

Original Article

A multi-disciplinary cancer program enhances hereditary colorectal cancer detection

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Abstract: Introduction: Five to ten percent of all colorectal cancers are related to an inherited syndrome and are often unrecognized. Collaborative clinical programs have the potential to increase the identification of hereditary colorectal cancer, by providing a systems-based approach to screening and detection. In 2010, a Multidisciplinary Colorectal Cancer Program was established with the goal of coordinating and standardizing the care of colorectal cancer patients at our institution. Prior to this program, no formalized system existed to identify at-risk patients. After 2010, all encountered patients were screened using National Comprehensive Cancer Network (NCCN) guidelines and high-risk patients were automatically referred for genetic counseling. Our goal was to determine the short-term impact of this program on the detection of hereditary colorectal cancer at our institution. Methods: This was an IRB-approved study that examined data from an Institutional Inherited Cancer Registry. Results: From 3/2003-1/2010, prior to the Colorectal Cancer Program, 114 patients were referred for genetic counseling and testing at our institution. Of the 114 patients, 96 patients underwent testing, leading to the identification of 32 (33.33%) patients with an inherited colorectal cancer syndrome (ICCS). Over this 7-year period, an average of 4.7 patients was diagnosed with an ICCS per year. From 2/2010-7/2013, following the establishment of this Program, 94 patients met NCCN guidelines and were referred for genetics counseling and testing. This led to the identification of 31 (32.98%) patients with inherited colorectal cancer syndromes over a 3.5-year period, an average of 9.0 patients per year. We found no statistically significant ICCS prevalence changes ($P=1.000$). However, the estimated yearly-identified ICCS in 2010, 2011, 2012 and 2013 were 5, 8, 8 and 17, respectively, suggesting a time associated improvement in detection of ICCS ($P=0.00363$). Conclusions: Implementation of a Multi-Disciplinary Colorectal Cancer Program led to an immediate and significant increase in genetic counseling referrals without ICCS prevalence changes, and a steady increase in inherited colorectal cancer detection over time. Improvements in systems processes can increase the quality of colorectal cancer care that is being provided.

Keywords: Colon cancer, genetic counseling, genetic testing, hereditary, multi-disciplinary cancer program

Introduction

It is estimated that 10-15% of all colorectal cancers are familial and 5% are associated with a known hereditary syndrome [1]. As the third most common cancer and second-leading cause of cancer-related death in the US, colorectal cancer accounts for roughly 140,000 new cases of colorectal cancer nationally each year, of which roughly 7000 are caused by a hereditary syndrome [2]. Identifying patients at risk for a hereditary syndrome is an essential component of any comprehensive cancer evaluation, with significant implications for patients

and their families. Unfortunately, hereditary syndromes often go undiagnosed without careful screening and testing.

The impact of a multi-disciplinary cancer program on the quality of cancer care has been well documented [3, 4]. For these reasons, a Colorectal Cancer Program was established at our institution, a tertiary academic medical center, in February 2010. This is a multi-specialty group that includes colorectal surgery, gastroenterology, medical oncology, pathology, radiology, radiation oncology, and a dedicated genetic counselor. Prior to the establishment of the

- Colorectal cancer diagnosed prior to age 50.
- Two or more separate colorectal and/or other cancers at any age.
- Colorectal cancer with abnormal tumor markers (MSI/IHC).
- Personal history of colorectal cancer and two or more first or second degree relatives with colorectal cancer or any other Lynch cancer (endometrial, ovarian, renal pelvis, stomach).
- History of >10 adenomas (colon polyps).
- Family history of inherited colorectal cancer syndrome such as HNPCC or FAP or a close relative meeting any of the above criteria.

Figure 1. The NCCN guidelines for inherited colorectal cancer screening.

program, genetics counselors were present at our institution and available for referrals but were not engaged in the screening process. A multi-disciplinary conference was held weekly to discuss patients that were referred into the program. While independent referrals were not impacted by the program, the major difference was that all patients who were referred to the Colorectal Surgery service for evaluation of colon polyps or cancer were automatically discussed at the weekly meeting. The goal of our program was to coordinate and standardize all phases of care, which ranged from screening to peri-operative management of patients with colorectal cancer.

A major emphasis of this program was to improve the identification of patients with hereditary colorectal cancer syndromes. Prior to the initiation of our program, patients were referred for genetics counseling and testing at the discretion of individual physicians. No systematic screening program was in place to determine which patients should be considered for testing. With the establishment of a multi-disciplinary colorectal cancer program, all patients with high-risk features, or with a diagnosis of colorectal cancer, were enrolled in this program and were discussed at a weekly multi-disciplinary conference. Risk factors were identified through all phases of their care, and included young age, family history, significant endoscopic findings such as multiple polyps, and post-operative pathologic testing. Patients who met criteria based on NCCN guidelines (**Figure 1**) were referred for genetic counseling and testing. The purpose of this study was to determine whether the implementation of a dedicated colorectal cancer program had any short-term impact on the rates of genetics counseling referrals and the identification of hereditary syndromes at our institution.

Methods

This was an Institutional Review Board (IRB)-approved study that examined both prospectively and retrospectively collected data from 2003 through 2013. The data of the patients that were referred for genetic counseling or testing were recorded through a database maintained by genetics counselors at our institution as part of an Inherited Cancer Registry, which began in 2003. All patients that

were referred for genetics counseling and testing were recorded in this database. A formal multi-disciplinary colorectal cancer program was established at our institution in February 2010. The number of patients referred to genetics counselors, and the outcomes of their testing, were compared before and after the initiation of the program. This included patients who were referred for genetic counseling who did not have a personal history of colorectal cancer but otherwise met criteria based on a strong family history or suspicious endoscopic findings.

Statistical analysis of the prevalence rates of inherited colorectal cancer syndromes over the time period studied, along with an analysis of annualized detection rates at our institution, was performed using the Chi-square test.

Results

Prior to the establishment of the Colorectal Cancer Program, a total of 114 patients were referred for genetic counseling and testing from 2003-2010 (**Table 1**). These included patients who were referred by their primary care or specialist physician based on a family history, or based on concerning endoscopic findings. This non-systematic approach led to an average of 16.9 referrals per year for genetic counseling over this 7-year time period. Of the 114 patients, 96 patients were tested for the following inherited colorectal cancer syndromes: hereditary non-polyposis colorectal cancer (HNPCC), familial adenomatous polyposis (FAP), and MYH-associated polyposis (MAP). This led to the identification of 32 (33.33%) patients with an inherited colorectal cancer syndrome. Seventeen patients were diagnosed with HNPCC, thirteen patients with FAP, and two patients with MAP, and these patients were

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Table 1. Comparison of rates of genetics referrals and hereditary cancer syndrome identification pre- and post-establishment of a colorectal cancer program in 2010

	#patients referred for genetics counseling/testing (yearly mean)	#patients identified with a hereditary syndrome (yearly mean)
3/03-1/10 (pre-program)	114 (16.9)	32 (4.7)
2/10-7/13 (post-program)	94 (27.5)	31 (9.0)

Table 2. Steady increase in detection of inherited colorectal cancer over time after establishment of the Multi-Disciplinary Colorectal Cancer Program

Year	Months included in the study	Case	Estimated yearly case	P value
2010	10	4	5	0.00363
2011	12	8	8	
2012	12	8	8	
2013	7	11	17	

subsequently enrolled in an Inherited Colorectal Cancer Registry. Over this 8-year period, an average of 4.7 patients was diagnosed with an inherited colorectal cancer syndrome per year.

From 2010-2013, following the establishment of this program, 94 patients were identified as meeting NCCN guidelines and were referred for genetics counseling and testing. This led to an average of 27.5 referrals per year for genetic counseling over this 3.5-year time period, an increase of over 10 patients per year. This led to the identification of 31 (32.98%) patients with inherited colorectal cancer syndromes (**Table 1**), an average of 9.0 patients per year.

We found no statistically significant ICCS prevalence rate changes (33.33% vs 32.98%, $P=1.000$). However, the estimated yearly-identified ICCS in 2010, 2011, 2012 and 2013 were 5, 8, 8 and 17, respectively, suggesting a time associated improvement in detection of ICCS (**Table 2**, Chi-square test, $P=0.00363$).

The male to female ratio was 1:1.1. Ages ranged from 19 to 84, with a mean age of 45 and a median age of 45. Twenty-seven out of the 31 patients (87%) had a positive family history of colorectal cancer. Thirteen patients (42%) did not have a personal history of colorectal cancer and were evaluated solely based on a concerning family history. Of the patients with a personal history of malignancy or polyposis, cancers were predominantly located more proximally and were found in the following locations: right colon (9), transverse colon (3), sigmoid colon (2), rectum (1), synchronous transverse

and left (1), synchronous right and transverse (1), diffuse polyposis (1). Twenty-seven patients were diagnosed with HNPCC, two patients with FAP, and 1 patient with MAP (**Table 3**).

Discussion and conclusion

Multi-disciplinary cancer programs have been shown to lead to demonstrable improvements in processes and outcomes of care [5, 6]. A multi-disciplinary colorectal cancer program was established at our institution in February 2010, with the goal of coordinating and standardizing care of the colorectal cancer patients, and patients at-risk for the development of colorectal cancer. As part of this program, there was a major effort to develop an Inherited Colorectal Cancer Registry, and to identify patients at risk for a hereditary syndrome. The program was anchored by a designated nurse coordinator, and not only included colorectal cancer specialists but also a dedicated genetics counselor. This team evaluated all patients that entered our program and shifted the responsibility of identifying at-risk patients from individual providers, who often had incomplete information, to a dedicated team of specialists.

In this study, the establishment of a multi-disciplinary colorectal cancer program led to an immediate and significant increase in the identification of hereditary syndromes at our institution. This increase occurred while the prevalence of inherited colorectal cancer syndromes remained unchanged over the time period studied. The impact of this program was quite dramatic, and resulted in better screening of both patients diagnosed with colorectal cancer, and patients who did not have a primary diagnosis of colorectal cancer but had a concerning family history or suspicious endoscopic findings. The ramifications of this are notable. The identification of a hereditary colorectal cancer syn-

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Table 3. Patients identified with a hereditary syndrome from 2010-2013

Appointment Date	Sex	Age at Diagnosis	Family History	Screening	Cancer Location	Type of Genetic Test	Test Result
2010	M	33	Positive	Yes	N/A	APC	APC+ (R332X)
2010	F	84	Positive	No	right colon	MYH	Apc Comp Neg, MYH G382D (1145G>A)
2010	F	42	Positive	Yes	screening N/A	HNPCC	MSH2+ (del exons 9-12)
2010	F	49	Positive	Yes	N/A	HNPCC	MSH2 VUS R534H (1601G>A)
2011	M	63	Negative	No	right colon	HNPCC	MSH6+ Y535X (1605C>G)
2011	F	54	Positive	No	synchronous transverse and descending; also uterine (age 38), renal (age 37), breast (age 64)	HNPCC	MSH2+ (1440delA)
2011	F	71	Positive	No	right colon	HNPCC	MLH1/PMS2 Comp. Neg., BRAF+ (V600E)
2011	M	55	Negative	No	transverse colon and esophagus	HNPCC	MSH6 VUS (L1201V 3601C>G); (R1242S 3724C>A)
2011	M	37	positive	No	sigmoid colon	HNPCC	PMS2+ (1112delATins4)
2011	F	29	Positive	Yes	N/A	HNPCC	MSH6+ (Y954X)
2011	M	45	Positive	No	polyposis	APC	APC+ (Y96X)
2011	M	19	Positive	Yes	N/A	HNPCC	MSH2+ (1906G>C)
2012	M	52	Positive	Yes	N/A	HNPCC	MSH2+ (1906G>C)
2012	M	28	Positive	No	transverse	HNPCC	MLH1+ (IVS5-1 G>C)
2012	F	26	positive	Yes	N/A	HNPCC	MSH2+ (186_187dupGG)
2012	M	26	Positive	No	Rectal	HNPCC	MSH2+ (S743X 2226C>G)
2012	M	19	Positive	Yes	N/A	HNPCC	MLH1+ (large deletion exons 3-4)
2012	F	45	Positive	Yes	N/A	HNPCC	MLH1/MSH2/MSH6 Comp Neg, EPCAM seq Neg, PMS2 VUS (H479Q)
2012	M	66	Positive	Yes	N/A	HNPCC	PMS2+ (1112delATins4)
2012	F	28	Positive	No	right colon	HNPCC	MSH2+ (del exons 4-6)
2013	M	45	positive	No	sigmoid colon	HNPCC	MSH2+ (IVS5+3A>T)
2013	F	55	Positive	No	cecum	HNPCC	MSH2+ (IVS5+3A>T)
2013	M	50	Positive	No	transverse	HNPCC	PMS2+ (R315X- deletion)
2013	M	60	Negative	No	right colon	HNPCC	MSH6 gene mutation
2013	F	22	Positive	Yes	N/A	HNPCC	MLH1 (1790delGGins9) mutation
2013	F	67	Positive	No	right colon	HNPCC	MSH2+ (c. 1786_1788delAAT)
2013	F	37	Negative	No	right colon	HNPCC	MSH2+ (EX3_15dup)
2013	F	69	Positive	No	right and transverse	HNPCC	hMLH-1 Absent
2013	F	41	Positive	Yes	N/A	HNPCC	MLH1 (IVS8-3T>A (c.678-3T>A)
2013	F	29	Positive	Yes	N/A	HNPCC	MSH2 deletion (Promotor_EX2del)
2013	M	49	Positive	No	right colon	HNPCC	MLH1 gene mutation

drome not only affects colorectal cancer treatment for the individual patient, but also affects the screening and treatment of other associated cancers that can affect multiple organs including the uterus, ovaries, small intestine, stomach, pancreas, and urinary tract. The impact also extends to generations of their family members, who may not have been aware of their cancer risk and may need to be counseled and screened as well.

The implementation of strategies aimed at increasing the identification of patients with a hereditary syndrome includes a careful and complete family history, and the identification of high-risk patient and tumor characteristics. These are often difficult for the individual provider to identify due to a lack of time for assessment, inadequate knowledge or awareness by the non-specialist physician, or a lack of follow up on data such as microsatellite instability (MSI) status, which is typically not available for weeks after the pathology results are made final. With a multi-disciplinary program, all patients were discussed at a weekly conference attended by specialists in this field and follow up of all patients and pathologic findings were discussed. Following the establishment of our program, we noticed a steady increase in the number of identified cases at our institution over time, with an annualized rate of identification that increased from 5 in 2010 to 17 in 2013.

Universal testing for mutations in DNA mismatch repair genes (MLH1, MSH2, MSH6, PMS2), which can be assessed by microsatellite instability (MSI) testing or immunohistochemical (IHC) staining, have been advocated for some time. Though universal MSI testing of all colorectal cancer pathology specimens was initiated at our institution in 2009, we did not see an increase in the diagnosis of HNPCC at our institution until after the development of our multi-disciplinary colorectal cancer program. This suggests that universal MSI testing is not sufficient without effective multidisciplinary communication and follow up, which was demonstrated in a previous study [7].

In conclusion, implementation of a multi-disciplinary colorectal cancer program was associated with an immediate and significant increase in the identification of hereditary colorectal cancer syndromes at our institution. The rea-

sons for this are multiple but likely include better identification of high-risk individuals and improved follow up of pathologic findings. Improvements on a system-wide level to integrate and standardize processes-of-care can directly impact the quality of cancer care.

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