The role of quantitative computed tomography perfusion in the assessment of colorectal thickening

Marwa Omran[a], Hisham Imam[b], Adel Gabr[c], Haisam Atta[a]

Departments of [a]Diagnostic Radiology, [c]Medical Oncology, South Egypt Cancer Institute[b], Department of Diagnostic Radiology, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Marwa Ali Mohamed, BSc, Demonstrator at Diagnostic Radiology Department, South Egypt Cancer Institute, Assiut University, Egypt.
Zip Code: 71511;
Tel.: 01066116189.
e-mail: marwa2311@aun.edu.eg

Received 28 October 2019
Revised 13 November 2019
Accepted 27 November 2019
Published 23 February 2021

Journal of Current Medical Research and Practice
2021, 6:76–81

Objective
To investigate the correlation between quantitative computed tomography (CT) perfusion findings in patients with colorectal thickening discovered at various imaging studies and histopathological examination.

Patients and methods
CT protocol included a precontrast scan. A region of 2 cm (four cuts) was selected based on the precontrast series. A dynamic study of the selected area was performed after contrast injection. Statistical analysis of the data was done.

Results
The current study enrolled 43 patients with suspected colorectal cancer; out of them, 39 patients were confirmed to have colorectal cancer based on the pathological evaluation. Blood flow of the thickened colon had 92% sensitivity and 50% specificity for diagnosing the malignant lesions, whereas blood volume had 97.4% sensitivity and 75% specificity. Permeability surface of the thickened part had 82% sensitivity and 75% specificity. Moreover, mean transit time had 44% sensitivity and 75% specificity.

Conclusion
Quantitative perfusion CT measurements enable differentiation and better discrimination between malignant and benign nature of colorectal thickening; however, the need for histopathological correlation cannot be omitted.

Keywords:
blood flow, blood volume, colorectal cancer, computed tomography perfusion

J Curr Med Res Pract 6:76–81

2357-0121

Introduction

The presence of large bowel wall thickening (BWT) on computed tomography (CT) is a common reason for gastroenterology consultation and often leads to colonoscopy, which affects health care resources and exposes patients to quantifiable risks [1].

Causes of large BWT are inflammatory, infectious, neoplastic, or ischemic conditions [2].

So the important question for the clinician, who may request CT for a variety of reasons, is whether an incidental finding of large BWT signifies the presence of colorectal cancer (CRC) [3].

In CRC, neovascularization was reported to arise early in the adenomacarcinoma sequence. Angiogenesis is an important process of CRC and plays an essential role in the process of growth and metastasis [4].

Perfusion CT is used to measure the vascular perfusion in tumors to gain insight into the functional nature of the neoplastic lesion. One of the exciting aspects of perfusion CT is its ability to quantify the degree of angiogenesis in solid tumors by providing quantifiable vascular parameters [5].

Changes observed at imaging are linked to differences in tumor pathophysiology. CT perfusion parameters represent the alteration of blood flow (BF), blood volume (BV), and permeability in tumor vessels secondary to their structural (chaotic structure, heterogeneity of vascular density, and dilated capillary beds) and functional (high permeability to macromolecules, intermittent flow, or arteriovenous shunts) abnormalities [6].

CT perfusion has shown significant differences in perfusion values when comparing normal tissue versus tumoral tissue. Significantly higher perfusion parameters have been reported in patients with rectal, hepatic, lung, and head and neck tumors [7].

The aim of the work of our study is to investigate the correlation between quantitative CT perfusion findings in patients with colorectal thickening discovered at various imaging studies and histopathological examination.

Patients and methods

Patients and masses

This prospective study was conducted at the South Egypt Cancer Institute Radiology Department, Assiut University, after approval of the local ethical committee of Faculty of Medicine, Assiut University. The study included 43 patients with colonic or rectal thickening discovered by various imaging modalities (12 were females and 31 were males), and their age ranged from 20 to 92 years, and then all patients underwent colonoscopy (except three patients who underwent surgical exploration without colonoscopy, and one patient in which punch biopsy was taken from the anal mass), and biopsy had to be considered for histopathological examination. After approval of the local ethical committee of Faculty of Medicine, Assiut University (IRB no 17100829). Informed written consent was taken from each patient.

Computed tomography scan technique

CT perfusion was done using a 16 multidetector CT scanner (GE Bright Speed 16 row; GE, GE United States, Chicago, Illinois). One abdominal scout was acquired in anteroposterior view, and then precontrast axial cuts were taken during a breath-hold at the end of inspiration to identify the colonic or rectal thickening (Fig. 1) using the following parameters: 120 kV, 140 mA, and 5-mm slice thickness. After colonic or rectal thickening localization, a region of 2 cm (four cuts) was selected based on the precontrast series for the dynamic study. A dynamic study of the chosen area was performed in a single breath-hold at the end of inspiration at a static table position. A total of 50 ml of nonionic iodinated contrast medium (iopromide, Ultravist 300; Schering, Berlin, Germany) was injected at a rate of 3.5: 4 ml/s. The following CT parameters were used to acquire dynamic data: 1 s gantry rotation time using a 'cine mode' acquisition, 120 kV, 200 mA, acquisition of four sections per gantry rotation, and 5-mm reconstructed section thickness. Scanning was initiated with no delay from the start of injection, and images were acquired for a total duration of 60 s.

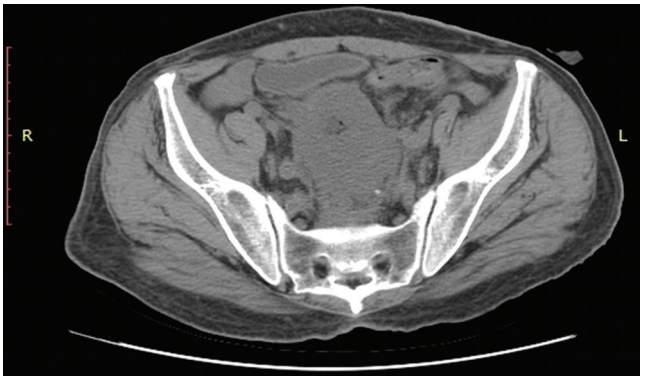
Image interpretation and analysis

Data were processed at a workstation (Advantage Windows 4.6; GE Medical Systems) (ADW, version 4.6) with CT perfusion software (GE Perfusion 4). The following steps calculated functional data: displaying images at an appropriate window, such as soft tissue for abdomen (width = 400 HU, level = 40 HU), obtaining a reference arterial input curve by placing a region of interest (ROI) within the best-visualized artery on the selected image, either the aorta or iliac arteries manually ensuring that the ROI did not include any mural calcification, another ROI was placed inside the visible colonic or rectal wall thickening taking care not to involve surrounding fat or intraluminal gas, additional ROI was placed within the apparently normal bowel wall, and the last ROI was placed within the ipsilateral visible gluteus or paraspinal muscle fibers (Fig. 2). Then perfusion maps and values are computed. The quantitative parameters, BF, BV, mean transit time, and permeability surface area product, were recorded in each patient (Fig. 3a and b).

Statistical analysis

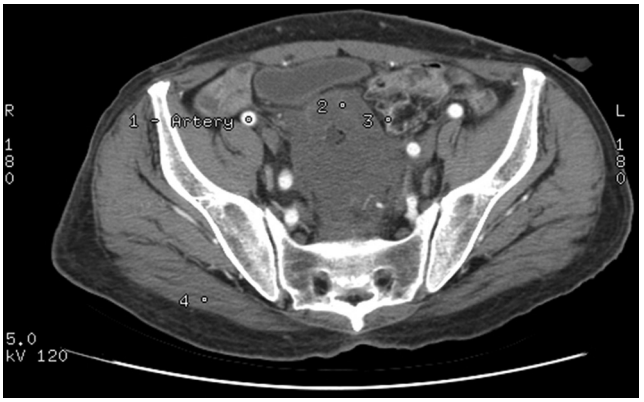
Data were collected and analyzed using Statistical Package for the Social Science (version 20; IBM, Armonk, New York, USA). Continuous data were expressed in the form of mean ± SD or median (range), whereas nominal data were expressed in the form of frequency (percentage). χ^2 test was used to compare the nominal data of different groups in the study, whereas the Student t test was used to compare the mean of different two groups and analysis

Figure 1



Precontrast series of CT perfusion. CT, computed tomography.

Figure 2



Sites of ROIs: ROI 1 was put within the best-visualized artery. ROI 2 was put within the visible colonic or rectal thickening. ROI 3 was put within the normal colonic wall if present. ROI 4 was put within the gluteus muscle. ROI, region of interest.

Figure 3

(a, b) Quantitative assessment of CT perfusion. CT, computed tomography.

of variance tests for more than two groups. Multivariate regression analysis was used for the prediction of the malignant nature of colorectal thickening. The receiver operating characteristic curve determined the diagnostic accuracy of different parameters of CT perfusion to diagnose the malignant colorectal thickening. *P* value was significant if less than 0.05.

Proof of diagnosis

Histopathological examination was performed in all patients using pathologic specimens obtained via colonoscopic examination in the planes that correspond to ROI of the CT imaging sections (where its distance is measured from the anal verge).

Results

The study enrolled 43 patients with suspected CRC, out of them, 39 patients were confirmed to have CRC based on the pathological evaluation.

Demographic and clinical data of the studied patients

The mean age of enrolled patients was 55.21 ± 18.87 years, with a range between 20 and 92 years, and out of them, 31 (72.1%) patients were males. Only two (4.7%) patients had a family history of CRC. It was noticed that 10 (23.3%), four (9.3%), and three (7%) were smokers, diabetic, and hypertensive, respectively (Table 1).

Colonoscopic, imaging findings, and pathological evaluation of the studied patients

Regarding CT findings, it was noticed that colonic thickening presented in all cases, whereas 17 (39.5%) cases had colonic mass. The most affected site was the anorectal region (46.5%) followed by the rectosigmoid junction (27.9%) and hepatic flexure (7%) (Table 2).

A biopsy was taken by colonoscopy in the majority (90.7%) of cases whereas the intraoperative biopsy was done in three (7%) cases, and punching through the anal canal was done in one patient. Based on the pathological evaluation of the biopsies, 39 (90.7%) cases showed evidence of malignancy (Table 3).

Table 3 shows that 27 (62.8%) biopsies revealed moderately differentiated adenocarcinoma, whereas each of the well and poorly differentiated adenocarcinoma presented in four (9.3%) patients.

Quantitative assessment of lesions by computed tomography perfusion

Table 4 shows the different CT perfusion parameters of malignant lesions in comparison with the benign lesions and muscle. It was noticed that malignant lesions had significantly higher mean BF, BV, and permeability surface in comparison with the benign lesions and muscle ($P < 0.05$), but the mean transit time had no significant difference between malignant lesions in comparison with benign lesions and muscle ($P < 0.05$). It was noticed that there were no significant differences between benign lesions and muscle regarding quantitative assessment.

Table 1 Demographic and clinical data of studied patients

Variables	*n*=43
Age (years)	55.21±18.87
Range	20-92
Sex	
Male	31 (72.1)
Female	12 (27.9)
Family history	2 (4.7)
Smoking	10 (23.3)
Hypertension	4 (9.3)
Diabetes mellitus	3 (7)

Data were expressed in the form of the mean±SD and *n* (%).

Table 2 Computed tomography Findings of the studied patients

CT findings	*n*=43
Presence of thickening	43 (100)
Presence of mass	17 (39.5)
Site of lesion	
Anorectal	20 (46.5)
Rectosigmoid	12 (27.9)
Descending colon	1 (2.3)
Splenic flexure	1 (2.3)
Transverse colon	1 (2.3)
Hepatic flexure	3 (7)
Ascending colon	2 (4.7)
Cecum	1 (2.3)
Site of anastomosis (previous surgery)	2 (4.7)

Data were expressed in the form of *n* (%). CT, computed tomography.

Table 3 Pathological evaluation of the studied patients

Pathological evaluation	*n*=43 [*n* (%)]
Method of obtaining biopsy	
Colonoscopy	39 (90.7)
Intraoperative	3 (7)
Punching	1 (2.3)
Pathological findings	
Benign	4 (9.3)
Malignant	39 (90.7)
Well differentiated adenocarcinoma	4 (9.3)
Moderately differentiated adenocarcinoma	27 (62.8)
Poorly differentiated adenocarcinoma	4 (9.3)
Mucinous adenocarcinoma	2 (4.7)
Signet ring adenocarcinoma	1 (2.3)
Carcinoma in situ	1 (2.3)

Data were expressed in the form of the *n* (%).

Diagnostic accuracy of quantitative computed tomography perfusion parameters in diagnosis of nature of colorectal thickening

BF of the thickened colon had 92% sensitivity and 50% specificity for diagnosing the malignant lesions when considering cutoff point of 31.82 ml/100 g/min with area under curve (AUR) was 0.71 and *P* value less than 0.001, whereas BV had 97.4% sensitivity and 75% specificity when considering cutoff point of 1.02 ml/100 g, with area under the curve of 0.86 and *P* value of 0.001.

Permeability surface of the thickened part had 82% sensitivity and 75% specificity when considering cutoff point of 4 ml/100 g/min, with AUR was 0.78, but was of insignificant values ($P < 0.14$). Moreover, mean transit time had 44% sensitivity and 75% specificity when considering cutoff point of 5.5 s, with area under the curve of 0.55 and *P* value of 0.19 (Table 5).

Multivariate regression analysis for prediction of malignant nature of colorectal thickening

In the logistic regression analysis, the statistical significance of individual coefficients was tested using the Wald x^2 statistic. It was noticed that increased BF, BV, and permeability surface had shown to be distinctive between malignant and benign lesions (Table 6). Those previously mentioned variables were significant predictors for the malignant nature of the colorectal thickening ($P < 0.05$). The inferential goodness of fit test was Hosmer and Lemeshow test, which showed a good fit of the current logistic regression model of the data, with overall accuracy of 76%. Cox and Snell R^2 was 0.65, and Nagelkerke R^2 was 0.68.

Discussion

CRC is the second most common cause of cancer mortality in developed countries with an increasing prevalence in developing countries owing to the changing eating habits and lifestyle [8].

The overall number of patients is 43 patients with suspected CRC; out of them, 39 patients were confirmed to have CRC based on the pathological evaluation.

It was noticed in the current study that 10 (23.3%), four (9.3%), and three (7%) were smokers, diabetic, and

Table 4 Quantitative assessment by computed tomography perfusion based on nature of lesions

Quantitative assessment	Malignant lesions	Benign lesions	Muscle
Blood volume	5.14±1.03	1.59±0.55	1.18±0.80
Blood flow	65.51±15.55	25.83±9.32	19.25±5.32
Mean transit time	6.32±1.03	5.20±2.11	5.98±2.01
Permeability surface	12.43±3.34	3.88±3.89	3.68±1.04
Significance	*P*1	*P*2	*P*3
Blood volume	0.01	0.01	0.34
Blood flow	0.02	0.01	0.45
Mean transit time	0.29	0.11	0.09
Permeability surface	0.02	0.02	0.06

Data were expressed in the form of the mean±SD. *P*<0.05. *P*1 compared between malignant and benign lesions. *P*2 compared between malignant lesions and muscle. *P*3 compared between benign lesions and muscle.

Table 5 Diagnostic accuracy of quantitative computed tomography perfusion parameters in diagnosing of nature of colorectal thickening

	Blood volume	Blood flow	Permeability surface	Mean transit
Sensitivity (%)	97.4	92	82	44
Specificity (%)	75	50	75	75
PPV (%)	97.4	95	97	94.4
NPV (%)	75	40	30	12
Cutoff point	1.02	31.82	4	5.5
AUC	0.86	0.71	0.78	0.55
P	<0.001	<0.001	0.14	0.19

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value. *P*<0.05.

Table 6 Multivariate regression analysis for prdiction of malignant nature of colorectal thickening

Parameters	Odd's ratio	95% confidence interval	*P*
Increased blood volume	2.23	2.01-3.99	0.01
Increased blood flow	1.98	1.23-3.98	0.00
Permeability surface	1.56	1.04-2.31	0.00

P<0.05.

hypertensive, respectively. This is in agreement with Ahmadi *et al.* [9], who reported that the prevalence of hypertension and type 2 diabetes mellitus in the patients with CRC was 13.38 and 8.69%, respectively, and Liang *et al.* [10], who reported that both past and current smokers have an increased risk of CRC incidence and mortality.

In this study, malignant lesions had significantly higher BV, BF, and permeability surface in comparison with the benign lesions and muscle ($P < 0.05$).

This is in agreement with Bellomi *et al.* [11], who reported that BF, BV, and permeability surface were significantly higher in rectal cancer than in normal rectal wall ($P < 0.001$).

Goh *et al.* [12], reported a significant difference in mean BV, BF, and permeability between patients with cancer and those with diverticulitis ($P < 0.0001$); patients with cancer had the highest BV, BF, and permeability surface.

However, mean transit time had no significant difference between malignant lesions in comparison with benign lesions and muscle ($P < 0.05$). However, Goh and colleagues, reported a substantial difference in mean transit time between patients with cancer and those with diverticulitis; patients with cancer had the shortest transit time. Bellomi and colleagues, reported that the mean transit time is lower ($P = 0.06$) in rectal cancer than in normal rectal wall.

Kambadakone and Sahani [13], reported that rectal cancer shows high BF and a shorter mean transit time compared with the normal rectum. Similarly, Tan and Iyer[14] also reported that rectal cancer showed higher tissue BF and shorter mean transit times than normal rectum.

BF of the thickened colon had 92% sensitivity and 50% specificity for diagnosing the malignant lesions when considering cutoff point of 31.82 ml/100 g/min, whereas BV had 97.4% sensitivity and 75% specificity when considering cutoff point of 1.02 ml/100 g.

In agreement with Goh and colleagues, who reported similar sensitivity for both BV and BF (80% for each) and specificity of 70 and 75%, respectively, when considering cutoff point of 4.8 ml/100 g for BV and 60.2 ml/100 g/min for BF.

Permeability surface of the thickened part had 82% sensitivity and 75% specificity when considering cutoff point of 4 ml/100 g/min. Moreover, mean transit time had 44% sensitivity and 75% specificity when considering cutoff point of 5.5 s.

Goh and colleagues, reported that sensitivity for permeability surface was 60% and specificity was 90% when considering cutoff point of 13.7 ml/100 g/min whereas sensitivity for mean transit time was 85% and specificity was 50% when considering cutoff point of 10.8 s.

Summary and conclusion

Perfusion CT has substantially affected the imaging and treatment aspect in the management of patients with CRC, particularly as a biomarker for monitoring the response of various treatment modalities, which may have further clinical usefulness in the staging of the disease and prognostic value as well.

In summary, we found that quantitative perfusion CT measurements enable differentiation and better

discrimination between malignant and benign nature of colorectal thickening; however, the need for histopathological correlation cannot be omitted.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1 Al-Khowaiter SS, Brahmania M, Kim E, Madden M, Harris A, Yoshida EM, *et al*. Clinical and endoscopic significance of bowel-wall thickening reported on abdominal computed tomographies in symptomatic patients with no history of gastrointestinal disease. Can Assoc Radiol J 2014; 65:67–70.

2 Fernandes T, Oliveira MI, Castro R, Araújo B, Viamonte B, Cunha R. Bowel wall thickening at CT: simplifying the diagnosis. Insights Imag 2014; 5:195–208.

3 Uzzaman M, Alam A, Nair M, Borgstein R, Meleagros L. Computed tomography findings of bowel wall thickening: its significance and relationship to endoscopic abnormalities. Ann Royal Coll Surg Engl 2011; 94:23–27.

4 Hayano K, Fujishiro T, Sahani DV, Satoh A, Aoyagi T, Ohira G, *et al*. Computed tomography perfusion imaging as a potential imaging biomarker of colorectal cancer. World J Gastroenterol 2014; 20:17345.

5 Dighe S, Castellano E, Blake H, Jeyadevan N, Koh M, Orten M, *et al*. Perfusion CT to assess angiogenesis in colon cancer: technical limitations and practical challenges. Br J Radiol 2012; 85:e814–e825.

6 Figueiras RG, Padhani AR, Goh VJ, Vilanova JC, González SB, Martín CV, *et al*. Novel oncologic drugs: what they do and how they affect images. Radiographics 2011; 31:2059–2091.

7 Petralia G, Bonello L, Viotti S, Preda L, d'Andrea G, Bellomi M. CT perfusion in oncology: how to do it. Cancer Imag 2010; 10:8.

8 Ghimire P. Perfusion computed tomography in colorectal cancer: protocols, clinical applications and emerging trends. World J Gastroenterol 2009; 26:005.

9 Ahmadi A, Mobasheri M, Hashemi-Nazari SS, Baradaran A, Choobini ZM. Prevalence of hypertension and type 2 diabetes mellitus in patients with colorectal cancer and their median survival time: a cohort study. J Res Med Sci 2014; 19:850.

10 Liang PS, Chen TY, Giovannucci E. Cigarette smoking and colorectal cancer incidence and mortality: systematic review and meta□analysis. Int J Cancer 2009; 124:2406–2415.

11 Bellomi M, Petralia G, Sonzogni A, Zampino MG, Rocca A. CT perfusion for the monitoring of neoadjuvant chemotherapy and radiation therapy in rectal carcinoma: initial experience. Radiology 2007; 244:486–493.

12 Goh V, Halligan S, Taylor SA, Burling D, Bassett P, Bartram CI. Differentiation between diverticulitis and colorectal cancer: quantitative CT perfusion measurements versus morphologic criteria—initial experience. Radiology 2007; 242:456–462.

13 Kambadakone AR, Sahani DV. Body perfusion CT: technique, clinical applications, and advances. Radiol Clin N Am 2009; 47:161–178.

14 Tan CH, Iyer R. Use of computed tomography in the management of colorectal cancer. World J Radiol 2010; 2:151.