Circulating Tumor DNA as Assessed by Next-Generation Sequencing is a Prognostic Biomarker in Patients with Localized Pancreatic Cancer

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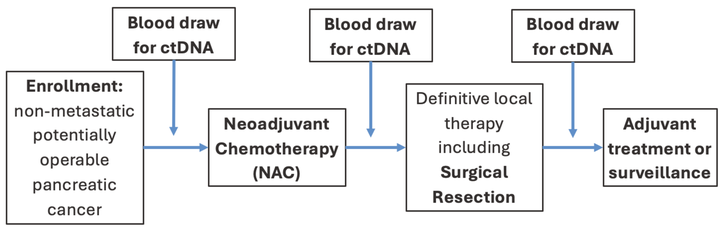
Background

- Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related death in the United States.[1]
- Circulating tumor DNA (ctDNA) is a promising blood-based biomarker with prognostic relevance in various cancers, but its clinical utility in localized PDAC remains unclear.[2]

Research Objectives

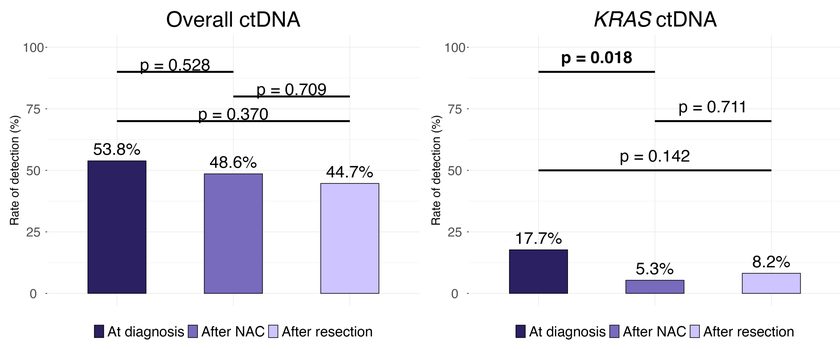
The primary objective was to evaluate the prognostic significance of circulating tumor DNA (ctDNA) detected by next-generation sequencing (NGS) in localized PDAC.

Methods



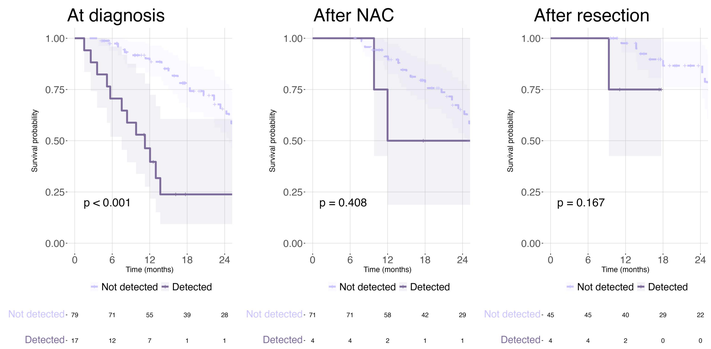
- Patients with localized PDAC were enrolled in a prospective study at Northwestern Medicine between October 2020 and November 2024.
- Samples underwent commercial, tumor-agnostic NGS.
- Analyses were conducted using RStudio (Version 2024.04.2+764) .

Figure 1: Overall and *KRAS*-specific ctDNA detection rates



- Overall ctDNA detection rates demonstrated no significant differences, while *KRAS*-specific detection rates declined after NAC

Figure 2: Overall survival stratified by *KRAS*-specific ctDNA detection



- *KRAS* detection at diagnosis was associated with shorter overall survival (OS) (median 11.2 vs 27.2 months; p<0.001).

Table 1: Multivariable Cox model with *KRAS* ctDNA detection at diagnosis predicting overall survival

Variable	aHR	95% CI
KRAS Detected	6.12	2.54 – 14.76

Table 2: Multivariable Cox model with overall ctDNA maximum allele frequency (MAF) change from diagnosis to post-NAC predicting overall survival

Variable	aHR	95% CI
Change in MAF	1.19	1.02 – 1.39

For both Cox regressions, age, gender, clinical stage, and pre-therapy serum CA 19-9 were not independently associated with survival.

Limitations

- Modest sample size
- Limited follow-up time
- Lower analytical sensitivity of NGS

Conclusions

- *KRAS*-specific ctDNA declined following NAC, suggesting treatment response.
- Baseline *KRAS* positivity and increases in overall ctDNA MAF predict shorter OS, suggesting utility as a prognostic biomarker.

References

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2. Dang DK, Park BH. Circulating tumor DNA: current challenges for clinical utility. *J Clin Invest*. Jun 15 2022;132(12)doi:10.1172/jci154941