Phrenic Nerve Function and Its Relationship to Atelectasis After Coronary Artery Bypass Surgery*

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Atelectasis following coronary artery bypass surgery (CAB) occurs in the majority of patients. To determine the importance of operative variables in the development of postoperative atelectasis and the incidence of phrenic nerve injury caused by topical cold cardioplegic solution, we studied 57 patients (53 male, four female) undergoing CAB. Their mean age, ± SD, was 58 ± 13 years. Transcutaneous stimulation was used to evaluate phrenic nerve function preoperatively and postoperatively in 52 patients. An unequivocal paresis of the phrenic nerve was documented in five patients. In an additional 27 patients, the amplitude of the compound diaphragm action potential was reduced postoperatively. However, methodologic limitations did not allow the conclusion that this was secondary to a phrenic axonal degeneration. Discriminant analysis of intraoperative variables showed more severe atelectasis with a larger number of grafts, with a longer operative and bypass time, when the pleural space was entered, when a right atrial drain and a cardiac insulating pad were not used, and with a lower body temperature. It is concluded that phrenic paresis may occur after CAB and topical cold cardioplegia, but that other factors must explain the atelectasis found in the majority of patients.

Impairment in gas exchange is one of the most significant postoperative complications of coronary artery bypass surgery (CAB). The postoperative period represents a time of particular susceptibility to the effects of hypoxemia because of increased myocardial irritability. A number of studies have addressed the etiology of the altered gas exchange,1,2 and although the mechanisms have not been clearly elucidated, a recurrent finding has been that of lower lobe atelectasis. Although both lower lobes may be affected, the loss of volume occurs predominantly on the left. The atelectasis has been attributed to decreased clearance of secretions secondary to impaired cough, decreased mobility, gastric distention, intraoperative lung con­fusion, and lack of postoperative positive end-expiratory pressure. More recently, it has been proposed that the left-sided predominance of the atelectasis may be explained by an intraoperative hypothermic injury to the left phrenic nerve.3,7 This nerve courses over the pericardium and consequently is exposed to cold from saline “slush” used for topical cold cardioplegia.

The incidence of cold injury to the phrenic nerve after CAB and the use of cold cardioplegia is unknown. One study in which phrenic nerve function was assessed six to eight days postoperatively showed a low incidence of conduction abnormalities.3 Transient early phrenic nerve dysfunction, however, could have been missed. In other studies, use of an insulating pad, designed to protect the phrenic nerve from intrapericardial ice, substantially decreased the incidence of postoperative atelectasis.6,7

We prospectively studied 57 patients with CAB to determine the incidence of postoperative right and left lung atelectasis and its relationship to changes in phrenic nerve conduction in the early postoperative period. We also evaluated the contribution of additional operative and postoperative variables to the incidence and severity of postoperative atelectasis.

METHODS

The study group consisted of 57 CAB patients (58 ± 13 years, mean ± SD; 53 men, four women) who were examined over eight months. Exclusion criteria consisted of the following: (1) another operative procedure in addition to CAB; (2) recent myocardial infarction or unstable ventricular arrhythmia; (3) the presence of a generalized neuropathy; and (4) the presence of a cardiac pacemaker. Postoperatively, patients were not studied until extubation and removal of the Swan Ganz catheter.

After informed consent had been obtained, the phrenic nerves were studied by measuring the latency to the compound diaphragmatic action potential (CDAP) following transcutaneous phrenic nerve stimulation. Both the right and left phrenic nerves were localized in the neck by stimulation at the posterior border of the sternocleidomastoid muscle at the level of the thyroid cartilage. A handheld felt-tipped bipolar stimulating electrode, connected to a stimulating unit, was used. Diaphragmatic response was measured using two surface disc electrodes, one placed over the xiphoid process of the sternum and the other over the seventh intercostal space at the costochondral junction.2 The position of both electrodes was recorded using the distances from two stable reference points: the suprasternal notch and the xiphoid process. This allowed reapplication of the electrodes in the same location for the postoperative studies. The position of the stimulating electrode was altered and the voltage was increased until a supramaximal stimulation was achieved (60 to 160 volts, 0.2 ms) as demonstrated by a maximal CDAP on the electromyograph (EMG) oscilloscope. A permanent record of a supramaximal stimulation was obtained using an oscilloscope camera for later analysis. The time from application of the

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stimulus to the onset of diaphragmatic activity was calculated. This represents the latency of conduction of the phrenic nerve. An upper limit of normal for this measurement was selected as 9.75 ms. As soon as possible postoperatively (day 1 to 3), transcutaneous phrenic nerve stimulation was repeated. Because of the invariable presence of a right-sided internal jugular line, right-sided phrenic nerve stimulation was obtained in only 8 subjects. In any patients demonstrating abnormalities of the left phrenic nerve postoperatively, follow-up studies of both phrenic nerves were performed at periodic intervals. In addition, in those patients with prolonged phrenic latencies on follow-up, sniff tests were performed to determine whether a paradoxical movement occurred to confirm phrenic paralysis.

Intraoperatively, several variables were recorded for later analysis. These included the number of grafts, the operative and bypass time, whether or not the pleural space was entered, and if a right atrial drain and polystyrene shield were used. In addition, the average body temperature, the volume of intravascular cardioplegic solution, and the amount of postoperative positive end-expiratory pressure (PEEP) were measured.

The bronchopulmonary anastomotic flow to the lung during bypass was also measured. The majority of the bronchial artery circulation anastomoses with the pulmonary microvasculature and returns to the left atrium. During bypass, when the aorta is cross clamped, the bronchopulmonary anastomotic flow represents the sole perfusion of the pulmonary parenchyma and is the major source of blood which reaches the left atrium. The bronchopulmonary anastomotic flow can be measured intraoperatively by collecting and measuring the drainage from the left ventricular sump. This is achieved by temporarily occluding the precollateral tubing leading from the cardiotomy reservoir which drains the left ventricle and timing the accumulation of blood. The bronchopulmonary anastomotic flow was expressed in absolute terms as milliliters per minute and as a percentage of total pump flow. A small amount of noncoronary collateral blood flow traverses the pulmonary circulation and will reach the left atrium if a right atrial drain is not used. In addition, the intravascular cardioplegic solution passes through the lung microvasculature if not drained by a right-sited sump. The measurement of bronchopulmonary anastomotic flow was made after drainage of all cardioplegic solution.

The presence and degree of atelectasis was evaluated roentgenographically. Chest x-ray films were routinely obtained preoperatively, on days 1, 2, and 3 postoperatively, and at the time of the patient's discharge. Further roentgenograms were taken at variable intervals throughout the recovery period depending on the clinical course of the patient. The roentgenograms were evaluated by a board-certified radiologist who evaluated them without knowing if they were taken preoperatively or on which day postoperatively. Atelectasis was graded using the following rating scale: 0, no atelectasis; 1, plate-like atelectasis; 2, mild lobar collapse; 3, moderate lobar collapse; and 4, complete lower lobar collapse. Separate results were compiled for the left and right lungs. The criteria used to evaluate atelectasis were position of the hemidiaphragm and hilum, and presence and characteristics of an opacity on chest roentgenograms.

Statistical Analysis

Contingency tables and nonparametric methods (Friedman rank sums and multiple comparisons) were used to evaluate the progression of atelectasis for the right and left lungs individually. The scores obtained on separate days for the left and right lungs were compared using Wilcoxon signed ranks for pairs (with ties). Individual relationships between the atelectasis scores, and the incidence and degree of atelectasis were evaluated by chi squared and likelihood ratio tests and by nonparametric methods based on ranks (Mann Whitney two sample test).

Discriminant analysis was used to evaluate which combination of categoric and continuous intraoperative variables best classified patients according to atelectasis score. The selection criteria were covariance controlled partial F values using an F to enter value of 1. This was a stepwise analysis whereby the variables with the best discrimination for atelectasis score were sequentially selected. Variables were no longer chosen when their relative importance, determined by the F statistic, was deemed insufficient. The ability to correctly classify patients according to atelectasis score on a given postoperative day could be calculated from a discriminant function derived from the multivariate discriminant analysis.

Results

Fifty-seven patients were studied over a period of eight months. Radiologic evidence of atelectasis was present at some time postoperatively in 50 of 57 patients in the left lung and 35 of 57 in the right lung. Atelectasis was more severe for the left lung than for the right for all postoperative days (p < 0.05). There was a progressive increase in the atelectasis score for the left lung until the fourth postoperative day (p < 0.02). There was no significant increase in the atelectasis score for the right lung after the first postoperative day. A large number of patients did not have chest roentgenography on the fifth and sixth postoperative days, and consequently these scores were not included in this analysis. Although the score values for both lungs had improved by the seventh postoperative day, they were still higher than preoperative values (p < 0.05).

Topical cold cardioplegia was used during the operative procedure in 56 of 57 patients. A polystyrene shield was used in 40 of 57 patients. Although there was a trend towards more severe left and right lower lobe atelectasis when the shield was not used, these differences were not statistically significant (atelectasis scores, mean ± SD, left lung, day 3: 1.8 ± 1.0 vs 1.5 ± 0.9; right lung, day 3: 0.7 ± 0.6 vs 0.5 ± 0.9, respectively).

Postoperative phrenic nerve studies were obtained.
Table 1—Phrenic Nerve Stimulation in Five Patients with Postoperative Phrenic Paresis

<table>
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<th>Patient No.</th>
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<th>Day of Final Test</th>
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<td>R (ms)</td>
<td>L (ms)*</td>
<td>R (ms)</td>
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*Ellipses indicate diaphragmatic CDAP unobtainable with phrenic nerve stimulation.

in 52 of 57 patients. Studies were performed on days 1, 2, and 3 postoperatively for 23, 26, and three patients, respectively. The preoperative conduction latency was within normal limits for all patients and was similar for right and left phrenic nerves (8.2 ± 0.1, and 8.1 ± 0.1 ms, respectively). Five patients had postoperative abnormalities in phrenic nerve function. In three patients (patients 1 to 3, Table 1) a left-sided diaphragmatic CDAP could not be elicited, and in two the latency of conduction was transiently prolonged (patients 4 and 5, Table 1). Left hemidiaphragmatic paralysis was confirmed in patients 1 to 3 by fluoroscopic demonstration of an elevated hemidiaphragm and paradoxical upward movement on sniffing. A markedly decreased action potential with palpable diaphragmatic contraction was subsequently elicited in two of the three on follow-up. At the time of follow-up, the phrenic latency was abnormally prolonged in one patient (patient 1) while it was within normal limits for the other (patient 2, Table 1). Fluoroscopy continued to show paradoxical movement, and the left hemidiaphragm remained elevated on roentgenography in these two patients. The third patient (patient 3) could not be restudied after being discharged because of the remote location of his residence. In all three of these, topical cardioplegia was used without the polystyrene shield. Studies of the right phrenic nerve in these three patients showed easily elicitable action potentials with normal conduction times. There were no roentgenographic abnormalities on the right and normal right hemidiaphragmatic descent with sniff maneuvers was present on that side on follow-up.

Two patients demonstrated a transient prolongation of phrenic latency after bypass (patients 4 and 5, Table 1). Both values returned to normal on retesting on the fifth and seventh day postoperatively, respectively. Topical cold cardioplegia and the polystyrene shield were used during CAB in both patients. In the remainder of the patients, there was no significant change in postoperative left phrenic nerve latencies in comparison to preoperative values (8.1 ± 0.1 vs 8.2 ± 0.1 ms).

The amplitude of the CDAP was measured in the 47 patients who had normal latencies of conduction. Preoperative CDAP amplitudes were found to be similar for the left (0.54 ± 0.18 mV) and right (0.57 ± 0.19 mV) hemidiaphragms. Overall, values for the postoperative left CDAP amplitudes were significantly lower when compared to the preoperative values (0.41 ± 0.13 mV vs 0.54 ± 0.18 mV). To test whether there was an association of reduced amplitude and postoperative atelectasis, patients were divided into those who showed a decrease in CDAP and those who did not. Preliminary work in our laboratory has shown an intrasubject coefficient of variation of 15 percent for the CDAP amplitude (unpublished data). In 20 patients, the preoperative and postoperative CDAP amplitudes were within 15 percent. In the remaining 27 patients, postoperative amplitudes were reduced in comparison to preoperative values by more than 15 percent. There was no difference in postoperative atelectasis scores (day 3) between the group with decreased or not decreased CDAP for either the left (1.5 ± 1.1 vs 1.7 ± 0.7) or right (0.65 ± 0.93 vs 0.68 ± 0.74) lungs. In the eight patients in whom both the left and right phrenic nerves were studied postoperatively, no difference in amplitude was found (left 0.39 ± 0.10 mV, right 0.44 ± 0.20 mV). Since a decreased CDAP amplitude could be secondary to diaphragmatic elevation, the effect of a change in electrode position on the CDAP amplitude was evaluated in several patients who had decreased postoperative amplitudes. In most cases, a larger CDAP was recorded by moving the electrodes in a cranial direction.

Follow-up phrenic nerve studies were not obtained in four patients. Three of these had complicated postoperative courses requiring prolonged intubation and the presence of Swan Ganz catheters. One suffered a perioperative myocardial infarction, one developed postoperative mediastinitis, and the third had hypoxic respiratory failure on the basis of pulmonary edema and left lower lobe atelectasis. At the time of discharge, all three had evidence of left lower lobe atelectasis.
with elevation of the left hemidiaphragm in one. The fourth patient had an uneventful postoperative course but declined to have the phrenic nerve studies repeated.

During the operative procedure, a number of variables potentially of importance in the development of atelectasis were tabulated. A right atrial sump was inserted in 28 of 50 patients. Entry of the pleural space occurred in 34 of 48 patients; bilaterally in nine, on the left in 21, and on the right only in four. In many instances, the pleural space was entered to harvest the inferior mammary arteries for grafting. The mean values, standard deviation and range for the continuous variables of body temperature, intravascular cardiopulmonary volume, bronchopulmonary anastomotic flow, and operative and bypass time are presented in Table 2. Although there was a trend towards more severe atelectasis in relation to several of these variables, only a larger number of grafts and longer operative time were found to be significant when analyzed in isolation from the other variables (p<0.05). There was no significant difference in any of the variables when comparing those patients with atelectasis scores of 0, 1, and 2 to those with scores of 3 and 4.

Discriminant analysis was used to determine which combination of variables would best predict the degree of postoperative left lower lobe atelectasis (Table 3). Using a stepwise procedure, the following variables were selected: (1) larger number of grafts; (2) longer operative and aortic cross-clamp time; (3) opening of the pleural space; (4) lack of use of the right atrial drain; (5) lack of use of the polystyrene pad; and (6) a lower body temperature. The p-values shown in Table 3 are dependent on inclusion in the model of the particular variable and all those listed above it. The discriminant function with these selected variables provided correct classification of atelectasis scores of 80 percent.

**DISCUSSION**

This study confirms the high prevalence of atelectasis in patients after CAB. Although this was more common and more severe in the left lower lobe, many patients developed similar changes on the right side. Several etiologic possibilities were addressed in this study. However, our major goal was to determine whether a relationship existed between postoperative phrenic nerve dysfunction and atelectasis. In 52 patients undergoing CAB, we found unequivocal postoperative abnormalities in left phrenic nerve conduction time in five patients with three of five developing a hemidiaphragmatic paralysis. In 27 of 47 patients, there was a decrement in the left CDAP postoperatively which could be explained by an axonal degeneration neuropathy or by an artifact resulting from surface EMG recording. Atelectasis of the left lower lobe occurred in approximately 90 percent of patients at some time after surgery. The data suggest that factors other than phrenic nerve injury account for the atelectasis in many patients.

In 1973, Scannell P first proposed an association between the use of topical cold cardioplegia during open heart surgery and impaired postoperative function of the left hemidiaphragm. The left phrenic nerve, during its course to the diaphragm, runs between the pericardium and the mediastinal reflection of the pleura on the left. In this exposed area, it is insulated from the cold saline "slush" only by the pericardium and perineural tissue. A direct injury of the phrenic nerve induced by hyperthermia would explain the predominant localization of the postoperative atelectasis to the left lower lobe.

It has been well established that cold may result in functional and structural abnormalities of peripheral nerves. A progressive decline in conduction velocity occurs when a nerve is cooled to below 17°C, culminating in a complete blockade below 5°C. Nerve conduction recovers rapidly upon rewarming. However, pathologic changes may occur at a later period, depending on both the temperature and duration of exposure. These consist of axonal degeneration predominantly affecting larger myelinated fibers and demyelination which is mainly paranodal in distribution. Although it has not been precisely measured, the perineural temperature may reach levels that are deleterious to the phrenic nerve during the application of topical cold cardioplegia. The pericardium is likely to afford limited insulation from the...
saline “slush” which may reach less than 0°C.

Since the study of Scannell et al., a number of other reports, corroborating the hypothesis of “phrenic frostbite,” have been published. In a prospective comparison of 40 patients undergoing CAB with or without topical cardioplegia, Benjamin et al found the incidence of left lower lobe atelectasis to be significantly higher in the former group (85 percent vs 33 percent). Sixty-nine percent (18 of 26) of patients with left lower lobe atelectasis were thought to demonstrate hemidiaphragmatic paralysis or paralysis as assessed by roentgenographic diaphragmatic excursion. More recently, Wheeler et al evaluated atelectasis after CAB in equal sized groups who differed only in the intraoperative use of a cardiac insulating pad (CIP). This Teflon device, inserted into the pericardial space, is designed to prevent direct contact between the “slush” and the area of pericardium containing the left phrenic nerve.

A significantly larger number of patients developed atelectasis in the group in whom the pad was not used (57 percent vs 22 percent). A study of comparable design substantiating these results was recently reported by Esposito and Spencer. The authors of these reports concluded that the use of this device diminished the hypothermia-induced injury to the phrenic nerve, thereby resulting in a lower incidence of atelectasis.

In contradistinction to this indirect evidence, there is limited objective documentation of phrenic nerve injury during CAB. It cannot be concluded that an impaired roentgenographic excursion of the diaphragm or lower lobe atelectasis is secondary to dysfunction of the phrenic nerve without specific electrophysiologic studies. In an animal model, Marco et al found a long-term phrenic nerve paresis in six of nine dogs when the phrenic nerve had been directly exposed to ice for 30 to 60 minutes. In five dogs where the experimental protocol more closely replicated the indirect exposure as in CAB, follow-up information was provided in only two. These dogs were found to have normal phrenic nerve function 53 days postoperatively; however, there was no information provided on the time course of recovery.

Markand et al studied 18 patients who had topical cold cardioplegia applied during bypass and documented abnormalities of the phrenic nerve in only three of them. However, because of the protracted time before they were studied postoperatively, an early neuropathy could have been missed. In this study, we addressed this possibility by performing phrenic nerve studies in the early postoperative period. Five patients had a left phrenic neuropathy as evidenced by a prolongation of latency or an inability to obtain a CDAP with left phrenic nerve stimulation. In two patients, a demyelinating neuropathy (prolongation of latency) had resolved one week postoperatively, and consequently, would have been missed if studied only at this time. Hemidiaphragmatic paralysis, substantiated by sniff testing, persisted on follow-up in the other three.

A demyelinating neuropathy of the left phrenic nerve can be excluded in the remainder of patients by the normal latencies of conduction. In an axonal degeneration neuropathy, however, the latency may be preserved but the amplitude of the CDAP reduced when fast fibers are spared. Normal ranges for the CDAP amplitude have not been established because of the large intersubject variability of this measurement. However, there was a significant decrease in mean left CDAP amplitude when comparing postoperative to preoperative studies. When results from individual patients were evaluated, 27 of 47 showed a significant decline. Before concluding that an axonal neuropathy of the left phrenic nerve occurred in these patients, an important caveat must be emphasized. A reduction in CDAP amplitude could be artifactual secondary to the problems inherent in surface recording of diaphragmatic EMG activity. Several factors suggest that this possibility must be strongly considered. First, atelectasis scores did not differ when comparing those patients with and without significant postoperative decreases in CDAP amplitude. Second, there was no difference in postoperative right and left CDAP amplitude in those patients in whom both phrenic nerves were studied. A discrepancy in amplitude would be evident with a localized injury of the left phrenic nerve sustained during bypass. Finally, we found that the left CDAP amplitude could be increased with a change in the electrode position from its preoperative site. This is not surprising given the frequently elevated position of the diaphragm postoperatively. At a later time of study, when this is presumably lessened, Markand et al were unable to demonstrate a reduction in postoperative left CDAP.

Given the limitations of surface EMG recording, we are therefore unable to accurately establish the incidence of an axonal degeneration neuropathy. A phrenic nerve paresis, presumably related to the application of topical cold cardioplegia, occurred in at least five patients in this study. The design of our study does not permit us to exclude a transient injury to the phrenic nerve that might have recovered by our evaluation at 24 to 72 hours after bypass surgery, in the remainder. Such an injury could lead to atelectasis initially, which may then be perpetuated by other mechanisms after recovery of phrenic function. Immediate postoperative phrenic nerve studies would be required to refute this possibility. Forty-four percent of our patients had phrenic nerve studies performed within 24 hours of surgery, and all but two had no abnormalities of phrenic latency. Therefore, we believe it unlikely that transient phrenic injury is the explanation for the almost routine
development of left lower lobe atelectasis.

As has been observed in other studies addressing this problem, we found the atelectasis to be related to a longer operative and bypass time. We hypothesized that atelectasis might be related to several operative factors including inadequate bronchopulmonary anatomic flow, intraoperative lung collapse due to entry of the pleural space, and pulmonary endothelial cell damage caused by the intravascular cardioplegic solution.

During CAB, the bronchial circulation is the sole nutrient flow to the lungs. If this relative ischemia predisposed to atelectasis, we should have observed a relationship between bronchopulmonary anatomic flow and the incidence and severity of postoperative atelectasis. Although there was a wide range of anatomic flows, such a relationship was not observed.

Atelectasis has been shown to occur experimentally when the lungs are ventilated and exposed to atmospheric pressure without PEEP. This is accentuated when there is cold exposure. The mechanism is unclear but may be related to the disruption of the surfactant layer. Several of these conditions may be present during CAB surgery. Both entry of the left pleural space and a lower body temperature were found to be related to the severity of postoperative left lower lobe atelectasis in this study.

The intravascular cardioplegic solution used during bypass, though isotonic, contains a high concentration of KCl (20 mEq/L). This solution returns to the right atrium, and subsequently, it may passively enter the pulmonary microvasculature unless removed by a right atrial cannula. Lack of use of a right atrial sump during bypass was found to be related to higher atelectasis scores. It is possible that the cardioplegic solution is toxic to endothelial cells, which in turn, may favor the production of atelectasis.

We therefore believe that atelectasis following CAB is multifactorial in etiology. One cause is an impairment of diaphragmatic activity secondary to neuromuscular dysfunction. Variability in the incidence of phrenic nerve paresis may occur because of differences in operative technique between surgeons. A precise quantitation of the temperature and duration of exposure necessary to cause phrenic nerve paresis is required. With this information, operative guidelines can be established to minimize this complication. In addition, the data from this study suggest that several other operative factors may contribute to the production of atelectasis following bypass surgery.

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