原文題目(出處)：	C-reactive protein levels: a prognostic marker for patients with head and neck cancer ? Head & Neck Oncology 2010;2:21
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內文：

Introduction

- C-reactive protein (CRP)
  - Acute-phase protein
  - Marker for inflammation
  - Synthesis in the hepatocytes
  - May be regulated by pro-inflammatory cytokines which are also influencing factors in various types of tumors
    - Interleukin-1
    - Interleukin-6
    - Tumor-necrosis factor
- Disease progression depends on
  - Tumor stage
  - Host's inflammatory response

- In 1863, Rudolf Virchow postulated the induction hypothesis
  - Cancer originated at site of chronic inflammation
    - Human immunodeficiency virus
    - Viral hepatitis B
    - Human papilloma virus
    - Long-term use of aspirin and other nonsteroidal anti-inflammatory drugs reduced risk for colorectal cancer
  - Chronic inflammation is associated with the increased risk of cancer

- Increased CRP levels associated with cancer

- Two hypotheses:
  - Induction hypothesis: chronic inflammation results in excessive cell proliferation and activation of a cascade of cellular actions, leading to induction of irreversible DNA damage
  - Response hypothesis: the immune response of the host as a consequence of tumor growth itself could be the reason for the elevation in CRP levels

- Findings from the studies have been inconsistent:
  - Elevated serum CRP levels are associated with colorectal and lung cancer
  - Doubt that CRP can be regarded as a prognostic marker
  - In patients with combined esophageal cancer and squamous cell carcinoma
    - Raised CRP concentrations have been regarded as an indicator of a poorer prognosis for squamous cell carcinoma
- However, it is still unclear whether an elevated CRP level is a risk factor for the development of cancer or CRP levels are elevated before the biological onset of cancer
- Only a very few studies have dealt with association between oral SCC and preoperative CRP levels (Table 1).

Table 1 Studies dealing with the association between oral SCC and preoperative CRP levels

Author	Number of patients	Results
Gallo et al. [10]	18	Significance of CRP and IL-6 in regard to tumour stage
Jablonska et al. [11]	42	CRP, IL-1b, IL-6, TNF-a serum levels related to clinical stage of disease
Khandavilli et al. [12]	60	CRP level is associated with worse overall outcome

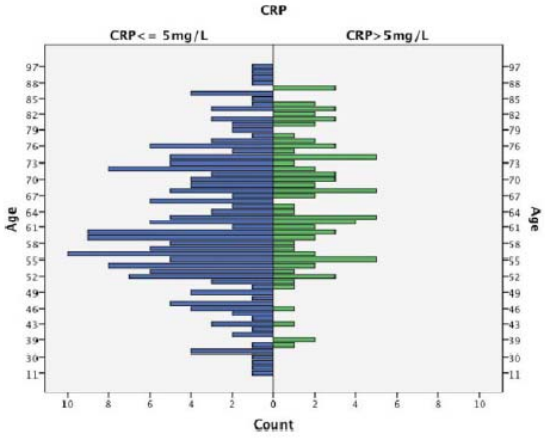
- All of these data are consistent with the hypothesis that CRP levels increase after onset of oral cancer.
- Aim of the current study: investigate the significance of preoperative CRP levels as a parameter for development of lymph node metastases or recurrence.

Materials and methods

- 278 patients with oral SCC (119 female,159 male)
- Treated at a single center (Department of Craniomaxillofacial and Oral Surgery, University Hospital Zurich) between 1999 and 2008.
- Minimum follow-up time:12 months
- Exclusion criteria: inadequate information, less than 12 months of follow-up time

- Serum CRP levels were obtained between 1 and 5 days prior to surgical treatment.
- According to the preoperative measure of CRP concentration, divided into two groups:
  - Normal CRP values: ≦ 5.0 mg/L
  - Elevated CRP levels: > 5.0 mg/L
- $P < 0.05$ was considered to be statistically significant
- Kaplan-Meier analysis with log-rank testing was used for univariate analysis.

Results



- Mean CRP: 7.36 mg/L
- 193 patients (69.4%): CRP level ≦ 5 mg/L
- 85 patients (30.6%): CRP level > 5 mg/L
  - The distribution was independent of age

- Local recurrence
  - 48 patients (17.3%): local recurrence, mean time of 24.31 months (range: 7-84 months)
  - 24 patients (8.6%): 2cd tumors
  - 206 patients (74.1%): no recurrence
- Lymph node metastases
  - 46 patients (16.5%): cervical lymph node metastases, mean time of 18.27 months (range: 4-71 months)
  - 14 patients (5%): distant metastases
  - 218 patients (78.5%): no metastases

- In the elevated CRP group:
  - Recurrence appeared earlier (Fig. 2)
  - No differences in the time of metastases (Fig. 3)

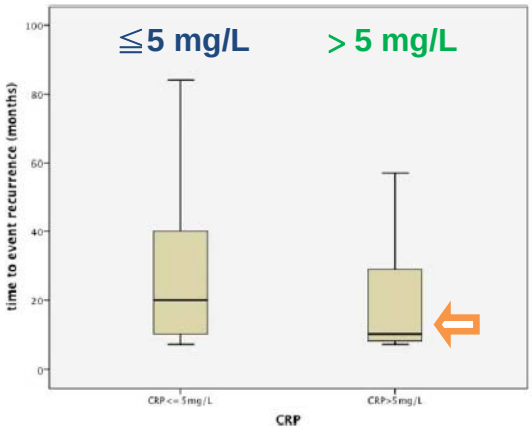


Figure 2 Distribution of time to recurrence dependent on CRP

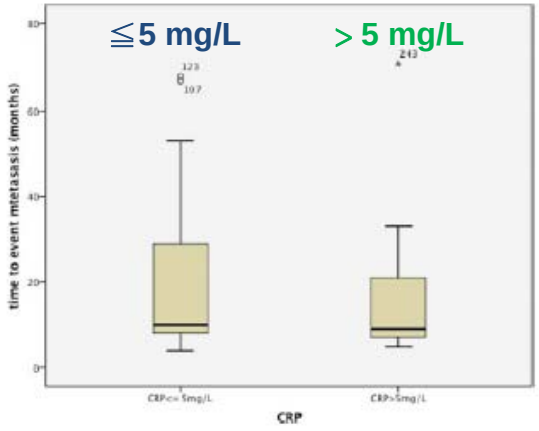


Figure 3 Distribution of time to metastases dependent on CRP level.

- Lymph node metastases:
  - Normal CRP group: 37 patients /193
  - Elevated CRP group: 9 patients /85
  - <u>No significant correlation was found for development of metastasis</u> (p = 0.468)

- Local recurrence:
  - Normal CRP group: 27 patients /193
  - Elevated CRP group: 21 patients /85
  - <u>No significant correlation was found for development of recurrence</u> (p = 0.137)

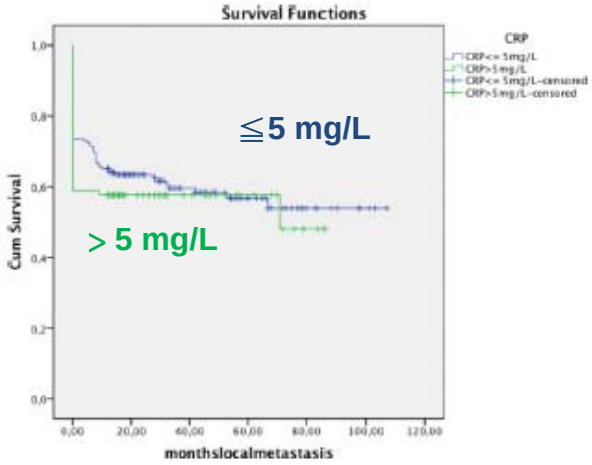


Figure 4 Kaplan-Meier analysis of development of metastasis in regard to CRP level.

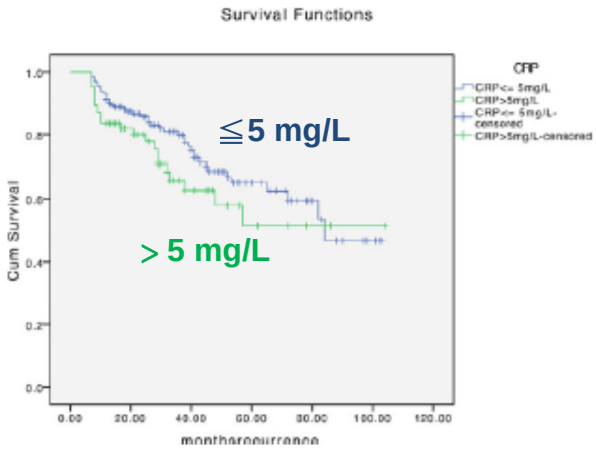


Figure 5 Kaplan-Meier analysis of development of recurrence in regard to CRP level.

Discussion

- The purpose of our study was to find a simple and cost effective indicator for oral SCC.
- Mean follow-up time: 35.97 months (range: 12-107 months)
- Elevated CRP levels:
  - The proportion of lymph node metastasis was smaller
  - No significant association with development of recurrence or metastases
- This study does not confirm the results from other studies (Table 1) and disagree with Zingg U et al.
  - In patients who have undergone neoadjuvant treatment for esophageal cancer
  - Suggested CRP-measurements in the re-staging process before surgery
  - Select patients who are likely to benefit from surgery
- There seems to be inconsistency concerning the CRP levels:
  - Khandavilli et al., Komai et al. : > 5 mg/L (raised CRP levels)
  - Other authors : < 1.0 mg/L (low), 1.0 - 3.0 mg/L (average), > 3.0 mg/L (high)
  - In our study : > 5 mg/L (raised CRP levels)

    (> 50 mg/L seen in infectious disease in 6 patients)

- CRP levels can be reduced with weight loss and smoking cessation
  - For esophageal cancer, a correlation has been shown between
    - Malnutrition with impaired immunity
    - Elevated serum CRP concentration
  - Smoking and alcohol abuse can lead to chronic inflammation in the oral mucosa
    - Investigate CRP levels in precancerous lesions (ex: erosive lichen)
    - Ki et al.
      - 40 patients with primary laryngo-pharyngeal cancer
      - During radiotherapy
      - Significant correlation between the presence of radiation-induced mucositis and CRP level

In our study

- Advantages: high number of patients
- Limitations:
  - CRP was measured at one point in time, therefore intra-individual variations were not considered
  - General diseases associated with possible higher inflammation markers like diabetes mellitus or Morbus Crohn were not taken into consideration

Conclusion

- Our findings do not appear to support a positive association between preoperative CRP levels and oral SCC.
- Further studies should examine CRP levels in precancerous lesions and in HPV positive patients with oral SCC.
- CRP is a nonspecific marker of inflammation, and additional studies of specific cytokines that regulate acute-phase response are necessary to elucidate the mechanisms by which inflammation influences the risk of cancer.

題號	**題目**
1	下列何者關於erosive lichen planus的敘述錯誤? (A) Confined to the gingival mucosa, producing the desquamative gingivitis (B) Periphery of the atrophic region is usually bordered by white radiating striae (C) Usually symptomatic (D) More common than the reticular type
答案(D)	出處：Oral and Maxillofacial PATHOLOGY, second edition, P680-681
題號	題目
2	下列何者不是可能引起SCC的因素之一?
	(A) Iron deficiency (B) Syphilis (C) Vitamin B deficiency (D) Phenols
答案(C)	出處：Oral and Maxillofacial PATHOLOGY, second edition, P358