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A familial component to human rectal cancer, independent of colon cancer risk

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Abstract

Background & Aims: The Utah Population Database (UPDB) is unique; it links genealogy for over 2 million Utah individuals to a statewide Cancer Registry. We have investigated the familial nature of rectal cancer, considered independently from colon cancer.

Methods: We estimated relative risks in relatives, and average relatedness among rectal cancer cases using matched controls from the UPDB.

Results: There is a significant increased risk for rectal cancer in first-degree relatives of rectal cancer cases (Relative Risk = 1.97), equivalent to the risk for colon cancer (RR = 2.11). The significant increased risk for rectal cancer extends to second- and third-degree relatives. The relative risk for rectal cancer among first-degree relatives of young-onset rectal cancer cases (< 55 years), is equivalent (RR = 3.34) to their risk of colon cancer (RR = 3.35).

Conclusions: The UPDB provides strong evidence for a familial component to rectal cancer that may include a genetic component in addition to shared environment. There is a significant increased risk of rectal cancer in the close and distant relatives of rectal cancer cases, which is even higher among relatives of young-onset cases. While it has been reported that relatives of colon cancer probands are at increased risk for colorectal cancer, the risk of large bowel cancer among relatives of rectal cancer patients has been less clear. Relatives of rectal cancer probands experience a risk of cancer of the large bowel that is at least as high as the risk previously reported for relatives of individuals with colon cancer.

INTRODUCTION

Of the projected nearly 150,000 new cases of large bowel cancer to be diagnosed in the U.S. in 2007, approximately 42,000 will be due to rectal cancer. Colon and rectal cancers combined will cause more than 55,000 deaths in the U.S. in 2007, accounting for approximately 10% of cancer deaths in this country¹. Inherited predisposition is recognized as a common risk factor for colorectal cancer. First-degree relatives of those with colorectal cancer exhibit a two- to three-fold increased risk for large bowel cancer;^{2,3,4,5,6,7} we observe similar risks in the UPDB. Colorectal cancers are usually considered as a group, rather than independently. Rectal cancer, however, is typically considered to have a less familial component than tumors occurring in the colon. Estimates for the relative risk of rectal cancer among first-degree

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relatives of colorectal cancer probands range from 0.98 to 1.89.^{7,8,9} Underestimation of this risk may affect the assiduity of screening for a potentially curable malignancy.

In this study, we use the unique Utah Population Database to explore the familial component of rectal cancer. The UPDB resource includes genealogical data representing up to 10 generations of the Utah pioneers and their descendants, representing approximately 2.2 million individuals, of whom approximately 90,000 have a cancer record in the Utah Cancer Registry (UCR) since 1966. We utilize this unique resource to define the familial nature of rectal cancer considered independent from other malignancies of the large bowel.

MATERIALS AND METHODS

Utah Population Database

The UPDB is a computerized archive that combines genealogy data originally contributed by the Family History Library of Utah, with Utah death certificate data since 1904 contributed by the Utah Department of Health, and cancer records since 1966 contributed by the Utah Cancer Registry.¹⁰ The Utah Cancer Registry contains records on all of the individuals with cancer diagnoses in Utah since 1966; it has been an NCI SEER (Surveillance, Epidemiology, and End Results Program of the National Cancer Institute Registry) since 1973. Cancer records in the Utah Population Database include information on site, stage, grade, age at diagnosis, and survival. Care is taken within the Cancer Registry to ensure that in the case of multiple cancers in one individual, only independent primary sites of cancer are reported. All of the data for this study was gathered with the approval of the University of Utah Institutional Review Board.

The UCR records have been record-linked to individual Utah genealogical records, allowing the relationships of individuals with cancer to be assessed.¹⁰ Over 50% of all Utah Cancer Registry records link to an individual in the genealogy; females have lower record linking rates than males due to name changes. The original Utah Mormon (The Church of Jesus Christ of Latter-day Saints or LDS) pioneers, who began arriving in Utah in 1847, were largely unrelated; the Utah population continues to have lower inbreeding than other areas in the United States.¹¹

The Mormons have strong proscriptions against the use of coffee, tea, alcohol and tobacco, and adherence is high. The association of some of these dietary components with attendant risks for cancer may partially explain lower cancer rates observed in Utah. For all malignancies combined, the standardized incidence ratios for cancer in Utah Mormons are 73 for males and 76 for females (with 100 being the nationwide value) whereas the corresponding values for Utah non-Mormons are 106 and 115.^{12,13}

Assessment of Cancer Risk

Evidence for a familial or genetic contribution to disease can be evaluated by estimating relative risk in relatives. Published relative risks for cancer in relatives are typically limited to close relationships (first-degree) and are estimated by comparison to population rates of disease. We estimate relative risks in both close and distant relatives in the UPDB, utilizing birth- and sex-specific cohort rates of cancer estimated internally from the UPDB as follows: All 2.2 million individuals in the UPDB genealogy were assigned membership in one of 132 birth year-, sex-, and birthplace-specific (Utah or not Utah) cohorts. Internal, cohort-specific rates of colon, rectal, and colorectal cancer were calculated for all 132 birth cohorts separately, by summing the number of individuals with the selected cancer in each cohort, and dividing by the total number of individuals in the cohort. Expected numbers of cancer cases for a set of individuals (e.g. first-degree relatives of rectal cancer cases) were estimated by counting all first-degree relatives of the set of rectal cancer cases by cohort, multiplying the number of relatives per

cohort by the cohort-specific cancer rate, and then summing over all 132 cohorts. The observed numbers of rectal cancer cases by site were counted, without duplication, in the set of relatives being considered. Relative Risk = observed/expected is an unbiased estimator of relative risk (also termed standardized morbidity rate), and can be calculated for multiple different relationships. One-sided probabilities for the alternative hypothesis test of relative risk > 1.0 were calculated under the null hypothesis relative risk = 1.0, under the assumption that the number of observed deaths follows a Poisson distribution with mean equal to the expected number of deaths. We have previously presented the data and methods used here to describe the familial and genetic contribution to multiple different diseases;^{14,15,16,17} a similar approach has been used for analysis of the similar Icelandic genealogical resource¹⁸.

Rectal and Colon Cancer Probands

Colon cancer is defined as cancer of the large intestine, excluding the rectum. Rectal cancer includes only primary malignancies involving the rectum. No rectal cancer cases in the UPDB had histology consistent with familial adenomatous polyposis. Young-onset rectal cancer is defined as a primary cancer diagnosed before the age of 55 years. Within the set of 2.2 million Utah individuals with at least 3 generations of genealogy data, there are 6,962 colon cancer cases and 2,684 rectal cancer cases. Of these, there are 798 colon cancer cases and 370 rectal cancer cases diagnosed before the age of 55 years.

Genealogical Index of Familiality

The genealogical index of familiality (GIF) statistic allows a test of the hypothesis of excess relatedness among disease cases in the UPDB.^{19, 20, 21} The GIF compares the pairwise average relatedness of a set of diseased individuals (cases) to the same measure in matched controls, using a coefficient of kinship to measure relatedness.²² Randomly selected controls are matched to cases by sex, 5-year birth cohort, and birth place (Utah or not Utah). The average relatedness is computed for 1,000 independent sets of matched controls, and the significance of the case GIF is assessed empirically by its position within the 1,000 control values.

RESULTS

Relative Risk in Relatives

We have estimated relative risks for rectal cancer in first-, second-, and third-degree relatives of rectal cancer cases. These are compared to relative risks for colon cancer among these same relatives. Table 1 shows the relative risk (RR) estimates for both rectal cancer and colon cancer among the first-degree relatives of the 2,684 rectal cancer cases that have genealogical records in the UPDB. The number of cases observed and expected among the relatives is shown, with the estimated relative risk, the significance of the test of the alternative hypothesis of $RR > 1.0$, and 95% confidence interval.

First-degree relatives of rectal cancer cases have a significantly increased risk of cancer throughout the colon and rectum. The relative risk for rectal cancer among first-degree relatives of rectal cancer patients is not significantly different from the risk for colon cancer among these relatives. Other studies have reviewed the risk of colon and rectal cancer by estimating risk from cohorts of patients diagnosed with colorectal cancer. These studies generally show that rectal cancer is less familial than colon cancer.^{23,24,25,26,27,28,29}

We also estimated the risks for rectal cancer and for colon cancer among second- and third-degree relatives of rectal cancer cases. Table 2 shows the relative risk estimates for rectal cancer and for colon cancer among the 82,945 second-degree relatives of the 2,684 rectal cancer cases. Table 3 shows the relative risks for rectal cancer and for colon cancer among the 158,435 third-degree relatives of the rectal cancer cases. Risks for both rectal cancer and colon cancer are

significantly increased in both the second- and third-degree relatives of rectal cancer cases, and are not significantly different from second and third degree risks for colon cancer in these individuals. No other studies have investigated risks in second- or third-degree relatives of rectal cancer cases.

It is well recognized for many cancer sites that relative risks are higher among the relatives of young cases. We have also estimated relative risks for colon and rectal cancer among the relatives of rectal cancer cases diagnosed before age 55 years. Table 4 shows the relative risk estimates for rectal cancer and colon cancer among the first-degree relatives of the 370 young rectal cancer cases with genealogical records in the UPDB (diagnosed < 55 years).

The relative risk of rectal cancer among the first-degree relatives of young rectal cancer cases (RR=3.34) is much higher than the risk of rectal cancer in first-degree relatives of all rectal cancer cases (RR=1.97), and is equivalent to the risk of colon cancer in these relatives. Published risk estimates for colorectal cancer among first-degree relatives of young colorectal cancer cases range from 4.36 to 5.37.^{23,2325,26} In the UPDB the risk of colorectal cancer in the first degree relatives of colorectal cancer cases is 2.79; 95%CI (2.41, 3.21).

Table 5 shows relative risk estimates for rectal cancer and for colon cancer among the 9,572 second-degree relatives of the 370 young rectal cancer cases. The relative risk for rectal cancer is increased among the second-degree relatives of young rectal cancer cases, but does not reach statistical significance (RR = 1.40, p = 0.07), while the risk for colon cancer in these relatives is increased significantly (RR=1.32, p = 0.03).

Genealogical Index of Familiality

We tested the hypothesis of no excess relatedness among the rectal cancer cases using the Genealogical Index of Familiality (GIF) statistic. Table 6 shows the average relatedness of the cases, the average relatedness estimated from 1000 sets of matched controls, and the empirical test of significance for the hypothesis for the rectal cancer cases. For purposes of comparison, we also show the average relatedness of the 6,962 colon cancer cases. Table 7 shows the results of the GIF analysis for young rectal and young colon cancer.

Figures 1 and 2 show the contribution to the GIF statistic by the genetic distance between pairs of relatives, for cases compared to controls; for rectal cancer (figure 1) and for colon cancer (figure 2). Both cancers show the same pattern, with excess relationships of cases over controls for first-, second- and third-degree relatives (genetic distances 1 - 4), but no excess observed for more distant relatives (genetic distances > 4).

DISCUSSION

Many published studies have established the familial nature of colorectal cancer and estimated the risk associated with positive family history among relatives of individuals diagnosed with colon and colorectal cancer.^{23,24,25,2627,28,29,30} Generally, rectal cancer is considered to confer less familial risk.^{27,29,30} Using the UPDB resource, we have shown that rectal cancer should be considered to have a strong familial component, and that the risk of malignancy associated with rectal cancer extends throughout the colon and rectum. The risk is comparable to that associated with a family history of colon cancer.

The UPDB resource allows nearly complete, unbiased ascertainment of all cancer cases in the state of Utah through the contributions of the Utah Cancer Registry data. Greater than 50% of these Utah cancer records link to individuals who also have genealogical data. This decades-long ascertainment of cancer in the state, coupled with the extensive genealogy representing the population of Utah, allows estimation of the risk of cancer for both close and distant family

relationships, and avoids the ascertainment and recall bias inherent in “cancer family” studies or studies relying on self-report of cancer family history.

A genetic component to rectal cancer is supported by several findings of this study. First, the risk of rectal cancer in first-, second-degree and third-degree relatives of rectal cancer cases is significantly increased. Many consider an excess risk to first-degree relatives to provide evidence of a genetic component to disease. In fact, such an excess could also be observed for a disease with a strong environmental component, since these individuals likely share many lifestyle factors. A significant excess observed in second- and third-degree relatives, on the other hand, provides very strong evidence for a genetic component, since such relatives typically share a less common environment and lifestyle than first-degree relatives.

Second, a heritable component of disease is commonly associated with a younger age of disease onset. We observed significantly increased relative risks among the first-degree relatives of young-onset rectal cancer cases. These risks were almost double the risks observed in relatives of all rectal cancer cases. Similar increased risks for both rectal cancer and colon cancer were also observed for the second-degree relatives of the young-onset rectal cancer cases, though the risk was not statistically significantly elevated for rectal cancer. The GIF analysis of familiarity for all rectal cancer cases also showed significant excess relatedness over expected ($p < 0.001$), with an observed excess of both close and distant relationships (Figure 1). This observation was similar to the pattern observed for colon cancer. The GIF for young-onset rectal cancer also showed significant excess relatedness.

We include relative risks and GIF calculations for colon cancer in addition to those for rectal cancer to allow comparisons of our resource to others, as well as to better understand the association of colon and rectal cancers. In the UPDB, the relative risk of colon cancer among first-degree relatives of colon cancer probands is 2.21 (95% CI 2.08-2.35). This estimate of risk is consistent with prior published estimates and demonstrates that the UPDB is not overestimating risk in these individuals.

In a smaller study, with 746 Icelandic rectal cancer cases, Stefansson et al (2006) reported that risk of rectal cancer was only increased among brothers, not sisters, of rectal cancer patients, and that the increased risk observed in first-degree relatives was due to increased risk in siblings only.³⁰ Although data are not shown, we observed significantly elevated risks of rectal cancer for all types of first-degree relatives of rectal cancer cases (children, siblings, parents, and separately for brothers and sisters).

In summary, this study uses the unique UPDB resource to examine the familial nature of rectal cancer. We have estimated relative risks in relatives and evaluated average relatedness among rectal cancer cases to assess the familial nature of rectal cancer. We have shown that the presence of rectal cancer in a relative confers a significantly increased risk of cancer in all areas of the large bowel, consistent with risks previously associated with colon cancer. The risk for rectal cancer in the first-degree relatives of young-onset rectal cancer cases is similar to the risks usually associated with young-onset colon and colorectal cancer. This risk warrants attention for screening strategies aimed at decreasing the risk of colorectal cancer in general. Further, due to the low frequency of known genetic syndromes conferring increased risk for rectal cancer in the population studied, our findings may suggest the presence of an independent genetic component for this disease. Multiple high-risk rectal cancer pedigrees have been identified in the UPDB resource and study of these high-risk pedigrees will allow increased understanding of rectal cancer predisposition.

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References

1. American Cancer Society. <http://www.cancer.org/docroot/home/index.asp>
2. Jemal A, Tiwari RC, Murray T, Ghafoor A, Samuels A, Ward E, Feuer EJ, Thun MJ. American Cancer Society Cancer Statistics 2004. *CA Cancer J Clin* Jan-Feb;2004 54(1):8–29. [PubMed: 14974761]
3. Woolf CM. A genetic study of carcinoma of the large intestine. *Am J Hum Genet* 1958;10:42. [PubMed: 13520697]
4. Lovett E. Family studies in cancer of the colon and rectum. *Br J Surg* 1976;63:13–18. [PubMed: 1267868]
5. Macklin MT. Inheritance of cancer of the stomach and large intestine in man. *J Natl Cancer Inst* 1960;24:551–571. [PubMed: 14419545]
6. Duncan JL, Kyle J. Family incidence of carcinoma in the colon and rectum in northeast Scotland. *Gut* Feb;1982 23:169–171. [PubMed: 7068040]
7. Potter JD. Colorectal cancer: molecules and populations. *J Natl Cancer Inst* 1999;91:916. [PubMed: 10359544]
8. Andrieu N, Launoy G, Guillois R, Ory-Paoletti C, Gignoux M. Estimation of the Familial Relative Risk of Cancer by Site from a French Population Based Study on Colorectal Cancer. *Gut* Sept;2004 53(9):1322–8. [PubMed: 15306593]
9. Slattey ML, Levin TR, Ma K, Goldgar D, Holubkov R, Edwards S. Family History and Colorectal Cancer: Predictors of Risk. *Cancer Causes and Control* Nov;2003 14(9):879–87. [PubMed: 14682445]
10. Skolnick, M. The Utah genealogical database: a resource for genetic epidemiology. In: Cairns, J.; Lyon, JL.; Skolnick, M., editors. *Banbury Report No 4; Cancer Incidence in Defined Populations*. Cold Spring Harbor Laboratory; New York: 1980. p. 285–97.
11. Jorde LB. Inbreeding in the Utah Mormons: an evaluation of estimates based on pedigrees, isonymy, and migration matrices. *Ann Hum Genet* 1989;53:339–355. [PubMed: 2624429]
12. National Research Council. *Diet, Nutrition and Cancer*. National Academy Press; Washington, DC: 1982. Committee on Diet, Nutrition and Cancer.
13. Lyon, JL.; Gardner, JW.; West, DW. Cancer risk and life-style: Cancer risk among Mormons from 1967–1975. In: Cairns, J.; Lyon, JL.; Skolnick, MH., editors. *Cancer Incidence in Defined Populations, Banbury Report 4*. Cold Spring Harbor Laboratory; New York: 1980. p. 3–30.
14. Cannon-Albright LA, Thomas A, Goldgar DE, Gholami K, Rowe K, Jacobsen M, McWhorter WP, Skolnick MH. Familiality of cancer in Utah. *Cancer Res* May 1;1994 54(9):2378–85. [PubMed: 8162584]
15. Allen-Brady K, Camp NJ, Ward JH, Cannon Albright LA. Lobular Breast Cancer: Excess Familiality Observed in the Utah Population Database. *Int J Cancer* 2005;117(4):655. [PubMed: 15929077]
16. Cannon Albright LA, Camp NJ, Farnham JM, MacDonald J, Abtin K, Rowe KG. A Genealogical Assessment of Heritable Predisposition to Aneurysm. *J Neurosurg* Oct;2003 99(4):637–43. [PubMed: 14567597]
17. Horne BD, Camp NJ, Muhlestein J, Cannon Albright LA. Evidence for a Heritable Component in Death Resulting from Aortic and Mitral Valve Diseases. *Circulation* Nov 9;2004 110(19):3143–8. [PubMed: 15520309]
18. Sveinbjornsdottir S, Hicks AA, Jonsson T, Petursson H, Gudmundsson G, Firgge ML, Kong A, Gulcher JR, Stefansson K. Familial aggregation of Parkinson's disease in Iceland. *N Engl J Med* 2000;343:1765–70. [PubMed: 11114315]
19. Hill, JR. A kinship survey of cancer in the Utah Mormon population. University of Utah; Salt Lake City, Utah: 1980a. Ph.D. Thesis

20. Hill, JR. A survey of cancer sites by kinship in the Utah Mormon population. In: Cairns, J.; Lyon, JL.; Skolnick, M., editors. Banbury Report 4: Cancer Incidence in Defined Populations. 299. Cold Spring Harbor Laboratory; Cold Spring Harbor, New York: 1980b. p. 318
21. Cannon L, Bishop DT, Skolnick MH, Hunt S, Lyon JL, Smart C. Genetic epidemiology of prostate cancer in the Utah Mormon genealogy. *Cancer Surveys* 1982;1:1.
22. Malecot G. *Les Mathematiques de L'heredite*. Paris: Masson. 1948
23. John DJ, McDermott FT, Hopper JL, Debney EA, Johnson WR, Hughes ES. Cancer risk in relatives of patients with common colorectal cancer. *Ann Intern Med* 1993;118(10):785–90. [PubMed: 8470852]
24. Planck M, Anderson H, Bladstrom A, Moller T, Wenngren E, Olsson H. Increased cancer risk in offspring of women with colorectal carcinoma: a Swedish register-based cohort study. *Cancer* 2000;89(4):741–9. [PubMed: 10951335]
25. Johns LE, Kee F, Collins BJ, Patterson CC, Houlston RS. Colorectal cancer mortality in first-degree relatives of early-onset colorectal cancer cases. *Dis Colon Rectum* 2002;45(5):681–6. [PubMed: 12004220]
26. Fuchs CS, Giovannucci EL, Colditz GA, Hunter DJ, Speizer FE, Willett WC. A prospective study of family history and the risk of colorectal cancer. *N Engl J Med* 1994;331(25):1669–74. [PubMed: 7969357]
27. Newcomb PA, Taylor JO, Trentham-Dietz A. Interactions of familial and hormonal risk factors for large bowel cancer in women. *Int J Epidemiol* 1999;28:603–8. [PubMed: 10480684]
28. Sondergaard JO, Bulow S, Lynge E. Cancer incidence among parents of patients with colorectal cancer. *Int J Cancer* 1991;47:202–6. [PubMed: 1988364]
29. Kune GA, Kune S, Watson LF. The role of heredity in the etiology of large bowel cancer: data from the Melbourne Colorectal Cancer Study. *World J Surg* 1989;13:124–9. [PubMed: 2728462]
30. Stefansson T, Moller PH, Sigurdsson F, Steingrimsdottir E, Eldon BJ. Familial risk of colon and rectal cancer in Iceland: evidence for different etiologic factors? *Int J Cancer* Jul 15;2006 119(2):304–8. [PubMed: 16477631]

Figure 1. Contribution to the GIF statistic for 2,684 rectal cancer cases by genetic between pairs of relatives.

Figure 2. Contribution to the GIF statistic for 6,962 colon cancer cases by genetic path length between pairs of relatives.

Table 1
Relative risk for rectal cancer and for colon cancer among the 25,274 first degree relatives of the 2,684 rectal cancer cases.

Disease in Relative	Observed Cases	Expected Cases	Relative Risk	One-sided p value	Confidence Interval (95%)
Rectal cancer	150	76.0	1.97	< 0.0001	1.67, 2.32
Colon cancer	393	186.0	2.11	< 0.0001	1.91, 2.33

Table 2
Relative risk of rectal and colon cancers among the 82,945 second-degree relatives of the 2,684 rectal cancer cases.

Disease in Relative	Observed Cases	Expected Cases	Relative Risk	One-sided p value	Confidence Interval (95%)
Rectal	158	124.5	1.27	0.002	1.08, 1.48
Colon	413	313.6	1.32	<0.0001	1.19, 1.45

Table 3
Relative risk of rectal and colon cancers among the 158,435 third degree relatives of the 2,684 rectal cancer cases.

Disease in Relative	Observed Cases	Expected Cases	Relative Risk	One-sided p value	Confidence Interval (95%)
Rectal	417	359.8	1.16	0.002	1.05, 1.28
Colon	1016	906.9	1.12	0.0002	1.05, 1.19

Table 4
Relative risk of rectal and colon cancers among the 3,037 first degree relatives of the 370 rectal cancer cases diagnosed age < 55 years.

Disease in Relative	Observed Cases	Expected Cases	Relative Risk	p value	Confidence Interval (95%)
Rectal	22	6.6	3.34	< 0.0001	2.09, 5.06
Colon	50	14.9	3.35	< 0.0001	2.49, 4.42

Table 5 Relative risk of rectal and colon cancers among the 9,572 second-degree relatives of the 370 young rectal cancer cases.

Disease in Relative	Observed cases	Expected Cases	Relative Risk	One-sided p value	Confidence Interval (95%)
Rectal	24	17.1	1.40	0.07	0.90, 2.09
Colon	57	43.5	1.31	0.03	0.99, 1.70

Table 6

Genealogical Index of Familiality analysis for rectal cancer and colon cancer

Disease	Number of Cases	Empirical p value	Case Gif	Mean Control Gif
Rectal	2,684	<0.001	3.27	2.95
Colon	6,962	<0.001	3.31	2.93

Table 7

Genealogical Index of Familiality test for rectal cancer and colon cancer.

Disease	Number of Cases	Empirical p value	Case Gif	Mean Control Gif
Rectal < 55 yrs	370	< 0.001	4.03	2.83
Colon < 55 yrs	798	< 0.001	4.84	2.84