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Right Ventricular Response to Hypercarbia after Cardiac Surgery

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The right ventricular responses to mild hypocarbia and hypercarbia were studied in 18 anesthetized and paralyzed patients following coronary artery bypass surgery. Maintaining constant tidal volume (8 ml · kg^{-1}), $F_{I_{O_2}}$ (0.5), and PEEP (5 cm H_2O), the ventilator rate was varied to sequentially produce: 1) normocarbia (Pa_{CO_2}, 38.3 ± 2.5 mmHg; mean ± SD), 2) hypocarbia (Pa_{CO_2}, 33.2 ± 2.8 mmHg), 3) hypercarbia (Pa_{CO_2}, 49.8 ± 2.9 mmHg) and 4) normocarbia (Pa_{CO_2}, 38.8 ± 3.6 mmHg). Pulmonary and right ventricular hemodynamics were assessed using a rapid-response pulmonary artery catheter after 10 min of stabilization at each Pa_{CO_2}. Pulmonary and right ventricular hemodynamics remained unaffected by slight hypocarbia. In contrast, hypercarbia increased pulmonary vascular resistance by 54% ($P < 0.001$) and mean pulmonary artery pressure by 34% ($P < 0.001$). This was accompanied by a 24% ($P < 0.001$) increase in right ventricular end-diastolic volume, a 38% ($P < 0.001$) increase in right ventricular end-systolic volume, and a 20% decrease ($P < 0.001$) in right ventricular ejection fraction. Despite an increase in right ventricular afterload, stroke volume was maintained unchanged because of a 45% ($P < 0.001$) increase in right ventricular stroke work index. Although the patients maintained pulmonary blood flow during hypercarbia using preload augmentation, compensatory reserve might be exceeded in patients with more compromised right ventricular function. (Key words: Acid-base equilibrium: respiratory acidosis; respiratory alkalosis. Carbon dioxide: hypercarbia; hypocarbia. Heart, myocardial function: carbon dioxide; right ventricle. Lung: blood flow; vascular resistance. Measurement techniques: ejection fraction; thermodilution.)

PULMONARY VASCULAR resistance (PVR) may be increased by even slight hypercarbia immediately after coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB).[1,2] In these patients who frequently have impaired right ventricular systolic function soon after CPB, acute increase in right ventricular afterload may by several mechanisms adversely affect right ventricular performance.[3–6] Although slight alterations in Pa_{CO_2} are relatively common in patients recovering from CABG, their effect on right ventricular function is unknown. The advent of a modified pulmonary artery catheter with a rapid response thermistor has enabled assessment of right ventricular performance at the bedside.[7–9] This study was designed to determine the effects of slight induced hypocarbia and hypercarbia on right ventricular function immediately after CABG in patients whose lungs are mechanically ventilated.

Methods

Eighteen hemodynamically stable patients were studied during controlled mechanical ventilation in the recovery room immediately after CABG and CPB. The study protocol was approved by the Ethics Committee of our institute, and each patient gave informed consent. Patients with impaired left ventricular function (ejection fraction < 0.4), valvular heart disease, major pulmonary dysfunction, or evidence of pulmonary hypertension[10] were excluded from the study. Twelve patients without sinus rhythm or with signs of intraoperative myocardial ischemia, those with postoperative bleeding, and those with temporary artificial pacemaker or faulty right ventricular ejection fraction (RVEF) measurement system operation also were excluded from the study after CABG. The patients' peroral, long-acting nitrate, beta-adrenergic blocker (atenolol in 8, metoprolol in 6, and timolol in 1) and calcium-entry blocker medications were continued until the morning of surgery. Four of our study patients were cigarette smokers, but none of them used pulmonary medications. The patients had a total of two or more coronary arteries stenosed, including significant involvement of the right coronary artery (RCA; ≥ 50% occlusion). Based on preoperative ECG, none had evidence of an old or recent right ventricular infarction.[11] The clinical characteristics of the study patients are given in table 1.

Anesthesia was induced with diazepam (2.5 to 10 mg) and fentanyl (30 μg · kg^{-1}) and maintained with a constant infusion of fentanyl at a rate of 0.3 μg · kg^{-1} · min^{-1} until the end of surgery. Muscle relaxation was achieved with pancuronium (0.1 mg · kg^{-1}), with additional 2-mg doses given to provide 90 to 100% relaxation (as estimated with the visual train-of-four method) up to the end of surgery. Ventilation was controlled to achieve normocarbia with a constant tidal volume of 8 ml · kg^{-1}, constant mixture of oxygen and air ($F_{I_{O_2}}$, 0.5), and constant PEEP of 5 cm

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TABLE 1. Characteristics of the 18 CABG Patients

Age (yr)	54.5 ± 5.1
Body surface area (m^2)	1.95 ± 0.12
LVEF	0.62 ± 0.10
FVC (% of predicted value)	96.4 ± 10.2
FEV1 (% of predicted value)	100.4 ± 13.5
Preoperative medication	
Nitroglycerin	15
Beta-adrenergic blocker	15
Calcium-entry blocker	14
Digoxin	2
Diuretic	2
Duration of aortic crossclamp (min)	53.9 ± 13.5
Duration of cardiopulmonary bypass (min)	110.1 ± 19.3

LVEF = left ventricular ejection fraction; FVC = forced vital capacity; FEV1 = forced expiratory volume in 1 s.
Means ± SD or number of patients presented.

H_2O (Servo 900C, Siemens-Elema, Sweden). Nonpulsatile CPB with bubble oxygenation, moderate hypothermia (nasopharyngeal temperature, 26–28°C), and mild hemodilution (hematocrit, 20–25) were used. Heparinization and its reversal with protamine chloride were accomplished using the activated coagulation time method. Sleep was ensured during CPB by giving diazepam in doses of 10 to 20 mg. Cold potassium cardioplegia and external cooling of the heart were used for myocardial protection. The pericardium was loosely closed in all patients. An $F_{I_{O_2}}$ of 1.0 was temporarily used after separation from CPB at rectal temperatures ranging from 34° to 36°C. No unexpected hemodynamic responses to protamine were noticed in any of the patients. Dopamine was infused at a dose of 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in three patients and at a dose of 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ together with an infusion of nitroglycerin at a dose of 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in one patient at separation from CPB and was continued unaltered until the end of the study. The number of coronary artery bypasses ranged from two to five, with RCA or one of its branches being bypassed in 17 of the 18 patients. Chest roentgenograms taken soon after recovery room admission were normal in all study patients.

Hemodynamic and blood oxygenation data were first obtained in premedicated patients breathing air and repeated 15 min after induction of anesthesia. The study interventions began about 3 hours after the end of CPB while patients were still asleep and while their lungs were being mechanically ventilated (Servo 900C, Siemens-Elema, Sweden). About 20 min before the beginning of the study period, diazepam (2.5 to 5 mg), oxycodone (3 to 6 mg), and pancuronium (3 to 6 mg) were given. Thereafter, oxycodone (3 to 6 mg) was occasionally given 15 min before the measurements to maintain stable oxygen consumption and carbon dioxide production as estimated using a metabolic monitor (Deltatrac™ Metabolic Monitor, Datex, Instrumentarium Corp, Finland). Ventilator rate was adjusted with a constant tidal volume of 8 $ml \cdot kg^{-1}$, constant mixture of oxygen and air ($F_{I_{O_2}}$, 0.5), and constant PEEP of 5 cm H_2O to sequentially produce normocarbia (Pa_{CO_2}, 36 to 40 mmHg), hypocarbia (Pa_{CO_2}, 32 to 36 mmHg), hypercarbia (Pa_{CO_2}, 46 to 50 mmHg), and finally again, normocarbia. The order of hypocarbia and hypercarbia was randomly varied.

Frequent blood gas analyses and continuous end-tidal CO_2 monitoring were used to direct changes in Pa_{CO_2} at constant $F_{I_{O_2}}$ (Multigas capnometer, Datex Instrumentarium Corp, Finland). Systemic and right ventricular hemodynamics, and arterial and mixed venous blood oxygen values were obtained after 10 min of stabilized Pa_{CO_2} at each stage. An average increase of 0.4° C in the rectal temperature from 34.9° C occurred during the study period (about 1½ h). Fluid management during the study consisted of balanced Ringer's solution infused at a rate of 1.5 $ml \cdot kg^{-1} \cdot h^{-1}$ and blood transfused according to losses measured every 15 min.

Systemic arterial pressure was measured *via* an indwelling catheter in the radial artery. A modified triple-lumen pulmonary artery catheter with a rapid response thermistor (Swan-Ganz Thermodilution Ejection Fraction/Volumetric Catheter, Model 93A-431H-7.5 F, American Edwards Laboratories) together with a computer (REF™-1 Ejection Fraction/Cardiac Output Computer, American Edwards Laboratories) was used for the measurement of pulmonary arterial pressures, pulmonary capillary wedge pressure (PCWP), right atrial (RAP), and right ventricular pressures, and for the measurement and computation of cardiac output (CO), RVEF, and right ventricular end-diastolic (RVEDV) and end-systolic (RVESV) volumes. For the measurement of right ventricular pressures, the proximal injectate port lumen of the pulmonary artery catheter was advanced into the right ventricle under continuous pressure monitoring. Intravascular pressures were obtained using AE (840 AME, Norway) transducers zeroed to the midchest level and recorded together with ECG leads II, V5, and RV4[11] on a multichannel recorder (Nihon Kohden, Corp., Japan).

End-expiratory pressure wave forms were used for the determination of intravascular pressures, right ventricular peak systolic pressure (RVPSP), and right ventricular end-diastolic pressure (RVEDP). The "v"-wave of RAP trace was evaluated for evidence of tricuspid regurgitation. The right ventricular injectate port lumen was positioned in the right atrium proximally to the tricuspid valve before each set of CO and RVEF measurements. Cardiac output and RVEF were determined by thermodilution using 10 ml of ice-cold 0.9 % saline solution (CO-set™, Model 93 500, American Edwards Laboratories, USA) injected at end-expiration. Three successful determinations within

TABLE 2. Minute Ventilation, Ventilator Rate, and Arterial and Mixed Venous Blood *p*H, P_{O_2} and S_{O_2}

Pa_{CO_2} (mmHg)	Awake 43.5 ± 3.7	Before CPB 39.4 ± 3.6	After CPB			
			Control 38.2 ± 2.5	33.2 ± 2.8	49.8 ± 2.9	38.8 ± 3.6
*p*Ha	7.38 ± 0.02	7.41 ± 0.03*	7.37 ± 0.02	7.42 ± 0.01†	7.28 ± 0.01†	7.37 ± 0.03
*p*Hv	7.35 ± 0.01	7.37 ± 0.02*	7.33 ± 0.02	7.37 ± 0.02†	7.26 ± 0.01†	7.33 ± 0.02
Pa_{O_2} (mmHg)	73.7 ± 7.7	203.8 ± 51.3	200.8 ± 60.0	221.0 ± 47.6*	177.8 ± 39.3*	211.9 ± 45.6
Pv_{O_2} (mmHg)	39.5 ± 3.6	42.8 ± 3.5†	38.3 ± 3.9	38.0 ± 3.5	42.4 ± 5.2	38.4 ± 4.7
Sa_{O_2} (%)	94.4 ± 2.6	98.6 ± 1.3	98.6 ± 1.5	98.8 ± 1.4	98.1 ± 1.7	98.6 ± 1.5
Sv_{O_2} (%)	73.2 ± 5.5	78.4 ± 5.3†	70.7 ± 4.8	71.2 ± 5.3	71.5 ± 6.6	70.6 ± 7.2
Minute ventilation (1 min^{-1})		7.7 ± 0.9	7.7 ± 1.2	9.5 ± 1.5*	5.2 ± 1.6†	8.3 ± 0.9
Ventilator rate (min^{-1})		12 ± 1	12 ± 2	15 ± 2*	8 ± 1	13 ± 1

Means ± SD.

* $P < 0.01$; † $P < 0.001$; compared to normocarbia (Control).

20% of each other were averaged. The RVEDV, RVESV, and cardiac index (CI) were calculated by the computer from measurements of CO, RVEF, and heart rate (HR).[7]

Arterial and mixed venous blood samples were immediately analyzed for blood gases and *p*H (ABL4, Radiometer, Denmark) and for hemoglobin oxygen saturation and hemoglobin content (CO-oximeter, IL 282, Instrumentation Laboratories, MA). Mean arterial (MAP) and mean pulmonary arterial (MPAP) pressures, pulmonary vascular (PVR) and systemic vascular (SVR) resistances, and right ventricular (RVSWI) and left ventricular (LVSWI) stroke work indices were derived using standard formulae.[12]

Hemodynamic responses to Pa_{CO_2} at different measurement stages were compared by the Wilcoxon signed rank test. Simple linear regression analysis was used for correlation between variables. A $P < 0.01$ was considered significant. Data are presented as means ± SD.

Results

The Pa_{CO_2} levels were 43.5 ± 3.7 mmHg when patients were awake, 39.4 ± 3.6 mmHg after induction of anesthesia (before CPB), and 38.3 ± 2.5, 33.2 ± 2.8, 49.8 ± 2.9, and 38.8 ± 3.6 mmHg at normocarbia, hypocarbia, hypercarbia, and second normocarbia after CPB, respectively. The corresponding ventilation and blood oxygenation data are given in table 2.

RIGHT VENTRICULAR HEMODYNAMICS AFTER CPB

Normocarbia (table 3). Right ventricular afterload was significantly increased after CPB as manifested by significant increases in MPAP, pulmonary artery diastolic to pulmonary capillary wedge pressure (DPAP–PCWP) gradient, PVR, and RVPSP, with essentially no change in RVESV. The RVEDV, RAP, and RVEDP remained unchanged. The significant 20% reduction in RVEF after CPB with no change in RVSWI suggests unaltered or reduced right ventricular contractility in the normocarbic CABG patients after CPB.

Hypocarbia (table 3, figs. 1 and 2). No significant changes were observed in right ventricular hemodynamics by slight hypocarbia.

Hypercarbia (table 3, figs. 1 and 2). Hypercarbia consistently increased right ventricular afterload and systolic

TABLE 3. Right Ventricular Hemodynamics in 18 CABG Patients

Pa_{CO_2} (mmHg)	Awake 43.5 ± 3.7	Before CPB 39.4 ± 3.6	After CPB			
			Control 38.3 ± 2.5	33.2 ± 2.8	49.8 ± 2.9	38.8 ± 3.6
MPAP (mmHg)	17.5 ± 4.0	13.8 ± 2.4†	18.1 ± 3.4	17.2 ± 3.2	24.2 ± 2.8†	19.6 ± 2.8
DPAP–PCWP (mmHg)	1.5 ± 1.6	1.5 ± 1.4†	5.1 ± 2.4	4.1 ± 1.7	7.8 ± 3.7*	5.1 ± 2.5
PVR (dyn · sec · cm^{-5})	105 ± 40	126 ± 52†	205 ± 70	159 ± 45	315 ± 137†	203 ± 75
RVPSP (mmHg)	29.2 ± 5.0	23.9 ± 3.4*	29.1 ± 3.8	29.4 ± 4.4	36.3 ± 5.5†	31.8 ± 3.7
RVESV (ml)	78 ± 32	62 ± 19	76 ± 37	84 ± 37	105 ± 35†	80 ± 30
RVEDV (ml)	157 ± 31	123 ± 22	123 ± 37	132 ± 35	153 ± 36†	130 ± 29
RAP (mmHg)	5.5 ± 2.3	5.7 ± 1.9	7.1 ± 2.5	7.6 ± 2.2	8.6 ± 2.5†	7.8 ± 2.1
RVEDP (mmHg)	7.8 ± 2.6	7.2 ± 2.3	8.6 ± 2.9	9.4 ± 2.6	10.9 ± 2.6†	9.9 ± 2.5
RAP/PCWP	0.51 ± 0.14	0.72 ± 0.15	0.86 ± 0.20	0.86 ± 0.19	0.95 ± 0.26	0.87 ± 0.25
RVEF	0.51 ± 0.12	0.50 ± 0.09*	0.40 ± 0.10	0.38 ± 0.11	0.32 ± 0.10†	0.39 ± 0.09
RVSWI (gm · m^{-2})	6.6 ± 3.0	3.4 ± 1.0	3.5 ± 1.2	3.1 ± 1.3	5.0 ± 1.5†	3.9 ± 1.2

Means ± SD.

* $P < 0.01$; † $P < 0.001$; compared to normocarbia (Control).

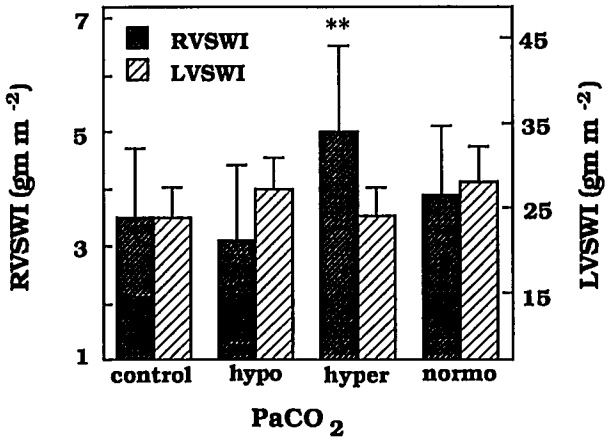

FIG. 1. Right ventricular (RVSWI) and left ventricular (LVSWI) stroke work indices during changes in Pa_{CO_2} in 18 CABG patients after CPB. Control = Pa_{CO_2} 38.3 ± 2.5 mmHg (mean ± SD); hypo = Pa_{CO_2} 33.2 ± 2.8 mmHg; hyper = Pa_{CO_2} 49.8 ± 2.9 mmHg; normo = Pa_{CO_2} 38.8 ± 3.6 mmHg. **$P < 0.001$.

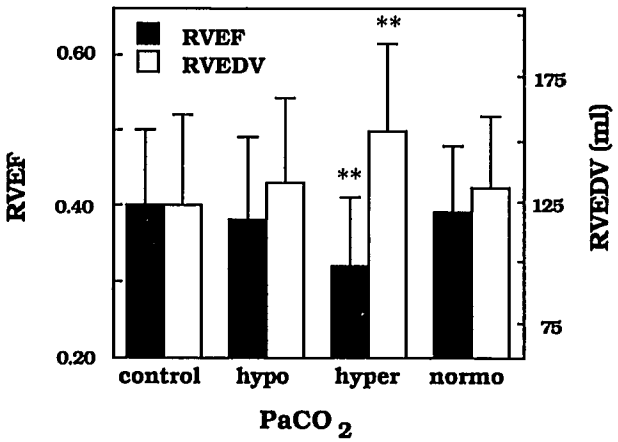

FIG. 2. Right ventricular ejection fraction (RVEF) and right ventricular end-diastolic volume (RVEDV) during changes in Pa_{CO_2} in 18 CABG patients after CPB. Control = Pa_{CO_2} 38.3 ± 2.5 mmHg (mean ± SD); hypo = Pa_{CO_2} 33.2 ± 2.8 mmHg; hyper = Pa_{CO_2} 49.8 ± 2.9 mmHg; normo = Pa_{CO_2} 38.8 ± 3.6 mmHg. **$P < 0.001$.

wall stress, as manifested by significant increases in PVR, MPAP, DPAP-PCWP gradient, RVPSP, and RVESV. The increase in right ventricular afterload was associated with a 45% increase in RVSWI and significant increases of RVEDV, RAP, and RVEDP while RVEF decreased significantly by 20%.

The effects of hypercarbia on right ventricular hemodynamics were completely reversed by restoring normocarbia. The RAP trace analysis revealed no detectable change in "v"-waves indicative of tricuspid insufficiency during the study. ST-segments in leads II, V5, and RV4 remained unaffected by Pa_{CO_2} changes.

Systemic Hemodynamics after CPB

See table 4.

Normocarbia. The only significant change in systemic hemodynamics after CPB was the 32% increase in HR.

Hypocarbia and Hypercarbia. The only significant changes in systemic hemodynamics produced by hypocarbia and hypercarbia were the 10% increases in MAP by hypocarbia and in PCWP by hypercarbia.

Discussion

The results of the current study indicate that in anesthetized, paralyzed patients whose lungs are being mechanically ventilated following CABG and CPB, slight hypercarbia induced by alveolar hypoventilation results in a significant increase in right ventricular afterload with significant right ventricular end-diastolic and end-systolic dilatation, increased chamber pressures, and reduced RVEF. Right ventricular forward stroke output is maintained unchanged by using preload augmentation for increased right ventricular work. The hemodynamic consequences of hypercarbia are completely reversed by restoring normocarbia.

The observed depression of the right ventricular ejection fraction and increased right ventricular volumes may be a physiologic compensation to the increased afterload. Alternatively, this may be due to the impairment of right ventricular contractility.[5,13,14] While the normal right ventricle is a low-pressure chamber, with limited contractility reserve and decreased ability for pressure develop-

TABLE 4. Systemic Hemodynamics in 18 CABG Patients

			After CPB			
Pa_{CO_2} (mmHg)	Awake 43.5 ± 3.7	Before CPB 39.4 ± 3.6	Control 38.3 ± 2.5	33.2 ± 2.8	49.8 ± 2.9	38.8 ± 3.6
HR (beats min^{-1})	66 ± 12	64 ± 10†	84 ± 13	86 ± 13	85 ± 13	87 ± 13
CI (1 min^{-1} m^{-2})	2.58 ± 0.96	1.98 ± 0.33	2.00 ± 0.33	2.09 ± 0.45	2.06 ± 0.45	2.16 ± 0.42
MAP (mmHg)	83 ± 10	72 ± 7	80 ± 15	88 ± 17*	79 ± 17	88 ± 15
PCWP (mmHg)	10.7 ± 3.0	8.0 ± 2.2	8.3 ± 2.5	9.0 ± 2.5	9.2 ± 2.2*	9.0 ± 2.2
SVR (dyn·sec·cm^{-5})	1,241 ± 277	1,388 ± 195	1,519 ± 377	1,639 ± 473	1,444 ± 388	1,520 ± 253
LVSWI (gm·m^{-2})	39.9 ± 13.5	27.3 ± 7.3	23.7 ± 7.8	26.9 ± 9.4	23.8 ± 9.4	27.9 ± 8.8

Means ± SD.

* $P < 0.01$; † $P < 0.001$; compared to normocarbia (Control).

ment under acute afterload stress, the degree of afterload elevation becomes critical for the hemodynamic course.[13–15] Thus, in patients with adult respiratory distress syndrome (ARDS) who have pulmonary hypertension without right ventricular contractile dysfunction, preload augmentation effectively increases RVSW and maintains stroke volume up to an MPAP of 30 mmHg.[13] Observations in previously healthy humans affected by acute pulmonary thromboembolism suggest that overt right ventricular failure and hemodynamic collapse may be expected beyond an MPAP of 30 to 40 mmHg.[15]

In our CABG patients, the hypercarbia-induced right ventricular end-diastolic dilatation at MPAP values of 18 to 30 mmHg caused a 45% increase in RVSWI. Foëx and Prys-Roberts reported a similar increase in RVSW in experimental animals with pulmonary hypertension as a consequence of a comparable degree of induced hypercapnia.[16] In patients with traumatic or ischemic reduction of right ventricular contractility, the Frank-Starling mechanism has been shown to exhaust early if right ventricular afterload is concomitantly increased.[17,18] Effective maintenance of right ventricular stroke volume in the face of significantly reduced RVEF by hypercarbia suggests that our CABG patients were on the ascending limb of the Frank-Starling curve, taking advantage of preload augmentation despite the significantly increased ejection pressure.

Because decreased contractility, by definition, is a decrease in cardiac function without a concomitant change in preload or afterload, we do not know whether the significant reduction in RVEF and increase in RVESV are indicative of reduced right ventricular contractility during hypercarbia in our study patients. While contractility was not directly measured in this study, we can only speculate about potential factors affecting right ventricular contractility in our CABG patients. During increased afterload, right ventricular performance critically depends on adequate coronary blood flow.[19] Thus, right coronary hypotension caused by acute pulmonary hypertension will rapidly decrease right ventricular contractility due to altered right ventricular transmyocardial blood flow distribution and subsequent development of subendocardial ischemia.[20] Moreover, carbon dioxide has been shown to be a direct vasodilator of the coronary vasculature, acting independently of changes in cardiac work, autonomic transmitters, and *p*H.[21] There is experimental evidence that changes in Pa_{CO_2} of 20 to 30 mmHg can markedly change myocardial blood flow.[21] On the other hand, adequate right ventricular perfusion is dependent on a sufficient systemic blood pressure level after CABG. In our patients with only a modest increase in right ventricular pressures and without a significant change in MAP,[2] the right ventricular perfusion apparently was maintained adequate during hypercarbia. This is supported by the absence of ST-segment changes in ECG leads II and RV4.[11]

Right ventricular contractility may increase with hypercarbia if it results in catecholamine release from sympathetic nerve endings.[22] Fifteen of our 18 patients were receiving β-adrenergic blockers, and residual β-blockade may thus have attenuated the adrenergic responses during hypercarbia in these patients.[23,24] A decrease in right ventricular contractility by β-adrenergic blockers has been observed in normal volunteers and patients with pulmonary hypertension during rest and exercise studies.[25,*] The involvement of the β-adrenergic component in the right ventricular response to increased afterload is further pointed out in the study by Rose *et al.* in which right ventricular dysfunction in awake dogs during hypercarbia was aggravated under β-blockade.[26] In accordance with our earlier findings,[2] HR did not significantly change during hypercarbia in the current study. This may be a sign of residual β-blockade. Alternatively, hypercarbia increased parasympathetic tone.[27]

The increase in central venous pressure (CVP) during hypercarbia-induced increase in CO has been assumed to be the result of a reflex-mediated peripheral venoconstriction.[28] The fact that in our patients CO, MAP, and SVR remained essentially unchanged during hypercarbia while RAP, RVEDV, and RVESV increased significantly may be compatible with right ventricular depression with or without peripheral venoconstriction.

Right ventricular pressure or volume overload can alter right ventricular diastolic mechanics.[5,29,30] The fact that both RVEDP and RVEDV were essentially unchanged after CABG and increased to a similar degree by hypercarbia may indicate that right ventricular compliance was not significantly affected after CABG and during hypercarbia in this study. As in our earlier studies,[1,2] PCWP and the ratio of RAP to PCWP increased concomitantly with right ventricular dilation by hypercarbia. Whether these findings indicate a decrease in left ventricular compliance *via* ventricular interaction is unknown but unlikely since CI and left ventricular work remained unchanged.

Changes in intrathoracic pressure–volume conditions caused by alterations in mechanical ventilation may induce changes in right ventricular filling.[30] Right ventricular pressure and volume measurements performed at end-expiration will tend to minimize this effect. Right ventricular pressure measurements, which were obtained from recordings at end-expiration, most likely were unaffected by transpulmonary pressure changes caused by differences in ventilator rate in the current study. In con-

* Matthay RA, Biondi JW, Schulman DS, Wiedeman HP: Acute right heart failure – Pathogenesis, diagnosis and therapy. Applied Cardiopulmonary Pathophysiology 2:59–83, 1988

trast, differences in ventilator rate may have affected the right ventricular volume measurements, because the manual timing of the right ventricular volume measurements may fail to occur exactly at end-expiration, especially at a higher ventilator rate. A more positive pleural pressure caused by higher ventilator rate in hypocarbia would decrease transmural diastolic filling pressure of the right ventricle and result in reduced RVEDV and stroke volume (SV). On the other hand, the increased lung volume above functional residual capacity (FRC) would increase PVR, RVESV, and RVEDV. In our study, use of increased ventilator rate to produce hypocarbia resulted in nonsignificant increases in RVEDV and RVESV. The changes in right ventricular volumes probably were not caused by increased airway pressure, however, since PVR simultaneously decreased. Reduced pleural pressure (less positive) during lower ventilator rate in hypercarbia would increase transmural diastolic filling pressure of the right ventricle, which would increase RVEDV and SV. However, the simultaneous increase in right ventricular afterload (either by hypercarbia-induced pulmonary vasoconstriction or by reduced FRC) would increase RVESV and offset any beneficial effect on SV caused by reduction in pleural pressure at a lower ventilator rate. The fact that no decrease in SV occurred during hypercarbia despite significant increases in RVESV and RVEDV may be caused partly by a reduction in ventilator rate. Thus, the influence of differences in mechanical ventilation on our results cannot be ruled out. We noticed previously, however, that there is no significant difference in the cardiopulmonary responses to hypercarbia produced either by decreasing minute volume or by adding CO_2 to the inspired gas.[2] We thus believe that the transpulmonary pressure changes during changes in ventilator frequency did not significantly affect our results.

The direct measurement of right ventricular volumes by the newly modified thermodilution method has clearly obviated some of the problems associated with estimation of right ventricular preload during alterations in intrathoracic pressure and ventricular compliance. The fact that the thermodilution method measures only forward flow may result in falsely low values in patients having pulmonary hypertension and tricuspid regurgitation.[8,14] Based on RAP trace analysis, tricuspid regurgitation was absent in our patients. Although the thermodilution RVEF measurement system generally functioned well in our hands, the capture of an adequate ECG signal was sometimes difficult, especially after CPB, leading to the exclusion of two patients from the study. The patients included in this study were without dysrhythmias or artificial pacemakers, both of which would adversely affect the RVEF measurement.[8,14] Recently, Spinale *et al.*[9] experimentally demonstrated that the thermodilution method is position sensitive, *i.e.*, bringing about significantly reduced RVEF values with increased thermistor distance from pulmonary valve. Moreover, although there was a strong correlation between thermodilution and biplane ventriculographic measurements of RVEF ($r = 0.74$), they noticed that the thermodilution method tended to underestimate RVEF, especially during hypovolemia. Since our patients were obviously not hypovolemic and the position of the catheter was carefully checked by pressure monitoring immediately before each set of CO and RVEF measurements, it is likely that the changes in RVEF during alterations in Pa_{CO_2} were reliably assessed by the thermodilution method.

Although the changes in intravascular volume may be accurately estimated by direct measurement of ventricular volumes and pressures, it still is difficult to separate the possible spontaneous intravascular volume changes occurring during the study period (about 1½ h) from those directly caused by carbon dioxide.[28,31] Our patients, however, were all hemodynamically stable at the beginning of the study. No significant bleeding was noticed in any of them. A standard continuous fluid infusion and blood transfusion regimen was used, and one-half of the patients were studied in reverse order in respect to changes in Pa_{CO_2}.

In a study by Wexels and Mjøs[32] concerning the effects of carbon dioxide and *p*H on myocardial function in anesthetized, mechanically ventilated dogs with acute, ischemic left ventricular failure, hypercarbia (Pa_{CO_2}, 83 ± 8.3 mmHg) was shown to aggravate left ventricular failure. This was indicated by a significantly increased left ventricular end-diastolic pressure, mean RAP, and mean MPAP while CO, HR, and MAP did not change significantly. These changes in central hemodynamics were reversed when *p*H was normalized during hypercarbia. The hemodynamic effects of acute right ventricular ischemia may be less conspicuous, but during a concomitant, acute, experimentally induced increase in right ventricular outflow pressure, CO and arterial pressure will rapidly decrease while RVEDP will increase.[33,34] Thus, it is probable that the existence of intraoperative right or left ventricular ischemia would have enhanced the adverse hemodynamic effects of hypercarbia observed in the current study.

The common occurrence of left ventricular dysfunction in patients with right ventricular dilatation and hypertrophy due to chronic lung disease and pulmonary hypertension may increase the sensitivity of these patients to even mild hypercarbia and the attendant increase in right ventricular afterload.[35] Thus, it is likely that chronic lung disease would have intensified the hemodynamic effects of hypercarbia seen in the current study.

In some experimental studies, the hemodynamic effects of hypercarbia have been shown to spontaneously atten-

uate with time[27]; thus, our results might be modified by increasing the duration of hypercarbia. Moreover, the hemodynamic changes generally associated with recovery from cardiac anesthesia and hypothermia were obviously attenuated by the use of the muscle relaxant and sedatives in this study.† Our results, therefore, cannot be applied directly to patients spontaneously recovering from CABG.

Mangano noted no relationship between the distribution of coronary artery disease and the degree of right ventricular dysfunction after CABG in 16 of 22 patients who had a 90% or greater occlusion of RCA.[3] Considering the only marginally occluded RCA in about one-half of our study patients, the lack of evidence of right ventricular infarction, and the presence of good preoperative RVEF (>40%) in 15 of 18 patients, we believe that the results of the current study also are applicable to patients without an RCA stenosis.

In conclusion, our results demonstrate that mild hypercarbia after CPB increases right ventricular afterload and right ventricular work load resulting in reduction of right ventricular ejection fraction at a higher right ventricular filling and pressure. The reduction in right ventricular ejection fraction occurred in the absence of changes in cardiac output or electrocardiographic evidence of myocardial ischemia. Restoration of normocarbia by adjusting mechanical ventilation under continuous end-tidal CO_2 monitoring totally reversed the potentially adverse hemodynamic effects of hypercarbia.

† Guffin A, Girard D, Kaplan JA: Shivering following cardiac surgery: Hemodynamic changes and reversal. Journal of Cardiothoracic Anesthesia 1:24–28, 1987

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