

Acute Ischemic Heart Disease

Regionalization of post-cardiac arrest care: Implementation of a cardiac resuscitation center

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Background Guidelines recommend standardized treatment of post-cardiac arrest patients to improve outcomes. However, the infrastructure, resources, and personnel required to meet the complex needs of cardiac arrest victims remain a barrier to care. Given that regionalization of time-dependent high-acuity illness is an emerging paradigm, the aim of the present study was to develop and implement a regionalized approach to post-cardiac arrest care.

Methods We performed a prospective observational study on all patients treated in a regionalized clinical pathway from November 2007 through June 2011. All patients were enrolled after admission to an urban academic medical center. Clinical data including arrest and treatment variables, complications, and outcome were collected on consecutive patients with the use of a preformatted standard data collection tool using Utstein criteria.

Results A total of 220 patients were enrolled; 127 (58%) patients were local direct admissions from our community, and 93 (42%) were transferred from 1 of 24 outlying referral hospitals. One hundred six (48%, 95% CI 38%-53%) patients survived to hospital discharge. The primary outcome of hospital survival with good neurologic function was observed in 94 (43%, 95% CI 32%-48%). There was no difference in survival with good neurologic outcome among local and referred patients. Overall 1-year survival was 44% (95% CI 38%-51%). Among patients discharged from the hospital with good neurologic function, 93% (95% CI 85%-97%) remained alive at 1 year.

Conclusion Development of a regionalized approach to post-cardiac arrest care using previously established referral relationships is feasible, and implementation of such an approach was clinically effective in our region. (Am Heart J 2012;164:493-501.e2.)

Sudden cardiac arrest is a leading cause of death in developed countries and affects over 300,000 patients in the United States per year.^{1,2} Less than one-quarter of patients with out-of-hospital cardiac arrest (OOHCA) survive to hospital admission.³ Among the subset of patients who achieve initial resuscitation, <50% survive to hospital discharge. One-third of patients die of refractory cardiovascular shock or the cause of the initial arrest. The remaining patients survive the initial insult only to later succumb to sequelae of the post-cardiac arrest syndrome, such as organ dysfunction and neurologic injury. Even among survivors, the burden of cardiac arrest persists, with many patients suffering permanent neuro-

logic injury and disability.^{4,5} These data underscore the impact of sudden cardiac arrest on organized healthcare systems and society.

Contemporary emergency care now emphasizes intensive support during the vulnerable but modifiable postarrest period.⁶ This phase has emerged as a critical window to impact the outcomes of patients with cardiac arrest. Improved morbidity and mortality achieved with therapeutic hypothermia (TH) prove the potential for therapies applied following return of spontaneous circulation (ROSC) to impact clinical outcome.^{7,8} Priorities of the postarrest period include stabilization of organ perfusion and oxygenation, identification and treatment of reversible causes of cardiac arrest and initiation of neuroprotective therapy.

Although standardized treatment of postarrest patients improves outcomes, the infrastructure, resources, and personnel required to meet the acute and complex needs of cardiac arrest victims remain a barrier.^{6,9} As a result, efficacious therapies that are logistically difficult to implement are not adopted into standard practice.^{10,11} This variability of practice is one possible explanation for regional and interhospital variation in survival following admission for OOHCA.^{2,12}

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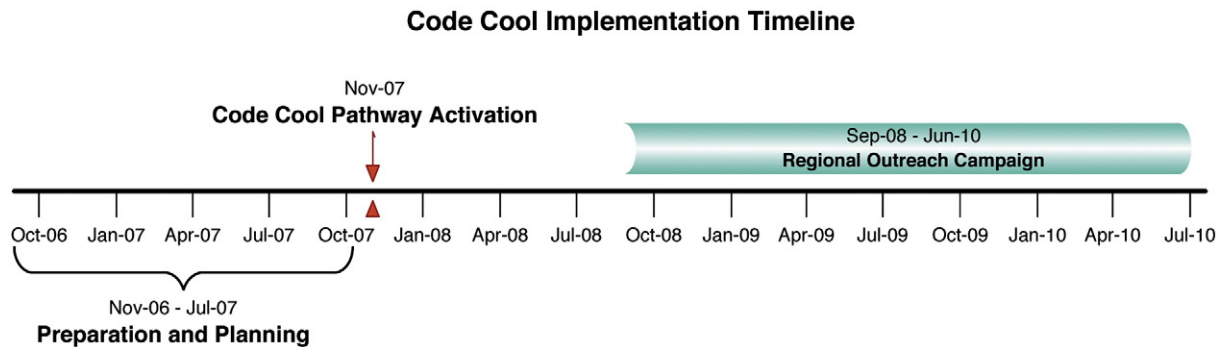
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Figure 1



Timeline for implementation of post-cardiac arrest care pathway.

Regionalization of complex time-dependent, high-acuity disease is an emerging paradigm for management of trauma, ST-elevation myocardial infarction (STEMI), and stroke.¹³⁻¹⁶ Extrapolation to regionalized care for cardiac arrest victims was recently endorsed by the American Heart Association (AHA).¹⁷ The objective of this report is to describe our 3-year experience with development and implementation of a regionalized approach for post-cardiac arrest care that incorporates TH.

Methods

Study design and setting

We performed a prospective observational study on all patients treated in our clinical pathway from November 2007 through June 2011. All patients were enrolled after admission to Carolinas Medical Center, an urban 900-bed teaching hospital. Our center is an STEMI-receiving hospital as designated by the American Heart Association Mission: Lifeline regional systems of care program and is accredited by the Society of Chest Pain Centers. This hospital is also the tertiary care medical center of Carolinas Healthcare System that includes 33 acute care facilities in 2 states. Before implementation, our emergency department and intensive care units (ICU) did not have a formal management protocol for post-cardiac arrest care. All study subjects were prospectively identified at admission. Clinical data including arrest and treatment variables, complications, and outcome data were collected on consecutive patients with the use of a preformatted standard data collection tool using Utstein criteria.¹⁸ This study was approved by the institutional review and privacy board at Carolinas Healthcare System.

Study subjects

Eligible patients were identified by the emergency medicine, critical care medicine, and cardiology services. Resuscitated victims of nontraumatic cardiac arrest with persistent coma (Glasgow Coma Scale ≤ 8 and/or unable to follow verbal commands) 15 minutes after ROSC were eligible. Our guideline emphasized the evidence for therapeutic cooling of patients with cardiac arrest due to ventricular fibrillation and tachycardia

(VT/VF). However, patients exhibiting any initial arrest rhythm or nontraumatic precipitant were eligible for the clinical pathway. Our guideline recommended strong consideration of cooling for patients with arrest with first recognized rhythm of pulseless electrical activity (PEA) or asystole if time of arrest to ROSC was <30 minutes.

Absolute contraindications to pathway implementation included an active do-not-resuscitate order or known severe terminal illness preceding the cardiac arrest. Relative contraindications included pregnancy, age >75 years, encephalopathy suspected unrelated to cerebral anoxia (eg, overdose, intoxication, intracranial hemorrhage, stroke, or trauma), active hemorrhage, severe systemic infection, moribund cardiovascular status or severe shock refractory to medical stabilization, arrest interval >60 minutes, and arrest to cooling initiation interval >6 hours. Clinical discretion was emphasized and superseded the relative contraindications if the perceived benefit of therapy outweighed the risk. Bundle implementation and continuation of TH initiated in the prehospital setting or by transferring facilities was not mandatory and was continued at the discretion of caring physicians upon arrival to our center. A group alert page including the in-hospital intensivist and cardiologist was activated following identification of potential pathway candidates to facilitate collective input and decision for pathway implementation including emergency percutaneous coronary intervention (PCI).

Treatment pathway development and implementation

A multidisciplinary clinical team from emergency medicine, critical care, and cardiology collaborated to develop a post-cardiac arrest management pathway (termed *Code Cool*) focused on comatose survivors of in- and OOHCA. Figure 1 illustrates the timeline for implementation of our hospital and regionalized care approach. Our *Code Cool* pathway was adopted as a new treatment protocol in November 2007.

To develop the pathway, the best available evidence was used to form a post-cardiac arrest care bundle guideline and order set. Core treatment elements included cardiopulmonary support goals, TH to a goal of 33°C for 24 hours, empiric antibiotic therapy for suspected pulmonary aspiration, and glycemic control (Table D).⁶ Recognizing the controversy surrounding emergency PCI in comatose victims of cardiac arrest,¹⁹ our

Table 1. Order set treatment bundle components

Cardiovascular goals
Fluid and catecholamine resuscitation
Goal MAP > 70 mm Hg, normalized perfusion and lactate clearance
Preferred vasopressor: norepinephrine
Preferred inotrope: dobutamine
Emergency PCI when indicated
Therapeutic cooling
Target 33°C as soon as possible postarrest
Induction via 30 mL/kg 4°C normal saline as tolerated
Cooling unit application with immediate cooling
Sedation and neuromuscular blockade
Ventilator management
Avoidance of hyperventilation and hyperoxia
Minute ventilation titrated to PaCO ₂ 38-42 mm Hg
FiO ₂ titrated to SpO ₂ >95%
Empiric antibiotics for suspected aspiration
Electrolyte repletion (potassium and magnesium)
Glycemic control: blood sugar goal <150 mg/dL
Critical care medicine consult
Cardiology consult
Physical medicine and rehabilitation consult

MAP, Mean arterial pressure; FiO₂, fraction of inspired oxygen.

group established a goal to facilitate emergency coronary angiography in all patients with STEMI or high clinical suspicion of acute coronary occlusion and time of arrest to ROSC <25 minutes.²⁰⁻²² The limited predictive value of a postresuscitation electrocardiogram for acute coronary occlusion was highlighted in our pathway, and clinical suspicion for acute coronary syndrome was left to the discretion of clinical teams.^{23,24}

Therapeutic hypothermia induction was performed with simultaneous intravenous chilled (4°C) isotonic crystalloid (30 mL/kg IV bolus as tolerated) and application of a servo-controlled external surface cooling unit (Medivance Inc, Louisville, CO) with core body temperature monitored via temperature sensing Foley thermistor. Therapeutic hypothermia induction was performed concurrent with emergency PCI when appropriate. The clinical pathway included continuous sedation regardless of neurologic status and use of neuromuscular blockade to thwart shivering and facilitate rapid TH induction.

Education and in-service classes were coordinated for clinical staff before implementation. A guidance document was designed to assist with patient selection and case management. Case review and quarterly task force meetings facilitated protocol revisions and ongoing education. Critical care medicine and cardiology consultations were administratively mandated for all patients entering this pathway. Recognizing the knowledge gap in validated prognostication for anoxic encephalopathy after therapeutic cooling, we did not implement a standardized approach for prognostication.^{9,25} This topic was discussed in a weekly multidisciplinary critical care conference before and during the study period. Neurology consultation was available but not mandated for patients entering the clinical pathway. Physical rehabilitation and neuropsychiatric evaluation and treatment were embedded in the treatment plan for all patients discharged from the ICU.

Regionalization strategies

Following implementation of our hospital postarrest bundle, we developed strategies to include referral hospitals in organized post-cardiac arrest care. Our center hosts an outreach

program that coordinates patient referrals. This and our participation in the Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments study allowed us to leverage existing relationships with regional referral hospitals.^{26,27} The existing database of referral hospitals was used to disseminate information on our *Code Cool* program (online Appendix [Supplementary Figure 1](#)). Regional hospital administrators and emergency department directors received information and criteria for our clinical pathway. A local clinical leader facilitated introduction of the care bundle. Structured goals including inclusion criteria, therapy end points, and a TH induction protocol using chilled saline and ice packs were developed and individualized at these referral centers. Some referral centers did not respond with a local champion or intent to develop a proactive treatment plan. In these situations, referring physicians were advised to initiate TH during telephone acceptance of patients to our center.

As a part of the regionalization of care, our hospital-based aeromedical and critical care transport services implemented TH via chilled intravenous fluids during interhospital transport and scene responses. In addition, our local county emergency medical services (EMS) group introduced intra-arrest TH whereby 4°C saline was administered via the first established venous or intraosseous access.²⁸ This plan was coordinated with 1 additional urban nonacademic hospital in our community that routinely provided TH. The EMS direction advised preferential transport of postarrest victims to 1 of the 2 hospitals active in the use of TH. Similar prehospital cooling was implemented by surrounding EMS agencies with preferential scene aeromedical transport requests for transport to our center.

Data analysis

The primary outcome was hospital survival with good neurologic outcome. We a priori defined clinical effectiveness as hospital survival with good neurologic outcome of >50% among patients with initial rhythm of VT/VF.^{7,8} Given our aim to modify local practice based on prior evidence, a formal sample size estimate was not calculated. Secondary outcomes were survival to hospital discharge, longitudinal survival at 1 year, and process-of-care measures. Cerebral functional status was determined at hospital discharge, and Pittsburgh cerebral performance category 1 to 2 was considered a good neurologic outcome.⁸ All patients admitted to the ICU with intention to receive the full care bundle including TH are included in this analysis.

For statistical analysis, categorical variables were assessed with the χ^2 or Fisher exact tests for small counts. Two-sample *t* tests and Wilcoxon rank sum tests were used for continuous data, depending upon the distribution of the data. Kendall rank correlation was used to assess annual changes in performance metrics. Our hospital system electronic health records and the social security death index were queried to determine the survival of subjects at 1-year postarrest. Kaplan-Meier survival analysis and log-rank test were used to evaluate survival. Two-sided *P* values <.05 were considered statistically significant. A multivariable logistic regression model was created using good neurologic outcome as the dependent variable. Candidate variables were selected based on significant (*P* <.05) differences in good neurologic outcome in the bivariate analysis, and the model was refined using backwards stepwise elimination. Model

Table II. Patient demographics

	Total (n = 220)	Local (n = 127)	Referred (n = 93)	P*
Age (mean years ± SD)	57 ± 15	58 ± 15	56 ± 15	.57
Male gender	132 (60%)	78 (61%)	54 (58%)	.62
Medical comorbidities				
Diabetes	63 (29)	40 (32)	23 (25)	.27
Hypertension	119 (54)	69 (54)	50 (54)	.94
Coronary artery disease	115 (52)	68 (54)	47 (51)	.66
Systolic dysfunction cardiomyopathy	81 (37)	45 (35)	36 (39)	.62
Atrial fibrillation	50 (23)	30 (24)	20 (22)	.71
Prior stroke	22 (10)	9 (7)	13 (14)	.09
End stage renal disease	45 (20)	27 (21)	18 (19)	.73
COPD	29 (13)	17 (13)	12 (13)	.92
Arrest location				
Out-of-hospital	209 (95%)	118 (93%)	91 (98%)	.12
In-hospital	11 (5%)	9 (7%)	2 (2%)	
Witnessed arrest	188 (86%)	106 (85%)	82 (88%)	.33
Bystander CPR (n = 186)	127 (68%)	82 (73%)	45 (62%)	.12
Time of arrest to ROSC (n = 162)†	19 (10-29)	19 (10-29)	20 (10-32)	.87
Initial rhythm				
VT/VF	136 (62%)	77 (61%)	59 (63%)	.80
PEA	48 (22%)	29 (23%)	19 (20%)	
Asystole	33 (15%)	20 (16%)	13 (14%)	
Unknown	3 (1%)	1 (1%)	2 (2%)	
Best GCS before TH	3 (3-3)	3 (3-3)	3 (3-3)	.86
Admission blood pressure (MAP ± SD) (n = 171)‡	80 ± 26	77 ± 25	85 ± 27	.07
STEMI at presentation	28 (13%)	10 (8%)	18 (19%)	.01

CPR, Cardiopulmonary resuscitation; GCS, Glasgow Coma Scale.

* P value comparisons between local and referred patient groups.

† Time in minutes with median and IQR.

‡ Excludes patients with a BP of 0 on admission.

fit was assessed using C-statistics and the Hosmer-Lemeshow goodness-of-fit test. Odds ratios (ORs) are presented for the final model. All analyses were conducted using SAS statistical software (SAS Institute, Cary, NC).

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Results

An alert page was activated for 248 patients, of which 26 patients were deemed ineligible. Moribund cardiovascular status (n = 13), neurologic improvement (n = 6), advanced comorbid disease, and directives status (n = 4) were the most common reasons for patient ineligibility. Overall, 222 patients were formally entered into the treatment pathway during the study period. Two patients were excluded from analysis due to incomplete data, leaving 220 patients for analysis. Demographics, comorbid status, and clinical variables are reported in Table II. Most patients had OOHCA (n = 209; 95%). The origin of enrolled patients was 127 (58%) patients had local arrest with primary medical care at our center and 93 (42%) patients underwent initial postarrest stabilization at a referral hospital with subsequent transport to our center.

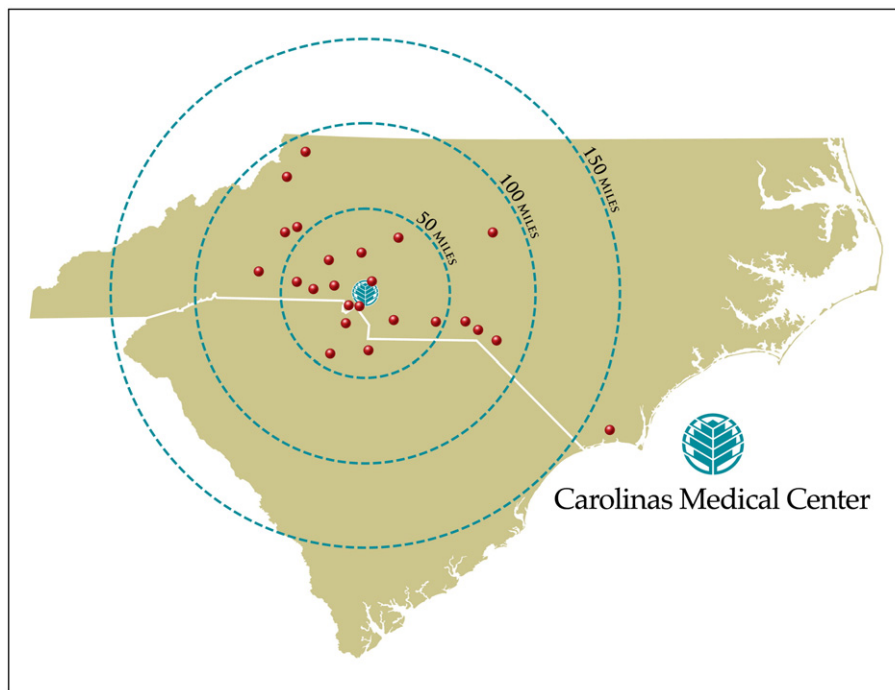
Patients transferred to our center originated from 1 of 24 outlying facilities within the region (Figure 2). ST-elevation myocardial infarction at presentation was the only statistically significant difference in demographic or arrest factors between local and referred patients (8% vs 19%, $P = .01$). Median time of arrest to ROSC was 19 minutes (interquartile range [IQR] 10-29 minutes) with arrest to ROSC interval ≥ 30 minutes occurring in 23% of enrolled patients with clear arrest timing.

Hospital survival and neurologic outcome

Overall, 106 (48%, 95% CI 42%-55%) patients survived to hospital discharge. The primary outcome of survival with good neurologic function was observed in 94 patients, which is 43% (95% CI 36%-49%) of the entire group and 86% (95% CI 81%-94%) of survivors. There was no statistical difference in good neurologic outcome or survival to hospital discharge based on arrest location or initial site of postarrest care (Table III).

A shorter interval of collapse to ROSC was associated with improved survival and survival with good neurologic outcome ($P < .001$). Survival with good neurologic outcome after arrest interval of 30 to 60 minutes was 14% (95% CI 5%-29%). Primary arrest rhythm of VT/VF was also associated with improved neurologic outcome ($P < .001$) and hospital survival ($P < .001$) compared

Figure 2



Geographic origin of referred subjects.

Table III. Primary outcome of survival and good neurologic function by patient subset

	Survival to discharge (n = 106)	P	Good neurologic outcome* (n = 94)	P
Initial care site				
Local patients (n = 127)	67 (53%)	.11	58 (46%)	.30
Referred patients (n = 93)	39 (42%)		36 (39%)	
Arrest location				
Out-of-hospital (n = 209)	100 (48%)	.67	90 (43%)	.76
In-hospital (n = 11)	6 (55%)		4 (36%)	
Initial rhythm				
VT/VF (n = 136)	81 (60%)	<.001	73 (54%)	<.001
PEA (n = 48)	17 (35%)		15 (31%)	
Asystole (n = 33)	7 (21%)		5 (15%)	
Unknown (n = 3)	1 (33%)		1 (33%)	

* Good neurologic outcome is a cerebral performance category of 1 or 2 at hospital discharge.

with patients with an initial nonshockable rhythm. Survival with good neurologic outcome was improved in patients with VT/VF compared with those demonstrating a primary nonshockable rhythm (54% vs 25%, $P = .001$).

Among nonsurvivors, 12 patients (11%) progressed to death by neurologic criteria, 11 patients (10%) died due to irrecoverable shock or recurrent cardiac arrest, and 91 (80%) patients had withdrawal of care for poor neurologic outcome or nonresolving organ failure. Withdrawal

of care occurred at a median of 4 (IQR 3-7, range 0-32 days) days after admission.

Clinical pathway performance

Clinical pathway quality measures are reported in [Table IV](#). Most patients reached goal temperature with a median time of 316 minutes (IQR 215-442 minutes) from ROSC. Time of ROSC to goal temperature was significantly longer in referred patients (267 vs 401 minutes, $P < .001$),

Table IV. Clinical pathway quality measures

	Total (n = 220)	Local (n = 127)	Referred (n = 93)	P*
All patients				
Achievement of target temperature	218 (99%)	126 (99%)	92 (99%)	>.99
Neuromuscular blockade at induction	164 (75%)	96 (76%)	68 (73%)	.68
Persistent hypotension [†]	37 (17%)	20 (16%)	17 (18%)	.62
Catecholamine infusion [§]	99 (45%)	54 (43%)	45 (49%)	.35
Emergency cardiac catheterization	48 (22%)	23 (18%)	25 (27%)	.12
Emergency cardiac catheterization for STEMI (n = 28)	28 (100%)	10 (100%)	18 (100%)	NA
ROSC to balloon time for STEMI patients (n = 19) [†]	110 (71-128)	69 (53-95)	122 (104-139)	.04
ROSC to target temperature (n = 193) [†]	316 (215-442)	267 (188-358)	401 (302-541)	<.001
Out-of-hospital arrests only n = 209		n = 117	n = 90	
ROSC to target temperature (n = 182) [†]	307 (206-435)	257 (185-350)	399 (302-536)	<.001
Resuscitation center arrival to target temperature [†]	253 (174-351)	244 (179-332)	279 (148-365)	.45

CMC, Carolinas Medical Center; NA, not available.

* P value comparisons between local and referred patient groups.

† Times in minutes with median and IQR.

‡ Defined as mean arterial pressure <65 mm Hg for >15 minutes.

§ Catecholamine infusion within first 6 hours of admission.

Table V. Results of logistic regression analysis for the end point of good neurologic outcome

Variable	OR	95% CI
Coronary artery disease	8.18	3.1-21.7
Catecholamine infusion*	0.44	0.20-0.97
Age	0.49	0.35-0.69
Arrest to ROSC interval	0.43	0.30-0.62

Model fit, C-statistic = 0.86; Hosmer-Lemeshow test, $P = .53$.

* Catecholamine infusion within first 6 hours of admission.

but there was no difference in time from medical center arrival to goal temperature between the 2 patient groups (244 vs 279 minutes, $P = .45$). Return of spontaneous circulation to goal temperature did not improve for the entire cohort ($P = .055$) but did improve among referred patients ($P = .008$) during the study period.

ST-elevation myocardial infarction was diagnosed in 28 (13%, 95% CI 9%-18%) of the entire patient group. All patients with STEMI underwent emergency coronary angiography, and 19 (68%, 95% CI 49%-82%) of these patients received a PCI. Twenty additional patients underwent emergency cardiac catheterization for suspected acute coronary syndrome despite a nondiagnostic electrocardiogram, of which 9 (45%, 95% CI 26%-66%) underwent PCI. Return of spontaneous circulation to balloon time for STEMI cases was longer in referred patients. In contrast, medical center arrival to balloon time for patients with STEMI was longer in local compared with referred patients (41 vs 28 minutes, $P = .03$).

Predictors of good neurologic outcome

Multiple regression analysis identified 4 variables independently associated with hospital survival with good neurologic outcome (Table V). Known coronary artery

disease was associated with improved survival, whereas acute postarrest catecholamine support, advancing age, and arrest interval were associated with adverse outcome. Each decade of age was associated with greater risk of experiencing poor neurologic outcome (OR 2.0). A patient was 2.3 times as likely to have good neurologic outcome for each 10-minute reduction in the interval of arrest to ROSC.

One-year outcome

Longitudinal 1-year survival was available for 210 patients. The remaining 10 excluded patients were alive but had not reached the 1-year analysis threshold. Overall, 93 (44%, 95% CI 38%-51%) of enrollees remained alive 1-year postarrest. Among patients discharged from the hospital with good neurologic function, 93% (95% CI 85%-97%) remained alive at 1 year. Local patients experienced improved longitudinal survival compared with referred patients (45% vs 32%, $P = .004$) (online Appendix Supplementary Figure 2) with referred patients having 1.5 times higher probability of death at 1 year compared with local patients (hazard ratio 1.5, 95% CI 1.03-2.1, $P < .035$).

Discussion

We report our initial experience in developing and implementing a regional cardiac resuscitation center. Our primary outcome measure of survival with good neurologic outcome is comparable with the landmark investigational studies and subsequent observational experiences supporting use of therapeutic hypothermia for comatose victims of cardiac arrest.^{29,30} This confirms the feasibility and clinical effectiveness of our treatment strategy to develop a regionalized approach to post-cardiac arrest care coordinated at a hub cardiac resuscitation center.

Our results are similar to the recent Minneapolis experience, which integrated TH into a regional STEMI network and demonstrated clinical effectiveness with similar hospital survival among local and referred patients.¹⁵ Our study provides an additional demonstration of stable survival 1-year after post-cardiac arrest care. Given the high proportion of patients with favorable neurologic function at hospital discharge, this finding illustrates an important long-term benefit of organized postarrest resuscitation care rather than just a short-lived victory. Differential long-term survival among local and referred patients contrasts with our findings between the 2 groups at hospital discharge. Although we note the survival plots of these 2 groups diverge early in care, we interpret this finding with caution given the potential for unidentified confounders. Further investigation via an adequately powered study design is warranted before drawing conclusions.

We believe that our observed results are directly attributable to the timely application of evidence-based practices capable of modifying outcomes rather than simply transfer of patients to a larger medical referral center. Delays in TH were observed among referral patients despite our attempts to coordinate induction with the referring hospitals and during transport. Differential time to coronary revascularization is likewise noted. We believe that these delays are likely surrogate markers for delayed implementation of other important bundle components including hemodynamic optimization.

Operational improvement on the metric of ROSC to goal temperature was achieved for referred patients during the study period. We attribute this to improved care coordination gained through experience and feedback from our regular quality review meetings. Precedence for the time-sensitive nature of therapeutic cooling to optimize neurologic recovery warrants future work to provide early and effective TH as an important component of the care bundle.^{31,32} Our rapid management of referred STEMI patients is consistent with previous experiences and likely stems from our prior steps to optimize emergency PCI including catheterization laboratory activation based on information from referral hospitals and direct transfer of patients to the catheterization suite upon arrival.^{27,32} Research on interventions to speed efficiency of postarrest critical care support is an important future opportunity.

Our treatment bundle attempted to distill the best evidence available for incorporation into medical practice. Many of these components have been subsequently endorsed by guideline recommendations, such that our experience substantiates these core treatment aims.⁶ Recent studies have identified modifiable factors in the early postarrest window capable of impacting the post-cardiac arrest syndrome, and TH should not be viewed as the sole treatment goal.^{33,34}

Our secondary analyses provide some additional insights into postresuscitation care. Age, arrest interval, and

postarrest shock necessitating catecholamine infusion were all independently associated with adverse outcome. Similar findings are previously reported.^{3,21,32,34} However, we demonstrate a 14% rate of good neurologic outcome among patients with arrest interval >30 minutes. Mooney et al³² describe 36% survival with good neurologic outcome in a group with similar arrest interval. Initial arrest rhythm was not independently associated with good neurologic outcome in our cohort, which is also reported by Mooney et al. Furthermore, good neurologic outcome occurred in 25% of our patients with an initial nonshockable rhythm, which compares to recent experiences of TH in this patient group.³⁵ These are important findings given the uncertain impact of TH on patients with nonshockable rhythms.^{36,37} We highlight these findings to reinforce the inaccuracy of early prognostication of cardiac arrest victims based on arrest factors, and we advise against the use of arrest interval or primary arrest rhythm as a primary determinant of patient eligibility for aggressive post-cardiac arrest care including TH.³⁸ Known coronary artery disease was associated with favorable outcome. We find no precedence for this finding and hesitate to draw conclusions based on the potential for unmeasured confounders to impact this result.

Regionalization of care for patients eligible for time-sensitive therapies is an important paradigm in critical illness. The Institute of Medicine highlighted the need for regionalized and coordinated emergency care for high-risk patients in 2006.³⁹ The rationale for such an approach includes broad underutilization of proven but logistically complex interventions, selective availability of specialized resources and expertise at specific centers, and the established correlation between case volume and patient outcome as highlighted in the recent AHA regionalization statement.¹⁷ In our report, coordinated referral enabled clinicians to provide patients with timely proven therapies unavailable at referring hospitals.

The AHA recently proposed adoption of a national standardization and designation system for postarrest care facilities analogous to the current US trauma center categorization.¹⁷ Although this is a laudable goal, our results serve as an alternative interim framework to support an immediate regionalization model. Medical centers providing state-of-the-art post-cardiac arrest care may impact a greater patient population by working toward local regionalization using previously established referral relationships for other high-acuity diseases such as STEMI, trauma, and acute stroke.³²

Our report has a number of important limitations. Although we developed a guideline for patient enrollment into our clinical pathway, we acknowledge this is an uncontrolled observational experience vulnerable to potential selection bias on the part of clinicians. However, this method of accrual is a more accurate representation of what might occur in a real world, nonresearch setting. Second, our pathway leveraged an

existing medical center outreach program that included prior experience with regionalized approaches to acute critical illness.²⁷ We therefore recognize our health care system size and structure is unique and that generalization of a similar regional strategy may be impacted by local geography, population density, bed capacity, prehospital support, and established referral relationships. Lastly, our study did not investigate adverse events during interfacility transport or the impact of patient transfer on referring hospitals.

Conclusions

A regionalized approach to post-cardiac arrest care based on a referral cardiac resuscitation center is feasible and effective. Established referral relationships for other high-acuity diseases such as STEMI, trauma, and stroke serve as a proposed model for immediate regionalization of post-cardiac arrest care. Recognizing the brief therapeutic window to impact the post-cardiac arrest syndrome, efforts to initiate best practice before and during interfacility transport should be prioritized.

Disclosures

Relationship with industry disclosure: Alan Heffner, MD, has received honoraria for educational lectures on the topic of therapeutic hypothermia from Medivance, Inc.


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Appendix

Supplementary Figure 1



Post-Cardiac Arrest Resuscitation Carolinas Medical Center CODE COOL™

**For Code Cool Transfer, contact: CMC Physician Connection Line (PCL)
704-512-7878, Toll Free 877-262-6397 or Yellow Phone**



Carolinas Medical Center

Inclusion Criteria

- Adults (age \geq 18 years)
- Return of Spontaneous Circulation (ROSC) within 60 minutes of arrest
- Persistent Coma: Inability to follow commands and/or GCS < 9

Exclusion Criteria

- Severe or terminal illness with anticipated non-aggressive care
- Active hemorrhage
- Systemic infection/sepsis
- Severe refractory shock

Resuscitation Priorities

- Airway: Intubation
- Breathing
 - Avoid hyperventilation (goal PaCO₂ of 38 – 42mmHg)
 - Avoid hyperoxia (rapidly decrease FiO₂ to maintain SpO₂ >95%)
- Circulation
 - Goal MAP >70
 - Anticipate and avoid hypotension
 - Norepineprine is the preferred vasopressor
 - ECG screen for STEMI

Cooling Induction

- Initiate cooling as soon as possible after ROSC
- Refrigerated (4°C) NS 30 cc/kg IV bolus as tolerated
- Ice packs to groin, axilla and neck
- Shivering control with Propofol 10 mcg/kg/min
- Paralyze patient with Vecuronium 0.1 mg/kg q1hr

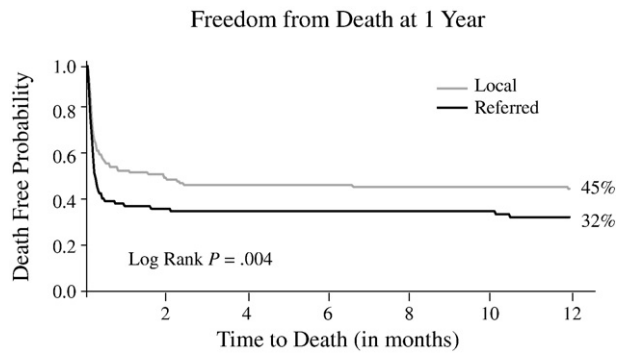
Do

- Initiate transfer early
- Use paralytics during induction phase of cooling
- Document time of arrest, time of ROSC and neuro exam

Don't

- Delay cooling for CT scanning or extensive testing before transfer, unless clinically indicated

Supplementary Figure 2



Kaplan-Meier survival analysis for freedom from death at 1-year postarrest.
