CLINICAL CHARACTERISTICS, SURVIVAL AND PROGNOSTIC FACTORS OF PATIENTS WITH ADRENOCORTICAL CARCINOMA: A TERTIARY CENTRE EXPERIENCE

ELEZOVIC V., MACUT DJ, OGNJANOVIC S., ISAILOVIC T., POPOVIC B., BOZIC ANTIC I., BOGAVAC T., ILIC D., DAMJANOVIC S.

CLINIC OF ENDOCRINOLOGY, DIABETES AND METABOLIC DISEASES; CLINICAL CENTER OF SERBIA

INTRODUCTION

Adrenocortical carcinoma (ACC) is rare malignancy associated with poor prognosis. The aim of this study was to present clinical characteristics and survival of patients with ACC and to analyse the effect of prognostic factors on survival.

METHODS AND RESULTS

We retrospectively analysed 69 patients (46 female and 23 males) with pathologically confirmed ACC who were treated in our hospital between January 2005 and December 2015.

The median age at diagnosis was 51,0 years (range 14-74), mean tumour size was 11.3cm (range 3,1-30cm) and median follow up duration was 36 month (range 3-240). Patients with hormone secreting ACC (43.5%) mainly presented with isolated Cushing's (21.7%), or combined with hyperandrogenism (20.3%); 56.5% of patients had non-functioning tumour. The group included 50% low-stage tumours (4 stage I, 29 stage II) and 50% high-stage tumours (no stage III, 33 stage IV). Metastatic disease was present in 33% of patient at the time of diagnosis and 39% had acquired metastasis. Surgical resection was performed in 89.9% of patients; 78.9% of patients were treated with mitotane, and 24% with chemotherapy *(table 1)*

Median overall survival (OS) was 71 months (95%CI 41-100), with 5 year OS 51% (75.1% in stage II, 26% in stage IV). The 5-year OS for hormone secreting and nonsecreting tumours were 33% and 62%. Median disease free survival was estimated 6 months (95%CI 0-12)- *figure 1 and 2.*

The results of <u>univariante</u> Cox regression analysis showed that gender, age, disease stage and tumour secretory activity were significant variables with patient survival and surgical resection and presence of metastatic disease at the diagnosis were highly significant. The results of <u>multivariate</u> Cox regression analysis showed that the surgical treatment (HR-7.16, 95%CI=1.48-34.55, p =0.014), age (HR-0.409, 95%CI=0.177-0.947, p =0.037), and presence of metastatic disease at the time of diagnosis (HR-0.217, 95%CI=0.101-0.729, p=0.010) were independent prognostic factors for survival (table 2 and 3).

Table 1. Basic demographics and clinical characteristics of patients with ACC

Variable	No	%
Gender		
Female	46	66,7
Male	23	33,3
Hormonal activity		
Nonsecreting tumour	39	56,5
Secreating tumour	30	43,5
Stage of disease		
I	4	6,1
II	29	43,9
III	0	
IV	33	50,0
Metastatic disease at diagnosis		
Yes	23	33,3
No	46	66,7
Surgery		
Yes	62	89,9
No	7	10,1
Mitotan		
Yes	54	78,3
No	15	21,7
Chemotherapy		
Yes	16	23,9
No	59	76,1

Fig.1. Kaplan-Meier survival curve for ACC

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
100.629	14.462	72.282	128.975	71.000	14.931	41.735	100.265

a. Estimation is limited to the largest survival time if it is censored.
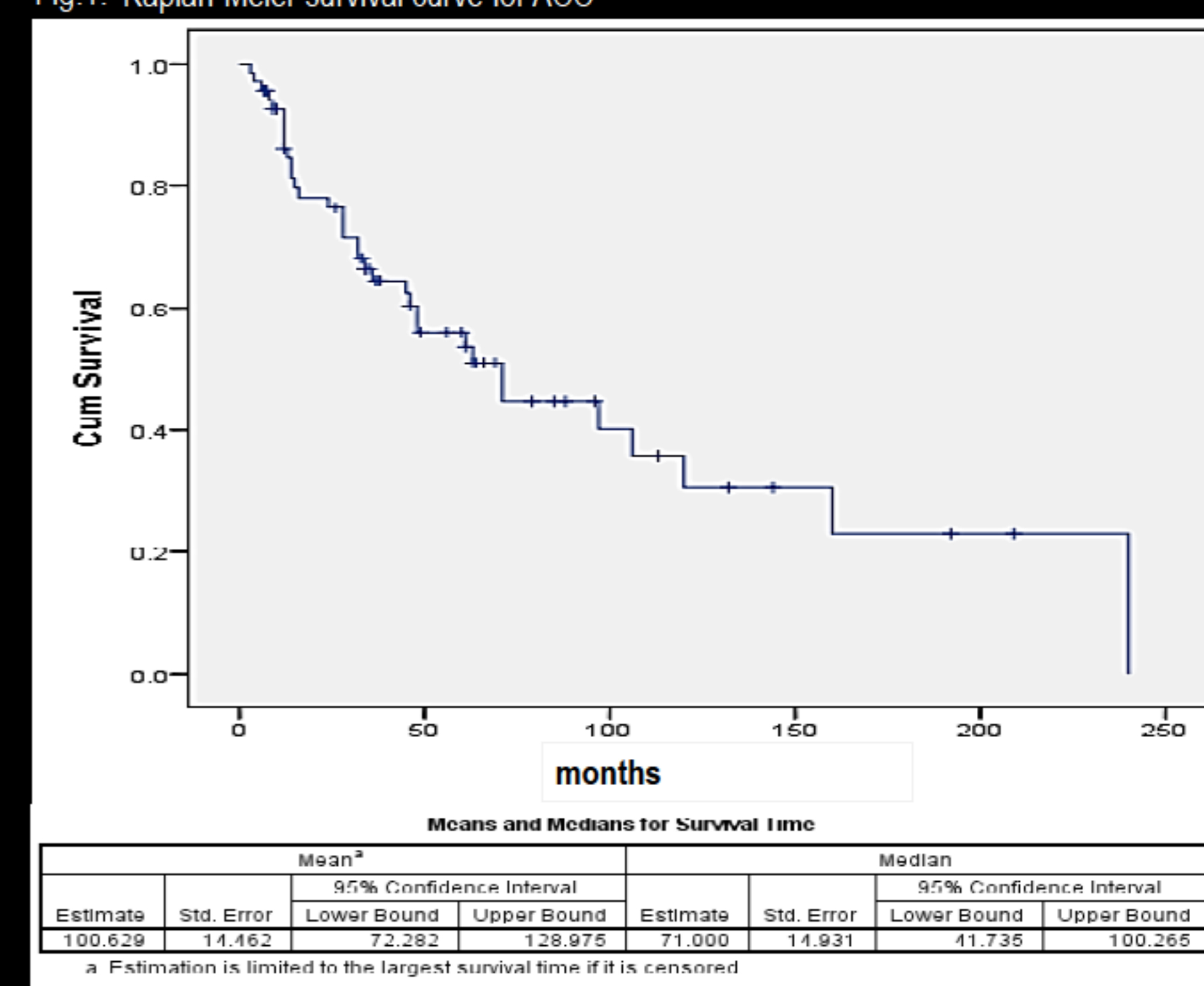
Fig.2. Kaplan-Meier survival curve for secreting vs. nonsecreating ACC
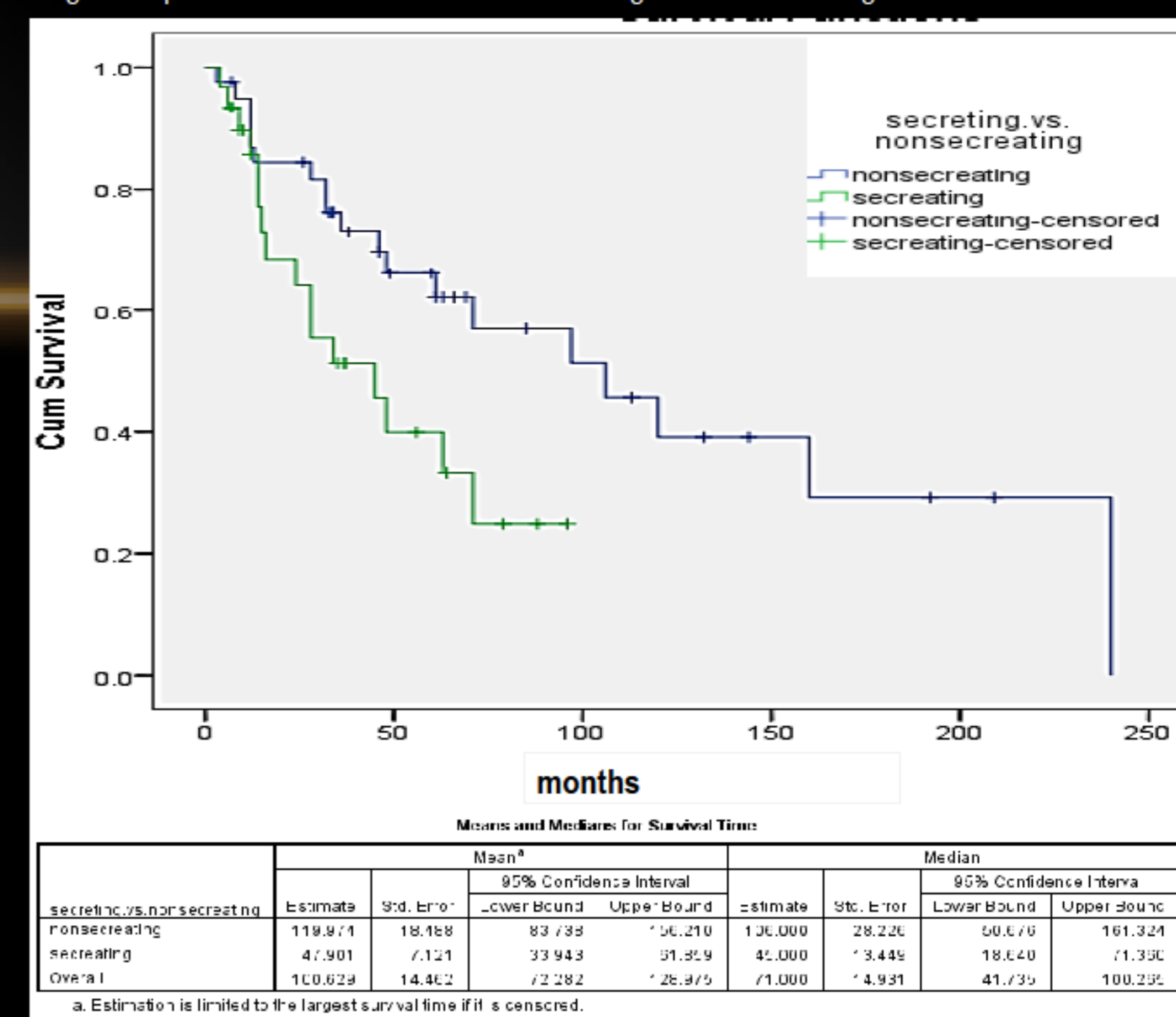
Table 2. Results of univariate Cox regression analyses

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
gender	.716	.356	4.039	1	.044	2.046	1.018	4.112
age (<50 vs >50)	-.803	.357	5.058	1	.025	.448	.223	.902
nonsecreting vs.secreating	-.804	.369	4.754	1	.029	.448	.217	.922
surgery	3.099	.611	25.748	1	.000	22.171	6.698	73.383
lowgrade.vs.high.grade	-1.816	.452	16.122	1	.000	.163	.067	.395
Mitotan	.180	.430	.175	1	.676	1.197	.515	2.783
chemotherapy	-.241	.372	.421	1	.517	.786	.379	1.628
metastasis at diagnosis	-2.168	.384	31.894	1	.000	.114	.054	.243
acquired metastasis	-.535	.351	2.318	1	.128	.586	.294	1.166

Table 3. Results of multivariate Cox regression analyses

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
gender	.815	.435	3.516	1	.061	2.260	.964	5.298
age (<50 vs >50)	-.893	.428	4.353	1	.037	.409	.177	.947
nonsecreting vs.secreating	-.879	.460	3.652	1	.056	.415	.168	1.023
surgery	1.969	.803	6.018	1	.014	7.165	1.486	34.557
lowgrade.vs.high.grade	-1.189	.653	3.314	1	.069	.305	.085	1.095
Mitotan	.451	.639	.498	1	.481	1.570	.449	5.493
chemotherapy	-.623	.556	1.256	1	.262	.536	.180	1.595
metastasis at diagnosis	-1.305	.504	6.695	1	.010	.271	.101	.729
acquired metastasis	.472	.620	.579	1	.447	1.603	.475	5.402

CONCLUSIONS

The presence of metastatic disease at the time of diagnosis is an unfavourable prognostic factor, while surgery and postoperative treatment with mitotane is a favorable prognostic factor for survival in patients with ACC.