Estimation of hazard rate of survival and relapse-free survival in a cohort of melanoma patients: a parametric approach

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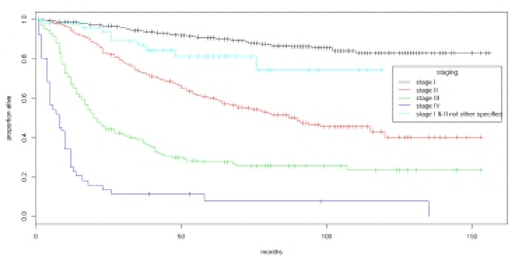
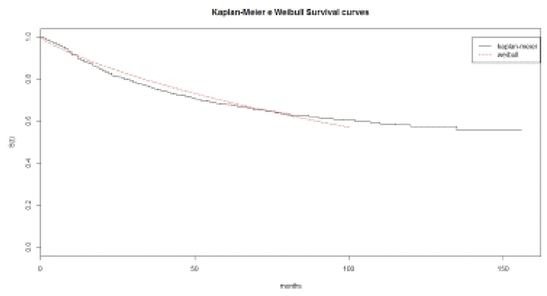
INTRODUCTION

After treatment of malignant diseases, patients are often followed up at regular intervals, however the schedule of visits and exams remains arbitrary with potential over or underuse of health resources.

The objective of this study is to evaluate hazard rates of patients with melanoma according to stage on presentation at pre-specified time-points.





MATERIALS AND METHODS

Cases of cutaneous melanoma treated at a single institution in the period between 1997 and 2006 were reviewed and socio-demographic, clinical and therapeutic features were abstracted.

Non-parametric survival curves (Kaplan Meier) and semi-parametric proportional hazards model (Cox) stratified by stage were constructed, parametric survival evaluation using time-accelerated Weibull distribution and predicted survival plots were performed. The hazard rate of the Weibull distribution model for each stage was estimated for months 6, 12, 24 and 60, as well as for years 1, 2 and 5.

Table 1: descriptive characteristics

Variable		Survival analysis (1414 individuals)
Sex (M:F)		675:739
Age (median)		57.1
Skin color	White	1243 (88%)
	Non-white	171 (12%)
School attendance	Illiterate	125 (8.8%)
	Fundamental	677 (47.9%)
	High-school	338 (23.9%)
	College	255 (18%)
Marital status	Married	874 (61.8%)
	Non-married	530 (37.5%)
Place of diagnosis	Cancer hospital	721 (51%)
	Public hospital	162 (11.5%)
	Private facility	295 (20.9%)
Topography	Head & neck	159 (11.2%)
	Trunk	491 (34.7%)
	Upper limbs	194 (13.7%)
	Lower limbs	276 (19.5%)
	Nails	58 (4.1%)
	Palms and soles	236 (16.7%)
Type	Superficial spreading	763 (53.9)
	Nodular	276 (19.5%)
	Lentigo maligna	32 (2.3%)
	Acrolentiginous	296 (20.9%)
Thickness (Breslow) (mean) (mm)*		2.00 (4.40)
Presence of ulceration **		509
TNM staging	I	632 (44.7%)
	II	475 (33.6%)
	III	205 (14.5%)
	IV	51 (3.6%)
	I & II NS***	51 (3.6%)
Sentinel lymph node biopsy		413
Palliative systemic therapy		167
Number of patients	1997	95 (6.7%)
	1998	111 (7.8%)
	1999	117 (8.3%)
	2000	145 (10.3%)
	2001	132 (9.3%)
	2002	140 (9.9%)
	2003	157 (11.1%)
	2004	195 (13.8%)
	2005	160 (11.3%)
	2006	162 (11.4%)

*information available from 1278 individuals

**information available from 961 individuals

***no information if stage I or II

RESULTS

There were 1414 cases with data available for overall survival and 1404 cases for relapse-free survival (table 1). Overall survival by stage was equivalent to those data presented in the literature. The parametric model estimates were similar to those generated by Cox model (table 2). Hazard rates for survival and relapse-free survival on months 6, 12, 24 and 60, and during the 1st, 2nd and 5th year of follow up were estimated for each stage (tables 3 and 4). The risk of death was stable for stage I, had a statistically significant increase for stage II and a decrease for stages III and IV, however with a higher magnitude. The risk of relapse decreased for stages I, II and III and was stable for stage IV. When overall survival analysis was restricted to patients with stage IV on presentation or to those who presented withmetastatic disease during the course of the treatment, the results remained similar.

Weibull

$$f(t) = \gamma\alpha^{\gamma}t^{\gamma-1}\exp(-(\alpha t)^{\gamma})$$

$$S(t) = \exp(-(\alpha t)^{\gamma})$$

$$\lambda(t) = \gamma\alpha^{\gamma}t^{\gamma-1}$$

Table2: coefficients of stratified models of overall survival (1414 individuals, 434 events)

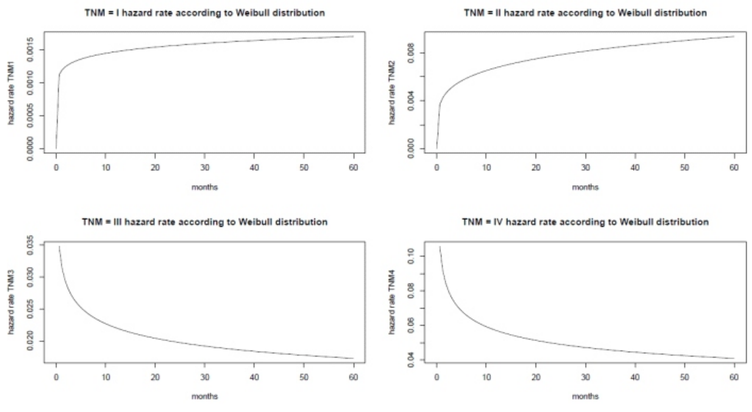
	Lognormal		Weibull		Cox	
Variable	coefficient	p-value	coefficient	p-value	coefficient	p-value
Educational level						
Fundamental	Ref.		Ref.		Ref.	
High school	0.3447	0.00744	0.2719	0.0189	-0.27764	0.038994
College	0.3896	0.00864	0.3989	0.00454	-0.291949	0.077696
Illiterate	-0.2491	0.169	-0.2681	0.0734	0.121255	0.440023
Type						
SSM	Ref.		Ref.		Ref.	
NM	-0.5560	0.0000157	-0.4093	0.000514	0.075640	0.570014
LMM	0.1217	0.707	0.0236	0.908	0.128797	0.727066
ALM	-0.4950	0.000264	-0.4629	0.0000785	0.089826	0.497146
Sex						
Woman	Ref.		Ref.		Ref.	
Male	-0.5687	<0.000001	-0.4809	<0.000001	0.440656	0.0000262
Age	-0.0110	0.00131	-0.0104	0.00146	0.009829	0.004363
Place of diagnosis						
Cancer Hospital	Ref.		Ref.		Ref.	
Public hospital	0.1087	0.504	0.0251	0.864	-0.022517	0.893073
Private facility	0.3574	0.0123	0.2573	0.0594	-0.223042	0.153442
Log(scale)						
TNM=1	0.1369	0.0218	-0.4973	<0.000001		
TNM=2	0.3066	<0.000001	-0.0851	0.151		
TNM=3	0.7175	<0.000001	0.4222	<0.000001		
TNM=4	1.0270	<0.000001	0.7635	<0.000001		

Table 3: Theoretical risk of death during months 6, 12, 24 and 60, and during years 1, 2 and 5 after diagnosis of melanoma, according to stage, parametric estimation - Weibull distribution

Risk of death	Stage I	Stage II	Stage III	Stage IV
6th month	0.00080	0.00273	0.02789	0.06125
12th month	0.00085	0.00313	0.02509	0.05198
24th month	0.00091	0.00359	0.02257	0.04412
60th month	0.00098	0.00431	0.01963	0.03551
1st year	0.0157	0.0877	0.2316	0.6093
2nd year	0.0166	0.1007	0.2084	0.5171
5th year	0.0180	0.1209	0.1812	0.4163
Trend (p-value)	0.452	0.0036	0.0141	0.0123

Table 4: Theoretical risk of relapse during months 6, 12, 24 and 60, and during years 1, 2 and 5 after diagnosis of melanoma, according to stage, parametric estimation - Weibull distribution

Risk of death	Stage I	Stage II	Stage III	Stage IV
6th month	0.00623	0.02124	0.03915	0.07442
12th month	0.00555	0.01892	0.03189	0.06662
24th month	0.00495	0.01686	0.02598	0.05964
60th month	0.00425	0.01447	0.01981	0.05152
1st year	0.0415	0.1630	0.2815	0.7979
2nd year	0.0369	0.1452	0.2293	0.7143
5th year	0.0317	0.1247	0.1749	0.6171
Trend (p-value)	0.0387	0.00062	<0.000001	0.123



CONCLUSION

Patients with stage I melanoma had low death and relapse hazard rates; patients with stage II had intermediate hazard rates that increased with time, reaching 0.121 in the 5th year of follow up; patients with stages III and IV disease had higher hazard rates that despite the decrease over time, remained high even during the 5th year. The hazard rates for relapse followed different trends, decreasing over time for stages I to III, and with higher magnitudes for stages I and II. These data may help in the definition of a policy of follow up, patients with stage should be followed in a more relaxed schedule with no complimentary exams but for a long period extending over 5 years, patients with advanced lesions should be followed in a more strict schedule, even after 2 years of diagnosis.

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