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Seasonal Incidence of Emergent Coronary Artery Bypass Grafting Surgery

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ABSTRACT

Background: Emergent coronary artery bypass grafting (CABG) surgery is often required in the case of severe coronary artery disease, which is refractory to traditional management. The objective of our study was to test the hypothesis that there is seasonal variation in the incidence of emergent CABG.

Methods: A sinusoidal logistic regression model was used to analyze operative data at our cardiovascular institute of 270 cases spanning 5939 calendar days.

Results: A cyclic peak risk for emergent CABG was observed for late winter (calendar day 66; $P = .036$). The odds ratios for the 1-, 2- and 3-month window surrounding this peak were 1.8 (95% CI = 0.94-3.5, $P = .072$), 1.6 (95% CI = 1.06-2.5, $P = .024$) and 1.4 (95% CI = 0.9-1.8, $P = .066$), respectively.

Conclusion: Our results suggest that a seasonal variation may exist in the incidence of patients presenting with severe coronary artery disease requiring emergent CABG. This information is useful in the scheduling of hospital resources and staff. It also provides important etiology clues underlying coronary artery disease that may lead to future interventions or targeted therapies.

INTRODUCTION

Emergent coronary artery bypass grafting (CABG) is a rarely performed procedure (~3.2-10.9% of CABG cases) that is reserved for the most severe cases of acute coronary syndrome (ACS) refractory to traditional management [Kaul 1995; Stone 2000; Kjaergard 2004]. The majority of patients presenting with ACS are assigned to medical management, fibrinolytic therapy, or primary percutaneous coronary intervention (PCI) [Hillis 2011]. Less than 1% of ACS cases involving PCI require emergent CABG [Roy 2009].

Variation in incidence of emergent CABG by season may be indicative of an underlying pathophysiological mechanism for severe CAD that has chronobiological significance. The aim of this study was to test the hypothesis that incidence of emergent CABG varies seasonally in patients presenting with ACS.

MATERIAL AND METHODS

Study Design

This study population included patients who were admitted for ACS and received primary isolated emergent CABG from January 1, 1995 to March 31, 2011. Demographics, comorbidities, and disease severity were collected at the time

Table 1. Patient Characteristics (n = 270)

Age, y, mean ± SD, median (IQR)	62 ± 12, 63 (16)
Male (%)	166 (61)
White (%)	230 (85)
BMI, kg/m^2, mean ± SD, median (IQR)	30 ± 5.9, 29 (6.4)
Hypertension (%)	193 (71)
Recent smoker (%)	67 (24)
Cerebrovascular disease (%)	19 (7)
Peripheral arterial disease (%)	35 (13)
Number of vessel disease	
One vessel	59 (22)
Two vessel	93 (34)
Three vessel	118 (44)
Left main disease	62 (23)
Diabetes	68 (25)
Chronic heart failure	41 (15)

IQR indicates interquartile range; SD, standard deviation; BMI, body mass index.

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of surgery. The analysis and waiver of consent were approved by the Institutional Review Board at the Brody School of Medicine, East Carolina University.

Emergent CABG

Patients receiving emergent CABG presented with left main and/or 3-vessel coronary artery disease (CAD), ongoing ischemia after failed PCI, coronary anatomy not amenable to PCI, a mechanical complication of STEMI, or cardiogenic shock [Hillis 2011].

Setting

Located in a rural and predominately agricultural region of the state, the East Carolina Heart Institute is the largest stand-alone tertiary referral hospital dedicated to cardiovascular care in North Carolina. Nearly all patients who underwent emergent CABG at our facility lived within 150-mile radius of the medical center. Complications of CAD are a leading cause of mortality in North Carolina with an unequal burden occurring in the eastern part of the state [Morris 2012].

Data Collection

Clinical data were obtained from the Society of Thoracic Surgeons Adult Cardiac Surgery Database and the electronic medical record at the Brody School of Medicine, East Carolina University. Validation and accuracy of the data are routinely checked by trained staff at the Center for Epidemiology and Outcomes Research at the East Carolina Heart Institute. Additionally, multiple logic algorithms are applied to reduce mismatching of patient data across clinics. Meteorological measurements over the timeframe of the study were obtained from the Meteorological Assimilation Data Ingest System and the Automated Surface Observing System (ASOS) [McMahon 1993].

Statistical Analysis

Categorical variables were displayed as frequency and percentage while continuous variables were presented as a mean (plus or minus 1 standard deviation [SD]), median, and interquartile range (IQR). Instead of using the number of events as the unit of analysis, we used calendar day in which the event occurred for seasonality comparisons, assuming that population denominators remained constant throughout the year. Case days were defined as those in which patients received emergent CABG, while referent days were defined as days with no event. Sinusoidal logistic regression was used to model seasonal risk of emergent CABG, adjusting for calendar year [Crump 2014]. In this method, peak calendar day of risk (tmax) is iteratively computed from the regression term for harmonic displacement, where (DOY) denotes calendar day of the year. The latter was plotted against harmonic displacement to graphically depict maximum and minimum seasonal risk. Odds ratios (OR) and 95% confidence intervals (CI) were used as the measure of association. The 1-, 2-, and 3-month OR windows were estimated by centering on the day of maximum versus minimum risk.

Rounding was performed using standard epidemiologic methods [Holly 1989]. Friedman's two-way analysis of variance was used to test the null hypothesis that meteorological measurement for case and referent days were the same, adjusting for year of admission [Friedman 1937]. Meteorological data were missing for ~7% of the days analyzed. An iterative expectation-maximization (EM) algorithm was used to impute missing values [Dempster 1977; Little 2012; Ware 2012]. Imputational relative efficacy for each variable exceeded 99%. Model calibration was assessed using the Hosmer-Lemeshow test [Hosmer 2013]. Statistical significance was defined as $P < .05$. SAS version 9.4 (Cary, NC) was used for analyses.

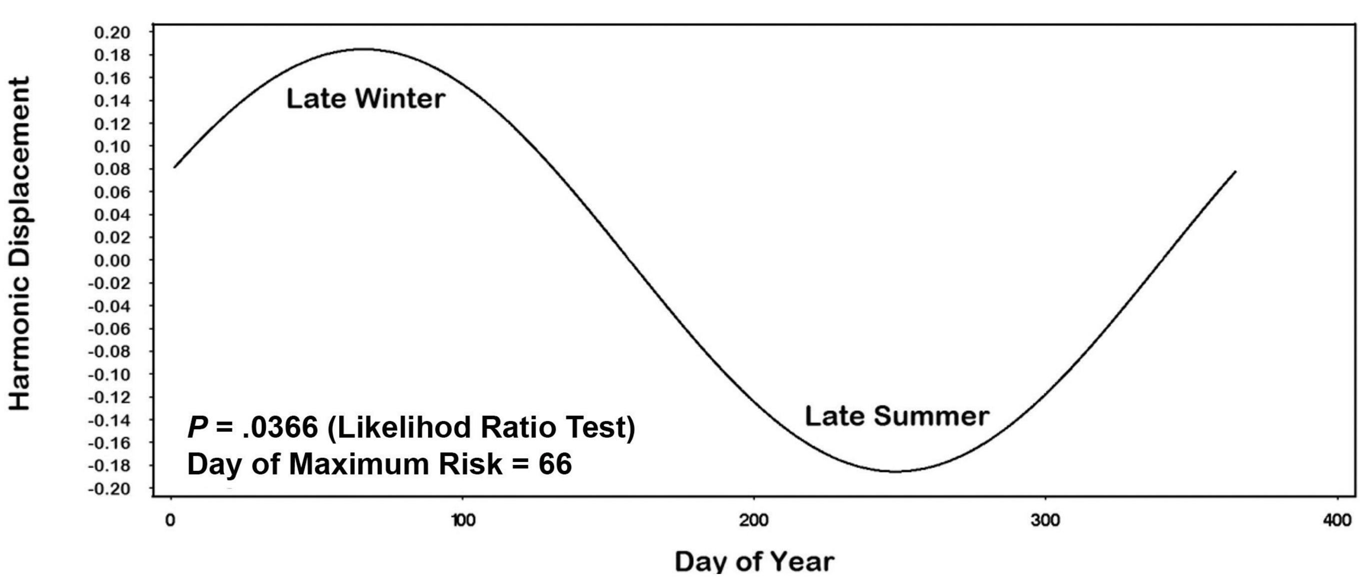

Figure 1. Sinusoidal risk model for emergent CABG.

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Table 2. One-, Two- and Three-Month Window Zenith to Nadir Comparisons

	Case days, n (%)	Referent days, n (%)	OR (95% CI)	*P*†*
1-month window				
Nadir	14 (35)	482 (49)	1.0 Referent	.072
Zenith	26 (65)	504 (51)	1.8 (0.94-3.5)	
2-month window				
Nadir	36 (38)	940 (49)	1.0 Referent	.024
Zenith	59 (62)	978 (51)	1.6 (1.06-2.5)	
3-month window				
Nadir	64 (42)	1393 (49)	1.0 Referent	.066
Zenith	88 (58)	1444 (51)	1.4 (0.98-1.9)	

CI indicates confidence interval; OR, odds ratio.
*Likelihood ratio test.
†Adjusted for calendar year.

Table 3. Daily Meteorological Measurements

	Case days (n = 270) mean ± SD, median (IQR)	Referent days (n = 5669) mean ± SD, median (IQR)	*P**
Barometric pressure (inches of Hg)†			
Maximum	30 ± 0.17, 30 (0.23)	30 ± 0.17, 30 (0.23)	.85
Minimum	30 ± 0.19, 30 (0.22)	30 ± 0.19, 30 (0.23)	.72
Humidity (%)			
Maximum	86 ± 11, 87 (13)	88 ± 10, 88 (12)	.85
Minimum	45 ± 16, 43 (21)	43 ± 16, 41 (19)	.64
Dew point (F)			
Maximum	54 ± 15, 57 (25)	55 ± 16, 57 (25)	.36
Minimum	42 ± 17, 43 (28)	43 ± 18, 45 (31)	.40
Temperature (F)			
Maximum	71 ± 16, 73 (24)	72 ± 16, 75 (26)	.32
Minimum	50 ± 16, 51 (28)	52 ± 16, 53 (29)	.33
Length of visible light (min)			
Mean	727 ± 97, 728 (189)	730 ± 100, 730 (193)	.65

IQR indicates interquartile range; Hg, hydragyrum (mercury).
*Friedman's non-parametric 2-way analysis of variance, controlling for calendar year.
†Sea level.

RESULTS

Our analysis included 270 case days and 5669 referent days. The mean age of patients undergoing emergent CABG was 62 ± 12 years (Table 1). Approximately 61% were males and 85% were white. The majority of cases involved 3-vessel CAD (44%) and 23% had left main disease.

A statistically significant peak risk for emergent CABG was observed for late winter (calendar day 66; *P* = .036) (Figure 1). The ORs corresponding to the 1-, 2- and 3-month window surrounding the day of peak risk were 1.8 (95% CI = 0.94-3.5, *P* = .072), 1.6 (95% CI = 1.06-2.5, *P* = .024) and 1.4 (95% CI = 0.9-1.8, *P* = .066) (Table 2). Average daily meteorological measurements by month were similar between case and referent days (Table 3, Figures 2 and 3).

DISCUSSION

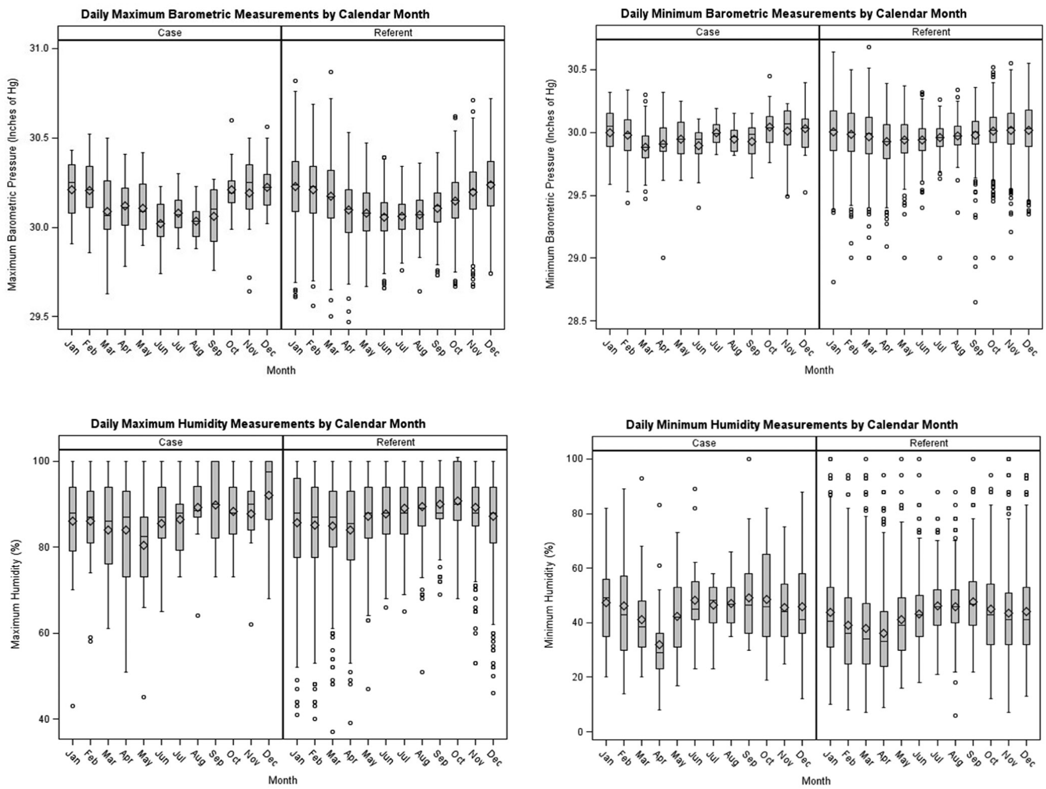
In this retrospective cohort series of 5939 consecutive days of risk, incidence of emergent CABG was observed to have a sinusoidal distribution with a peak in late winter. To our knowledge, this is the first manuscript to address the seasonal incidence of emergent CABG.

Several studies have examined the relationship between season and incidence of cardiovascular disease [Stewart 2002; Konuralp 2002; Spencer 1998; Arntz 2000; Efird 2014; Master 1937]. Increased morbidity and mortality of acute myocardial infarction (AMI) during winter was first reported in the 1930s [Master 1937]. Recently, seasonal variation in incidence of AMI was observed in a large multi-centric study in the United States, with the highest relative difference (43%) occurring during winter versus summer months in the South Atlantic region [Spencer 1998]. Similarly, peak seasonal incidence for sudden cardiac death (SCD) was observed during winter in a population-based analysis of over 20,000 cases in Germany [Arntz 2000]. In another study conducted in Olmstead County, Minnesota, incidence of SCD, but not MI, reportedly increased in winter compared with summer [Gerber 2006]. In contrast, some studies observed a peak incidence during spring and summer for AMI and coronary stent thrombosis, respectively [Mahmoud 2011; Kriszbacher 2008].

Limited data exist on seasonal incidence of specific interventions for MI. A single center study in Istanbul, Turkey, reported that more CABG procedures were performed in winter (28%) than summer (24%). However, these results may have been attributable to patient or surgeon preference for scheduling elective CABG [Konuralp 2002]. To our knowledge, no studies to date have been conducted on severe CAD requiring invasive emergent interventions such as CABG.

Our findings of a late winter peak for emergent CABG may be explained by seasonal variation of cardiovascular risk factors such as increases in sympathetic tone, respiratory tract infections, prothrombotics, and blood viscosity in winter months [Scherlag 1990; Woodhouse 1994; Keatinge 1984; Horan 2001]. Cumulative seasonal exposure to environmental and behavioral factors also may underlie our result. For example, dietary cholesterol has been shown to fluctuate seasonally with a winter peak. The Seasonal Variation of Blood Cholesterol Study (SEASONS) of 600 patients at 3-week

A



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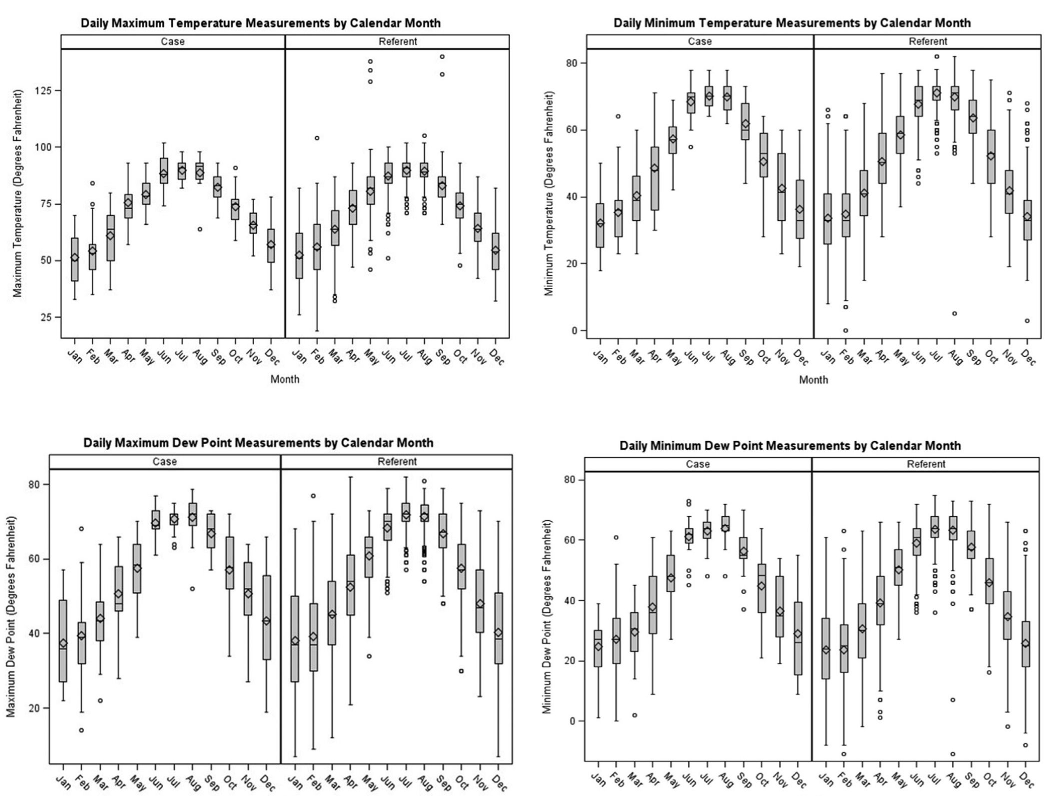

Figure 2. A, Maximum (left) and minimum (right) daily averages of barometric pressure and humidity by month for case (left panel) and referent days (right panel). B, Maximum (left) and minimum (right) daily averages of temperature and dew point by month for case (left panel) and referent days (right panel).

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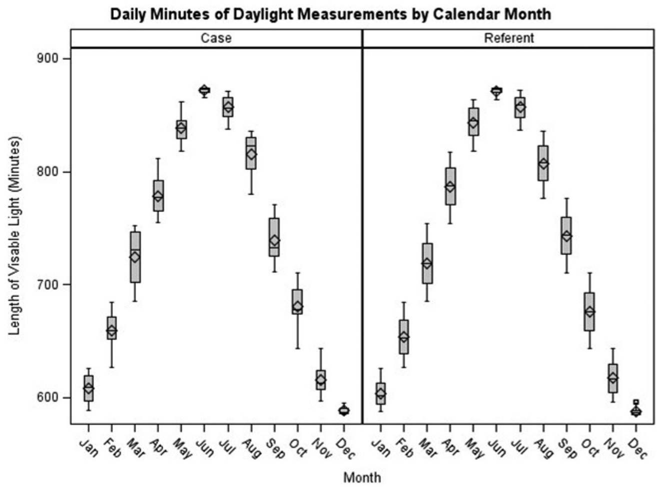

Figure 3. Monthly averages for daily minutes of sunlight between case (left panel) and referent (right panel).

intervals observed a 22% increase in total blood cholesterol during winter versus summer months [Ockene 2004; Merriam 1999]. Similarly, physical inactivity, poor diet and exposure to second hand smoke have been noted to peak during winter [Ma 2006; Arku 2015]. Conceivably, ignoring symptoms and delaying care for chest pain during the winter holiday season may underlie the degree of severity of CAD that was observed in patients requiring emergent CABG.

Another potential explanation of our results may be seasonal variation of meteorological conditions as reported in some studies of AMI and arrhythmias [Schneider 2008; Marchant 1993]. However, we did not observe any statistically significant differences between case and referent days for temperature, barometric pressure, humidity, dewpoint, and hours of sunlight.

Several limitations should be noted when evaluating our results. Those who died prior to surgery were not included in this analysis. However, any bias associated with case-fatality likely would have been non-differential in nature. Our unit of analysis was calendar day and thus we were unable to control for demographic and clinical factors. The assessment of environmental and behavioral exposures was outside of the scope of the current study.

In conclusion, we observed a seasonal variation in incidence of emergent CABG with a late winter peak. Further studies allowing for the inclusion of clinical, environmental, and behavioral factors are warranted to better understand the pathophysiologic mechanisms underlying our results.

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