

Serum YKL-40 as a Prognostic Marker in Patients with Advanced Non-small Cell Lung Cancer

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Introduction

- Advanced non-small cell lung cancer (NSCLC) has a disappointing long-term prognosis.
- To minimize toxicity and improve efficacy as well as the quality of life (QOL) of patients with advanced NSCLC
 - It is necessary to find accurate prognostic and predictive factors.

YKL-40

- YKL-40 is a 40 kDa mammalian chitinase-like protein produced by cancer cells and tumor-associated macrophage.
- It may play a role in tissue remodeling, cancer cell proliferation and angiogenesis.

- Johansen JS, Jensen BV, Roslind A, Nielsen D, Price PA: Serum ykl-40, a new prognostic biomarker in cancer patients? *Cancer Epidemiol Biomarkers Prev* 2006;15:194-202.

Introduction (2)

- YKL-40
- not a cancer-specific biomarker
- An increase the level of YKL-40 in serum has been reported in patients with cancers such as breast cancer, ovarian cancer and colon cancer.
- associated with a poor prognosis in cancer patients.

Eur J Cancer 1995;31A:1437-1442.

Br J Cancer 1999;79:1494-1499.

Acta Obstet Gynecol Scand 2003;82:287-293.

Patients and Methods (1)

- This retrospective study compared the blood samples obtained from patients with advanced NSCLC to a control group.
- The serum levels of YKL-40 were determined in duplicate by ELISA.
- The serum samples obtained from healthy volunteers and patients with benign hematological disorders were used to determine the serum levels of YKL-40 in the control group.

Patients and Methods (2)

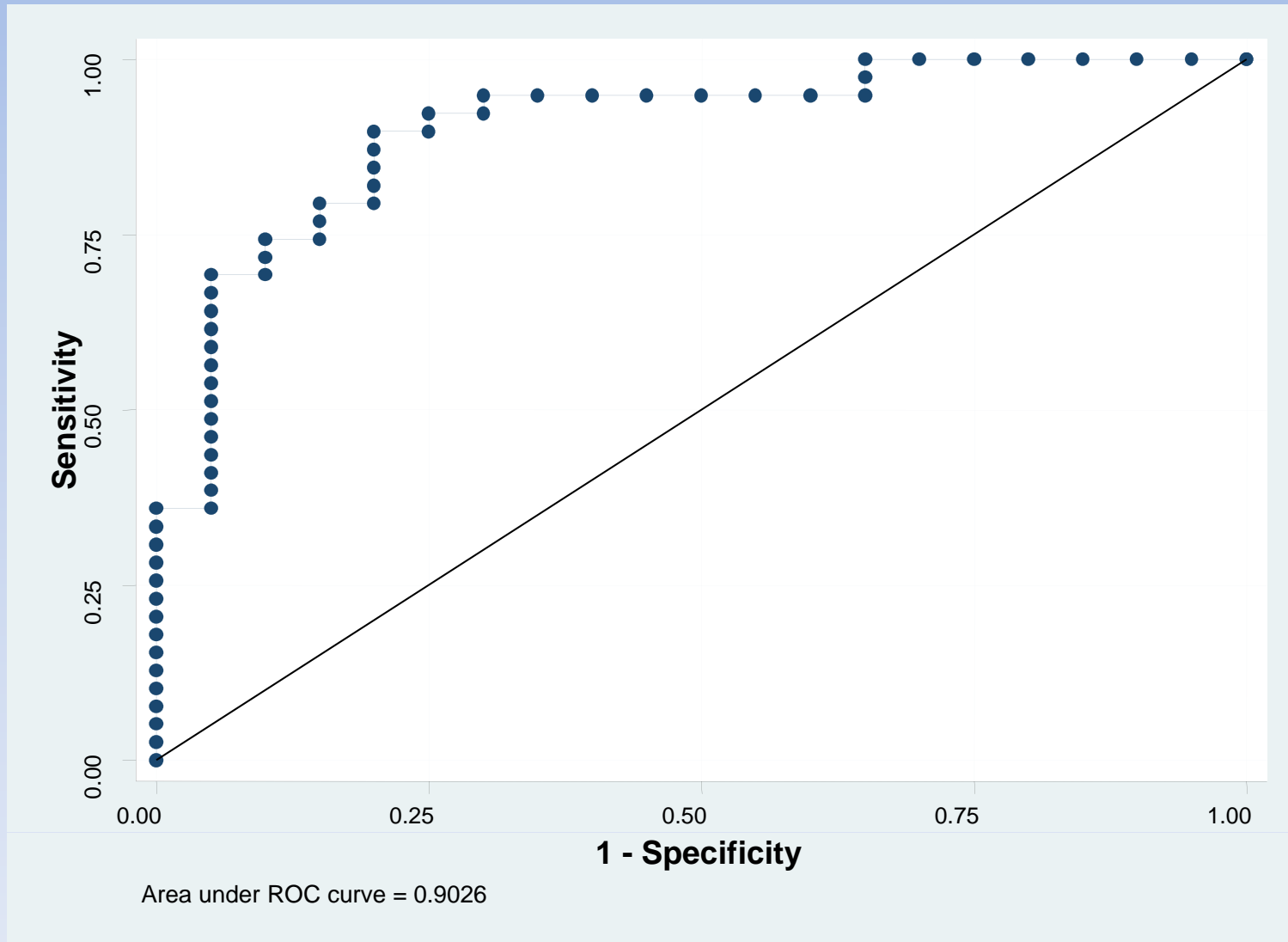
- Healthy control group
- not taking medication
- had no signs or clinical symptoms of cancer, joint, liver, metabolic or endocrine diseases
- Serum was separated from cellular components by centrifugation within one hour after blood sampling.
- stored at -80 °C until analysis.

Patients Characteristics

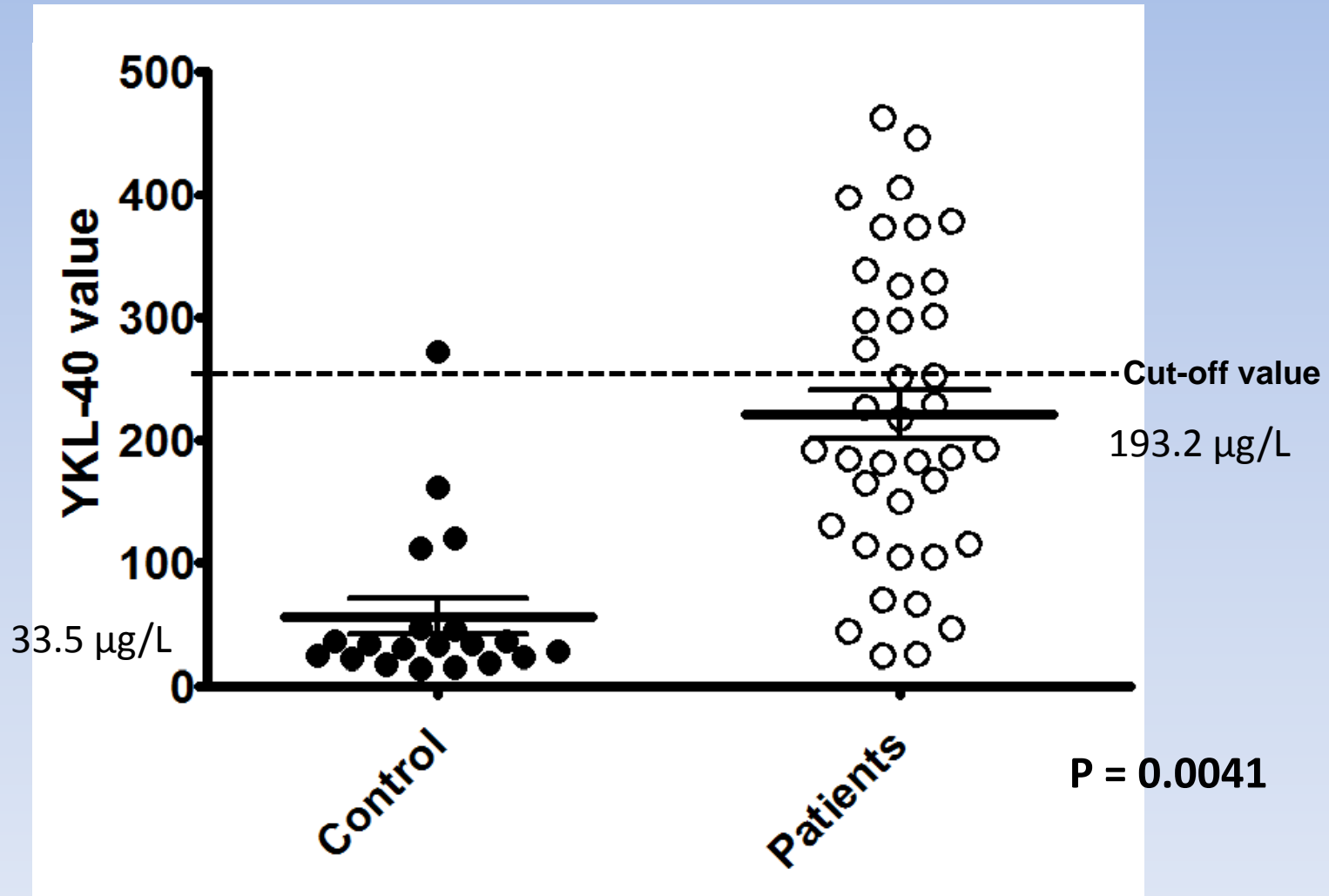
Number of patients	39
Age	
< 60	16 (41.0%)
≥60	23 (59.0%)
Sex	
Male	27 (69.2%)
Female	12 (30.8%)
Stage	
Stage IIIb	9 (23.1%)
Stage IV	30 (76.9%)
Performance	
0, 1	26 (59.0%)
2, 3	13 (41.0%)

Continued..	
Histologic type of NSCLC	
Adenocarcinoma	22 (56.4%)
Squamous cell carcinoma	14 (35.9%)
Poorly differentiated	3(7.7%)
Response of chemotherapy	
CR	1 (3.3%)
PR	12 (40.0%)
SD	8 (26.7%)
PD	9 (30.0%)
Smoking	
No	11 (28.2%)
Yes	28 (71.7%)
YKL-40	
Low	11 (28.2%)
High	28 (71.7%)

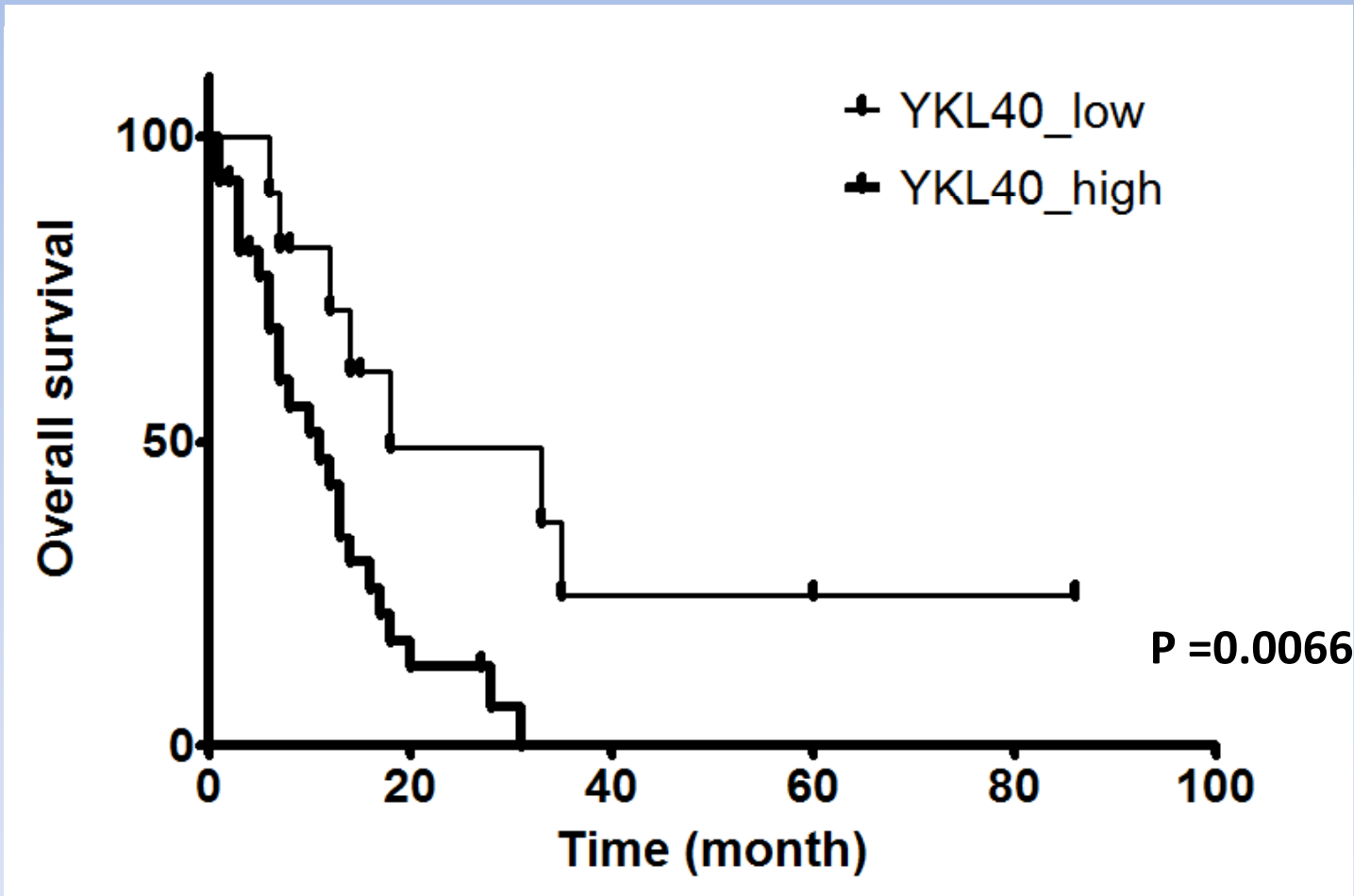
The optimal cutoff point for the YKL-40 level



Results (1)



Results (2)



- Patients with progressive disease tended to have higher serum levels of YKL-40 compared to the patients with a good response [median YKL-40: 251 vs. 165 $\mu\text{g/L}$, $p=0.067$].

Prognostic factors

- We conducted univariate and multivariate analyses of baseline characteristics such as age, sex, stage, performance status, pathology, smoking, alcohol and YKL-40 in order to evaluate the prognostic factors for overall survival.

Cox proportional hazard analysis of overall survival

Variables	Number	Hazard ratio (95% CI)	
		Univariate	Multivariate
Age			
< 60	16	1	
≥60	23	2.25 (1.06 – 4.75)	1.74 (0.79 – 3.84)
Sex			
Female	12	1	
Male	27	0.80 (0.38 – 1.69)	
Stage			
IIIB	9	1	
IV	30	1.38 (0.60 – 3.14)	
Performance*			
0, 1	26	1	
2, 3	13	2.38 (1.22 – 6.59)	3.94 (1.58 – 9.82)*

Pathology			
Adenocarcinoma	22	1	
Squamous cell cancer	14	1.49 (0.67 – 3.28)	
Undifferentiated	3	0.48 (0.06 – 3.63)	
Smoking			
No	11	1	
Yes	28	1.16 (0.52 – 2.55)	
Alcohol			
No	16	1	
Yes	23	0.75 (0.36 – 1.60)	
YKL-40[†]			
Low	11	1	
High	28	3.55 (1.32 – 9.56)	3.60 (1.25 – 10.39) [†]

*P value = 0.003

+P value =0.018

Conclusions (1)

- The levels of YKL-40 in patients with NSCLC were found to be higher than in controls.
- Performance status and YKL-40 were statistically significant in Cox proportional hazard regression analysis .
- These results suggest that YKL-40 may be useful prognostic factor in patients with advanced NSCLC.

Conclusions (2)

- YKL-40 may also be a good predictor to evaluate and modify cancer treatments.
- These potentially useful findings warrant further study and confirmation in patients with NSCLC.