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Utilization and Outcomes of Multigene Panel Testing in Patients With Pancreatic Ductal Adenocarcinoma

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ABSTRACT

PURPOSE Guidelines recommend germline genetic testing (GT) for patients with pancreatic ductal adenocarcinoma (PDAC). This study aims to evaluate the utilization and outcomes of multigene panel GT in patients with PDAC.

METHODS This retrospective, multisite study included patients with PDAC diagnosed between May 2018 and August 2020 at Mayo Clinic Arizona, Florida, and Minnesota. Discussion, uptake, and outcomes of GT were compared before (May 1, 2018-May 1, 2019) and after (August 1, 2019-August 1, 2020) the guideline update, accounting for a transition period.

RESULTS The study identified 533 patients with PDAC, with 321 (60.2%) preguideline and 212 (39.8%) postguideline. Patient characteristics did not differ between the preguideline and postguideline periods. GT was discussed in 34.3% (110 of 321) of preguideline and 39.6% (84 of 212) of postguideline patients (odds ratio [OR], 1.26 [95% CI, 0.88 to 1.80]) and subsequently performed in 80.9% (89 of 110) of preguideline and 75.0% (63 of 84) of postguideline patients (OR, 1.10 [95% CI, 0.75 to 1.61]). Of 152 tested patients, 26 (17.1%) had a pathogenic variant (PV), of whom 17 (11.2%; 17 of 152) were PDAC-associated. Over the entire study period, GT was more likely in younger patients (65 *v* 70 years; $P < .001$), those seen by a medical oncologist (82.9% *v* 69.0%; $P < .001$), and those surviving more than 12 months from diagnosis (70.4% *v* 43.4%; $P < .001$). Demographics and personal/family cancer history were comparable between patients with and without a PDAC PV.

CONCLUSION GT remains underutilized despite National Comprehensive Cancer Network guideline recommendations. Given the poor prognosis of PDAC and potential implications of GT, efforts to increase utilization are needed to provide surveillance and support to both patients with PDAC and at-risk family members.

ACCOMPANYING CONTENT

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INTRODUCTION

The incidence of pancreatic ductal adenocarcinoma (PDAC) is increasing at a rate of about 1% per year, with little improvement in survival.[1] Consequently, PDAC is soon expected to become the second-leading cause of cancer-related mortality in the United States.[2,3] Early detection is crucial as surgical resection is presently the only curable treatment available. Unfortunately, most patients present with unresectable or metastasized disease because of the lack of early symptoms.[4]

Population-wide screening for PDAC is not feasible.[5] However, evidence suggests that screening can benefit subpopulations with higher hereditary risk, potentially improving outcomes.[6-9] Main PDAC susceptibility genes are *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, *STK11*, *MLH1/MSH2/MSH6*, *PALB2*, and *TP53*.[10-12] Around 4%-11% of seemingly sporadic PDAC cases harbor a pathogenic variant (PV) in these genes.[13-16] Identifying hereditary cancer syndromes within families is crucial to enrich the high-risk populations for pancreatic cancer surveillance.[17,18] Moreover, identifying specific germline PVs offers opportunities for personalized therapies like poly adenosine diphosphate-ribose polymerase inhibitors and platinum-based chemotherapy, which appear to be effective in treating individuals with germline *BRCA1* and *BRCA2* PVs.[19-21]

Despite the considerable preventive implications for patients and at-risk relatives of patients with PDAC, genetic testing (GT) for hereditary cancer syndromes remains severely underutilized.[22-24] Besides known barriers such as financial

CONTEXT

Key Objective

This study aimed to evaluate the utilization and outcomes of multigene panel genetic testing (GT) for patients with pancreatic cancer in accordance with the National Comprehensive Cancer Network guidelines.

Knowledge Generated

Despite guidelines recommending germline GT for patients with pancreatic cancer, this study reveals a notable underutilization of GT. Only 36% of patients had genetic counseling, of whom 78% subsequently underwent GT. Notably, approximately one in 10 patients who underwent GT were found to have a pathogenic variant associated with pancreatic cancer, highlighting the critical importance of germline GT.

Relevance

Given the poor prognosis associated with pancreatic cancer and the potential benefits of GT for both patients and their at-risk family members, efforts to increase utilization are needed to provide surveillance and support to both patients with pancreatic ductal adenocarcinoma and at-risk family members.

burden, poor provision of information, and lack of referral, a specific obstacle for GT in patients with PDAC is the short time window inherent to the poor prognosis.[25]

Recent guidelines from ASCO published in 2018 recommend offering germline GT to individuals with features suggestive of a genetic cancer susceptibility and that testing has a clinical consequence for the patient or family members at risk of hereditary cancer.[26] Moreover, GT may be discussed in patients with personal diagnosis of pancreatic cancer, even if family history is unremarkable. More recently, the National Comprehensive Cancer Network (NCCN) updated their guidelines in 2019,[27] recommending that all patients with PDAC should be offered genetic counseling and germline GT, irrespective of family cancer history. However, limited data exist on the impact of these updated guidelines on the management of patients with PDAC.

Despite recent guideline updates, we suspect that there is still significant underutilization of GT. Therefore, this study aims to evaluate the uptake and outcomes of multigene GT in patients with PDAC, specifically focusing on adherence to recently updated guidelines. The findings have the potential to raise awareness of the uptake and benefits of germline GT in patients with PDAC, contributing to efforts that may positively affect the future landscape of PDAC management.

METHODS

Study Population and Setting

Patients 18 years and older who presented with a diagnosis of PDAC between May 1, 2018, and August 1, 2020, at one of the three Mayo Clinic sites: Arizona, Florida, and Minnesota, were identified from the Mayo Clinic Cancer Registry and included in this study. Pancreatic malignancies other than adenocarcinoma (eg, neuroendocrine tumors, squamous cell carcinoma, colloid carcinoma, or metastatic disease to the pancreas) were excluded. This study was approved by the Mayo Clinic Institutional Review Board (IRB 21-011326).

Data Collection and Definitions

Data on demographics, diagnosis, and treatment of PDAC were derived from the Mayo Clinic Cancer Registry. Additional characteristics (eg, personal and family cancer histories) were extracted from the electronic medical record (EMR). Next, EMR data were reviewed to determine whether a treating physician had discussed GT with the patient. A systematic search was conducted using both structured data fields (eg, GT orders or referrals) and a natural language processing algorithm to analyze unstructured clinical notes. Multigene panel test results were evaluated for patients who underwent GT. A variety of multigene panels were used, which all (at a minimum) tested *APC*, *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, *MLH1*, *MLH2*, *MSH6*, *PALB2*, *PMS2*, *STK11*, and *TP53*. In addition, we evaluated outcomes of tumor tissue genotyping and liquid biopsy for somatic actionable variants (eg, *BRCA* PVs or mismatch repair–deficient [dMMR] tumors) and/or germline PVs (tissue genotyping only). Finally, a qualified physician researcher (D.C.F.K.) manually reviewed all GT referrals and outcomes.

Guideline Adherence

The NCCN Guideline update recommending GT for all patients with PDAC was published in May 2019.[27] A 3-month transition period was allowed for implementation in clinical practice. We compared two periods: a 12-month period before guideline publication (May 1, 2018-May 1, 2019; preguideline) and a 12-month period after guideline publication and the transition period (August 1, 2019-August 1, 2020; postguideline; Data Supplement, Fig S1, online only). For patients with a confirmed PV, we evaluated their

TABLE 1. Demographic and Clinical Characteristics of Patients With PDAC Subdivided by Diagnosis in the Preguideline (May 1, 2018-May 1, 2019) and Postguideline (August 1, 2019-August 1, 2020) Period

Characteristic	Total (N = 533)	Preguideline (n = 321)	Postguideline (n = 212)	*P*
Age at diagnosis, years, mean (SD)	68.4 (10.5)	68.0 (10.5)	69.0 (10.4)	.276
Sex, No. (%)				.868
Female	250 (46.9)	152 (47.4)	98 (46.2)	
Male	283 (53.1)	169 (52.6)	114 (53.8)	
Race or ethnicity, No. (%)				.506
Non-Hispanic White	467 (87.6)	283 (88.2)	184 (86.8)	
Non-Hispanic Black	25 (4.7)	12 (3.7)	13 (6.1)	
Hispanic	11 (2.1)	6 (1.9)	3 (1.4)	
Asian	9 (1.7)	7 (2.2)	7 (3.3)	
Other	14 (2.6)	7 (2.2)	4 (1.9)	
Unknown	7 (1.3)	6 (1.9)	1 (0.5)	
Smoking, No. (%)				.235
Never	283 (53.1)	159 (49.5)	124 (58.5)	
Current	37 (6.9)	25 (7.8)	12 (5.7)	
Former	199 (37.3)	128 (39.9)	71 (33.5)	
Unknown	14 (2.6)	9 (2.8)	5 (2.4)	
PDAC stage, No. (%)				.282
High-grade dysplasia	7 (1.3)	3 (0.9)	4 (1.9)	
I	133 (25.0)	79 (24.6)	54 (25.5)	
II	72 (13.5)	44 (13.7)	28 (13.2)	
III	124 (23.3)	85 (26.5)	39 (18.4)	
IV	194 (36.4)	108 (33.6)	86 (40.6)	
Unknown	3 (0.6)	2 (0.6)	1 (0.5)	
Visit with a medical oncologist, No. (%)	389 (73.0)	250 (77.9)	139 (65.6)	.002
Distance to clinic, miles, median (IQR)	83.9 (25.9-214.7)	80.9 (27.9-225.3)	87.9 (21.6-195.1)	.649
Surgical resection, No. (%)	186 (34.9)	115 (35.8)	71 (33.5)	.645
Summary of treatment, No. (%)				.716
No treatment	114 (21.4)	68 (21.2)	46 (21.7)	
Surgery only	26 (4.9)	17 (5.3)	9 (4.2)	
STx and/or RTx only	223 (41.8)	129 (40.2)	94 (44.3)	
Surgery with STx and/or RTx	170 (31.9)	107 (33.3)	63 (29.7)	
Follow-up time since diagnosis, median (IQR)	13.1 (4.6-22.5)	14.1 (5.1-28.8)	12.3 (3.8-18.3)	<.001
Survived >12 months, No. (%)	272 (51.0)	172 (53.6)	100 (47.2)	.174

Abbreviations: PDAC, pancreatic ductal adenocarcinoma; RT, radiotherapy; SD, standard deviation; STx, systemic therapy (chemotherapy and/or immunotherapy).

potential indication for GT on the basis of previous guidelines from the American College of Medical Genetics and Genomics (2015) and NCCN Guidelines on genetic high-risk assessment for breast and ovarian and colorectal cancers (2017).[28-30]

Statistical Analysis

A sample size calculation was performed to detect a 15% GT difference between the pre- and postguideline periods[31] with 80% power and a two-tailed significance level of 0.05, which led to a minimum sample size of 165 patients in each group. Characteristics were compared using chi-square tests, Fisher's exact tests, or *t*-test as appropriate. Odds ratio (OR) for univariable and multivariable analyses were calculated using logistic regression. $P < .05$ was considered to be statistically significant. All statistical tests were two-sided. All analyses were performed using R version 4.2.2.

Ethics Declaration

This study was approved by the Mayo Clinic Institutional Review Board (IRB 21-011326). Because of the retrospective nature of this study and no associated risks to patients, informed consent was waived.

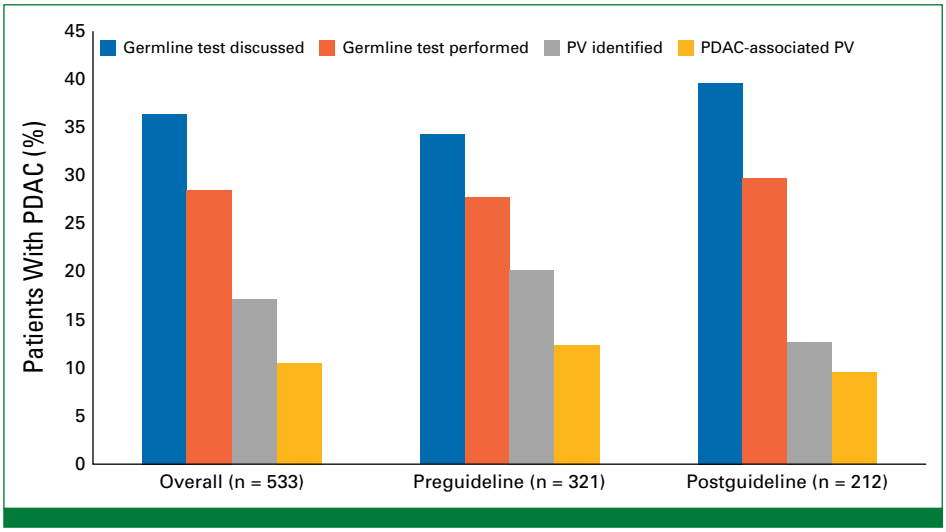

FIG 1. Overview of germline GT discussion, performance, and identification of PVs in the total study population (n = 533), preguideline cohort (n = 321), and postguideline cohort (n = 212). No significant increase in discussion or performance of GT was found between the preguideline cohort and the postguideline cohort (OR, 1.26 [95% CI, 0.88 to 1.80] and OR, 1.10 [95% CI, 0.75 to 1.61], respectively). A PDAC-associated PV was found in 12.4% and 9.5% of the tested patients preguideline and postguideline, respectively. GT, genetic test; OR, odds ratio; PDAC, pancreatic ductal adenocarcinoma; PV, pathogenic variant.

RESULTS

Study Population

A total of 533 patients with PDAC were included in this study, of whom 321 (60.1%) were preguideline and 212 (39.8%) were postguideline. The mean age at diagnosis was 68.4 (standard deviation, 10.5) years, and 46.9% were female. Most patients were White (89.7%) and of non-Hispanic origin (96.2%). Characteristics of patients in the preguideline and postguideline periods were comparable (Table 1) although patients in the postguideline period were less likely to be seen by a medical oncologist (77.9% *v* 65.5%; $P = .002$).

Discussion and Uptake of Germline GT

Most patients were referred for germline GT to the Department of Clinical Genomics by one of their treating physicians for pretest counseling by a genetic counselor or a physician geneticist. In total, 36.4% (194 of 533) of patients had documented discussions of GT with their treating physicians, of whom 78.4% (152 of 194) underwent subsequent testing (Fig 1; Data Supplement, Fig S2). No significant increase in GT discussion and performance was observed after guideline publication. A GT discussion was documented in 34.3% (110 of 321) of patients preguideline versus 39.6% (84 of 212) postguideline (OR, 1.26 [95% CI, 0.88 to 1.80]). GT was subsequently performed in 27.7% (89 of 321) of preguideline and 29.7% (63 of 212) of postguideline patients (OR, 1.10 [95% CI, 0.75 to 1.61]). In 42 patients, GT was discussed, but not performed. In 26 (61.9%) of those, the reason was not documented, and in 11 (26.2%), GT was refused by the patient. Two patients had a known germline PV at the time of diagnosis (*BRCA2* and *MLH1*/*MSH2*/*MSH6*) and did not receive additional GT. Overall, GT was performed in 48.8% (81 of 167) of patients in Mayo Clinic Arizona, 23.6% (41 of 174) in Florida, and 15.5% (30 of 193) in Minnesota ($P < .0001$).

Figure 2 illustrates the distribution of patients who underwent germline GT relative to the total number of PDAC diagnoses during the study period. Notably, a decrease in GT rates was observed during the first months of the COVID-19 pandemic (January–April 2020). Subsequently, testing rates returned to levels similar to those observed before the onset of the pandemic.

Characteristics of Patients With and Without GT Completed

Patients who completed GT (n = 152) were on average 5 years younger than patients who did not receive GT (n = 381; $P < .001$; Data Supplement, Table S1). Males and females were equally likely to have GT. Pancreatic cancer stage did not differ between tested and untested patients although tested patients more often had extensive treatment (surgery in combination with systemic and/or radiotherapy; 55.3% *v* 36.5% of tested and untested patients, respectively; $P < .001$). Tested patients were more frequently seen by a medical oncologist (tested 82.9% *v* untested 69.0%) and had more visits ($P < .001$). Tested patients also resided closer to

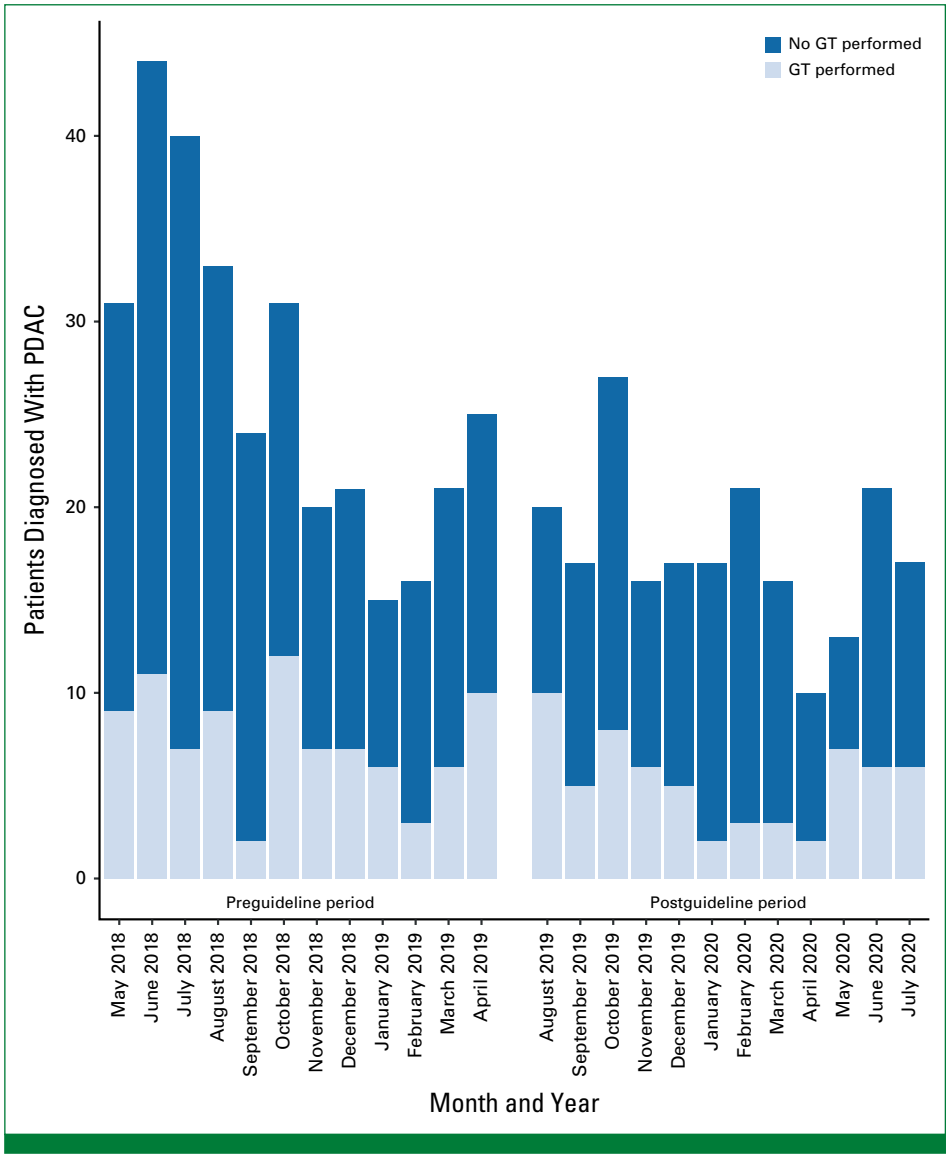

FIG 2. Number of patients per month during the study period who were diagnosed with PDAC and proportion of patients who received germline GT (blue) or did not receive germline GT (light blue). GT, genetic test; PDAC, pancreatic ductal adenocarcinoma.

the clinic (P = .001). A higher proportion of tested patients (70.4%) survived for more than 12 months compared with untested patients (43.3%; P < .001).

Demographics of patients who received GT in the pre- versus postguideline period were similar. However, preguideline patients were more likely to be seen by medical oncologists (91.0% *v* 71.4%; P = .003) and had higher survival rates beyond 12 months (78.8% *v* 58.7%; P = .014) compared with postguideline patients (data not shown).

Factors associated with GT were analyzed in univariable and multivariable analyses (Table 2). In multivariable analysis, older age (OR, 0.96 [95% CI, 0.94 to 0.98]), non-Hispanic White race (OR, 0.47 [95% CI, 0.26 to 0.86]), and living farther from the clinic (OR, 0.50 [95% CI, 0.28 to 0.85]) inversely correlated with GT. Conversely, receiving treatment (OR, 4.96 [95% CI, 2.17 to 13.44]) and surviving more than 12 months (OR, 2.20 [95% CI, 1.41 to 3.74]) strongly associated positively with GT.

Figure 3 depicts the distribution of personal and family cancer histories among tested and untested patients. Specifically, in the preguideline period, patients with GT were more likely to have a family history of cancer. For example, 27.0% of tested patients had one or more first-degree relatives (FDRs) with pancreatic cancer, compared with 7.3% in untested patients (P < .001). Except for family history of breast or colorectal cancer, the distribution of a positive family history of any type of cancer in tested and untested patients was comparable in the postguideline period.

TABLE 2. Factors Associated With Germline Genetic Testing in Univariable and Multivariable Analyses

	Univariable Analysis		Multivariable Analysis	
Factor	OR (95% CI)	*P*	OR (95% CI)	*P*
Age at diagnosis (cont.)	0.95 (0.93 to 0.97)	<.001	0.96 (0.94 to 0.98)	.001
Race (non-White[a] *v* non-Hispanic White)	0.46 (0.27 to 0.78)	.003	0.47 (0.26 to 0.86)	.014
Visit with a medical oncologist (no *v* yes)	2.17 (1.37 to 3.55)	.001	1.54 (0.93 to 2.60)	.100
Distance to clinic (≤250 miles *v* >250 miles)	0.56 (0.33 to 0.91)	.023	0.50 (0.28 to 0.85)	.012
Treatment (none *v* any)	9.62 (4.48 to 25.08)	<.001	4.96 (2.17 to 13.44)	<.001
Survival time (≤12 months *v* >12 months)	3.11 (2.09 to 4.69)	<.001	2.20 (1.41 to 3.74)	.001

Abbreviations: cont., continuous; OR, odds ratio.
[a]Non-White includes non-Hispanic Black, Hispanic, Asian, and other races or ethnicities.

Identification of Germline PVs

Germline PV was identified in 17.1% (26 of 152) of patients tested, of whom 16 (10.5%; 16 of 152) were associated with PDAC (Figs 1 and 4). Comparatively, germline PV was found in 20.2% (18 of 89) of patients tested preguideline and 12.7% (8 of 63) of patients tested postguideline, of whom 12.4% (11 of 89) and 9.5% (6 of 63), respectively, were associated with PDAC. Overall, demographics and personal and family histories of cancer were similar between patients with (n = 16) and without (n = 136) a PDAC PV identified (Data Supplement, Table S2). However, those with a PDAC PV were more frequently diagnosed at stage I (31.2% *v* 19.1%), underwent surgical resection more often (62.5% *v* 34.6%), and had higher 12-month survival rates (93.8% *v* 67.6%), as compared with PDAC-PV–negative patients. Among the 110 tested patients with any relevant family history of cancer, 14 (9.2%) had a PDAC PV. Two of 42 (1.3%) without any relevant family history of cancer had a PDAC-associated PV (*P* = .256).

Of the 16 patients with a PDAC PV, seven patients (43.8%; 7 of 16) would not have an indication for GT if previous guidelines were applied (Fig 4). From the 12 patients with a germline PV in one of the hereditary breast and ovarian cancer genes (*BRCA1*, *BRCA2*, *PALB2*, *ATM*), two (16.7%) patients had a completely negative personal or family history for relevant cancers. One of the two patients with Lynch syndrome (*MLH1*/*MSH2*/*MSH6*) had a completely negative personal or family history for relevant cancers.

Outcomes of Tumor Genotyping and Liquid Biopsy

The Venn diagram provided in the Data Supplement (Fig S3) depicts the number of patients who had germline GT (A; n = 152), tumor genotyping (B; n = 75), liquid biopsy (C; n = 80), or a combination of those. Actionable variants (*BRCA1*/2 or dMMR) were found in five (6.7%) of 75 patients who had tumor genotyping and in six (7.5%) of 80 patients who had a liquid biopsy. In five (6.7%; 5 of 75) patients, a germline PV in *ATM*, *MLH1*/*MSH2*/*MSH6*, *CHECK2*, and *MUTYH* was diagnosed through tumor genotyping. In four of these five patients, these germline PVs were confirmed through germline GT. In one patient with a germline *CHEK2* PV detected through tumor genotyping, germline GT was not performed.

DISCUSSION

This study conducted in a tertiary care center shows that multigene germline GT was performed in approximately one third of patients diagnosed with PDAC. Although recent guidelines advocate offering GT for all patients with PDAC,[27] regardless of personal or family history of cancer, we did not observe a substantial increase in GT after guideline publication. These results are consistent with others showing that guidelines can take many years to impact practice.[32]

Patients who received GT were more likely to have a family history of cancer, particularly pancreatic cancer, suggesting that patients with a higher perceived genetic risk are more likely to receive testing. However, patients with or without a germline PDAC PV had similar personal and family cancer histories, consistent with previous studies.[33-37] Moreover, a relevant number of patients would not have met previous guidelines for GT, indicating that a suspicion of a hereditary cancer syndrome because of family history should not be the sole determinant for testing and that all patients with newly diagnosed PDAC should be offered GT. In addition, significant variations in uptake were noted among the different Mayo Clinic sites. Geographic differences between Minnesota, Arizona, and Florida likely contribute to this difference, with the latter two having larger local populations that may facilitate multiple visits. Conversely, patients visiting Mayo Clinic Minnesota may often do so for a second-opinion consultation. This is supported by the fact that patients who underwent GT were more likely to reside in closer proximity to the clinic. Recognizing the potential advantages for both patients and their family members, it is crucial to make collaborative endeavors aimed at promoting increased uptake of GT in the future.

The low rates of testing might stem from physician's lack of awareness or understanding of the guideline's benefits.[38,39]

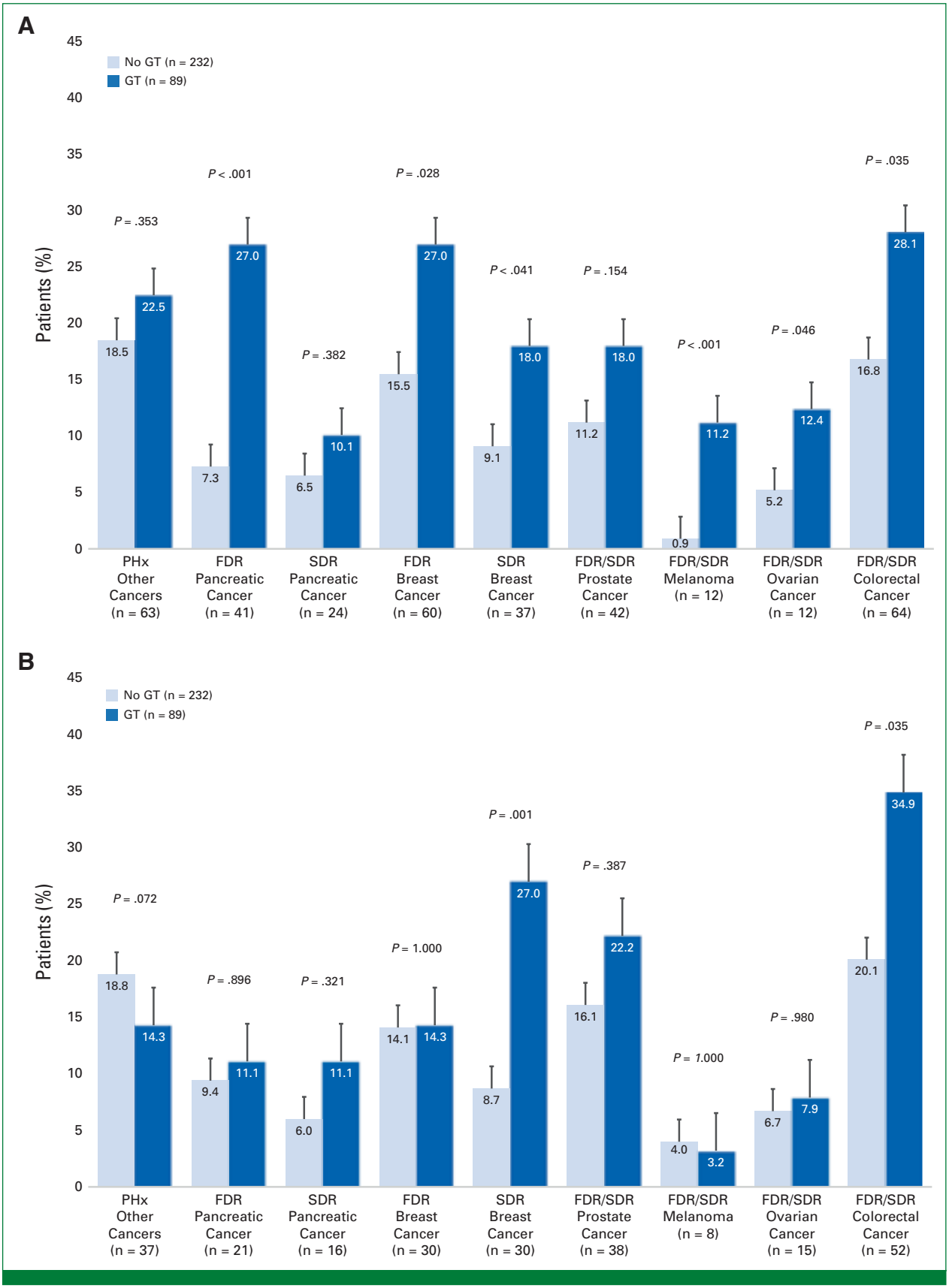

FIG 3. Distribution of personal and family cancer histories of patients who had germline GT (n = 152; blue) and did not have GT (n = 381; light blue), subdivided by the preguideline (A) and postguideline (B) period. FDR, first-degree relative; GT, germline genetic testing; PHx, personal history; SDR, second-degree relative.

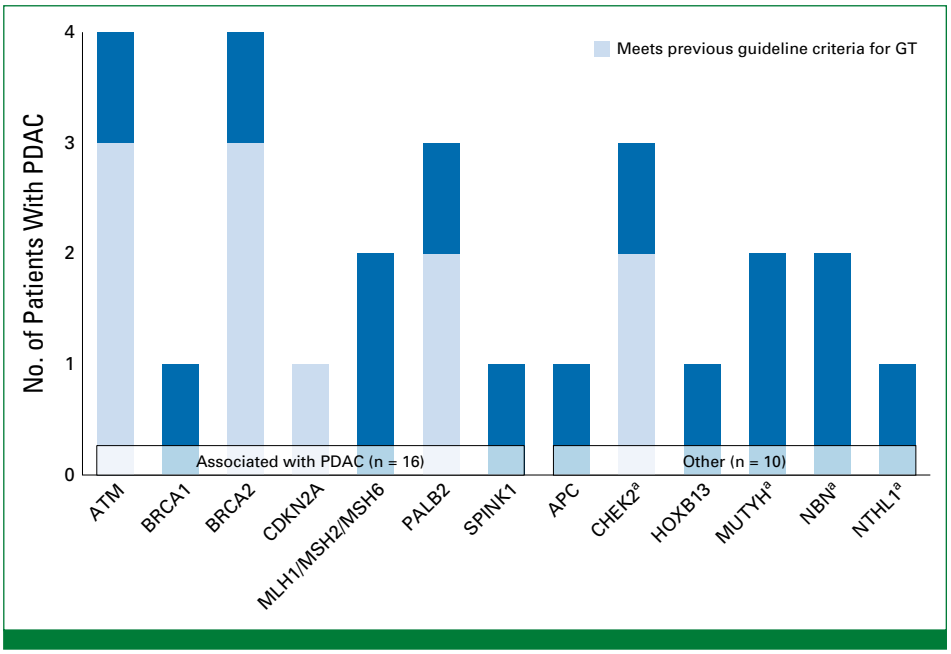

FIG 4. Germline PVs identified with germline GT. Personal and family cancer histories were reviewed for each patient with a PV identified and assessed whether they would have met criteria for referral for GT on the basis of 2015 ACMG[28] and 2017 NCCN Guidelines,[29,30] the proportion of which is depicted in light blue. ACMG, American College of Medical Genetics and Genomics; GT, germline genetic testing; NCCN, National Comprehensive Cancer Network; PDAC, pancreatic ductal adenocarcinoma; PV, pathogenic variant. [a]Indicates heterozygous for PV.

We found that most patients did not have a documented discussion of GT with their physician. However, when GT was discussed, the subsequent uptake of GT was high (78%). We also observed that patients who were seen by medical oncology were more likely to complete GT, possibly because of their awareness guidelines, interest in GT for treatment planning, and likeliness to have multiple encounters with a patient. This highlights the importance of continuing education and dissemination of guidelines among all treating physicians who effectively implement the latest recommendations.

Two recent studies have found similar rates of GT completion in patients with PDAC. Drogan et al[40] found that GT was recommended in 53% of cases and completed 37% of the time. Similarly, they found that younger patients and those with a positive family history of cancer were more likely to receive GT. Similarly, although in a more diverse patient population, Crowley et al[41] found that 44% of patients underwent GT, with testing rates increasing annually from 33% in 2019 to 61% in 2021. Streamlined genetic counseling with multigene testing has proven to be effective in boosting GT rates in various studies.[37,42-44] For instance, implementation of automated referrals at the Dana-Farber Cancer Institute increased GT from 16.5% to 38.0%.[37] Currently, our institution uses multiple approaches like raising awareness in meetings, staff education, and electronic health record advisories to implement guideline updates. Our next step involves implementing and evaluating an automated referral workflow for GT in all patients with newly diagnosed PDAC to enhance uptake.

Our findings confirm earlier estimations that approximately one in 10 patients with PDAC carry a PDAC susceptibility gene.[12,13] Cascade testing of FDRs of the index patient offers an opportunity to enrollment in cancer surveillance programs, which has demonstrated the potential to improve outcomes.[7-9] We did assess discussions and rates of cascade testing among at-risk relatives, which would have provided a more comprehensive representation of the benefits of GT. Earlier studies showed that testing results were communicated to at-risk relatives in approximately 80% of cases,[45,46] yet recent findings by Wang et al[46] showed that only 31% of FDRs pursued subsequent testing. Understanding barriers to cascade testing is crucial for developing strategies to enhance testing rates among at-risk family members, fully harnessing potential benefits of GT in PDAC.

More than half of the identified PDAC-associated PVs involved DNA damage response (DDR) genes (*BRCA1/2*, *PALB2*) or mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*). Discovering a DDR gene mutation suggests potential sensitivity to platinum chemotherapy, leading to improved overall survival.[47] While occurrence of dMMR/microsatellite instability-high in advanced/metastatic PDAC is rare (around 1%), it is imperative that this is not missed as

immunotherapy could change the trajectory of the disease dramatically.[48] These examples emphasize the critical role of identification of PVs in guiding personalized treatment options. Our study highlights tumor genotyping and liquid biopsy as additional strategies to identify actionable alterations. This is exemplified by another recent study showing that tumor molecular profiling after germline GT increased the detection of actionable alterations by five-fold, indicating that these strategies are important to maximize options in therapeutic decision making.[49]

A limitation is that the Mayo Clinic is a tertiary referral center, and it is therefore likely that a proportion of patients had GT performed at an outside center. Although we extensively searched medical records, including information provided by referring centers, the resulting GT rates presented here are likely to be an underestimate. Moreover, although we diligently collected patient history data, retrospective nature might limit its accuracy and completeness. Second, our patient demographics at Mayo Clinic may not be generalizable to other centers in and outside the United States. This is for example reflected by the predominantly White study population, which in general is more likely to receive GT as compared with Black, Latino, or Native American patients,[50-52] although we did not observe evident differences in our data. Third, the study period coincided with the early phases of the COVID-19 pandemic, likely affecting testing rates, underestimating the true impact of the guideline update. Finally, the NCCN Guideline stipulates that if patients with PDAC cannot be tested, their FDRs should be offered testing. We unfortunately did not investigate if GT was offered to these relatives, which might have underestimated the eventual guideline adherence.

In conclusion, this study underscores the underutilization of germline GT despite guideline recommendations for all patients with PDAC. Those with a family history, particularly of pancreatic cancer, were more prone to testing. Yet, a significant number would not have met previous guidelines, suggesting that a family history alone should not dictate testing. Considering PDAC's poor prognosis and the potential benefits for patients and at-risk relatives, streamlining genetic counseling and testing is essential to boost uptake in this population.

AFFILIATIONS

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PRIOR PRESENTATION

This study was previously presented as a poster presentation at the Conference ASCO Gastrointestinal Cancers Symposium, San Francisco, CA, January 19-21, 2023, Title: Guideline Adherence and Outcomes of Genetic Testing in Pancreatic Cancer Patients and Conference Digestive Disease Week, Chicago, IL, May 6-9, 2023, Title: Guideline Adherence and Outcomes of Genetic Testing in Pancreatic Cancer Patients.

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DATA SHARING STATEMENT

The deidentified data that support the findings of this study are available upon reasonable request from the authors.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Utilization and Outcomes of Multigene Panel Testing in Patients With Pancreatic Ductal Adenocarcinoma

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