Coronary Artery Disease in Patients Undergoing Lung Volume Reduction Surgery for Emphysema*

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**Objectives:** Most patients with severe pulmonary emphysema referred for lung volume reduction surgery (LVRS) have a long-standing history of cigarette smoking. Coronary artery disease (CAD) predisposes to perioperative cardiac complications. Since symptoms and signs of myocardial ischemia are often absent in patients with severe ventilatory impairment even during exercise, we investigated the prevalence of CAD in candidates for LVRS by angiography. 

**Design:** We prospectively studied the prevalence of CAD by angiography and assessed the CAD risk factor profile in 41 candidates for LVRS (26 men, 15 women; mean age, 66±6.8 years; range, 52 to 76 years), who had no current symptoms or a history of myocardial ischemia.

**Results:** In six patients (15%), asymptomatic but significant coronary lesions (>70% stenosis) were detected. In five patients, these findings altered the clinical management. Patients with CAD had significant higher cholesterol levels, tended to have smoked more, and had more often additional vascular risk factors.

**Conclusions:** We found a high prevalence of angiographically significant but clinically silent CAD in this particular population of heavy smokers with advanced emphysema. 

*(CHEST 1997; 112:122-28)*

**Key words:** coronary artery disease; lung volume reduction surgery; pulmonary emphysema

**Abbreviations:** CAD = coronary artery disease; CHF = congestive heart failure; LAD = left anterior descending (artery); LVRS = lung volume reduction surgery; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; py = pack-year; RCA = right coronary artery; VAT = video-assisted thoracoscopic

LVRS. According to our own experience* and that of others,1-4 this population consists of approximately two thirds of men with a mean age of over 60 years and a history of heavy cigarette smoking.

A lack of cardiac symptoms (eg, chest pain) does not exclude the presence of relevant CAD in patients with serious impairment of exercise performance due to severe obstructive ventilatory defect. Therefore, treadmill or bicycle stress exercise testing, the most widely used screening method for CAD, is of limited value. To obtain unequivocal information on coronary anatomy as well as on left ventricular function, we performed left heart catheterization with coronary angiography in all candidates for LVRS.

The goal of this prospective study was to assess the prevalence of CAD, particularly the occurrence of asymptomatic but significant CAD, in candidates for LVRS. In addition, we evaluated whether the presence of risk factors other than smoking and advanced age can discriminate between patients with and without significant CAD.

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**Materials and Methods**

**Patient Selection for LVRS**

*Inclusion Criteria:* According to criteria published previously,13 potential candidates for LVRS had the following profile: the patient has severe COPD with an FEV₁ of <35% predicted and is considerably hyperinflated (residual lung volume >200%, total lung capacity >130% predicted). Radiologic signs of pulmonary emphysema with flat diaphragms are present on conventional chest radiograph and emphysema is confirmed on a high-resolution CT scan. The patient is highly motivated and has stopped smoking for >6 months. No further improvements could be achieved by antiobstructive pharmacotherapy, including systemic corticosteroids.

*Exclusion Criteria:* Exclusion criteria were as follows: age older than 75 years; PaCO₂ >55 mm Hg; diffusing capacity for carbon monoxide (single breath) <20% predicted; bronchiectases; acute bronchopulmonary infection; neoplastic disease with a life expectancy of <2 years; and psychiatric disturbance. Patients with a previous Q-wave myocardial infarction (MI) and/or congestive heart failure (CHF) were also no longer considered to be candidates for LVRS.

**Functional Assessments**

Lung volumes were measured according to standard criteria9,10 (using the Sensor Medics 66200 Autobox; Yorba Linda, Calif). Results were expressed as the best values after inhalation of two puffs of salbutamol. Diffusing capacity for carbon monoxide was measured using specific equipment (66200/Sensor Medics). Reference values were according to the European Community for Steel and Coal.13 Arterial blood gases were analyzed (AVL 999-S; AVL Medical Instruments; Schaffhausen, Switzerland) as were oxygen saturation and carboxyhemoglobin with a co-oximeter (IL 482; Radiometer; Copenhagen).

*Exercise:* For a 12-min walking distance, the patients walked along the same hospital hallway without oxygen supplementation, encouraged by a technician.11,12 Cardiopulmonary stress tests were performed by the metabolic measurement cart (Sensor Medics 2900) on an electronically braked cycle ergometer (Bosch; Medicare; Zurich, Switzerland). After 2 min of unloaded cycling at 50 rpm, the workload was increased by 5 W/min according to a ramp protocol until the patient was unable to continue. Maximal values for cardiorespiratory variables were taken at the highest oxygen uptake. Predicted maximal heart rate was 215–age (years). Heart rate reserve was defined as the difference between predicted maximum heart rate and maximal achieved heart rate and breathing reserve as the difference between maximal ventilation and the product of FEV₁ \times 37.

**Cardiac Evaluation**

We obtained a careful history seeking to identify prior angina, MI, chronic heart failure, or symptomatic arrhythmias. All patients had a standard 12-lead ECG. An abnormal ECG was defined as any rhythm other than normal sinus rhythm, right or left bundle-branch block, pathologic Q waves, repolarization abnormalities, or T-wave inversions.

Women older than 55 years and men older than 50 years, who qualified for LVRS according to our criteria and who had no previous Q-wave MI by ECG criteria or documented CHF, underwent coronary angiography as well as left heart catheterization. Multiple views of the right and left coronary arteries were obtained. Significant CAD was defined as narrowing of one or more vessels by at least 70% or the left main coronary artery of at least 50%.13 Biplane left ventricular ejection fraction was calculated according to Wynne et al.14

**Vascular Risk Profile**

Patients were asked for their smoking history (cumulative pack-years [py]) and a positive family history (ie, CAD in first-degree relatives younger than 60 years). We looked for a history and clinical findings of peripheral and/or cerebrovascular diseases. Other risk factors such as arterial hypertension (ie, systolic BP >160 mm Hg or diastolic BP >95 mm Hg), diabetes mellitus (fasting glucose >140 mg/dL or 7.7 mmol/L), and hypercholesterolemia (serum cholesterol >6.2 mmol/L) were investigated during the preoperative in-hospital evaluation.

If coronary angiography revealed CAD neither accessible to coronary angioplasty nor to bypass surgery, the candidates were not accepted for LVRS. The decision to perform a coronary intervention or to exclude a patient from LVRS was the result of an interdisciplinary discussion and based on a synoptic view of cardiac findings and noncardiac LVRS inclusion and exclusion criteria.

The following adverse perioperative cardiac outcomes were considered: cardiac-related death, nonfatal MI, unstable angina, CHF, and ventricular tachycardia.

**Statistical Analysis**

Continuous data are presented as means±SD. Categorical data were analyzed by Fisher’s Exact Test, and continuous variables were compared by the Mann-Whitney U test. Two-sided p values <0.05 were considered to be significant.

**Results**

Between January 1995 and June 1996, 86 patients were referred for evaluation for LVRS. Thirty-six patients were excluded from a further workup owing to various noncardiac reasons (eg, impairment not severe enough, perioperative risk not accepted, emotional instability) (Fig 1). Four patients were not evaluated further for cardiac reasons: two had a documented history of transmural MI and two patients suffered from ischemic left heart failure.

The remaining population that was evaluated further consisted of 46 patients (Fig 1). Forty-three had no history of CAD. The anthropometric and physiologic data of this subpopulation are summarized in Table 1. All suffered from severe bronchial obstruction and their chests were markedly hyperinflated. Their exercise capacity was considerably reduced as a consequence of impaired pulmonary mechanics with a mean breathing reserve of 1.6±0.7 L/min. The mean maximal heart rate achieved was only 117±15 resulting in a mean heart rate reserve of 33±16. The median (range) rate-pressure product15 was 13,850 (8,100 to 20,480) at rest and increased to 21,285 (10,925 to 28,440) at maximal exercise.

All patients, except one woman younger than 55 years and one man younger than 50 years, underwent left heart catheterization and coronary angio-
Evaluation

n = 86: referred for LVRS evaluation

n = 36: excluded for various non-cardiac reasons

n = 4: excluded for:
  n=2: history of MI
  n=2: history of CHF

n = 46: further evaluation

n = 43: no hx of CAD and/or CHF

n = 2: no coronary angiography 1 male <50 y, 1 female <55 y

n = 3: history of CAD

n = 3: coronary angiography

n = 41: coronary angiography and left heart catheterization

Findings

n = 35: no significant CAD

n = 6: significant CAD

n = 3: significant CAD

n = 2: accepted

n = 4: excluded

Intervention

n = 1: no intervention

n = 1: PTCA

n = 1: no intervention

n = 2: 1 CABG 1 stent

LVRS

Figure 1. CAD in candidates for LVRS: evaluation, findings, and interventions. CABG=coronary artery bypass grafting.
Table 1—Anthropometric and Physiologic Characteristics (n=41)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, mean (range)</td>
<td>66 (52-76)</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>26/15</td>
</tr>
<tr>
<td>FEV1, mL</td>
<td>805±388</td>
</tr>
<tr>
<td>FEV1, % pred</td>
<td>30±7</td>
</tr>
<tr>
<td>TLC, L</td>
<td>8.3±1.45</td>
</tr>
<tr>
<td>TLC, % pred</td>
<td>136±15</td>
</tr>
<tr>
<td>RV, L</td>
<td>5.3±1.01</td>
</tr>
<tr>
<td>RV, % pred</td>
<td>231±47</td>
</tr>
<tr>
<td>PaO2 at rest, mm Hg</td>
<td>65.2±13.3</td>
</tr>
<tr>
<td>PaCO2 at rest, mm Hg</td>
<td>37.5±7.3</td>
</tr>
<tr>
<td>12-min walking distance, m</td>
<td>504±176</td>
</tr>
<tr>
<td>Maximum work rate, W</td>
<td>34±14</td>
</tr>
<tr>
<td>Vo2 max, mL/kg/min</td>
<td>9.5±2.9</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>65±5.5</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>8.1±3.9</td>
</tr>
</tbody>
</table>

*Results are mean±SD; TLC=total lung capacity; RV=residual lung volume; PCWP=pulmonary capillary wedge pressure; Vo2 max=maximum oxygen consumption.

raphy. None of them had ECG signs of ischemic heart disease or arrhythmias.

Three patients were estimated to be good candidates for LVRS despite a history of symptomatic CAD and underwent coronary angiography.

Coronary Angiography Findings and Left Heart Function in Asymptomatic Patients

In 35 patients, no significant CAD was found, but 6 of 41 patients (15%) without a history of CAD were documented to have significant CAD by coronary angiography. All had an ejection fraction above 50% and a mean pulmonary capillary wedge pressure within the normal range (<15 mm Hg) as assessed by right and left heart catheterization (Table 1).

Three of the patients had severe two-vessel disease and one had a one-vessel disease (stenosis of the right coronary artery [RCA] ostium) not accessible to percutaneous transluminal coronary angioplasty (PTCA) (Table 2). These four patients were no longer considered as candidates for LVRS (Fig 1). The two other patients underwent LVRS despite significant CAD. In one of them, showing a 50% stenosis of the left anterior descending (LAD) artery and a 90% stenosis of the circumflex artery, dipyridamole99m technetium methoxy-isobutyl-isonitrile (MIBI)-single photon emission CT (SPECT) revealed no myocardial ischemia. One patient underwent preoperative PTCA.

Coronary Angiography Findings and Left Heart Function in Symptomatic Patients

In all three symptomatic patients, CAD was documented angiographically. None of them had impaired left ventricular systolic function. One patient underwent preoperative bypass grafting and one underwent preoperative stenting of the LAD.

Cardiovascular Risk Profile

All asymptomatic patients were former smokers. There were no differences between asymptomatic patients with CAD and those without CAD with regard to age and sex (Table 3). The 35 patients in whom no CAD was found by coronary angiography had smoked somewhat less (43 py) than patients with significant CAD (59 py). Furthermore, the percentage of patients with a smoking history of more than the arbitrary cutoff of 45 py tended to be higher in the group with documented CAD (p=0.09).

The prevalence of cardiovascular risk factors other than smoking was low in the overall study popula-

Table 2—Coronary Angiography Findings in Candidates for LVRS With Significant Lesions

<table>
<thead>
<tr>
<th>Patient/Age, yr/Sex</th>
<th>Findings</th>
<th>Procedure</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>No history for CAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/68/F</td>
<td>70-80% RCA</td>
<td>No intervention</td>
<td>Uneventful</td>
</tr>
<tr>
<td>2/56/F</td>
<td>75% RCA</td>
<td>PTCA</td>
<td>Uneventful</td>
</tr>
<tr>
<td>3/73/M</td>
<td>75% LAD, 80% diagonal artery, 80% RCA</td>
<td>Rejected*</td>
<td>—</td>
</tr>
<tr>
<td>4/69/M</td>
<td>60% LAD, 70% RCA</td>
<td>Rejected*</td>
<td>—</td>
</tr>
<tr>
<td>5/63/M</td>
<td>90% RCA-ostium, right dominant</td>
<td>Rejected*</td>
<td>—</td>
</tr>
<tr>
<td>6/73/F</td>
<td>70-80% LAD, 50% RCA</td>
<td>Rejected*</td>
<td>—</td>
</tr>
<tr>
<td>History for CAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/73/M</td>
<td>50% LAD, 70% circumflex artery</td>
<td>No intervention</td>
<td>Uneventful</td>
</tr>
<tr>
<td>2/66/M</td>
<td>90% LAD, 50% diagonal artery, RCA occluded (chronic infarction of posterior wall), collateral arteries</td>
<td>PTCA of LAD, stent</td>
<td>Postoperative death</td>
</tr>
<tr>
<td>3/64/M</td>
<td>50-70% main LCA,* 90% circumflex artery, 70% LAD</td>
<td>CABG*</td>
<td>Uneventful</td>
</tr>
</tbody>
</table>

*LCA=left coronary artery.

*Stenosis not accessible for PTCA.

*Dipyridamole 99mTc-MIBI (methoxy-isobutyl-isonitrile): no signs for ischemia.

*Underwent CABG without our knowledge in another hospital; bypasses were patent on subsequent angiography.
tion, and there were no statistical differences with regard to a family history of cardiovascular diseases, a history of diabetes, or arterial hypertension between the two groups (Table 3). However, mean serum cholesterol levels and levels above a cutoff of 6.2 mmol/L were higher in the group with significant CAD. Of the patients with CAD, one third (33%) had at least one additional vascular risk factor besides smoking and high cholesterol levels (>6.2 mmol/L) in contrast to the patients without CAD, where in only 9% were diabetes, hypertension, or a family history of CAD present (p<0.05). We found one patient with concomitant peripheral vascular disease. He had no CAD. None of the patients had a history of cerebrovascular disease.

**Perioperative Course**

In the group without cardiac symptoms, none of the patients died perioperatively. In the symptomatic group, consisting of three patients who finally underwent LVRS, one died on the second postoperative day. He had received a preoperative stent of the LAD and his intraoperative and early postoperative course was uneventful. He developed cardiopulmonary decompensation 10 h after surgery without evidence for MI or ischemic left ventricular failure. Autopsy was refused by the patient’s family. The two other patients had an uncomplicated course.

**DISCUSSION**

We found a high prevalence of asymptomatic CAD in a population of candidates for LVRS, who were mainly elderly patients and exclusively former heavy smokers.

LVRS is a novel surgical approach that is successfully applied in a selected group of patients with COPD who are considerably hyperinflated owing to severe pulmonary emphysema.1-5 LVRS can be performed by median sternotomy1,2 or by video-assisted thoracoscopic.3-5 For both operations, the patient is intubated with a double-lumen endotracheal tube, and single lung ventilation is performed on the nonoperated-on side. Hypoxia, hypercapnia, acidosis, pulse and BP alterations, pain, and emotional stress may occur in the perioperative period. Hence, an already compromised cardiopulmonary system may be further stressed. Recent studies have suggested that adverse cardiac events in the perioperative phase result from stress with excessive catecholamine levels, which cause an imbalance between myocardial oxygen supply and oxygen demand.16

Therefore, reliable information about the coronary circulation seems mandatory for the perioperative risk assessment. The goal is to find either cases in which coronary revascularization is an option or to exclude patients from the operation when a coronary intervention is not feasible and the perioperative risk is considered to be not acceptable.

Different strategies for the preoperative cardiac risk assessment in patients scheduled for noncardiac surgery have been published.17-19 Recently, the American College of Cardiology and the American Heart Association published guidelines on perioperative cardiac evaluation for noncardiac surgery in different settings; however, LVRS was not discussed.20

Since LVRS is a relatively new surgical intervention, only scant information on preoperative cardiac risk assessment strategy is available in patients scheduled for this type of operation.3,4,21 The detection of CAD by ECG during treadmill or bicycle stress test is not sensitive in this population of patients who are severely limited in their exercise capacity due to airway obstruction. Our patients reached their maximal exercise level using up the breathing reserve without achieving heart rates or rate pressure products, where signs of myocardial ischemia can be expected to reliably predict significant CAD.15

The patients of the group of Cooper and Patter-
son\textsuperscript{21} underwent left and right heart catheterization if “clinically” indicated. Miller and coworkers\textsuperscript{3} evaluated all of their patients by dobutamine stress echocardiography and right heart catheterization. Left heart catheterization was restricted to those with an abnormal dobutamine stress echocardiogram. Others\textsuperscript{4} performed left heart catheterization or dobutamine stress tests selectively in patients with a history or symptoms of CAD. However, no detailed information or results of cardiac evaluation are presented in these\textsuperscript{3,4,21} and other publications on LVRS.\textsuperscript{2,6,22,23}

Similar problems arise with potential lung transplantation candidates. Two studies in which ischemic heart disease was evaluated concluded that coronary angiography can be limited to a subgroup of patients with additional coronary artery risk factors besides smoking.\textsuperscript{24,25} However, since these studies were retrospective and performed in a younger population than ours, no firm conclusions can be drawn with regard to the evaluation for LVRS.

Due to the lack of information in regard to possible perioperative cardiac complications of LVRS, we decided to start with invasive cardiac examinations. We expected to obtain definitive information on coronary morphologic features and left ventricular function and to have the opportunity of performing PTCA with or without stenting at the same time, if deemed to be mandatory.

We diagnosed CAD by angiography in 6 of 41 (15\%) entirely asymptomatic patients who satisfied our primary selection criteria for LVRS. In four of these patients, surgery was canceled based on these findings and one patient underwent preoperative revascularization. The cardiovascular complication rate was low in our operation population. The only perioperative death occurred in a patient who preoperatively received a stent in the LAD for symptomatic CAD. We observed no additional adverse cardiac events. This low cardiac complication rate is in accordance with the published observations of others, who reported perioperative cardiac events in only 3 of 233 patients.\textsuperscript{1-4,23}

However, based on these reports and our experience, it is not possible to draw any conclusions to what degree revascularization contributes to a reduction of the perioperative risk in emphysema patients scheduled for LVRS. In analogy to the strategy in patients who have to undergo major vascular surgery, we assume that a similar risk stratification is appropriate prior to LVRS.

We found that patients with significant CAD tended to have smoked more and to have higher serum cholesterol levels. However, risk factor profiles may not reliably predict coronary findings in an individual patient.

The two most widely applied methods for preoperative evaluation of patients unable to exercise are dobutamine stress echocardiography and dipyridamole thallium-201 perfusion scintigraphy. By infusion of dobutamine, myocardial oxygen demand is increased and abnormalities of ventricular contraction due to ischemia are detected by echocardiography.

However, transthoracic echocardiography is often not practicable in emphysema patients with a severely hyperinflated chest since image quality is likely to be poor. In a small population of 23 lung transplantation candidates with a variety of end-stage lung diseases, dobutamine thallium-201 stress test had a high sensitivity but a low specificity for the detection of CAD, i.e., a normal scintigram reliably excluded the presence of significant CAD.\textsuperscript{26} Another noninvasive test known to provide information about coronary reserve is dipyridamole-thallium-201 imaging. In a recently published meta-analysis of noninvasive stress imaging for risk stratification before vascular surgery, dipyridamole-thallium-201 imaging had a high prognostic value for perioperative ischemic events in patients with a high CAD prevalence.\textsuperscript{27} The same authors concluded, based on secondary economic analyses, that this method is more cost effective compared to the routine use of coronary angiography.\textsuperscript{27} Regarding these recent results, it seems appropriate to use a noninvasive stress imaging method for cardiac evaluation also in patients undergoing LVRS.

We conclude that the prevalence of asymptomatic CAD is high in candidates for LVRS. Coronary angiography is known to be the most accurate but also most expensive method to assess CAD. Based on the known high negative predictive value and safety of dipyridamole-thallium-201 scintigraphy, we assume that this procedure may be applied as a screening method to exclude significant CAD and reduce the number of coronary angiograms. Furthermore, left heart catheterization reveals no additional information that is necessary for the management of this highly selected population.

REFERENCES