Author's response to reviews

Title: Association of nutritional status and serum albumin levels with development of toxicity in patients with advanced non-small cell lung cancer treated with paclitaxel-cisplatin chemotherapy: A prospective study

Authors:

Oscar Arrieta (ogar@servidor.unam.mx)
Rosa Mayela Michel Ortega (mayela_michael@yahoo.com.mx)
Geraldine Villanueva-Rodríguez (geral_vr2@yahoo.com)
Maria Guadalupe Serna-Thomé (gpeserna@hotmail.com)
Diana Flores (dfg15@yahoo.com.mx)
Susana Torres (susana.araiza@hotmail.com)
Cindy M. Rodríguez (nut_cindy@hotmail.com)
Karla Sánchez-Lara (kpao82@hotmail.com)
Luis Martínez (luismartinbarr@yahoo.com.mx)
Norma Ortiz-Arellanes (normaortizarellanes@gmail.com)

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Author's response to reviews:

Professor
Melissa Norton, MD
Editor-in-Chief
BMC Cancer

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Title: Association of nutritional status and serum albumin levels with development of toxicity in patients with advanced non-small cell lung cancer treated with paclitaxel-cisplatin chemotherapy: A prospective study#

Dear Dr. Norton:

We appreciate the comments made to our manuscript; undoubtedly they have increased the quality of our paper. Enclosed please find the revised manuscript and a detailed description point by point addressing the reviewers' comments.

All authors have read and approved the final version of this manuscript, and concur with the submission.

Waiting your reply, I remain.

Yours sincerely,

Oscar Arrieta M.D.
Referee 2. Donald C McMillan (Comments to author):

With the inclusion of a measure of the systemic inflammatory response the authors have confirmed the hypothesis of my previous review that "It has long been recognised that hypoalbuminaemia is associated with nutritional decline and poor survival in patients with cancer. However recent evidence points to such relationships being secondary to the presence of a systemic inflammatory response (McMillan, 2008, 2009). Indeed, this has been shown clearly in patients with advanced NSCLC (Forrest et al., 2003; 2004; 2005)

We have included and extended the cited articles and consider the information described in them quite important for the development and enrichment of our study, however, our objective since the enrollment of patients started, was to describe the relationship between hypoalbuminemia and the development of chemotherapy-related toxicity in NSCLC patients treated with paclitaxel and cisplatin. We deem significant the contribution that our research can make in the field of NSCLC as it objectively describes a cohort of patients with NSCLC, all treated with paclitaxel and cisplatin, in whom albumin was measured as were also NLR and PLR, and toxicity was evaluated. Information that has not been previously been documented and which in turn is helpful for the initial evaluation and support considerations in this type of patients.

However, they do not comment on the importance of their observation that hypoalbuminaemia was associated with both the NLR and PLR. That is "is the relationship between hypoalbuminaemia and toxicity merely a reflection on an ongoing systemic inflammatory response rather than a reflection nutritional status?"

The authors should comment on the importance of their observation that hypoalbuminaemia was associated with both the NLR and PLR and that these, in addition to hypoalbuminemia, were also associated with toxicity. Also, they should address whether the relationship between hypoalbuminaemia and toxicity merely a reflection on an ongoing systemic inflammatory response rather than a reflection nutritional status

This relationship is mentioned in the discussion of our study: “Besides, albumin synthesis may diminish with SIR found in patients with advanced NSCLC [18]. We found a relationship between #5 NLR and baseline hypoalbuminemia and also of PLR #150 with baseline hypoalbuminemia and low BMI.” (page 9, paragraph 3, line 1)

We have also added: “Clinical evidence has shown that the activation of the SIR
is one of the earliest and most important contributory factors of cachexia, moreover these findings help explain the failure of simple nutritional programs to reverse weight loss adequately in patients with cancer [34].

The SIR can be measured with albumin levels, PLR and NLR, the albumin levels are also useful as indicators of nutritional status. Still, as the SIR and malnutrition are processes that can be present simultaneously we did not dare to make a causal inference as hypoalbuminemia is associated with both. We did add the following: “Albumin levels, PLR and NLR were all related to the development of chemotherapy-induced toxicity. We therefore consider that the SIR, hypoalbuminemia and malnutrition in unison contribute to further toxicity development.”

We also included in the conclusions: “Therefore, early nutritional assessment and detection of SIR markers might allow identification of patients at higher risk of developing chemotherapy toxicity”