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The need for lung transplantation in The Netherlands

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Abstract The aim of this study was to assess the future need for lung transplantation in the Netherlands in the absence of limiting factors, such as a shortage of donor organs. The need was estimated using two different methods. In method 1, estimation of the need was based on data from the Dutch lung transplantation program, collected during a 4-year period (1 April 1992 until 31 March 1996). In method 2, the need was estimated using national mortality data over a 5-year period (1987–1991) preceding the start of the Dutch lung transplantation program. The results of both methods were corrected for known factors of distortion. The number of lung transplantations needed in the Netherlands in the future was esti-mated to range from 50 to 80 a year, which corresponds to 3.2–5.2 trans-plantations per million inhabitants per year. Considering the current supply of donor lungs in the Nether-lands, only about one-third of the patients in need of a lung transplant in the future will be able to receive one.

Key words Lung transplantation, needs assessment · Needs assessment, lung transplantation

Introduction

In 1989 the first lung transplantation was performed in the Netherlands. At that time, little was known about the effects of lung transplantation on survival, quality of life, or resources. Before deciding whether or not to incorporate lung transplantation into the Dutch health care benefits package, the Dutch National Health Insurance Board initiated a technology assessment (TA) in which the 5-year experience (1990–1995) of the Dutch lung transplantation program was investigated [4, 15]. The TA provided information on clinical effectiveness, quality of life, costs, and the need for, and supply of, donor organs. At the time of the TA, the Dutch lung transplantation program was only being carried out at one center, the University Hospital Groningen (UHG).

At the start of the TA it was already clear that, as in other countries, the demand for donor lungs would be greater than the supply. However, the extent of the shortfall was not known. Therefore, studies of both the supply of donor lungs and of the need for lung transplantation were included in the TA.

The aim of the present study was to determine the future need for lung transplantation in the absence of limiting factors, such as the shortage of donor organs or financial restrictions. The need was estimated using two different methods. In method 1, estimation of the need was based on data from the Dutch lung transplantation program, which was collected during a 4-year period (1 April 1992 until 31 March 1996). In method 2, the need was estimated using national mortality data over a 5-year period (1987–1991) preceding the start of the

Dutch lung transplantation program. A third method, using epidemiological data (incidence and prevalence) on patients with end-stage lung diseases, was not feasible because additional information on the stage or severity of the diseases was lacking [7].

Materials and methods

Method 1: The experience of the Dutch lung transplantation program

The number of patients who were accepted as candidates for lung transplantation and put on the waiting list of the UHG was used as an estimate of the total need for lung transplantation. As the UHG was the only center in the Netherlands to which these patients could be referred during the study period, all of the patients could be identified. By using the number of patients on the waiting list instead of the number of patients who had already undergone lung transplantation, the shortage of donor lungs did not influence the estimation of future need.

Patients who were accepted as candidates for lung transplantation had to be suffering from irreversible, progressively disabling end-stage pulmonary or cardiopulmonary disease, with a predicted life expectancy of less than 12–18 months. Detailed criteria for patient selection in the Dutch lung transplantation program are described elsewhere [12]. The diagnoses of patients accepted as candidates for transplantation are listed in Table 1.

The calculation of the need for lung transplantation was based on the number of patients placed on the waiting list between 1 April 1992 and 31 March 1996. Patients listed during the first 2 years of the program (1990–1991) were not included in the calculation. The outcome of the calculation was a weighted mean of the annual number of patients listed, and the most recent years had the highest weight. This way, estimation of the need was mainly determined by the number of patients placed on the waiting list in the most recent years; however, by also using the number of patients listed in previous years, the estimation could be corrected for accidental fluctuations. The following formula, in which # 92/93 represents the number of patients accepted between 1 April 1992 and 31 March 1993, was used: Total annual need = $(0.1 \times \# 92/93) + (0.2 \times \# 93/94) + (0.3 \times \# 94/95) + (0.4 \times \# 95/96)$.

Method 2: National mortality data

In method 2, mortality data were used to estimate the need for lung transplantation. All deaths in the Netherlands are registered with the Bureau of Statistics (CBS), and the causes of death are listed in accordance with the International Classification of Deaths (ICD, 9th revision). The CBS provided us with national age-specific mortality data for the period 1987–1991 that included deaths from lung diseases that are considered to be indications for lung transplantation. Had a lung transplantation program been available, some of the people who died of these diseases could have been suitable candidates for it.

To estimate the total future need, mortality data were analyzed according to the following stepwise approach:

1. Selection of diseases that might be an indication for lung transplantation and that are included in the national mortality data (Table 1). Since secondary pulmonary hypertension is caused by other

Table 1 Diseases that can be indications for lung transplantation and their ICD codings

Disease	ICD
α_1-Antitrypsin deficiency	277.6
COPD/emphysema	491.2/492/496
Cystic fibrosis	277.0
Primary pulmonary hypertension	416.0
Secondary pulmonary hypertension	–
Idiopathic pulmonary fibrosis	516.3
Pulmonary fibrosis due to inhaled mineral or organic dusts, sarcoidosis, scleroderma, Sjögren's syndrome, other collagen diseases or histiocytosis X	135/277.8/500/501/502/ 506.4/710.1/710.2/710.9
Bronchiectasis	494

Table 2 Disease and age-specific selection fractions for contraindications used in method 2 (*a1ATD* α1-antitrypsin deficiency, *COPD* chronic obstructive pulmonary disease, *CF* cystic fibrosis, *PPH* primary pulmonary hypertension, *IPF* idiopathic pulmonary fibrosis, *PF other* pulmonary fibrosis due to known causes, *Br* brochiectasis)

Disease	Age (years)					
	< 20	20–29	30–39	40–49	50–59	> 59
α1ATD	–	0.8	0.8	0.8	0.8	0.8
COPD	–	0.6	0.6	0.6	0.4	0.1
CF	0.7	0.7	0.7	0.7	0.7	–
PPH	1.0	1.0	1.0	0.8	0.5	0.5
IPF	0.8	0.8	0.8	0.8	0.2	0.2
PF other	0.2	0.2	0.2	0.2	0.2	0.2
Br	0.5	0.5	0.5	0.5	0.5	0.5

(primary) diseases, such as congenital heart disease or pulmonary thromboembolic disease, it is not included in the mortality data. Therefore, this method could not give an estimate of the number of patients with end-stage secondary pulmonary hypertension.

2. Calculation of the average annual number of deaths in the Netherlands based on the mortality data in the period 1987–1991

3. Deselection of patients under 10 and over 61 years of age. Although age is not one of the selection criteria for lung transplantation, patients under 10 or over 61 years of age were not accepted for transplantation in the UGH during the study period.

4. Deselection of patients who died of extrapulmonary complications. Some of the diseases that are indications for lung transplantation can also lead to fatal extrapulmonary complications. Patients who died of extrapulmonary complications were not considered to be suitable candidates for lung transplantation and were, consequently, excluded from the analysis.

Based on the literature the following selection fractions, representing the fraction of deaths caused by pulmonary complications, were used: sarcoidosis 0.75 [9]; scleroderma 0.5 [11]; Sjögren's syndrome 0.33 [1]; other collagen diseases 0.5. For cystic fibrosis and α_1-antitrypsin deficiency, no selection fraction was used because more than 95 % of deaths were caused by pulmonary complications of the disease [10, 14].

Fig. 1 Annual number of patients accepted as candidates for transplantation in the Dutch lung transplantation program during the period 1 April 1990 until 31 March 1996, according to specific disease ($a1ATD$ α1-antitrypsin deficiency, *COPD* chronic obstructive pulmonary disease, *CF* cystic fibrosis, *PH* pulmonary hypertension, *PF* pulmonary fibrosis, *Br* brochiectasis)
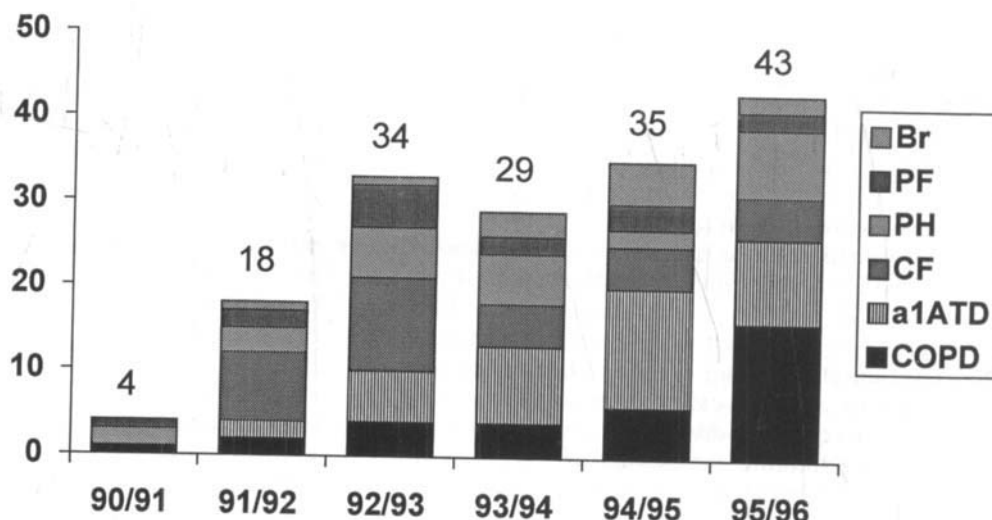
5. Deselection due to contraindications. Some patients with end-stage lung disease are not considered suitable candidates for lung transplantation because of contraindications. Based on the experience of the lung transplantation program of the UHG, selection fractions were determined for the seven diseases shown in Table 2. The disease-specific selection fraction was the ratio of patients placed on the waiting list to the total number of patients who were accepted or rejected. Patients who died during assessment or who were still under consideration were excluded from computations. The selection fractions were determined per age category. If there was no clear trend in the relationship between age and the presence of contraindications, one selection fraction for all age categories was used.

Results

Method 1: The experience of the Dutch lung transplantation program

During the period 1 April 1990 until 31 March 1996, a total of 163 patients were accepted as candidates for lung transplantation and put on the waiting list of the UHG. The median age of these patients was 43 years (range 10–61 years), and 55 % were men. Figure 1 shows that the total number of new patients increased over the years. This was particularly true for patients with COPD and α_1-antitrypsin deficiency. COPD and α_1-antitrypsin deficiency together accounted for about 60 % of all new patients on the waiting list during the last 2 years. As shown in the calculation below, the total need was estimated to be 37 transplantations a year.

Total annual need = $(0.1 \times 34) + (0.2 \times 29) + (0.3 \times 35) + (0.4 \times 43) = 37$

Method 2: National mortality data

Following the first two steps of the analysis of the national mortality data, it was estimated that during the period 1987–1991, an average of 5517 deaths per year in the Netherlands were caused by diseases that were indications for lung transplantation. About 94 % of these patients were older than 61 years of age. Less than 0.02 % were younger than 10. Deselection of patients under 10 and over 61 years of age (step 3) resulted in 344 deaths per year. Of these deaths, about 80 % were caused by emphysema/COPD. After applying the fourth step, the deselection of patients with fatal extrapulmonary complications, 334 deaths remained in the analysis. The fifth, and last, step of the analysis, the deselection of patients with contraindications, resulted in an estimated total need for 122 lung transplantations per year (Table 3). The most frequent diagnosis was COPD, followed by cystic fibrosis and pulmonary fibrosis.

Table 3 The results of the stepwise analysis of the National mortality data (method 2) ($a1ATD$ α1-antitrypsin deficiency, *COPD* chronic obstructive pulmonary disease, *CF* cystic fibrosis, *PPH* primary pulmonary hypertension, *IPF* idiopathic pulmonary fibrosis, *PF other* pulmonary fibrosis due to known causes, *Br* brochiectasis)

Disease	Age (years)						
	Total	10–19	20–29	30–39	40–49	50–59	60–61
α1ATD	6.2	0.0	0.5	0.7	1.7	3.0	0.2
COPD	86.8	0.0	0.9	1.3	14.1	62.2	8.4
CF	12.9	6.4	4.9	1.2	0.4	0.0	0.0
PPH	7.3	1.2	1.0	1.2	1.7	1.6	0.6
IPF	6.3	0.2	0.2	0.0	1.1	0.6	0.2
PF other	4.0	0.1	0.2	0.5	1.0	1.7	0.5
Br	3.0	0.0	0.1	0.0	0.5	1.9	0.5
Total	122.5	7.9	7.8	4.9	20.5	71.0	10.4

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Discussion

In this study, we used two methods to estimate the future need for lung transplantation in the Netherlands. According to method 1, future need was estimated at 37 a year, while method 2 revealed an estimate of 122 lung transplantations. In fact, method 1 underestimates the future need for lung transplantations since what it really provides is an estimation of the manifest demand rather than the need for lung transplantation. Potential candidates who were not placed on the waiting list of the transplantation center could not be identified; these were patients with so-called unrecognized need [5]. These patients could be divided into two groups, the first one including suitable candidates who died during assessment before being placed on the waiting list, in particular, patients with rapidly progressive lung diseases like primary pulmonary hypertension and idiopathic pulmonary fibrosis. A more timely referral of these patients to the transplantation center could have led to their acceptance as candidates for transplantation and placement on the waiting list. Analysis of the patient flow through the assessment phases of the program showed that, annually, between five and ten potential candidates died before they could be placed on the waiting list. The second group of patients with unrecognized need was the effect of incomplete referral to the transplantation center. The TA of the Dutch liver transplantation program revealed that the number of patients accepted as candidates for transplantation from provinces near the UHG was 1.9 times higher than the number from other parts of the country, indicating incomplete referral of candidates from other parts of the country [2]. Therefore, we compared the standardized (total number per 10^6 inhabitants) number of patients who live in the northern provinces of the Netherlands, where the UHG is situated, and who had been placed on the waiting list for lung transplantation with the number of patients from other parts of the country. Unlike in the liver transplantation program, the regional distribution of patients accepted as candidates for lung transplantation appeared to be rather even. However, this does not imply that all potential candidates are referred to the UHG. The total number of new patients on the waiting list has been increasing in the last few years, and this number is likely to continue to increase in the years to come. Therefore, we estimated the total future need for lung transplantation to be at least 50 a year.

Method 2 provides an overestimation of the total future need because it insufficiently accounts for patients with contraindications for lung transplantation. Contraindications may exclude patients from transplantation either before or during the selection process. The selection process in the UHG is known, and the mortality data were corrected for this selection. However, it is obvious that an unknown, but substantial, number of patients with end-stage lung disease were not referred to the transplantation center because of contraindications. In particular, patients with COPD, who are mostly over 50 years of age, often have contraindications, such as side effects of systemic corticosteroids and severe atherosclerosis. Based on interviews with clinicians who work with patients with end-stage lung disease, we estimated that over one-third of all possible candidates for lung transplantation are not referred to a transplantation centre because of relevant contraindications. If, we exclude these patients, the total need for lung transplantation in the Netherlands would be as high as 80 a year.

One should note that, using method 2, it was impossible to estimate the number of lung transplantation candidates with secondary pulmonary hypertension. In mortality data, these patients are coded according to their primary disease that resulted in pulmonary hypertension and, therefore, they cannot be identified. However, it is unlikely that this would amount to more than a few patients a year.

In conclusion, the total need for lung transplantation in the Netherlands was estimated to range from 37 to 122 a year; after correction, this was 50–80 transplantations a year, which corresponds to 3.2–5.2 per million inhabitants per year. This estimate is in line with figures published in a preliminary study by Brutel de la Rivière et al. [3] for the Netherlands (3–3.5 a year). Estimates made by Evans et al. [6] for the United States were much higher (13.7–46.9 a year), but these estimates were criticized by others as being unduly high [13]. The actual rate of lung transplantation in other countries, even in countries with a high donor supply such as Austria, does not exceed 4.0 transplants per million inhabitants per year.

Based on an analysis of the supply of donor lungs, the maximum number of future lung transplantations in the Netherlands was estimated to range from 17 to 27 a year [8]. This estimation applies to the Dutch situation, where over 80 % of the transplants are double lung transplants. As a consequence of the limited supply of donor lungs, only about one-third of all future patients needing a lung transplant will be able to receive one. This will lead to a further increase in the number of patients on the waiting list and, consequently, to high mortality rates among these patients, very likely over 50 %.

Based on the technology assessment of the lung transplantation program, the Dutch National Health Insurance Board advised the Minister of Health to defer the decision on whether or not to incorporate lung transplantation into the Dutch health care benefits package. Ways to prevent increasingly long waiting lists and to lower the costs involved in lung transplantation need to be addressed in further studies before a final decision on coverage of lung transplantation can be made.

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