Colorectal Neoplasia among Patients with and without Human Immunodeficiency Virus

Adil Faqih[1], Amit G. Singal[1,2,3], Hannah M. Fullington[2], Benjamin Hewitt[1], Ezra Burstein[1,3], Purva Gopal[3,4], Annika Wylie[5], John Abrams[3,5], and Caitlin C. Murphy[1,2,3]

ABSTRACT

Background: Increasing availability of highly active antiretroviral therapy (HAART) for human immunodeficiency virus (HIV) has led to prolonged survival and rising incidence of non-HIV–defining cancers among patients with HIV. Compared with the general population, risk of colorectal cancer may differ among those with HIV due to immunosuppression, oncogenic viral coinfections, and higher prevalence of risk factors.

Methods: We identified patients (age ≥50 years) diagnosed with HIV, prescribed HAART for ≥6 months, and receiving care in two large health care systems in Dallas, TX. Patients received a first colonoscopy between January 2009 and December 2017. We calculated a standardized prevalence ratio as the ratio of observed to expected number of advanced neoplasia (high-risk adenoma or colorectal cancer) using an age- and sex-matched cohort of patients without HIV ($n = 10{,}250$).

Results: Among patients with HIV ($n = 839$), about two thirds (60.1%) had normal findings at colonoscopy; 6.8% had hyperplastic polyps only, 20.4% had low-risk adenomas, 11.7% had high-risk adenomas, and 1.1% had colorectal cancer. Prevalence of advanced neoplasia was similar between patients with and without HIV, with a standardized prevalence ratio of 0.99 (95% confidence interval, 0.81–1.19).

Conclusions: There was no difference in the prevalence of colorectal neoplasia between patients with and without HIV.

Impact: Patients with HIV appear to have similar risk of colorectal neoplasia compared to those without HIV and can therefore follow average-risk colorectal cancer screening guidelines.

Background

Since the introduction of highly active antiretroviral therapy (HAART), the population of persons with human immunodeficiency virus (HIV) has dramatically increased. HAART suppresses HIV viremia and has lowered incidence of acquired immune deficiency syndrome (AIDS)–defining illnesses and mortality. As a result, cancer and other chronic conditions have become significant causes of morbidity and mortality among persons with HIV; risk of cancer in this population may be higher compared with the general population due to immunosuppression, oncogenic viral coinfection, and higher prevalence of risk factors (1). For example, persons with HIV have higher incidence rates of Hodgkin lymphoma, lung, liver, and human papillomavirus–associated cancers (2). Persons with HIV may also be at higher risk for colorectal cancer (CRC) but prior studies conflict (3, 4). To address this gap in the literature, we (i) compared prevalence of advanced neoplasia among patients with HIV to an adult, non-HIV population, and (ii) identified correlates of advanced neoplasia among those with HIV.

Methods

Study setting and population

We identified screen-eligible patients (i.e., age ≥50 years, no prior colorectal cancer or colonoscopy) diagnosed with HIV and who received a first colonoscopy between January 1, 2009 and December 31, 2017 at Parkland Health & Hospital System and UT Southwestern Medical Center in Dallas, TX ($n = 1{,}526$). To avoid misclassification of HIV diagnosis (i.e., codes used for rule-out diagnoses; ref. 5), we restricted the sample to patients prescribed HAART for ≥6 months prior to colonoscopy ($n = 839$).

For comparison with a general population, we identified screen-eligible patients without HIV, who attended a primary care visit at Parkland or UT Southwestern and received a colonoscopy during the study period ($n = 10{,}250$).

We used a structured data form to collect information from colonoscopy and pathology reports, including polyp number, size, and histology (6). We categorized colonoscopy findings as: normal findings, hyperplastic polyps only, low-risk adenomas, high-risk adenomas, and colorectal cancer.

Statistical analysis

Our primary outcome was advanced neoplasia, defined as any high-risk adenoma (any adenoma with villous histology, high-grade dysplasia, or ≥10 mm, or ≥3 adenomas of any size or histology) or colorectal cancer. Given our sample size, we had 80% power to detect a 3.5% difference in advanced neoplasia between patients with and without HIV. We estimated a standardized prevalence ratio to compare prevalence in the two groups, accounting for differences in the distribution of age and sex.

To assess robustness of the standardized prevalence ratio, we used a logistic regression model to estimate the association of HIV and advanced neoplasia.

Finally, we used a logistic regression model to identify correlates of advanced neoplasia among patients with HIV. Correlates included age,

[1]Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas. [2]Department of Population & Data Sciences, University of Texas Southwestern Medical Center, Dallas, Texas. [3]Harold C. Simmons Comprehensive Cancer Center, Dallas, Texas. [4]Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas. [5]Department of Cell Biology, University of Texas Southwestern Medical Center, Dallas, Texas.

Corresponding Author: Caitlin C. Murphy, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75390. Phone: 214-648-9551; Fax: 214-648-3934; E-mail: caitlin.murphy@utsouthwestern.edu

Cancer Epidemiol Biomarkers Prev 2020;29:1689–91

doi: 10.1158/1055-9965.EPI-20-0021

sex, race/ethnicity, viral load (±200 copies/mL), CD4 count (cells per mm^3), and time on HAART.

Results

Characteristics of patients with ($n = 839$) and without ($n = 10,250$) HIV are shown in **Table 1**. About two thirds of patients with HIV (60.1%) had normal findings at colonoscopy; 6.8% had hyperplastic polyps only, 20.4% had low-risk adenomas, 11.7% had high-risk adenomas, and 1.1% had colorectal cancer.

Prevalence of advanced neoplasia was similar between patients with and without HIV [standardized prevalence ratio 0.99; 95% confidence interval (CI), 0.81–1.19; **Table 2**]. We observed similar results comparing prevalence of any neoplasia between the two groups (standardized prevalence ratio 0.95; 95% CI, 0.84–1.06). In the logistic regression model, HIV was not associated with advanced neoplasia, after adjusting for age, sex, race/ethnicity, and insurance (OR = 0.94; 95% CI, 0.76–1.18).

In correlates analysis, older age (≥60 years: OR, 1.95; 95% CI, 1.16–3.28) was associated with advanced neoplasia among patients with HIV. Viral load, CD4 count, and time on HAART were not associated with advanced neoplasia.

Discussion

Studies estimating risk of colorectal cancer and neoplasia among patients with HIV conflict, with some suggesting higher risk and others reporting no or small differences compared with the general population (3, 4). In a diverse cohort of patients, we observed no significant difference in the prevalence of advanced neoplasia between patients with and without HIV.

Some have hypothesized HAART reduces risk of certain cancers by mitigating consequences of derepressed retrotransposons associated with p53 mutations (7). However, in our study, time on HAART and other clinical factors (e.g., CD4 count, viral load) were not associated with advanced neoplasia among persons with HIV. Instead, traditional colorectal cancer risk factors, such as older age, were associated with a higher prevalence.

Although Dallas ranks high among U.S. cities by rate of HIV infection, our findings are limited to two health systems and may not be generalizable to the entire United States. We also limited the study population to screen-eligible patients, and the association between HIV and advanced neoplasia may differ in younger patients.

In summary, prevalence of advanced neoplasia did not differ by HIV infection. Combined with findings of others (8), our study underscores the importance of HIV-infected persons continuing colorectal cancer screening according to average-risk guidelines.

Table 1. Characteristics of patients with HIV ($n = 839$) and without HIV ($n = 10,250$) and who received colonoscopy, Parkland Health & Hospital System and UT Southwestern Medical Center, 2009–2017.

	Patients with HIV[a] ($n = 839$)		Patients without HIV ($n = 10,250$)	
	N	%	*N*	%
Age, median (IQR)	54 (51–59)		57 (53–61)	
Race/ethnicity				
Non-Hispanic white	302	36.0	1,698	16.7
Non-Hispanic black	367	43.7	3,607	35.4
Hispanic	152	18.1	4,235	41.5
Other	18	2.2	658	6.5
Sex				
Male	669	79.7	3,759	36.6
Female	170	20.3	6,494	63.4
Insurance				
Private/commercial	42	5.0	756	7.4
Medicare	382	45.5	959	9.4
Medicaid	128	15.3	1,265	12.4
County assistance	270	32.2	7,192	70.7
Other	17	2.0	78	0.8
CD4 count, median (IQR)	493 (329–711)		—	—
Viral load ≤200 copies/mL	784	93.4	—	—
Concurrent hepatitis B	112	13.4	—	—
Time on HAART				
6 months to <1 year	96	11.4	—	—
≥1 year to <3 years	304	36.2	—	—
≥3 years	439	52.3	—	—
Colonoscopy outcomes				
Normal findings	504	60.1	6,155	60.0
Hyperplastic polyps only	57	6.8	921	9.0
1–2 small (<1 cm) adenomas	171	20.4	2,114	20.6
Any large (≥1 cm) adenoma	36	4.3	458	4.5
>3 adenomas, any size	62	7.4	545	5.3
Colorectal cancer	9	1.1	57	0.6

[a]Patients with HIV also prescribed HAART for at least 6 months prior to colonoscopy.

Disclosure of Potential Conflicts of Interest

A.G. Singal is a consultant for Exact Sciences. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the official views of CPRIT or NIH.

Table 2. Standardized prevalence ratio comparing prevalence of advanced neoplasia among patients with HIV ($n = 839$) to patients without HIV ($n = 10,250$).

Strata	Stratum-specific prevalence (A)	Population size (B)	Expected cases (AxB)	Observed cases	Standardized prevalence ratio
Men, age 50–59 years	13.6	531	72	62	
Women, age 50–59 years	7.4	125	9	13	
Men, age ≥60 years	16.3	138	23	28	
Women, age ≥60 years	9.6	45	4	4	
Total	10.3	839	108	107	0.99 (0.81–1.19)

Authors' Contributions

Conception and design: A. Faqih, A.G. Singal, E. Burstein, A. Wylie, J. Abrams, C.C. Murphy
Development of methodology: A. Faqih, J. Abrams, C.C. Murphy
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): A. Faqih, H.M. Fullington, B. Hewitt, J. Abrams
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): H.M. Fullington, J. Abrams, C.C. Murphy
Writing, review, and/or revision of the manuscript: A. Faqih, A.G. Singal, H.M. Fullington, E. Burstein, P. Gopal, J. Abrams, C.C. Murphy
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): H.M. Fullington, B. Hewitt, J. Abrams
Study supervision: J. Abrams, C.C. Murphy

Acknowledgments

Research reported in this publication was supported by the Cancer Prevention Research Institute of Texas under award number PP160075 (to A.G. Singal) and the NCI of the NIH under award number P30CA142543.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received January 9, 2020; revised March 27, 2020; accepted May 19, 2020; published first May 28, 2020.

References

1. Deeken JF, Tjen-A-Looi A, Rudek MA, Okuliar C, Young M, Little RF, et al. The rising challenge of non-AIDS defining cancers in HIV-infected patients. Clin Infect Dis 2012;55:1228–35.
2. Hernandez-Ramirez RU, Shiels MS, Dubrow R, Engels EA. Cancer risk in hiV-infected people in the USA from 1996 to 2012: a population-based, registry-linkage study. Lancet HIV 2017;4:e495–e504.
3. O'Neill TJ, Nguemo JD, Tynan AM, Burchell AN, Antoniou T. Risk of colorectal cancer and associated mortality in HIV: a systematic review and meta-analysis. J Acquir Immune Defic Syndr 2017;75:439–447.
4. Bini EJ, Park J, Francois F. Use of flexible sigmoidoscopy to screen for colorectal cancer in HIV-infected patients 50 years of age and older. Arch Intern Med 2006; 166:1626–31.
5. Leibowitz AA, Desmond K. Identifying a sample of HIV-positive beneficiaries from Medicaid claims data and estimating their treatment costs. Am J Public Health 2015;105:567–74.
6. Murphy CC, Sigel BM, Yang E, Skinner CS, Halm EA, Gupta S, et al. Adherence to colorectal cancer screening measured as the proportion of time covered. Gastrointest Endosc 2018;88:323–31.
7. Wylie A, Jones AE, D'Brot A, Lu WJ, Kurtz P, Moran JV, et al. p53 genes function to restrain mobile elements. Genes Dev 2016;30:64–77.
8. Lam JO, Hurley LB, Udaltasova N, Alexeeff SE, Klein DB, Corley DA, et al. Colorectal cancer screening in people with and without HIV in an integrated health care setting. J Acquir Immune Defic Syndr 2019;81: 284–91.