Appraisal of Choice and Results of Treatment for Bronchogenic Carcinoma*

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I have been kindly invited to present a scientific paper and have chosen to talk on a subject or, more correctly on two subjects which are dear to me. As to the first part, appraisal of choice of treatment for bronchogenic carcinoma, I have in Toronto a feeling of carrying coals to Newcastle because there are few places where this problem has been more thoroughly investigated than here. During the last few years this problem seems also to have been a matter of considerable dispute, partly because of misunderstanding and partly because of different attitudes about certain medical problems.

Although the main cause of lung cancer now is well known, its incidence will in coming decades continue to rise to epidemic proportions and, unfortunately, a great majority of the victims will continue to be unsuitable for curative treatment. In most of these patients a simple physical examination may be sufficient to exclude them from operation. In the remaining smaller part, the reliability of several diagnostic procedures has been questioned. In the latest report from the Veterans Administrations Surgical Adjuvant Cancer Chemotherapy Group published a few months ago, the authors1 stress that the factors which enable a patient to survive five years or longer after resection of a bronchial tumor are ill-defined. During recent years, however, great experience has been gained from combinations of different prognostic signs, and international organizations have sought to establish uniform principles and rules for presentation of treatment results and permitting statistical evaluation.

One of these is the TNM system recommended by the International Union Against Cancer.2 In this, “T” stands for size and location of tumor and “M” for remote metastases. The significance of these variables has not given rise to much discussion. This has, however, been the case in “N,” which denotes regional lymph nodes.

All agree that tumor invasion of lymph nodes is evidence of a more advanced stage. Independently of how they are examined, there is, however, rather great confusion both to the significance of localization and of the extent of tumor invasion. There are now several series published with a relatively high percentage of five-year survivals among lung cancer patients with invaded intrathoracic lymph nodes. Whether these are mediastinal, hilar or intrapulmonary is, however, often difficult to ascertain from these reports. In other series in which there is documented invasion of mediastinal nodes, the five-year survival rate is almost without exception less than 10 percent. Consequently, it is a serious prognostic sign that must be evaluated together with the results of other investigations before operation. I would like to stress, however, that lymph node invasion alone is not always a real sign that operation should not be performed. I will discuss that problem later on.

Some authors cannot find a reason for a lymph node examination before operation because they have found a resectability rate of 50 percent, even in patients with tumor-invaded nodes. The information on which nodes are found invaded is, however, scanty and the longterm results are mostly missing. Unfortunately, some data are also uncritically quoted in some surveys on the subject, furthering the confusion. It may be stressed that the aim of the lymph node examination is intended as a guide for curative resection.

In two large studies this year from Sweden3 and France5 further attempts have been made to determine the route of the lymphatic spread and to evaluate the seriousness of the tumor invasion in the mediastinal lymph nodes.

In a study by Larsson5 in Gothenburg observations are reported relative to 500 patients, all considered candidates for operation, for more than three years. He has presented a modified classification within the frame of the TNM system, and in all patients the regional lymph nodes were examined mediastinoscopically. I would like to concentrate on the prognostic significance of these findings. Larsson5 has distinguished between ipsi- and contralateral spread and also, as Bergh and Scherstén4 in the same clinic, taken into consideration whether the nodes microscopically have shown perinodal growth or not.

Tumor invasion of the mediastinal lymph nodes was detected before operation in 157 cases or in 32 percent of the whole series. Of these, 38 patients

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were assigned to the contralateral metastases group. Most of these patients were excluded from operation.

There was a highly significant association between histologic tumor type and mediastinal lymph node metastases. In both small cell anaplastic carcinoma and adenocarcinoma mediastinal node involvement was detected in 47 percent, but only in 17 percent in epidermoid carcinoma.

As to the extent of lymph node involvement the perinodal growth was predominant in all of the histologic types. Real intranodal growth was found in only 15 percent in the whole investigated material. The differentiation between intra- and perinodal growth had, moreover, great prognostic significance. The three-year survival rate in the resected group is shown in Figure 1.

No patient with perinodal growth was alive two years after the resection. This indicates a further support of the findings made by Bergh and Scherstén.4 Perhaps the few reported long-term survivors among patients with invaded mediastinal lymph nodes would all have shown intranodal growth when examined.

Many have questioned the diagnostic and prognostic value of the mediastinal exploration. It is said not to give sufficient information because many invaded nodes may be overlooked. As for all procedures, the results depend to a large extent on the examiner. It may, however, be remembered that the method was suggested as a screening test and must be evaluated together with other investigations. Invaded lymph nodes in the actual region may sometimes be overlooked even by an experienced examiner. Larsson4 found, however, that most of these at

\[ \text{% Survival Rate} \]

\[ \begin{array}{l}
\text{Right} \\
64 \\
48 \\
32 \\
39 \\
\text{Upper} \\
42 \\
43 \\
12 \\
14 \\
46 \\
43 \\
\text{Lower} \\
42 \\
46 \\
21 \\
20 \\
45 \\
50 \\
\end{array} \]

\( \times \) Cancer metast.

\( \times \) Colour spread

\text{FIGURE 1. Prognostic significance of type of mediastinoscopically detected ipsilateral lymph node metastases in patients with resection (deaths at operation included).}

\text{FIGURE 2. Comparison of mediastinoscopic findings in 243 patients with bronchogenic carcinoma in different parts of lungs and mediastinal spread after color injection in same region in human cadavers according to J.F. Dyon.}

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has offered great problems. In bronchogenic carcinoma, however, the situation is unique. The most important mediastinal lymph node groups are accessible and the presence of metastases may be confirmed by biopsy, rendering the reliability of the diagnosis extremely high. For that purpose it does not matter what method is used. Some prefer the open parasternal mediastinal exploration and others the mediastinoscopy.

With a slight modification of the proposed TNM system Larsson found very good correlation between survival of the patients and staging of the disease as estimated on the basis of studies before operation. It is to be hoped that this staging system will be studied in other lung cancer centers.

May I repeat that for scientific staging and to avoid confusion it is absolutely necessary to distinguish between the different intrathoracic lymph node stations? According to Salzer, there are four stations, and several authors have confirmed that tumor spread to each of them has prognostic significance.

In a series of lung cancer patients with resectable tumors, Nohl found that those with mediastinal spread (stage 3) had a four-year survival rate of 9.7 percent, a low figure compared to stage 1 and 2. The question now arises, may it by any means be possible to select these few patients before operation and to save the majority from the pain and expense of an unnecessary resection?

It has been shown by Bergh and Scherstén, and now in a larger series before operation, by Larsson, that perinodal tumor growth is a serious sign, with no patient alive two years after resection. If these results are confirmed by those surgeons who already have made this distinction it suggests that patients with contralateral spread or perinodal growth be excluded from operation (Fig 3). Among those patients with invaded mediastinal nodes there will then remain 12 percent located ipsilaterally and showing only intranodal growth, a figure corre-

![Figure 3. Estimated distribution of mediastinoscopically detected lymph node metastases in bronchogenic carcinoma.](image1)

![Figure 4. Right-sided resection of middle and lower lobes in 67-year-old man with epidermoid carcinoma.](image2)

![Figure 5. Showing 69-year-old patient with inoperable epidermoid carcinoma. Cytostatic treatment.](image3)

responding fairly well with the four-year survival rate in Nohl's series.

Now finally a few words about appraisal of the results of lung cancer treatment. As yet, only surgical treatment has been discussed. We know from experience that in selected patients radiotherapy in different forms and also chemotherapy may have a beneficial effect on the patients' well-being. These treatments may be used in combination with operation, and some encouraging results are reported. In incurable patients so-called "palliative" treatment has been tried, palliative in the sense of alleviation of symptoms. Sometimes, however, this same type of treatment may have a deleterious effect, prolonging death rather than life, as it were.

There is another question. Do all patients surviving five years, that is, those few with the most successful treatment, enjoy a meaningful life? Are they free from pain and dyspnea and how is their ability to work? It may be difficult to answer many of these questions when dealing with cancer patients. Because of the seriousness of the disease we have
usually measured the results of treatment only in months of survival. There seems to be a real need for a method capable of evaluating the beneficial and the harmful effects of the methods commonly accepted.

I will quote Feinstein et al.9 “A prime target of future clinical research will be the development of scientific methods to evaluate quality rather than mere quantity of survival in cancer.” Thus, quality of life measured in some way or other, has to be taken into account. We have made a preliminary attempt to measure this.

For each patient a “vitagram” was constructed as an expression of the quality of survival. The survival time was denoted along the x-axis of a graph in months and the points of quality of life per month along the y-axis. The measured area gives the total sum of points as an expression of the total quality of survival. Examples of such two-dimensional vitagrams are given in Figure 4 and 5. Every month of survival was judged and graded according to a scale of 0–20 points:

1 Full capability of work during one month + 20 p
2 Partial capability of work + 16 p
3 Ambulant without work + 12 p
4 Confined to bed + 8 p
5 Symptoms such as fever, pain or cachexia during nos. 1–4 — 4 p
6 Hospitalization during nos. 3–4 — 2 p

Those above working age have been classified according to their real capacity.

According to these lines a prospective investigation started two years ago at the Lung Clinic in Uppsala. To achieve statistically reliable results comparable patient groups were given randomized treatment. When patients suitable for operation are excluded, we presume that most colleagues consider such a randomized selection of treatment justifiable from an ethical point of view. We have not seen the results yet and, as I said, it is a preliminary attempt open for criticism.

Finally, many of you may consider my suggestions sophisticated. Maybe they are. But until the worldwide smoking habit has been changed or more effective forms of therapy have been developed we must work hard to give the selection of cases for different treatment and the appraisal of the therapeutic results at least a scientific touch, which, I am sure, in the long run will be for the benefit of our patients.

REFERENCES

5 Dyon JF: Contribution a l'étude du drainage des lymphatiques du poumon. Université Scientifique et Medicale de Grenoble, 1973