MACHINE LEARNING-BASED EVALUATION OF THE COMPLEX LINKS EXISTING BETWEEN COSTS AND THE CLINICAL AND SOCIO-DEMOGRAPHIC CHARACTERISTICS IN A LARGE ITALIAN COHORT OF MELANOMA PATIENTS

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Objective

We aimed to characterize the influence on costs exerted by the main clinical, sociodemographic and laboratory variables in cutaneous melanoma patients (CMM).

Materials & Methods

This study evaluated a collaborative registry of 556 patients (Veneto Tumor Registry & Veneto Oncology Network), who were diagnosed with CMM in 2015 in 4 of the 7 provinces of the Veneto Region (Belluno, Padova, Rovigo and Verona) in Northern Italy (1). For each patient, the CMM registry includes a set of clinical, therapeutic, socio-demograhic characteristics and CMM-specific mortality. Costs were assessed from the perspective of the Italian National Health System (Italian NHS), taking only direct costs into account.

Patients were linked via unique anonymous identification codes to all administrative data regarding their hospital admissions, day hospital service use, drug usage, visits to emergency services, medical devices used at home, and hospice admissions. These data were used to compute the direct costs for each patient in the 5 years after diagnoses of their CMM.

Descriptive analyses were performed using absolute and relative frequencies for categorical variables.

Machine Learning Evaluation

A semantic connectivity map was constructed using Auto Contractive Map (AutoCM, Semeion©, Rome, Italy) to elucidate variable links (2). The system highlights the natural links on a graph based and distances between variables reflect the weights of the ANN (Appendix S12). AutoCM has many relevant features: (i) non-linear associations among variables are preserved; (ii) patterns of connections between clusters of variables are captured; and (iii) complex similarities among variables emerge.

Variables	Characteristics	%	(n)
Sex	male	47.66%	265
	female	52.34%	291
Age (years)	under 30	3.78%	21
	30-40	9.53%	53
	40-50	24.64%	137
	50-60	20.68%	115
	60-70	17.99%	100
	over 70	23.38%	130
Married status	single	7.37%	41
	married	30.22%	168
	separated	2.16%	12
	widowed	1.98%	11
	undefined	58.27%	324
Education	uneducated	7.91%	44
	primary school	16.01%	89
	secondary school	24.46%	136
	high school	41.91%	238
	university degree	8.81%	49
T stage	IA	58.63%	326
	IB	24.10%	134
	IIA	5.22%	29
	IIB	3.96%	22
	III	6.83%	38
	IV	1.26%	7

Table I. Characteristics of the included cohort

Figure 1. Semantic map clustering CMM patients in 4 main endotypes predictive of costs.
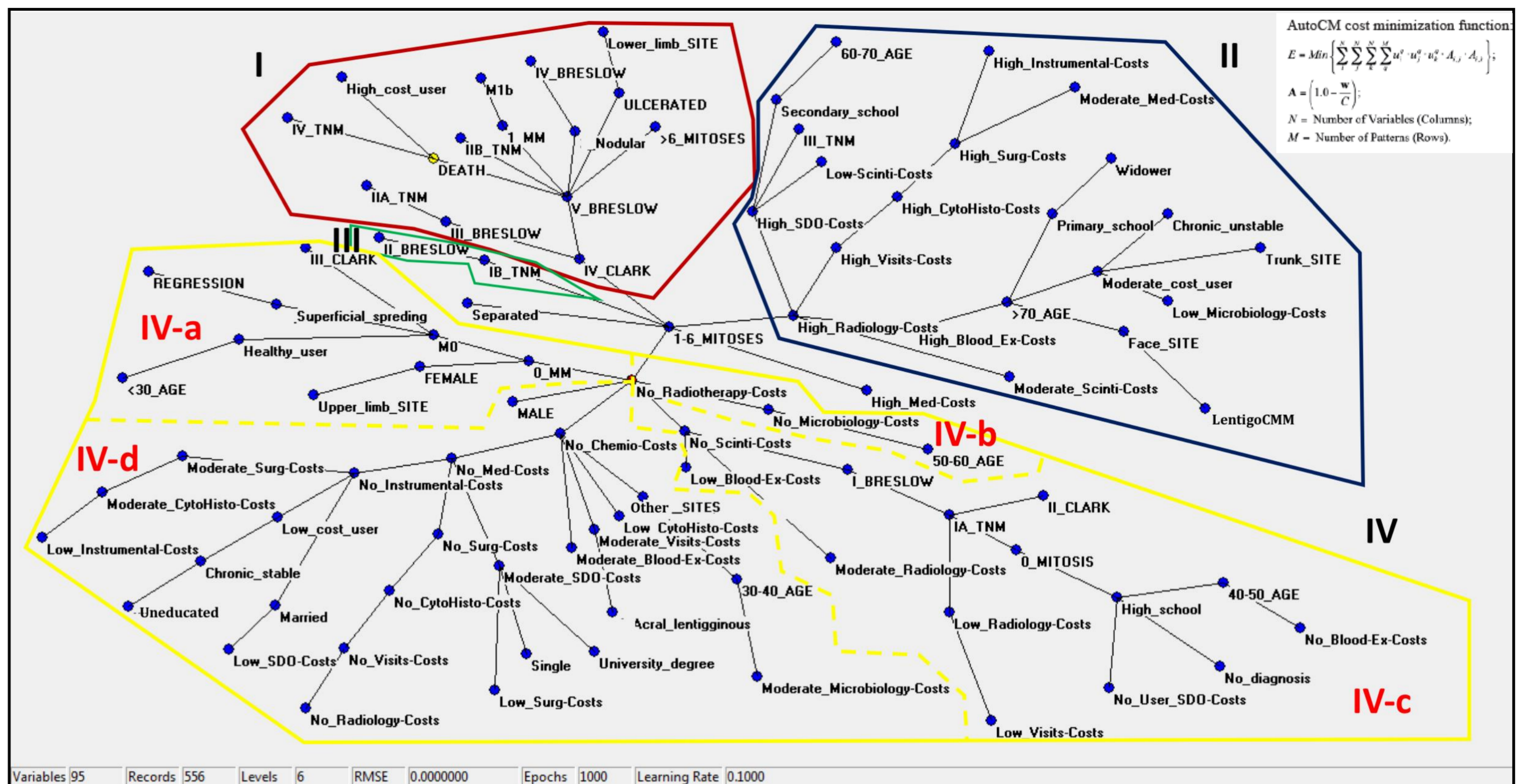
Results

Demographics and clinical characteristics are summarized in **Table I**. In the semantic map, we opted to exclude branches radiating from "1–6 mitoses" (which has a bond strength <0.60) as endotypes, so the branches "separated" and "high costs of medical therapies" were excluded (**Figure 1**). Four main endotypes were identified (I, II, III, IV). The endotypes are as follows: (I) advanced-stage patients: with nodular and ulcerated CMM on lower limbs (Clark IV, Breslow III–IV, TNM IV or II with metastases and >6 mitoses), high risk of death, and heavy economic burden; (II) patients >60 years, widowed, with primary school diploma, with unstable chronic disease, non-nodular CMM on the trunk, or lentigo maligna on the face,

with 1–6 mitoses, associated with high costs of SDO (Hospital Discharge Form), diagnostic procedures (visits, cytohistology, radiological and instrumental investigations), and therapies (medical, surgical); (III) patients with stage Ib disease: patients with TNM Ib, and Breslow II with 1–6 mitoses; (IV) a cluster around the absence of costs for radiotherapy.

It includes 4 main subsets, each with their own biological and socioeconomic items: (IV-a) female under 30 years old with non-metastatic, regressive and superficial spreading CMM of the upper limb, with 1–6 mitoses; (IV-b) male aged 50–60 years with CMM with 1–6 mitoses, and without microbiological costs; (IV-c) male aged 40–50 years with a high-school diploma, with TNM Ia, Clark II, Breslow I CMM, with no mitosis, associated with moderate radiology costs; (IV-d) a miscellany of CMM patients with 1–6 mitoses.

Conclusion

The socioeconomic impact of education level and/or income is likely to be mitigated in a universalistic health system like the Italian NHS. In conclusion, in CMM, clinical variables together with costs were indispensable to cluster patients in endotypes by ANN. Endotypes-guided management is affirming as new promising strategy to guide medical and surgical therapies.

References

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