学位論文（博士）

Hemodynamic changes of abdominal organs after CT colonography with transrectal administration of CO2: evaluation with early-phase contrast-enhanced dynamic CT
（経直腸的炭酸ガス注入による CT コロノグラフィー後の腹部臓器の血行動態変化：造影ダイナミック CT 早期相による評価）

氏名　伊原　研一郎
所属　山口大学大学院医学系研究科
医学専攻　放射線医学講座

令和３年 11 月

学位論文の関連論文の研究背景及び要旨

所属　放射線医学講座
氏名　伊原　研一郎

〔題名〕

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〔研究背景〕

CT コロノグラフィー（以下 CTC）は 大腸癌の低侵襲で信頼性の高い診断法として広く利用されている。CTC は、内視鏡検査が困難な患者であっても、大腸癌やポリープを高感度で検出でき、また病期分類のための局所進行度を決定することができる。しかし、スクリーニング検査としての CTC で、造影 CT を日常的に使用する必要性はない。

一方で、大腸癌の患者では、術前に転移病変の有無を評価することが治療方針を決定する上で重要であり、そのためには dynamic 造影 CT（以下 DCE-CT）が有用である。したがって、CTC と CTC 直後に DCE-CT を組み合わせることは、大腸と大腸外の両方の所見を詳しく調べるために有効であると考えられる。しかし、炭酸ガス拡張を用いた CTC の直後に行う DCE-CT では、大腸壁から吸収された炭酸ガスによって腹部臓器や血管の血行動態が影響を受け、内臓の造影効果の変化や血流変化に関連した肝偽病変が生じる可能性があると考えられるが、CTC 後に行われた DCE-CT における腹部臓器の血行動態の変化を評価した報告はこれまでにない。

本研究の目的は、炭酸ガス拡張を用いた CTC 直後の DCE-CT 早期相において、腹部臓器・血管の血行動態の変化と、血流に関連する肝偽病変の有無を、CTC 併用時と非併用時の DCE-CT を比較して明らかにすることである。

〔要旨〕

方法：

2010 年 10 月から 2019 年 9 月までに山口大学医学部附属病院および川崎医科大学附属病院で画像検査を受けられた患者を後ろ向きに検討した。炭酸ガス拡張を用いた CTC 直後に DCE-CT を実施した 82 例を CE-CTC 群とした。CE-CTC 群と同様の DCE-CT プロトコールで撮像された CTC 非併用の DCE-CT の症例のうち、年齢や性別をマッチさせた 77 例を対照群とした。CE-CTC 群は男性 48 名、女性 34 名で年齢は 21～85 歳（平均 60 歳）、対照群は男性 46 名、女性 31 名で年齢は 20～84 歳（平均 60 歳）であった。

CT は多列検出器 CT 装置（Optima CT660 Pro または LightSpeed Ultra 16、ともに GE 社製）を用いて行った。CE-CTC 群では、大腸の拡張は自動低圧炭酸ガス送出装置（HP-2®；堀井薬品工業

社製）を用いて行った。

胃、肝臓（右葉、左葉）、膵尾部、門脈（PV）、脾静脈（SpV）、上腸間膜静脈（SMV）、下腸間膜静脈（IMV）の CT 値を、それぞれ非造影 CT と早期 CT で測定した。造影 CT 値として、非造影 CT 画像と DCE-CT 早期相画像の CT 値（Hounsfeld unit 値）の差を算出した。これらの測定は、2 名の放射線科医がワークステーション（EV InsiteS；PSP 社製）で各々行い、各臓器、血管の画像上に円形または楕円形の関心領域（ROI）を設定し、2 人の測定した造影 CT 値の平均を算出した。また、肝偽病変の有無を共同で記録した。肝偽病変は、DCE-CT 早期相で、肝左葉内側区の後縁または胆嚢窩の周囲にある高または低吸収領域として定義した。

Mann-Whitney U 検定を用いて各臓器と血管ごとの造影 CT 値を比較した。また、カイ二乗検定を用いて CE-CTC 群と対照群の間で肝病変の発症頻度を比較した。

結果：

CE-CTC 群と対照群の各臓器・血管における造影 CT 値の平均値の比較は表 1 のとおりで、CE-CTC 群の肝実質(図 1)、PV、SMV・IMV(図 2)の造影 CT 値は、対照群に比べて有意に高かった。一方で、CE-CTC 群の胃(図 3）、膵尾部、SpV の造影 CT 値は、対照群に比べて有意に低かった。

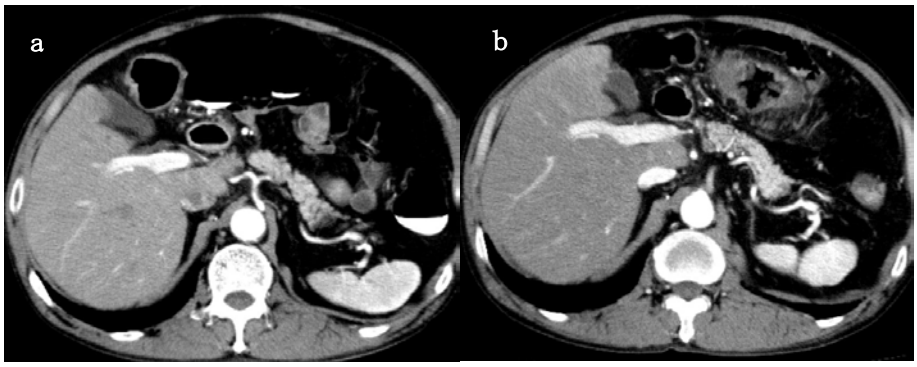
肝偽病変は、CE-CTC 群の 6 例（7%）において、肝左葉内側区の後縁（n＝5）または胆嚢窩周囲（n＝1）に低吸収領域として認められた（図 4）が、対照群では認められなかった（p＝0.016）。表 2 は、CE-CTC 患者で肝偽病変がある場合とない場合の肝臓の造影 CT 値を比較した結果で、肝偽病変のある CE-CTC 患者の肝の造影 CT 値は、肝偽病変のない CE-CTC 患者の造影 CT 値よりも有意に高かった。

表 1．各臓器・血管における造影 CT 値の平均値の比較

臓器・血管	平均造影 CT 値 (HU)		
	CE-CTC 群	対照群	*P* 値
肝右葉	33.94±16.06	26.55±15.97	0.003
肝左葉	41.06±18.03	33.05±17.79	0.003
胃	53.78±19.39	73.46±24.12	<.0001
膵尾部	69.81±18.69	83.08±20.95	<.0001
PV	155.1±37.23	139.24±46.69	0.013
SMV	139.42±53.08	98.91±55.94	<.0001

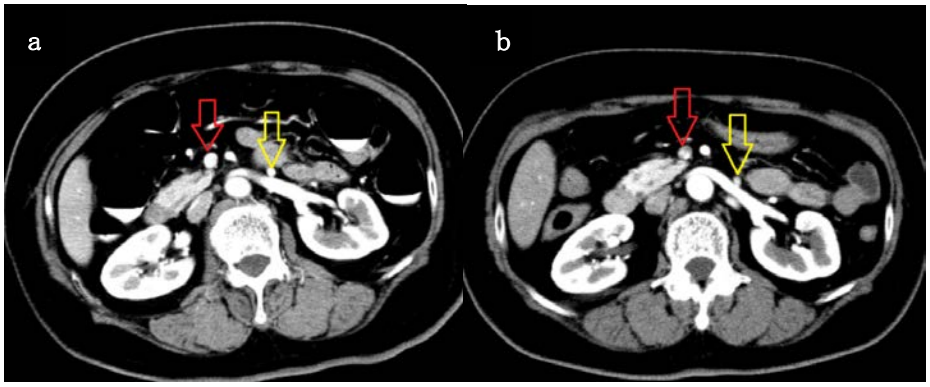
IMV	162.64±54.95	65.72±56.27	<.0001
SpV	163.31±38.46	186.31±48.26	0.014

図１．CTC 併用 DCE-CT 早期相画像(a)と CTC 非併用 DCE-CT 早期相画像(b) ：肝臓の比較



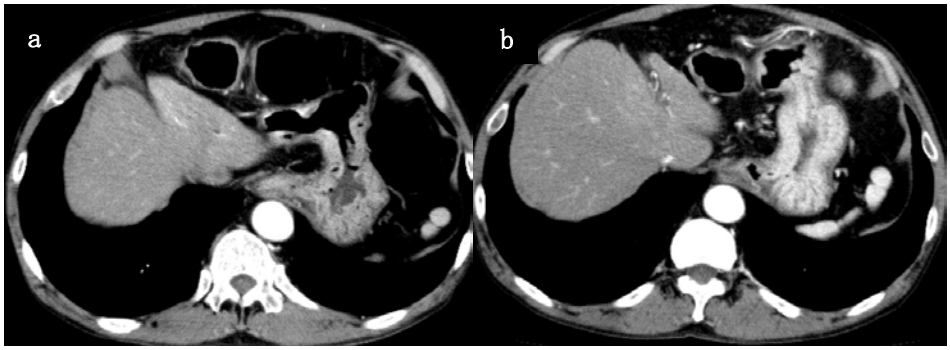
CTC 併用 DCE-CT 早期相(a)では、CTC 非併用 DCE-CT 早期相(b)に比べて、肝実質の造影効果が高い。　＊a、b とも同一患者

図 2. CTC 併用 DCE-CT 早期相画像(a)と CTC 非併用 DCE-CT 早期相画像(b)：SMV、IMV の比較



CTC 併用 DCE-CT 早期相(a)では、SMV（赤矢印）および IMV（黄矢印）の造影効果が、CTC 非併用 DCE-CT 早期相(b)よりも高い。SMV と IMV の拡張も観察された。　＊a、b とも同一患者

図 3. CTC 併用 DCE-CT 早期相画像(a)と CTC 非併用 DCE-CT 早期相画像(b)：胃の比較



CTC 併用 DCE-CT 早期相(a)では、CTC 非併用 DCE-CT 早期相(b)に比べて、胃の造影効果が低い。

＊a、b とも同一患者

表 2.

	平均造影 CT 値 (HU)		
	肝偽病変		
	あり (n=6)	なし (n=76)	*P* 値
肝右葉	51.81±11.6	32.5±15.1	0.005
肝左葉	62.9±13.8	39.3±16.7	0.005

考察：

肝臓、SMV および IMV の造影 CT 値が CE-CTC 群で対照群よりも有意に高かったことから、大腸からの静脈還流が増加していることが示唆された。大腸壁から吸収された二酸化炭素が、大腸壁の血管平滑筋に影響を与え、血管拡張が引き起こされ、その結果、SMV および IMV を介して肝臓への早期血流還流が増加したと推測される。

一方、胃、膵尾部、脾静脈の造影 CT 値は、CE-CTC 群が対照群に比べて有意に低かったことから、CE-CTC 群では、腸間膜血流の増加により、腹腔動脈系の血流が相補的に減少したことが示唆された。

また、CE-CTC 群では肝偽病変の発現頻度は対照群に比べて有意に高かった。炭酸ガス拡張による CTC 後の DCE-CT では、SMV と IMV からの門脈還流が増加するため、肝実質の造影効果が高まり、また third inflow からの血流が減少することで肝偽病変が相対的低吸収域として現れやすくなったと考えられる。

炭酸ガス拡張を用いた DCE-CT では、このような血行動態の変化に伴う画像所見の変化が引き起こされることを知っておくことは臨床的に重要であると考えられる。

結語：

炭酸ガス拡張による CTC の直後の DCE-CT では、血行動態の変化によって引き起こされる画像所見に注意することが重要であると考えられる。

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ORIGINAL ARTICLE

Hemodynamic changes of abdominal organs after CT colonography with transrectal administration of CO2: evaluation with early-phase contrast-enhanced dynamic CT

Kenichiro Ihara[1] · Hideko Onoda[1] · Masahiro Tanabe[1] · Akihiko Kanki[2] · Katsuyoshi Ito[1]

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Abstract

Purpose To evaluate the hemodynamic changes in the liver, pancreas, gastric mucosa and abdominal vessels in early-phase dynamic contrast-enhanced (DCE) CT immediately after CT colonography (CTC) with carbon dioxide expansion.

Materials and methods This study included 82 patients with DCE-CT after CTC (CTC group) and 77 patients without CTC (control group). Contrast enhancement values of the gastric mucosa, liver, pancreas, portal vein (PV), splenic vein (SpV), superior mesenteric vein (SMV), and inferior mesenteric vein (IMV) in early-phase CT were measured. The presence of hepatic pseudolesions were also recorded.

Results The mean contrast enhancement values of the gastric mucosa, pancreas and SpV in the CE-CTC group were significantly lower than those in the control group ($p<0.001$, $p<0.001$, $p=0.014$). Conversely, the mean contrast enhancement values of the liver, PV, SMV and IMV in the CE-CTC group were significantly higher than those in the control group ($p=0.003$, $p=0.013$, $p<0.001$, $p<0.001$). Hypovascular hepatic pseudolesions were seen in early-phase CT in six patients after CTC, while they were not seen in the control group.

Conclusions On DCE-CT performed immediately after CTC with carbon dioxide expansion, it is important to be aware of the imaging findings induced by visceral hemodynamic changes.

Keywords CT colonography · Hemodynamic · Hepatic pseudolesion

Introduction

Computed tomography (CT) colonography (CTC) has been widely used as a minimally invasive, reliable diagnostic technique for colorectal cancer [1–5]. CTC allows for the detection of colorectal cancers and polyps with high sensitivity, determination of local progression for staging, and depiction of synchronous lesions in the colon, even in patients with endoscopic inaccessibility. With standard CTC as a screening examination, the routine use of contrast medium is not necessary.

✉ Kenichiro Ihara
k.ihara@yamaguchi-u.ac.jp

[1] Department of Radiology, Yamaguchi University Graduate School of Medicine, 1-1-1 Minami-Kogushi, Ube, Yamaguchi 755-8505, Japan

[2] Department of Diagnostic Radiology, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama 701-0192, Japan

However, in patients with colorectal cancer, the preoperative detection of metastases is extremely important for deciding on the therapeutic strategy. Positive or negative extra-colonic findings can be as valuable as colonic findings in the management of patients with colorectal cancer [6, 7]. Therefore, the combination of CTC and dynamic contrast-enhanced (DCE) CT of the body performed immediately after CTC is considered efficient for the further investigation of both colonic and extra-colonic findings.

However, in DCE-CT performed immediately after CTC with carbon dioxide expansion, it is likely that hemodynamics of the abdominal organs and vessels will be affected by carbon dioxide absorbed through the colonic wall, possibly causing visceral enhancement alteration and perfusion-related hepatic pseudolesions. However, few previous reports have assessed the hemodynamic changes in the abdominal organs in DCE-CT performed after CTC.

Hence, the purpose of this study was to elucidate hemodynamic changes of the abdominal organs and vessels and the presence of perfusion-related hepatic pseudolesions in

early-phase DCE-CT immediately after CTC with carbon dioxide expansion, comparing DCE-CT combined with and without CTC.

Materials and methods

Study population

Our Institutional Review Board approved this retrospective study and waived the requirement for informed consent. DCE-CT immediately after CTC with carbon dioxide expansion was performed in 106 patients from October 2010 to September 2019 (CE-CTC group). Among these patients, those with the following were excluded: retention of oral contrast agents in the gastrointestinal tract causing artifacts ($n=11$); a history of gastrectomy ($n=3$) or splenectomy ($n=1$); presence of gastric diseases ($n=4$) or huge liver metastasis ($n=1$) affecting gastric mucosa or hepatic enhancement; heart failure ($n=1$); the development of obvious collateral pathways such as gastric varices caused by portal vein hypertension ($n=1$); and insufficient colon expansion ($n=2$). Ultimately, 82 patients were included in the CE-CTC group. These included patients with colon cancer ($n=43$), inflammatory bowel diseases (Crohn disease; $n=12$, ulcerative colitis; $n=9$), colon polyp ($n=2$), colon adenoma ($n=2$), diverticulitis ($n=2$), and miscellaneous ($n=12$).

DCE-CT immediately after CTC was performed to investigate extra-colonic abnormalities in patients with suspected malignant colonic diseases. In 16 of these 82 patients, DCE-CT without CTC had already been performed, namely five patients were performed within 1 month before CTC, while 11 patients were performed within 10 months after CTC. Thus, we additionally selected 66 age- and gender-matched patients randomly who underwent DCE-CT of the abdomen without CTC using the same contrast enhancement techniques during the same research period as the control group. Among these 66 patients, five were excluded because of the presence of obvious collateral pathways. The remaining 61 patients underwent DCE-CT for the further evaluation of suspected abdominal diseases such as hepatocellular carcinoma ($n=10$), fever of unknown origin ($n=3$), hematuria ($n=3$), adrenal lesions ($n=3$), malignant lymphoma ($n=2$), liver metastasis ($n=2$), benign hepatic lesions ($n=2$), for the screening of malignancies ($n=8$), and miscellaneous ($n=28$). Ultimately, 77 patients in the control group were also included in this study. Chronic liver injury was found in four patients (chronic hepatitis B; $n=2$, chronic hepatitis C; $n=1$, alcoholic hepatic disease; $n=1$) in the CTC group and 15 patients (chronic hepatitis B; $n=2$, chronic hepatitis C; $n=10$, fatty liver disease; $n=3$) in the control group.

The CE-CTC group included 48 men and 34 women 21–85 years old (mean, 60 years), and the control group included 46 men and 31 women 20–84 years old (mean, 60 years).

Imaging technique

CT was performed on a multidetector CT (MDCT) unit (Optima CT660 Pro, GE Healthcare or LightSpeed Ultra 16, GE Healthcare, Tokyo, Japan). The imaging parameters were as follows: tube voltage of 120 kVp, tube current of 180–250 mA, pitch 1.375 or 1.75, collimation 20 mm, and matrix, 512× 512. The direction of all scans was craniocaudal. All patients received 600 mgI/kg body weight nonionic contrast material (iopamidol [Oypalomin 300 or 370, Konica Minolta, Tokyo, Japan and Iopamiron 370, Bayer, Osaka Japan]; or iohexol [Omnipaque 300, Daiichi Sankyo, Tokyo Japan]; or iomeprol [Iomeron 300 or 350, Eisai, Tokyo Japan]). The contrast material was administered at a rate of 3.3–5.0 mL/s using a mechanical power injector (Dual Shot; Nemotokyorindo, Tokyo Japan). Because a fixed injection duration of 30 s was used, the injection rate was automatically decided according to the patients' weights. The contrast medium was injected through a 20- or 22-gauge plastic intravenous (IV) catheter placed in an antecubital vein. The section thickness and reconstruction interval were 5 mm. Total scan numbers of CTC and dynamic CT were four (two times scans for CTC with supine and prone position, and two times scans for dynamic contrast CT with early and late phases), and averaged estimated total radiation dose (CTDIvol) to the patients was 37 mGy. In the CE-CTC group, colonic distention in CTC was achieved using an automatic low-pressure with carbon dioxide delivery device (HP-2®; Horii Pharmaceutical Industry, Osaka, Japan) via a flexible rectal catheter. At first, unenhanced CT images were obtained for the purpose of CTC. DCE-CT during the early and late phases was then performed in all patients. Early- and late-phase images were obtained with delays of 40 and 210 s, respectively.

Image analyses

The CT values of the gastric mucosa, liver (right lobe and left lobe), tail of pancreas, portal vein (PV), splenic vein (SpV), superior mesenteric vein (SMV), and inferior mesenteric vein (IMV) were measured in unenhanced and early-phase CT, respectively. The CT values of the pancreatic head were not measured, because they could be affected by the flow from both celiac artery and superior mesenteric artery. The contrast enhancement value was calculated as the difference in Hounsfield unit values between the unenhanced image and early-phase CT image. These measurements were conducted by two radiologists with 4 and 18 years of

experience in abdominal CT interpretation blinded to the clinical data on a workstation (EV InsiteS; PSP Corporation, Tokyo, Japan) where patients' information was anonymized, and CT data sets were randomized for blind-reading purpose.

The two radiologists set a circular or oval region of interest (ROI) on the images of each organ and vessel. The average contrast enhancement values of the two observers were calculated. The presence of hepatic pseudolesions was also recorded by collaboration. Hepatic pseudolesions were defined as hyper- or hypo-attenuating areas at the posterior edge of the left medial segment or surrounding the gallbladder fossa on early-phase CT. True lesions such as cyst, hemangioma and metastasis in these locations were carefully excluded based on unenhanced and late-phase CT findings.

Statistical analyses

All data were analyzed using the JMP Pro software program (JMP Version 14; SAS Institute Inc., Cary, NC, USA). The Mann–Whitney *U* test was used to compare the mean contrast enhancement value in each organ and vessel, and the chi-square test was used to compare the presence of hepatic pseudolesions between the CE-CTC and control groups. A p value of < 0.05 was considered to indicate a statistically significant difference.

Table 1 Comparison of mean contrast enhancement CT values of each organs and vessels

Organ or vessel	Mean contrast enhancement values (HU)		
	CE-CTC group	Control group	*p* value
Right hepatic lobe	33.94 ± 16.06	26.55 ± 15.97	0.003
Left hepatic lobe	41.06 ± 18.03	33.05 ± 17.79	0.003
Gastric mucosa	53.78 ± 19.39	73.46 ± 24.12	< .0001
Tail of pancreas	69.81 ± 18.69	83.08 ± 20.95	< .0001
PV	155.1 ± 37.23	139.24 ± 46.69	0.013
SMV	139.42 ± 53.08	98.91 ± 55.94	< .0001
IMV	162.64 ± 54.95	65.72 ± 56.27	< .0001
SpV	163.31 ± 38.46	186.31 ± 48.26	0.014

Results

The comparisons of the mean contrast enhancement value in each organ and vessel between the CE-CTC group and the control group are summarized in Table 1. The mean contrast enhancement values of the right and left hepatic lobes, PV, SMV and IMV in the CE-CTC group were significantly higher than those in the control group (33.9 ± 16.1 vs. 26.6 ± 16.0 HU, $p = 0.003$; 41.1 ± 18.0 vs. 33.1 ± 17.8 HU, $p = 0.003$; 155.1 ± 37.2 vs. 139.2 ± 46.7 HU, $p = 0.013$; 139.4 ± 53.1 vs. 98.9 ± 55.9, $p < 0.001$; 162.6 ± 55.0 vs. 65.7 ± 56.3, $p < 0.001$, respectively) (Figs. 1 and 2). Conversely, the mean contrast enhancement values of the gastric mucosa, tail of pancreas and SpV in the CE-CTC group were significantly lower than those in the control group (53.8 ± 19.4 vs. 73.5 ± 24.1 HU, $p < 0.001$; 69.81 ± 18.69 vs 83.08 ± 20.95 HU, $p < 0.001$; 163.3 ± 38.5 vs. 186.3 ± 48.3 HU, $p = 0.014$, respectively) (Fig. 3).

Hepatic pseudolesions were seen as hypo-attenuating areas on early-phase CT in six patients (7%) of the CE-CTC group at the posterior edge of the left medial segment ($n = 5$) or the surrounding gallbladder fossa ($n = 1$) (Fig. 4) while they were not seen at all in the control group ($p = 0.016$). Table 2 shows the results of the comparison of the mean contrast enhancement values of the liver between the CE-CTC patients with and without hepatic pseudolesions. The mean contrast enhancement values of the right and left hepatic lobes in the CE-CTC patients with hepatic pseudolesions were significantly higher than those in the CE-CTC patients without hepatic pseudolesions (51.8 ± 11.6 vs. 32.5 ± 15.1 HU, $p = 0.005$, 62.9 ± 13.8 vs. 39.3 ± 16.7 HU, $p = 0.005$, respectively).

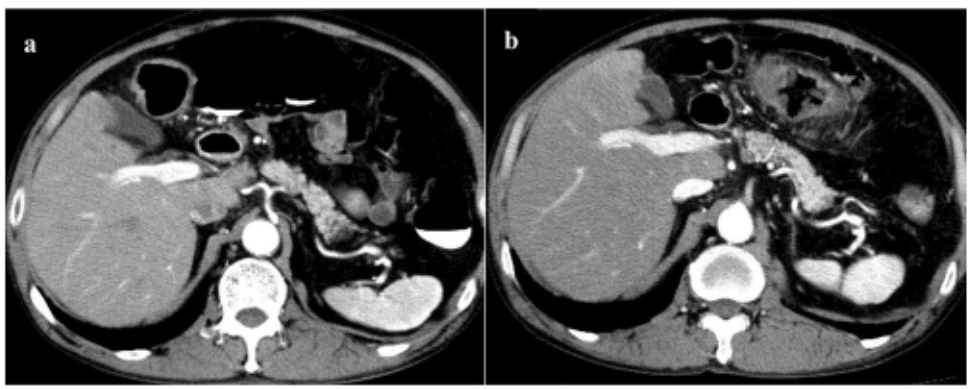

Fig. 1 Early-phase CT (**a**) obtained after CTC with carbon dioxide expansion (CE-CTC), and early-phase CT (**b**) obtained without CTC procedures (control) from a same 73-year-old man. The contrast enhancement effect of the liver parenchyma in the early-phase CT obtained after CTC with carbon dioxide expansion was higher than that obtained without CTC procedures

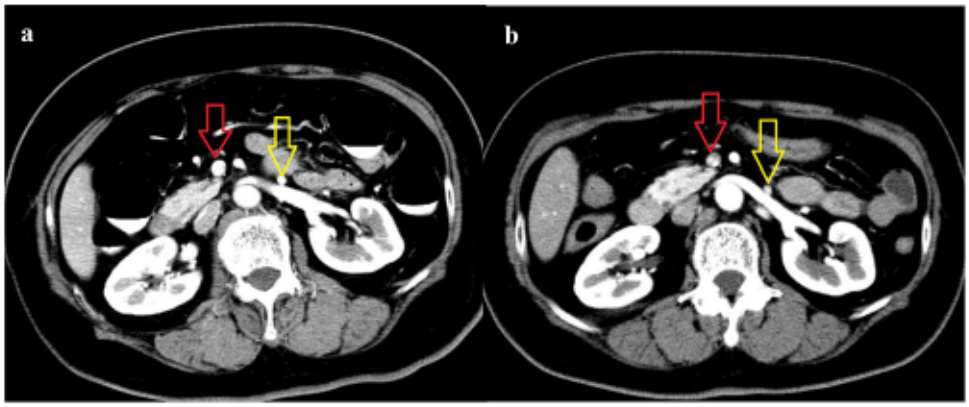

Fig. 2 Early-phase CT (**a**) obtained after CTC with carbon dioxide expansion (CE-CTC), and early-phase CT (**b**) obtained without CTC procedures (control) from a same 63-year-old woman. The contrast enhancement effect of the SMV (red arrow) and IMV (yellow arrow) in the early-phase CT obtained after CTC with carbon dioxide expansion was higher than that obtained without CTC procedures. Dilatation of the SMV and IMV in a) was also observed

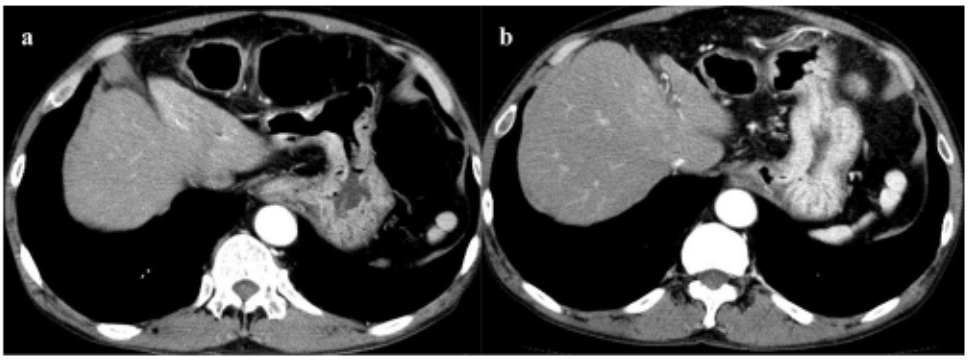

Fig. 3 Early-phase CT (**a**) obtained after CTC with carbon dioxide expansion (CE-CTC), and early-phase CT (**b**) obtained without CTC procedures (control) from a same 73-year-old man. The contrast enhancement effect of the gastric mucosa in the early-phase CT obtained after CTC with carbon dioxide expansion was lower than that obtained without CTC procedures

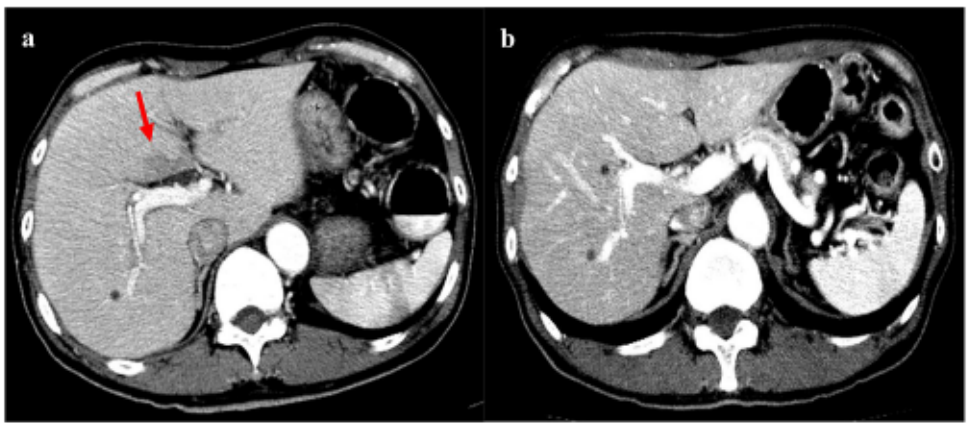

Fig. 4 Hypovascular pseudolesion observed in a 58-year-old man. Early-phase CT (**a**) obtained after CTC with carbon dioxide expansion (CE-CTC) showed a hepatic pseudolesion seen as a hypo-attenuating area at the posterior edge of the left medial segment (arrow). On the early-phase CT (**b**) obtained without CTC procedures, a hepatic pseudolesion was not demonstrated. The contrast enhancement value of the liver parenchyma after CTC was higher than that without CTC procedures (right lobe: 66 vs. 51, left lobe: 75 vs. 67)

Table 2 Comparison of mean contrast enhancement CT values of the liver between the CE-CTC group with and without hepatic pseudolesions

	Mean contrast enhancement values (HU)		
	Hepatic pseudolesion		
	Positive ($n=6$)	Negative ($n=76$)	p value
Right hepatic lobe	51.81 ± 11.6	32.5 ± 15.1	0.005
Left hepatic lobe	62.9 ± 13.8	39.3 ± 16.7	0.005

Discussion

In the present study, the mean contrast enhancement CT values of SMV and IMV were significantly higher in the CE-CTC group than in the control group, suggesting an increased venous return from the large intestine. In addition, the mean contrast enhancement CT values of the liver were significantly higher in the CE-CTC group than in the control group, suggesting an increased portal venous flow, probably due to the early venous return from the SMV and IMV. Although the precise mechanism remains unclear, these findings may have been caused by carbon dioxide expansion of the colon during CTC.

Automated carbon dioxide insufflation is commonly used during CTC procedures, significantly improving colonic distention [8, 9]. Carbon dioxide is readily absorbed through the colonic wall approximately 20 times faster than room air because of a steep diffusion gradient [10]. Absorbed carbon dioxide affects the vascular smooth muscle of blood vessels in the colonic wall, causing arterial and venous vasodilation. Although several mechanisms of vasodilatation effect of carbon dioxide have been proposed, the major mechanism is considered to be related to a direct effect of extracellular H^+ on vascular smooth muscle, causing a decrease in the pH and the subsequent reduction of free Ca^{2+} [11]. Therefore, it is speculated that vasodilatation was induced in the blood vessels of the large intestine that absorbed carbon dioxide and, as a result, the increased early venous return to the liver through the SMV and IMV was thereby promoted. In contrast, the mean contrast enhancement CT values of the gastric mucosa, tail of pancreas and splenic vein were significantly lower in the CE-CTC group than in the control group, suggesting that the blood flow in the celiac artery system such as gastric and splenic circulation in the CE-CTC group was complementarily reduced due to the increase in the mesenteric vascular circulation. While the routine use of contrast agents in CTC is not necessary for screening examinations, performing contrast-enhanced CT after CTC can be justified by the need for information about intra-abdominal organs other than colon. Therefore, it is essential to understand the changes in the contrast enhancement effect of the abdominal organs after CTC.

In the present study, hepatic pseudolesions were seen as hypo-attenuating areas at the posterior edge of the left medial segment or surrounding the gallbladder fossa on early-phase CT in six patients (7%) of the CE-CTC group, a significantly higher frequency than in the control group. The posterior edge of the left medial segment or surrounding the gallbladder fossa have been the characteristic locations of hepatic hypervascular pseudolesions sometimes observed on early-phase contrast-enhanced CT [12] or MRI [13, 14], angiography [15] or CT during arterial portography [16]. In early-phase CT and MRI immediately after IV contrast injection, these pseudolesions were seen as hyper-enhanced areas. These hypervascular pseudolesions are attributed to early drainage from a "third flow" source, such as cholecystic or aberrant gastric venous systems. It is likely that the blood flow from the cystic or aberrant gastric veins drains more rapidly into the sinusoids of the focal liver through the anatomical portal-systemic shunts than the flow from the vessels of the usual portal venous system, such as the superior mesenteric and splenic veins [13, 17].

However, the hepatic pseudolesions seen after CE-CTC in our study at the posterior edge of the left medial segment or surrounding the gallbladder fossa showed hypo-enhancement compared with the surrounding liver parenchyma. In CTC with carbon dioxide expansion, the liver parenchyma showed increased enhancement due to the increased early portal venous return from the SMV and IMV, and as a result, pseudolesions were more likely to appear as areas of relative hypo-enhancement, because they received a decreased blood flow from the third inflow. Similar findings may be seen on CT during arterial portography, where pseudolesions appears as areas of diminished portal perfusion (hypo-enhancement). One advantage of CTC over colonic endoscopy is that extra-colonic findings, including the preoperative detection of metastases, may strongly influence the accurate therapeutic management of patients with suspected colonic malignancies [7, 18, 19]. Therefore, being aware of the presence of these perfusion-related hypo-enhanced pseudolesions in characteristic locations on CE-CTC with carbon dioxide expansion will be clinically important for differentiation from true metastatic lesions.

Several limitations associated with the present study warrant mention. First, this was a retrospective study, and there might have been a potential risk of selection bias. Second, images from different CT machines were included. However, to minimize variability among different CT scanners, a uniform contrast injection protocol was used. Third, individual differences in hemodynamics and the duration of colon distension are unavoidable, even though we used the same imaging protocol. Fourth, in this study, there were no patients with hepatic pseudolesions in the control group, but

it might be necessary to evaluate large number of patients to clarify the more exact frequency of hepatic pseudolesions. Finally, pathologic proof was not obtained in any patients with hepatic pseudolesions on CE-CTC with carbon dioxide expansion. However, the location of these pseudolesions was already well-known, so a percutaneous biopsy would not have been practical.

In conclusion, on DCE-CT performed immediately after CTC with carbon dioxide expansion, it is clinically important to be aware of the imaging findings induced by hemodynamic changes, such as increased contrast enhancement of the liver, SMV and IMV; decreased enhancement of the gastric mucosa; and the presence of perfusion-related hypoenhanced hepatic pseudolesions at the posterior edge of the left medial segment or surrounding the gallbladder fossa, probably due to the increased early venous return from the large intestine caused by carbon dioxide expansion.

Declarations

Conflict of interest No financial support for this study was provided, and we have no disclosure.

Ethical statement This study was approved by the institutional review board.

References

1. Johnson CD, Dachman AH. CT colonography: the next colon screening examination? Radiology. 2000. https://doi.org/10.1148/radiology.216.2.r00au47331.
2. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med. 2003. https://doi.org/10.1056/NEJMoa031618.
3. Pineau BC, Paskett ED, Chen GJ, Espeland MA, Phillips K, Han JP, et al. Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. Gastroenterology. 2003. https://doi.org/10.1016/s0016-5085(03)00885-0.
4. Fenlon HM, Nunes DP, Schroy PC 3rd, Barish MA, Clarke PD, Ferrucci JT. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. N Engl J Med. 1999. https://doi.org/10.1056/nejm199911113412003.
5. Gluecker TM, Johnson CD, Harmsen WS, Offord KP, Harris AM, Wilson LA, et al. Colorectal cancer screening with CT colonography, colonoscopy, and double-contrast barium enema examination: prospective assessment of patient perceptions and preferences. Radiology. 2003. https://doi.org/10.1148/radiol.2272020293.
6. Spreng A, Netzer P, Mattich J, Dinkel HP, Vock P, Hoppe H. Importance of extracolonic findings at IV contrast medium-enhanced CT colonography versus those at non-enhanced CT colonography. Eur Radiol. 2005. https://doi.org/10.1007/s00330-005-2798-6.
7. Tolan DJ, Armstrong EM, Chapman AH. Replacing barium enema with CT colonography in patients older than 70 years: the importance of detecting extracolonic abnormalities. AJR Am J Roentgenol. 2007. https://doi.org/10.2214/ajr.07.2026.
8. Nagata K, Fujiwara M, Shimamoto T, Iida N, Mogi T, Mitsushima T. Colonic distention at CT colonography: randomized evaluation of both IV hyoscine butylbromide and automated carbon dioxide insufflation. AJR Am J Roentgenol. 2015. https://doi.org/10.2214/ajr.14.12772.
9. Patrick JL, Bakke JR, Bannas P, Kim DH, Lubner MG, Pickhardt PJ. Objective volumetric comparison of room air versus carbon dioxide for colonic distention at screening CT colonography. Abdom Imaging. 2015. https://doi.org/10.1007/s00261-014-0206-x.
10. Sumanac K, Zealley I, Fox BM, Rawlinson J, Salena B, Marshall JK, et al. Minimizing postcolonoscopy abdominal pain by using CO(2) insufflation: a prospective, randomized, double blind, controlled trial evaluating a new commercially available CO(2) delivery system. Gastrointest Endosc. 2002. https://doi.org/10.1016/s0016-5107(02)70176-4.
11. Kontos HA, Raper AJ, Patterson JL. Analysis of vasoactivity of local pH, PCO2 and bicarbonate on pial vessels. Stroke. 1977. https://doi.org/10.1161/01.str.8.3.358.
12. Ito K, Awaya H, Mitchell DG, Honjo K, Fujita T, Uchisako H, et al. Gallbladder disease: appearance of associated transient increased attenuation in the liver at biphasic, contrast-enhanced dynamic CT. Radiology. 1997. https://doi.org/10.1148/radiology.204.3.9280250.
13. Ito K, Choji T, Fujita T, Matsumoto T, Nakada T, Nakanishi T. Early-enhancing pseudolesion in medial segment of left hepatic lobe detected with multisection dynamic MR. Radiology. 1993. https://doi.org/10.1148/radiology.187.3.8497615.
14. Ito K, Honjo K, Fujita T, Awaya H, Matsumoto T, Matsunaga N. Hepatic parenchymal hyperperfusion abnormalities detected with multisection dynamic MR imaging: appearance and interpretation. JMRI. 1996. https://doi.org/10.1002/jmri.1880060604.
15. Matsui O, Takashima T, Kadoya M, Konishi H, Kawamura I, Hirose J, et al. Staining in the liver surrounding gallbladder fossa on hepatic arteriography caused by increased cystic venous drainage. Gastrointest Radiol. 1987. https://doi.org/10.1007/bf01885168.
16. Matsui O, Takahashi S, Kadoya M, Yoshikawa J, Gabata T, Takashima T, et al. Pseudolesion in segment IV of the liver at CT during arterial portography: correlation with aberrant gastric venous drainage. Radiology. 1994. https://doi.org/10.1148/radiology.193.1.8090916.
17 Yoshimitsu K, Honda H, Kuroiwa T, Irie H, Aibe H, Shinozaki K, et al. Unusual hemodynamics and pseudolesions of the noncirrhotic liver at CT. Radiographics. 2001. https://doi.org/10.1148/radiographics.21.suppl_1.g01oc06s81.
18. Ozsunar Y, Coskun G, Delibas N, Uz B, Yukselen V. Diagnostic accuracy and tolerability of contrast enhanced CT colonoscopy in symptomatic patients with increased risk for colorectal cancer. Eur J Radiol. 2009. https://doi.org/10.1016/j.ejrad.2008.05.013.

19. Mainenti PP, Cirillo LC, Camera L, Persico F, Cantalupo T, Pace L, et al. Accuracy of single phase contrast enhanced multidetector CT colonography in the preoperative staging of colo-rectal cancer. Eur J Radiol. 2006. https://doi.org/10.1016/j.ejrad.2006.08.001.