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The Pressure Rate Quotient Is not an Indicator of Myocardial Ischemia in Humans

An Echocardiographic Evaluation

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Background: **The pressure rate quotient (PRQ; mean arterial pressure/heart rate [MAP/HR]) less than one (PRQ < 1) has been proposed as a simple, clinically available hemodynamic index of myocardial ischemia. Recent investigations using electrocardiography (ECG) detection of myocardial ischemia have not found this index reliable. We prospectively compared PRQ < 1 to detection of myocardial ischemia *via* transesophageal echocardiography (TEE) and ECG in patients undergoing elective coronary artery bypass graft.**

Methods: **Forty-six of 50 patients admitted into the study had acceptable data acquisition. Calibrated ECG leads II and V_5 were recorded with a computerized ST-segment analyzer. Hemodynamic data were stored at 2-min intervals. After tracheal intubation, a 5.0-MHz TEE probe was inserted. Electrocardiography-detected ischemia was defined as new onset ST-segment deviation (≥1 mm) lasting for >1 min. Transesophageal echocardiography determination of ischemia was worsening of wall motion ≥1 grade and lasting >1 min. PRQ < 1 was compared to ECG and/or TEE as a predictor or indicator of myocardial ischemia.**

Results: **Electrocardiography ischemia occurred during 230 intervals in 10 patients, and in only 41 of 230 (18%) was PRQ < 1. Transesophageal echocardiography-defined ischemia occurred during 592 intervals in 9 patients, and in 119 of 592 (20%) PRQ < 1. Compared to ECG and TEE, PRQ < 1 had a low sensitivity (21%) and poor positive predictive value (25%).**

Conclusions: **Pressure rate quotient < 1 is an unreliable indicator and predictor of myocardial ischemia when evaluated by ECG, TEE, and the combination of these modalities in patients undergoing coronary artery bypass graft surgery. (Key words: Anesthesia: cardiac. Heart: coronary artery disease; ischemia. Monitoring: electrocardiography; pressure rate quotient; transesophageal echocardiography; Surgery, cardiac: coronary artery bypass grafting.)**

INTRAOPERATIVE ischemia is a harbinger of perioperative morbidity and mortality.[1–3] Electrocardiography (ECG) is used widely for ischemia detection, despite its inherent limitations.[4,5] Consequently, investigators have sought supplemental means to diagnose myocardial ischemia. Hemodynamic indexes have been proposed as simple, clinically available methods to aid in detection of myocardial ischemia.[6,7] Recently, the pressure rate quotient (PRQ, mean arterial pressure/heart rate [MAP/HR]) less than one (PRQ < 1) has undergone scrutiny in canine models and human applications. Although one clinical report supports this concept, other investigators have been unable to consistently validate the efficacy of PRQ < 1 as a predictor of ischemia in patients with coronary artery disease.[8,9] Using ECG as evidence of ischemia, Gordon *et al.* were unable to find a relationship between ECG evidence of ischemia and PRQ < 1.[10] They concluded that in patients undergoing elective coronary artery bypass operations PRQ < 1 was a poor indicator or predictor of myocardial ischemia. Buffington's original animal experiments employed ultrasound as a gold standard for ischemia detection. Our previous use of ECG as a sole means for ischemia detection may not have been as sensitive or specific as the ultrasound standard in Buffington's original investigation. In recent years, transesophageal echocardiography (TEE) has been touted as the new gold standard of ischemia detection in the operating room.[11,12] The availability of a specific, early means of ischemia detection is desirable, considering the cost of perioperative ischemia and its ensuing morbidity and mortality. Using this mode of ischemia detection, Leung *et al.* compared indexes of myocardial

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oxygen supply and demand against ischemia detection *via* TEE during the perioperative period in a similar patient population.[13] Although PRQ < 1 was evaluated in that study, it was not the main focus of the experimental design. Hemodynamic indexes, rate pressure product, and PRQ were compared only to TEE evidence (regional wall motion abnormalities [RWMA]) of ischemia. They concluded that perioperative TEE episodes were triggered infrequently by changes in hemodynamics. However, in everyday clinical practice, the clinician may have both modalities available for intraoperative use. The combination of two calibrated leads available for ECG monitoring *and* the ability to use a TEE for ischemia detection is a reality now, and their combined use has the potential to make intraoperative ischemia detection more thorough *via* these two different technologies. As a result of the availability of this technology, we believed a more systematic evaluation of PRQ < 1 using ultrasound (2-D TEE), in addition to calibrated ECG monitoring, as ischemia detection was warranted as a follow-up to our previous study. That study evaluated PRQ < 1 compared to ECG as our gold standard for ischemia detection. Therefore, we prospectively evaluated PRQ < 1 as an indicator and/or predictor of myocardial ischemia occurring before cardiopulmonary bypass in patients undergoing elective coronary artery bypass grafting (CABG) operations. PRQ < 1 was compared to TEE and/or computerized ECG ST-segment analysis for the detection of myocardial ischemia.

Methods

This study was approved by the Human Investigation Committee of the authors' institution. Fifty (50) patients with multi-vessel coronary artery disease as verified by cardiac catheterization and selected for elective coronary artery bypass surgery were admitted to the study. All patients received 0.1 mg/kg morphine sulfate and 0.005 mg/kg scopolamine intramuscularly 90 min before arrival in the operating room. They also received their usual anti-anginal medications and were transported to the operating room breathing oxygen delivered by nasal cannula at 3 L/min. Intraoperative monitoring included ECG (leads II and V_5 calibrated one 1 mV = 10 mm − diagnostic mode), pulse oximetry, end tidal carbon dioxide concentration, and arterial and pulmonary artery pressure catheters (inserted prior to anesthesia induction). In addition, all patients were monitored with the Hewlett-Packard computer-processed electrocardiogram ST-segment analyzer (Andover, MA, model HP 78534L) with a frequency response of 0.05–100 Hz using leads II and V_5. This monitor measures the vertical difference between the isoelectric point (80 ms before the R wave) and the ST segment (120 ms after the R wave). The settings for isoelectric and ST-segment points were adjusted for HR. The ST-segment deviation in leads II and V_5 were updated and averaged over 15 s and then displayed. Hard copy of the ECG was obtained at specific times (during preinduction, induction/intubation, incision/sternotomy, and aortic cannulation) and whenever ST-segment deviation > 1 mm appeared on the monitor. In addition, someone continually viewed the monitor for ST-segment changes. Upon later review, hard copies of the ECG were used to verify changes in the ST-segment deviation. The intraoperative team were shown the data from the ST-segment analyzer displayed alongside the hemodynamic information and therefore were not blinded to the occurrence of ST-segment deviation > 1 mm. In all patients, a standardized anesthetic was induced with sufentanil 5–10 μg/kg administered over 10 min during induction and endotracheal intubation. A sufentanil infusion (total 15–20 μg/kg) was administered 60–90 min following induction of anesthesia. Pancuronium (0.1 mg/kg) was used for neuromuscular relaxation. Based on clinical judgment, enflurane (<0.5%) was administered for supplemental anesthesia. Immediately after intubation, a 5.0-MHz phased array transducer (Hewlett-Packard) was inserted under direct vision and positioned at a transgastric short axis view of the left ventricle at the midpapillary level and recording on videotape was begun.

Patients were excluded from the study if they had abnormal myocardial repolarization (*e.g.*, digitalis effect, left ventricular hypertrophy, left bundle branch block) on preoperative (baseline) 12 lead ECG, preoperative placement of an intraaortic balloon pump, or contraindications to TEE. All patients who evidenced unstable anginal patterns (failed angioplasty, heparin and nitroglycerin infusions, preoperative intraaortic balloon pump insertion) were omitted from the study similarly.

ST-segment deviation, HR, and arterial, right atrial, and pulmonary artery pressures were recorded at 2-min intervals following placement of the monitors in the preinduction period (before induction of anesthesia) until initiation of cardiopulmonary bypass. Patients were considered to have new onset myocardial ischemia if they had longer than 1 min of ST-segment

deviation that was greater than or equal to 1 mm from their preoperative baseline ECG.

Transesophageal echocardiography was monitored on-line in the operating room. Specific intervals of videotaping were obtained at 5 min before, during, and after events usually associated with hemodynamic responses. These included: immediately after intubation, incision, sternotomy, isolation of left internal mammary artery, aortic cannulation, and immediately preceding cardiopulmonary bypass. In addition, whenever there was ECG evidence of ischemia or an alteration of hemodynamics (greater than 20% change from baseline), videotaping began and continued until resolution or onset of cardiopulmonary bypass. The transgastric short axis view of the left ventricle was divided into four quadrants with the use of papillary muscles as a guide to reference level. Left ventricular systolic endocardial excursion and wall thickening was evaluated by inspection. Although the TEE was available for intraoperative use, the wall motion scoring was not performed intraoperatively. Unedited tapes were subsequently reviewed and graded, 4–6 weeks after the study by two observers blinded to clinical events. The grading system for each quadrant was 0 = normal wall motion or thickening, 1 = hypokinesis, 2 = akinesis, and 3 = dyskinesia. Transesophageal echocardiography episodes of ischemia, RWMA, were defined as new onset of wall motion worsening $\geq$1 grade and lasting >1 min.

Postoperatively, 12-lead electrocardiograms were obtained daily for 3 days. Blood samples were obtained for measurement of creatine phosphokinase × MB% U/L fractions at the following times: immediately before cardiopulmonary bypass, upon arrival into the intensive care unit, and every 8 h for 48 h. Postoperative myocardial infarction was defined as peak creatine phosphokinase × myocardial bands (MB%) > 80 U/L and ECG changes (new significant Q waves and/or development of left bundle branch block).

The intraoperative period was composed of 2-min intervals of measurement. Data were obtained for each 2-min interval (ST-segment analysis and all hemodynamic indexes) with the average value calculated over this period. All data were stored on a Hewlett-Packard Vectra Computer on Microsoft (Redmond, WA) Excel spreadsheet. To clarify the definition of predictors and indicators of myocardial ischemia, the term predictor is employed whenever onset of PRQ < 1 occurs within 15 min of ECG and/or TEE evidence of ischemia. This would suggest a temporal relationship between the occurrence of TEE and/or ECG ischemia and PRQ < 1. An indicator of myocardial ischemia identifies simultaneous occurrence of ischemia by PRQ < 1 with ECG and/or TEE evidence of ischemia. PRQ < 1 was evaluated *via* calculation of sensitivity, specificity, and positive and negative predictive values by using both ECG and TEE as gold standards for ischemia detection. Transesophageal echocardiography interobserver agreement using data from a random number of tapes was performed using Cohen's kappa as a measure of agreement.[14] Interobserver agreement for TEE grading, or discrepancy between observers, was defined as differences in scoring of a particular segment by two or more grades. By kappa analysis, the wall motion scoring showed 100% agreement. Parenthetically, if only one grade difference was seen, interobserver agreement decreased to 0.66, a kappa value indicating moderate agreement.

Results

Demographics

For the 50 patients studied, 46 were deemed by the investigators to have acceptable data acquisition (hemodynamics, ECG, and TEE). Mean age was 65 yr (range 41–83 yr) with a mean preoperative left ventricular ejection fraction (LVEF) of 54% (range 35–73%). The majority of the population was male, 38 of 46 (82.6%). Only 2 of 46 (4.3%) experienced myocardial infarction less than 1 week prior to surgery, and 24 of 46 (52%) of the patients had no history of previous myocardial infarction. Preoperative beta blocker therapy was present in 26 of 46 (56%) of patients, 34 of 46 (74%) received calcium channel blocker therapy, and 20 of 46 (43%) were treated with both beta blockers and calcium channel blocker therapy preoperatively.

ECG

For ECG determination of ischemia, 3,326 of the possible 3,365 2-min intervals were available for study. Prior to cardiopulmonary bypass, 10 of 46 (22%) patients experienced one or more ECG ischemic events. These 10 patients had a total of 230 ischemic 2-min intervals detected by ECG, whereas only 41 of 230 (18%) intervals had PRQ < 1 (fig. 1A). There were 3,096 intervals when no ECG ischemia was detected, and 564 of 3096 (18%) of these 2-min intervals had PRQ < 1.

Four patients (4 of 10) had ECG evidence of ischemia upon arrival in the operating room. Only one of these

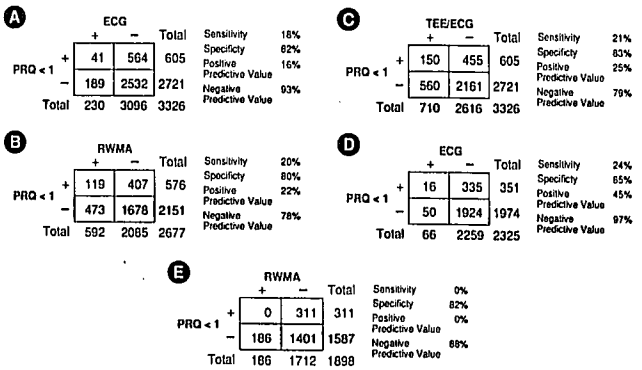

Fig. 1. Analysis of 2-min intervals in which the presence or absence of electrocardiography (ECG) and/or transesophageal echocardiography (TEE)-defined ischemia occurred ("gold standard") compared to whether the pressure rate quotient (PRQ) was <1 or >1. *(A)* The entire study population (n = 46) experienced 230 ischemic ECG intervals, and in only 41 (18%) was the corresponding PRQ <1. Note that, of the 3,096 intervals in which there was no ECG-detected ischemia, there were 564 intervals in which PRQ < 1 was a false-positive indicator of ischemia. *(B)* Of the 592 ischemic TEE intervals, in only 119 (20%) was PRQ < 1. In the 2,085 intervals in which no ischemia was detected by TEE, there were 407 in which PRQ < 1 was a false-positive indicator of ischemia. *(C)* Data presentation comparing the simultaneous detection of ischemia by ECG and TEE compared to the occurrence of PRQ < 1. Combining modalities did not reveal PRQ < 1 to be a better indicator of ischemia. *(D)* Analysis for subset of population with a preoperative LVEF ≥ 55% (n = 31). In the 66 intervals in which ECG ischemia was detected, 16 (24%) were associated with PRQ < 1. PRQ < 1 was a false indicator of ischemia in 85% of the nonischemic ECG intervals. *(E)* Data analysis for same population in *D*. In the 186 intervals in which RWMA was detected, PRQ < 1 never occurred. PRQ < 1 was present in 311 of 1712 intervals in which regional wall motion abnormalities was not detected. In this subset of the study population, this analysis shows low sensitivity and positive predictive value.

four patients had simultaneous PRQ < 1 at this time. The distribution of onset of all ischemic ECG intervals occurred as follows: 5 of 10 occurred in the preinduction interval; 1 of 10 during induction and intubation; 1 of 10 after TEE insertion; 2 of 10 at aortic cannulation; and 1 of 10 just prior to cardiopulmonary bypass. Three patients (3 of 10) had ECG evidence of ischemia upon arrival in the operating room lasting up to cardiopulmonary bypass.

TEE

When comparing onset of new RWMA to PRQ < 1, 2,677 2-min intervals were available for study (fig. 1B). Of the total patients studied, 15 of 46 (32%) evidenced new onset of RWMA. Nine of these patients had PRQ < 1 at some time during the pre-period. These 9 patients experienced a total of 592 intervals when RWMA were detected. Only 119 of 592 (20%) intervals in which RWMA occurred were associated with PRQ < 1. There were 2,085 intervals without RWMA detection, and 407 of 2,085 (19%) of these were associated with PRQ < 1.

The distribution of RWMA episodes detected by TEE was as follows: 6 of 15 were observed immediately after TEE probe insertion; 2 of 15 occurred from sternotomy continuing to the end of the left internal mammary artery isolation; 4 of 15 started during left internal mammary artery isolation and persisted through aortic cannulation; 1 of 15 occurred with aortic cannulation only; and 2 of 15 occurred immediately prior to cardiopulmonary bypass. Once a patient ceased having RWMA, it did not recur in the pre-bypass period.

In terms of PRQ < 1 predicting ischemia as detected by TEE, only 3 of 15 patients who exhibited RWMA pre-bypass had onset of PRQ < 1 within 15 min of TEE-defined ischemia. One patient had onset of PRQ < 1 and RWMA occurring simultaneously. Two patients had PRQ < 1 occurring *after* onset of RWMA (fig. 2).

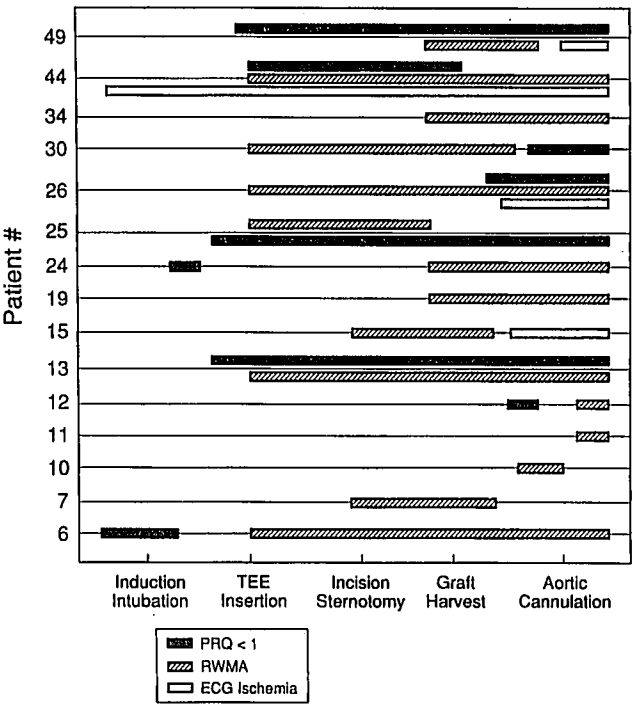

Fig. 2. Plot of entire population who experienced ultrasound-defined ischemia, regional wall motion abnormalities. The relationship to the stressful components of the intraoperative (before cardiopulmonary bypass) period as well as presence or absence of electrocardiographic ischemia and a pressure rate quotient <1 are presented.

ECG and TEE

Previous evaluations have been concerned with comparing PRQ < 1 to either TEE *or* ECG determinations of ischemia. In clinical practice, both modalities are available for use. To determine whether combined use of TEE *and* ECG improved the sensitivity and specificity of PRQ, we compared both techniques with the incidence of PRQ < 1 (fig. 1C). Of the 3,326 total intervals available for study, 710 were associated with positive ECG and/or TEE-defined ischemia. In 150 of 710 (21%) 2-min intervals, the TEE and ECG were positive with PRQ < 1. No ischemia was detected by TEE and/or ECG in 2,616 intervals, whereas 455 of 2,616 (17%) of these had PRQ < 1.

The Non-failing Heart: LVEF ≥ 55%

When compared to the entire study population, there was a subset of patients whose preoperative LVEF was ≥55% (n = 31) with a total of 2,325 intervals available for analysis (fig. 1D). Of the patients in this subset, 5 of 31 (16%) experienced ECG detected ischemia. These 5 patients had a total of 66 intervals when there was ECG-detected ischemia, whereas only 16 of 66 (24%) were associated with PRQ < 1. There were 2,259 intervals without ECG-defined ischemia, and 335 of 2,259 (15%) were associated with PRQ < 1.

In examining the comparisons between TEE and PRQ < 1, there were 1,898 intervals available (fig. 1E). Here only 4 of 31 (13%) patients experienced RWMA in the pre-cardiopulmonary bypass period. None of the 186 intervals in which RWMA was detected had concurrent PRQ < 1. In 1,712 intervals, no RWMA was detected, whereas 311 of 1,712 (18.1%) of these were associated with PRQ < 1. Closer evaluation revealed only two patients who experienced both RWMA and PRQ < 1. One patient had PRQ < 1 for 20 min during the induction and intubation portion of the anesthetic without ECG evidence of ischemia. This resolved, and 24 min later, RWMA were observed without concomitant PRQ < 1. A second patient experienced PRQ < 1 lasting 10 min near the end of saphenous vein graft harvesting that also resolved, and RWMA occurred 12 min later just after aortic cannulation. In this subset of patients with a preoperative LVEF ≥ 55%, PRQ < 1 was a poor predictor or indicator of ischemia when evaluated by ECG and by TEE (fig. 3).

Patients with Ischemia

Patients who experienced ECG-determined ischemia at no time had PRQ < 1 herald the onset of these events.

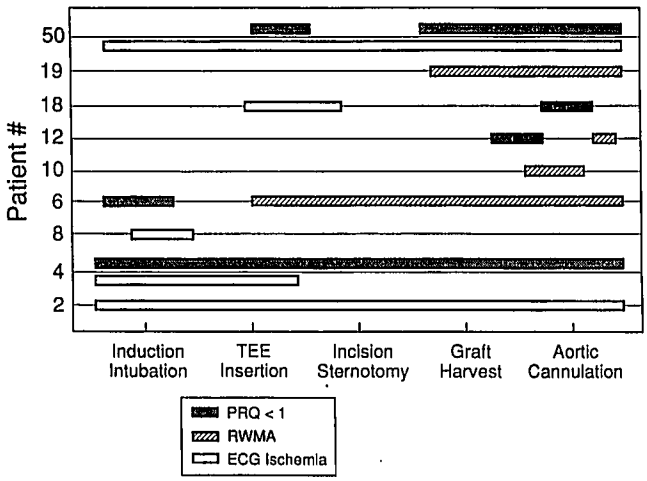

Fig. 3. Plot of all patients with preoperative left ventricular ejection fraction ≥55% who experienced electrocardiography and regional wall motion abnormalities before cardiopulmonary bypass (9 of 46). The relationship to the intraoperative period as well as presence and absence of a pressure rate quotient <1 are presented.

One patient had simultaneous ECG ischemia and PRQ < 1. This patient had significant three-vessel disease by catheterization report, was treated with calcium channel blocker therapy only, and had PRQ < 1 duration of 86 min. Another patient experienced RWMA prior to onset of PRQ < 1, which then occurred 20 min prior to onset of ECG ischemia. This patient was receiving only calcium channel blocker therapy, had significant three-vessel disease, and experienced a total of 18 min of PRQ < 1.

Three patients all had PRQ < 1 occur within 15 min of TEE-defined ischemia (RWMA). One patient received only calcium channel blocker therapy, had three-vessel disease, and had a duration of PRQ < 1 of 20 min. The second patient received only beta blocker therapy, had an isolated left anterior descending coronary artery lesion, and had PRQ < 1 duration of 62 min. The third patient had a significant left main lesion, was on no antianginal therapy, and had PRQ < 1 duration of 86 min. The latter two patients, who both had significant single vessel disease, received esmolol infusions for treatment of HR increases greater than 20% from resting baseline values. Despite this intervention to lower HR and to indirectly increase PRQ > 1, these patients did not resolve their RWMA.

Nine patients experienced PRQ < 1 and RWMA pre-cardiopulmonary bypass (regardless whether PRQ < 1 predicted or indicated this event). Of these nine, eight had three-vessel disease, two were receiving beta ad-

renergic blockade alone, four were receiving calcium channel blockers alone, and two were receiving both beta blocking and calcium channel blocking-therapy. Seven patients who experienced ECG-defined ischemia and PRQ < 1 pre-cardiopulmonary bypass (regardless whether PRQ < 1 predicted or indicated this event). Of these seven, six had three-vessel disease, three were receiving beta blockers only, two were receiving calcium channel blockers only, and two received combination therapy. Except for two patients, one with left main coronary artery disease and the other with an isolated left anterior descending coronary artery lesion, all who experienced ischemia as detected by ECG or TEE had significant three-vessel disease.

Postoperatively, 4 of 46 patients (8%) experienced a postoperative myocardial infarction with both peak creatine phosphokinase × MB% > 80 U/L and diagnostic ECG changes. Of these four patients, one had PRQ < 1 immediately preceding cardiopulmonary bypass with no evidence of ischemia detected by ECG or TEE. One had ECG evidence of ischemia without PRQ < 1 or TEE findings. One had evidence of RWMA without ECG or PRQ < 1. One had no evidence of ECG, RWMA, or PRQ < 1.

Discussion

This study evaluated PRQ < 1 as a predictor and/or indicator of myocardial ischemia when compared to computer-assisted ECG ST-segment trend analysis and/or 2-D TEE during the pre-cardiopulmonary bypass period in patients undergoing elective CABG. Using ultrasound, as did Buffington in his earlier studies,[8] we confirmed our previous study that PRQ < 1 was neither a predictor or indicator of myocardial ischemia. Of the ischemic ECG intervals noted, only 18% occurred while there was PRQ < 1 (fig. 1A). A high percentage of all ischemic ECG episodes were associated with PRQ > 1 (false-negative). The low sensitivity (18%) and low positive predictive value (16%) limit its clinical usefulness. When compared to ECG, PRQ < 1 was an excellent negative predictor (93%) of ischemia. Transesophageal echocardiography evidence of ischemia compared to PRQ < 1 revealed that 20% of all RWMA were associated with PRQ < 1, which is similar to our findings with ECG as seen in figure 1B. Thus, a large percentage of RWMA occurred when PRQ > 1 (false-negative). When RWMA occurred, it was predicted by onset of PRQ < 1 within 15 min in only 3 of 15 patients; simultaneous occurrence was seen in 1 of 15 patients; and RWMA preceded PRQ < 1 in 2 of 15 patients (fig. 4).

A majority of our study population had normal ventricular function (preoperative LVEF ≥ 55%). In this population, ECG-defined ischemia showed slightly better specificity (24%) compared to 18% for the entire patient population. Transesophageal echocardiography- defined ischemia was evident in only 4 of 31 (13%) patients in this subset. Further evaluation revealed that PRQ < 1 preceded (within 15 min) RWMA only once and that intervals in which RWMA did occur showed no association with PRQ < 1. (fig. 3)

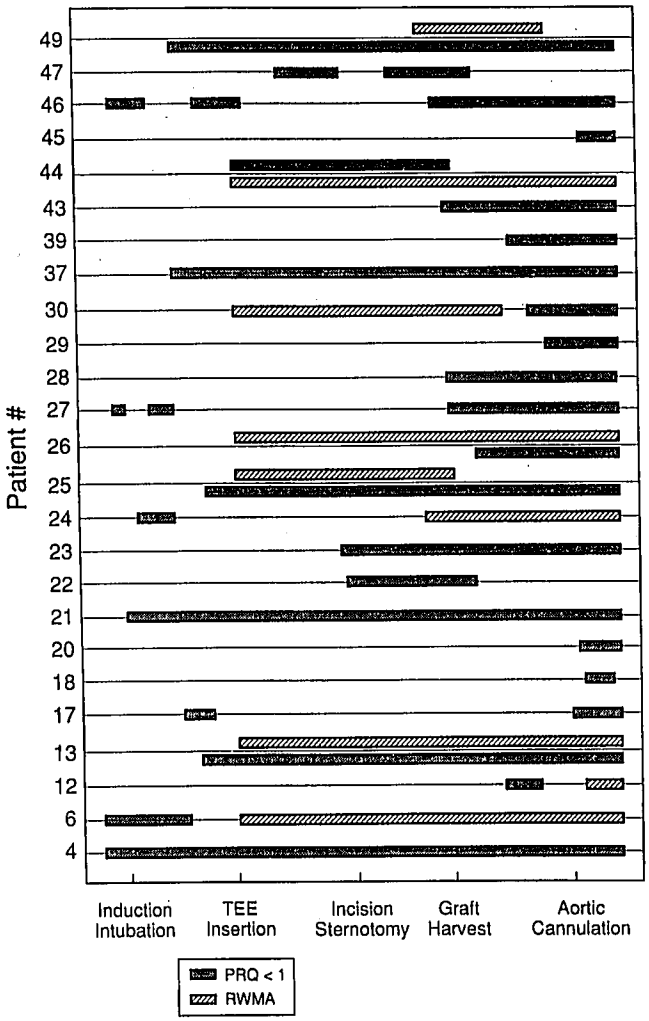

Fig. 4. Plot of all patients who experienced a pressure rate quotient <1 before cardiopulmonary bypass. The relationship to the intraoperative period and presence of regional wall motion abnormalities as detected by ultrasound are shown here.

Duration of PRQ < 1 did not correlate with a higher incidence or duration of ischemia (ECG or TEE). The mean duration of PRQ < 1 in patients who experienced either ECG- or TEE-defined ischemia was 38.8 ± 38.19 (SD) min with a range of 2–114 min. No one patient dominated the ischemia data. There was no correlation with presence or absence of medical therapy, or duration of PRQ < 1, and the occurrence of ECG- or TEE-defined ischemia. Of the nine patients who had RWMA and PRQ < one, four, of nine received an esmolol infusion to treat a HR increase greater than 20% from baseline. Despite this intervention, ongoing RWMA did not resolve. The above findings bring out three important points. First, by controlling HR and blood pressure, we cannot influence other factors that may cause ischemia, *i.e.*, spasm and platelet plugging, which have been proven to cause myocardial ischemia. Second, following an acute occlusion, patients with significant single-vessel disease may not have time to develop collateral circulation, which may be beneficial in times of low supply (decreased MAP) and of high demand (increased HR). Third, preoperative medical therapy aimed at protecting the heart from ischemia, *i.e.*, beta blockers calcium channel blockers, may not be protective in this setting.

In a previous evaluation of hemodynamic indexes and their relationship to TEE-defined myocardial ischemia, PRQ < 1 was compared to presence of RWMA in a similar patient population before and after cardiopulmonary bypass as well as postoperatively.[13] Despite differences in methodology (50% of patients with unstable angina, varied anesthetic agents and intraoperative management, PRQ < 1 evaluated 10 min prior to TEE episodes, not by ECG or the combination of the two), Leung *et al.* found PRQ < 1 associated with only 27% RWMA episodes occurring during their entire study. In the precardiopulmonary bypass period, there were 16 TEE episodes, which were associated with PRQ < 1 and 3 of 16 (19%) had concurrent RWMA and PRQ < 1. Pressure rate quotient < 1 also was a poor predictor of TEE-defined ischemia in this population. Only 2 of 16 (13%) TEE episodes were predicted by PRQ < 1 within 10 min of RWMA in the pre-cardiopulmonary bypass period. Our data are similar to the findings of Leung *et al.* We observed 20% of our TEE episodes associated with PRQ < 1 and 3 of 15 (20%). TEE episodes were predicted by PRQ < 1 within 15 min of onset of RWMA.

The original work by Buffington was performed in a canine model in which alterations of blood flow in the left circumflex coronary artery distribution were evaluated by sonomicrometry.[8] An experimental stenosis (concentric, rigid, nondynamic, 10–12-mm length of a 6-mm OD glass tubing) was created following ligation of obvious collateral flow between the left circumflex and the anterior descending coronary arteries. Blood pressure was maintained with a phenylephrine infusion and HR was controlled with ventricular pacing ranging from 50–150 beats/min. During varying combinations of blood pressure and HR, systolic wall thickening was determined for the area under question. Buffington found that the regional dysfunction that resulted from severe stenosis and hemodynamic perturbations were seen most commonly with tachycardia and hypotension. He concluded that ischemic myocardial dysfunction occurred rarely with the combination of hypertension and bradycardia whereas increases in HR caused dysfunction at any arterial pressure, which worsened with decreases in arterial pressure. As a result of these findings, he suggested that ischemic dysfunction was unlikely if the MAP exceeded the HR (MAP/HR > 1). Extrapolation of these findings to the clinical situation should be taken with caution. Significant differences exist between the canine experimental model and the patient with coronary artery disease presenting for CABG surgery. The majority of our patient population presented with disease in multiple coronary arteries and variable etiologies of stenosis ranging from intermittent spasm to eccentric and/or concentric lesions. The presence of collateral flow in the detail of the coronary anatomy was not uncommon. The anesthetic team intervened when there were elevations in HR ≥ 20% from baseline values, so increases in HR to 125 and 150 beats/min as well as MAP reaching 120 mmHg were not encountered. All patients exhibited stable preoperative anginal patterns and were on chronic anti-anginal therapy. There was no evidence of overt heart failure as documented by elevated pulmonary artery, pulmonary capillary wedge pressures, or increased end diastolic area as noted on TEE.[15,16]

In patients presenting for CABG, medical management aimed at maximizing supply and minimizing demand has failed. Coronary lesions are dynamic rather than stable, so that when the medical management fails or symptoms worsen, these patients will present for CABG surgery. This is a more accurate reflection of our everyday practice rather than a patient with a single highly specific lesion without variability and coronary artery disease management lacking anti-anginal medications. The presence of significant lesions (>70%) may

induce low-grade ischemia, vasodilation, and subsequent collateral flow formation. This may help preserve flow to watershed areas during episodes of low perfusion pressure and/or times of high demand (MAP/HR < 1). Conversely, an increased MAP may enhance coronary perfusion and preserve flow through watershed areas through collateral flow, but at the expense of increasing myocardial work. Even if the HR remains low for a favorable PRQ > 1, the increases in wall tension that ensue may not favor subendocardial blood flow, especially in the setting of left ventricular hypertrophy. In this setting, PRQ > 1 may not preclude the development of ischemia in this patient population.

Because of the unpredictable nature of coronary disease, patients who are well managed medically still experience episodic angina or constant, subclinical ischemia.[17,18] These people have had their lesions progress despite management designed to maximize supply (beta blockers, anti-platelet agents, angioplasty) and minimizing demand (ACE inhibitors and calcium channel blockers). The goals of beta blockade are to decrease HR, maximize coronary perfusion time across stenotic lesions, and decrease myocardial oxygen consumption. Calcium channel blocker therapy also may be beneficial by helping to decrease myocardial oxygen demand by improving the ability of the ventricle to relax, slowing HR and inducing coronary vasodilation. These medications would be expected to decrease HR and induce coronary vasodilation (supply) or enable more complete diastolic relaxation with less overall energy consumed (demand). During an acute decrease in arterial pressure, a decrease in supply may be offset by the concomitant decrease in demand as a result of the beneficial effect of the beta blockers and/or calcium channel blockers, if given in therapeutic doses. In our population, the presence of beta blocker and calcium channel blocker therapy did not prevent the development of PRQ < 1 and ECG- and/or TEE-defined ischemia. This could be because of the occurrence of local factors responsible for producing ischemia, which we were unable to control.

Limitations of our methods used for ischemia detection are well known and have been discussed extensively.[4,5,19] Myocardial ischemia detection may be increased by the number, location, and configuration of additional ECG leads. An increase in the number of leads monitored (II, V_4, V_5) has been shown to increase the sensitivity of ECG-defined ischemia.[20] The addition of a right-sided precordial electrode (V_4R) may increase the sensitivity for right ventricular and inferior ischemia.[21,22] Our method of ST-segment analysis had the amount of deviation of ST segments displayed on the monitoring screen. Since we were involved directly in patient care, we were not blinded to this information. However, we believe that the information gathered and the conclusions drawn from them are not hindered by this limitation in methodology.

Transesophageal echocardiography-defined ischemia (RWMA) detection also has inherent limitations. Placement of the probe after tracheal intubation may miss ongoing ischemia, which was present upon arrival to the operating room or acutely precipitated during the induction, laryngoscopy, and tracheal intubation.[23] Traditional TEE views monitored for ischemia detection have been the short axis mid-papillary view of the left ventricle. This area of myocardium may not yield as comprehensive a picture of ischemia as we think. Apical, basal, as well as right ventricular RWMA may occur without detection.[24,25] Certain RWMA may be due to areas of previous infarction, abrupt changes in loading conditions and inotropic state, as well as variants of normal processes inherent to cardiac surgery.[26,27] The introduction of biplane as well as future use of omniplane, TEE as imaging modalities may help to image once ignored or missed areas of myocardium for a more sensitive mode of ischemia detection.

In summary, this investigation reports that a specific hemodynamic index, PRQ < 1, did not prove to be an adequate predictor or indicator of pre-cardiopulmonary bypass myocardial ischemia. This was evident in our entire population, as well as our subset of patients with a preoperative LVEF ≥ 55%, when they were evaluated by ECG, TEE (ultrasound), and the combination of these modalities. This study reinforces the hypothesis that a single highly specific hemodynamic index, despite many theoretical advantages, currently has little clinical application for patients with multiple coronary lesions presenting for elective CABG surgery.

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