Pulmonary capillary wedge pressure (PCWP) is monitored during anesthesia in an attempt to detect changes in myocardial function in patients at risk of preoperative cardiac complications. Because the sensitivity with which preoperative PCWP monitoring indicates myocardial ischemia is uncertain, we monitored PCWP, 12-lead electrocardiogram, and left ventricular wall motion abnormalities as defined by transesophageal echocardiography (TEE) in 98 anesthetized patients before coronary artery bypass grafting. Measurements were made five times in each patient, before and after induction of anesthesia. Myocardial ischemia was identified by TEE in 14 patients; in 10 of these, it was associated with concomitant ST segment depression of at least 1 mm. The onset of ischemia, as defined by TEE, was accompanied by a mean increase in PCWP of 3.5±4.8 mm Hg, as compared with a mean change of 0±2.2 mm Hg between observations not associated with the onset of ischemia (p<0.01). An increase in PCWP of at least 3 mm Hg, tested as an indicator of ischemia, had a sensitivity of 25% and a positive predictive value of 15%; after correction for background changes associated with anesthetic induction, the sensitivity of this indicator was 33%, and its positive predictive value was 16%. These figures were not improved by selecting cutoff points higher or lower than 3 mm Hg. In this study, the onset of myocardial ischemia was associated with a small yet significant increase in mean PCWP at group level. Wide variation in PCWP changes, however, resulted in many false-positive and false-negative observations when a rise in PCWP was used to test for ischemia in individual patients; thus, the value of PCWP as a monitoring technique for preoperative myocardial ischemia was limited. (Circulation 1990;81:865–871)

Pulmonary capillary wedge pressure (PCWP) is widely used to monitor cardiac function in patients who are undergoing major surgery, primarily as an indirect indicator of left ventricular (LV) preload. The direct determinant of preload, however, is end-diastolic fiber length or its correlate, LV end-diastolic volume, which are influenced by myocardial diastolic compliance as well as by LV end-diastolic pressure. As PCWP assesses only one of these variables, the end-diastolic pressure, it is not surprising that studies performed during cardiac and vascular surgery have demonstrated a poor correlation between PCWP and end-diastolic volume, and the PCWP is, thus, frequently misleading when it is used as the sole indicator of preload.

PCWP is also used to detect intraoperative myocardial ischemia in patients with ischemic heart disease. This approach is based on the theory that ischemia leads to a decrease in compliance, resulting in an increase in filling pressure as reflected by a rise in PCWP. The precise value of PCWP as a monitor of myocardial ischemia, however, remains
uncertain. Previous studies have demonstrated that there is, indeed, a significant increase in PCWP during ischemia that is acutely induced by cardiac pacing or coronary angioplasty, but it is unknown whether such observations can be extrapolated to the insidious onset of spontaneous ischemia during anesthesia. It is also uncertain whether such an increase, if apparent, can be useful in clinical practice as an early and reliable indicator of myocardial ischemia.

To assess the clinical value of PCWP monitoring for the detection of ischemia, we studied the relation between the onset of myocardial ischemia and changes in mean PCWP. Ischemia was detected by both 12-lead electrocardiography and transesophageal echocardiography (TEE). The standard 12-lead body-surface electrocardiogram (ECG) was used because it is the most widely accepted technique although its sensitivity to detect subendocardial ischemia is limited. Furthermore, 12-lead electrocardiography is impractical during surgery and, therefore, rarely used. TEE was also chosen for comparison with changes in PCWP because new regional wall motion abnormalities (RWMA) of the left ventricle are accepted as the most sensitive indicators of intraoperative myocardial ischemia.

Methods

One hundred patients who were scheduled for elective coronary artery bypass grafting gave informed consent for this prospective study, which was approved by the Medical Ethical Committee of the University Hospital Rotterdam. The patients selected were at risk of developing spontaneous myocardial ischemia because they all had angiographically documented coronary artery disease and symptoms for which surgery was required. Patients with preexisting, documented arrhythmias, bundle branch block, or valve disease were excluded. In two patients, the study was aborted before introduction of the transesophageal probe because they had angina pectoris before the induction of anesthesia with ST segment depression, which continued after induction. Thus, 98 patients completed the study. Their ages were in the range of 39–79 years (mean, 59±11 years), and 79 were men. LV ejection fraction determined by preoperative ventriculography was in the range of 0.23–0.80 (mean, 0.53±0.15). Six patients had one-vessel disease, 18 had two-vessel disease, and 74 had three-vessel disease. One patient in the series died because she could not be weaned from cardiopulmonary bypass; she had no ischemia detected by any method during the study, and her data were included.

Data were obtained during a concomitant study to determine whether the addition of nitrous oxide to the inspiratory gas mixture increases the risk of myocardial ischemia in patients with ischemic heart disease. Reports of the results in 68 patients of that investigation have appeared elsewhere. After induction of anesthesia (fentanyl 15 µg/kg by bolus injection and, then, 0.2 µg/kg/min as maintenance infusion) patients were ventilated with 100% oxygen for 15 minutes. They were then randomized to receive either 60% nitrous oxide or 60% nitrogen added to the inspired gas mixture for 10 minutes, before receiving 100% oxygen for a further 10 minutes. Finally, they again received 40% oxygen, with 60% nitrous oxide or 60% nitrogen, whichever was not administered before, also for 10 minutes. The possibly different effects of nitrous oxide versus nitrogen on PCWP were studied, and these, in fact, were found to be identical; changing the gas mixture from 100% oxygen to 60% nitrogen decreased PCWP for the whole group by 0.17±1.4 mm Hg, and to 60% nitrous oxide, the change in PCWP was −0.17±1.5 mm Hg.

Surgery was delayed until the completion of the study, so that data were not influenced by surgical stimuli, blood loss, or fluid therapy; patients were specifically informed of this delay before they were asked to give consent. Apart from changes in the ventilator gas mixture, all treatment was kept constant throughout the study, with the exception of nitroglycerin. This was administered by intravenous infusion after the diagnosis of myocardial ischemia but, as described herein, subsequent measurements were excluded from the analysis.

In the anesthetic induction room, electrodes were placed on limbs and chest to record a standard 12-lead ECG (Hewlett-Packard model 4750A with diagnostic quality electrical filtering). A preoperative ECG (1 day before surgery) was also obtained for comparison.

A 7.5F fiberoptic thermodilution catheter (American Edwards) was inserted by subclavian vein puncture and advanced to the distal pulmonary artery. A correct position for recording PCWP was confirmed by observing a clear change in the pressure waveform when the balloon was inflated, and by measuring the oxygen saturation of blood at the tip of the catheter. Pressure transducers were calibrated before every study over the range of 0–100 mm Hg with a standard mercury manometer. Zero-level was set by opening to atmospheric pressure at the level of left atrium, as determined by the midaxillary line. The zero-value was checked before every measurement and always found to be within ±1 mm Hg of the initial calibration. Before induction of anesthesia, PCWP was measured during normal respiration, and after induction, it was measured while the patient was temporarily disconnected from the ventilator. Mean PCWP was determined as an electronic mean during eight beats.

The transesophageal catheter (Hewlett-Packard 5 MHz probe, connected to a Hewlett-Packard 77020 AC ultrasonograph) was introduced immediately after tracheal intubation and positioned in the stomach to obtain an LV short-axis view through the middle of the papillary muscles. This view was selected because it images regions of myocardium supplied by all three main coronary arteries. The
transducer remained in the same position relative to the heart throughout the study, and the LV short-axis views were recorded on VHS videotape for subsequent analysis.

Data were collected five times in each patient. Baseline recordings of PCWP and the 12-lead ECG were made immediately before induction of anesthesia. These parameters were measured four other times, at the end of each period (before changing the inspiratory gas mixture), and simultaneously, the TEE LV short-axis view was recorded for 1 minute.

Because of technical problems, no electrocardiographic data were obtained in one patient, and in another, no ECG was obtained during one study period. In four patients, less than 12 leads were recorded during part of the study. None of these developed ST segment depression in the leads that were recorded, nor did any of them develop RWMA's. A transeosophageal echocardiographic LV short-axis view was obtained in all patients but, in one patient, image quality was considered insufficient for wall motion analysis. This patient had no ST depression or significant PCWP changes. In three other patients, the posterior wall could not be analyzed adequately, and in another, the lateral wall could not be analyzed. In this last patient, RWMA's were detected in the posterior wall and septum. Adequate PCWP recordings were obtained before induction of anesthesia in all but two patients. After induction of anesthesia, PCWPs were recorded in all 98 patients but, in one further patient, one PCWP recording was missed. None of these patients was excluded. There were no clinical problems or complications related to the study.

Data Analysis

The 12-lead ECGs were analyzed by two observers who were blinded to other patient data. ST segment depression was measured in millimeters at 80 msec after the J-point. Ischemia was diagnosed if new (compared with the preoperative ECG) ST segment depression of 1 mm or more occurred in any electrocardiographic lead except aVr.

Analysis of PCWP was performed using changes in PCWP calculated in each patient from one measurement to the next because our aim was to study the relation between acquired ischemia and changes in PCWP rather than absolute values of PCWP. Thus, from the five measurements obtained in every patient, four changes in PCWP were calculated. The mean values of PCWP in the group of patients who did not have myocardial ischemia were also calculated for each set of measurements, to establish any temporal drift in PCWP after the induction of anesthesia, which would not be caused by ischemia but that might mask its manifestation. Individual changes in PCWP were then corrected according to the mean PCWP change for the nonischemic group during that particular period of the study. The mean PCWP of the 98 patients decreased slightly during the early part of the study from 11.0±4.1 mm Hg during the first set of measurements (before induction of anesthesia) to 9.2±4.2 mm Hg during the second set of measurements, and to 8.7±4.2 mm Hg during the third. Because these changes were statistically significant (p<0.01 and p<0.05), we normalized for this temporal drift by adding 1.8 mm Hg to PCWP changes between the first and second measurements and 0.5 mm Hg to changes between the second and third. Thereafter, mean PCWP did not change, and no adjustments were required. It was 8.5±3.5 mm Hg during the fourth, and 8.6±3.5 mm Hg during the fifth set of measurements.

The LV short-axis views were analyzed off line for RWMA's by two independent observers who were blinded to the ECG and other patient data. Every short-axis view was divided into four segments: posterior (or inferior), lateral, anterior, and septal. As landmarks for this division, we used the anterolateral papillary muscle and the insertion of the right ventricular free wall to the left ventricle (Figure 1). These criteria are a slight modification of the method originally used by Smith et al.19 They used both papillary muscles as landmarks for the division into segments. We choose to modify this scheme because, in our experience, the position of the postero-medial papillary muscle is variable in the short-axis view and usually not at 90° from the anterolateral papillary muscle. Each myocardial segment was scored "de novo" by subjective grading on the following scale: 1) normal, that is, more-than-30% shortening of the radius of the LV cavity and clearly visible myocardial wall thickening during systole, 2) mildly hypokinetic, that is, radial shortening estimated to be 10–30%, 3) severely hypokinetic, that is, radial shortening estimated to be less than 10%, 4) akinetic, and 5) dyskinetic, that is, outward bulging during systole with thinning of the myocardium. The presence of ischemia was detected when the wall motion score for a segment of myocardium was two or more classes worse than that obtained for the same segment of myocardium during another period of the study, if it was identified by both observers, independently.
A total of 389 data points (four changes in PCWP per patient, 98 patients, three PCWP observations missing) were available for analysis. The changes in PCWP associated with new RWMA on TEE were compared with PCWP changes not associated with new ischemia (no change in wall motion or ECG). PCWP changes measured during persisting or resolving ischemia, including those recorded in patients who received nitroglycerin (in total, 42 data points) were excluded from this analysis.

Statistics

Data were compared to confirm or reject the hypothesis that PCWP changes associated with the onset of ischemia are significantly different from “at random” PCWP changes, occurring in the absence of ischemia. Thereafter, we used the mean change in PCWP associated with the onset of ischemia as an indicator of myocardial ischemia in individual patients, and calculated its sensitivity, specificity, and positive predictive value. Other increases in PCWP were also tested as potential markers of ischemia, and the sensitivity, specificity, and positive predictive value of each were calculated. Results are quoted as mean±1 SD. Data were compared using unpaired two-tailed t tests, and statistical significance was assigned if the p value was less than 0.05.

Results

Myocardial ischemia was diagnosed by TEE in 14 of the 98 patients. In two, dyskinesia of the left ventricle and ST segment depression were present from the start of the study, thus, “new” ischemia was observed in 12 patients. The echocardiographic diagnosis of ischemia was based on the observation of a period of severe hypokinesia (grade 3) in an otherwise normal (grade 1) segment in six patients, akinnesia (grade 4) in an otherwise mildly hypokinetic (grade 2) segment in one patient, dyskinesia (grade 5) versus mild hypokinesia (grade 2) in one patient, and dyskinesia (grade 5) versus severe hypokinesia (grade 3) in four patients. In these 12 patients, the onset of ischemia was associated with an increase in PCWP of 3.5±4.8 mm Hg, as compared with a change of −0±2.2 mm Hg between 335 pairs of “at random” PCWP observations, which were not associated with ischemia (p<0.01).

In most patients, only one segment of myocardium met the echocardiographic criteria for ischemia. In total, we identified ischemia in 10 posterior segments, six septal segments, one anterior segment, and one lateral segment. There was no clear correlation between the localization or severity of the RWMA and the change in PCWP. However, the number of observations available for such an analysis was small. In fact, only three patients had ischemia associated with an increase in PCWP of at least 3 mm Hg (Table 1); all three had their RWMA (two dyskinesia, one severe hypokinesia) in the posterior wall of the left ventricle.

Table 1. Numbers of Observations in Each Category Obtained by Using Different Criteria for Change in Pulmonary Capillary Wedge Pressure Indicative of Ischemia

<table>
<thead>
<tr>
<th>Increase in PCWP</th>
<th>True-positive</th>
<th>False-positive</th>
<th>True-negative</th>
<th>False-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncorrected data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3 mm Hg</td>
<td>3</td>
<td>17</td>
<td>318</td>
<td>9</td>
</tr>
<tr>
<td>Corrected data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 mm Hg</td>
<td>9</td>
<td>110</td>
<td>225</td>
<td>3</td>
</tr>
<tr>
<td>≥2 mm Hg</td>
<td>6</td>
<td>47</td>
<td>288</td>
<td>6</td>
</tr>
<tr>
<td>≥3 mm Hg</td>
<td>4</td>
<td>21</td>
<td>314</td>
<td>8</td>
</tr>
<tr>
<td>≥4 mm Hg</td>
<td>3</td>
<td>14</td>
<td>321</td>
<td>9</td>
</tr>
</tbody>
</table>

Total n=347. PCWP, pulmonary capillary wedge pressure.

When an increase in uncorrected PCWP of at least 3 mm Hg was used to detect the onset of myocardial ischemia in each individual patient, its sensitivity when compared with TEE was 25%, its specificity was 96%, and its positive predictive value was 15% (Table 2). After correction for the mean temporal drift in PCWP, which is not possible in the individual patient, these values were not improved. Selecting a value lower than 3 mm Hg as the indicator of ischemia increases sensitivity but lowers specificity; as a result, there is a marked increase in the number of false-positive observations as compared with only a small reduction in the numbers of false negatives (Table 1).

Ten of the 14 patients in whom ischemia was identified by TEE had concomitant ST segment depression of at least 1 mm on the ECG. One other patient had ischemia diagnosed by ECG but not by TEE; ST segment depression was present from the initial recording until the third recording, and then resolved, whereas no significant change (improvement) in wall motion was observed. Reporting numbers of observations rather than numbers of patients, 22 of 32 ischemic periods were accompanied by simultaneous ST segment depression of at least 1 mm. When electrocardiographic changes were compared with TEE as the “gold standard” for the detection of ischemia, a 1-mm-or-greater ST segment

Table 2. Performance of Different Increments in Pulmonary Capillary Wedge Pressure When Used as a Test of Myocardial Ischemia

<table>
<thead>
<tr>
<th>Increase in PCWP</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncorrected data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3 mm Hg</td>
<td>25</td>
<td>96</td>
<td>15</td>
</tr>
<tr>
<td>Corrected data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 mm Hg</td>
<td>75</td>
<td>67</td>
<td>8</td>
</tr>
<tr>
<td>≥2 mm Hg</td>
<td>50</td>
<td>86</td>
<td>11</td>
</tr>
<tr>
<td>≥3 mm Hg</td>
<td>33</td>
<td>94</td>
<td>16</td>
</tr>
<tr>
<td>≥4 mm Hg</td>
<td>25</td>
<td>96</td>
<td>18</td>
</tr>
</tbody>
</table>

PCWP, pulmonary capillary wedge pressure.
depression in any lead of the 12-lead ECG had a sensitivity of 69% and a specificity of 99%.

Ischemic changes in the ECG were present in 13 patients (the 10 patients with concomitant RWMA, one patient without ischemia by TEE, and two patients in whom ST segment depression resolved before introduction of the TEE transducer). The ECG lead most involved was V5; there was ST segment depression in V5 in 10 of the 13 patients in this group with predominantly posterior wall RWMA.

The interobserver variability of the echocardiographic gradings was tested. The subjective gradings of the two independent observers were identical in 77% of segments, whereas they differed by one grade in 19% of segments and by two grades in 4% of segments. Disagreement occurred mainly in grading mild (grade 2) versus severe (grade 3) hypokinesia. In two patients, interobserver variability affected the diagnosis of ischemia, as one observer saw a deterioration of wall motion by 2 grades, whereas the other did not. They were not included in the ischemia group, however, as our criterion for ischemia was that both observers agree. Neither of these patients had 1-mm-or-greater ST segment depression.

Intraobserver variation in echo-gradings revealed identical gradings in 97% of segments for one observer and 84% for the second observer. Intraobserver variation never affected the diagnosis of ischemia.

Discussion

Previous studies have reported an increase in PCWP when myocardial ischemia was provoked by atrial pacing or angioplasty.10-15 We found that PCWP also increases during nonprovoked spontaneous myocardial ischemia during anesthesia, but the rise in PCWP was not consistent, and it was not a reliable indicator of newly developing ischemia. These conclusions are supported by two other recent studies on spontaneous ischemia during surgery. Leung et al22 investigated 40 patients undergoing elective coronary artery bypass grafting and observed that only 10% of all RWMA were associated with an acute rise in PCWP. Hägmark et al23 compared different indicators of intraoperative myocardial ischemia in 53 patients with ischemic heart disease undergoing vascular surgery. They observed that neither elevation of the PCWP, nor the appearance of an abnormal PCWP waveform (which was not analyzed in our study) discriminated sensitively between the presence or absence of myocardial ischemia.23 Our study differs from the study by Leung et al22 because their study was performed during and after surgery, so that hemodynamic changes because of anesthesia and surgery can also have influenced PCWP. In contrast to Hägmark et al,23 who used cardiokymography and single-lead (V5) ECG to detect ischemia, we used TEE and 12-lead ECG, assuming that this provides a more sensitive and reliable means of detecting ischemia.

In most patients who developed new ischemia during anesthesia, the increase in PCWP was absent or small. In those who did show changes, these most frequently involved the posterior wall of the left ventricle. Thus, it is possible that the rise in PCWP seen during spontaneous ischemia was not the result of any change in compliance but occurred as a result of transient papillary muscle dysfunction and mitral valve regurgitation. The data obtained in this study and others, however, are insufficient to allow comment on this hypothesis. Color flow mapping and Doppler interrogation of mitral valve flow during transient myocardial ischemia might give more insight into the role of the mitral valve and subvalvular apparatus in altered filling pressures during ischemia.

The value of monitoring mean PCWP as a means of detecting ischemia can be even less in clinical practice than it was in this study because, during surgery, PCWP is also influenced by noncardiac factors such as fluid therapy, blood loss, sympathetic reaction to surgical stimuli, and hemodynamic changes because of anesthetic agents. Such external factors were absent or were corrected for in this study. A standard deviation of 2.2 mm Hg in nonischemic PCWP changes means that the normal range (including 95% of nonischemic observations) ranges from −4.4 to +4.4 mm Hg in this experimental setting. During surgery, this range will be much wider, and as a result, the overlap with ischemic changes in PCWP will be even larger.

In this study, data were collected while the patients received alternating ventilatory regimens. It was possible that the inhalation of nitrous oxide during part of the study might have induced PCWP changes not related to ischemia or might have masked ischemia-induced changes. Retrospective analysis of changes in PCWP associated with the addition of either nitrous oxide or nitrogen to the ventilator gas, however, showed that these had no effect on mean PCWP. Previous studies have also demonstrated that nitrous oxide does not change PCWP in anesthetized patients before coronary bypass grafting, either in those with normal or in those with elevated PCWP.24 Thus, it seems reasonable to accept the data in this present report as a true reflection of changes in PCWP occurring with spontaneous ischemia during anesthesia.

Another theoretical disadvantage of this study is that we might have missed brief periods of ischemia occurring between measurements because these were made at set intervals. It is not possible, however, to record PCWP continuously because of the risk of pulmonary infarction. Additionally, because we were comparing different indicators rather than studying the true incidence of myocardial ischemia, we believe the observations remain valid.

We observed the ECG to be more sensitive in identifying ischemia detected by TEE than has been reported previously.19 The most obvious explanation is that we used 12-lead ECGs whereas others used seven or fewer leads.19 It is also known from exercise
testing that the sensitivity of ECG is increased if more leads are used.25

TEE represents a major advance in preoperative monitoring of cardiac function. It can provide information on LV volumes as well as on myocardial ischemia, and thus, as described in this study, it might overcome some of the limitations of monitoring with pulmonary artery catheters. On the other hand, it should be realized that TEE also has some limitations compared with pulmonary artery catheter monitoring and ECG. In particular, it is impractical to use TEE before the induction of anesthesia and in the postoperative period in awake patients, yet both periods are associated with a high risk of ischemia in patients with coronary artery disease. Furthermore, on-line subjective analysis of RWMA for clinical monitoring can be less accurate than off-line analysis conducted for research. Additionally, the subjective impression of deterioration by two grades is only a crude assessment, and especially in previously damaged, poorly contracting ventricles, subjective analysis of changes in wall motion is difficult. Computer-aided systems for on-line quantitative wall motion analysis are now being developed, and in the future, they are likely to increase the sensitivity with which small changes in wall motion can be detected.

Although there are limitations to the current subjective detection of RWMA, there is no doubt that changes in LV myocardial function occur as the earliest and most sensitive indicator of ischemia, preceding both electrocardiographic or hemodynamic changes.26–29 PCWP, in contrast, is a non-specific indicator because it is influenced by many factors affecting myocardial function that can have opposite effects (e.g., cardiac failure and intraoperative blood loss). Detection of acute and large changes in PCWP can be invaluable in clinical practice (e.g., to assess the effects of fluid therapy or to detect acute LV failure) but our data suggest that a change in the mean PCWP is neither a sensitive nor a reliable early indicator of myocardial ischemia.

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