Author's response to reviews

**Title:** Clinical and prognostic significance of preoperative plasma hyperfibrinogenemia in gallbladder cancer following surgical resection

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**Version:** 2  
**Date:** 13 May 2014

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Dear Editors:

We would like to submit the enclosed manuscript entitled “Clinical and prognostic significance of preoperative plasma hyperfibrinogenemia in gallbladder cancer following surgical resection”, which we wish to be considered for publication in “BMC Cancer”. The aims of this study were to elucidate the prognostic significance of blood coagulation tests and various clinicopathological characteristics in patients with gallbladder cancer (GBC) after surgery with curative intent. Our results indicate that plasma levels for all coagulation tests, with the exception of INR, revealed a significant difference between patients with malignancies and those with controls (p<0.001). Hyperfibrinogenemia (>402 mg/dL) was associated with poorly differentiated tumors, advanced tumor invasion, lymphatic metastasis, and advanced tumor stage (p<0.001) and had a statistically significant adverse effect on survival (p=0.001). In the multivariate analysis, hyperfibrinogenemia (p=0.031) was independently associated with poorer OS. Moreover, cell migration and invasion in vitro were significantly enhanced by fibrinogen. Taken together, the results indicate that preoperative plasma fibrinogen levels was associated with tumor progression and may represent an independent marker of poor prognosis in patients with GBC. Furthermore, fibrinogen may contribute to cell migration by inducing the epithelial-mesenchymal transitions (EMT).

To the best of our knowledge, a long term study on the association between preoperative plasma fibrinogen levels and GBC patient survival has not been reported. Neither the entire paper nor any part of its content has been published or has been accepted elsewhere. It is also not being submitted to any other journal. We shall greatly appreciate hearing from you as soon as possible.

Thank you very much for your attention and consideration!

Sincerely yours,

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