TREE BASED MODELS FOR THE PREDICTION OF IGAN PROGRESSION IN YOUNG PATIENTS

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INTRODUCTION and OBJECTIVES

The multifactorial nature of making a clinical prediction makes it difficult for doctors to simultaneously evaluate multiple risk factors to produce an accurate estimate of patients' risk. To overcome this problem, during the past two decades, many multivariable risk prediction models have been developed over a wide range of conditions and populations. Usually, these models are mathematical equations relating multiple predictors to the individual risk.

Tree Based Models (TBMs) are exploratory techniques for uncovering interactions among predictors, defining patient subgroups with a simple and intuitive method for model representation.

THE AIM OF THIS STUDY WAS TO TEST THE APPLICATION OF DIFFERENT TBMs ON A COHORT OF CHILDREN AND YOUNG ADULTS AFFECTED BY IgAN.

METHODS

The cohort included 261 children and young adults aged < 23 years (median 15.6, IQR 11.7 - 19.1) enrolled in the **VALIGA study**.

Variables included in the analysis were both demographic (age, gender), clinical (baseline eGFR, MAP, Proteinuria) and pathological (MEST score).

We used 3 different TBMs to identify risk model for: i) 15 years survival to combined endpoint (50% reduction in eGFR or ESRD), ii) time-average (TA) proteinuria during follow-up and iii) proteinuria remission.

The differences among defined subgroups were evaluated respectively with Cox, linear or logistic regression and performances were internally validated by bootstrap procedures.

RESULTS

Survival tree model identified subjects at higher risk of combined event those with mesangial hypercellularity (High-Risk Group; survival = 46.8%, p <0.001 vs. Low-Risk Group)), followed by cases with no mesangial lesions, proteinuria ≥ 0.4 g/die and eGFR <90 ml /min (Medium-Risk, survival=56.5%, p=0.009 vs Low-Risk) and patients with proteinuria <0.4 g/day or eGFR >90 ml/min (Low-Risk, survival = 90.3%). The c-statistics revealed a good discrimination of the tree model (c-index 0.81, 95%CI 0.71 - 0.92) higher, even if not statistically different, than a Cox regression model built with the same covariates (0.76, 0.63 - 0.88).

The regression tree to identify subgroups with higher TA-Proteinuria (multivariate R-squared = 0.2) showed that subjects whit persistent high proteinuria at follow-up were positive for mesangial hypercellularity at renal biopsy (p <0.0001) or had eGFR <90 ml/min (p = 0.0007).

The classification tree analysis to identify patients with different probabilities of remission to a TA-Proteinuria <0.5, identified a specific group with higher chance of remission composed by no mesangial hypercellularity patients younger than 16.4 with a baseline eGFR over 90.4 ml/min not treated with immunosuppressant (remission rate: 10/16). Also in this case the c-statistics revealed a good discrimination of the classification tree model (AUC 0.8, 95%CI 0.69 - 0.9) comparable to a Logistic regression model built with the same covariates (AUC 0.77, 0.7 - 0.87).

CONCLUSIONS

IN CONCLUSION, TREE BASED ANALYSIS IS SUITABLE FOR THE IDENTIFICATION OF PROGNOSTIC MODELS DEFINED BY COMBINATION OF DIFFERENT PATIENTS' DATA, SHOWING PREDICTIVE PERFORMANCE COMPARABLE TO STANDARD STATISTIC TECHNIQUES AND PRESENTING INTUITIVE MODEL TO BE USED IN CLINICAL PRACTICE.

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