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Coronary: Short Report

Gradual Oxygen Exposure During Coronary Bypass for Acute Myocardial Infarction: A Retrospective Cohort Study

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ABSTRACT

BACKGROUND This study aimed to analyze the effect of venous vs arterial blood cardioplegia and gradual oxygen exposure during emergency bypass surgery for acute myocardial infarction (MI) and to determine its causal impact on mortality, ventricular function, readmission, and defibrillator requirement in consecutive patients.

METHODS This is a retrospective cohort study, reviewing the records of patients with acute MI brought directly to surgery during 8 years at a single center. Tabular analyses were undertaken, followed by logistic regression analysis adjusting for shock, preoperative left ventricular ejection fraction (LVEF), diabetic status, and status of ST-segment MI. Post-acute MI, post-surgery LVEF was analyzed in both groups.

RESULTS After screening of 113 charts, the analysis included 21 of 66 patients displaying hemodynamic instability or overt shock. Crude mortality was lower in treated vs control patients (2.4% vs 16%; risk ratio [RR], 0.15; 95% CI, 0.02-1.29; $P = .049$). If cardiogenic shock was present, mortality was (7.1% vs 42.9%; RR, 0.17; 95% CI, 0.018-0.98; $P = .015$). Readmission for heart failure was 12.2% vs 40.0% (RR, 0.30; 95% CI, 0.12-0.79; $P = .009$), and requirement for automatic implantable cardioverter-defibrillator was 4.9% vs 20% (RR, 0.24; 95% CI, 0.051-1.16; $P = .053$). Left ventricle functional profiles showed improvement in LVEF in the treated compared with the untreated patients (+9.5; 95% CI, +2.7-+16.3; $P = .007$).

CONCLUSIONS Early, purposeful deoxygenated blood cardioplegia administration was safe and led to improved mortality, decreased readmission for any heart failure, the requirement for an implantable defibrillator, and better ventricular recovery.

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Acute myocardial infarction (MI) with acute ventricular dysfunction leading to shock has been treated within rigid reperfusion protocols. Whether approached percutaneously (percutaneous coronary intervention [PCI]) or surgically (coronary artery bypass grafting [CABG]), outcomes remain poor. Mortality for acute MI with cardiogenic shock at 30 days is 30% to 40% and is higher when intubation or mechanical

IN SHORT

- Venous blood as a protective measure for patients with evolving myocardial infarction led to fewer deaths and readmissions for heart failure.
- Significant improvement in left ventricular function was also observed.
- This effect was enhanced in the shock subgroup, illustrating heterogeneity of treatment effect.

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circulatory support is required.[1] Survivors remain costly to care for and often require readmission, and mortality at 1 year is approximately 50%.[2] Attempts have been made to reduce infarct size by applying percutaneous mechanical circulatory support for left ventricle unloading[3] or by adding "surgical protection" (eg, cooling) to PCI but have not improved outcomes overall.[4] Exposure to hyperoxia during surgery is known to unintentionally create cardiac injury in adults and in children with cyanotic conditions.[5] Our primary aim was to study whether more gradual reoxygenation during high-acuity CABG could improve outcomes.

PATIENTS AND METHODS

This was a retrospective cohort study reviewing 113 consecutive patients admitted for CABG directly from the catheterization laboratory during 8 years at Northwestern Medicine Central DuPage Hospital. Central DuPage Hospital is a 350-bed regional referral center near Chicago. We excluded patients with anything other than acute MI and those who underwent operation on the same day for convenience. No patient was allowed to go the intensive care unit to "cool off." High-risk stress tests, even harboring critical anatomy, were excluded if the patient presented electively. Only patients with acute MI were included (ie, positive enzymes, acute unstable chest discomfort or dyspnea, and an injury pattern on 12-lead electrocardiogram). Patients with prior CABG, with prior heart failure, or on dialysis and anyone with a serum creatinine concentration above 2.5 mg/dL (men) or above 2.0 mg/dL (women) were also excluded.

DATA COLLECTION AND PRIMARY/SECONDARY OUTCOME ANALYSES. Records were reviewed by investigators from Northwestern Medicine. Acuity was confirmed, and demographic data, comorbidities, and hemodynamics were recorded. To comport with recent, "shock team" classifications, acute MI with cardiogenic shock was defined by the Society for Cardiovascular Angiography and Intervention criteria stages: stages A and B (none vs early—not in shock) to stages C to E (shock). Preoperative echocardiographic assessments were available in all cases. Follow-up echocardiograms from 3 to 6 months were accepted. Information on readmission for heart failure and defibrillator requirement was collected. Surgical mortality was the primary outcome. Readmission for heart failure with reduced ejection fraction (HFrEF), the requirement for an implantable cardioverter-defibrillator, and assessment of postoperative left ventricular function (left ventricular ejection fraction [LVEF]) were secondary outcomes. Follow-up was considered complete at 6 months for the cohort.

SURGICAL PROCEDURES. Operations were performed on bypass. Techniques of anesthesia and operation were left to the discretion of the surgeon and anesthesiologist. In the treated group, hyperoxygenation during intubation was avoided unless necessary as judged by the anesthesiologist. Initiation of bypass was adjusted. Oxygen/air mixture was 30% and raised to a maximum 50% only after the warm induction phase. Warm Buckberg cardioplegia (4:1) was given in both groups. The initial Po_2 of cardioplegia is documented in Table 1, and in the treated group, the "ramp-up" strategy was complete within approximately 10 minutes in all patients. The strategy was accomplished without the need for a second oxygenator. Oxygen administration was liberalized during and after coming off bypass. Transfusion of blood or blood products was decided by the teams.

STATISTICAL ANALYSIS. Data analysis was carried out in R version 4.2.2 (R Foundation for Statistical Computing). We assumed no unmeasured confounding at baseline and monitored death during follow-up by EPIC medical records. We used tabular analyses of the dichotomous exposure and outcomes to obtain crude risk ratios (RRs), where appropriate, and calculated z-squared statistics and a χ^2 distribution with 1 degree of freedom. Repeated measures of LVEF were unbalanced. Paired t-test analysis of the mean response differences within groups was carried out, followed by a between-group 2-sample t-test. We estimated mean values at baseline and at the repeated measurement times and assumed missing data points for follow-up LVEF were missing at random (R-code; see Supplemental Appendix). Approval was obtained from the institutional review board at Northwestern Medicine Central DuPage Hospital.

RESULTS

Descriptive statistics and baseline clinical characteristics are shown in Table 1. Continuous data are reported as mean ± standard deviation and dichotomous variables as proportions. There is relative homogeneity of patient characteristics supporting our assumption of a lack of important baseline confounding. Only the Po_2 of the initial cardioplegia differed importantly between the groups, mean of 404 ± 105 mm Hg vs 49 ± 14

mm Hg (difference, 355 mm Hg; 95% CI, 317-395 mm Hg; $P < .0001$), and clamp and bypass times were similar (Supplemental Figure).

The treated group experienced lower overall mortality (2.44% vs 16%; RR, 0.15; 95% CI, 0.018-1.29; $P = .049$). The difference on the additive scale (Table 2) was even more pronounced in patients with cardiogenic shock (7.1% vs 42.9%; RR, 0.17; 95% CI, 0.018-0.980; $P = .015$; Supplemental Figure). We observed improvement in ventricular function on follow-up in the treated patients vs a clinically unimportant decrease in LVEF in the untreated patients (paired *t*-test for the mean within-group difference in the treated group was +8.48% (95% CI, +5.2-+11.8; $P < .0001$) vs -1.0% (95% CI, −7.7% to +5.0%; $P = .24$) in the untreated group. The between-group difference gave an estimate of +9.5% in the treated patients (95% CI, +5.4%-+16.9%; $P = .007$). Readmission for HFrEF, within 3 to 6 months, was less common in the treated patients (12.2% vs 40%; RR, 0.305; 95% CI, 0.12-0.79; $P = .009$), as was any diagnosis of ambulatory HFrEF up to 6 months of follow-up (9.8% vs 28%; RR, 0.35; 95% CI, 0.11-1.07; $P = .054$). Last, the requirement for insertion of a permanent defibrillator during 6 months of follow-up was 4.9% vs 20% (RR, 0.24; 95% CI, 0.05-1.16; $P = .053$). Parametric logistic regression analysis (Supplemental Table), using both crude and adjusted models for variables assumed to be strong potential predictors of the outcome, confirmed the reported findings as observed with the tabular analysis. We assessed the length of stay as a surrogate for overall morbidity and found no difference between the groups.

TABLE 1 Demographic and Clinical Characteristics

Variable	Hyperoxic (n = 25)	Controlled Oxygen (n = 41)	Total (N = 66)
Age, y	65.7 ± 9.98	62.4 ± 10.1	63.7 ± 10.1
Sex			
Male	19 (76.0)	36 (87.8)	55 (83.3)
Female	6 (24.0)	5 (12.2)	11 (16.7)
Hypertension			
Yes	13 (52.0)	20 (48.8)	33 (50.0)
No	12 (48.0)	21 (51.2)	33 (50.0)
Diabetes mellitus			
Diabetic	7 (28.0)	13 (31.7)	20 (30.3)
Not diabetic	18 (72.0)	28 (68.3)	46 (69.7)
Preoperative EF, %	41.2 ± 9.90	43.6 ± 13.1	42.7 ± 12.0
Shock			
Yes	7 (28.0)	14 (34.1)	21 (31.8)
No	18 (72.0)	27 (65.9)	45 (68.2)
STEMI			
Non-STEMI	18 (72.0)	27 (65.9)	45 (68.2)
STEMI	7 (28.0)	14 (34.1)	21 (31.8)
IABP			
Yes	21 (84.0)	36 (87.8)	57 (86.4)
No	4 (16.0)	5 (12.2)	9 (13.6)
Cardioplegia Po_2, mm Hg	404 ± 125	48.7 ± 14.0	183 ± 190
Time on bypass, min	89.0 ± 36.3	84.3 ± 26.5	86.1 ± 30.4
Cross-clamp, min	36.6 ± 11.5	44.2 ± 16.2	41.3 ± 15.0
Smoker			
Nonsmoker	19 (76.0)	29 (70.7)	48 (72.7)
Smoker	6 (24.0)	12 (29.3)	18 (27.3)
Any_hypotension	0.360 ± 0.490	0.463 ± 0.505	0.424 ± 0.498
Acute HF			
No	21 (84.0)	30 (73.2)	51 (77.3)
Yes	4 (16.0)	11 (26.8)	15 (22.7)
HgA_{1c} on admission, %	6.79 ± 1.92	6.27 ± 1.68	6.47 ± 1.78
ASA			
Not on ASA	13 (52.0)	22 (53.7)	35 (53.0)
ASA	12 (48.0)	19 (46.3)	31 (47.0)

Categorical variables are presented as number (percentage). Continuous variables are presented as mean ± SD. ASA, aspirin; EF, ejection fraction; HF, heart failure; HgA_{1c}, glycated hemoglobin; IABP, intra-aortic balloon pump; STEMI, ST-segment elevation myocardial infarction.

COMMENT

Our analysis describes improvement in outcomes after controlling oxygen tension during early resuscitation of the heart, a therapy directed at the molecular consequences of reperfusion/reoxygenation itself. As ischemic conditions progress with time, it is recognized that hyperoxia leads to oxidative damage by a variety of mechanisms published elsewhere.[5,6] We did not specifically measure indices of postoperative cellular injury because they are difficult to interpret in this setting. We are aware of no prior report showing a clear causal contrast in mortality using a therapy designed to mitigate reperfusion injury by confronting this known molecular mechanism. By comparison, other observational reports seem methodologically confounded and either allow patients to "cool off" before surgery or exclude the sickest patients. Herein, we report mortality lower than outcomes from The Society of Thoracic Surgeons database[7] and the National Cardiogenic Shock Initiative,[8] improved recovery, and lower readmission in a retrospective cohort displaying no important baseline confounding. This supports the idea that individualized myocardial protection and percutaneously applied strategies mimicking surgical protection during acute ischemia should be explored further. This report suggests a promising solution because myocardial protection science and PCI have never converged as, for example, with transcatheter valve interventions (transcatheter aortic valve replacement). "One-size-fits-all" but "hurry-up"

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TABLE 2 Outcomes

Variable	Treated, No. (%)	Control, No. (%)	Risk Ratio (95% CI)	*P* Value
Mortality				
Entire group	1 (2.4)	4 (16)	0.152 (0.018–1.29)	.043
N = 66	n = 41	n = 25		
Shock	1 (7.1)	3 (42.9)	0.168 (0.02–1.32)	.049
N = 21	n = 14	n = 7		
Readmission	5 (12.2)	10 (40)	0.305 (0.118–0.789)	.009
Ambulatory CHF	4 (9.8)	7 (28)	0.348 (0.113–1.07)	.054
AICD	2 (4.9)	5 (20)	0.244 (0.051–1.16)	.053
Follow-up LVEF, *t*-test				
Within group δ	+8.5% (5.1–11.5)*	−1.0% (−2.0 to −7.7)**		
Between group δ	+9.5% (2.7–16.3)			.007

*Within group-paired *t*-test; **between group-two sample *t*-test. AICD, automatic implantable cardioverter-defibrillator; CHF, congestive heart failure; LVEF, left ventricular ejection fraction.

strategies and the administration of supplemental oxygen remain almost routine, despite this and other compelling clinical observations suggesting potential harm.[9]

No baseline imbalance was observed in potential confounding variables, supporting a causal contrast, always challenging with observational data.[10] The analysis also illustrates the important notion of "heterogeneity of treatment effect" in the consideration of tailoring individual therapy (Supplemental Figure). The enhanced effect observed in the shock subgroup is not surprising because advanced ischemic conditions are known to set the stage for the additive injury described. The improvement in recovery of left ventricular function in the treated group was not surprising, given our inferences regarding enhanced protection.

The major limitation of the analysis is sample size, even with data gathered at a busy community referral center (Supplemental Table). As a result, the estimates lack precision. The analysis is retrospective, which is a valid limitation of such studies. A randomized trial is required because such patients have seemed to present an unsolvable problem with high mortality and morbidity among survivors; however, our report is promising.

The Supplemental Material can be viewed in the online version of this article [https://doi.org/10.1016/j.atssr.2025.01.013] on http://www.annalsthoracicsurgery.org.

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DISCLOSURES

Neil J. Thomas reports a relationship with Rheoxtech, Inc that includes: board membership and equity or stocks; and has a patent issued to Rheoxtech, Inc. Arif Jivan reports a relationship with Rheoxtech, Inc that includes: consulting or advisory. Paul Connors reports a relationship with Rheoxtech, Inc that includes: employment.

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