Whole exome sequencing of circulating tumor dna to determine treatment response and detect recurrence in gastroesophageal cancer

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Abstract

Background

The gastroesophageal cancers (GEC) have some of the worst cancer-related mortality rates. This is partly due to the lack of efficient biomarkers for monitoring treatment response and minimal residual disease (MRD) in GEC patients. Here, circulating tumor DNA (ctDNA) has emerged as a potential clinical tool for monitoring MRD during the disease course of GEC patients. However, ctDNA detection methods, such as whole exome sequencing (WES), still require extensive research and development for clinical implementation.

Objective

The aim of this study is to investigate WES-based ctDNA analysis as a potential tool for determining treatment response after neoadjuvant chemotherapy and detecting MRD at the time of recurrence.

Methods

Five patients with locally advanced GEC treated for curative intent were included in this study. Blood samples were collected at baseline, after neoadjuvant chemotherapy before surgery, and at the time of recurrence. Tumor tissue was collected at baseline or at the time of surgery. Whole exome sequencing was performed on extracted DNA from plasma, buffy coat, and tumor tissue, where copy number analysis was performed using Sequenza. Variant calling was performed on tumor tissue using the SomaticSeq ensemble pipeline consisting of eight variant callers, namely LoFreq, Scalpel, MuTect2, VarScan, SomaticSniper, MuSE, Strelka, and VarDict. Tumor-guided ctDNA analysis will be performed to detect tumor-specific alterations in ctDNA.

Results

CtDNA copy number analysis lacked copy number alterations before and after neoadjuvant chemotherapy, whereas copy number alterations were discovered in tumor tissue. This suggests that ctDNA was not detected before and after neoadjuvant chemotherapy.

Four of the five included patients experienced post-surgery recurrence. Copy number analysis on ctDNA obtained at the time of recurrence had clear indications of copy number alterations in one patient and slight indications in another patient, suggesting that ctDNA was able to detect MRD in these two patients.

Tumor-guided ctDNA variant analysis remains to be performed.

Conclusion

This study shows the potential of WES-based ctDNA analysis in detecting MRD at the time of recurrence, which could provide clinicians with an additional tool to monitor MRD in GEC patients. However, ctDNA analysis was not able to capture treatment response after neoadjuvant chemotherapy.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.