0%)
Measurements at emergency room	*Pulse rate, bpm, median, (Q1-Q3)*	95 (80–117)	90 (73–111)
	Systolic blood pressure (mmHg) median (Q1-Q3)	130 (107–149)	125 (109–161)
	Glasgow Coma Scale, median (Q1-Q3)	3 (3–4)	3 (3–3)
	Troponin-T (ng/L) at admission to hospital, median (Q1-Q3)	51 (25–149)	54 (23–92)
First arterial blood gas	*pH (Q1-Q3)*	7.2 (7.1–7.3)	7.2 (7.1–7.3)
	PaO2 (kPa), median, (Q1-Q3)	16.2 (11.1–39.8)	18.5 (12.1–35.4)
	PaCO2 (kPa) median (Q1-Q3)	5.7 (4.7–8.5)	5.9 (5.1–8.0)
	Lactate (mmol/l) at admission, median (Q1-Q3)	7.9 (5.7–9.9)	7.5 (5.7–9.7)
Presenting ECG	*ST-elevation*	2 (5.2%)	0 (0%)
	ST-depression	5 (13.2%)	6 (15.0%)
	Right bundle branch block	10 (26.3%)	7 (17.5%)
	Known Left bundle branch block	5 (13.2%)	4 (10.0%)
	New Left bundle branch block	0 (0%)	1 (2.5%)
	Q-wave	1 (2.6%)	1 (2.5%)
	T-wave inversion	1 (2.6%)	2 (5.0%)
	Other, incl normal	13 (34.2%)	16 (40.0%)
ECG rhythm	*Sinus rhythm*	26 (68.4%)	25 (62.5%)
	Atrial fibrillation	9 (23.7%)	11 (27.5%)
	Ventricular tachycardia	1 (2.6%)	0 (0%)
	Other, incl AV-block	2 (5.2%)	3 (7.5%)

Categorical variables are presented as numbers (%). Continuous variables are presented as medians (Q1-Q3). Abbreviations: CPR: Cardio pulmonary resuscitation, VT: Ventricular Tachycardia, VF: Ventricular fibrillation, PEA: Pulseless electric activity, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass grafting, COPD: Chronic obstructive pulmonary disease.

Table 2
Outcome measures.

Outcome measures	No ST elevation		P-value
	Immediate CAG n = 38	Standard care n = 40	
Ejection Fraction (%) median (Q1-Q3) at 24 h	47 (30–55) [n = 28]	46 (35–55) [n = 30]	0.74
Troponin-T (ng/L) peak value, median (Q1-Q3)	362 (174–2020) [n = 31]	377 (205–1078) [n = 31]	0.77
NT-proBNP (ng/L) at ICU admission, median (Q1-Q3)	749 (356–2945) [n = 28]	1431 (160–2390) [n = 26]	0.75
NT-proBNP (ng/L) at 72 h, median (Q1-Q3)	931 (396–2845) [n = 20]	1913 (489–3140) [n = 17]	0.64
Lactate clearance at 6 hours[1]*, (%)*	70.7 (56.0–79.5) [n = 30]	75.2 (68.1–85.0) [n = 34]	0.08
Lactate clearance at 24 h[1]*, (%)*	81.5 (75.0–88.0) [n = 26]	79.5 (66.0–85.4) [n = 32]	0.31

[1] Lactate clearance at xh was calculated as (Lactate at admission – Lactate at xh)/Lactate at admission * 100. Continuous variables are presented as medians (Q1-Q3). Mann-Whitney *U* test for continuous variables.

Q3; 68.1–85.0) in the standard-of-care group (p = 0.08). The lactate-clearance difference between the groups was less at 24 h, the figures being 81.5% (immediate-angiography group) and 79.5% (standard-of-care group) (Table 2).

5. Discussion

In patients with ROSC after OHCA randomized to immediate coronary angiography with the possibility for PCI after OHCA we found no significant differences in LVEF at 24 h after the arrest or levels of cardiac biomarkers or lactate clearance within three days compared with patients randomized to standard-of-care with deferred angiography. This study sheds light on the very early phase after ROSC and not the effect of PCI on LV function during the whole hospitalization period and beyond.

5.1. Left ventricular ejection fraction

Coronary angiography and PCI have the potential to increase myocardial contractility in the post resuscitation-phase. When measuring LVEF at 24 h we detected no difference between the groups. Using PCI as a surrogate marker of a culprit lesion or a

Table 3
Impact of PCI in patients undergoing immediate angiography divided in four subgroups.

	No ST-elevation ST-elevation					
Outcome measures	Immediate coronary angiography – PCI n = 15	Immediate coronary angiography – no PCI n = 23	P-value	Observation – PCI n = 26	Observation – no PCI n = 13	P-value
Ejection Fraction (%) at 24 h, median, (Q1-Q3)	50 (30–55) [n = 11]	45 (40–55) [n = 17]	0.80	45 (33–55) [n = 20]	40 (34–50) [n = 10]	0.72
Troponin T (ng/L) at hospital admission, median (Q1-Q3)	102 (29–789) [n = 14]	49 (23–127) [n = 17]	0.14	173 (53–903) [n = 22]	93 (31–264) [n = 12]	0.14
Troponin T (ng/L) peak value, median (Q1-Q3)	1395 (408–2500) [n = 14]	227 (145–379) [n = 17]	0.04	3100 (903–8650) [n = 22]	854 (463–1820) [n = 12]	0.03
NTproBNP (ng/L) at ICU admission, median (Q1-Q3)	870 (250–3160) [n = 11]	1274 (373–2945) [n = 17]	0.67	380 (111–1490) [n = 20]	1355 (67–3110) [n = 10]	0.83
NTproBNP (ng/L) at 72 h, median (Q1-Q3)	1260 (773–3200) [n = 7]	939 (400–4030) [n = 13]	1.0	1260 (934–1953) [n = 18]	975 (422–1821) [n = 8]	0.33
Lactate clearance at 6h[b] median, (Q1-Q3)	64.3 (37.8–78.5) [n = 10]	71.1 (60.6–76.3) [n = 20]	0.33	71.3 (54.2–79.6) [n = 24]	83.9 (76.1–87.9) [n = 11]	0.01
Lactate clearance at 24h[b] Median, (Q1-Q3)	80.5 (70.4–88.8) [n = 11]	83.6 (79.3–86.7) [n = 15]	0.50	75.7 (66.7–86.8) [n = 24]	85.1 (79.8–88.7) [n = 11]	0.07

Lactate clearance at xh was calculated as (Lactate at admission – Lactate at xh)/Lactate at admission * 100. Continuous variables are presented as medians (Q1-Q3). Mann-Whitney *U* test for continuous variables.

recently occluded coronary vessel, we compared patients randomized to immediate coronary angiography where PCI was performed with patients in this group that did not undergo PCI and noted that the LVEF was numerically slightly higher in those patients where PCI was performed. This finding needs to be explored in a larger population. The median post-resuscitation LVEF in our study was 46% which was is similar to a report by Jentzer et al. [10] but slightly higher than that reported by Bro-Jeppesen et al. (median LVEF of 40% at day one after the arrest) [11]. This could be explained by the high proportion of ST-elevation-patients in their study.

5.2. Cardiac biomarkers

In the absence of ST-elevation on the presenting ECG after ROSC, hs-cTn has the potential, as a diagnostic tool, to detect a recent coronary event [12,13]. However, elevated Troponin levels are observed in most resuscitated OHCA patients admitted alive to hospital [7], either as a consequence of a coronary event or a result of the cardiac arrest itself and resuscitation efforts.

As expected, we detected elevated hs-cTnT levels in all OHCA patients after resuscitation. Hs-cTnT has high sensitivity as regards cardiomyocyte injury and high sensitivity for myocardial infarction, but at the price of low specificity [14]. However, the median level of hs-cTnT in the first-collected blood sample was lower in this study than in that reported by Geri et al. [12], being 52.5 ng/L in our study compared with 551 ng/L in the study conducted by Geri et al. [12]. One explanation could be that in the present study the first blood sample was collected earlier, immediately after ROSC in the emergency room and before coronary angiography had been performed. In the observational study by Geri et al. the blood sample was collected after coronary angiography.

When comparing patients who underwent PCI vs no PCI we noted that the median Hs-cTnT level in the first-collected blood sample, taken before coronary angiography, was higher in patients who underwent PCI (102 ng/L vs. 49 ng/L. However, in prior studies the initial Troponin levels after ROSC have shown a low positive predictive value as regards recent coronary events after cardiac arrest [12,15]. Hs-cTnT levels and the timing of multiple samples early during the treatment needs to be explored further in order to be able be to use Hs-cTnT as a tool to identify whether the cardiac arrest may be of ischemic origin, and if there could be a potential benefit with revascularization.

None of the differences in NT-proBNP levels were statistically significant. However, when comparing NT-proBNP levels between the randomized groups, the levels were numerically higher in the immediate-angiography group at ICU admission and after 72 h.

5.3. Lactate clearance

Blood lactate concentrations may be considered as a marker of prolonged hypoperfusion or poor resuscitation. The results of some studies have suggested that lactate clearance during the first phase of post-resuscitation care may correlate with a more favorable outcome [16–19].

In our population, concerning OHCA patients without ST-elevation on admission, lactate clearance at six hours was faster than in some other studies [18,20] which have included broader populations including patients with ST-elevation, who are more prone to hemodynamic instability.

Studies in post-cardiac-arrest patients, have shown that rapid lactate clearance is favorable and is associated with a better outcome, both in terms of a lower mortality rate and a better neurological function [16,18]. However, lactate clearance could be a misleading expression, partly since lactate levels are dependent on both production and elimination. It is a balance and is thus more complex than the word clearance suggests [21]. In the present study the use of target temperature management (TTM) was relative low and applied in 55% of the patients in the immediate-angiography group compared with 75% in the standard-of-care group. TTM 33 °C is associated with elevated lactate levels, a low cardiac index and increased doses of vasopressors [1,11]. The proportion TTM 33 °C patients in the present study, as well as those not receiving any TTM at could have influenced our lactate-clearance and LVEF results.

How common is PRMD in the absence of preexisting or acute ischemic cardiomyopathy? Cha et al. excluded cardiac etiology and reported that only 20% of their patients had signs of PRMD, defined as reduced global left ventricle systolic function [22]. This may imply that a considerable amount of the PRMD is due to pre-existing or new coronary/cardiac events.

In comparison with previously published studies, in this study we compared prospectively collected data in randomized patients, which eliminates the risk of confounding factors.

5.4. Limitations

The potential benefit of immediate coronary angiography when assessing LVEF at 24 h is probably because of revascularization of a culprit lesion by means of PCI. The main purpose of this secondary analysis was to describe myocardial dysfunction during the early phase after ROSC. LVEF has the potential to improve during the months after revascularization, but long-term follow-up was not in the scope of this study. The small sample size and the low rate of PCI in this study make it difficult to find an effect on LVEF. Furthermore, 25% of the patients had no echocardiographic examination at 24 h either because of early withdrawal of life-sustaining treatment for ethical reasons or missing examinations for other reasons. Factors with a potential influence on NT-proBNP and Troponin levels, such as pre-existing heart failure, age and kidney function could have influenced the levels of these cardiac biomarkers.

6. Conclusion

In this secondary analysis of OHCA patients without ST-elevation on the ECG randomized to immediate coronary angiography or standard-of-care, we found no significant differences in post-resuscitation myocardial dysfunction parameters between the groups. This finding was consistent also in patients randomized to immediate coronary angiography where PCI was performed compared to those where PCI was not performed.

CRediT authorship contribution statement

Ludvig Elfwén: Writing - original draft, Writing - review & editing, Conceptualization. **Rickard Lagedal:** Conceptualization, Investigation. **Sten Rubertsson:** Conceptualization, Funding acquisition. **Stefan James:** Conceptualization, Writing - review & editing. **Jonas Oldgren:** Conceptualization, Writing - review & editing. **Jens Olsson:** Writing - review & editing, Investigation. **Jacob Hollenberg:** Conceptualization, Investigation. **Ulf Jensen:** Writing - review & editing, Investigation. **Mattias Ringh:** Writing - review & editing, Investigation. **Leif Svensson:** Conceptualization, Supervision. **Per Nordberg:** Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

None of the authors report conflicts of interest related to this manuscript.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100483.

References

[1] J. Grand, J. Kjaergaard, J. Bro-Jeppesen, M. Wanscher, N. Nielsen, M.G. Lindholm, et al., Cardiac output, heart rate and stroke volume during targeted temperature management after out-of-hospital cardiac arrest: Association with mortality and cause of death, Resuscitation 142 (2019) 136–143.
[2] J.P. Nolan, J. Soar, A. Cariou, T. Cronberg, V.R. Moulaert, C.D. Deakin, et al., European resuscitation council and european society of intensive care medicine guidelines for post-resuscitation Care 2015: section 5 of the european resuscitation council guidelines for resuscitation 2015, Resuscitation 95 (2015) 202–222.
[3] R.W. Neumar, J.P. Nolan, C. Adrie, M. Aibiki, R.A. Berg, B.W. Bottiger, et al., Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A consensus statement from the International Liaison Committee on Resuscitation (American Heart Association, Australian and New Zealand Council on Resuscitation, European Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Asia, and the Resuscitation Council of Southern Africa); the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; and the Stroke Council, Circulation 118 (23) (2008) 2452–2483.
[4] W. Bougouin, A. Cariou, Management of postcardiac arrest myocardial dysfunction, Curr. Opinion Crit. Care 19 (3) (2013) 195–201.
[5] I. Laurent, M. Monchi, J.D. Chiche, L.M. Joly, C. Spaulding, B. Bourgeois, et al., Reversible myocardial dysfunction in survivors of out-of-hospital cardiac arrest, J. Am. Coll. Cardiol. 40 (12) (2002) 2110–2116.
[6] A. Chalkias, T. Xanthos, Pathophysiology and pathogenesis of post-resuscitation myocardial stunning, Heart Fail Rev. 17 (1) (2012) 117–128.
[7] L.J. Morrison, S.M. Devlin, M.C. Kontos, S. Cheskes, T.P. Aufderheide, J. Christenson, et al., The association of maximum Troponin values post out-of-hospital cardiac arrest with electrocardiographic findings, cardiac reperfusion procedures and survival to discharge: A sub-study of ROC PRIMED, Resuscitation 111 (2017) 82–89.
[8] L. Elfwen, R. Lagedal, P. Nordberg, S. James, J. Oldgren, F. Bohm, et al., Direct or subacute coronary angiography in out-of-hospital cardiac arrest (DISCO)-An initial pilot-study of a randomized clinical trial, Resuscitation 139 (2019) 253–261.
[9] R. Lagedal, L. Elfwen, S. James, J. Oldgren, D. Erlinge, O. Ostlund, et al., Design of DISCO-direct or subacute coronary angiography in out-of-hospital cardiac arrest study, Am. Heart J. 197 (2018) 53–61.
[10] J.C. Jentzer, M.D. Chonde, A. Shafton, H. Abu-Daya, D. Chalhoub, A.D. Althouse, et al., Echocardiographic left ventricular systolic dysfunction early after resuscitation from cardiac arrest does not predict mortality or vasopressor requirements, Resuscitation 106 (2016) 58–64.
[11] J. Bro-Jeppesen, M. Annborn, C. Hassager, M.P. Wise, P. Pelosi, N. Nielsen, et al., Hemodynamics and vasopressor support during targeted temperature management at 33 degrees C Versus 36 degrees C after out-of-hospital cardiac arrest: a post hoc study of the target temperature management trial*, Crit. Care Med. 43 (2) (2015) 318–327.
[12] G. Geri, N. Mongardon, F. Dumas, C. Chenevier-Gobeaux, O. Varenne, X. Jouven, et al., Diagnosis performance of high sensitivity troponin assay in out-of-hospital cardiac arrest patients, Int. J. Cardiol. 169 (6) (2013) 449–454.
[13] D.A. Pearson, C.M. Wares, K.A. Mayer, M.S. Runyon, J.R. Studnek, S.L. Ward, et al., Troponin marker for acute coronary occlusion and patient outcome following cardiac arrest, West J. Emerg. Med. 16 (7) (2015) 1007–1013.
[14] J. Mair, B. Lindahl, O. Hammarsten, C. Muller, E. Giannitsis, K. Huber, et al., How is cardiac troponin released from injured myocardium?, Eur. Heart J. Acute Cardiovasc. Care 7 (6) (2018) 553–560.
[15] V. Agusala, R. Khera, D. Cheeran, P. Mody, P.P. Reddy, M.S. Link, Diagnostic and prognostic utility of cardiac troponin in post-cardiac arrest care, Resuscitation 141 (2019) 69–72.
[16] M.W. Donnino, L.W. Andersen, T. Giberson, D.F. Gaieski, B.S. Abella, M.A. Peberdy, et al., Initial lactate and lactate change in post-cardiac arrest: a multicenter validation study, Crit. Care Med. 42 (8) (2014) 1804–1811.
[17] T.R. Lee, M.J. Kang, W.C. Cha, T.G. Shin, M.S. Sim, I.J. Jo, et al., Better lactate clearance associated with good neurologic outcome in survivors who treated with therapeutic hypothermia after out-of-hospital cardiac arrest, Crit. Care (London, England) 17 (5) (2013) R260.
[18] K. Hayashida, M. Suzuki, N. Yonemoto, S. Hori, T. Tamura, A. Sakurai, et al., Early lactate clearance is associated with improved outcomes in patients with postcardiac arrest syndrome: a prospective, multicenter observational study (SOS-KANTO 2012 Study), Crit. Care Med. 45 (6) (2017) e559–e566.
[19] A.M. Dell'Anna, C. Sandroni, I. Lamanna, I. Belloni, K. Donadello, J. Creteur, et al., Prognostic implications of blood lactate concentrations after cardiac arrest: a retrospective study, Ann. Intensive Care 7 (1) (2017) 101.
[20] M.W. Donnino, J. Miller, N. Goyal, M. Loomba, S.S. Sankey, B. Dolcourt, et al., Effective lactate clearance is associated with improved outcome in post-cardiac arrest patients, Resuscitation 75 (2) (2007) 229–234.
[21] J.L. Vincent, E.S.A. Quintairos, L. Couto Jr., F.S. Taccone, The value of blood lactate kinetics in critically ill patients: a systematic review, Crit. Care 20 (1) (2016) 257.
[22] K.C. Cha, H.I. Kim, O.H. Kim, Y.S. Cha, H. Kim, K.H. Lee, et al., Echocardiographic patterns of postresuscitation myocardial dysfunction, Resuscitation 124 (2018) 90–95.