Prediction of Pulmonary Function Loss Due to Pneumonectomy Using $^{133}$Xe-Radiospirometry*

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Nineteen patients on whom pneumonectomy was performed because of bronchial cancer were investigated preoperatively with spirometry and $^{133}$Xe-radiospirometry. Postoperative lung function was predicted from these examinations. One month to one year postoperation the patients were reinvestigated with spirometry and arterial blood gas analyses and the obtained values were compared with the preoperative values. The prediction of postoperative VC and FEV$_{1.0}$ was found satisfactory for clinical purposes, ie about as good as that obtained by previous authors using bronchospirometry.

Patients with lung cancer often have other pulmonary diseases such as chronic bronchitis, emphysema and tuberculosis.¹ If a complicating disease is more pronounced in the noncancerous lung,² unsuspected postoperative ventilatory insufficiency may appear. For this reason it is desirable to be able to predict the postoperative lung function after pneumonectomy by preoperative investigations. Conventional lung function tests are insufficient to predict the course in any individual patient.²,⁵ Snider,⁸ and Neuhaus and Cherniack⁷ used bronchospirometry to predict pulmonary function after pneumonectomy for tuberculosis. They found a reasonable correlation between predicted values for maximal breathing capacity and measured values after operation. Ranson-Bitker and associates¹⁰ using the same methods in pneumonectomy for either bronchogenic carcinoma or tuberculosis also showed good predictability of postoperative function. However, bronchospirometry has not become widely used in routine investigation before lung surgery probably because it is relatively cumbersome for both patient and doctor. The technique of $^{133}$Xe-radiospirometry, with the use of radioactive xenon and external scintillation detectors gives the same information as does bronchospirometry regarding the distribution of ventilation, perfusion and lung volume between the two lungs.¹¹ In the present study $^{133}$Xe-radiospirometry was used together with conventional spirometry in an attempt to predict changes of pulmonary function (vital capacity, ventilatory capacity, arterial blood gases) after pneumonectomy in lung cancer.

Material

The material consisted of 19 patients, aged 44 to 73, on whom pneumonectomy was performed for treatment of bronchial cancer during the years 1967 to 1970 at the Clinic of Thoracic Surgery, Malmö General Hospital, Malmö, Sweden. The patients are identified by the letters A through T (Table 1). One patient, E, had been treated for bilateral pulmonary tuberculosis when the cancer was discovered. Two patients, I and L, had sarcoidosis in addition to cancer. Twelve of the patients had left-sided bronchial cancer and seven right-sided. Preoperative examinations were performed one week to one month before the operation, and the postoperative examinations between one month and one year after the operation.

Methods

Spirometry was performed preoperatively with the use of the modified Bernstein spirometer described by Berglund and co-workers.¹² The predicted normal values were obtained from Berglund and associates¹² and Birath and colleagues.¹³ Functional residual capacity was measured by wash-out of nitrogen during oxygen breathing, which also permitted an estimation of the efficiency of the alveolar ventilation¹⁴-¹⁷ (normal values from unpublished data in this laboratory). Arterial oxygen and carbon dioxide tensions were determined with electrode systems manufactured by Instrumentation Laboratory, Inc, Boston. The distribution of ventilation, perfusion and volume between the two lungs was measured with...
133Xenon and external scintillation detectors\textsuperscript{18,19} using a technique described by Mörner.\textsuperscript{11} The patient was investigated in the supine position with four frontal and four dorsal scintillation detectors, suitably collimated so that the radioactivity from each lung could be recorded separately. In addition, it was possible to record the activity from one basal and one apical field of each lung. The pulses from the ventral and dorsal detector over each field were added and recorded in one of four channels. After subtraction of the preceding background activity, the activity registered over the four fields was added and the activity registered for each lung was expressed as a percentage of the sum, as in bronchospirometry. Thus the possibility of studying apical and basal fields separately was not used for the present purpose.

The distribution of perfusion between the lungs was estimated during breath-holding after an intravenous injection of about 0.2 mc of 133Xe. The partition of ventilation was measured after three normal breaths of 133Xe from a closed spirometer system containing 0.5 mc of 133Xe per liter air. The regional lung volume was estimated after rebreathing in this closed spirometer system, absorbing carbon dioxide and adding oxygen to keep the volume constant, until the concentration of radioactive xenon was the same throughout the lung-spirometer system. Regional vital capacity was measured as the difference in radioactivity between a maximal inhalation and a maximal exhalation when this equilibrium was reached. 133Xe-radiospirometry performed in this way gives essentially the same information as bronchospirometry regarding the distribution of volume, ventilation and perfusion between the lungs (Fig 1).\textsuperscript{11}

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\begin{figure}
\centering
\includegraphics[width=\textwidth]{distribution_of_ventilation}
\caption{Distribution of ventilation in 35 patients with lung distress. X-axis: the ventilation of the right lung in percent of the ventilation of both lungs estimated with bronchospirometry (Br). Y-axis: the ventilation of the right lung in percent of the ventilation of both lungs estimated with radiospirometry (Ra).}
\end{figure}

\begin{table}
\centering
\begin{tabular}{|c|c|c|c|c|c|c|c|c|c|c|c|c|c|}
\hline
Subject & Age & Site of Cancer & VC & FEV\textsubscript{1.0} & FEV\% & FRC & Washout & LCI & P\textsubscript{CO2} & VC & FRC & Vent & Perf & Survival Time (mo) \\
\hline
A & 68 & R & 69 & 71 & 97 & 106 & 130 & 8.6 & 43 & 52 & 56 & 59 & 55 & 7 \\
B & 55 & L & 68 & 68 & 99 & 92 & 95 & 10.0 & 40 & 68 & 65 & 75 & 64 & 21 \\
C & 68 & L & 97 & 90 & 90 & 86 & 103 & 10.1 & 43 & 59 & 61 & 60 & 17 & 6 \\
D & 66 & L & 73 & 63 & 84 & 61 & 136 & 13.9 & 34 & 76 & 80 & 77 & 6 & 9 \\
E & 51 & L & 93 & 73 & 78 & 136 & 139 & 8.4 & 37 & 56 & 62 & 67 & 72 & 6 \\
F & 64 & L & 63 & 62 & 97 & 111 & 89 & 9.7 & 36 & 59 & 61 & 66 & 69 & 6 \\
G & 57 & L & 90 & 88 & 94 & 79 & 76 & 7.9 & 41 & 55 & 59 & 57 & 56 & 5 \\
H & 73 & L & 77 & 75 & 94 & 98 & 149 & 14.2 & 35 & 64 & 60 & 69 & 71 & 17 \\
I & 71 & R & 68 & 77 & 109 & 82 & 85 & 9.0 & 37 & 57 & 57 & 63 & 65 & 19 \\
J & 44 & R & 59 & 84 & 84 & 115 & 125 & 9.2 & 34 & 50 & 50 & 53 & 56 & 20 \\
K & 48 & L & 74 & 59 & 80 & 137 & 156 & 14.0 & 38 & 66 & 70 & 74 & 72 & 17 \\
\hline
\hline
\textbf{X} & 61 & 79.2 & 73.6 & 91.5 & 100.3 & 116.6 & 12.7 & 37.7 & 58.5 & 61.3 & 65.7 & 64.2 & 13.0 \\
\textbf{SE} & 3.9 & 3.2 & 2.8 & 7.1 & 8.4 & 0.72 & 1.2 & 2.0 & 2.1 & 2.5 & 2.3 & 2.0 \\
\hline
M & 68 & R & 85 & 75 & 85 & 114 & 142 & 8.0 & 33 & 53 & 53 & 47 & 53 & \\
N & 65 & R & 50 & 45 & 85 & 43 & 74 & 10.9 & 37 & 88 & 68 & 86 & 91 \\
O & 49 & L & 69 & 78 & 114 & 82 & 62 & 8.5 & 42 & 65 & 65 & 65 & 72 \\
P & 61 & L & 69 & 74 & 106 & 86 & 55 & 9.4 & 31 & 85 & 89 & 84 & 78 \\
Q & 71 & R & 89 & 96 & 104 & 75 & 109 & 10.9 & 33 & 54 & 51 & 60 & 59 \\
R & 61 & L & 81 & 78 & 96 & 81 & 110 & 9.7 & 36 & 65 & 69 & 70 & 74 \\
S & 49 & R & 101 & 98 & 95 & 130 & 130 & 10.0 & 8.3 & 36 & 56 & 63 & 57 & 57 \\
T & 57 & R & 87 & 85 & 97 & 77 & 81 & 9.9 & 36 & 63 & 63 & 65 & 85 \\
\hline
\textbf{X} & 60 & 78.9 & 78.6 & 97.8 & 86.0 & 87.9 & 9.5 & 35.5 & 66.1 & 64.9 & 66.7 & 71.0 \\
\textbf{SE} & 5.6 & 5.8 & 3.6 & 9.3 & 8.1 & 0.4 & 1.2 & 4.7 & 4.1 & 4.7 & 4.9 & 4.9 \\
P & >0.05 & >0.05 & >0.05 & >0.05 & <0.05 & >0.05 & >0.05 & >0.05 & >0.05 & >0.05 & >0.05 & >0.01 \\
\hline
\end{tabular}
\caption{The Results of Preoperative Lung Function Studies.}
\end{table}

The P-values indicate the probability that the difference in a given function between those who are dead (A-L) and those who have survived (M-T) is statistically significant.

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The postoperative value for vital capacity was predicted from the preoperative vital capacity measured with conventional spirometry, multiplied by the percentage of vital capacity on the nonoperated side determined from the preoperative $^{133}$Xe-radiospirometry. The postoperative ventilatory capacity ($FEV_{1.0}$) was predicted in the same way but with the use of the percentage of ventilation in the nonoperated lung.

**RESULTS**

The results of the preoperative investigations are given in Table 1 which also includes survival times after surgery. There was no operative mortality. Of the 11 patients (A–L) who died, one died of pneumonia five months after surgery and the other ten from their cancer. There was little difference between those who have survived and those who are dead in regard to preoperative lung function.

In Figures 2 and 3, the predicted values for vital capacity and $FEV_{1.0}$ are given on the X-axis and the actual values obtained one to 12 months after pneumonectomy are shown on the Y-axis. In Figure 2, the values for vital capacity are evenly distributed around the line of identity. The 95 percent confidence interval of the y intercept includes zero. The correlation coefficient is 0.73 and the standard deviation is 16 percent (0.35 liter). The prediction of $FEV_{1.0}$ is somewhat less precise as judged from Figure 3, the correlation coefficient being 0.63. The y intercept is outside the 95 percent confidence interval. However, it should be pointed out that only 6 of 19 subjects are located below the line of identity. The standard deviation is 12 percent (0.20 liter). The arterial oxygen tension rose postoperatively in all subjects except E, who was very ill of metastases at the time of the postoperative investigation and subsequently died in a matter of weeks (Fig 4). The mean preoperative arterial oxygen tension was 71.4, the mean postoperative, 82.6. The difference is significant ($P<0.001$). There was no significant correlation between preoperative and postoperative arterial oxygen tension. In none of the cases did the oxygen tension decrease to a critical level.

**DISCUSSION**

The present group of patients, subjected to pneumonectomy because of lung cancer, is small and select. It should be noted, however, that the preoperative lung function was quite poor in some cases, eg subject N had an $FEV_{1.0}$ of 1.4 liter. The postoperative $FEV_{1.0}$ was between 1.2 and 1.4 in four subjects. Thus, several subjects had a ventilatory capacity quite close to what we consider the lower limit of operability, ie a predicted postoperative value of $FEV_{1.0}$ less than 1.0 liter. The present results confirm the opinion that conventional lung function tests are of little value in predicting the outcome of surgery in the individual case (Table 1). The $FEV_{1.0}$, FEV percent and nitrogen wash-
out during O₂-breathing were somewhat worse among the group of patients who died during the first year after surgery than among the surviving patients. The difference was most pronounced when studying intrapulmonary gas mixing with the nitrogen wash-out technique.

The prediction of ventilatory capacity after pneumonectomy with ¹³³Xe-radiospirometry seems roughly as good as that obtained with bronchospirometry. It should be noted that with ¹³³Xe-radiospirometry as well as with bronchospirometry the distribution of ventilation is measured at rest. The predicted value for FEV₁₀ is thus obtained as a product of one measurement at rest (¹³³Xe-radiospirometry) and one forced expiration (FEV₁₀). It does not seem unlikely that the precision in the prediction would improve if the preoperative measurements of the distribution of ventilation and volume in the lungs were obtained during forced breathing, eg during an exercise test. Such measurements are feasible with the xenon method but difficult with the bronchospirometric technique. The value of a preoperative assessment of the distribution of ventilation during exercise or otherwise increased ventilation remains to be studied.

In the present investigation all subjects were studied in the supine position and we have no information about the pulmonary artery pressure.

However, the fact that arterial oxygen tension rose in most subjects after pneumonectomy and that no patient had a postoperative arterial oxygen tension less than 55 mm Hg speaks against a serious reduction of the pulmonary capillary bed.

The rise in postoperative arterial oxygen tension is probably due to the elimination of a V-A shunt. However, there was no significant difference in V/Q index between the cancerous and noncancerous lung using ¹³³Xe-radiospirometry. This may be due to the fact that resolution with the present technique is too poor to detect smaller areas with a change in V/Q index. It may be possible to discover such small defects by further separation of the information from different parts of the lungs, ie by using either more detectors or a gamma-camera.

Svanberg in a study of 180 patients found that the decrease in regional lung function caused by cancer was closely related to the involvement of the regional lymph glands and hence to operability and five-year survival rate. He and James and co-workers concluded that the information obtained from radiospirometry or scanning regarding the patient's respiratory function in the affected and contralateral lung is valuable in deciding whether a patient is to be treated by surgery.

The distribution of pulmonary blood flow may also be studied with labeled macroaggregates and lung scan or gamma-camera. This technique is likely to give better anatomic resolution but the perfusion data obtained in this way cannot readily be related to regional or total ventilation and volume. Nevertheless, Secker Walker and Provan found lung scanning valuable in the preoperative assessment of lung cancer.

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REFERENCES

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Another indication that single organisms generally have inherent potentialities for both sexes is found in the existence of intersexes, individuals more or less intermediate between male and female. The Greeks had words for six sexes in people. No objective evidence bears out the number of sexes they recognized, but the implications of varying degrees of masculinity and femininity is quite in conformity with modern views. The consensus among biologists is that there is a balance of male and female tendencies in the hereditary complement of an individual, and that the mechanisms like XY ordinarily serve to trip the balance in one direction or another. Sometimes, however, other factors enter onto the scales and alter or reverse the effect of the normal mechanism for sex determination.