

Critical Review Form Therapy

PGY-4

Early cardiac catheterization is associated with improved survival in comatose survivors of cardiac arrest without STEMI. Resuscitation. 2013 Aug 6. doi:pii: S0300-9572(13)00396-1.

Objectives: "To determine if early CC [cardiac catheterization] is associated with improved survival in comatose patients who are resuscitated after cardiac arrest due to ventricular arrhythmia when electrocardiographic evidence of STEMI is absent."
(p. 2)

Methods: This retrospective observation study was performed using prospectively collected data from the [International Cardiac Arrest Registry \(INTCAR\)](#) on consecutive comatose patients admitted to any of 6 large tertiary care centers in the US following cardiac arrest. All patients aged 18 years or older who survived to hospital admission following out of hospital cardiac arrest (OHCA) due to ventricular fibrillation (VF) or ventricular tachycardia (VT), without signs of STEMI on ECG, and remained comatose, were eligible for inclusion. All patients received [therapeutic hypothermia](#) to a core body temperature of 32-34 °C for 24 hours following return of spontaneous circulation (ROSC).

Outcomes were assessed for 2 groups: those who received early CC, defined as catheterization performed during the first 24 hours; and those who underwent late CC, defined as catheterization at any other time during hospitalization, or underwent no CC. The primary outcome measured was survival to hospital discharge. Secondary outcomes included survival to discharge with good neurologic function ([CPC score](#) of 1 or 2), left ventricular function at discharge, survival to follow-up, and neurologic function at follow-up. Left ventricular systolic function, as measured by transthoracic echocardiogram, was defined as normal (<50%), moderately impaired (30-49%), or severely impaired (<30%). Shock was defined as a systolic blood pressure (SBP) < 90 mmHg despite vasoactive medications, or the need for intra-aortic balloon counter-pulsation.

A total of 754 consecutive comatose patients survived to hospital admission following OHCA at the 6 study sites, of whom 435 had VF/VT as the initial documented rhythm. Of these, 269 had no signs of STEMI on their ECG and were included in the analysis. Out of this cohort, 122 (45.3%) patients received early CC, while 147 (54.6%) did not receive early CC. Of those who did not receive early CC, 41/147 (27.9%) received late CC (> 24 hours after admission) and 106/147 (72.1%) did not receive CC during hospitalization. The two groups (early CC and no early CC) were similar with respect to mean age (60.4 vs. 59.9 years), rates of bystander CPR (54.6% vs. 59.7%), percent with witnessed arrest (85.3% vs. 85.6%), and mean time to ROSC (22.0 minutes vs. 21.9 minutes). Patients in the early CC were more likely to be in

shock at hospital admission (40.5% vs. 25.7%, $p = 0.013$), and were more likely to receive aspirin (36.9% vs. 13.6%), antithrombin agents (32.8% vs. 12.9%), and glycoprotein IIb/IIIa inhibitors (9.8% vs. 1.4%).

Guide		Comments
I.	Are the results valid?	
A.	Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?	
1.	Were patients randomized?	No. This was a retrospective, observational study. The decision regarding if and when to perform cardiac catheterization was at the discretion of the treating physicians, and may have been based on factors that would influence prognosis with regards to the outcomes of interest. This selection bias is only partially overcome by the calculation of an adjusted odds ratio, due to the inability to correct for all known confounding factors, and the presence of unknown confounding factors .
2.	Was randomization concealed (blinded)?	No. Patients were not randomized.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. While patients were not randomized, they were analyzed according to the predefined groups set by the authors, namely whether they received CC early (within 24 hours) or not.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. While patients who received early CC were similar to those who did not with respect to mean age (60.4 vs. 59.9 years), rates of bystander CPR (54.6% vs. 59.7%), percent with witnessed arrest (85.3% vs. 85.6%), and mean time to ROSC (22.0 minutes vs. 21.9 minutes), patients in the early CC were more likely to be in shock at hospital admission (40.5% vs. 25.7%, $p = 0.013$), and were more likely to receive aspirin (36.9% vs. 13.6%), antithrombin agents (32.8% vs. 12.9%), and glycoprotein IIb/IIIa inhibitors (9.8% vs. 1.4%).
B.	Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?	
1.	Were patients aware of group allocation?	Yes. While the study consisted only of patients who were comatose following ROSC, patients would be made aware

		of whether or not they received CC upon awakening. It is unlikely that this would result in performance bias on the part of the subjects.
2.	Were clinicians aware of group allocation?	Yes. The decision to perform CC in this observational trial was at the discretion of the treating physicians, who hence could not be blinded to group allocation. The possible influence of performance bias must be considered.
3.	Were outcome assessors aware of group allocation?	Uncertain. The authors do not provide the details of their chart review methodology (Gilbert 1996 and Worster 2004), and do not mention blinding of the outcome assessors, potentially introducing observer bias .
4.	Was follow-up complete?	No. All data was obtained from the International Cardiac Arrest Registry (INTCAR) , which contained information regarding in-hospital death or survival to discharge and CPC score at discharge among those who survived. Follow-up data (with variable time to follow-up) was only available for 139 patients (52%): 73 in the early CC group, 66 in the no early CC group.
II.	What are the results (answer the questions posed below)?	
1.	How large was the treatment effect?	<ul style="list-style-type: none"> • There was no significant difference in the rate of acute coronary occlusion diagnosed at CC between those receiving early CC and those receiving late CC (26.2% vs. 29.3%, $p = 0.381$), or in the rates of PCI (32.8% vs. 39.0%, $p = 0.628$). • Of those receiving early CC, 33% (40/122) received successful PCI. • Overall 56.5% of patients survived to discharge: more patients in the early CC group survived compared to those who did not receive early CC (65.6% vs. 48.6%, $p = 0.017$) with an adjusted OR of death of 0.35 (95% CI 0.18-0.70, $p = 0.003$). • Within the early CC group, survival rates were similar between those who received PCI and those who did not (60% vs. 68.3%, $p = 0.386$), as were rates of good neurologic outcome (60% vs. 62.2%, $p = 0.669$). • Survival was higher among those who received early CC compared to those who received no CC (65.6% vs. 28.6%, $p < 0.001$) with an adjusted OR of 0.14 (95% CI 0.06-0.32, $p < 0.001$); a higher rate of favorable neurologic outcome was seen among survivors as well

		<p>(95.2% vs. 83.3%, $p = 0.037$).</p> <ul style="list-style-type: none"> • More patients in the early CC group survived with good neurologic outcome compared to the group without early CC (60.7% vs. 44.5%, $p = 0.017$). • There was no statistically significant difference in the percent of patients with normal left ventricular systolic function between those who received early CC and those who did not (37.9% vs. 27.6%, $p = 0.282$). • The median follow-up interval was 5 months for those who received early CC and 6 months for those who did not receive early CC. Survival to follow-up was higher in the early CC group (60% vs. 40.4%, $p = 0.005$), as was survival with good neurologic function at follow-up (60% vs. 39.7%, $p = 0.004$).
2.	How precise was the estimate of the treatment effect?	See above.
III.	How can I apply the results to patient care (answer the questions posed below)?	
1.	Were the study patients similar to my patient?	Yes. These were successfully resuscitated patients suffering OHCA with an initial rhythm of VF or VT. Patients were typically older and male, similar to anecdotal observations in our institution. Rates of bystander CPR were above 50% in both groups, and this rate may be higher than in our community, potentially favoring overall survival in the study.
2.	Were all clinically important outcomes considered?	Yes. The authors considered both survival and survival with good neurologic function, and looked at outcomes at follow-up, with a median of 5 months and 6 months follow-up in the early and not early CC groups respectively. While the authors did not assess cost, length of stay, length of ICU stay, or number of days on a ventilator, the most important patient-centered outcomes were considered.
3.	Are the likely treatment benefits worth the potential harm and costs?	No. While this was an observation trial subject to selection bias , the results indicate a significant survival benefit among patients undergoing early CC (RR 1.35), this benefit was seen despite a higher rate of shock among patients who underwent early CC (40.5% vs. 25.7%). The presence of shock has been shown to be predictive of worse outcomes following cardiac arrest (Kilgannon

		<p>2008, Trzeciak 2009). This improvement in survival persisted after adjustment for known confounders (OR of death of 0.35; 95% CI 0.18-0.70, p = 0.003).</p> <p>Surprisingly, among those in the early CC group, successful PCI was <i>not</i> associated with improvement in survival rates (60% for those with successful PCI vs. 68.3% for those without successful PCI, p = 0.386). This suggests that other factors led to the improved outcomes seen in the early CC group, rather than catheterization itself. It is possible that the increased use of other interventions, such as the use of anti-thrombin and antiplatelet agents, could have led to improved outcomes in the early CC group. More likely, given the retrospective nature of the study, it seems plausible that selection bias played a significant role: patients suspected of having a better prognosis may have been referred for CC, whereas those in whom aggressive care was felt to be futile would be treated more conservatively.</p> <p>While a randomized controlled trial would eliminate some of this bias, such a study would be costly and difficult to achieve, and this observational trial is currently the best evidence available.</p>
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Limitations:

1. This was a retrospective, observational trial. It is quite likely that [selection bias](#) played a confounding role.
2. While the two treatment groups reportedly had similar proportions of "previously healthy" patients, details of past medical history were not provided. Differences in underlying rates of potentially serious illness (i.e. cancer) or previous cardiac illness could affect the decision to provide more aggressive testing or treatment, and could influence the likelihood of survival.
3. There was a higher rate of shock among patients who underwent early CC (40.5% vs. 25.7%) which is predictive of worse outcomes following cardiac arrest ([Kilgannon 2008, Trzeciak 2009](#)).
4. Within the early CC group, survival rates were similar between those who received PCI and those who did not, suggesting that the survival benefit was

either a result of prognostic imbalance, or due to other aspects of treatment (antithrombins, antiplatelet agents).

5. There was no logistic regression, or other [method to adjust for the presence of confounding](#).

Bottom Line:

This study demonstrated higher rates of survival and neurologically intact survival among patients with ROSC following OHCA due to ventricular fibrillation or ventricular tachycardia, without ST-elevation, who underwent early cardiac catheterization compared to those who did not. However, in the early catheterization group, there was no survival difference between those with successful PCI and those without successful PCI, suggesting that the perceived benefit may not have been due to the catheterization itself. Given the retrospective nature of the study, it is possible that clinicians selected patients with overall better prognosis to undergo catheterization; less likely, it is possible that differences in treatment aside from cardiac catheterization, such as increased use of antiplatelet and antithrombin agents, led to the perceived survival benefit.