Author's response to reviews

Title: Elevated CRP values predict nodal metastasis in patients with penile cancer

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Author's response to reviews: see over
Dear Hayley Henderson,

On behalf of my colleagues, I would like to re-submit to “BMC Urology” this manuscript of original research entitled:

“Elevated CRP values predict nodal metastasis in patients with penile cancer “.

Squamous cell carcinoma (SCC) of the penis, which accounts for >95% of penile cancer cases, is relatively uncommon in the Western world, but its incidence has increased slightly and varies markedly in some parts of Europe with an annual rate of 0.5 to 1.6 per 100,000 men. Its incidence in the United States is affected by race and ethnicity, being low for Asian-Pacific Islanders and American Indians and highest for Hispanics and Southern Blacks.

Classical molecular markers are of no clinical value in SCC of the penis, therefore identifying preoperative prognostic factors, including a serum biomarker, would allow a better therapeutic approach. Particularly biomarkers in body fluids could offer the opportunity for more objective and reproducible measurement and risk stratification prior to surgery. Therefore, the area of defining new prognostic markers is of active interest, especially biomarkers in body fluids offer the opportunity for more objective and reproducible measurement prior to surgery.

C-reactive Protein (CRP) is an acute phase protein produced almost exclusively by the liver. Elevated CRP levels can be a result of an underlying cancer and a premalignant state, respectively, as well as due to tumour growth associated tissue inflammation. A study published in 2009 by Allin et al. involving 10,408 individuals showed that elevated CRP is associated with increased risk of cancer, e.g. lung or colorectal malignancies. Furthermore, an elevated CRP level was associated with an early death, even in patients without metastases.

Our article describes the results of a retrospective trial that includes 94 patients with penile cancer from two German high volume centers. This study demonstrates for the first time in SCC of the penis that elevated CRP levels are associated with higher tumor stages and nodal disease, the most important prognostic factor in penile carcinoma. In fact, multivariate analysis even showed that a high CRP value was the only independent predictor of lymph node metastasis which could have direct clinical relevance (e.g. for the prognosis, indication for lymph node dissection, potentially neoadjuvant systemic therapy).

We have received your comments and revised the manuscript accordingly.

We appreciate your time and interest, and are looking forward to your answer.

Sincerely yours

Sandra Steffens