

Colorectal cancer screening in human immunodeficiency virus population: Are they at average risk?

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Abstract

AIM: To evaluate if human immunodeficiency virus (HIV) population is getting adequate screening for colon cancer in the highly active anti-retroviral treatment (HAART) era with improved longevity, and the prevalence of polyps and adenomas in this population, when compared with the general population.

METHODS: We conducted retrospective chart review of average-risk HIV population for colon cancer attending our infectious disease clinic. Individuals who underwent diagnostic colonoscopy were excluded. We extracted various demographic, HIV disease-specific and colonoscopy data including histo-pathological reports in the last 10 years. Total population was divided into a study group, who underwent screening colonoscopy and a control group who did not. We analyzed data using standard statistical methods and software.

RESULTS: We found that 25% of average-risk HIV-infected population was screened for colon cancer using colonoscopy. There was no difference in gender and ethnic distribution between the groups. We found

wider distribution of age (50-84 years with mean 56 years) in the control group when compared to (50-73 years with mean 58 years) the study group. However, there were 89% of subjects with well-controlled HIV disease measured by HIV RNA copies of < 75 in the study group when compared with 70% in the control group ($P < 0.0001$). We noticed polyp detection rate of 55% and adenoma detection rate of 32% in HIV population.

CONCLUSION: It is unclear whether HIV or HAART medications play a role in increased prevalence of adenomas. We suggest that when estimating the risk for colonic neoplasms, HIV population should be considered as a high-risk group and screened accordingly.

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Key words: Colorectal cancer; Screening; Human immunodeficiency virus; Highly active anti-retroviral treatment

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INTRODUCTION

Human immunodeficiency virus (HIV) infection and its spectrum of clinical features including acquired immunodeficiency syndrome (AIDS) are associated with significant morbidity and mortality^[1]. Introduction of highly active anti-retroviral treatment (HAART) and chemoprophylaxis for opportunistic infections has significantly influenced mortality, leading to longer survival

rates in the HIV-infected population^[2-10]. This lead to increase in mortality due to non-HIV-related pathologies, including non-AIDS-defining malignancies among these individuals^[11-16].

Non-AIDS defining cancers include various hematological and solid organ malignancies including colon^[17-19]. However the existing data suggest that colon cancer presents at younger age, at an advanced stage and unfavorable prognosis in the HIV population^[17,20-24]. There have also been reports of various etiological agents, including genetic, immunological and viruses like human papilloma virus playing a role in colon cancer development in this population, which is different from the general population^[25-27].

There is limited data available on screening colonoscopy trends in HIV population^[28,29]. We wanted to study if HIV population is getting adequate screening for colon cancer in the HAART era with increased longevity, and prevalence colonic polyps and adenomas which may be different from general average-risk population.

MATERIALS AND METHODS

The study protocol was approved by Institutional Review Board at Bronx Lebanon Hospital Center. Retrospective chart review of electronic medical records was conducted for patients attending Infectious Disease Clinic of the hospital. At our institution, patients diagnosed with HIV are referred and followed up in Infectious Diseases Clinic equipped with other clinical and supportive services providing comprehensive health-care for individuals infected with HIV. Electronic database of endoscopic procedures performed by gastroenterologists of the hospital was used to extract colonoscopy information.

The study included individuals aged 50 years and above, diagnosed with HIV infection by confirmatory tests, who have seen their physician at least twice.

Individuals who were classified at average risk for colon cancer according to the current guidelines were included^[30]. Patients who underwent diagnostic colonoscopy or surgical removal of colon for various reasons were excluded from the study. Multiple modalities were used to confirm if individuals in the study underwent screening colonoscopy in the last 10 years, including physician documentation in medical records, referral to a gastroenterologist and gastroenterology clinic visit by the patient. Patients' self-reporting documented in medical charts and endoscopy data base of the hospital were used to confirm screening colonoscopy status of subjects. All the individuals in the study were divided into two groups based on whether they underwent screening colonoscopy in the last 10 years. Individuals who underwent screening colonoscopy are grouped as the "study group" and those who did not undergo screening colonoscopy are grouped as the "control group".

Demographic data of all subjects including age, gender, and ethnicity was obtained. HIV viral load of

all study subjects measured by serum HIV RNA copies were obtained. Viral suppression was defined based on present antiretroviral guidelines^[31] and standards of hospital laboratory. Patients with HIV RNA of < 75 copies were defined to have adequate viral suppression and well-controlled disease. Similarly, patients with HIV RNA of > 75 copies were defined to have inadequate viral suppression and uncontrolled disease. When individuals had multiple viral load results and results are falling in both categories, persistent levels were taken into consideration. Colonoscopy findings and pathology results of biopsies were also extracted.

Two-sample *t*-test is used to measure the difference in mean age in both groups. The association between gender and prevalence of screening colonoscopy was analyzed using contingency analysis by Fisher's Exact Test. The association between ethnicity and prevalence of colonoscopy was analyzed using contingency analysis by pearson χ^2 test. The association between viral suppression and having colonoscopy done was analyzed using contingency analysis by Fisher's exact test. *P* value of < 0.05 was considered as statistically significant. All statistical procedures were performed using SAS JMP statistical software (Version 8.0.2., SAS Institute Inc, Cary, NC, 1989-2011).

RESULTS

There were in total 565 subjects fulfilled the inclusion criteria and were included in the study. All individuals were confirmed to have been offered screening colonoscopy by their respective physicians. Of these 565 individuals 142 (25%) underwent screening colonoscopy and 423 (75%) never underwent screening colonoscopy in the last 10 years which was verified by all sources of information mentioned earlier. Based on these pre-defined criteria 142 and 423 individuals are classified as "study group" and "control group" respectively.

There was no significant distribution in age, gender and ethnicity between the study and control groups (Table 1). Mean age in the control group was 58 years (\pm 5 years) with a range of 50-73 years compared with 56 years (\pm 6 years) in the control group (with a range of 50-84 years (*P* = 0.05). There were 45 (32%) females and 97 (68%) males in the study group and 147 (35%) females and 276 (65%) males in the control group (*P* = 0.54). Ethnic distribution in the study group revealed Hispanics 77 (54%), African Americans 64 (45%), and others 1 (1%). In the control group, there were 207(49%) Hispanics, 208 (49 %) African Americans, and others 8 (2%) (*P* = 0.45).

However there were 126 (89%) individuals with well-controlled HIV measured by HIV RNA levels of less than 75 copies and 16 (11%) with higher viral load in the study group compared to 295 (70%) individuals with well-controlled HIV disease and 128 (30%) with uncontrolled HIV disease in the control group (*P* < 0.0001).

The study group that included 142 individuals was

Table 1 Age, gender and ethnicity in the study and control groups *n* (%)

	Underwent screening colonoscopy	Did not undergo screening colonoscopy	<i>P</i> value
Total	142 (25)	423 (75)	
Age, yr (mean ± SD)	58 ± 5	56 ± 6	0.05
Gender			
Men	97 (68)	276 (65)	0.54
Women	45 (32)	147 (35)	
Ethnicity			
African Americans	64 (45)	207 (49)	0.45
Hispanics	77 (54)	208 (49)	
Others	1 (1)	8 (2)	
HIV viral load			
< 75 Copies	126 (89)	295 (70)	< 0.0001
> 75 Copies	16 (11)	128 (30)	

HIV: Human immunodeficiency virus.

Table 2 Study group was further analyzed based on macroscopic findings during colonoscopy and cyto-pathological examination *n* (%)

	Total number	<i>P</i> value
Individuals underwent screening colonoscopy	142	
Polyps		
Total	78 (55)	
Men	54 (56)	0.85
Women	24 (53)	
Diverticulosis	44 (31)	
Others	14 (10)	
Pathology		
Hyperplastic polyps	23 (16)	
Normal colonic mucosa	10 (7)	
Tubular adenoma		
Total	45 (32)	
Men	33 (34)	0.44
Women	12 (27)	

further analyzed based on macroscopic findings during colonoscopy and cyto-pathological examination (Table 2). Polyps were detected during colonoscopy in 78 (55%) subjects, diverticulosis in 44 (31%), and other non-specific changes in 14 (10%) subjects. Polyp detection rate was 56% in men and 53% in women (*P* = 0.85).

Biopsies were performed during colonoscopy in 86 individuals which includes 78 patients with polyps and 8 for various other macroscopic abnormalities. On pathology examination of polyps 23 (16%) had hyper-plastic changes, 45 (32%) had tubular adenomas and 10 (7%) had normal colonic mucosa. The remaining 8 individuals who underwent biopsy had nonspecific pathological changes. However, adenoma detection rate was 34% in men when compared with 27% in women (*P* = 0.44).

DISCUSSION

Because of the introduction of HAART and chemoprophylaxis for opportunistic infections survival rates among HIV-infected population have been dramatically improved^[9,10,32-35]. However non-HIV-related causes of death have been increasingly reported in the recent past^[2,36-39]. Non-HIV causes may include but are not limited to various systemic diseases and non-AIDS defining malignancies^[2,36,40-50].

Colon cancer is one of the important malignancies among hematological and solid organ cancers reported in HIV infected individuals^[13,15,18,49,51]. Immunological, genetic and viral factors may play a vital role in the etiopathogenesis of colon cancer in this population^[52,53]. Cancer of colon may present at an earlier age, advanced stage and more aggressively in HIV infected individuals^[17,20,22].

Prevalence of screening for colorectal cancer by endoscopic measures varies between 52% and 74% in different geographical areas of the United States^[54,55] among the average risk population. However, in our study, only 25% of the average-risk patients diagnosed with HIV underwent screening colonoscopy, which is far lower

than national and state prevalence rates. There are no genders or ethnic differences between the patients who underwent screening colonoscopy when compared with patients who did not. Although mean age is slightly higher in those who underwent colonoscopy (58 years *vs* 56 years), the age range is wider (50-84 years) in the group that did not have screening, indicating lower prevalence of screening colonoscopy in older HIV population.

However, disease severity measured by viral load showed strong association with the rate of screening colonoscopy being done in HIV population. HIV patients who had screening colonoscopy had well-controlled disease compared with the other group. Viral suppression resulting from treatment adherence could explain higher compliance to screening colonoscopy. However it may not always be true as drug resistance mutations^[56-58] could enhance viral replication even in good treatment adherence cases.

Interestingly, we found higher polyp (55%) and adenoma (32%) detection rates in HIV population when compared with the average-risk population^[59,60]. The average adenoma detection rates reported in men and women of general population are 25% and 15%, respectively. However, in our study, adenoma detection rate is high in both genders with men (34%) and women (27%). These finding in accordance with the existing data on colon cancer in HIV individuals and strongly support aggressive screening in this particular group of population. However, the present guidelines stratify colon cancer risk based on family history and other variables and recommend colorectal cancer screening for average risk population starting at 50 years of age^[30]. HIV status of the individual is not considered in the present guidelines to stratify the risk of colon cancer and subjecting for screening^[30]. There is increased incidence of malignancies in immunosuppressive states even though colon cancer is rarely reported^[52,61]. The prognosis of HIV patients with malignancies depends on the extent of immune-suppression and mortality is higher for non-AIDS-defining malignan-

cies^[53,62]. However, in our study, HIV patients with less severe immunosuppression are screened more frequently, leaving patients with severe immunosuppression without screening where mortality is high^[62].

At this point it is uncertain whether HIV or HAART medications are increasing the risk of non-AIDS-defining malignancies^[14,18,49,51,53,62-64]. However, there is definitely higher incidence of non AIDS defining malignancies in HIV population on HAART prompting timely screening and diagnosis^[13,14,18].

Our study lacks definitive advantages of prospective cohort or more refined randomized controlled studies. There was no matching between subjects in the study and control groups. As we collected data from old medical records, the accuracy of the information is not always perfect. However, the observations in our study, especially polyp and adenoma detection rates cannot be ignored. There were no cancers detected during screening colonoscopy in this group. We can explain this by the fact that patients might have undergone screening colonoscopy at an earlier stage of the disease process or it may be an incidental finding.

We conclude that there has been existing evidence showing early and aggressive presentation of colon cancer in HIV population. Our study provided further data on higher polyp and adenoma detection rate in HIV-infected population. Although further prospective studies are needed to have more refined results, we suggest that HIV-infection status may have to be considered while assessing colon cancer risk, and individuals with HIV infection should be considered at higher risk for colon cancer and screened accordingly. Currently there are no published guidelines on how to screen HIV infected population for colon cancer. However as suggested for other high risk patients it may be reasonable to screen HIV infected population starting at age 40, but further studies needed to evaluate and support this recommendation^[65].

COMMENTS

Background

Human immunodeficiency virus (HIV) infection has been linked to many cancers and with the advent of newer medications people infected with HIV are living longer. There is no data available on how to screen this population for colon cancer.

Research frontiers

Results may provide new findings which may influence current practice methodology in HIV population.

Innovations and breakthroughs

Existing data suggests that colon cancer presents at younger age, at an advanced stage and has unfavorable prognosis in the HIV population.

Applications

The study results suggest that prevalence of precancerous lesions of colon cancer is high in HIV population. Considering HIV infected population as high risk for colon cancer may guide physicians to offer colonoscopy at an earlier age. Detecting colon cancer at an earlier stage has been associated with improved mortality and morbidity.

Peer review

The authors analyzed in their study the risk of HIV infected population. The results as well as the study design are well presented.

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