FIRST REPORTS OF COMPUTED TOMOGRAPHIC COLONOGRAPHY FOR THE SCREENING OF COLORECTAL POLYPS IN ACROMEGALIC PATIENTS

[1§]Ramos Jr.,Odery – Ph.D. and Professor at the Departments of Medical Clinic and Gastroenterology, Hospital de Clínicas, Universidade Federal do Paraná

[2] Boguszewski, César Luiz – Ph.D. and Professor at the Departments of Medical Clinic and Endocrinology, Hospital das Clínicas, Universidade Federal do Paraná

[3]Teixeira, Sandra – Physician at the Endoscopy Service, Hospital de Clínicas, Universidade Federal do Paraná

[4] Boeving, Anke – Physician at the Endocrinology Service, Hospital de Clínicas, Universidade Federal do Paraná

[5]De Bem, Ricardo – Physician at the Gastroenterology Service, Hospital de Clínicas, Universidade Federal do Paraná

[6] Parolim, Benito – Radiologist at the Center of Computed Tomography of Curitiba

[7]Pisani, Júlio César – Ph.D. and Professor at the Departments of Medical Clinic and Gastroenterology, Hospital de Clínicas, Universidade Federal do Paraná

[8]Prolla, João Carlos – Ph.D. and Professor/Advisor at the Post-Graduate Studies in Gastroenterology, Universidade Federal do Rio Grande do Sul, Porto Alegre

§Corresponding author: Dr. Odery Ramos Junior ---- Address: Rua Saldanha Marinho, 1422 , CEP 80430-160, Curitiba, Paraná, Brazil; Telephone/Fax numbers: 55-41-3232-9649; e-mail: oderyramos@gmail.com

ABSTRACT

Aim: To analyze the CTC performance for the screening of colorectal polyps in acromegalic patients.

Materials and Methods: A prospective study of 21 acromegalic patients, 12 male and 9 female, average age 49, who underwent CTC and CC. CTC was performed with a GE Helical Multislice Computed Tomography Apparatus. The colonoscopy was performed, in the same day, without previous knowledge of the CTC diagnostics. The study evaluated the capacity of CTC to detect patients with colorectal polyps and identify each colorectal lesion described by CC.

Results: In two patients (2/21), CC was incomplete. However, in all patients CTC was complete. In Phase I ("Per Patient"), CTC diagnosed 8 of the 9 patients with colorectal polyps and showed 88% sensitivity, 75% specificity and 81% accuracy. In Phase II ("Per Polyp"), out of the 21 acromegalic patients included in this study, 12 presented normal findings at CC. A total of 19 polyps were identified in 9 patients. 10 of the 19 polyps were smaller than 10 mm, and 9 were equal to or larger than 10. CTC identified 7 of the 9 polyps $\geq$ 10 mm described by CC and only 6 of the 10 small polyps identified at CC were detected by CTC. The histological analysis of resected lesions revealed 12 tubular adenomas, 6 hyperplastic polyps and 1 colonic tubulo-villous adenoma with an adenocarcinoma focus.

Conclusion: In this study, CTC was performed without complications and a complete and safe colorectal evaluation was possible in all acromegalic patients. Moreover, CTC showed good sensitivity to identify acromegalic patients with colorectal polyps.

Key words: Colorectal Polyps; Computed Tomographic Colonography; Acromegaly; Colonoscopy; Virtual Colonoscopy

INTRODUCTION

It is generally accepted that patients with acromegaly are at a moderately increased risk of developing colorectal cancer [1], and for this reason, many centers all over the world offer at least one screening colonoscopy to such patients.[2] Studies of acromegalic patients show that colonoscopy is technically difficult to be performed due to the increased bowel length and the loop complexity. These factors increase the risks of complications during colonoscopy in acromegalic patients[3].

The most feared complication related to colonoscopy is perforation[4] and 50% of these patients require surgery, with a concomitant increase in morbidity[5]. Perforation, on its turn, depends on whether polypectomy and/or biopsy is performed, the endoscopist`s experience, and in theory, the length of the large intestine, technical difficulties, and the time used for the colonoscopic procedure [6].

Decisions related to colonoscopy policies should also consider potential risks and benefits. The risk of death related to colonoscopy for the general population is 1in every 10.000 exams[6]. In acromegalic patients the estimate death rate associated with the colonoscopic procedure can be as high as 1 in 2898 procedures. Considering risk and benefit, the cost/benefit rate is high, meaning that in every 5 deaths prevented by means of a colonoscopic screening in acromegalic patients, there is a theoretical risk of 1 death due to screening procedures[7]. These observations must be considered when we propose developing a screening strategy for colorectal neoplasia in acromegalic patients.

Computed Tomographic Colonography (CTC), also named Virtual Colonoscopy (CV), is an innovative technology which is revolutionizing the diagnosis of colon and rectum cancers. Described by Vining[8] in 1994, this technique has been researched widely in the last years. CTC

has presented promising initial results for the detection of colorectal polyps and cancers, offering safety and possibility to evaluate the whole colon structure without sedation or anesthesia. However, this procedure is exclusively a diagnostic one, so therapeutic CC is necessary when positive results are obtained.

Conflicting data have been published about the CTC sensitivity for the detection of colorectal polyps. Some researchers have reported a higher than 90% sensitivity for the diagnosis of ≥10 mm polyps[9], whereas others have reported negative results with sensitivity ranging between 55% and 64%[10].

CTC has been proposed for colon and rectum diagnostic studies specially for the evaluation of the colon above the obstructed segment[11], colon evaluation after unsuccessful conventional colonoscopy[12], patients with higher risks of colonic perforation, anesthetic complications, and colorectal neoplasia screening in risk-factor populations[13,14].

Hence, due to the increase risk of CC complications in acromegalic patients such as colonic perforation, associated with the need of periodic screening for colorectal neoplasia in these patients, led the authors to consider, for the first time, the use of CTC as a safe procedure to identify colorectal polyps in acromegalic patients who then should be recommended additional procedure with CC.

MATERIALS AND METHODS

MATERIALS

From August 2005 to April 2007, 21 acromegalic patients, assisted at the Neuroendocrinology and Metabolism Service of the Clinic Hospital, Universidade Federal do Paraná (HC-UFPR), underwent both CTC and CC, on the same day, to screen for polyps and colorectal cancer.

Twelve of the 21 acromegalic patients were male and 9 female, average age 49. The youngest was 35 and the oldest 65. CTC was performed at CETAC – Center of Computed Tomography of Curitiba – by a radiologist, graduated from the Brazilian College of Radiology, and with a learning curve for CTC performed in 60 non-acromegalic patients recommended to undergo CC. CC was performed at the Digestive Endoscopy Unit of the Clinic Hospital, UFPR, by an endoscopist graduated from SOBED – Brazilian Society of Digestive Endoscopy. All patients were informed about the purpose of the study, and only the ones who signed the consent form were selected. The project was approved by the Committee of Ethics and Research on Human Beings of HC-UFPR, protocol CEP/HC 941.171/2004-10.

METHODS

CTC was performed with a GE Helical Multislice Computed Tomography Apparatus. CC was performed with an Olympus videocolonoscope, model CV 160. The findings described at CC as well as at CTC were evaluated according to the characteristics of each colorectal lesion, number, location and diameter. At CTC, each polyp diameter was measured in 3D with an electronic ruler and at CC, the length of an open biopsy tweezers, estimated at 5mm, was used as a measurement reference. To determine the location of each lesion, colorectal evaluation was divided into six segments: rectum, sigmoid, descendent, transverse, ascendant e cecum.

CC was considered incomplete when, for any reason, the equipment was not able to reach cecum. CTC, on the other hand, was considered incomplete when at least one colon segment could not be studied appropriately.

CTC TECHNIQUE

CTC techniques and interpretations were established according to conventional protocols[15]. Helical multislice computed tomography images were taken from the abdomen and the pelvic

region. Images were obtained by means of 5-mm collimation, 2.5 mm increments, at 110 mA and 110 kV. Further colonic reconstructions were performed at a GE AW 4.0 05 workstation, with the GE TEKTRONIK software, version AW 4.0-05.2.5 S017 navigator 3225012684. The colon segments were analyzed individually, being correlated simultaneously with the axial slices, the multiplanar and tri-dimensional reconstructions, considering the insufflation, topography, caliber, surface and loop walls of these colon segments.

Intestinal preparation for CTC and CC was the same. A liquid diet without residues, prescribed for a period of 48 hours, included the oral intake of 1 liter of 20% mannitol solution and one additional liter of water administered at least 12 hours before the examination. After intestinal cleaning, the colon distension was performed by means of insufflation of approximately 1.2 to 1.8 liters of atmospheric air trying to avoid any patient discomfort. The patient was laid in a dorsal decubitus position. An image was obtained to verify whether distension was appropriate, and additional air was insufflated, if necessary. Next, computed tomography of the whole abdomen and pelvis was performed during a breath pause. The same procedure was performed with the patient in ventral decubitus position.

Data were transferred to a workstation, where the images were analyzed by a radiologist. With the help of the software, a fly-through examination in the colon was performed. When the examination was completed and a report issued, the patient underwent CC to take advantage of the same bowel preparation.

STATISTICAL ANALYSIS

As acromegaly is not very frequent, we have selected all eligible patients from the Neuroendocrinology Service, at the Clinic Hospital of UFPR. The statistical analysis comprised

determination of CTC sensitivity, specificity, positive and negative predictive values, and accuracy in relation to the number of acromegalic patients with colorectal polyps.

RESULTS

In 2 patients, CC was incomplete. In both cases, CTC was complete for the evaluation of all colon segments and did not detect lesions in the colonic segments not reached by CC. In one case, CTC identified a 10mm polyp confirmed by CC in the descendant colon and did not detect other lesions in the right colon. In the other patient, CTC evaluated all the colonic segments not reached by CC, without detecting any lesion, thus complementing the colon screening which could not be performed at CC.

Phase – I ("Per Patient"): When CTC capacity to diagnose in acromegalic patients colorectal polyps of any size was considered (Table 1), 9 of the acromegalic patients presented polyps, 8 of them diagnosed at CTC, with 1 false negative. Twelve patients did not present polyps: 9 were confirmed at CTC, and 3 patients presented false positive results. Seven of the 9 patients with polyps presented polyps equal to or higher than 10mm; 6 of them were diagnosed at CTC. Out of the 14 patients who did not present large polyps, CTC confirmed 12 of them and revealed two false positives. Out of the 9 patients who presented polyps, 6 presented polyps smaller than 10mm, 4 of them detected at CTC. The 15 acromegalic patients who did not present polyps of this size, only one had the polyp diagnosed at CTC. There was 1 false positive and 2 false negative.

Table 1 Sensitivity (SE), Specificity (SP), Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Accuracy of CTC according to the number of acromegalic patients who present polyps of any size detected by means of both methods.

		CC		
		Patients with polyps	Patients without polyps	Total
		+	-	
CTC	+	8	3	11
	-	1	9	10
Total		9	12	21

Sensitivity (SE) = 0.88 (95% IC: 0.65, 0.97)
Specificity (SP) = 0.75 (95% IC: 0.57, 0.81).
Positive Predictive Value (PPV) = 0.72 (95% IC: 0.53, 0.80).
Negative Predictive Value (NPV) = 0.90 (95% IC: 0.68, 0.98).
Accuracy = 0.81 (95% IC: 0.60, 0.88)

Phase - II ("Per Polyp"): Analysis of CTC was also performed based on the identification of each colorectal polyp, according to its diameter, reported at CC, in the acromegalic patients. Out of the 21 acromegalic patients included in this study, 12 presented normal findings at CC. A total of 19 polyps were identified in 9 patients. 10 of the 19 polyps were smaller than 10 mm, and 9 were equal to or larger than 10 mm. There were 4 false negative and 1 false positive results for < 10 mm polyps. Only 6 small polyps identified at CC were detected by CTC. The false positive result in the re-evaluation of the CTC images was considered a residue and 4 < 10 mm polyps were not identified even after a careful CTC re-evaluation examination was performed. When we studied the reasons for the 2 false negative results for ≥ 10 mm polyps at CTC, a further analysis of CTC images revealed that one image was interpreted as a thick fold in the sigmoid and the other undetected polyp was interpreted as a residue. The two false positive findings of ≥ 10 mm polyps at CTC are accounted for as a wrong interpretation of the residues as polyps.

The 19 identified polyps were dissected successfully and examined histologically: 12 were adenomatous and 6 hyperplastic. In a 65-year old male patient, with 30-year acromegaly but no symptomatic colorectal disease, CTC detected a 15 mm polypoid lesion in the transverse colon. This finding was confirmed at CC. The polyp was dissected and the anatomopathologic

diagnostic revealed a tubulo-villous colonic adenoma with a multifocal high-degree epithelial dysplasia and a focus of well-differentiated adenocarcinoma (Table 2).

Table 2 Results of histological analysis of polyps removed from acromegalic patients.

Histology of Colorectal Lesions				
	Total N=19	Tubular Adenoma N=12	Hyperplastic Polyps N=06	Colorectal Cancer N=01
Diameter				
< 10 mm	10	06	04	-
Polyps ≥ 10 mm	09	06	02	1*

*Obs.: Colonic Tubulo-Villous Adenoma with a well differentiated adenocarcinoma focus (Intramucous and with lesion-free pedicle).

DISCUSSION

In this study, CC was performed as control on acromegalic patients, and the endoscopist described that there were some difficulties to pass through the sigmoid colon with the colonoscope. In two cases, due to redundant intestinal loops, despite the several maneuvers tried, colonoscopy could not be completed. The examinations were interrupted to avoid potential risks and complications. CTC in these two patients was complete; however, because of the complexity of the intestinal loops, more time was necessary to interpret the data collected. The two patients whose CC was not complete and whose CTC did not detect any lesions were recommended for a follow-up procedure after one year.

In Phase I (Per Patient), the authors analyzed the diagnostic of acromegalic patients with polyps of any size. The results of the 21 CTC were classified as 8 true positive, 9 true negative, 3 false positive and 1 false negative results. The performance per patient improved as the polyp size increased. With < 10 mm polyps, sensitivity decreased significantly. We point out that in the per-patient analysis only the lesions which were combined with the polyps at CC were considered true positive findings. We consider that the results obtained with the per-patient approach are

more important since the purpose is to identify only the patients who might need to undergo colonoscopy.

The patient with colonic tubulo-villous adenoma with a well differentiated adenocarcinoma focus, resected by CC, was also diagnosed correctly by CTC. Consequently, the authors acknowledge that CTC was able to detect colorectal cancer in this acromegalic patient.

In this study, around 20% (4/21) of the acromegalic patients reported that they had not obtained a good response from the preparation used to cleanse the bowel. In these cases, it was necessary to repeat the same mannitol dose determined by the protocol to perform CTC and CC. All colonic segments could be evaluate by CTC and CC appropriately. However, the presence of residues contributed to false positive findings. This situation was also described by Renehan et al.[7] who associated this difficulty in cleansing the bowel with a longer colonic transit time in acromegalic patients and suggested, as we have done, that the standard cleansing for colon preparation can be inappropriate for such patients.

When CTC analysis was performed per polyp, the low sensitivity obtained for the small polyps in this study was also shown in non-acromegalic patients[10]. It is no surprise to find out that CTC can better detect large polyps – larger than 10 mm - than smaller polyps. However, the definition of what constitutes a clinically important polyp in regard to its size and morphology is very important to evaluate CTC accuracy. It is a debatable issue.[16]

There are two limitations that need to be acknowledged and addressed regarding the present study. The first one concerns the small cohort of patients in this study due to the low prevalence of acromegaly accounts. However, the authors register the multiprofessional initiative to conduct this study and demonstrate the feasibility of performing CTC to detect colorectal adenoma in acromegalic patients. Another limitation is the radiologist's experience which can be considered

limited by a short learning curve due to CTC availability and cost in our region. This fact may have influenced the false positive and negative results. Finally, although it is not a limitation, the authors believe that if new software could be used, such as the V3D Colon System developed by Dr. Pickhardt`s team in Madison, Wisconsin, USA, more precise results could have been obtained. In the studies reported by this team, they demonstrated that sensitivity to detect polyps with the V3D Colon System was higher when compared with the Navigator System[17].

This study presents the first records of CTC in the screening of colorectal polyps in acromegalic patients. The results reveal that CTC was able to perform a complete colorectal evaluation without complications and had good sensitivity to identify acromegalic patients with colorectal polyps.

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