Title: Accuracy of Electronic Health Record Family History in Predicting Genetic Susceptibility to Pancreatic Ductal Adenocarcinoma

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Background: Electronic health records (EHR) are a widely utilized tool for healthcare providers (HCPs) and researchers, allowing for rapid centralized access to patient information, but previous studies have demonstrated decreased accuracy in documentation of a patient's cancer family history (FH) by HCPs when compared to history obtained by trained genetic professionals. Accurate FH information is imperative for genetic risk assessment in individuals with pancreatic adenocarcinoma (PC) since current practice guidelines for genetic testing in individuals with PC primarily focus on cancer FH. We hypothesized that the EHR-documented cancer FH would fail to identify individuals with PC that meet established genetic testing criteria and limit the identification of clinically actionable genetic variants.
Methods: We reviewed the EHR of 186 consecutive, unselected patients with PC who participated in a study that included collection of 3-generation pedigrees by a genetic counselor and testing for 32 cancer susceptibility genes. A cancer FH was ascertained by reviewing the available FH from HCP clinical notes prior to study enrollment. Data was also extracted from the FH tab in the EHR. The FH information from these sources and from the pedigree was used to determine if patients met current criteria for genetic evaluation or testing using the National Comprehensive Cancer Network (NCCN) guidelines for BRCA1 and BRCA2 testing and Lynch syndrome evaluation and the American College of Gastroenterology (ACG) guidelines for familial PC.
Results: As shown in Table 1, a lower percentage of patients met criteria for genetic testing based on data obtained from the FH tab (16%) and clinical notes (24%) compared to the pedigree (41%); the differences were statistically significant ($p = <0.00001$ when comparing the FH tab to the pedigree and $p=0.0006$ when comparing clinical notes to the pedigree). Of the 22 patients who had a clinically actionable variant (pathogenic or likely pathogenic), a lower percentage of patients met criteria for genetic testing based on data obtained from the FH tab (36%) and clinical note (50%), compared to the pedigree (73%); the difference between the FH tab and the pedigree was significant ($p= 0.0154$).
Conclusion: Our findings suggest that providers should take caution when utilizing FH documented in the EHR to guide decisions about genetic testing. Our data demonstrate that using the EHR alone to determine genetic testing eligibility based on current guidelines results in the failure to identify a genetic susceptibility in up to 64% of individuals with PC; whereas, 27% of clinically actionable variants would be missed when using the pedigree. Identifying genetic susceptibility in individuals with PC is increasingly important given its potential implications for PC treatment and in directing testing for at-risk family members.

Table 1. Individuals who meet criteria[1] for genetic evaluation and testing

	Patients	***p*-value[2]**
Total Cohort	n=186	
Family History Tab	30 (16%)	<.00001
Clinical Note	45(24%)	.000602
Genetic Counselor	76 (41%)	
Mutation Carriers[3]	n=22	
Family History Tab	8 (36%)	.01543
Clinical Note	11(50%)	.121606
Genetic Counselor	16(73%)	

[1] NCCN guidelines for BRCA1/2 and Lynch syndrome; ACG guideline for familial pancreatic cancer.

[2] When compared to genetic counselor pedigree using Chi-Square.

[3]Clinically actionable variants were identified in ATM (4), BRCA1 (4), BRCA2 (3), CDKN2A (1), CHEK2 (6), MSH6 (1), PALB2 (1), PMS2(1) and TP53 (1).