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Intraoperative Systolic Blood Pressure Variability Predicts 30-day Mortality in Aortocoronary Bypass Surgery Patients

Solomon Aronson, M.D.,* Mark Stafford-Smith, M.D.,* Barbara Phillips-Bute, Ph.D.,† Andrew Shaw, M.D.,‡ Jeffrey Gaca, M.D.,§ Mark Newman, M.D.*; for members of the Cardiothoracic Anesthesiology Research Endeavors‖

ABSTRACT

Background: Few data support an association between blood pressure variability and clinical outcomes during cardiac surgery. We tested the hypothesis that intraoperative systolic blood pressure variability outside a targeted blood pressure range predicts 30-day mortality in patients undergoing cardiac surgery.

Methods: Electronically captured blood pressure data from 7,504 consecutive coronary bypass surgery procedures between September 1, 1996, and December 31, 2005, were divided into development and validation cohorts. Systolic blood pressure variability episodes outside a blood pressure range (*e.g.*, higher than 135 or lower than 95 mmHg) were characterized by number of episodes, magnitude of episode, duration of episode, and magnitude × duration of excursion (*i.e.*, area under the curve). Multiple logistic regression analysis was used to assess 30-day mortality association. The most predictive mortality risk characteristic and blood pressure range was tested in the validation cohort.

Results: A total of 3.1 million intraoperative blood pressure evaluations were analyzed. Systolic blood pressure variability was derived in 5,038 patients and validated in 2,466 patients (8% without cardiopulmonary bypass and 6% with valve procedure). Among all tested indices of blood pressure variability, mean duration of systolic excursion (outside a range of 105–130 mmHg) was most predictive of 30-day mortality (odds ratio = 1.03 per minute, 95% CI 1.02–1.39, $P < 0.0001$).

Conclusions: Intraoperative blood pressure variability is associated with 30-day postoperative mortality in patients undergoing aortocoronary bypass surgery.

What We Already Know about This Topic

- Blood pressure variability during surgery has been associated with postoperative adverse events
- These studies included a small number of patients and intermittent manual recording of blood pressure

What This Article Tells Us That Is New

- In electronically captured blood pressure recording in more than 7,500 consecutive cardiac surgery patients, blood pressure variability was independently associated with an increased 30-day mortality, and although the absolute increased risk was small (3% for systolic blood pressure outside 105–130 mmHg), intraoperative systolic blood pressure variability may represent an important modifiable risk factor for 30-day mortality

FOR nearly a century, arterial blood pressure has been adopted as the cornerstone for clinical evaluation of cardiovascular function and risk. Poorly controlled blood pressure represents a major risk factor for cardiac, renal, cerebral, and metabolic dysfunction outcomes.[1–3]

Hypertension, as a preexisting condition, exists in more than two thirds of the elderly surgical population in the United States, with upward of 80% prevalence in those requiring cardiac surgery,[1,2,4–6] and remains a significant contributor to postoperative risk.[4–10]

Acute intraoperative changes in blood pressure, although a common consequence of preexisting hypertension, may also be a consequence of excessive release of catecholamines, rapid intravascular volume shifts, peripheral vasoconstriction, reduced

* Professor, † Assistant Professor, ‡ Associate Professor, Department of Anesthesiology, § Assistant Professor, Department of Surgery, Cardiovascular Division, Duke University Medical Center, Durham, North Carolina. ‖ See appendix for members of Cardiothoracic Anesthesiology Research Endeavors.

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Address correspondence to Dr. Aronson: Professor of Anesthesiology, Department of Anesthesiology, Duke South, Baker House Room 102, DUMC Box 3094, Durham North Carolina, 27710. arons002@mc.duke.edu.

baroreceptor sensitivity, renin-angiotensin activation, altered cardiac reflexes, inadequate anesthesia, reperfusion injury, aortic occlusive clamps, as well as neural, humoral, and cellular responses.[11] These factors, separately or in combination, could trigger hyperinflammatory and procoagulation conditions,[12] including platelet activation,[13] which may compromise microvascular blood flow. In addition, perioperative hypertension increases myocardial oxygen consumption, increases left ventricular end-diastolic pressure, and increases the risk of surgical bleeding from anastamotic sites,[11] whereas perioperative hypotension contributes to subendocardial hypoperfusion and myocardial ischemia.

Despite what has been learned about characterization of blood pressure subtypes, associated risk of hypertension or hypotension, autoregulation shifts, and efficacy of therapy,[4,9,10,14–16] few data have been presented regarding optimal intraoperative blood pressure, with treatment guidelines poorly defined and nearly untested in this setting.

An association between perioperative systolic blood pressure bandwidth (in other words, systolic blood pressure excursions outside a target systolic blood pressure range; *e.g.*, systolic blood pressure higher than 135 or less than 65 mmHg) and 30-day adverse events has been found.# Data demonstrating increased therapeutic differentiation (*i.e.*, drug differences, based on class and or pharmacokinetics, to control blood pressure within a target range) as blood pressure bandwidth narrowed (*e.g.*, higher than 135 or less than 95 mmHg) have also been reported.[17] However, these data were limited because of a relatively small sample size, reliance on manual recording of blood pressure, infrequent blood pressure capture frequency, and *post hoc* analysis. Here we test a large cohort of similar cardiac surgical patients, using nearly continuous electronic data that capture the association between intraoperative systolic blood pressure variability as a surrogate of blood pressure control and 30-day postoperative mortality.

Materials and Methods

Study Population

With Institutional Review Board approval (Duke University Medical Center, Durham, North Carolina), we retrospectively studied a cohort of 7,808 consecutive patients undergoing primary nonemergent aorto-coronary bypass surgery procedures performed at Duke University Medical Center between September 1, 1996, and December 30, 2005. Intraoperative blood pressure was captured electronically after arterial line placement every 30 s in all patients. In addition, perioperative data, including 30-day mortality data, were accessed from the prospectively collected Duke Databank for Cardiovascular Diseases. In-hospital complications were classified using the Society of Thoracic Surgeons criteria.** The Databank is prospectively compiled from contemporaneous medical records, custom datasheets, and records of laboratory results. Database quality assurance involves random chart review for data confirmation and assessment of data completeness.

Long-term follow-up data were obtained from the follow-up group of the Duke Clinical Research Institute, which collects annual follow-up mortality data and nonfatal endpoint information for the Duke Databank for Cardiovascular Diseases. The annual surveys collect data on general health, hospitalizations, myocardial infarction, stroke, cardiac procedures, and medication use. Patients are surveyed 6 months after an index visit and yearly thereafter with a mailed, self-administered survey or a phone-administered survey to nonresponders.

Follow-up is 95% complete for mortality, and patients who are lost to follow-up (2%) or who have asked to be withdrawn (3%) are submitted for an annual search of the National Death Index. Death information is collected from next-of-kin interviews, hospital discharge summaries, death certificates, or cause of death provided from the National Death Index. Cause of death is assigned after agreement from independent reviews by a death committee from the Duke Clinical Research Institute.

Study Design and Conduct

For analysis, the study sample was *a priori* divided randomly into hypothesis development and validation cohorts using a 66 to 33% sample division. All endpoints were specified in advance of data gathering and analysis. The study was conceived and designed by S.A., the data gathered and analyzed by S.A., M.S.S., A.S., and B.P.B. The manuscript was reviewed by J.G. and M.N.

Blood Pressure Analysis

Intraarterial catheter blood pressure values were recorded in the operating room every 30 s using an automated anesthesia record-keeping system. For purposes of the study, baseline blood pressure was defined as the median of the first five values recorded while the patient was awake and mildly sedated before anesthesia induction.

Development Phase

Independent Variable—Systolic Blood Pressure Variability. Systolic blood pressure values recorded less than 20 or greater than 299 mmHg were considered erroneous and excluded from analysis. Measurements made during cardiopulmonary bypass were excluded. Based on *a priori* evidence,[17] the systolic blood pressure variability index area under the curve was assessed. Area under the curve is a continuous variable that reflects an integral of degree and duration of pressure incursions described in units of millimeters of mercury per minute.

- Three area under the curve variables were calculated for various systolic threshold criteria: area above a value (*e.g.*,

Aronson S, Dyke C, Kereiakes D, Levy JH, Lumb P, Cheung A, Corwin H, Stierer K, Newman M: Blood pressure control is an independent predictor of short-term mortality in cardiac surgery patients: Analysis from the three randomized ECLIPSE trials. ACC 07 Late-Breaking Clinical Trials II. Presented at the American College of Cardiology 56th annual scientific session, March 24–27, 2007, New Orleans, LA, presentation number: 412–5.

** Society of Thoracic Surgeons Web site for complication criteria definition. Available at: http://www.sts.org. Accessed February 25, 2010.

135 mmHg), area below a value (*e.g.*, 95 mmHg), or the combined areas beyond a range (*e.g.*, higher than 135 or less than 95 mmHg).
- In addition, the isolated systolic blood pressure variables of, magnitude of excursion above or below a criteria blood pressure range, duration of episodes above or below a criteria blood pressure range, and number of episodes above or below a criteria blood pressure range were described separately and tested as outlined below to better understand which blood pressure index most likely predicts adverse postoperative outcome.
- Magnitude of excursion was characterized as an absolute value by the difference between the criteria threshold (*e.g.*, higher than 135 or less than 95 mmHg) and peak (for excursions above) or nadir (for excursions below) systolic blood pressure values. Peak or nadir values were averaged for a subject to determine the mean excursion value (millimeters of mercury). For values beyond a range (*e.g.*, higher than 135 or less than 95 mmHg), a mean maximum excursion value was also determined.
- Duration of excursion variables were described and calculated for various systolic threshold criteria: above a value (*e.g.*, 135 mmHg), below a value (*e.g.*, 95 mmHg), or the combined duration of excursion beyond a range (*e.g.*, higher than 135 or less than 95 mmHg).
- Number of excursions above (*e.g.*, 135 mmHg), below (*e.g.*, 95 mmHg), and above or below range criteria (*e.g.*, higher than 135 or less than 95 mmHg) was also tested.

Dependent Variable—Postoperative Mortality. Mortality risk factors evaluated were those identified by Parsonnet *et al.*[18] in their assessment of preoperative risk factors specific to coronary bypass surgery and coronary bypass surgery/valve surgery. In addition, the parameter of surgery duration was included for analysis as a marker of procedure complexity and risk, because it is directly correlated with factors such as number of coronary grafts performed and is significantly associated with in-hospital mortality.[19] Finally, we further assessed the association of systolic blood pressure variability during surgery with outcome by including an investigation of possible confounding effects of aprotonin use.[20]

Statistical Analysis

Associations between measures of systolic blood pressure variability and 30-day mortality were investigated using separate multivariable logistic regression models, adjusted for surgery length and Parsonnet score. Because previous research# has suggested that cumulative perioperative blood pressure excursion (area under the curve) beyond a systolic blood pressure range (*e.g.*, higher than 135 or less than 95 mmHg) predict adverse outcome after cardiac surgery, our initial analyses sought to validate this association.

In addition, we sought to determine whether other systolic blood pressure index or thresholds also demonstrated a predictive association with 30-day mortality, thus we then explored other characteristics of "systolic blood pressure variability," as outlined earlier, for their association with mortality (30 day and long term). Candidate criteria for systolic blood pressure variability were those surrounding the confirmed values from the previously published criteria (*i.e.*, $>$ 135 or $<$ 95 mmHg).# For the upper bound, thresholds considered were 120, 125, 130, 135, 140, 145, 150, and 180 mmHg. For the lower bound, thresholds considered were 110, 105, 100, 95, 90, 85, 80, and 60 mmHg. Each value was investigated separately in a multivariable model including case length and Parsonnet score. The three most predictive upper and lower blood pressure values were then com-

Table 1. Patient Characteristics

	Development Sample (N = 5,038)	Validation Sample (N = 2,466)
Age, median (IQR), yr	65 (56–73)	66 (57–73)
Male, %	68	68
White, %	86	86
History of hypertension, %	70	70
Congestive heart failure, %	17	17
Chronic obstructive pulmonary disease, %	11	11
Previous myocardial infarction, %	42	42
CABG, % Previous	18	17
Diabetes, %	33	33
Intraaortic balloon pump, %	9	8
Aprotinin given, %	10	7
Baseline systolic, median (IQR)	141 (122–161)	141 (122–161)
Baseline diastolic, median (IQR)	64 (56–72)	64 (55–72)
Preoperative creatinine, median (IQR)	1.0 (0.9–1.2)	1.0 (0.9–1.2)
Preoperative hematocrit, median (IQR)	40 (36–43)	40 (36–42)
BMI, median (IQR)	28 (25–32)	28 (25–31)
Nitroprusside, %	45	45
Parsonett risk score, median (IQR)	7 (3–12)	7 (3–13)
Surgery duration, min, median (IQR)	197 (132–286)	190 (131–288)
CPB duration, min, median (IQR)	106 (83–133)	109 (85–134)
Cross-clamp duration, min, median (IQR)	60 (45–80)	60 (46–81)
Procedure type		
CABG Only on pump (%)	86	86
CABG + valve	6	6
Off pump	8	8

BMI = body mass index; CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; IQR = interquartile range (25th–75th percentile).

Table 2. Characterizations of Blood Pressure Variability and Association with 30-day Mortality in the Development Sample

Blood Pressure Descriptor	*P* Value	Odds Ratio	95% CI	Median (25th–75th Percentile)
AUC for 95/135 (mmHg · min)	0.006	1.03*	1.007–1.044	930 (424–2707)
AUC < 95 (mmHg · min)	0.03	1.02*	1.002–1.041	447 (130–1584)
AUC > 135 (mmHg · min)	0.16	1.02*	0.991–1.055	207 (71–443)
AUC for 20% (mmHg · min)	0.85	1.00*	0.994–1.008	2268 (702–5698)
Total Incursions	0.03	0.96	0.926–0.997	13 (9–17)
Incursions > 135	0.79	0.99	0.929–1.058	4 (2–6)
Incursion < 95	0.02	0.95	0.916–0.994	9 (5–13)
Cumulative minutes > 135 or < 95 mmHg	0.02	1.01	1.001–1.012	17.7 (3.1–6.8)
Minutes > 135 or < 95 mmHg per incident	< 0.0004	1.02	1.011–1.038	4.8 (3.3–7.8)
Minutes > 135 mmHg per incursion	0.04	1.03	1.001–1.055	3.7 (2.3–5.7)
Minutes < 95 mmHg per incursion	0.003	1.03	1.008–1.042	4.9 (2.8–10.8)
Mean incursion nadir < 95 mmHg	0.002	1.05	1.019–1.084	13 (9–17)
Mean incursion peak > 135 mmHg	0.14	1.01	0.989–1.016	21 (12–31)

All models are adjusted for case length and Parsonnet score.

* Per 100 (mmHg · min).

AUC = area under the curve, measures both magnitude and duration of excursions. The units are mmHg (magnitude) × min (duration); AUC for 20% = boundaries for range determined by a 20% increase above the patient's baseline systolic blood pressure and 20% decrease below their baseline systolic blood pressure; CI = confidence interval.

bined to create nine predictive combined ranges. The final validation analysis was conducted using the best combined predictive systolic blood pressure range. The other systolic blood pressure ranges were compared with the most predictive blood pressure range to determine their relative predictive value for 30-day mortality. In addition, to address the question of whether systolic blood pressure above or below the range is a more powerful predictor of 30-day mortality, we independently evaluated from multivariable logistic regression models mean duration both above and below threshold.

Because of the number of analyses conducted, all findings in the development dataset analysis were considered preliminary only, and no adjustments were made for multiple comparisons. After the single primary hypothesis was tested in the validation dataset, receiver operating characteristic curves from the development and validation samples were plotted for comparison. Randomization of samples was achieved with the use of a random number function to generate a uniform distribution (SAS statistical software version 9.1; SAS Institute, Inc., Cary, NC).

In addition, the relationship of the validation blood pressure criteria with long-term survival was also evaluated using an adjusted Cox proportional hazards analysis. Parsonnet score was included in the survival model. All analyses were performed using SAS statistical software (version 9.1). A value of *P* less than 0.01 was considered significant, with a more conservative significance level chosen because of the size of the dataset.

Results

Seven thousand eight hundred eight patients were enrolled and underwent surgery during the period of the study. Three hundred four were excluded for having insufficient pressure data. This sample (n = 7,504) was divided into a development sample of 5,038 and a validation sample of 2,466. The average age was 65 yr; 68% were men; 86% white; and 70% had a history of hypertension, 8% underwent coronary bypass surgery without cardiopulmonary bypass, and 6% underwent combined coronary bypass surgery/valve surgery (table 1). The 30-day mortality was 2.1% (n = 99) in the development sample and 2.6% (n = 62) in the validation sample.

Our initial hypothesis, that cumulative perioperative blood pressure excursion (area under the curve) beyond a systolic blood pressure range more than 135 or less than 95 mmHg predicted adverse outcome after cardiac surgery, was confirmed (odds ratio [OR] = 1.03 per mmHg min, 95% CI 1.007–1.044, $P < 0.006$; table 2). Additional characteristics

Table 3. Multivariable Logistic Regression Model for Mean Duration < 95 mmHg

Predictor	*P* Value	Odds Ratio
Episode duration < 95 mmHg	< 0.0001	1.025 (1.013–1.036)
Case length	0.81	1.000 (0.998–1.002)
Parsonnet score	< 0.0001	1.086 (1.067–1.105)

Table 4. Multivariable Logistic Regression Model for Mean Duration > 130 mmHg

Predictor	*P* Value	Odds Ratio
Episode duration > 130 mmHg	0.005	1.029 (1.009–1.05)
Case length	0.20	1.000 (0.999–1.003)
Parsonnet score	< 0.0001	1.085 (1.066–1.105)

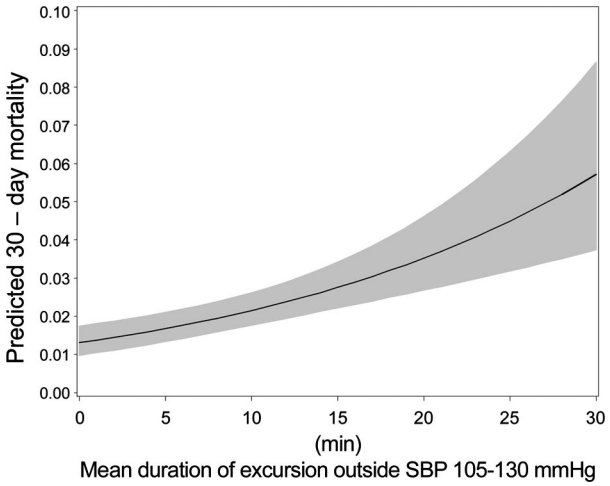

Fig. 1. Predicted association of mean duration per incursion (minutes) outside of threshold (105–130 mmHg) and 30-day mortality in the combined sample (n = 7504). *Shaded area* represents the 95% confidence intervals for the predicted values.

of systolic blood pressure variability were calculated for threshold values of 135 and 95 mmHg for each patient and evaluated separately with logistic regression for its ability to contribute to a model in predicting 30-day mortality, after adjusting for length of surgery and Parsonnet score. The characteristic most highly associated with 30-day mortality (identified by *P* value and odds ratio) was mean duration of systolic blood pressure excursions beyond threshold values (OR 1.03, 95% CI 1.02–1.39, $P < 0.0001$). *P* values and

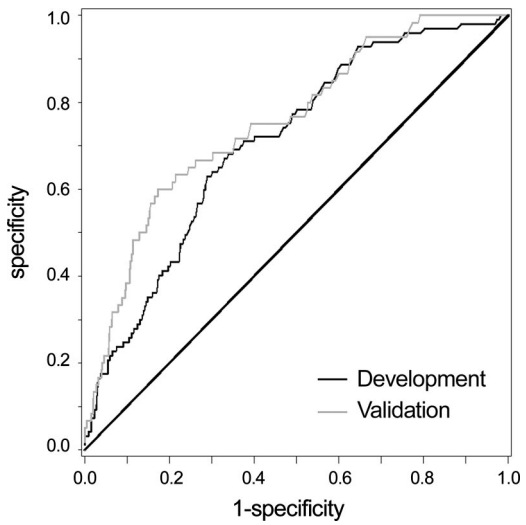

Fig. 2. Receiver operating characteristic curves showing association between duration of incursions and 30-day mortality in the development and validation samples. Results are graphically presented using the complete dataset divided into two parts, development and validation. The c index for the logistic regression model in the development sample (equivalent to the area under the receiver operating characteristic curve) is 0.703. The c index for the validation sample is 0.79. A reference line has been included to illustrate a c index of 0.5, indicating no association.

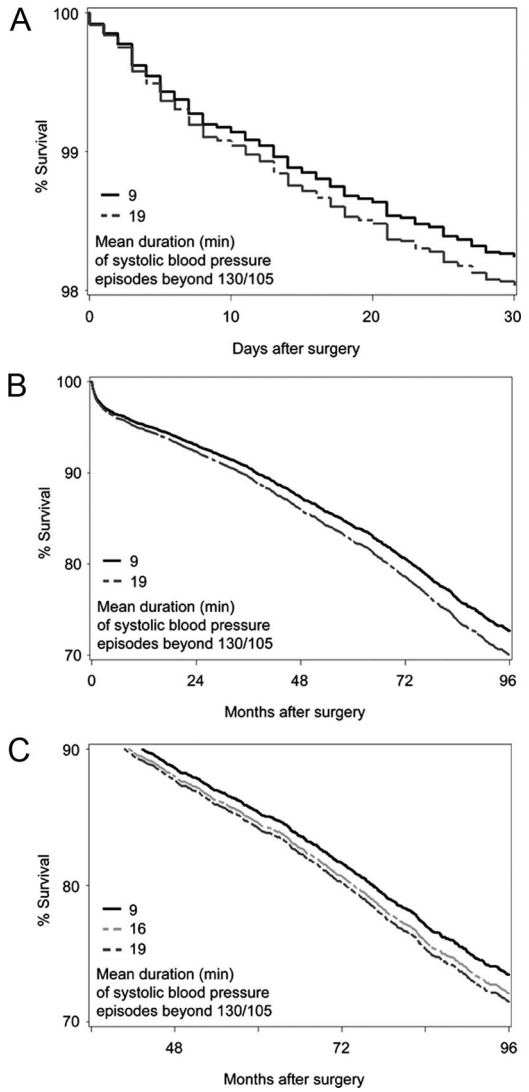

Fig. 3. (*A*) Close-up view of the first 30 days of the survival curves, showing risk adjusted survival estimates using the Cox proportional-hazard method for two mean incursion values outside the range of 105–130 mmHg: 9 and 19 min (25th and 75th percentiles). (*B*) Risk-adjusted survival estimates using the Cox proportional-hazard method for two mean incursion values outside the range of 105–130 mmHg: 9 and 19 min (25th and 75th percentiles). *P* value for the continuous variable is less than 0.0001. (*C*) Risk-adjusted survival estimates using the Cox proportional-hazard method for three mean incursion values outside the range of 105–130 mmHg: 9, 16, and 19 min (25th, 50th, and 75th percentiles). *P* value for the continuous variable is less than 0.0001.

odds ratios for the other variables are presented in table 2. The best upper and lower thresholds, as tested using the association of criteria to describe episodes of systolic blood pressure variability with 30-day mortality, were 130, 135,140, and 95, 100, 105 mmHg, respectively. The nine combinations using these thresholds were all evaluated as ranges for their association with 30-day mortality. The upper and lower thresholds were also evaluated independently for their respective associations with 30-day mortality.

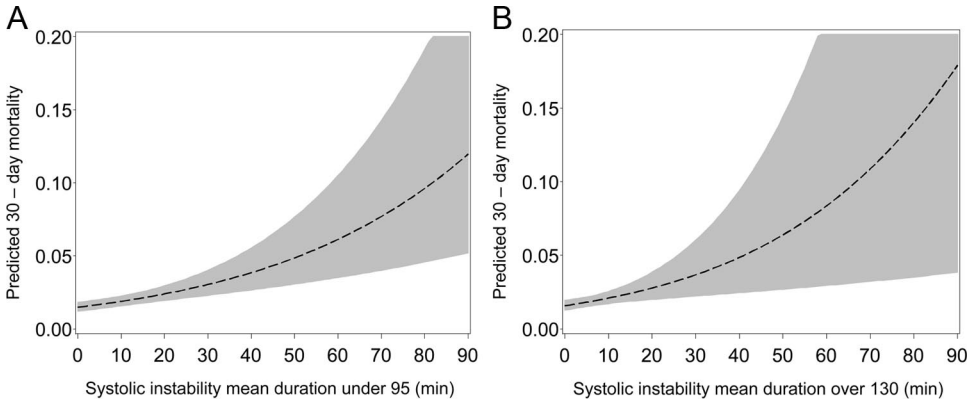

Fig. 4. (*A*) Predicted association of mean duration per incursion (minutes) below the threshold 95 mmHg and 30-day mortality in the combined sample (n = 7504). *Shaded area* represents the 95% confidence intervals for the predicted values. (*B*) Predicted association of mean duration per incursion (minutes) above the threshold 130 mmHg and 30-day mortality in the combined sample (n = 7504). *Shaded area* represents the 95% confidence intervals for the predicted values.

All range combinations were highly associated with 30-day mortality. The systolic blood pressure upper threshold of 130–140 mmHg and the systolic blood pressure lower threshold of 100–105 mmHg demonstrated the strongest odds ratio, *P* values, and 95% confidence interval (for the range greater than 130 and less than 105 mmHg, $P < 0.0001$, OR 1.028, CI 1.016–1.040 and for the range greater than 140 through less than 105 mmHg, $P < 0.0001$, OR 1.028, CI 1.015–1.041). Blood pressure excursions greater than 130 mmHg ($P < 0.005$, OR 1.03, 95% CI 1.01–1.05) and less than 95 mmHg ($P < 0.0001$, OR 1.03, 95% CI 1.01–1.04) were tested in separate multivariable logistic regression models and each was associated with 30-day mortality (tables 3 and 4).

The developed primary hypothesis was that the mean duration of excursions beyond the threshold criteria of the strongest systolic blood pressure range signal, 130/105 mmHg, is associated with 30-day mortality, after adjustment for case length and Parsonnet score. Aprotinin use (10% of patients) showed no significant association with mortality ($P = 0.58$), whereas mean duration of excursions outside 130/105 continued to be associated ($P < 0.0001$), hence aprotinin use was not included in the final model.

The logistic regression model primary hypothesis test confirmed a strong association ($P = 0.0008$, OR 1.03, 95% CI 1.01–1.05). The mean duration of an independent excursion more than 130 mmHg was 5.12 ± 4.6 min and that less than 105 mmHg was 11.06 ± 9.6 min. The mean duration of a combination excursion more than 130 mmHg and less than 105 mmHg was 8.03 ± 5.4 min. There was a direct and a progressive predicted probability of mortality with mean duration of excursion such that for a mean duration of 8 min, the predicted probability of mortality was 1.9%; for mean duration of 10 min, predicted probability of mortality was 2.1%; and for mean duration of 20 min, predicted probability of mortality was 3.5%. The exact magnitude of this effect, per minute increase, can be seen in figure 1. Odds ratios represent an effect for a per-unit change. For example, for the duration variables, which are characterized by minutes outside a range, the odds ratio is per-minute effect. The interpretation is that for every minute outside the range, the odds ratio for 30-day mortality increases by the amount of the odds ratio.

Figure 2 portrays the receiver operating characteristic curves generated from the logistic regression models in the development and validation samples. Results from the final validated model are graphically presented using the complete dataset (development and validation together). The c index for the logistic regression model in the development sample (equivalent to the area under the receiver operating characteristic curve) is 0.703. The c-index for the validation sample is 0.79.

The secondary long-term survival analysis was performed using the whole dataset (combined development and validation). Median follow-up time for survivors was 74 months. One thousand six hundred fifty-three patients died during follow-up time; the remaining patients were censored at the date of last follow-up. Risk-adjusted survival estimates are shown in figs. 3A–C and show a highly significant association of the mean duration of intraoperative systolic blood pressure variability episodes with short-term and long-term survival ($P < 0.0001$; hazard ratio per minute 1.009 [95% CI 1.005–1.012]). An assessment, excluding patients who died within 30 days of surgery, noted similar findings ($P < 0.0001$; hazard ratio = 1.009, 95% CI 1.004–1.013).

Figures 4A and B depict the magnitude of the effect, per minute increase, of blood pressure excursions less than 95 mmHg and more than 130 mmHg, respectively. Figures 5A–C depict unadjusted data of 30-day mortality within each tertile of the dataset, based on blood pressure variability (minutes per episode spent outside the range).

Discussion

This study reports that a strong association exists between intraoperative blood pressure variability and postoperative 30-day mortality in a nearly continuous electronically captured evaluation of blood pressure from a large database

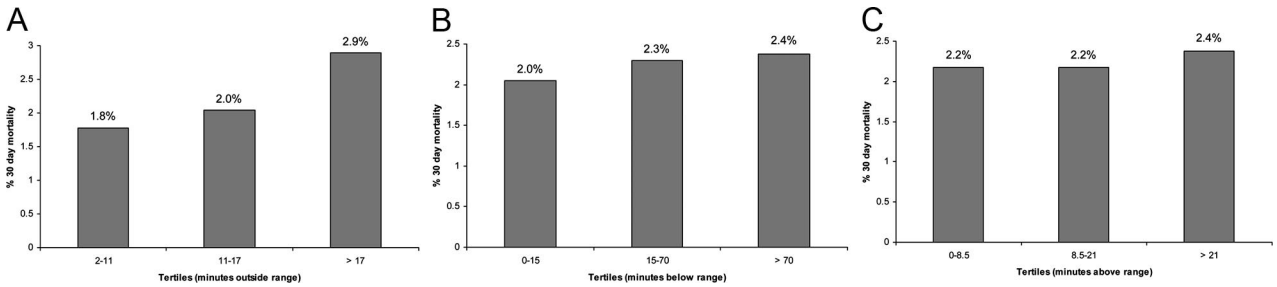

Fig. 5. (*A*) Unadjusted data of 30-day mortality within each tertiles of dataset, based on blood pressure variability (minutes per episode spent outside the range). (*B*) Unadjusted data of 30-day mortality within each tertiles of dataset, based on blood pressure variability (minutes per episode spent below the range). (*C*) Unadjusted data of 30-day mortality within each tertiles of dataset, based on blood pressure variability (minutes per episode spent above the range).

among a homogenous subset of patients undergoing cardiovascular revascularization.

Manipulation of blood pressure during cardiac surgery is common because of safety concerns related to ischemia modulation, the need for aortovascular stress-strain modulation (*e.g.*, clamping, unclamping), maintaining adequate perfusion conditions during cardiopulmonary bypass, and balancing these pressure–perfusion requirements with surgical bleeding concerns throughout surgery and especially during the postoperative period when requirements for weaning from mechanical ventilation and analgesia are additional stresses for poor blood pressure control.

Although blood pressure abnormalities have been reported to be associated with death, stroke, cognitive and renal dysfunction, perioperative myocardial infarction, and increased mortality,[6,7,14,16] many of these studies used a small sample size and lacked statistical power, used a discontinuous data analysis, did not include patient- or surgery-specific characterizations, and were not analyzed to determine specific target blood pressure thresholds and therefore provide limited information on the impact of blood pressure control to postoperative outcome.

In the elderly population with a high prevalence of systolic and pulse pressure hypertension, it has been demonstrated that acute pulsatile stress in conduit vessels cause the elastic elements in the vessel wall to break down, producing vessel dilation and stiffening,[21,22] which may contribute to plaque rupture by a mechanical fatiguing effect.[21,23] Blood pressure stress and increase in pulsatile load seen in patients with preexisting hypertension may further contribute to endothelial dysfunction.[24,25] These mechanical stress induced changes in arterial pathology are uniquely vulnerable to the acute physiologic perturbations seen during surgery and anesthesia. In addition, blood pressure target depends on vascular properties, which include a shift in the autoregulatory range in those persons who have pre-existing disease, which thereby further increases the risk for organ hypoperfusion.

This study presents data on an association of intraoperative blood pressure variability to 30-day mortality in a relatively homogeneous population of patients undergoing coronary revascularization surgery. Although an odds ratio of 1.03 represents a modest effect, it is important (1) to realize that this effect size is per-minute effect, such that for every minute outside the 105–130 mmHg range, the odds ratio for 30-day mortality increases by 0.03 and (2) intraoperative blood pressure is a modifiable risk factor.

We understand that a target systolic blood pressure bandwidth or a "sweet spot" may be different in this population compared with other populations with different conditions or situations (*e.g.*, non-cardiac surgery, acute stroke, or other hypertensive emergencies); nevertheless, we believe that these data strongly suggest a need to explore that such a "sweet spot" exists and should be the basis for further investigation.

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Appendix: Cardiothoracic Anesthesiology Research Endeavors, Duke University Medical Center

Anesthesiology: Solomon Aronson, M.D., Katherine P. Grichnik, M.D., Steven Hill, M.D., G. Burkhard Mackensen, M.D., Ph.D., Joseph P. Mathew, M.D., Mark F. Newman, M.D., Barbara Phillips-Bute, Ph.D., Mihai V. Podgoreanu, M.D., Andrew D. Shaw, M.D., Mark Stafford-Smith, M.D., Madhav Swaminathan, M.D., Ian Welsby, M.D., William D. White, M.P.H., Lisa Anderson, Lauren Baker, B.S., Jerry Dove, R.N., Bonita L. Funk, R.N., Roger L. Hall, A.A.S., Gladwell Mbochi, A.A.S., Tiffany Bisanar, R.N., Prometheus T. Solon, M.D., Peter Waweru.

Perfusion Services: Kevin Collins, B.S., C.C.P., Greg Smigla, B.S., C.C.P., Ian Shearer, B.S., C.C.P.

Surgery: Thomas A. D'Amico, M.D., R. Duane Davis, M.D., Donald D. Glower, M.D., R. David Harpole, M.D., G. Chad Hughes, M.D., James Jaggers, M.D., Shu Lin, M.D., Andrew Lodge, M.D., James E. Lowe, M.D., Carmelo Milano, M.D., Peter K. Smith, M.D., Jeffrey Gaca, M.D., Mark Onatis, M.D.