



## Research Article

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# Prealbumin as Tumor Marker in Head and Neck Cancer in Adults

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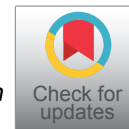
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## Abstract

**Introduction:** Nowadays clinicians don't have a useful tumoral marker to perform the follow up of patients affected of head and neck cancers (H&NC).

**Objectives:** To analyse the operative characteristics of prealbumin (PRB) as a tumoral activity marker in those affected of head and neck cancer compared with albumin, total proteins, carcinoembryonic antigen, and alfa fetoprotein.

**Methods:** It was performed an observational prospective study with patients visited in Hospital Universitari Arnau de Vilanova de Lleida (Spain) with the main diagnosis of H&NC. During study time main epidemiological, clinical, and analytical (including PRB) characteristics were collected in 3 times: at diagnosis, after finishing the treatment and 12 months later.

**Results:** Blood samples were obtained from 138 patients from the 1<sup>st</sup> January 2007 till the 1<sup>st</sup> February 2010. Median age was 62.5 (29-89) years and 121 (88%) were males. Most frequent histological diagnosis was squamous carcinoma 87 cases (63%). 19 patients (14.5) died during that time. Sensitivity, specificity, positive and negative predictive values of PRB were 63%, 100%, 100%, 87% respectively. The area under receiver operating characteristic curve was 0.87 (CI 0.76-0.98), that was better than other parameters studied.

**Conclusions:** Prealbumin is a useful tumoral activity marker in those affected of head and neck cancer and it could be a useful tool in these patients follow up.

## Keywords

Head and neck cancers, Tumor marker, Prealbumin

## Abbreviations

H&NC: Head and Neck Cancers; CR: Complete Remission at 12 months; NCR: Non Complete Remission at 12 months; PRB: Prealbumin; PPV: Positive Predictive Value; NPV: Negative Predictive Value; AUROC: Area under Receiver Operating Characteristic Curve; CI: Confidence Interval; AJCC: American Joint Committee on Cancer; NCCN: National Comprehensive Cancer Network; CEA: Carcinoembryonic Antigen; AFP: Alfa Fetoprotein

## Introduction

Head and neck tumors (H&NC) require a great effort for their diagnosis, treatment, and follow-up. Previous studies found a prevalence between 5 and 15 % of all neoplasms [1].

In a H&NC mortality study, done by cancer research foundation, H&NC was the sixth among men and the fourteen in woman [2]. The most common risk factors for developing H&NC are tobacco and alcohol use [3].

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Nowadays clinicians don't have a useful tumor marker to perform the follow up of patients affected of H&NC.

The nutritional assessment of H&NC patients can help in the prognosis and follow-up of these patients. Prealbumin levels (PRB), better than albumin, have been used for nutritional evaluation [4-6].

The purpose of this study is to analyse the operative characteristics of PRB as a tumor activity marker in adults affected of H&NC compared to other tumor markers with common use in clinical practice.

## Methods

It was performed an observational prospective study with patients visited in Hospital Universitari Arnau de Vilanova de Lleida with the main diagnosis of H&NC.

Inclusion criteria were age older than 18 years, histology of H&NC and to get informed consent. Lack of follow-up or consent were used as exclusion criteria.

Before starting oncological treatment (surgery, chemotherapy, radiological oncology, or a combination of them, following NCCN guidelines), it was performed a nutritional assessment a nutritional support and a follow up [7].

During study time main epidemiological, clinical, and analytical (including PRB) characteristics were collected in 3 times: at diagnosis, after finishing the treatment and 12 months later. The data that were analysed correspond to the second visit carried out a month after the initial treatment ended. In this visit, it was done a blood sample, determining level of total proteins, albumin, and prealbumin. We also checked tumoral markers such as carcinoembryonic antigen (CEA) and alfa fetoprotein (AFP) [8,9].

The CEA and FPA variables were categorical (positive or negative value). The cut-off points of positivity for CEA and AFP according to our laboratory were 5 and 10 ng/ml respectively.

**Table 1:** Patient characteristics, extent and location of the neoplasm, and treatment received according to evolution.

Variables	Study group n = 138	CR n = 77	NCR n = 61	p-value
Age, median (range)	62 (54-71)	61 (54-70)	65 (54-72)	0.565
Sex (% male)	121 (87.7)	68 (88.3)	53 (86.9)	0.800
<b>Neoplasm location</b>				0.469
Oral cavity	26 (18.8)	16 (20.8)	10 (16.4)	
Pharynx	29 (21.0)	14 (18.2)	15 (24.6)	
Larynx	50 (36.2)	28 (36.4)	22 (36.1)	
Cavum	8 (5.8)	5 (6.5)	4 (6.6)	
Paranasal sinuses	10 (7.2)	5 (6.5)	5 (8.2)	
Thyroid	2 (1.4)	1 (1.3)	1 (1.6)	
Multiple	1 (0.7)	1 (1.3)	0 (0.0)	
Primary unknown	12 (8.7)	7 (9.1)	5 (8.2)	
<b>Histology</b>				< 0.001
Squamous cell carcinoma	87 (63.0)	57 (74.0)	30 (49.2)	
Small cell carcinoma	4 (2.9)	3 (3.9)	1 (1.6)	
Epidermoid	29 (21.0)	5 (6.5)	24 (39.3)	
In situ	9 (6.5)	9 (11.7)	0 (0.0)	
Undifferentiated	7 (5.1)	1 (1.3)	6 (9.8)	
Adenoid cystic carcinoma	2 (1.4)	2 (2.6)	0 (0.0)	
<b>AJCC stage 6<sup>th</sup> edition</b>				< 0.001
I	10 (7.2)	10 (13.0)	0 (0.0)	
II	10 (7.2)	10 (13.0)	0 (0.0)	
III	38 (27.5)	33 (42.9)	5 (8.2)	
IV	80 (58.0)	24 (31.2)	56 (91.8)	
<b>Surgery</b>	65 (47.1)	35 (45.5)	30 (50.0)	0.597
<b>Chemotherapy</b>	110 (79.7)	68 (88.3)	42 (68.9)	0.005
<b>Radiotherapy</b>	91 (65.9)	59 (76.6)	32 (54.2)	0.006

Values as median (interquartile range) or n (percentage); CR: Complete Remission; NCR: Non Complete Remission; AJCC: American Joint Committee on Cancer. p-value: Calculated with the chi-square test or Mann-Whitney test.

The patients were classified according to whether they reached the state of complete remission (CR) or not (NCR) at the end of the treatment (at 12 months).

## Statistical Analyses

With an estimated NCR percentage, according to a previous study, of 40-45% and for a precision of 95% (alpha error of 0.05) and a power of 90% (beta error of 0.1) a size between 135 and 225 patients was calculated. Results are shown as median (interquartile range), or percentage. Comparisons among groups were done by chi-square test, and by non-parametric test of Mann-Whitney for quantitative variables. All statistical analysis got a significance level lower than 0.05. Calculations of Sensitivity, specificity, positive and negative predictive values, and calculation of the area under receiver operating characteristic curve (AUROC) for comparing analysed tests by the statistical package R (version 2.9.0).

## Results

Of the 140 patients chosen, 2 were excluded: one due to lack of follow-up and the other decided not to follow the treatment. Therefore, blood samples were obtained from 138 patients from January 1, 2007, to February 1, 2010. Median age was 62.5 (29-89) years and 121 (88%) were males. Table 1 shows the results of the study group and divided according to whether they achieve CR (55.8%) or do not achieve it (44.2%).

Most frequent histological diagnosis was squamous carcinoma 87 cases (63%), and the most frequent location was larynx. More than half of the patients were diagnosed in stage IV. Mortality during the follow-up period was 19 patients (14.5%).

Table 2 shows the analytical values studied. Significant differences are observed in albumin and prealbumin values. And Table 3 shows the accuracy values achieved by the different analytical parameters. Figure 1 shows the differences in the AUROC of albumin, prealbumin and total protein values.

## Discussion

There are no previous studies about PRB as a tumoral marker for H&NC in adults. Our sample of patients with HN agrees with others in the values of remission and mortality [9]. We also agree in other studies in the proportion of men and in the age, values found [10]. Regarding the location, we obtain similar results to the series published by the Cancer Research Foundation in Spain with most patients diagnosed at advanced stage (III or IV) [11].

The most common histology in our population was in 63% of cases de scamous carcinoma, followed by epidermoid carcinoma in 21% patients and, less frequent carcinoma "in situ", small cell carcinoma, undifferentiated and adenoid-cystic carcinoma. What is different from previous studies, where the most frequent is epidermoid carcinoma [12,13].

Limitations of our work include the limited sample size and the need to validate our results in an external population.

In summary, we considered PRB as a tumor marker in the follow-up of adult patients with H&NC.

## Conclusions

1. PRB is a useful tumoral marker in adults with H&NC.
2. Albumin and total proteins are not useful tumoral marker in adults with H&NC.

**Table 2:** Analytical parameters according to evolution (n = 138).

Analytical parameters	Study group n = 138	RC n = 77	NRC n = 61	p-value
Prealbumin g/dL	0.22 (0.16-0.28)	0.24 (0.17-0.30)	0.17 (0.14-0.26)	0.002
Total proteins g/dL	7.2 (6.8-7.7)	7.3 (6.9-7.8)	7.2 (6.7-7.6)	0.411
Albumin g/dL	4.2 (3.7-4.4)	4.2 (3.8-4.5)	3.9 (3.4-4.3)	0.009
CEA (≥ 5 ng/ml)	112 (81.2)	61 (79.2)	51 (83.6)	0.671
AFP (≥ 10 ng/ml)	131 (95.0)	74 (96.1)	57 (93.4)	0.779

Values as median (interquartile range) or n (percentage); CR: Complete Remission; NCR: Non Complete Remission; CEA: Carcinoembryonic Antigen; AFP: Alfa Fetoprotein. p-value: Calculated with the Mann-Whitney test.

**Table 3:** Precision of the analytical parameters evaluated (n = 138).

Variable	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	AUROC (CI 95 %)
Prealbumin g/dL	100	87	63	100	0.87 (0.76-0.98)
Total proteins g/dL	52	70	9	90	0.55 (0.41-0.69)
Albumin g/dL	85	98	11	98	0.66 (0.54-0.79)
CEA ng/ml	100	65	31	22	---
AFP ng/ml	77	63	31	91	---

PPV: Positive Predictive Value; NPV: Negative Predictive Value; AUROC: Area Under Receiver Operating Characteristic Curve; CI: Confidence Interval; CEA: Carcinoembryonic Antigen; AFP: Alfa Fetoprotein

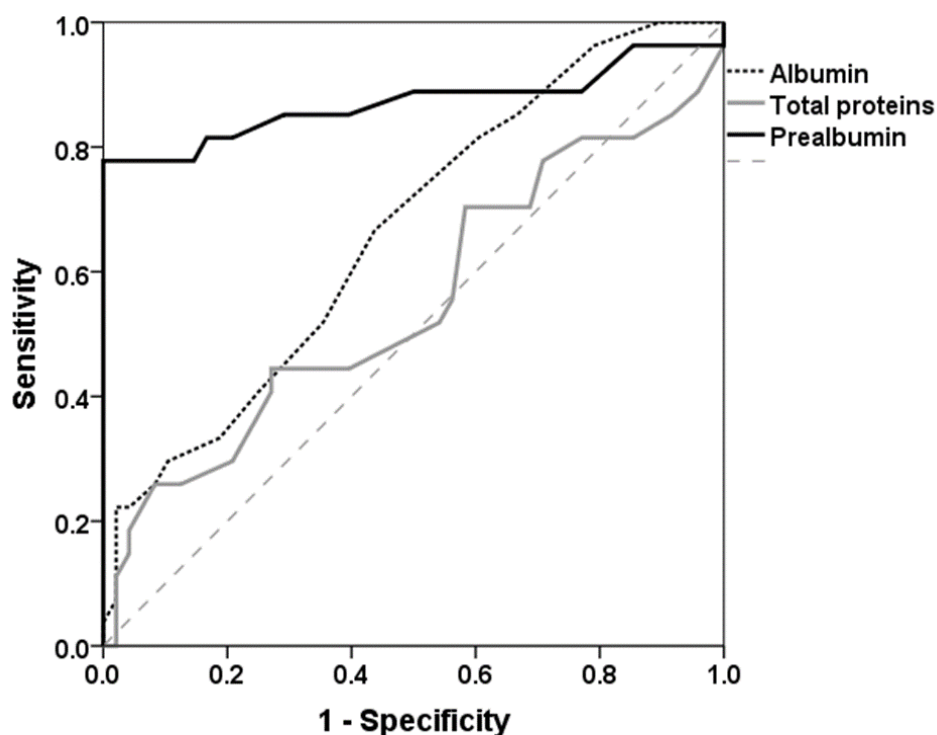


Figure 1: ROC curves of prealbumin, albumin and total proteins.

## Declarations

### Ethics approval and consent to participate

All the procedures used in the present study were in conformity with the current revision of the Helsinki Declaration. All participants were informed of the objectives of the study, and they were enrolled only after providing a signed consent form.

### Consent for publication

All the authors approved the final version of the manuscript and consented for its publication.

### Availability of data and materials

Data will be made available by the corresponding author upon request.

### Competing interests

All the authors declared no competing interest.

### Funding

None.

### Authors' contributions

Study conception: CM, RA, TJ; Data collection: CM, GC, BM, SM, BP, SE. Data analysis and Manuscript drafting: CM, RA, TJ, CM. All authors read and approved the final manuscript.

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