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Abdominal Imaging of Pancreatic Cysts and Cyst-Associated Pancreatic Cancer in BRCA1/2 Mutation Carriers: A Retrospective Cross-Sectional Study

Carrie X Cao, MD^{1,*}, Jeremy S Sharib, MD^{1,*}, Amie M Blanco, MS^{2,3}, Dena Goldberg, MS², Paige Bracci, PhD⁴, Rita A Mukhtar, MD, FACS^{1,3}, Laura J Esserman, MD, MBA, FACS^{1,3}, Kimberly S Kirkwood, MD, FACS^{1,3}

¹Department of Surgery, University of California San Francisco, San Francisco, CA

²University of California San Francisco Cancer Genetics and Prevention Program, San Francisco, CA

³University of California San Francisco Heller Diller Family Comprehensive Cancer Center, San Francisco, CA

⁴Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA

Abstract

Background: Direct-to-consumer BRCA testing will increase BRCA diagnoses and subsequent abdominal imaging. It is unclear whether BRCA-carriers are at higher risk of developing pancreatic cysts (PCs) or cyst-associated pancreatic adenocarcinoma (PDAC). We investigate the prevalence of PCs in BRCA-tested patients, and whether BRCA-carriers have higher rates of PDAC when PCs are found.

Study Design: This is a retrospective cross-sectional study of patients with BRCA testing and abdominal imaging between 1996-2018. PCs were identified on original imaging reports.

Corresponding Author Address: Jeremy S Sharib, MD, 600 16th St, S514, San Francisco, CA 94158, Phone: 415-476-1239, Jeremy.Sharib@ucsf.edu.

*Drs Cao and Sharib contributed equally to this work.

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Prevalence and risk characteristics of PCs, as well as incidence of PDAC, were compared between BRCA+, BRCA–, and BRCA-untested patients.

Results: PCs were identified in 4045 patients among 128,164 unique patients with abdominal imaging, including 33 patients with PCs in 1,113 BRCA-tested patients. There was no difference in PC prevalence between BRCA+, BRCA– and untested patients (3.6%, 2.6%, 3.2% respectively; $p=0.64$). PCs were diagnosed in BRCA+ patients at a younger age (57.1 vs 65.3 years, $p<0.001$), however there was no difference in risk stratification compared to BRCA– or untested patients by consensus criteria. Across the population of imaged patients, patients with PCs had significantly higher rates of PDAC compared to those without PCs (18.2% vs 2.4%, $p<0.001$). Incidence of cyst-associated PDAC was similar in BRCA+ and BRCA– patients (13.3% vs 22.2%, $p=0.84$).

Conclusion: BRCA+ patients have similar rates of PCs, high-risk features in their cysts, and PDAC as BRCA– and untested patients. BRCA+ patients likely do not require dedicated abdominal imaging to evaluate for PCs and should follow similar management guidelines as the untested general population if an incidental PC is identified.

Graphical Abstract

Precis

BRCA+ patients do not have higher rates of pancreatic cysts (PCs), high-risk features in their cysts, or cyst-associated pancreatic adenocarcinoma compared to BRCA– and untested patients. BRCA+ patients likely do not require dedicated abdominal imaging to evaluate for PCs and should follow management guidelines for incidental PCs when identified.

Keywords

pancreatic cysts; pancreatic cancer; BRCA; genetic testing; abdominal surveillance; abdominal imaging

Introduction

Since 2006, there has been a rapid growth in the development and accessibility of direct-to-consumer genetic testing.¹ In April 2018, the United States Food and Drug Administration (FDA) authorized the first direct-to-consumer genetic test for 3 founder mutations of the BRCA gene.² Additionally, several multi-gene full sequencing panels for inherited cancer predispositions are now provided by several companies, and increasingly these tests are performed in healthy individuals.³⁻⁴ Mutations in the BRCA gene are strongly associated with increased risks of several malignancies, particularly breast, ovarian, and prostate cancers, which has led to the implementation of robust screening programs for these cancers in BRCA mutation positive (BRCA+) individuals.⁵ More recently, there has been a strong push for screening for other BRCA-associated cancers as well, particularly pancreatic cancer in BRCA2 mutation carriers.⁶ Some proponents advocate for more frequent abdominal surveillance of BRCA+ patients using computed tomography (CT), magnetic resonance imaging (MRI), or endoscopic ultrasound (EUS).⁷⁻⁹ Pancreatic cancer screening in BRCA+ patients remains controversial, however, because the potential harm of over-treatment is high, including the risks of procedure-related complications, morbidity of pancreatic surgery, as well as the psychoemotional and financial burdens of over-testing.¹⁰⁻¹³ Additionally, as access to genetic information becomes more widespread and the diagnostic sensitivity of imaging modalities continues to improve, the demand for screening will likely contribute to an increase in incidental findings such as pancreatic cysts, the optimal management of which remains unclear.

Pancreatic cysts are frequent incidental findings in patients undergoing abdominal imaging, with a reported prevalence ranging from 2.6%-21.5% in the general population and greater than 50% in patients over the age of 70.¹⁴⁻¹⁸ Mucinous pancreatic cystic neoplasms such as intraductal papillary mucinous neoplasms (IPMNs), which have a potential risk for malignant transformation to invasive ductal adenocarcinoma of pancreas (PDAC), represent the majority of pancreatic cysts found incidentally.¹⁸⁻²⁰ The precise risk of this malignant transformation is unclear, with estimates ranging from a 2.8% long-term risk of developing cancer in a cohort of patients with suspected branch duct IPMNs, to a 15% incidence of high-grade dysplasia and invasive carcinoma in a large series of surgically resected IPMNs.^{21,22}

Currently, consensus guidelines recommend that patients who are found to have pancreatic cysts on abdominal imaging undergo risk stratification.²³ Those with characteristics considered worrisome or high-risk for suspected malignancy—such as clinical symptoms, ductal dilatation, mural nodules, or elevated biochemical markers—are recommended for further evaluation with endoscopic ultrasound, fine needle aspiration, and potential surgical resection. Cysts that do not immediately require resection are recommended for interval surveillance with CT, MRI, or EUS.^{21,23} Risk stratification of pancreatic cysts is a significant challenge because while the majority of pancreatic cysts are benign, it is important to identify those that do have malignant potential given the high mortality of pancreatic cancer.^{24,25} Balancing the benefits of potential cancer prevention with the risks and morbidity of overtreatment continues to be an area of controversy, with several different

guidelines currently available that vary in their assessment of high-risk cysts, indications for surgical resection, and frequency and preferred modality of surveillance.^{23,25-28}

Current guidelines for risk stratification do not include genetic factors that may predispose patients to malignancies. Patients with known genetic predispositions to pancreatic cancer, who make up approximately 10% of the pancreatic cancer population, are one group to whom consensus guidelines may not apply.^{21,29} Inherited mutations in the BRCA gene, particularly BRCA2, are associated with a significantly increased risk of pancreatic cancer.³⁰⁻³⁹ Recent cohort studies have found that BRCA2 mutations are associated with a 2- to 4-fold increased risk of pancreatic cancer, with emerging evidence suggesting an association with BRCA1 mutations as well.^{29,40,41} Given this elevated risk, some providers advocate for increased pancreatic cancer screening and surveillance of individuals with BRCA mutations, with the goal of detecting and prophylactically resecting premalignant lesions. Emerging evidence suggests that pancreatic cysts are the most frequent abnormalities detected on imaging in these high-risk individuals.^{42,43} Additionally, a higher prevalence of IPMNs with high grade dysplasia has been found in the resected lesions of patients with familial PDAC, compared to patients with sporadic PDAC.⁴⁴ However, whether individuals with BRCA mutations in fact have higher rates of pancreatic cysts and pancreatic cancer in their cysts compared to the general population has not been well-studied. The optimal management of pancreatic cysts in these patients, including whether screening, frequent surveillance, or other more aggressive interventions are effective, remains unclear.^{7,45,46}

In this retrospective, cross-sectional study, we aim to investigate the prevalence and clinical features of pancreatic cysts found on abdominal imaging in patients who underwent BRCA1/2 testing. The knowledge of pancreatic cyst and cancer rates in the BRCA population has significant implications. As genetic testing becomes increasingly accessible, demand for imaging increases, and image resolution improves, the pool of individuals with potential mutations and incidental pancreatic findings is expected to increase.⁴⁷⁻⁵⁰ It is important to better characterize the risk profile of these patients in order to provide a more evidence-based recommendation regarding the clinical management of pancreatic cysts in high-risk populations.

Methods

Study design and population

This is a retrospective cross-sectional study of patients at the University of California, San Francisco who underwent genetic testing at the Cancer Genetics and Prevention Program (UCSF CGPP) between January 1, 1996 and April 1, 2018 and received abdominal imaging (CT or MRI) at UCSF in the same time period. Consecutive adults >18 years old referred for BRCA testing at UCSF were identified from a CGPP clinical database. Sociodemographic information, including age, gender, and race, and clinical history including personal oncologic history were self-reported at the time of genetic testing. Patients with pancreatic cysts were identified from a UCSF Department of Radiology imaging database containing searchable, archived original reports entered into the medical record at the time of each scan. Radiographic findings of pancreatic cysts, clinical indications for each scan, imaging modality, as well as limited sociodemographic information including age at the time of scan

and gender, were abstracted from these archived imaging reports; raw scans were not reviewed centrally.

All patients with BRCA test results were considered *BRCA-tested*; patients who tested positive for one or more mutations in BRCA1 or 2 were considered *BRCA-positive (BRCA+)*, and those without mutations were considered *BRCA-negative (BRCA-)*. All patients with abdominal imaging but without BRCA testing were included in a *BRCA-untested* group, distinct from BRCA- patients. For the purposes of our analysis, these patients were considered to represent the general population; patients with an encounter at a tertiary academic center, with undetermined genetic risk.

Additional review of the electronic medical charts of all BRCA-tested patients with pancreatic cysts was performed to further characterize their cysts, including size, radiographic characteristics, and pathologic diagnoses when available. Cysts with high-risk features were defined according to the 2017 International Association of Pancreatology (IAP) consensus guidelines for worrisome features and high-risk stigmata of malignancy in pancreatic cysts.²³ A diagnosis of pancreatic cancer was confirmed by reference to a pathology report or medical record where available. Routine abdominal screening for BRCA carrier was not conducted.

Statistical analysis

Demographic and clinical characteristics of the study cohort were summarized by descriptive statistics. Categorical variables were summarized using percentages and proportions, and continuous variables were described using mean with standard deviation or median with interquartile range. Comparison of categorical variables such as proportion of patients with PCs was performed using the Pearson chi-squared test, while continuous variables were analyzed using Wilcoxon rank-sum test. Correction for multiple testing was not performed. Statistical significance was defined as a two-sided p-value less than 0.05. Power was set at 1-beta=0.8, with a predicted effect size of 2 for the prevalence of pancreatic cysts among BRCA+ and BRCA- or untested groups based on estimates of an at least 2-fold increased risk of pancreatic cancer associated with BRCA mutations as reported by prior studies.^{29,40,41} All statistical analyses were performed using the statistical computing software R (R Foundation for Statistical Computing, Vienna, Austria. 2017. <https://www.R-project.org/>).

Results

We identified 128,164 unique patients with abdominal CT or MRI between 1996 and 2018. Five-thousand four-hundred eight patients with BRCA testing available through the UCSF CGPP database were cross-referenced with this imaged cohort, which yielded 1,113 patients with both BRCA testing and imaging data, and 127,051 BRCA-untested patients with imaging data only. Of those BRCA-tested and imaged patients, there were 33 patients with pancreatic cysts, including 15 BRCA+ and 18 BRCA-. In addition, 4,012 BRCA-untested patients had pancreatic cysts (Figure 1).

Over the study period, the number of patients undergoing BRCA testing at UCSF each year increased from 6 patients in 1996 to 234 in 2017, the last full year included in the study (Figure 2a). The frequency of abdominal imaging at UCSF each year increased from 3,883 scans in 1996 to 20,428 scans in 2017 (Figure 2b). The number of new patients with pancreatic cysts found on imaging each year also increased from 33 patients in 1996 to 340 patients in 2017 (Figure 2c). Only partial data from 2018 was available at the time of this study.

Demographic and clinical characteristics of BRCA-tested patients are summarized in Table 1. Patients with BRCA testing were more likely to be female compared to the BRCA-untested group (92% vs 52%, $p < 0.001$). BRCA+ patients were also diagnosed with pancreatic cysts at a younger age than the BRCA-untested population (57.1 yrs vs 65.3 yrs, $p = < 0.001$), despite a similar age at which the first abdominal imaging was performed (51.3 yrs vs 53.5 yrs, $p = 0.32$). Eighty-four percent of BRCA+ and 91% of BRCA- patients reported a personal history of at least one type of cancer, including 70% and 78% with a personal history of breast or ovarian cancer in BRCA+ and BRCA- patients, respectively. Eight percent of BRCA+ and 10% of BRCA- patients reported a history of three or more discrete cancers.

Patterns of abdominal imaging in BRCA-tested patients

In our cohort of BRCA-tested patients, the overall prevalence of abdominal imaging was 20.6% (1,113/5,408), with no significant difference between BRCA+ and BRCA- groups ($p = 0.14$) (Table 2). Notably, the percentage of patients who received MRI or multimodal imaging was slightly higher in the BRCA+ group compared to BRCA- (20.0% vs 14.6%, $p = 0.018$) and the untested population (20.0% vs 14.2%, $p = 0.0067$). The median number of scans per patient in the BRCA+ group was 3, while BRCA- patients and the untested population had a median of 2 scans per patient and 1 scan per patient, respectively.

Greater than 90% of axial abdominal imaging in BRCA-tested patients were done for reasons unrelated to pancreatic cysts or cancer, indicating that most cyst diagnoses were in fact made incidentally. Figure 3 depicts the most common clinical indications for abdominal imaging among all BRCA-tested patients, based on a total of 6,341 abdominal scans of 1,113 patients. BRCA+ and BRCA- patients had a similar distribution of indications for abdominal imaging, likely due to similar indications for BRCA testing. Greater than 50% of scans were completed for clinical indications related to breast or ovarian cancer, and 9.6% of BRCA+ and 17.7% of BRCA- patients had abdominal imaging for other non-hepatobiliary malignancies. Approximately 6% of scans were done to further characterize or follow a previously diagnosed pancreatic cancer, 1% of scans were for follow-up of a pancreatic cyst, and 0.4-2.2% of scans were due to clinical suspicion of a pancreatic malignancy based on symptoms of abdominal pain, jaundice, or weight loss. From these studies, 3/15 BRCA+ patients and 2/18 BRCA- were diagnosed with a pancreatic cyst on serial imaging. Screening for pancreatic cancer, or any other cancer, was not routinely performed for BRCA tested patients and as a result, only 0.4% and 0.1% of BRCA+ and BRCA- patients were imaged for this indication. The remaining 20% of scans had a variety of other, unrelated, clinical indications.

Rates of pancreatic cysts and cancer

The overall prevalence of patients with pancreatic cysts among all patients with abdominal imaging was 3.2% (4,045/128,164) over the 22-year study period. Among BRCA-tested individuals, 4% of BRCA+ patients had pancreatic cysts, while 3% of BRCA– patients had pancreatic cysts. There was no significant difference in the prevalence of pancreatic cysts between BRCA+ patients compared to BRCA– patients (RR=1.4, 95% CI [0.7-2.7], $p=0.35$), or between BRCA+ patients compared to the BRCA-untested population (RR=1.1, 95% CI [0.7-1.9], $p=0.62$). In addition, while the numbers were low, there was no difference in the prevalence of pancreatic cysts in patients with BRCA1 and BRCA2 mutations (3% vs 4%, $p=0.61$). Finally, rates of high-risk pancreatic cysts based on consensus definitions for worrisome features or high-risk stigmata were not statistically significantly different in BRCA+ and BRCA– patients (Table 3).

Pancreatic cancer rates in patients with or without pancreatic cysts indicate that those with a diagnosed cyst on imaging are significantly more likely to have pancreatic cancer at some point during the study period (18% with cysts vs 2% without cysts; RR=7.5, 95% CI [3.3–17.1], $p<0.001$) (Table 4). However, there was no statistically significant difference in pancreatic cancer prevalence in BRCA+ patients with cysts compared to BRCA– patients with cysts (13.3% BRCA+ vs 22.2% BRCA–; RR=0.60, 95% CI [0.1-2.8], $p=0.84$) or in BRCA+ patients with cysts compared to BRCA-untested patients (13.3% vs 18.2%; RR=0.73, 95% CI [0.2-3.2], $p=0.68$). Additional descriptive statistics of the 33 BRCA-tested patients' pancreatic cysts, including average size, location, and pathologic findings on biopsy or excision, are summarized in eTable 1.

Discussion

This is the first study to examine the prevalence and clinical features of pancreatic cysts in a BRCA-tested population. Understanding the risk of pancreatic cysts and cyst-associated cancer in these patients has important implications in the context of increasingly accessible genetic testing and high-resolution abdominal imaging. As some clinicians advocate for more aggressive strategies such as universal BRCA testing and surveillance abdominal imaging of all BRCA+ patients, the population of individuals with known BRCA mutations and incidental pancreatic cysts is expected to grow^{51,52}. Pancreatic cysts are increasingly common, while the majority are often found to be low-grade or benign,⁵³ thus the potential for overdiagnosis and overtreatment is high. Moreover, the availability of full sequencing panels has led to the identification of additional genetic variants of unclear significance in terms of pancreatic cancer risk (eTable 2),⁵⁴⁻⁵⁷ which further contributes to an increasingly complicated landscape of risk stratification.

Our study reports a 3.2% overall prevalence and a 4.0% prevalence in the last five years of pancreatic cyst diagnoses in adult patients who underwent abdominal imaging studies over a 22-year period at a large tertiary university hospital. This is consistent with the rates of pancreatic cysts found on CT reported by several recent studies, although other studies have reported rates of up to 20%.^{14,58-60} Notably many of these latter studies utilized MRI or EUS which have better sensitivity for detecting cysts; also, cyst diagnoses were usually made by radiologists reviewing or re-reviewing raw scans for research purposes, rather than

using original imaging reports, a factor that likely contributed to a higher yield of pancreatic cysts in those studies.^{15,18,61} Inter-observer variation in the diagnostic assessment of pancreatic cysts on imaging has been found by prior studies to affect the reliability of cyst identification and classification, which may also have lowered our cyst diagnosis rates.^{14,62,63}

Identifying pancreatic cysts in BRCA+ patients is thought to be particularly important due to the increased risk of pancreatic cancer in this population.^{40,42,64} The goal for increased surveillance with abdominal imaging is to detect more pancreatic cysts, dysplastic features, and ultimately cyst-related cancer in these high-risk patients. However, in our study cohort, we found no significant differences in pancreatic cyst diagnosis rates among BRCA+, BRCA-, and BRCA-untested patients. BRCA+ patients with cysts did not have higher rates of worrisome features or high-risk stigmata in their cysts, despite being more likely to be imaged with MRI or multimodal imaging which have superior sensitivities for cyst detection and characterization.⁶⁵ Also, while overall patients with cysts had a higher rate of pancreatic cancer compared to those without cysts, which is consistent with prior reports,⁶⁶ there was no difference in pancreatic cancer prevalence among BRCA+ or BRCA- and BRCA-untested patients with cysts. In other words, for patients with diagnosed cysts, BRCA-positivity does not appear to confer any additional risks of having pancreatic cancer.

These results are important within the context of abdominal screening for pancreatic cancer in patients with BRCA mutations and other high-risk genetic syndromes. The recently updated USPTF guidelines for Pancreatic cancer screening confirmed the long held conclusion that screening for pancreatic cancer is not warranted in asymptomatic patients.⁶⁷ However, the guidelines did not take up the open question about screening for patients with known high-risk genetic syndromes. The American College of Gastroenterology conditionally recommends surveillance for pancreas cancer for certain high-risk populations, including BRCA carriers.⁶⁸ Unclear and inconsistent screening practices in high-risk populations are likely to identify increasing amounts of pancreatic cysts in BRCA carriers. Our results suggest that current abdominal imaging practices do not in fact detect higher rates of malignant features in the pancreatic cysts of BRCA+ patients. As such, it is unlikely that more frequent abdominal imaging, such as abdominal surveillance practices, would be a high-yield intervention for identifying high-risk pancreatic cysts or cyst-related pancreatic cancer in these individuals. There is no clear evidence at this time to support that BRCA+ patients should undergo different or more aggressive management of their pancreatic cysts relative to the untested population.

Our study has several strengths. The study population, particularly our untested group, is composed of a very large, heterogeneous cohort of patients that is assumed to be representative of the general population. The BRCA-tested group is also large, and while different in certain demographic parameters (e.g. gender) from the general population, is largely representative of the patients typically undergoing BRCA testing at this time. The fact that the majority of abdominal scans were done for non-pancreatic indications demonstrates that most pancreatic cysts were in fact detected incidentally, which captures the types of cyst diagnoses currently of great interest and challenge for investigators. Additionally, despite extensive ongoing discussions regarding abdominal surveillance

practices in BRCA mutation carriers, the prevalence and outcomes of pancreatic cysts has never been studied in these patients. This is the first study to our knowledge that begins to quantify these risks and provide data to guide the optimal management of cysts in high-risk patients.

There are several limitations of this study. First, BRCA1 and BRCA2 are not the only predisposing genes for pancreatic cancer; several others, including CDKN2A, Lynch Syndrome (MLH1, MSH2, PMS2, and MSH6), PALB2, and ATM, have also been implicated in patients with a family history of pancreatic cancer.^{68,69} Inherited mutations in these genes are also thought to increase the risk of pancreatic cancer and may prompt consideration for screening abdominal imaging.^{7,70} Thus, while the results of our study do not support extensive abdominal surveillance for BRCA mutation carriers, high-risk individuals with mutations in other pancreatic cancer susceptibility genes, as well as patients with familial pancreatic cancer, may warrant more aggressive management. Second, given that this is a retrospective, cross-sectional study, we are limited in the ability to estimate the true incidence of pancreatic cysts and pancreatic cancer in patients with positive BRCA testing. A longitudinal cohort study is required to identify these data and strengthen the conclusions regarding the development of these pathologies over time. Third, the power of some sub-analyses was limited due to the very low rates of pancreatic cancer and BRCA testing in the population, with a <1% prevalence of BRCA testing among all patients with abdominal imaging, and a 2.9% prevalence of pancreatic cancer diagnoses among all BRCA tested patients. Given the number of BRCA+ patients we identified, our study is powered to detect an at least two-fold difference in the prevalence of PCs in BRCA+ patients compared to BRCA-, an estimated effect size based on prior studies looking at the risk of pancreatic cancer BRCA mutation carriers.^{29,38} However, given the low numbers of patients with both BRCA testing and PC diagnoses, the study may not be adequately powered to detect such a difference in the prevalence of cyst-associated pancreatic cancer among the BRCA-tested with PCs, so there may be a statistically significant effect size that was not accounted for by our study. The decision to undergo abdominal screening for the low risk of finding a malignancy must be weighed against the probability of finding a PC where surgical intervention is undertaken but may not have been necessary. The mortality and morbidity risks associated with the latter may well outweigh the benefit of surveillance.

Of note, however, as the rates of pancreatic cyst diagnoses and genetic testing increase (Figure 2) and are expected to continue to increase with the approval of direct-to-consumer genetic testing and improved imaging, the population of BRCA+ patients are PCs is expected to grow in the coming years. As such, this current retrospective, cross-sectional study is limited in its capacity to assess long-term outcomes of PCs in this population, demonstrating a need for more longitudinal prospective data on the risks of developing pancreatic cancer over time among BRCA-tested patients with PCs. Finally, participants were recruited from a single tertiary academic center, which may limit the current study's generalizability.

Conclusions

Pancreatic cysts are detected at similar rates in BRCA mutation carriers compared to patients without BRCA mutations and the untested population. The prevalence of high-risk features as defined by IAP consensus guidelines are also similar in BRCA+ and BRCA– patients. Across the entire population of BRCA tested individuals, patients with pancreatic cysts reported higher rates of pancreatic cancer compared to those without. However, among those with cysts, there was no statistically significant difference in cancer rates between BRCA+ and BRCA– patients. At this time, carriers of BRCA mutations should follow similar management guidelines for their pancreatic cysts as the untested general population if they are diagnosed. Our results demonstrate a need for larger prospective cohort studies, which would yield a larger group of BRCA-tested patients with pancreatic cysts and provide more longitudinal data on the long-term outcomes of cysts in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Study patient selection using 2 clinical databases, the University of California San Francisco (UCSF) Cancer Genetics and Prevention Program and the UCSF Department of Radiology.

Figure 2.

Data from the University of California San Francisco. (A) Genetic testing by year, 1996 to 2018. Bars represent number of new patients (pts) undergoing BRCA testing each year. Data from 2018 includes January to April only. (B) Abdominal imaging by year, 1996 to 2018. Bars represent number of total abdominal CTs and MRIs completed each year, with gray shaded portion representing CTs and black shaded portion representing MRIs. Data from 2018 includes only scans completed between January and April. (C) Pancreatic cysts by year, 1996 to 2018. Bars represent number of new patients (pts) diagnosed with pancreatic cysts each year; gray or black shaded portions represent patients whose cysts were diagnosed on CT or MRI, respectively. Data from 2018 includes only scans completed between January and April.

Figure 3.

Summary of indications for abdominal imaging in BRCA-tested patients. Percentages are calculated from a total of 2,254 scans of 419 BRCA+ patients and 4,087 scans of 694 BRCA – patients. More than 90% of scans were for indications unrelated to known or suspected pancreatic cysts or cancer. abd, abdominal; wt, weight.

Table 1. Sociodemographic and Clinical Characteristics of Study Population: Patients with BRCA Testing and Abdominal Imaging 1996 to 2018

Characteristic	BRCA1 (n = 202)	BRCA2 (n = 217)	All BRCA+ (n = 419)	All BRCA- (n = 694)	Untested population (n = 127,051)	p Value	
						BRCA+ vs BRCA-	BRCA+ vs untested
Pancreatic cyst, n	6	9	15	18	4,012	<0.001	<0.001
Sex, n (%)							
Male	17 (8)	38 (18)	55 (13)	36 (5)	61,749 (48)	-	-
Female	185 (92)	179 (82)	364 (87)	658 (95)	65,302 (52)	-	-
Mean age							
Genetic testing, y $\pm$ SD	52.5 $\pm$ 14.2	53.5 $\pm$ 13.2	53.0 $\pm$ 13.7	54.3 $\pm$ 13.4	Not applicable	0.19	-
First abdominal imaging, y $\pm$ SD	50.6 $\pm$ 12.2	52.0 $\pm$ 13	51.3 $\pm$ 12.6	50.9 $\pm$ 12	53.5 $\pm$ 19	0.32	0.001
Cyst diagnosis, y $\pm$ SD	52.7 $\pm$ 10.6	60.8 $\pm$ 9.9	57.1 $\pm$ 10.7	60.4 $\pm$ 12.2	65.3 $\pm$ 16	0.84	<0.001
Race/ethnicity, n (%) *					(n = 2,565)		
White	148 (73)	140 (65)	288 (69)	514 (74)	1,582 (62)	-	-
Black	5 (2)	12 (6)	17 (4)	22 (3)	186 (7)	-	-
Asian/Pacific Islander	27 (13)	24 (11)	51 (12)	91 (13)	490 (19)	-	-
Other	9 (4)	16 (7)	25 (6)	19 (3)	307 (12)	-	-
Unknown	13 (6)	25 (12)	38 (9)	47 (7)	-	-	-
Personal cancer history, n (%)							
Breast	81 (40)	102 (47)	183 (44)	438 (63)	-	-	-
Ovarian	75 (37)	33 (15)	108 (26)	103 (15)	-	-	-
Prostate	2 (1)	7 (3)	9 (2)	10 (1)	-	-	-
Colon	4 (2)	10 (5)	14 (3)	14 (2)	-	-	-
Thyroid	3 (1)	3 (1)	6 (1)	13 (2)	-	-	-
Melanoma	7 (3)	6 (3)	13 (3)	31 (4)	-	-	-
Lymphoma	2 (1)	2 (1)	4 (1)	7 (1)	-	-	-
Pancreas	4 (2)	14 (6)	18 (4)	14 (2)	-	-	-
Number of cancers, n (%)							

Characteristic	BRCA1 (n = 202)	BRCA2 (n = 217)	All BRCA+ (n = 419)	All BRCA- (n = 694)	Untested population (n = 127,051)	p Value	
						BRCA+ vs BRCA-	BRCA+ vs untested
0	25 (12)	41 (19)	66 (16)	59 (9)	-	-	-
1	119 (59)	131 (60)	250 (60)	412 (59)	-	-	-
2	39 (19)	32 (15)	71 (17)	152 (22)	-	-	-
3	19 (9)	13 (6)	32 (8)	71 (10)	-	-	-

Personal cancer history and number of cancers available only for BRCA-tested patients.

* Race/ethnicity data available for a subset of pancreatic cyst patients.

Table 2.

Rates of Abdominal Imaging in Patients with BRCA Mutations

Variable	BRCA1 (n = 910)	BRCA2 (n = 1,024)	All BRCA+ (n = 1,934)	All BRCA- (n = 3,474)	Untested population with abdominal imaging
With abdominal imaging, n (%) [*]	202 (22)	217 (21)	419 (22)	694 (20)	127,051
Modality, n (%) [†]					
CT only	158 (78)	177 (82)	335 (80)	593 (85)	108,997 (86)
MRI only	17 (8)	14 (6)	31 (7)	27 (4)	8,279 (7)
Multimodal	27 (13)	26 (12)	53 (13)	74 (11)	9,775 (8)
Median number of studies per patient	3	2	3	2	1
25 th to 75 th percentile	1-7	1-6	1-7	1-6	1-3

p = 0.007, BRCA+ vs untested population, distribution of imaging modalities.

^{*} p = 0.14, BRCA+ vs BRCA-, proportion with abdominal imaging.[†] p = 0.018, BRCA+ vs BRCA-, distribution of imaging modalities.

Table 3.
Pancreatic Cyst Diagnoses in BRCA-Tested and Untested Patients with Abdominal Imaging

Diagnosis	BRCA1 (n = 202)	BRCA2 (n = 217)	All BRCA+ (n = 419)	All BRCA- (n = 694)	p Value		Untested population (n = 127,051)
					BRCA+ vs BRCA-	BRCA+ vs untested	
Pancreatic cyst, n (%)	6 (3)	9 (4)	15 (4)	18 (3)	0.35	0.62	4,012 (3)
Worrisome or high-risk feature, n (%)	1 (17)	2 (22)	3 (20)	6 (33)	0.64	-	-
Pancreatic cancer, n (%)	1 (17)	1 (11)	2 (13)	4 (22)	0.84*	-	-

* BRCA+ vs BRCA- (with cysts and pancreatic cancer).

Table 4.

Pancreatic Cancer in BRCA-Tested Patients with and without Pancreatic Cysts

Variable	BRCA1	BRCA2	All BRCA+	All BRCA-	Total BRCA-tested	p Value*
Pancreatic cancer, n (%)	1 (17)	1 (11)	2 (13)	4 (22)	6 (18.2)	<0.001
With cyst, n	6	9	15	18	33	<0.001
Pancreatic cancer, n (%)	3 (1.5)	13 (6.3)	16 (4.0)	10 (1.5)	26 (2.4)	<0.001
Without cyst, n	196	208	404	676	1,080	<0.001

* Patients with cysts who developed pancreatic cancer vs pancreatic cancer in patients without cysts (total BRCA-tested).