

Survival of patients with asbestosis can be assessed by risk predicting models

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1. ABSTRACT

Objectives: Our aim was to investigate the pulmonary function test (PFT) results of asbestosis patients and determine whether baseline PFTs and the risk predicting models such as gender, age and physiologic variables (GAP)-model and composite physiologic index (CPI) would be useful in predicting survival in these patients.

Methods: Demographics and PFTs of 100 patients with asbestosis were evaluated. The survival difference between the GAP stages was determined with Kaplan-Meier survival curves with statistical significance analysed with log-rank test. The suitability of the risk predicting models and baseline PFTs to predict the survival of patients was analysed with Cox regression.

Results: At baseline, the mean value of diffusion capacity for carbon monoxide (DLCO) was 65%; for forced vital capacity (FVC) it was 81%, with restrictive lung function being the most common impairment. The median estimated survival of the patients was 124 months, i.e. 171 months in GAP stage I, 50 months in stage II and 21 months in stage III ($p < 0.001$). CPI, DLCO % predicted, age at baseline and GAP stage were significant predictors of mortality (all p-values under 0.001).

Conclusions: GAP and CPI as well as baseline DLCO % predicted were significant parameters in the evaluation of the prognosis of the patients with asbestosis; they may be useful in clinical practice when considering treatment strategies of individual patients.

Key Messages

What is already known about this subject?

- Decreased values of pulmonary function tests (PFT), especially forced vital capacity (FVC) and diffusion capacity (DLCO) are typical findings in patients with pulmonary fibrosis
- The association of baseline PFT with survival in patients with asbestosis is unclear
- Gender, age and physiologic variables (GAP)-model and composite physiologic index (CPI) are risk-predicting models developed for patients with idiopathic pulmonary fibrosis
- The suitability of risk predicting models is recognized in several types of interstitial lung diseases but not in patients with asbestosis

What are the new findings?

- Restrictive lung function was the most common lung function impairment observed in patients with asbestosis
- GAP model, CPI as well as baseline DLCO % predicted were significant predictors of mortality in asbestosis patients
- Spirometry variables were not useful in predicting survival

How might this impact on policy or clinical practice in the foreseeable future?

- GAP model, CPI or DLCO may be used in clinical practice when evaluating the prognosis of an individual patient with asbestosis
- These risk-predicting models may be beneficial when considering treatment strategies in the future

Keywords: asbestosis, mortality, pulmonary function test, diffusion capacity, gender age and physiologic variables, composite physiologic index

List of abbreviations: Asbestos body (AB), bronchoalveolar lavage (BAL), chronic hypersensitivity pneumonitis (CHP), composite physiologic index (CPI), diffusion capacity for carbon monoxide

(DLCO), potential value of diffusion capacity per liter of lung volume (DLCO/VA), forced vital capacity (FVC), forced expiratory volume in one second (FEV1), gender age and physiologic variables (GAP), high resolution computed tomography (HRCT), interstitial lung disease (ILD), idiopathic pulmonary fibrosis (IPF), Oulu University Hospital (OUH), rheumatoid arthritis associated interstitial lung disease (RA-ILD)

2. INTRODUCTION

In asbestosis, as well as in other types of pulmonary fibroses, the evaluation of prognosis and disease progression in an individual patient is often challenging. In previous studies, baseline pulmonary function tests (PFT) have been used to evaluate the prognosis in other types of pulmonary fibroses, but as far as we are aware, in the English literature, there are no previous studies which have attempted to associate baseline PFT values with survival in patients with asbestosis [1-4]. Although a restrictive pattern in spirometry and decreased diffusion capacity for carbon monoxide (DLCO) are commonly encountered in asbestosis, similarly as in other types of pulmonary fibroses, the significance of these findings in the assessment of prognosis in asbestosis is still unclear.

Risk predicting models such as the gender, age and physiologic variables (GAP)-model and composite physiologic index (CPI) were originally developed for patients with idiopathic pulmonary fibrosis (IPF) [5,6]. CPI has proved to be better in the evaluation of the prognosis than any single pulmonary function measurement [6]. These risk predicting models have also been examined in patients with other types of interstitial lung diseases (ILD), but not in patients with asbestosis [2-4,7-9]. Several studies have focused on GAP and CPI assessments in both genders with ILD in many countries throughout the world, but only few have reported details of the spirometry device models [1,2,5,6,10-16]. Thus, CPI and GAP models seem to be functional in both genders, in different ethnic backgrounds and with several types of spirometry equipment.

The examination of asbestos bodies (AB) in bronchoalveolar lavage (BAL) fluid has been commonly used in the evaluation of asbestos exposure, with more than 1 AB/ml being generally considered as a probable sign of asbestos exposure, although AB do not always exist in BAL despite the existence of a significant exposure [17,18]. In our previous study, we found that several BAL differential cell

counts predicted survival in asbestosis patients, thus offering a novel tool for risk prediction in asbestosis [19].

Prognostic factors in asbestosis are presently poorly understood. The aim of our study was to investigate the PFT results at the time when investigations start in a case of suspected asbestosis. In addition, we aimed to determine whether baseline PFTs and the risk predicting models such as GAP and CPI would be useful in predicting survival in these patients.

3. METHODS

3.1 Patient and data collection

The study population was identified from the database of Oulu University Hospital (OUH) using the International Classification of Diseases 10th edition (ICD-10) code J61 "asbestosis" as previously described [19]. We collected the patients with asbestosis who had been treated in the hospital between the years 1996-2015. We verified the diagnoses from the medical records of the hospital by applying the Helsinki criteria for asbestosis [18,20] i.e. we excluded those patients who did not display the diagnostic criteria for asbestosis as described previously [19]. All the included patients had moderate or high asbestos exposure and radiological findings typical of asbestosis. We collected information from their PFTs such as spirometry and diffusion capacity from the examination conducted closest to their initial visit at the hospital at the time of diagnosis. All of the asbestosis patients treated in OUH between 1996-2015 and for whom we were able to find information of the initial hospital visit during asbestosis diagnosis as well as sufficient data from the follow-up visits were included in this study. Most patients with suspected ILD in OUH have undergone an assessment in a multidisciplinary meeting. In addition, the patients in whom there was a suspicion of an occupational exposure such as an exposure to asbestos, have been handled in an occupational multidisciplinary meeting.

Clinical information of the patients was collected from the patient records of OUH which have used electronic medical records for over 20 years. In addition to electronic data, information was retrieved from card files from the patients investigated prior to the introduction of electronic medical records. In addition to the PFTs, the data included date of birth, date of investigations, date of asbestosis diagnosis, gender, occupation, information about exposure to asbestos, high resolution computed tomography (HRCT) records and smoking habits. Data of the results of the BAL-examination, was collated as previously described [19].

PFT included results of spirometry i.e. forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1 / FVC ratio as well as diffusion capacity for carbon monoxide i.e. DLCO (haemoglobin corrected) and potential value of diffusion capacity per liter of lung volume (DLCO/VA). PFT were evaluated by applying the Finnish reference values [21,22]. The PFT laboratory used the Jaeger Master Diffusion spirometry device between 1996-2011, Jaeger MasterScreen PFT devices since 1998 and also Carefusion PFT Pro devices since 2013.

Smoking status i.e. whether a patient was a non-smoker, ex-smoker or current smoker, was determined at the time of spirometry. Patients whose smoking history was not more than three pack years (n=8) were classified as non-smokers as previously described [19]. Survival time was calculated from the time of spirometry to death from all causes or to the latest visit to the hospital. Vital status was updated until June 2018. Date of death was collected from death certificates housed in the national registry of Statistics Finland.

3.2 Risk prediction models

The GAP score was determined based on the patient's gender, age, FVC% predicted and DLCO% predicted. Patients were classified into three GAP stages, namely as stage I (0-3 points), stage II (4-

5 points) and stage III (6-8 points), as previously described [5]. The formula for CPI calculation was:
$$\text{CPI} = 91.0 - (0.65 \times \text{DLCO \% predicted}) - (0.53 \times \text{FVC \% predicted}) + (0.34 \times \text{FEV1 \% predicted})$$
[6]. We used a cut-off value of 41 for the CPI score based on the previous study of survival predictors in IPF patients [15].

3.3 Statistical analyses

The data was analysed with IBM SPSS Statistics version 26. Variables were evaluated as means and standard deviation. The median value was used for variables with extremely skewed distributions. Differences between groups were evaluated with the one-way ANOVA followed by Tukey's test, Kruskal-Wallis, Chi-Square and Fisher's Exact test. In the survival analyses, we used Kaplan-Meier survival curves with statistical significance being evaluated with the log-rank test. Survival was evaluated in median survival time values. The mortality risk was analysed with Cox regression. P-value <0.05 was considered as statistically significant.

4. RESULTS

4.1 Characteristics, GAP stages and CPI of the patients

The study cohort included 100 asbestosis patients diagnosed by the Helsinki criteria, and treated in the Respiratory Medicine clinic of the OUH [18,20]. The vast majority of the patients were male (96%) and most of the patients were ever-smokers (Table 1). The mean age was 68.6 years at spirometry and 68.0 years at the time of diagnosis. The most common occupations were construction worker (24%), plumber (17%) and car mechanic (11%). A large proportion, 39%, of the patients had emphysema in HRCT and almost all of the patients (97%) had pleural lesions. Asbestosis (39%) and cardiovascular diseases (31%) were the most common causes of death.

The results of GAP and CPI are presented in detail in Table 1. There were no differences in either smoking habits or BAL parameters in the various GAP stages (Table 1) although the BAL

macrophage differential count was lower and neutrophil differential counts were higher in GAP stage III in comparison with stages I and II but the differences were not statistically significant ($p=0.092 / 0.578$). In contrast, the CPI score differed significantly between all of the GAP stages (all p -values $p<0.001$).

Table 1. Characteristics of the patients in different GAP stages

		All (n=100)	GAP I (n=71)	GAP II (n=24)	GAP III (n=5)
Gender	male	96 (96.0)	67 (94.4)	24 (100.0)	5 (100.0)
Survival	dead	71 (71.0)	47 (66.2)	19 (79.2)	5 (100.0)
Age at diagnosis		68.0±8.7	66.8±9.3	70.2±5.9	74.9±6.6
Age at spirometry		68.6±8.8	67.2±9.3	71.5±5.9	75.1±6.5
Smoking	smoker	17 (17.0)	12 (16.9)	5 (20.8)	0 (0.0)
	ex-smoker	54 (54.0)	39 (54.9)	12 (50.0)	3 (60.0)
	non-smoker	29 (29.0)	20 (28.2)	7 (29.2)	2 (40.0)
BAL macrophages		73.6±18.1	74.5±15.7	74.8±20.8	54.4±29.0
BAL lymphocytes		17.0±15.7	17.6±15.4	14.7±16.3	21.4±20.8
BAL neutrophils		6.8±11.7	5.6±6.5	7.3±15.7	21.4±30.5
BAL eosinophils		2.5±2.9	2.2±2.9	3.1±2.8	2.6±3.2
BAL AB/ml ^A		2.1	1.6	2.3	1.5
CPI		32.2±15.2	26.3±11.9	43.0± 9.9	64.9±4.8

Values are expressed as numbers of patients (%) or mean ± standard deviation except those with an “A” superscript which are median values.

BAL cell differential counts were analysed after May-Grünwald-Giemsa -staining.

BAL was performed in 86 patients (missing 12 GAP I, 1 GAP II and 1 GAP III patients) and ABs had been counted in 84 patients (missing 13 GAP I, 2 GAP II and 1 GAP III patients).

Abbreviations: asbestos body (AB), bronchoalveolar lavage (BAL), composite physiologic index (CPI) and gender age and physiologic variables (GAP)

4.2 Pulmonary function tests

The results of spirometry at the baseline were nearly within normal values i.e. mean FVC was 81% and mean FEV1 was 78% whereas mean DLCO was mildly decreased, being 65%. (Table 2). There were no significant differences in spirometry values between the smoking statuses. The DLCO ($p=0.011 / 0.010$) and DLCO/VA ($p=0.037 / 0.105$) of smokers were decreased when compared to non-smokers and ex-smokers, the results are presented in detail in Table 2. In addition, smokers had higher CPI compared to non- and ex-smokers ($p=0.033/0.007$). Restrictive lung function was the most common lung function impairment encountered in the study cohort. An obstructive pattern was

uncommon, being mostly associated with smoking since only one patient with an obstructive pattern was a non-smoker. The PFT results were slightly decreased since about 50% of the patients with decreased FVC had a result which was over 70% of reference value. Similarly, about every second patient with decreased DLCO had a result of over 60% at baseline.

Table 2. Pulmonary function measurements in patients with asbestosis

	Total (n=100)	Non-smokers (n=29)	Ex-smokers (n=54)	Smokers (n=17)	p-value
FVC % pred	81.2±16.8	80.4±14.7	84.0±18.1	73.7±13.6	NS
FEV1 % pred	77.9±17.0	79.4±16.2	79.2±18.5	71.2±11.5	NS
FEV1/FVC % pred ^A	96.2±11.7	97.8±9.0	94.9±12.8	97.7±11.8	NS
DLCO % pred	65.0±18.9	68.3±17.0	67.2±18.6	52.1±18.5	0.007
DLCO/VA% pred ^B	79.4±19.4	84.0±17.0	80.2±19.7	69.4±19.4	0.043
CPI	32.2±15.2	30.9±13.4	29.7±15.1	42.3±15.0	0.009
Restrictive ^A	35 (36.1)	12 (44.4)	13 (24.5)	10 (58.8)	NS ^C
Obstructive ^A	9 (9.3)	1 (3.7)	7 (13.2)	1 (5.9)	
Combined ^A	12 (12.4)	3 (11.1)	7 (13.2)	2 (11.8)	
FVC and FEV1/FVC normal ^A	41 (42.3)	11 (40.7)	26 (49.1)	4 (23.5)	
FVC and DLCO normal	21 (21.0)	6 (20.7)	14 (25.9)	1 (5.9)	NS ^D

Data are presented as mean ± standard deviation or numbers of patients (%)

^AInformation is missing for 3 patients (2 non-smokers and 1 ex-smoker)

^BInformation is missing for 1 patient (non-smoker)

Means are compared with ANOVA

^CComparing all 4 lung function profiles with Fisher's test

^DComparing with Chi-Square test

Restrictive (FVC% pred <80 and FEV1/FVC% pred ≥88), obstructive (FVC% pred ≥80 and FEV1/FVC% pred <88), combined (FVC% pred <80 and FEV1/FVC% pred <88), FVC normal ≥80% pred, FEV1/FVC normal ≥88% pred and DLCO normal ≥74% pred

Abbreviations: composite physiologic index (CPI), diffusing capacity of the lung for carbon monoxide (DLCO), potential value of diffusion capacity per liter of lung volume (DLCO/VA), forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and nonsignificant (NS)

4.3 Survival analyses and mortality predictors

The estimated median survival in the study cohort was 124.4 months. Median estimated survivals were 170.7, 50.0 and 20.5 months in GAP stages I, II and III, respectively, when the difference between GAP stages were statistically significant (p<0.001) (Figure 1). The median estimated survival was 163.8 months in the group with CPI score ≤41 and 46.6 months in the group with CPI score >41 (p<0.001) (Figure 1). The observed cumulative mortalities in different GAP stages and CPI scores are shown in Table 3 (Table 3).

Table 3. Observed cumulative mortality

Mortality (years)	1	2	3	5	10
GAP Stage					
I (n=71)	0 (0.0)	3 (4.2)	3 (4.2)	7 (10.0)	23 (39.0)
II (n=24)	1 (4.2)	6 (25.0)	8 (33.3)	14 (58.3)	18 (85.7)
III (n=5)	0 (0.0)	3 (60.0)	3 (60.0)	4 (80.0)	5 (100.0)
CPI score					
≤41 (n=76)	0 (0.0)	3 (3.9)	5 (6.6)	11 (14.7)	27 (42.2)
>41 (n=24)	1 (4.2)	9 (37.5)	9 (37.5)	14 (58.3)	19 (90.5)

Values are presented as number of patients (%)

12 patients in GAP stage I and 3 patients in GAP stage II were alive and followed for less than 10 years (1 GAP I patient had been followed for less than 5 years) at the end of follow-up time.

12 patients with CPI score ≤41 and 3 patients with CPI score >41 were alive and followed less than 10 years (1 patient with CPI score ≤41 had been followed for less than 5 years) at the end of follow-up time.

CPI, GAP stage, DLCO% predicted and age at spirometry were all statistically significant predictors of mortality (Table 4), the results of which remained significant also in multivariate analyses (Supplementary material Table 5 and Table 6). For every ten point increase in the CPI score, the mortality risk increased by 68%, for every ten percentage points decline in DLCO%, the mortality risk increased by 38% and for every increased year of age, the mortality risk increased by 8%. In GAP stage II patients, the mortality risk was 3.6 times higher and in GAP stage III, it was as much as 12.7 times higher than the risk associated with GAP stage I.

Table 4. Univariate analysis of mortality predictors in asbestosis patients

	HR (95% CI)	p-value
FVC% pred	0.99 (0.97-1.00)	NS
FEV1% pred	0.99 (0.98-1.01)	NS
DLCO% pred	0.95 (0.94-0.97)	<0.001
CPI	1.05 (1.03-1.07)	<0.001
Age at spirometry	1.08 (1.05-1.12)	<0.001
GAP I	Ref	
GAP II	3.58 (2.03-6.34)	<0.001
GAP III	12.69 (4.55-35.43)	<0.001
Non-smoker	Ref	
Ex-smoker	1.12 (0.65-1.95)	NS
Smoker	1.27 (0.63-2.54)	NS
No emphysema	Ref	
Emphysema	0.94 (0.58-1.53)	NS

Abbreviations: composite physiologic index (CPI), confidence interval (CI), diffusing capacity of the lung for carbon monoxide (DLCO), emphysema in HRCT, forced expiratory volume in one second (FEV1), forced vital capacity (FVC), gender-age-physiology stage (GAP), hazard ratio (HR), nonsignificant (NS) and reference group (Ref)

5. DISCUSSION

We have examined the association of baseline PFTs and risk-predicting models with survival in a relatively large cohort of asbestosis patients. As far as we are aware, the results of our study are novel since there are no previous published studies on GAP and CPI models nor has the correlation between baseline PFTs and survival in asbestosis been evaluated, at least in the English literature. We observed that GAP and CPI as well as DLCO were significant predictors of mortality. In addition, this is the first time that BAL cell counts and the number of asbestos bodies have been analysed in asbestosis patients subdivided into different GAP stages. It also seems that BAL results and GAP stages have not been associated previously in any type of ILDs.

We observed that the mean FVC % predicted at the time of the diagnosis was nearly 80 % when DLCO had slightly declined; these results are in line with a previous study [23]. In a Chinese study, Yang et al. estimated the mean FVC as being 76.7% and that of DLCO as 59.9%; their cohort consisted of 281 newly diagnosed asbestosis patients with a mean age of 65 years, which is nearly the same as the mean age of the individuals examined here. The gender distribution of Yang's study, however, was different since 40% of the patients were men whereas 96% of our subjects were males [23]. Walters et al. observed mean FVC 84.5% and mean DLCO 52% at the time of the diagnosis of asbestosis, the results of which are approximately in a similar direction as found here [24]. In a previous study on IPF, lower mean FVC (76.7%) and DLCO results (56.1%) were observed which are comparable to the values in our asbestosis patients [25]. In another recent study on rheumatoid arthritis associated ILD (RA-ILD)-patients, however, mean FVC (84.8%) and DLCO (71.1%) at the time of diagnosis were higher than the values in asbestosis patients [2].

The results of the previous studies investigating asbestos exposure and airway obstruction have been contradictory. Ameille et al. did not detect any association between cumulative asbestos exposure and airway obstruction in an asbestos exposed cohort, whereas Yang et al. observed an association between the duration of asbestos exposure and the FEV1/FVC ratio in non-smoking asbestosis patients [23,26]. In our study, most of the patients with impaired lung function had a restrictive pattern, those with an obstructive pattern were almost invariably smokers or ex-smokers. The present results are in a similar direction as those described in a Finnish study of 130 patients published over 40 years ago, which reported that 10 % of patients had obstruction [27].

The association of baseline PFTs with survival in asbestosis has not been studied previously in the English literature. We observed that DLCO, but not FVC or FEV1, associated with the survival of our asbestosis patients. When examining patients with other types of ILDs, the results have been partly similar and partly different than those found here in asbestosis patients. In a study on RA-ILD patients, Nurmi et al. observed a similar kind of association i.e. DLCO, but not FVC, was correlated with mortality [2]. FVC and DLCO have been shown to associate with the prognosis of IPF in several previous studies [28]. In a recent Finnish study, Kärkkäinen et al. stated that both FVC and DLCO were feasible ways of predicting survival, however DLCO appeared to be more sensitive than FVC [1]. In addition to DLCO, both FVC and FEV1 were significantly associated with mortality in chronic hypersensitivity pneumonitis (CHP) patients [3]. In addition to the above mentioned studies published in English, one abstract of a study published in Russian can be found in PubMed, which investigated the association of baseline PFT values with the prognosis in asbestosis [29]. In summary, baseline spirometry results have been shown to be useful in predicting survival in some ILD types such as IPF and CHP. In contrast, we did not detect a similar result in asbestosis; in these patients, the value of baseline DLCO seemed to be more useful in predicting survival.

We observed that the GAP stage predicted survival in patients with asbestosis although the observed mortality in asbestosis was smaller than the predicted mortality of IPF [5]. The difference between IPF and asbestosis was most evident in GAP stage I. In IPF, the predicted 3-year mortality in GAP stage I was 16.3%, which was higher than the observed mortality in asbestosis (4.2%) [5]. Similarly, the predicted 3-year mortality risks in GAP stages II and III in IPF were higher i.e. 42.1% and 76.8%, respectively, as compared to the observed values for asbestosis i.e. 33.3% (GAP stage II) and 60.0% (GAP stage III) [5]. When asbestosis was compared to RA-ILD, GAP stage I in asbestosis revealed a longer survival (observed 3-year mortality 4.2% in asbestosis vs 17.6% in RA-ILD), while survival in asbestosis GAP stage II was shorter since both 2-year (25.0% in asbestosis vs 9.1% in RA-ILD) and 3-year mortalities were higher (33.3% in asbestosis vs 27.3 in RA-ILD) [2].

We have shown that both CPI and GAP are functional if one wishes to estimate a prognosis in asbestosis, a situation similar to other ILDs. Few previous studies have reported spirometer devices. The Ohio water-seal spirometer, P.K Morgan respirometer and Chestac-55 V devices have been utilized in other studies, while we used Jaeger Master and Carefusion equipment [13,16]. The above mentioned results suggest that different spirometry devices can be used for the risk prediction in ILD. We have chosen the PFT results near to the time of the asbestosis diagnosis, which in practice is the earliest time point if one wishes to obtain the necessary PFT parameters for risk prediction models, although the time at diagnosis does not necessarily represent the early stages of asbestosis. The mean CPI (27.2) at the time of diagnosis in patients with RA-ILD was nearly the same as in our present study and further, both CPI and GAP models were statistically significant predictors of mortality [2]. It is noteworthy that few of the asbestosis patients were in GAP stage III, a situation reminiscent of those with RA-ILD i.e. only 5% of the patients with asbestosis revealed GAP stage III and none of the patients with RA-ILD had GAP III [2]. Jacob et al. observed that CPI was feasible also in

predicting survival in CHP [3]. Previously the cut-off value of 41 for the CPI score in IPF patients and the preoperative cut-off value of 41 for the CPI score in lung cancer patients with combined pulmonary fibrosis and emphysema who have undergone surgery, seemed to be useful in predicting survival [15,30]. We found this cut-off value was also workable in asbestosis patients. In summary, it seems that both GAP and CPI are useful in risk prediction of several types of ILDs.

An evaluation of prognosis of an individual patient may be useful when considering treatment strategies. Currently the treatment options for most of the patients with asbestosis are mainly symptomatic although in some cases, lung transplantation may be considered. Antifibrotic drugs, namely pirfenidone and nintedanib, are currently used for the treatment of patients with IPF. The recent INBUILD study revealed that nintedanib was efficacious also for the treatment of other types of progressive fibrotic ILDs [31]. Therefore, it may be possible that nintedanib may be used for the treatment of some asbestosis patients in the future.

One study limitation is its retrospective nature, which meant that some information was missing including the FEV1/FVC, DLCO/VA and BAL-examinations. Despite these limitations inherent in a retrospective study design, the data was reasonably comprehensive and thus we were able to determine how well the two predicting models such as GAP and CPI functioned in 100 patients with asbestosis. Therefore, we believe that the missing information did not exert any significant impact on the accuracy of the results. Another study limitation was the small number of GAP stage III patients, but nonetheless the results of survival analyses were statistically significant revealing that GAP stage III patients have a poor prognosis. Furthermore, a comparison of the survival curves with a same aged general population would have been relevant, but this kind of data was not available for our analysis.

6. CONCLUSIONS

GAP and CPI as well as baseline DLCO were functional in the evaluation of the prognosis of asbestosis patients, which may be useful in clinical practice when considering treatment strategies of the individual patient.

7. STATEMENTS

7.1 Acknowledgements

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7.2 Contributors

Eerika Keskitalo collected the study material, analysed and interpreted the data and prepared the draft of the manuscript. Johanna Salonen participated in the interpretation of data. Hannu Vähänikkilä participated in the statistical data analyses. Riitta Kaarteenaho managed and designed the study, planned the data collection form and interpreted the data. All authors have read and approved the final manuscript.

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7.4 Competing interests

The authors have the following competing interests that have not affected the contents of this study: Eerika Keskitalo reports congress fees and travel costs from Orion Pharma. Johanna Salonen reports congress fees and travel costs from Boehringer-Ingelheim, Novartis, Orion Pharma, Ratiopharm and Roche, and lecture fees from Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Mundipharma, Orion Pharma and Roche. Riitta Kaarteenaho has received a congress travel cost from Orion Pharma; consulting fees from Boehringer-Ingelheim and lecture fees from Roche, Boehringer-Ingelheim and Ratiopharm. Hannu Vähänikkilä declare no competing interests.

7.5 Patient consent for publication

Not applicable

7.6 Ethics approval

The study protocol was approved by the Research Ethics Committee of the Northern Ostrobothnia Hospital District. The permission to use data from death certificates was given by Statistics Finland. This study was conducted in compliance with the Declaration of Helsinki. No consents for the inclusion into this study were collected because of its retrospective design and due to the fact that most of the patients were already deceased. In addition, in accordance with Finnish legislation, consent would not be required because of the register-based nature of the project.

7.7 Data availability statement

The datasets generated and analysed during the current study are not publicly available since they contain information that could compromise research participant privacy but are available from the corresponding author on reasonable request.

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9. FIGURE LEGENDS

Figure 1. The Kaplan-Meier survival curve of the patients with asbestosis revealed a correlation between both GAP stages and survival (A) and CPI score and survival (B).