Pulse Pressure and Risk of Adverse Outcome in Coronary Bypass Surgery

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BACKGROUND: Among ambulatory patients, an increase in pulse pressure (PP) is a well-established determinant of vascular risk. The relationship of PP and acute perioperative vascular outcome among patients having coronary artery bypass graft (CABG) surgery is less well known.
METHODS: We conducted a prospective observational study involving 5436 patients having elective CABG surgery requiring cardiopulmonary bypass. Of these, 4801 met final inclusion criteria. Comprehensive data were captured for medical history, intraoperative and postoperative physiologic and laboratory measures, diagnostic testing, and clinical events. The relationship between preoperative hypertension (systolic, diastolic, PP) and ischemic cardiac and cerebral outcomes and death was assessed using multivariable logistic regression; $P < 0.05$ was considered significant.
RESULTS: Nine hundred and seventeen patients (19.1%) had fatal and nonfatal vascular complications, including 146 patients (3.0%) with cerebral and 715 patients (14.9%) with cardiac events. In-hospital mortality occurred in 147 patients (3.1%). Among all blood pressure variables measured preoperatively, PP was most strongly associated with an increased risk of postoperative complications. PP increments of 10 mm Hg (above a threshold of 40 mm Hg) were associated with an increased risk of cerebral events (adjusted odds ratio: 1.12; 95% CI [1.002–1.28]; $P = 0.026$). The incidence of a cerebral event and/or death from neurologic complications nearly doubled for patients with PP >80 mm Hg versus ≤80 mm Hg (5.5% vs 2.8%; $P = 0.004$). PP more than 80 mm Hg was also found to be associated with cardiac complications, increasing the incidence of congestive heart failure by 52%, and death from cardiac cause by nearly 100% ($P = 0.003$ and 0.006, respectively).
CONCLUSION: An increase in PP was independently and significantly associated with greater fatal and nonfatal adverse cerebral and cardiac outcomes in patients having CABG surgery. These findings highlight the associated risks of preoperative PP on acute postoperative vascular outcomes.
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Hypertensive disease is a prevalent and important risk factor for cardiac, cerebral, and other vascular events in the general population.[1,2] Since first accepted as vital physiologic measures, the systolic (SBP) and diastolic (DBP) component of arterial blood pressure have been the cornerstone of blood pressure characterization and evaluation for secondary vascular fatal and nonfatal events.[3] Perhaps, nowhere is the assessment, characterization, and management of blood pressure more important than in the setting of coronary artery bypass graft (CABG) or major vascular surgery, a period marked by an acute and stressful physiologic perturbation involving excessive release of catecholamines, reperfusion injury,[4] humoral and cellular inflammatory responses,[5,6] and platelet activation, which can compromise microvascular blood flow.[7] Whereas several studies have indicated an association between preexisting hypertension (HTN) and perioperative complications after cardiac surgery including stroke,[8] myocardial infarction, congestive heart failure (CHF),[9,10] bleeding, and renal dysfunction,[11] only a few have distinguished relations between categories of blood pressure [isolated systolic (ISH), isolated diastolic (IDH), and combined systolic and diastolic HTN] and postoperative vascular outcomes.[12]

Pulse pressure (PP) (difference between SBP and DBP) reflects the stiffness of conduit vessels and the rate of pressure wave propagation within the arterial tree.[13–15] With stiffening that occurs with aging, propagated and reflected waves within the arterial tree travel much more rapidly, resulting in early

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return of the propagated wave to the central aorta[13,14] during late systole as opposed to early diastole. This increased systolic load along with a lower diastolic perfusion pressure and relative intravascular volume depletion may, in part, set up a unique pathophysiologic basis for perioperative vascular injury including cerebral, cardiac, and renal dysfunction.[16–23]

We recently reported that in patients undergoing CABG surgery, an increase in preoperative PP by increments of 20 mm Hg (above a reference point of 40 mm Hg) was associated with a 50% increase in the risk of postoperative renal events.[24] To further evaluate the importance of perioperative blood pressure characterization, we investigated the relationship between SBP, DBP, and PP and adverse cerebral and cardiac outcomes in patients having coronary surgery with cardiopulmonary bypass (CPB).

Table 1. Categories of Blood Pressure (BP) According to the JNC VII Report (Modified): Natural History of Hypertension Subtypes[26]

BP characteristics	
Optimal	<120/80
High normal	130–139/85–89
Stage 1	140–159/90–99
Stage 2	160–179/100–109
Stage 3	>180/110
ISH	>140 SBP/<90 DBP
IDH	<140 SBP/>90 DBP
Combined systolic and diastolic HTN	>140 SBP/>90 DBP
Mean PP	Difference between mean SBP and mean DBP
MAP	1/3 SBP + 2/3 DBP

All values are given in mm Hg.

SBP = systolic blood pressure; DBP = diastolic blood pressure; ISH = isolated systolic hypertension; IDH = isolated diastolic hypertension; PP = pulse pressure; MAP = mean arterial blood pressure.

Study Design

The Multicenter Study of Perioperative Ischemia Epidemiology II (*McSPI*-EPI II) initiated enrollment in November of 1996 and was completed in June of 2000. The methods of this study have been previously described in detail and are briefly summarized here.[25] A total of 5436 patients from 72 centers among 17 countries requiring elective CABG surgery with or without valve repair/replacement were enrolled (Appendix). After IRB approval at each center, 100 patients per center provided written informed consent and were enrolled according to a systematic sampling scheme that allowed a random sampling of patients at each institution among all patients undergoing surgery at that institution over 1 yr. Eligible patients were between the ages of 18 and 100 yr, able to complete the preoperative interview, not involved in another study, and scheduled to have coronary bypass using CPB.

Study Data

Comprehensive information totaling more than 7500 data fields per patient, including demographic, historical, clinical, laboratory, electrocardiographic, specialized testing, resource utilization, and adverse outcome, were recorded from the period of hospital admission until hospital discharge.

Derivation of Study Groups

We applied recently published definitions for categorizing blood pressure[26] (Table 1). A standardized procedure was used to measure blood pressure preoperatively as the average of two seated measurements. For each patient, up to five blood pressure recordings were captured in the case report form from the time of hospital admission to the morning of surgery. These were averaged and the mean SBP, mean DBP, and mean PP (difference of mean SBP and mean DBP) were calculated for each patient.

Measurement of Outcomes

The primary outcome measures were cerebral or cardiac events occurring postoperatively and all-cause mortality. A cerebral event was defined as new nonfatal stroke, transient ischemic attack, or encephalopathy, coma at the time of discharge, or death due to stroke or encephalopathy.[25] Postoperative stroke was defined as an increase in score on the National Institutes of Health Stroke Scale of four points or more or was diagnosed on the basis of a focal or global defect on physical examination, tomographic scan, magnetic resonance imaging, or autopsy. A cardiac event included new myocardial infarction [diagnosis requiring either: the development of new Q waves (as defined by MN Code 1-1-1 or 1-2-7)[25,27]; new persistent ST-segment or T-wave changes (MN Code 4-1, 4-2, 5-1, 5-2 or 9-2) associated with autopsy evidence of acute myocardial infarction], or new CHF diagnosed by either the use of a ventricular assist device or the use of at least two inotropic infusions continuously for at least 24 h, or autopsy evidence of heart failure.[25,27]

Study Sample and Statistical Analysis

After enrollment, 635 patients were excluded because of the following: change in procedure (132 patients who did not undergo CPB); cancellation or rescheduling of surgery (97 patients); incomplete data (97 patients); patient withdrawal (32 patients); inadvertent enrollment in another study (11 patients); death before surgery (2 patients); concurrently undergoing additional procedures (256 patients); and incomplete or questionable blood pressure recording.[8] Thus, the final study population was 4801 participants.

Descriptive statistics were performed on all study variables. Comparison between patients with and without HTN was performed using the two-tailed *t*-test, χ^2 test, or Fisher's exact test, as appropriate. For these analyses, odds ratios and 95% confidence intervals are reported when applicable, with associated *P* values.

Univariate and multivariate analyses were performed to identify potential risk factors for each individual ischemic outcome. The risk factors included medical history, categories of blood pressure

Table 2. Demographics and Perioperative Characteristics

Characteristics	$N = 4801$
Age (yr)	
Mean ± SD	64.0 ± 9.8
Median (Q1, Q3)	65.0 (57.0, 71.0)
Gender, *n* (%)	
Male	3833 (79.8)
Female	968 (20.2)
Medical history, *n* (%)	
Congestive heart failure	1737 (36.4)
Myocardial infarction	3035 (63.8)
Diabetes	1476 (30.8)
Hypertension	3213 (67.2)
Renal disease	762 (15.9)
Pulmonary disease	1008 (21.1)
Neurological event	514 (10.7)
Vascular disease	812 (17.0)
Chronic obstructive pulmonary disease	554 (11.5)
Prior coronary artery bypass graft	284 (5.9)
Prior valve surgery	31 (0.7)
Currently smoke	549 (11.5)
Left ventricular hypertrophy	1327 (27.7)
Left ventricular dilation	398 (8.3)
Preoperative medication, *n* (%)	
β-blockers	3297 (68.7)
Angiotensin converting enzyme inhibitors	2105 (43.9)
Calcium channel blockers	1748 (36.4)
Diuretic	1369 (28.5)
Peripheral vasodilators	479 (10.0)
Intraoperative factors, *n* (%)	
β-blockers	652 (13.6)
Inotropes (≥2)	1111 (23.1)
IABP	122 (2.5)
CPB time (min)	
Mean ± SD	102.1 ± 42.0
Median (Q1, Q3)	95.0 (74, 122)
Cross-clamp-time (min)	
Mean ± SD	64.6 ± 31.6
Median (Q1, Q3)	59.0 (43, 79)

COPD = chronic obstructive pulmonary disease; CABG = coronary artery bypass graft; ACE = angiotensin converting enzyme; IABP = intraaortic balloon pump; CPB = cardiopulmonary bypass. Q1, Q3 = interquartiles 1 and 3.

Note: data were missing as follows: in 32 patients for congestive heart failure; in 41 patients for myocardial infarction; in 1 for diabetes; in 17 for hypertension; in 15 for renal disease; in 20 for pulmonary disease; in 31 for vascular disease; in 18 for history of current smoking; in 7 for left ventricular hypertrophy, and in 40 for aortic cross-clamp-time.

(Table 1), demographics, laboratory, physiologic, and surgical characteristics, and medications administered. Only those predictors showing a two-tailed nominal *P* value of <0.15 in univariate analyses were entered into stepwise multivariable logistic regression analysis. The multivariable model identified significant independent risk factors with a two-tailed nominal *P* value of <0.05. All categories of blood pressure and subtypes of HTN (ISH, IDH, combined systolic and diastolic) were entered into the regression model along with other known preoperative and intraoperative risk factors. SBP and DBP were also interrogated as continuous variables and PP was interrogated in increments of 10 mm Hg above a threshold of 40 mm Hg. Logistic regression analyses was also performed with the presence of PP ≤80 vs >80 mm Hg as the predictor of interest for postoperative fatal or nonfatal vascular complications and all-cause mortality. A *P* value <0.05 was considered statistically significant. Statistical analysis was performed with SAS Version 8.12 software (SAS Institute, Cary, NC).

Table 3. Characterization and Distribution of Preoperative Blood Pressure

Systolic blood pressure (mm Hg)	
Mean ± SD	134 ± 18
Median (Q1, Q3)	132 (120, 145)
Diastolic blood pressure (mm Hg)	
Mean ± SD	75 ± 10
Median (Q1, Q3)	75 (69, 81)
PP (mm Hg)	
Mean ± SD	59 ± 15
Median (Q1, Q3)	57 (49, 68)
Isolated systolic hypertension, *n* (%)	1180 (25.0)
Systolic (mean ± SD)	153 ± 10
Diastolic (mean ± SD)	77 ± 8
Isolated diastolic hypertension, *n* (%)	23 (0.5)
Systolic (mean ± SD)	133 ± 7
Diastolic (mean ± SD)	94 ± 3
PP, *n* (%)	
≤40 mm Hg	492 (10.3)
>40–50 mm Hg	1061 (22.1)
>50–60 mm Hg	1359 (28.3)
>60–70 mm Hg	983 (20.5)
>70–80 mm Hg	524 (10.9)
>80–90 mm Hg	239 (5.0)
>90 mm Hg	143 (3.0)

PP = pulse pressure.

RESULTS

Sixty-seven percent of this international cohort with typical multivessel coronary heart disease reported past or current HTN (Table 2). Overall, the mean preoperative SBP for this surgical cohort was mildly increased (134 ± 18 mm Hg), whereas the mean DBP was minimally reduced (75 ± 10 mm Hg) (Table 3). ISH was present in 1180 patients (25%) whereas IDH and combined systolic and diastolic HTN were present in 23 patients (0.5%) and 230 patients (4.8%), respectively. Nearly half of the cohort presented with PP values between 40 and 60 mm Hg; however, a third had moderate increases in PP of 60–80 mm Hg, and 382 (8%) had excessive increase in PP of >80 mm Hg (Table 3).

Cerebral Events

One hundred and forty-six (3.0%) patients suffered cerebral events; 83 (1.7%) patients experienced strokes. PP was independently associated with an increased risk of developing a postoperative cerebral event. For every 10 mm Hg increment in PP (above a threshold of 40 mm Hg), the odds of experiencing a cerebral event increased by 12% (adjusted odds ratio: 1.12; 95% CI [1.002–1.28]; $P = 0.026$). Importantly, the incidence of a cerebral event and/or death from neurologic complications nearly doubled for patients with PP >80 mm Hg versus ≤80 mm Hg (5.5% vs 2.8%; $P = 0.004$) (Fig. 1). The univariate frequency of major vascular outcomes according to increment of PP above a threshold of 40 mm Hg is presented in Table 4. Independent predictors of a cerebral event are listed in Table 5.

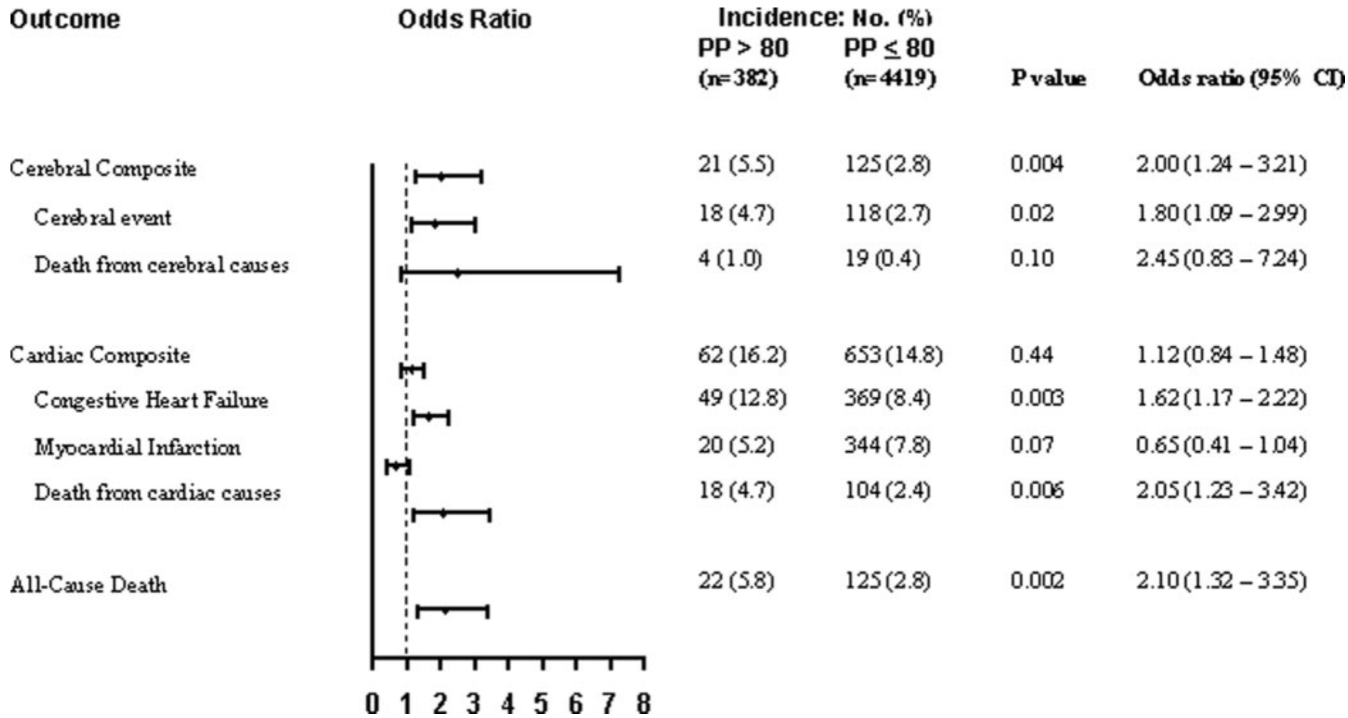

Figure 1. Postoperative fatal and nonfatal outcomes in patients with pulse pressure (PP) <80 mm Hg versus those with PP ≥80 mm Hg. Individuals with PP >80 mm Hg were nearly twice more likely to experience a cerebral event (neurologic death, stroke, transient ischemic attack, encephalopathy, coma, or stupor), congestive heart failure (52% more), death from cardiac causes (96% more), and overall mortality (twice more) when compared with those with PP <80 mm Hg.

Table 4. Univariate Frequency of Outcomes for Each Level of Pulse Pressure

Pulse pressure	No. of patients	Cerebral events no. (%)	Cardiac outcomes no. (%)	In-hospital mortality no. (%)
≤40 mm Hg	492	11 (2.2)	71 (14.4)	13 (2.6)
>40–50 mm Hg	1061	14 (1.3)	164 (15.5)	29 (2.7)
>50–60 mm Hg	1359	39 (2.9)	203 (14.9)	35 (2.6)
>60–70 mm Hg	983	32 (3.3)	155 (15.8)	30 (3.1)
>70–80 mm Hg	524	22 (4.2)	60 (11.5)	18 (3.4)
>80–90 mm Hg	239	12 (5.0)	43 (18.0)	15 (6.3)
>90 mm Hg	143	6 (4.2)	19 (13.3)	7 (4.9)
Overall	*4801*	*136 (2.8)*	*715 (14.9)*	*147 (3.1)*

Table 5. Multivariable Analysis of Preoperative and Intraoperative Predictors of Postoperative Cerebral Events

Predictor	Odds ratio (95% CI)	*P*
Pulse pressure (per 10 mm Hg increment)	1.123 (1.002–1.259)	0.046
Age (per 10 yr increment)	1.51 (1.22–1.86)	<0.001
Medical history		
Neurological event	2.80 (1.88–4.15)	<0.001
COPD	1.73 (1.12–2.67)	0.014
ACE inhibitor	1.47 (1.04–2.09)	0.030
Intraoperative predictor		
CPB time (per 1 min increment)	1.005 (1.002–1.009)	0.002

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ACE = angiotensin converting enzyme inhibitor; and CPB = cardiopulmonary bypass.

Cardiac Events

Postoperative cardiac complications were noted in 715 (14.9%) patients including 418 (8.7%) patients with a diagnosis of CHF, another 364 (7.6%) patients having Q-wave myocardial infarction, and 122 (2.5%) deaths attributed to cardiac causes. PP above a threshold of 80 mm Hg was found to be significantly associated with a cardiac event, increasing the incidence of CHF by 52%. Nearly twice as many deaths from a cardiac cause were associated with a preoperative PP >80 mm Hg (Fig. 1). Multivariable analysis, however, demonstrated no association between the category of blood pressure and the composite cardiac outcome (Table 6).

Mortality

Death occurred in 147 patients (3.1%). After controlling for SBP and DBP and all known perioperative predictors, multivariable logistic regression identified the following independent predictors of postoperative all-cause mortality: PP, age, history of CHF, chronic obstructive pulmonary disease, intraoperative treatment with intraaortic balloon pump and inotropes for ventricular dysfunction, and duration of CPB (Table

Table 6. Multivariable Analysis of Preoperative and Intraoperative Predictors of Postoperative Cardiac Outcomes

Predictor	Odds ratio (95% CI)	*P*
Pulse pressure (per 10 mm Hg increment)	0.96 (0.91–1.02)	0.190
Age (per 10 yr increment)	1.06 (0.96–1.17)	0.273
Gender (female vs male)	1.26 (1.03–1.54)	0.026
Medical history		
Congestive heart failure	1.61 (1.36–1.92)	<0.001
Myocardial infarction	1.27 (1.05–1.53)	0.012
Carotid disease	1.52 (1.20–1.91)	<0.001
Pulmonary disease	1.34 (1.11–1.63)	0.003
ACE inhibitor	1.22 (1.03–1.45)	0.024
Intraoperative predictor		
>2 intraoperative inotropes	1.60 (1.32–1.93)	<0.001
IABP	3.82 (2.56–5.71)	<0.001
CPB time (per 1 min increment)	1.006 (1.004–1.008)	<0.001

ACE = angiotensin converting enzyme; CHF = congestive heart failure; CI; confidence interval; CPB = cardiopulmonary bypass; IABP = intraaortic balloon pump; MI = myocardial infarction.

Table 7. Multivariable Analysis of Preoperative and Intraoperative Predictors of In-Hospital Mortality

Predictor	Odds ratio (95% CI)	*P*
Pulse pressure (per 10 mm Hg increment)	1.13 (1.01–1.27)	0.037
Age (per 10 yr increment)	1.59 (1.29–1.97)	<0.001
Medical history		
Congestive heart failure	1.82 (1.27–2.60)	0.001
COPD	1.57 (1.01–1.45)	0.044
Intraoperative predictor		
>2 intraoperative inotropes	2.73 (1.86–4.02)	<0.001
IABP	7.16 (4.30–11.93)	<0.001
CPB time (per 1 min increment)	1.006 (1.003–1.009)	<0.001

COPD = chronic obstructive pulmonary disease; IABP = intraaortic balloon pump; CPB = cardiopulmonary bypass.

7). When analyzed by subtypes of HTN or as continuous variables, SBP and DBP (independent of PP) were not associated with mortality.

DISCUSSION

Our findings indicate that in this cohort of elderly patients presenting for CABG surgery an increase in PP of 10 mm Hg (above a threshold of 40 mm Hg) was associated with both fatal and nonfatal postoperative major vascular complications. These observations raise important questions regarding current approaches to evaluate, treat, and counsel patients undergoing elective CABG surgery.

For over a century, health care practice has adopted arterial blood pressure as a cornerstone for clinical evaluation of cardiovascular function and risk.[1–3] In this time span, much has been learned about characterization of hypertensive states, associated morbidity and mortality, efficacy and safety of antihypertensive therapy,[18–22,28] and the understanding of the relative importance of systolic and diastolic HTN. While DBP has served as the primary marker for blood pressure management, including screening, antihypertensive therapy, and design of clinical trials,[29] a number of longitudinal trials have shown that in individuals older than 50 yr, ISH is far more prevalent and significant than IDH for predicting greater risk of both fatal and nonfatal stroke and coronary heart disease.[30,31] Indeed, ISH was present in 25% of our surgical cohort (Table 3), whereas IDH was found in only 0.5% of patients.

According to the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure,[26] optimal SBP and DBP are <120/<80 mm Hg indicating a normal PP of near 40 mm Hg. However, only 10% of patients in our study had PP <40 mm Hg, whereas half of the cohort presented with PP of 40–60 mm Hg and, notably, another 40% had excessive preoperative PP of >60 mm Hg.

Blood Pressure and Cerebral Events

Preoperative HTN *per se* has been implicated as a risk factor for stroke after cardiac surgery but specific subtypes of HTN have not been investigated as potential risk predictors. In the current study, we explored such thresholds and in addition explored PP as well as SBP and DBP as continuous predictors for cerebral outcomes. We found that an increase of 10 mm Hg in PP above a threshold of 40 mm Hg increased the odds of a cerebral event by 12%. Importantly, for those patients with PP >80 mm Hg, the incidence of cerebral event and/or death from neurologic complications was nearly doubled. No other threshold of SBP or DBP was related to cerebral complications. Our results are supported by several longitudinal studies in ambulatory subjects identifying PP as a better predictor of stroke than SBP or DBP[19] in both normotensive and in hypertensive individuals. Franklin et al. reported that increases in PP at fixed SBP are associated with a much greater risk of ischemic outcomes than increase in SBP at a fixed PP.[23]

Blood Pressure and Cardiac Events

Myocardial work is closely linked to SBP, which is as a marker of afterload. As afterload increases, myocardial oxygen demand and delivery must be matched, otherwise, injury in the form of ischemia, infarction, and/or CHF can ensue. DBP, on the other hand, is critically important for coronary perfusion. Those patients in our study with a preoperative PP >80 mm Hg were nearly twice more likely to die of a cardiac cause and were 52% more likely to develop CHF (Fig. 1).

In the context of CABG surgery, this result is both relevant and consistent with known cardiovascular pathophysiology. That is, cardiac events such as myocardial infarction are generally attributed to technical problems during surgery, including inadequate revascularization, early graft occlusion, poor myocardial protection, or the inflammatory response to CPB. Thus, it is not surprising that PP was not associated with postoperative myocardial infarction since CABG surgery generally improves coronary perfusion, thereby reducing cardiac events. However, a benefit from coronary revascularization was not evident at the extreme of widened PP with regards to CHF and cardiac-related death. The former may have very well arisen from abnormal myocardial relaxation. Widened PP is closely linked to left ventricular hypertrophy, which is an important cause of diastolic dysfunction and cardiac mortality. It is also possible that in patients with significant atherosclerotic disease and stiffened arteries manifested as a PP ≥80 mm Hg, attempts to treat postoperative systolic HTN or to normalize blood pressure results in profound, clinically significant diastolic hypotension leading to coronary hypoperfusion. In fact, Somes et al.[31] found that in treating ISH, decreasing of DBP by just 5 mm Hg significantly increases the risk of coronary heart disease and stroke.

Blood Pressure and Mortality

During the index hospitalization, PP was the only component of blood pressure to be associated with higher mortality. According to multivariable analysis, a 10 mm Hg increment in PP resulted in a 13% increased odds of death (Table 7). These findings are consistent with those of Glynn et al.[32] and colleagues who reported that the death rate is highest in hypertensive individuals with SBP of 160 mm Hg or more and DBP of <70 mm Hg, a PP value >90 mm Hg.

Pathophysiology

The etiology of a detrimental effect of widened PP upon perioperative organ function is uncertain, but may be related to the following factors. PP is an index of stiffness in the larger "cushioning" vessels and the rate of pressure wave propagation within the arterial tree.[13–15] As the ventricle ejects,[32,33] the resultant systolic pressure generated on the aortic wall is dependent on the ejected volume and the compliance of the larger arterial vessels.[15] Arterial compliance, in turn, relates to the change in volume (stroke volume) and inversely to the ensuing change in pressure (PP).[14,15,34] When stiffening of the aorta occurs as with aging, propagated and reflected waves within the arterial tree travel much more rapidly, resulting in early return of the propagated wave to the central aorta[13,34] during late systole as opposed to early diastole. This augmented systolic component thereby effectively increases afterload and diminishes diastolic pressure augmentation, leading to alterations in coronary, cerebral, and renal perfusion pressure.[13] The latter two organs, in particular, have very low resistance and consequently experience much higher PP. Generally, once PP widens, the pulsatile stress that vessels are exposed to may cause the elastic elements in the vessel wall to break down, thereby producing vessel dilation and stiffening.[14,32,35,36] Further, remodeling changes lead to vessel wall medial necrosis, stiffening, increased vascular resistance, and additional reduction in cerebral and renal perfusion.[14,37] Finally, a widened PP also contributes to endothelial dysfunction[36] and disruption of atherosclerotic plaques, enhancing both local and distal thrombotic events. Only 10% of our study cohort had normal PP (<40 mm Hg), suggesting that vascular changes associated with endothelial dysfunction were common in our study population. Lee et al.[13] demonstrated that markers of vascular thrombosis (plasma viscosity, fibrinogen levels, von Willebrand factor, flow-mediated dilation, D-dimer, and platelet activation) were significantly increased in patients with PP >50 mm Hg when compared with those without high PP. The combination of such preexisting vasculopathy with aortic-wall injury from surgical manipulation, and inflammatory response associated with CPB[5–7] provide, in part, a pathophysiologic basis for the increased postoperative vascular complications observed in patients with increased PP.

Implication for Surgical Patients

In patients undergoing CABG surgery, critical decisions regarding risk assessment, informed consent, or cancellation/alterations of procedures center on known preoperative risks and patient stability. In this regard, our findings may have major clinical importance, particularly for older persons with increased PP. Although data from the nonsurgical population suggest that PP is modifiable with exercise, diet, caloric restriction, and weight loss,[38] whether the risk associated with increased PP can be acutely modified preoperatively or intraoperatively (e.g., use of higher perfusion pressures during CBP) is unknown. Our findings would suggest that either prevention or management of high PP perioperatively is prudent.

Study Limitations

Characterization of preoperative blood pressure based on clinic (in-hospital) measurements can often over-estimate "actual" blood pressure, thereby increasing the diagnosis of HTN.[39,40] In addition to this so-called "white coat" effect, diurnal change in blood pressure is an important source of variability in measurement.[40] To overcome these limitations, in part, we obtained up to five measurements in each patient and averaged these to derive the preoperative categories of blood pressure. In this large, surgical cohort with relatively well controlled blood pressure, the mean SBP was 134 ± 18 mm Hg, suggesting minimal white coat influence. We also analyzed SBP and DBP as continuous variables and did not find any association with vascular outcomes. A second limitation of our study is the fact that patients with aortic insufficiency were included in the analyses. However, the association between PP and cerebral events and mortality remained true even when the patients with aortic insufficiency were excluded. Lastly, this being an observational study, we did not standardize either the anesthetic technique or the surgical techniques among the centers. The effects of anesthetic on PP, as well as the management of PP perioperatively, would be interesting and deserving of further investigation.

CONCLUSIONS

In patients undergoing CABG, increase in preoperative PP is associated with both fatal and nonfatal vascular outcomes. Our results call for reevaluation of risk assessment, monitoring, and management of blood pressure in the perioperative setting.

APPENDIX

The Ischemia Research and Education Foundation (IREF) is an independent nonprofit foundation, formed in 1987, which develops clinical investigators via observational studies and clinical trials addressing ischemic injury of the heart, brain, kidney and gastrointestinal tract. IREF provided all funding for execution of the study, collection of the data, and analysis and publication of the findings. The Multicenter Study of Perioperative Ischemia (*McSPI*) Research Group, formed in 1988, is an association of 160 international medical centers located in 23 countries, organized through, and supported by grants from, IREF.

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