

The increment in prognostic discrimination and calibration of the TNM 8th edition on prediction 5-year overall survival in head and neck cancer

Leonardo F Rios, PhD¹; Pamela O Soares, MSc¹; Keila T Macedo²; Fabio D Nunes³, PhD; Raquel A Moyses, PhD¹

1. Head and Neck Surgery Department - LIM28 – Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil;
2. Hospital Heliópolis, São Paulo, SP, Brazil
3. School of Dentistry, Universidade de São Paulo, SP, Brazil



Objective

The aim of this study is to compare the prognostic value of the new (8th) edition of TNM classification for squamous cell carcinoma (SCC) in head and neck with the previous one, in terms of discrimination ability and calibration to predict 5-year overall survival.

Methods

We performed a retrospective review of demographic and clinical data from 1811 patients with SCC prospectively enrolled in GENCAPO, a consortium of five hospitals in São Paulo, Brazil. All the patients were categorized according the 7th and 8th TNM Staging Classification. 119 patients from a total of 398 with oropharynx cancer had HPV status, and the remained were classified as unknown according to the TNM 8th edition. Prognostic models were created using logistic regression (LR), classification and regression trees (CART), and neural networks (NN) for each TNM staging edition. The performance of each model was compared.

Results

1789 (98.8%) patients had TNM Staging information. When comparing the two editions, we found that for 1398 (78.14%) there were no changes in the stage classification. Among the 367 (20.5%) patients that were upstaged, 245 were dead and 122 were alive, while among the 24 (1.3%) who were downstaged, 13 were dead and 11 were alive in five years. When comparing the 7th and 8th edition models we found no significant difference in discrimination ability by LR (AUC 7th=0.65 and AUC 8th=0.66 p=0.069) or CART (AUC 7th=0.65 and AUC 8th=0.66 p=0.0586). However, we could observe a greater discrimination by NN for the 8th edition (AUC 8th=0.66 and AUC 7th=0.64; p=0.0101). We averaged the death probability predicted for each patient using LR, CART and NN for the 7th and 8th editions to analyze the increment in calibration of the new edition. Due to limitations in the assumptions required, no statistical tests were performed to address the differences in calibration. However, we found that the prognostic ability of the recent TNM is better in patients with more advanced tumors while for early tumors, the seventh edition seemed to better predict the risk of death.

Discussion

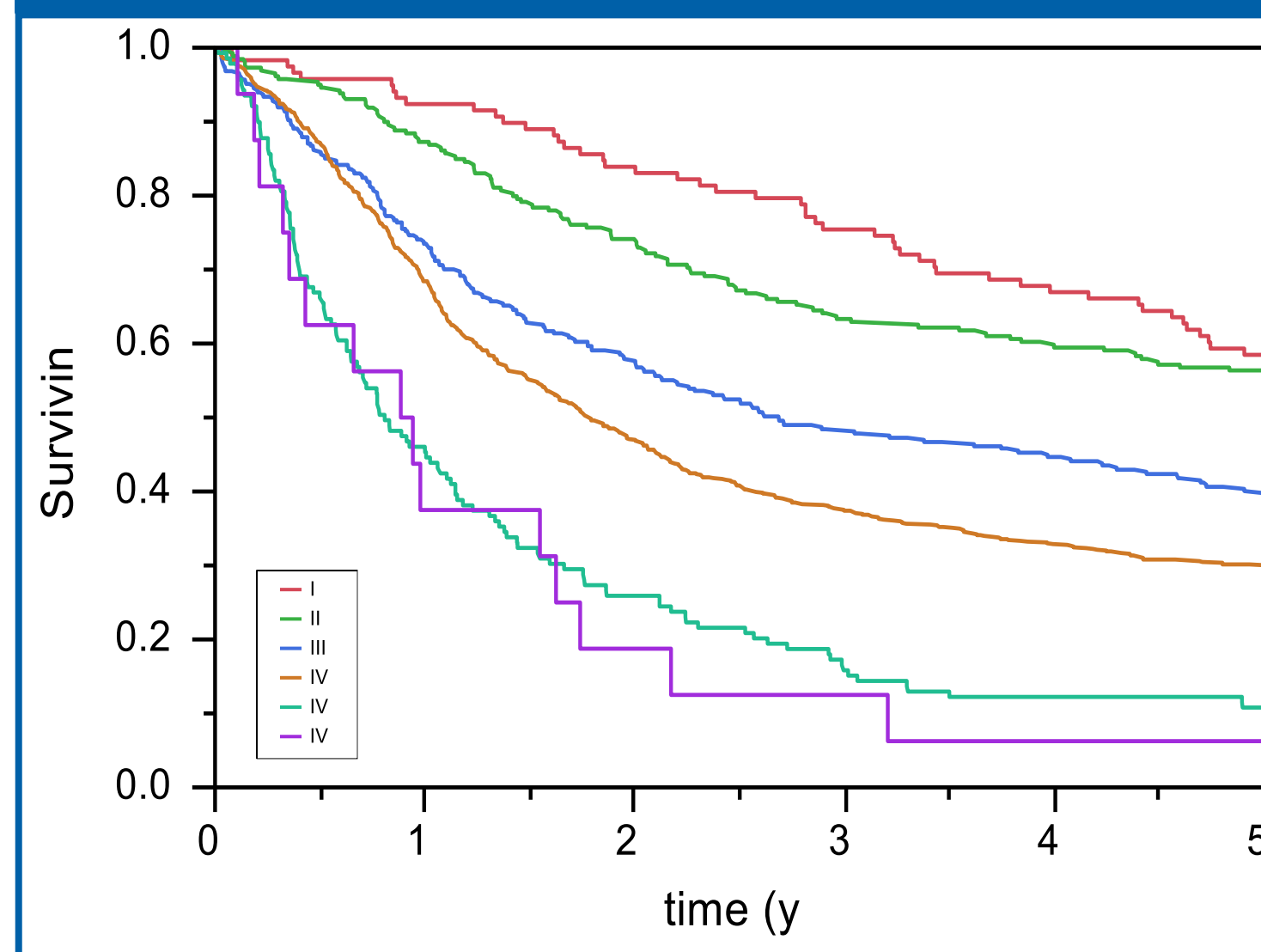
Analyzing the modifications adopted by TNM 8th edition, we observed a change in the stage of about one fifth of the patients, especially those with oral cavity cancer. Oropharyngeal and hypopharyngeal tumors also changed, mainly due to HPV status for the former and to a higher prevalence of extracapsular extension for the latter. Laryngeal tumors were less frequently changed by the TNM 8th edition. Analysis stratified by sites might give more insights in terms of limitations of both editions.

Conclusion

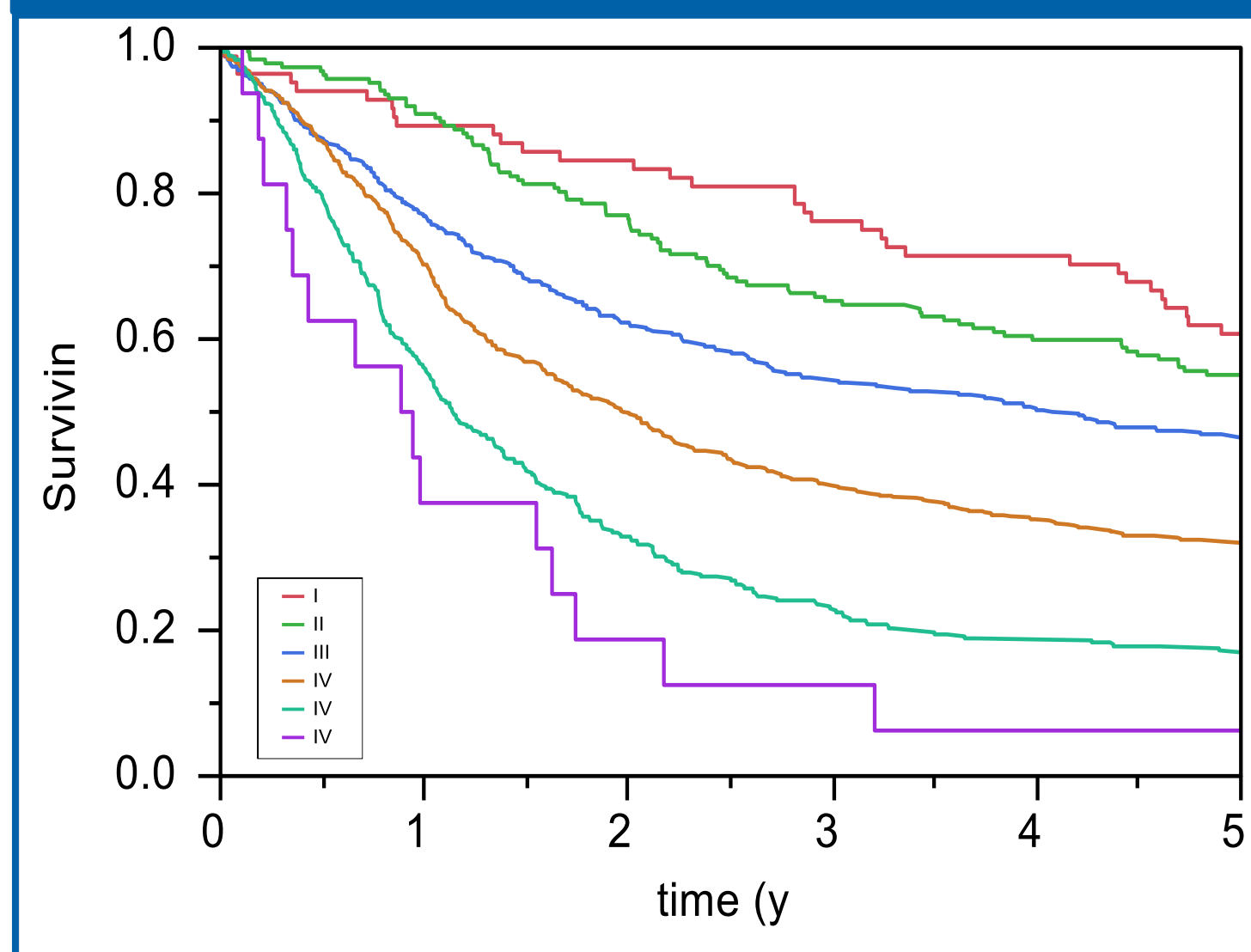
Compared with the seventh edition, the eighth edition of the AJCC cancer staging system represented an increase in discrimination of the 5-year overall survival of patients with diagnosis of head and neck cancer. When analyzing risk classification by each stage group, we observed that the 8th edition may have lost in calibration for early tumors. These findings illustrate the complexity of prediction models and the need for continuing research on the field.

Stage	n	
	TNM 7 th edition	TNM 8 th edition
I	118 (6.6%)	84 (4.7%)
II	259(14.5%)	187 (10.5%)
III	347 (19.4%)	424(23.7%)
IVa	909 (50.8%)	712(39.8%)
IVb	140 (7.8%)	366(20.5%)
IVc	16 (0.01%)	16 (0.01%)
Total	1789(100%)	1789 (100%)

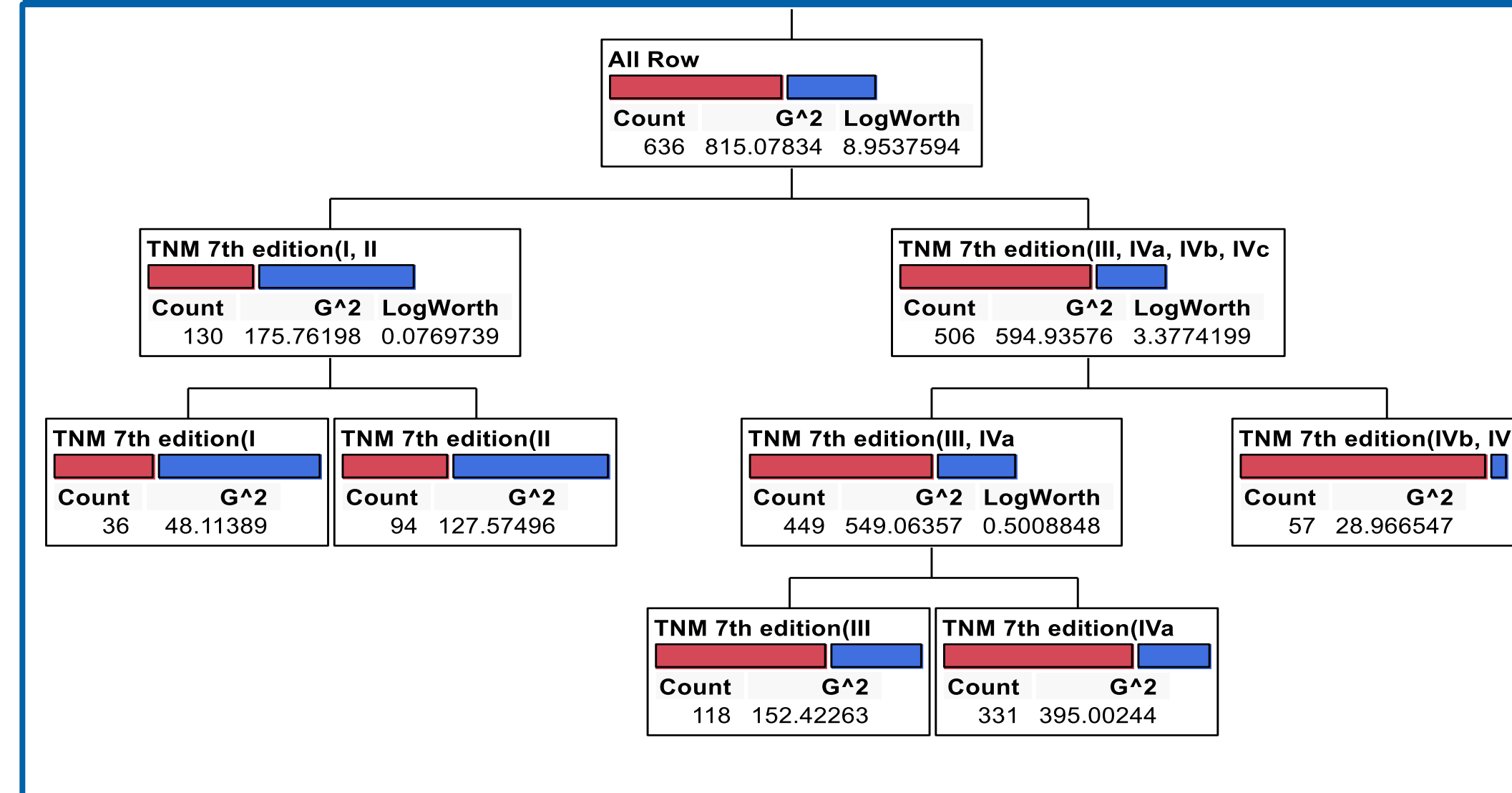
Survival plot – TNM 7th edition



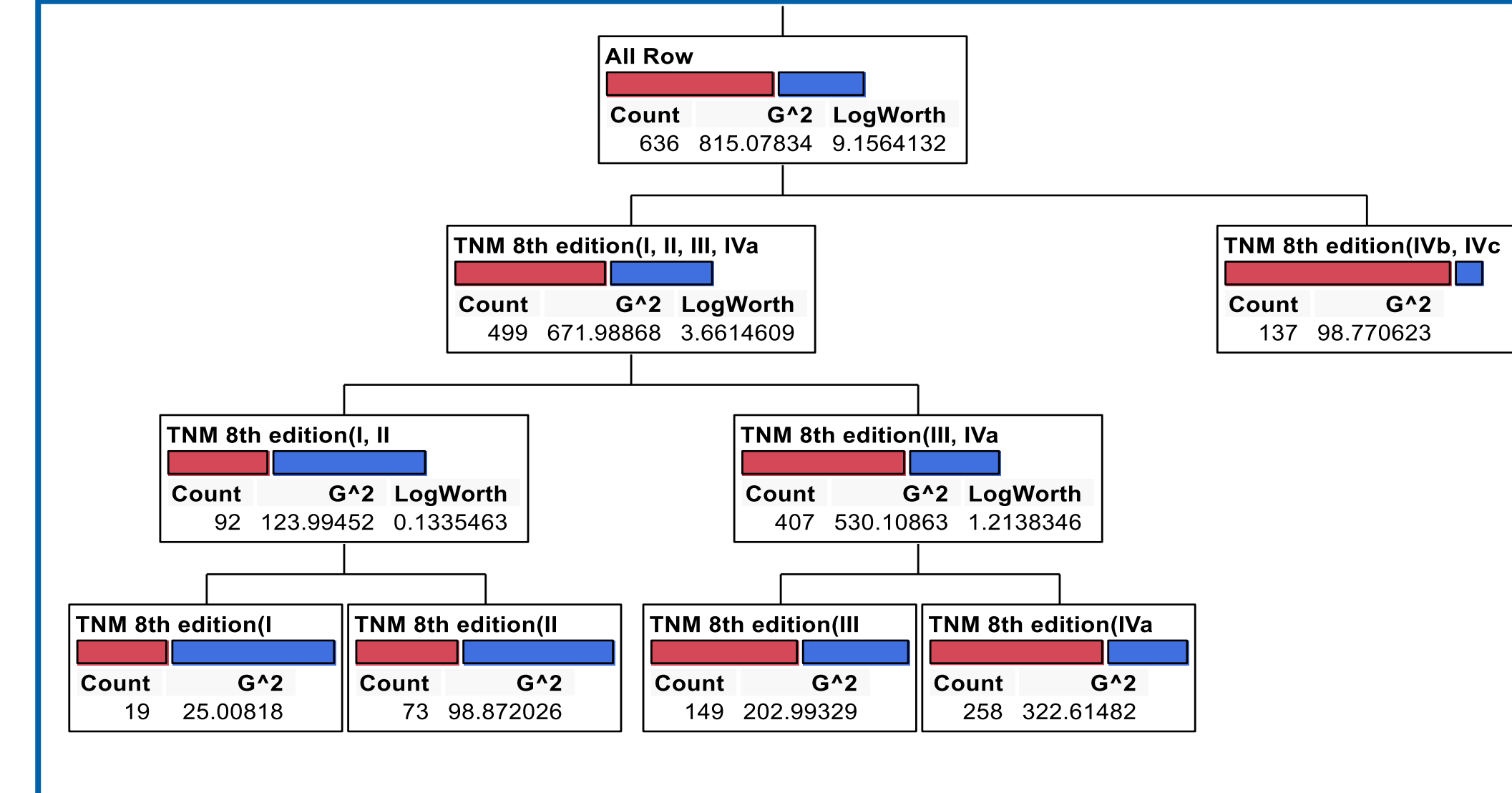
Survival plot – TNM 8th edition



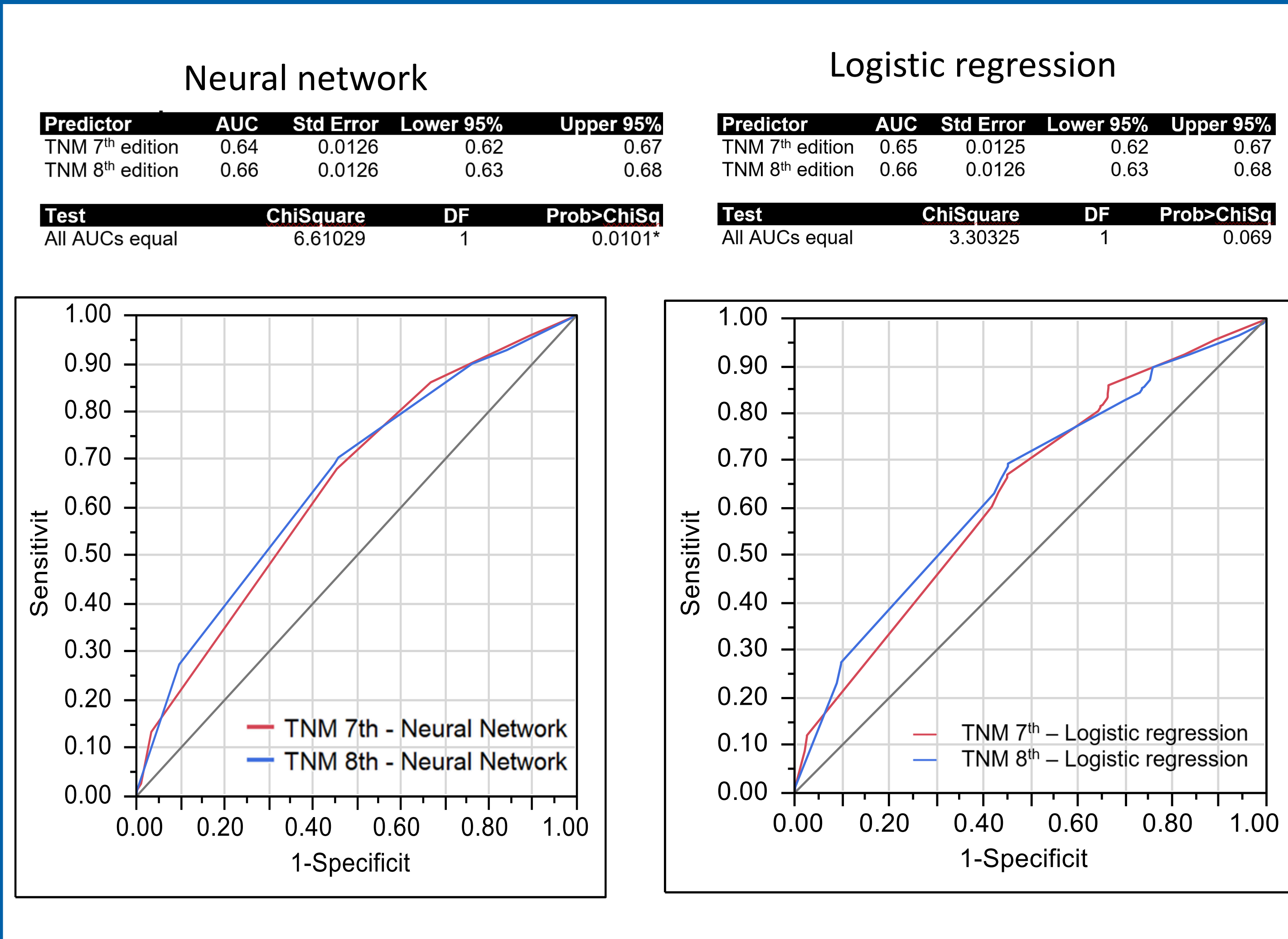
CART model plot – TNM 7th edition



CART model plot – TNM 8th edition



Models comparison



Risk reclassification

		TNM 8th edition						
TNM 7th edition			I	II	III	IVa	IVb	IVc
	I	Odeaths	37.7	54.5	42.1			
		P7th	43.6	43.6	43.6			
		P8th	46.4	43.4	50.2			
	II	Odeaths	50	42.3	45.4			
		P7th	40	40	40			
		P8th	46.4	43.4	50.2			
	III	Odeaths	100	83.3	57.3		77.5	
		P7th	59.7	59.7	59.7		59.7	
		P8th	46.4	43.4	50.2		78.3	
	IVa	Odeaths		33.3	20	68	79.4	
		P7th		70.2	70.2	70.2	70.2	
		P8th		43.4	50.2	69.5	78.3	
	IVb	Odeaths			66.7		89.8	
		P7th			84.4		84.4	
		P8th			50.2		78.3	
	IVc	Odeaths						93.8
		P7th						78.2
		P8th						81.6
Comparison: observed death (red) vs. the predicted risk by TNM 7 th edition (green) vs. the predicted risk by 8 th edition (blue). Grey background cell informs which probability calculated was closer to the outcome observed								

Comparison: observed death (red) vs. the predicted risk by TNM 7th edition (green) vs. the predicted risk by 8th edition (blue). Grey background cell informs which probability calculated was closer to the outcome observed

Key findings

- Visually analyzing the survival curves, we observed a better separation of the curves using TNM 8 edition
- None of the three models created (CART, neural networks and logistic regression) showed a statistically significant difference when using TNM 7th and 8th edition, although in all TNM 8th models they are slightly better at discrimination
- Analyzing the calibration of the logistic regression models, we observed that the TNM 7th model is more calibrated in stage 1, whereas the TNM 8th model is more calibrated in more advanced tumors.

Contact:

Leonardo Rios, MD, PhD
Universidade de São Paulo
Departamento de Cirurgia de Cabeça e Pescoço
Av. Dr. Enéas Carvalho de Aguiar, 255
São Paulo - SP, 05403-000
lfbrios@gmail.com