The prevalence and characteristics of incidental colorectal polyps in patients undergoing colonoscopy at a South African tertiary institution.

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Master of Medicine (MMed) in Medicine

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DECLARATION

I, *Jean-Jacques Kruger*, hereby declare that the work on which this dissertation/thesis is based, is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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DISSERTATION ABSTRACT

Abstract

Background

There is a lack of data on the frequency, and pattern of colorectal adenomas in sub-Saharan Africa, to guide diagnostic and preventative strategies for CRC in the region. This study aimed to describe polyp characteristics, and adenoma frequency in patients at average risk of CRC undergoing colonoscopy for bowel symptoms at a tertiary hospital in South Africa.

Methods

Colonoscopy records from the prospective endoscopy database at Groote Schuur Hospital for the period August 2014 to February 2017 were retrieved. The presence of polyps, and their morphology, size, site and number in relation to ethnicity, symptoms, and colonoscopy quality indicators were analysed. The histological type and grade were obtained from laboratory records, and analysed. The primary endpoint was the adenoma detection rate. Age, gender, ethnicity, symptoms, bowel preparation, and caecal intubation rates were also compared between patients with adenomas, and those without adenomas.

Results

Of 1334 colonoscopies, 342 were in patients at increased risk of premalignant lesions, and these were excluded from analysis. Polyps were identified in 172 of the remaining 992 patients (17.3%), whose self-declared ethnicity was: mixed race 76%, white 12%, black African 11%, and Asian 1%. The quality of the bowel preparation and caecal intubation rate was similar between patients with polyps and those without. Individuals with polyps were older than those without polyps (mean age 61. 5 ±12,9 versus 56.3 ±17,4 years, $p<0.002$). On histology of these polyps, 119 were adenomas, 26 hyperplastic and 27 normal. The majority of the adenomas were tubular (80%), and only 6% had high grade dysplasia. Half (51%) of the adenomas were in the proximal colon, and the overall adenoma detection rate was 12%. The adenoma detection rate (prevalence) was highest in white, and Asian South Africans (18% each), followed by mixed race (13%), and much lower in black South Africans (5%).

Conclusions

This study provides a benchmark adenoma detection rate for our catchment population and potentially across Africa. There is evidence of a continuing differential colorectal neoplasia risk according to ethnicity, with fewer adenomas being detected in black South Africans.

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Professor Sandie Thomson for all his help in developing the study , writing and presenting it at SAGES and winning best presentation. Without his valuable time, knowledge and patience this project would not be possible.

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Professor Mashiko Setshedi for her contribution and input with regards to statistical analysis.

Dr Leolin Katsidzira for his tremendous help and knowledge of medical gastroenterology that contributed to the final article.

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Contributions of Authors

Jean-Jacques Kruger developed the study protocol, collected and analysed the data and wrote the manuscript. Professor Sandie Thomson, Professor Mashiko Setshedi and Dr Leolin Katsidzira contributed to the study design, data analysis and reviewing and editing of the manuscript.

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The prevalence and characteristics of incidental colorectal polyps in patients undergoing colonoscopy at a South African tertiary institution.

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Abstract

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Introduction

Colorectal cancer (CRC) is the second most common cancer in women, and the third most common in men, and accounts for 10% of all cancers worldwide.[1] Classically, colorectal cancers arise from adenomas, through the adenoma-carcinoma sequence described by Fearon and Vogelstein.[2] The prevalence of adenomas in a population generally correlates with the incidence of colorectal cancer. The incidence of CRC varies widely across the globe, with the USA and Western European countries reporting age standardised incidence rates per 100,000 averaging 29.5 for men and 23.2 for women.[1] This is in sharp contrast to SubSaharan Africa countries that report much lower age standardised incidence ranging from 6·3 in men and 2·7 in women in Mozambique, to the highest of 15.6 in men and 9.5 in women in South Africa.[1,3]

Although there are reasonably adequate reports on the epidemiology of CRC in sub-Saharan Africa, data on the prevalence of adenomas is sparse. In an analysis of 91 surgical resections for CRC in Pretoria between 1996 and 1997, 48 in white people, and 43 in black Africans, adenomas were found in 25% and 20% respectively .[4] A retrospective review, reported in 1999, of 172 CRC resections in black Africans, from Witwatersrand reported that 5% had synchronous adenomas.[5] Apart from the small numbers, these studies were in patients at high risk of having adenomas by virtue of having invasive CRC already, and were based on segmental colonic resections, rather than the entire colon. Thus, the figures cannot be generalised to the ordinary, average risk population. While colonoscopy-based studies would give more accurate data, very few have been performed. In a review of 460 colonoscopies in Zimbabwe, mainly in symptomatic patients, polyps were found in 5% .[6] Similarly, in a review of 415 colonoscopies in Nigeria, adenomas were present in 7% .[7] In contrast, the prevalence of adenomas in asymptomatic individuals in the USA at screening colonoscopy is as high as 37%, and the prevalence of advanced adenomas is 6–8%.[8,9] Data in sub-Saharan Africa is further limited by low numbers, and lack of systematic histological examination of the polyps.

Recent data from Zimbabwe shows the incidence of CRC is on the increase, possibly due to a combination of improved diagnosis and a true increase in new cases .[10,11] These increases have also been reported in several countries across Africa, and clearly, South Africa should be no exception. There is limited knowledge on the pattern of neoplastic polyps in South Africa and the region, which can guide prevention strategies, and help estimate the trajectory of CRC. Therefore, we reviewed data of patients with an average risk of CRC using a prospective colonoscopy registry at a tertiary hospital in the Cape Metropole and estimated the adenoma detection rate that clinicians can use as a benchmark in South Africa, and the rest of Africa. Furthermore, we comprehensively described the pathological patterns of colorectal polyps in this population.

Methods

A cross-sectional study was conducted at the Gastrointestinal Clinic at Groote Schuur Hospital, a tertiary institution in Cape Town, South Africa. Data of all adult (>18years) patients who had a colonoscopy between August 2014 to February 2017 was retrieved from the prospective endoscopy registry. Cases of inflammatory bowel disease, flexible sigmoidoscopies and incomplete colonoscopies due to inadequate bowel preparation were excluded from analysis. Repeat colonoscopies performed within 6 months of the initial procedure were considered as one single procedure. Data on age, gender, ethnicity, number of polyps, morphology, size, location were extracted from the database. Adenoma Detection Rate (ADR) was calculated as the number of patients with at least one adenoma divided by the number of colonoscopies performed

Bowel preparation was routinely assessed segmentally, and graded and recorded as good, adequate, or poor (but proceeded with colonoscopy), and ceacal intubation rate automatically recorded. Data on histological findings was obtained from the National Health Laboratory Services (NHLS). Data on the histological sub-type and degree of dysplasia were extracted from the narrative reports, and merged with the endoscopic dataset using the patients' unique hospital numbers. Ethical approval was obtained from the University of Cape Town Human Research Ethics Committee (HREC REF 617/2018).

Continuous data was summarised using mean values with standard deviations, or median values with interquartile range as appropriate. The various proportions were summarised using percentages and confidence intervals. The χ^2 test or Fisher's exact test t were used to compare categorical data, and the student t-test was used for continuous variables. All the analyses were carried out using STATA 14 (Stata Corp, College Station, Texas).

Results

Of 1334 colonoscopies in the database over the study period, 342 were in patients at increased risk of developing colorectal cancer, and these were excluded from analysis. Figure 1 shows how the cohort was derived and the histological findings.

Figure 1. Consort diagram showing selection criteria and histological findings

Of the 992 colonoscopies analysed, 70% were performed in patients older than 50 years, 76% were in individuals of mixed race, 12% were in black Africans, and 11% were in white individuals.

Rectal bleeding was the most common indication for a colonoscopy, followed by abdominal pain and change in bowel habit.

Table 1. Baseline clinical and demographic features in cohort

Out of the 992 patients colorectal polyps were identified in 172 (17.3%) patients, of which 119 (12%) had confirmed adenomas. Table 1 Compares the baseline clinical and demographic features in the 119 individuals with adenomas versus those individuals without adenomas. Generally, patients with adenomas were significantly older than those with no adenomas (61. 5 years ±12,9 versus 56.3 ±17,4 years, $p<0.002$), and 82% of those with adenomas were older than 50 years. The result of bowel preparation was good in 54%, adequate in 28% and poor in 18%, though a complete colonoscopy was performed. The quality of bowel preparation, and the caecal intubation rate were similar between the two groups.

Two hundred and forty-six polyps were visualised, and 42% were <5mm in size, with 72% sessile. Two hundred and six were removed and on histology, 27 had normal mucosa, 26 were hyperplastic and 148 were adenomas. The latter were detected in 119 patients. Seven patients had 2, three had 3 and one had 6 adenomas. The most advanced histology for these adenomas per patient were: tubular with low grade dysplasia in 96, tubular with high grade dysplasia in one, 15 tubulo-villous with low grade dysplasia, tubulo-villous high-grade dysplasia in three, and serrated in four patients (Fig. 1).

Figure 2. Anatomical distribution of the histological types of adenomas.

The anatomical distribution of the adenomas is shown in Figure 2.

Approximately 51% of the adenomas were in the proximal colon, and 22% were located in the rectum. The adenoma detection rate (ADR) was 12 % (119/992) in all age groups, and 14% (97/693) in the over 50's, with equal gender distribution. The ADR by ethnicity was as follows: mixed race 13%, white 18%, Asian 18%, and black African 5%.

Discussion

We describe the findings of 992 colonoscopies performed in patients presenting to Groote Schuur hospital at average risk of developing CRC with the aim of estimating the frequency, and pathological spectrum of the adenomas. Overall, we found that the overall adenoma detection rate was 12% in all age groups and this did not vary between men and women. In those over 50 years of age, the ADR was 14% This is lower than the recommended adenoma detection rate of > 25% in men in North American and Western European guidelines, but closer to the target of > 15% in women.[12] Interestingly, the rate of advanced adenomas in our study of 6%, of average risk symptomatic patients was comparable to rates of 6 – 8% found in the asymptomatic screening population in the USA.[8,9] However, it is unclear whether our presumed average risk population, originating from a hospital setting, would be comparable to the asymptomatic screening population in the USA. Nonetheless, our findings represent the first comprehensive report on adenomas in a South African tertiary state institution.

South Africa is a diverse, multi-cultural country with marked provincial variation in the ethnic proportions and wide variations in CRC risk based on ethnicity.[13] South Africa's population is estimated at 58,8 million, of which black Africans constitute 81%, mixed race 9%, white 8%, and Asian population 2%. In contrast, the population our catchment area, the

Cape Town Metropole, was 3.7 million in 2012, with 42% being of mixed race, 39% black Africans, 15.7% white, and 1.4% Asian.[14] Our findings reflect the differences in CRC risk between the diverse ethnic groups in our population. The lowest rate of adenomas of 5% was in the black African patients, which is similar to reports from Nigeria and Zimbabwe.[6,7] In contrast, the frequency of adenomas was much higher in the mixed race, and white patients, reflecting a higher risk of CRC in these populations. There was a predominance of adenomas in the proximal colon, which is similar to the traditional high incidence countries, and may reflect the impact of obesity and lifestyle related factors.[15,16] Colorectal neoplasia has a stronger association with lifestyle in the proximal colon compared to the distal colon.[17-20] The higher frequency of colonic compared to rectal adenomas is similar to a previous study of CRC in the Northern Cape, in which 64% were located in the colon rather than the rectum.[21] However, colorectal cancers in this population are rather enriched with Lynch syndrome, which is known to have a predilection for the proximal colon. Nonetheless, our study excluded patients with high risk of premalignant lesions, therefore our results are probably a true reflection of the distribution of adenomas in this population.

Several factors contribute to the ADR at colonoscopy in this study. Key amongst these is the efficacy of bowel preparation, which was poor in 18% of our study participants. This does not meet the key performance indicator in international guidelines, which aim for at most, 5 – 15 % .[12,22] Thus, it is possible that there may be under-detection of polyps in our practice. It could be argued that the outcomes from our colonoscopies were affected by the varying levels of experience of the clinicians performing them, who ranged from novice gastroenterology, and surgical trainees to senior consultant gastroenterologists. However, our training is modelled on the UK JAG Endoscopy Training System (JETS) principles, and trainees are usually supervised by a gastroenterologist or colorectal surgeon.[23] Thus, it is

unlikely that the inclusion of data from trainees had a negative effect on the ADR. Moreover, evidence from an earlier study on this registry showed that mature trainees had as good an ADR as consultants, suggesting that the effect is negligible.[24] Another potential limitation is selection bias inherent in data obtained from a single tertiary hospital. To our credit, the caecal intubation rate of 90% was in keeping with both UK and US recommendations for colonoscopy in symptomatic patients, who constituted the majority of our cohort.[12,25] However, withdrawal time was not documented.

Despite these limitations, our study represents the first attempt to determine the ADR in South Africa, and is the biggest dataset to describe the pathological spectrum of polyps. As such it provides a benchmark for clinicians providing diagnostic, and screening colonoscopies, both in the state and in the private sector. Practice should be individualised, given the differences in adenoma frequency between different population groups.

Furthermore, this data reaffirms the higher risk of CRC in the mixed race and white patients, and the threshold for opportunistic screening in these groups should be low, while population based screening may be merited. While the low frequency of adenomas in the black population suggest a relatively low incidence of colorectal cancer, a registry of this nature can act as an early warning system of changes in CRC risk. Finally, these findings should not detract from the need to provide timely colonoscopy in all symptomatic patients regardless of the perception of CRC risk.

Declaration. The research for this study was done in partial fulfilment of the requirements for JK's MMed (Internal Medicine) degree at the University of Cape Town.

Acknowledgements. None.

Author contributions. JK developed the study protocol, collected and analysed the data and wrote the manuscript. SRT, MS and LK contributed to the study design, data analysis and reviewing and editing of the manuscript.

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Conflicts of interest. None

Figure 1. Consort diagram showing selection criteria and histological findings

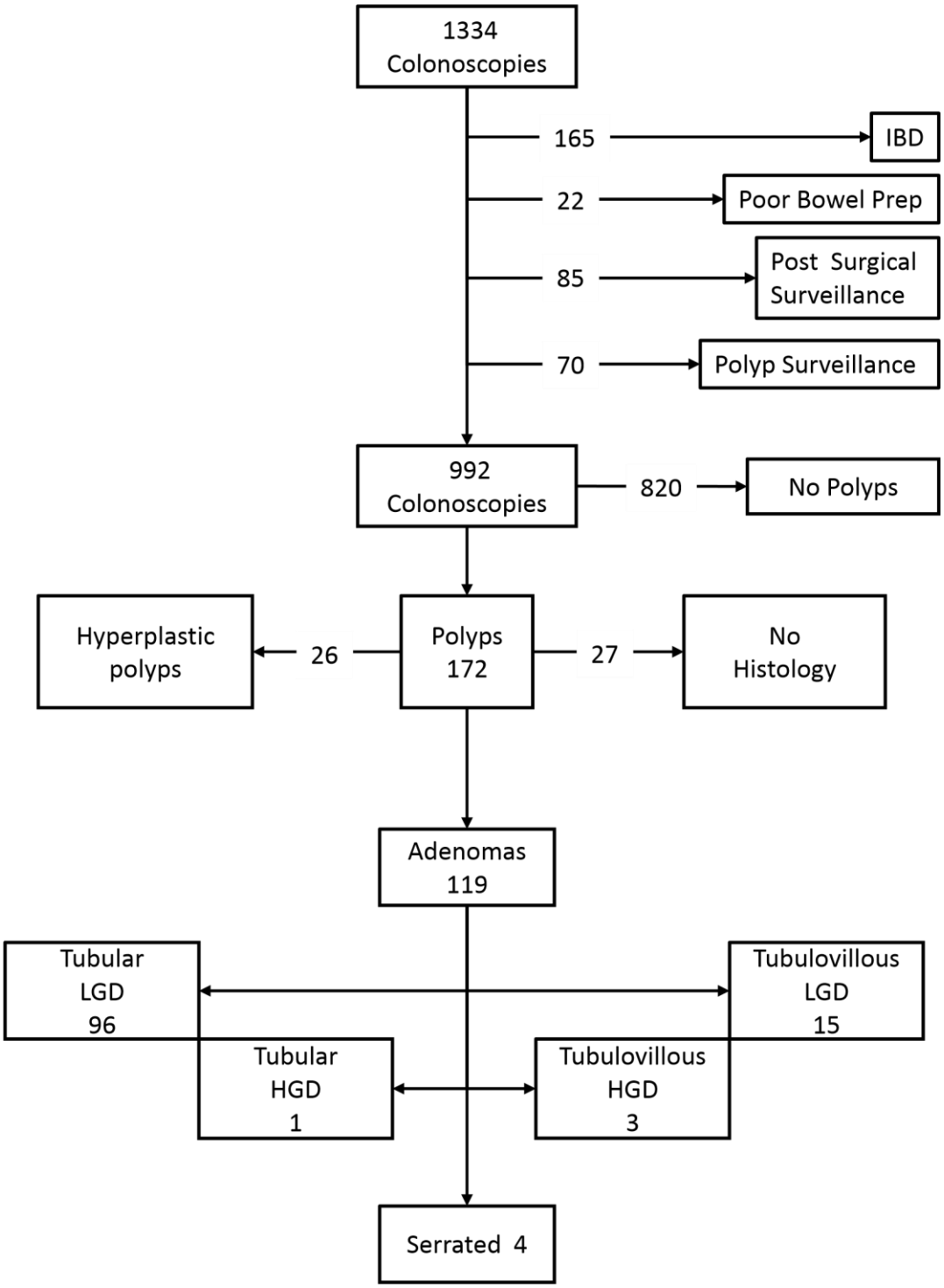
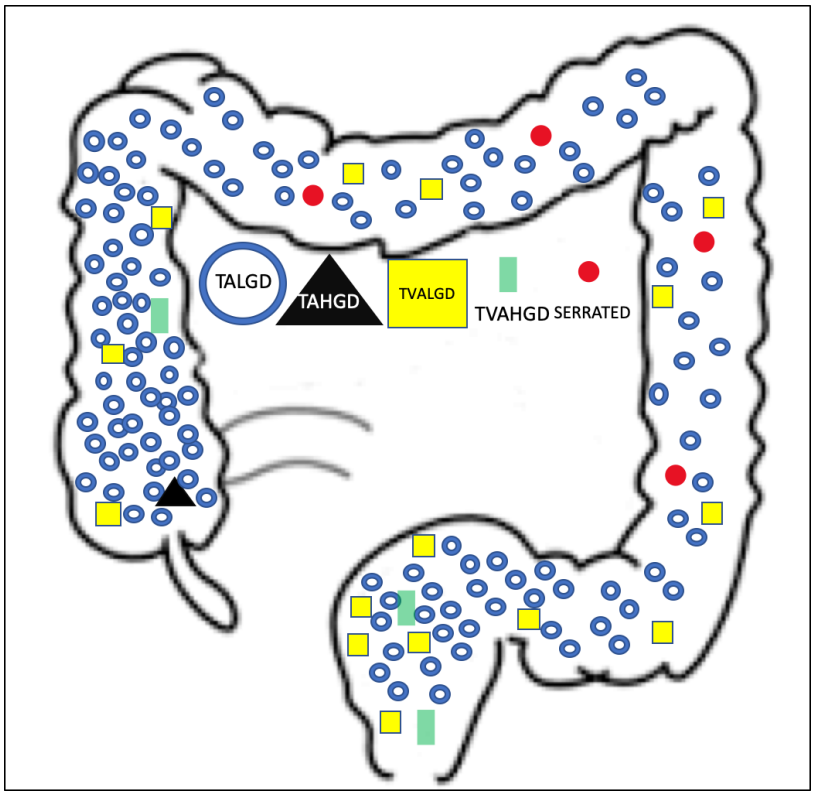


Table 1. Baseline clinical and demographic features in cohort

Variables	Colonoscopies without adenomas N = 873	%	Patients with adenomas N = 119	%
Gender				
Male	325	37%	44	37%
Female	548	63%	75	63%
Ethnicity				
Mixed race	662	76%	95	80%
Black	113	14%	6	5%
White	87	10%	16	13%
Asian	11	2%	2	2%
Mean age (SD)	56.3 (17.4)		61.5 (12.9)	
Age categories				
> 50	596	70%	97	82%
< 50	277	30%	22	18%
Weight loss	165	14%	22	16%
Rectal bleeding	203	18%	27	19%
Diarrhoea	128	11%	7	5%
Constipation	180	16%	24	17%
Asymptomatic	49	4%	5	4%
Anaemia	160	14%	19	14%
Alteration in bowel habit	65	6%	10	7%
Abdominal pain	198	17%	25	18%
Bowel Preparation				
Good	409	47%	64	54%
Adequate	293	34%	33	28%
Poor	171	20%	22	18%
Caecal intubation rate	784	90%	107	90%

Figure 2. Anatomical distribution of the histological types of adenomas



TALGD Tubular Adenoma with low grade dysplasia
TAHGD Tubuloadenoma with high grade dysplasia,
TVALGD Tubulovillous adenoma with low grade dysplasia
TVAHGD Tubulovillous adenoma with high grade dysplasia

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26 September 2018

HREC REF: 617/2018

Prof Sandie Thomson
Division of Gastroenterology
E23, NGSH

Dear Prof Thomson

PROJECT TITLE: THE PREVALENCE AND CHARACTERISTICS OF COLORECTAL POLYPS IN PATIENTS UNDERGOING COLONOSCOPY AT GROOTE SCHUUR HOSPITAL (MMED Candidate - Mr J Kruger)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 September 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

The HREC acknowledge that the student, Jean-Jacques Kruger will also be involved in this study.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

Research Protocol

The prevalence and characteristics of colorectal polyps in patients undergoing colonoscopy at Groote Schuur Hospital.

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Introduction

Colorectal cancer is the second most common cancer in women and the third most common in men and accounts for 10% of all cancers worldwide [1]. Classically, almost all colorectal cancers are adenomas, following the adenoma-carcinoma sequence [2]. The prevalence of adenomas in a population generally correlates with the colorectal cancer rate. There is little data on the prevalence of adenomas in sub-Saharan Africa. the prevalence of adenomas in asymptomatic individuals during screening colonoscopy in the USA was as high as 37%, and the prevalence of advanced adenomas was 6–8%[19,20]. In an analysis of 91 surgical resections from patients with colorectal cancer in Pretoria, South Africa, between 1996 and 1997, adenomas were found in 10% of patients. In a retrospective review of 172 cases of colorectal cancer in the Witwatersrand, South Africa, 5% of patients had synchronous adenomas [3,4]. These studies were based on partial colonic resection and not on the entire colon. Colonoscopy based studies would give more accurate data but very few have been performed. In a review of 460 colonoscopies in Zimbabwe, mainly in symptomatic patients, polyps were found in 5% [5]. In a review of 415 colonoscopies in Nigeria, adenomatous polyps were found in 7% [6].

Recent data from Zimbabwe shows the incidence of colorectal cancer in Sub Saharan Africa is on the increase in their country due to both improved diagnosis and a true increase in new cases [7,8]. There is limited knowledge on the pattern of neoplastic polyps in Sub Saharan Africa. Knowledge of these frequencies can help in estimating the future trajectory of colorectal cancer incidence in our population and determine the need for and guide to the implementation of preventative strategies.

Colonoscopy is the gold standard for colorectal cancer screening as it allows for the detection and removal of adenomas [9,10]. Its use can reduce colorectal cancer mortality through the detection of early-stage adenocarcinomas and the detection and removal of precursor adenomatous polyps [11,12]. Histopathological examination of colon polyps

contributes to the determination their malignant potential; diminutive and small adenomas are considered to be advanced if they contain at least 25% villous features, high-grade dysplasia, or carcinoma.[13,4,15]

Among different quality indicators, the most common used is the adenoma detection rate, which is the percentage of average risk patients undergoing screening colonoscopy in which an adenoma or cancer is found [16] .This is the main measure of colonoscopy performance quality; these rates predict subsequent colorectal cancer risk following a screening colonoscopy [17]. Current guidelines suggest that adenomas should be detected in ≥15% of women and in ≥25% of men who undergo screening colonoscopy [18] .This benchmark quality indicator is used for population-based screening colonoscopy which is not practiced in South Africa. The only indicator available in our population is the adenoma detection rate in those being colonoscoped for symptoms of large bowel disease.

Research question

What is the prevalence and characteristics of colorectal polyps in patients undergoing colonoscopy at the gastrointestinal clinic at Groote Schuur Hospital.

Objectives

Study population:

All patients that underwent a colonoscopy at the gastrointestinal clinic at Groote Schuur Hospital between August 2014 to February 2017.

The objectives of this study are:

1. Determine the macroscopic and histological types of polyps detected during colonoscopy.

2.To determine the frequency of adenomatous polyps in relation to other histological types and their size, site, morphology and degree of dysplasia.

3. Determine the adenoma detection rate in the clinic.

Methods

Study design: Registry-based cross-sectional study.

Study procedures

All colonoscopies performed in the Gastrointestinal Clinic at Groote Schuur Hospital between August 2014 and February 2017 will be retrieved from the gastrointestinal endoscopy database and sub classified according to the total number, type of polyp the size, location and how they were removed. The patients GSH folder number will be used to cross reference the database with the histology of biopsies and polypectomies from the NHLS records.

Repeat colonoscopies performed within 6 months of the initial procedure will be recorded as one procedure.

Inclusion criteria

1. All patients above the age of 18 years undergoing colonoscopy will be included.

Exclusion criteria

1. All cases of inflammatory bowel disease.
2. Flexible sigmoidoscopies.
3. Procedures abandoned because of a poor bowel preparation.

Sample Size

1500 Colonoscopies from August 2014 to February 2017 will be reviewed.

The estimated frequency of adenomas is 25% and the number of colonoscopies performed is sufficient for the cohort.

Variables and measurements

Data collection sheets and electronic databases will be used to collect the following information

Variable	Numerical	Categorical Ordinal	Categorical Nominal	Possible values
Indication for colonoscopy		X		
Biopsy site		X		
Polyp size	X			
Morphology		X		
Histology		X		
Racioethnic frequency		X		
Age	X			18-80
Gender			X	M, F

Statistical methods

The data will be extracted from the database and stored in excel spreadsheets. Upon cleaning the data using Microsoft excel pivot tables, it will be exported to STATA 14 (Stata

Corp, College Station, Texas) for analysis. Statistical tests will be performed according to whether the variable is continuous or categorical. Continuous data will be expressed as mean values ± SD or median values (IQR) depending on the normality of data. For categorical data the χ^2 test or Fisher exact test and the Z test will be used to test for a statistical difference between variables and proportions, respectively. The Mann – Whitney, and Student t-test will be used to test the association between continuous and categorical variables.

1. Descriptive statistics will be used to analyse the proportion and pathological characteristics of the neoplastic polyps and to determine the adenoma detection rate. Chi-squared tests will be used to compare the differences in neoplastic polyps across different patient age groups. Polyps of different categories of patients.

STRENGTHS AND LIMITATIONS

Limitations:

The Adenoma detection rate is a screening tool and is not used for symptomatic patients. Not all polyps would have been biopsied or removed. There is no standardized pathology reporting system.

Strengths:

There is minimal data on polyp and colorectal cancer frequency in Sub Saharan Africa, this will be a benchmark.

Ethical considerations

Ethical approval will be sought from the UCT Faculty of Health Sciences Human Research Ethics Committee. The study is a registry-based review, and there is no physical risk to patients. There is a potential risk of breach of confidentiality but this will be mitigated by allocating identification numbers at data retrieval and these will be used for analysis. There is no direct benefit to the patients, but the data obtained will be invaluable in guiding policy on a growing public health threat.

BUDGET

Currently there is no additional cost to carry out this research: the electronic database has already been set up and maintained by the gastroenterology department at the University of Cape Town. Funding will be sought to allow for presentation of data at a local conference and for publication in a peer review journal.

Study timelines

Literature Review	June 2018	July 2018							
Preparing Protocol	June 2018	July 2018							
Protocol Assessment		Sept 2018	Oct 2018						
Collecting Data		Sept 2018	Oct 2018	Nov 2018					
Data Analysis			Oct 2018	Nov 2018					
Writing up - Thesis				Nov 2018	Dec 2018	Jan 2019	Feb 2019	March 2019	
Writing up - Paper							Feb 2019	March 2019	

Prevalence and characteristics of incidental colorectal polyps in patients undergoing colonoscopy at a South African tertiary institution

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Background. There is a lack of data on the frequency and pattern of colorectal adenomas in sub-Saharan Africa to guide diagnostic and preventive strategies for colorectal cancer (CRC) in the region.
Objectives. To describe polyp characteristics and adenoma frequency in patients at average risk of CRC, who are undergoing colonoscopy for bowel symptoms at a tertiary hospital in South Africa (SA).
Methods. Colonoscopy records from the prospective endoscopy database at Groote Schuur Hospital, Cape Town, SA, from August 2014 to February 2017, were retrieved. The presence of polyps, and their morphology, size, site and number in relation to ethnicity, symptoms and colonoscopy quality indicators were analysed. The histological type and grade were obtained from laboratory records and analysed. The primary endpoint was the adenoma detection rate (ADR). Age, gender, ethnicity, symptoms, bowel preparation and caecal intubation rates were also compared between patients with adenomas and those without.
Results. Of 1 334 colonoscopies, 342 were performed in patients at increased risk of premalignant lesions; these were excluded from the analysis. Polyps were identified in 172 of the remaining 992 patients (17.3%), whose self-declared ethnicity was mixed race (76%), white (12%), black African (11%) or Asian (1%). The quality of bowel preparation and caecal intubation rate were similar between patients with polyps and those without. Patients with polyps were older than those without polyps (mean age 61.5 (standard deviation 12.9) v. 56.3 (17.4) years; $p<0.002$). On histological examination of these polyps, 119 were adenomas, 26 were hyperplastic and 27 were normal. The majority of the adenomas were tubular (80%), and there were only 6% with high-grade dysplasia. Half (51%) of the adenomas were in the proximal colon, and the overall ADR was 12%. The ADR (prevalence) was highest in white and Asian South Africans (18% each), followed by that in persons of mixed race (13%), but much lower in black Africans (5%).
Conclusions. This study provides a benchmark ADR for our catchment population and potentially across Africa. There is evidence of a continuing differential colorectal neoplasia risk according to ethnicity, with fewer adenomas being detected in black South Africans.

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Colorectal cancer (CRC) is the second most common cancer in women, and the third most common in men, and accounts for 10% of all cancers worldwide.[1] Classically, CRCs arise from adenomas, through the adenoma-carcinoma sequence described by Fearon and Vogelstein.[2] The prevalence of adenomas in a population generally correlates with the incidence of CRC. The latter varies widely across the globe, with the USA and Western European countries reporting age-standardised incidence rates per 100 000 population, averaging 29.5 for men and 23.2 for women.[1] This is in sharp contrast to sub-Saharan African countries that report much lower age-standardised incidence rates, ranging from 6.3 in men and 2.7 in women in Mozambique, to the highest rates, i.e. 15.6 in men and 9.5 in women in South Africa (SA).[1,3]

Although there are reasonably adequate reports on the epidemiology of CRC in sub-Saharan Africa, data on the prevalence of adenomas are sparse. In an analysis of 91 surgical resections for CRC between 1996 and 1997 in Pretoria, SA (white: n=48; black African: n=43), adenomas were found in 25% of whites and 20% of black Africans.[4] A retrospective review in 1999 reported that of 172 CRC resections in black Africans on the Witwatersrand, SA, 5% had synchronous adenomas.[5] Apart from the small numbers, these studies were in patients at high risk of adenomas by virtue of them already having invasive CRC, and were based on segmental colonic resections, rather than removal of the entire colon. Therefore, the figures cannot be generalised to the average-risk population. While colonoscopy-based studies would give more accurate data, very few have been performed. In a review of 460 colonoscopies in Zimbabwe, mainly in symptomatic patients, polyps were found in 5%.[6] Similarly, in a review of 415 colonoscopies in Nigeria, adenomas were present in 7% of patients.[7] In contrast, the prevalence of adenomas in asymptomatic individuals in the USA at screening colonoscopy was as high as 37%, and the prevalence of advanced adenomas was 6 - 8%.[8,9] Data in sub-Saharan Africa are further limited by low numbers and a lack of systematic histological examination of the polyps.

Recent data from Zimbabwe show that the incidence of CRC is increasing, possibly owing to a combination of improved diagnosis and a true increase in new cases.[10,11] These increases have also been reported in several countries across Africa, and SA should be no exception. There is limited knowledge on the pattern of neoplastic

polyps in SA and the sub-Saharan African region, which could guide prevention strategies and help to estimate the trajectory of CRC. Therefore, we reviewed data of patients with an average risk of CRC using a prospective colonoscopy registry at a tertiary hospital in the Cape Metropole, and estimated the adenoma detection rate (ADR) for clinicians to use as a benchmark in SA and the rest of Africa. Furthermore, we comprehensively described the pathological patterns of colorectal polyps in this population.

Methods

A cross-sectional study was conducted at the Gastrointestinal Clinic at Groote Schuur Hospital, a tertiary institution in Cape Town, SA. Data of all adult patients (>18 years old), who had undergone a colonoscopy between August 2014 and February 2017, were retrieved from the prospective endoscopy registry. Cases of inflammatory bowel disease, flexible sigmoidoscopies and incomplete colonoscopies due to inadequate bowel preparation were excluded from the analysis. Repeat colonoscopies performed within 6 months of the initial procedure were considered as a single procedure. Data on age, gender, ethnicity, number of polyps, morphology, size and location were extracted from the database. The ADR was calculated as the number of patients with at least one adenoma divided by the number of colonoscopies performed.

Bowel preparation was routinely assessed segmentally, and graded and recorded as good, adequate or poor (but proceeded with colonoscopy), and caecal intubation rate was automatically recorded. Data on histological findings were obtained from the National Health Laboratory Service (NHLS). Data on the histological subtype and degree of dysplasia were extracted from the narrative reports and merged with the endoscopic dataset, using the patients' unique hospital numbers.

Continuous data were summarised using mean values with standard deviations (SDs), or median values with interquartile range (IQR), as appropriate. The various proportions were summarised using percentages and confidence intervals (CIs). The χ^2 test or Fisher's exact test were employed to compare categorical data, and the student *t*-test was used for continuous variables. All the analyses were carried out using Stata 14 (Stata Corp., USA).

Ethical approval

Ethical approval was obtained from the University of Cape Town Human Research Ethics Committee (ref. no. HREC REF 617/2018).

Results

Of 1 334 colonoscopies in the database over the study period, 342 were performed in patients at increased risk of developing CRC; these were excluded from the analysis.

Fig. 1 shows how the cohort was derived and the histological findings.

Of the 992 colonoscopies analysed, 70% were performed in patients >50 years of age, 76% were in patients of mixed race, 12% were in black Africans and 11% were in whites. Rectal bleeding was the most common indication for a colonoscopy, followed by abdominal pain and change in bowel habit.

Colorectal polyps were identified in 172 of the 992 patients (17.3%), of whom 119 (12%) had confirmed adenomas.

Table 1 compares the baseline clinical and demographic features of the 119 individuals with adenomas with those of individuals without adenomas. Generally, patients with adenomas were significantly older than those with no adenomas (61.5 (12.9) v. 56.3 (17.4) years; $p<0.002$), and 82% of those with adenomas were >50 years of age. The result of bowel preparation was good in 54%, adequate in 28% and poor in 18%, although a complete colonoscopy was performed. The quality of bowel preparation and the caecal intubation rate were similar between the two groups.

A total of 246 polyps were visualised, and 42% were <5 mm in size, with 72% sessile. Two hundred and six were removed, and on histological examination, 27 had normal mucosa and 26 were hyperplastic. Adenomas (n=148) were detected in 119 patients. Seven patients had 2 adenomas, 3 had 3 adenomas and 1 had 6 adenomas.

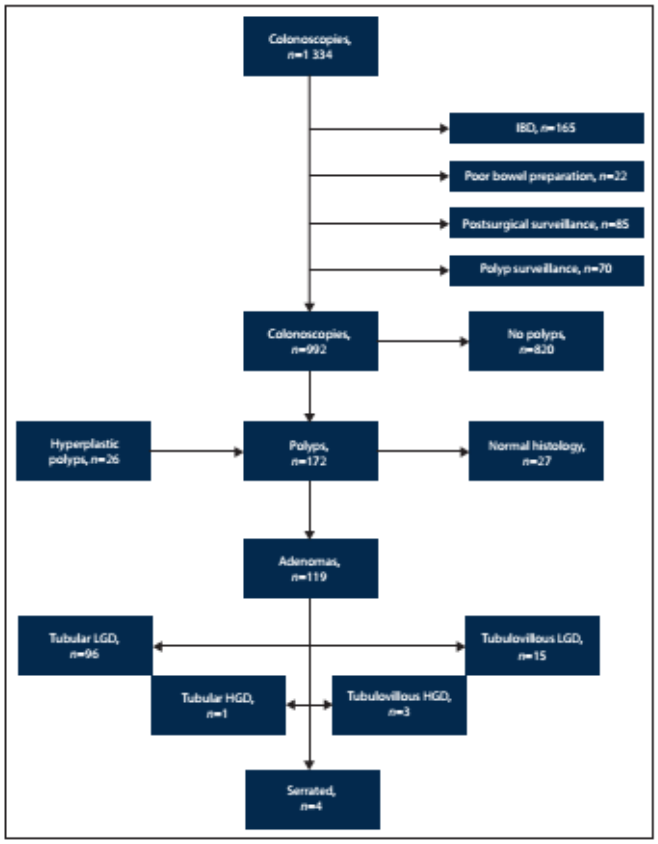

Fig. 1. Consort diagram showing selection criteria and histological findings. (IBD = inflammatory bowel disease; LGD = low-grade dysplasia; HGD = high-grade dysplasia.)

The most advanced histology for these adenomas per patient were: tubular with low-grade dysplasia (*n*=96), tubular with high-grade dysplasia (*n*=1), tubulovillous with low-grade dysplasia (*n*=15), tubulovillous with high-grade dysplasia (*n*=3) and serrated (*n*=4) (Fig. 1).

The anatomical distribution of the adenomas is shown in Table 2. Approximately 51% of the adenomas were in the proximal colon, and 22% were located in the rectum. The ADR was 12% (119/992) in all age groups, and 14% (97/693) in those >50 years of age, with equal gender distribution. The ADR by ethnicity was as follows: mixed race (13%), white (18%), Asian (18%) and black African (5%).

Table 1. Baseline clinical and demographic features in the cohort

Variables	Colonoscopies in patients without adenomas (*N*=873), *n* (%)*	Colonoscopies in patients with adenomas (*N*=119), *n* (%)*
Gender		
Male	325 (37)	44 (37)
Female	548 (63)	75 (63)
Ethnicity		
Mixed race	662 (76)	95 (80)
Black	113 (14)	6 (5)
White	87 (10)	16 (13)
Asian	11 (2)	2 (2)
Mean age (SD), years	56.3 (17.4)	61.5 (12.9)
Age categories, years		
≥50	596 (70)	97 (82)
<50	277 (30)	22 (18)
Weight loss	165 (14)	22 (16)
Rectal bleeding	203 (18)	27 (19)
Diarrhoea	128 (11)	7 (5)
Constipation	180 (16)	24 (17)
Asymptomatic	49 (4)	5 (4)
Anaemia	160 (14)	19 (14)
Alteration in bowel habit	65 (6)	10 (7)
Abdominal pain	198 (17)	25 (18)
Bowel preparation		
Good	409 (47)	64 (54)
Adequate	293 (34)	33 (28)
Poor	171 (20)	22 (18)
Caecal intubation rate	784 (90)	107 (90)

SD = standard deviation.
*Unless otherwise indicated.

Discussion

We describe the findings of 992 colonoscopies performed at Groote Schuur Hospital in patients at average risk of developing CRC. The aim was to estimate the frequency and pathological spectrum of the adenomas. The overall ADR was 12% in all age groups, which did not vary between men and women. In those >50 years of age, the ADR was 14%. This percentage is lower than the recommended ADR of >25% in men, according to North American and Western European guidelines, but closer to the target of >15% in women.[12] Interestingly, the rate of advanced adenomas in our study (6%) in average-risk symptomatic patients was comparable with rates of 6 - 8% in the asymptomatic screening population in the USA.[8,9] However, it is unclear whether our presumed average-risk population, originating from a hospital setting, would be comparable with the asymptomatic screening population in the USA. Nonetheless, our findings represent the first comprehensive report on adenomas in an SA tertiary state institution.

SA is a diverse, multicultural country with marked provincial variation in the ethnic proportions and wide variations in CRC risk based on ethnicity.[13] SA's population is estimated at 58.8 million, of which black Africans constitute 81%, mixed race 9%, whites 8% and Asians 2%. In contrast, the population in our catchment area, the Cape Town Metropole, was 3.7 million in 2012, with 42% being of mixed race, 39% black African, 15.7% white and 1.4% Asian.[14] Our findings reflect the differences in CRC risk between the diverse ethnic groups in our population. The lowest rate of adenomas (5%) was in black African patients, which is similar to rates in Nigeria and Zimbabwe.[6,7] However, the frequency of adenomas was much higher in patients of mixed race and white patients, reflecting a higher risk of CRC in these populations. There was a predominance of adenomas in the proximal colon, which is similar to that in the traditional high-incidence countries, and may reflect the impact of obesity and lifestyle-related factors.[15,16] Colorectal neoplasia has a stronger association with lifestyle when it occurs in the proximal colon compared with the distal colon.[17-20] The higher frequency of colonic compared with rectal adenomas is similar to a previous study of CRC in the Northern Cape, in which 64% of adenomas were located in the colon - not in the rectum.[21] However, CRC in this population is rather enriched with Lynch syndrome, which is known to have a predilection for the proximal colon. Nonetheless, our study excluded patients with a high risk of premalignant lesions; therefore, our results are probably a true reflection of the distribution of adenomas in this population.

Study limitations

Several factors contributed to the ADR at colonoscopy in this study. Key among these is the efficacy of bowel preparation, which was poor in 18% of the participants. This does not meet the key performance

Table 2. Anatomical distribution of the histological types of adenomas

Polyp site	Polyp histology				
	TALGD	TAHGD	TVALGD	TVAHGD	Serrated adenoma
Caecum	15	1	1	0	0
Ascending colon	20	0	2	1	0
Transverse colon	19	0	2	0	2
Descending colon	12	0	3	0	2
Sigmoid colon	16	0	2	0	0
Rectum	14	0	5	2	0
Total	96	1	15	3	4

TALGD = tubular adenoma with low-grade dysplasia; TAHGD = tubuloadenoma with high-grade dysplasia; TVALGD = tubulovillous adenoma with low-grade dysplasia; TVAHGD = tubulovillous adenoma with high-grade dysplasia.

indicator in international guidelines, which aims for at most 5 - 15%.[12,13] Therefore, it is possible that there may be under-detection of polyps in our practice. It could be argued that the outcomes of our colonoscopies were affected by the varying levels of experience of the clinicians, who ranged from novice gastroenterology and surgical trainees to senior consultant gastroenterologists. However, our training is modelled on the UK Joint Advisory Group (JAG) Endoscopy Training System (JETS) principles, and trainees are usually supervised by a gastroenterologist or colorectal surgeon.[28] Therefore, it is unlikely that the inclusion of data from trainees had a negative effect on the ADR. Moreover, evidence from an earlier study using this registry showed that the ADR of mature trainees was as good as that of consultants, suggesting that the effect is negligible.[14] Another potential limitation is selection bias inherent in data obtained from a single tertiary hospital. To our credit, the caecal intubation rate of 90% was in keeping with both UK and US recommendations for colonoscopy in symptomatic patients, who constituted the majority of our cohort.[12,28] However, withdrawal time was not documented.

Conclusions

Despite these limitations, our study represents the first attempt at determining the ADR in SA, and is the largest dataset describing the pathological spectrum of polyps. It provides a benchmark for clinicians who perform diagnostic and screening colonoscopies, both in the state and in the private sector. This should be individualised, given the differences in adenoma frequency between different population groups. Furthermore, these data reaffirm the higher risk of CRC in mixed race and white patients. The threshold for opportunistic screening in these groups should be low, while population-based screening may be merited. Whereas the low frequency of adenomas in the black population suggests a relatively low incidence of CRC, a registry of this nature can act as an early warning system of changes in CRC risk. Finally, these findings should not detract from the need to provide timely colonoscopy in all symptomatic patients, regardless of the perception of CRC risk.

Declaration. The research for this study was done in partial fulfilment of the requirements for JK's MMed (Internal Medicine) degree at the University of Cape Town.

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Author contributions. JK developed the study protocol, collected and analysed the data and wrote the manuscript. SRT, MS and LK contributed to the study design, data analysis and reviewing and editing of the manuscript.

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Conflicts of interest. None.

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The prevalence and characteristics of incidental colorectal polyps in patients undergoing colonoscopy at a South African tertiary institution.

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Abstract

Background

There is a lack of data on the frequency, and pattern of colorectal adenomas in sub-Saharan Africa, to guide diagnostic and preventative strategies for CRC in the region. This study aimed to describe polyp characteristics, and adenoma frequency in patients at average risk of CRC undergoing colonoscopy for bowel symptoms at a tertiary hospital in South Africa.