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EMERGENCY RADIOLOGY SPECIAL FEATURE: FULL PAPER

Reperfusion in non-occlusive mesenteric ischaemia (NOMI): effectiveness of CT in an emergency setting

¹MARIA A MAZZEI, MD, Prof., ¹SUSANNA GUERRINI, MD, ¹NEVADA CIOFFI SQUITIERI, MD, ²CARLA VINDIGNI, MD, ¹GIUSI IMBRIACO, MD, ¹FRANCESCO GENTILI, MD, ³DANIELA BERRITTO, MD, ⁴FRANCESCO G MAZZEI, MD, ⁵ROBERTO GRASSI, MD, Prof. and ¹LUCA VOLTERRANI, MD, Prof.

¹Department of Medical, Surgical and Neuro Sciences, Diagnostic Imaging, University of Siena, Azienda Ospedaliera Universitaria Senese, Siena, Italy

²Division of Pathological Anatomy, Azienda Ospedaliera Universitaria Senese, Siena, Italy

³Department of Diagnostic Imaging, Casa di Cura Villa dei Fiori Srl, Acerra, Napoli, Italy

⁴Department of Diagnostic Imaging, Azienda Ospedaliera Universitaria Senese, Siena, Italy

⁵Department of Radiology, Second University of Naples, Naples, Italy

Address correspondence: Professor Maria Antonietta Mazzei

E-mail: mamazzei@gmail.com

Objective: To investigate the CT features of reperfusion (presence/absence) in non-occlusive mesenteric ischaemia (NOMI) and their prognostic value in an emergency setting.

Methods: A revision was undertaken of imaging from 20 patients (16 males/4 females) with a dismissal summary of NOMI. All patients had previously undergone a minimum of one multidetector CT examination, and consequently underwent surgery ($n = 8$), autopsy ($n = 2$), angiography ($n = 1$) or endoscopy ($n = 9$). An evaluation of the CT scans was conducted to determine vessels, mesentery, bowel and peritoneal cavity features. The superior mesenteric artery (SMA) average diameter of NOMI cases were compared with 30 controlled cases. Kappa, Kolmogorov-Smirnov (K-S) and Fisher's exact tests were used for statistical analysis.

Results: A mean SMA diameter significantly smaller than that of the controlled cases was found for patients with

NOMI (K-S test: $D = 0.75$, $p = 3.7 \times 10^{-08}$). Fisher's exact tests showed a strong connection between the presence of reperfusion and mesenteric fat stranding ($p = 0.026$), bowel wall thickening ($p = 3.2 \times 10^{-05}$) and a high attenuation of the bowel wall on unenhanced CT images ($p = 2.8 \times 10^{-04}$). A reduction in mortality was significantly linked to the combination of normal mesenteric vessels and wall thickening ($p = 0.034$).

Conclusion: Analysis of not only vessels findings but also mesentery and bowel CT features will support the identification of NOMI with or without a reperfusion event in an emergency setting. A strong correlation between some CT features and lower mortality exists.

Advances in knowledge: CT features of NOMI with or without reperfusion are demonstrated. Correctly assessing the presence of reperfusion in NOMI, may allow better management of these conditions in the emergency setting.

INTRODUCTION

Non-occlusive mesenteric ischaemia (NOMI) is an abdominal emergency that accounts for 20–30% of all intestinal ischaemic events.¹ Bowel ischaemia and infarction in NOMI are present as a result of reduced mesenteric blood supply without vascular occlusion, because of a mesenteric arterial vasoconstriction on reflex to hypotension owing to various forms of shock, septicemia, dehydration, heart or major abdominal surgery followed by hypotension and overuse of vasoconstrictive agents.^{1,2} From a pathological viewpoint, the ischaemic injury may range from reversible superficial damage, localized to the watershed areas to a more severe form that extends to the entire bowel. The diagnostic criteria of NOMI includes the

absence of vascular occlusion (both mesenteric artery or vein), the presence of ischaemic and necrotic spots and segments involving non-consecutive tracts of a wide area of the intestine and haemorrhagic and necrotic changes without fibrin plugs as histopathological findings.³ NOMI is the most lethal form of acute mesenteric ischaemia (AMI) (58–70%) because of the delayed diagnosis related to the non-specific symptoms and signs at imaging. Nevertheless, recognition of NOMI from other conditions and in particular from occlusive ischaemia is critical because of the different treatment required. In fact, medical treatment, and more recently perfusion therapy using vasoactive substances, has achieved a pivotal position in the effective treatment of NOMI, whereas surgery is only performed in

advanced forms of NOMI with necrosis of the involved tract due to an ineffective reperfusion event;^{4,5} therefore, its definition should be a target of imaging.^{6,7} Notwithstanding the technical evolution of non-invasive techniques, for example, multi-detector CT (MDCT), many authors still believe angiography to be the only diagnostic modality that can reliably establish NOMI in an early phase, by identifying the presence of mesenteric vasospasm.^{8,9} Only a few articles have explored the effectiveness of MDCT for NOMI diagnosis, with a very limited cohort of patients.^{3–5,10} However, these studies explored the only vessel features [morphology and diameter of the superior mesenteric artery (SMA)], whereas MDCT not only analyses mesenteric vessels but other features, for example, abnormalities in the bowel wall, mesentery and peritoneal cavity. CT imaging of AMI changes is widely dependent upon the cause and the underlying physiopathology, on the severity of bowel ischaemia (*i.e.*, superficial mucosal or transmural bowel wall necrosis), duration and severity of the ischaemic event (*i.e.*, only small bowel, small and large bowel), the state of collateral circulation and any potential reperfusion occurrences that are more common in NOMI than in AMI of an occlusive type. Thus, NOMI imaging may be different dependant upon this criteria and the specific time when the CT examination is undertaken.^{11,12} In this study, the MDCT features of 20 patients (28 CT examinations) with NOMI, with or without reperfusion, were reviewed with the purpose of identifying those imaging features related to this condition and to determine their potential prognostic value in the emergency setting.

METHODS AND MATERIALS

Patients

This study received institutional review board approval for a retrospective review, with a waiver of informed consent. The study complies with current ethical considerations. The

dismissal summary between 1 July 2003 and 1 July 2014 was queried for the terms “intestinal ischaemia”. We identified 131 patients fitting our search criteria over the time period. 110 patients were excluded because of the lack of a CT examination ($n = 93$), or because of the occlusive aetiology ($n = 17$). The inclusion criteria were as follows: CT examination undertaken in the radiology department of University Hospital of Siena; NOMI diagnosis verified by angiography, by autopsic or surgical pathology or by endoscopy associated with CT examination (the absence of occlusion of mesenteric vessels). The exclusion criteria were the absence of an abdomen CT examination and occlusive aetiology of proved intestinal ischaemia. A cluster of 20 subjects (16 males, 4 females; average age 73.7 years, range 49–88 years) with a NOMI dismissal summary were included. The clinical suspicion of NOMI was restricted to the presence of abdominal pain to include a minimum of one of the following symptoms: pain out of proportion to clinical findings; biochemical evidence of ischaemia, such as heightened lactate levels or unexplained metabolic acidosis; patient risk factors for NOMI, such as shock, septicaemia, hypotension following heart or major abdominal surgery and low flow (history of hypotension or vasopressor therapy). As a control for the SMA evaluation, a group of 30 patients, matched for age and gender, who underwent MDCT for a non-related condition were randomly selected from our institutional database. Those patients who suffered from gastrointestinal symptoms, cardiac failure, kidney failure, high blood pressure and arterial sclerosis were excluded from controls. All the controls were revealed as not having any disorders at the time of the MDCT scan as well as during the 6-month follow-up after the MDCT scan.

Multidetector CT

MDCTs were obtained using a 16-detector row scanner (LightSpeed® 16 Pro; General Electric Healthcare, Milwaukee, WI) for

Figure 1. Example of the multiplanar reconstruction image (a) used for measuring superior mesenteric artery (SMA) proximal and distal diameters: in a case of non-occlusive mesenteric ischaemia, the proximal diameter (measured immediately below the inferior pancreaticoduodenal artery bifurcation, white arrow in a) was 6 mm, as demonstrated in axial image (b, white arrow), and the distal diameter (measured immediately below the inferior ileocolic artery bifurcation, arrowhead in a) was 3.2 mm, as demonstrated in axial image (c, arrowhead). The average diameter of the SMA in this patient was 4.6 mm.

3 patients and with a 64-detector row scanner (LightSpeed™ VCT; General Electric Healthcare) for the other 17 patients, 4 of whom were studied 3 times (for a total of 28 MDCT examinations). Studies were performed in the supine position, with a spiral method in the craniocaudal direction (from the base of the lungs to the pelvic brim). One patient underwent only a contrast-enhanced CT scan while a CT examination performed only with unenhanced scans was obtained for two patients. These patients had 3 examinations and only the last CT examination was unenhanced for both the 2 patients mentioned above, whereas the first and the second CT examination were conducted similar to the remaining 21 CT examinations with unenhanced and contrast-enhanced scans. For all patients, contrast-enhanced scans were performed in two phases, late arterial (45–50 s) and portal venous phase (70–80 s). An intravenous injection of 2 ml kg^{-1} of non-ionic contrast material (Iopamiro® 370; Bracco Diagnostics, Milan, Italy), followed by 40 ml of saline solution, was administered through an 18-gauge needle in the antecubital vein, using a semi-automated power

injector. All patients were instructed not to breath during CT scans to prevent motion artefacts, and none of them received oral contrast medium. CT technical parameters included: in 16-row CT—slice thickness of 3.75 mm for plain acquisition and 2.5 mm for contrast-enhanced CT, beam pitch of 1.375/0.937, reconstruction interval of 0.8 mm; tube voltage of 120–140 kVp and reference mAs of 250–500 mAs; in 64-row CT—slice thickness of 3.75 mm for plain acquisition, 1.25 and 2.5 mm in the late arterial and portal venous phase, respectively; beam pitch of 0.938, reconstruction interval of 0.8 mm, tube voltage of 120–140 kVp and reference mAs of 250/700. A standard reconstruction algorithm and an automatic tube current modulation were also utilized.

All the 28 CT examinations were independently analysed by two radiologists (blinded 1 and blinded 2, with 25 and 10 years' of experience in abdominal imaging, respectively). Readers were asked to review NOMI cases in a random manner, avoiding all pathological and clinical information. The chart review and

Table 1. Patients' demographic characteristics

Patient	Sex	Age (years)	Pre-existing disease	Number of CT	Diagnostic proof	Status at discharge
1	M	67	Heart failure	1	S	D
2	F	83	Heart failure	1	S	L
3	M	52	Heart failure	1	S	L
4	F	65	Dilatative cardiomyopathy	3	S	L
5	M	81	Ischaemic heart disease, FFAA, arteriosclerosis, renal failure	1	A	D
6	M	49	Bentall procedure for aortic dissection type A, Marfan syndrome	3	S	D
7	M	84	Heart failure	1	S	L
8	M	76	Arteriosclerosis, ischemic heart disease	1	E	D
9	M	63	Ischemic heart disease, pacemaker	1	E	D
10	M	75	Heart failure	1	S	L
11	M	84	AAA treated with surgery	1	S	L
12	M	75	AAA	1	AN	L
13	M	70	Lymphoma, Parkinson	1	A	D
14	M	74	Ischaemic heart disease	1	S	L
15	M	88	Dilatative cardiomyopathy	1	E	D
16	M	83	Ischaemic heart disease, pacemaker, AAA treated with surgery, thrombotic disease	3	E	D
17	F	85	Ischaemic heart disease	1	E	D
18	F	75	AAA, arteriosclerosis	1	S	D
19	M	63	Ischaemic heart disease	1	E	D
20	F	82	Ischaemic heart disease, arteriosclerosis	3	S	L

A, autopsy; AAA, aortic abdominal aneurism; AN, angiographic study; D, died; E, endoscopy; F, female; FFAA, fragmented focal arterial activity; L, living; M, male; S, surgery.

randomization of the cases were performed by one resident in radiology who was not involved in reading the cases (blinded 3). The MDCT examinations were evaluated for evidence of:

- *vessel features*: (a) SMA diameter: the largest proximal diameter immediately below the inferior pancreaticoduodenal artery bifurcation and the shortest distal diameter below the inferior ileocolic artery bifurcation were measured using a two-dimensional multiplanar oblique reformat. Each observer obtained the measurement, and the average measurements were evaluated; (b) diameter of the superior mesenteric vein (SMV): measured before the confluence of the splenic vein (Figure 1)
- *mesenteric features*: (a) mesenteric vessels (visual assessment): normal appearance (“normal mesenteric vessels”), increased or reduced (“pale mesentery”) calibre and number of mesenteric vessels; (b) mesenteric fat stranding or mesenteric fluid: presence or absence
- *bowel features*: the following features were evaluated in terms of presence or absence: (a) paper thin; (b) bowel wall thickening; (c) pneumatosis of the bowel wall; (d) high attenuation of the bowel wall on unenhanced CT images; (e) hyperperfusion of the mucosal layer and hypoattenuation of the submucosal layer upon contrast-enhanced CT; (f) absent or diminished contrast enhancement of the bowel wall; (g) dilatation of the bowel lumen, known as hypotonic reflex ileus, in the digiuneal and ileal tract; (h) dilated colon
- *peritoneal features*: the following features are evaluated in terms of presence or absence: (a) peritoneal fluid; (b) free air in peritoneal cavity.

Table 2. The percentage value of each of the CT features in the 20 patients with non-occlusive mesenteric ischaemia (28 CT examinations)

Mesenteric features	
Pale mesentery (reduction in calibre and number of mesenteric vessels)	46.42% (13)
Normal (normal mesenteric vessels)	53.57% (15)
Mesenteric fat stranding	82.14% (23)
Bowel features	
Paper thin	60.71% (17)
Bowel wall thickening	57.14% (16)
Pneumatosis of the bowel wall	32.14% (9)
High attenuation of the wall on unenhanced CT images	75% (21)
Absent or diminished contrast enhanced of the bowel wall	42.85% (12)
Dilatation of the bowel lumen (HRI)	67.85% (19)
Dilated colon	67.85% (19)
Peritoneal features	
Peritoneal fluid	78.57% (22)
Free air in peritoneal cavity	7.14% (2)

HRI, hypotonic reflex ileus.

STATISTICAL ANALYSIS

The interobserver agreement was obtained by applying a Kappa test. The Kappa unit ranged from 0 (chance agreement) to 1 (total agreement), in particular K -values were deciphered in the following way: $K < 0.20$, poor agreement; $K = 0.21$ – 0.40 , fair; $K = 0.41$ – 0.60 , moderate; $K = 0.61$ – 0.80 , good; $K = 0.81$ – 1.00 , very good. Average SMA and SMV diameters were provided through the results of each reviewer from each CT examination. Mean value and standard deviation were computed for the SMA and SMV in both the NOMI cases and control sample. The same was carried out for NOMI cases with or without reperfusion events. Kolmogorov–Smirnov (K–S) tests were run to compare the distributions of SMA and SMV values in both samples. K–S test output parameters are the statistic, named D and its significance level, Prob. The D statistic symbolises the maximum vertical deviation between the cumulative distribution functions (CDFs) of the comparative data sets. The CDFs are presented in a fractional way, and thus D ranges between 0 and 1, with low values meaning that the CDFs are similar, whereas large numbers represent severe discrepancies. The scope of the Prob parameter is between 0 and 1, and a small value implies significantly different CDFs. We interpret the K–S test as follows: if $D < 0.5$ and Prob $> 1\%$, the values of a given parameter measured in NOMI and control samples are consistent. On the contrary, when $D > 0.5$ and Prob < 0.01 , there is a significant discrepancy of the parameter values in the two samples. The prognostic significance of mesenteric, bowel and peritoneal features, as well as their relationship with the reperfusion event, was tested using Fisher’s exact test. We generated contingency tables by relating the NOMI features with mortality and reperfusion. The same was performed while combining in twos, the NOMI CT features. For the four patients with multiple CT examinations, we considered the status at the time of discharge, as with the remaining patients. All tests were two-sided, and we considered a 5% significance level (*i.e.* the result is statistically significant for each contingency table to which Fisher’s test assigned a p -value ≤ 0.05).

RESULTS

An excellent agreement (kappa test value of 0.81–1) was found between the two readers and no severe discrepancies concerning the distribution of MDCT findings were highlighted between unenhanced and contrast-enhanced CT examinations, reviewed separately in all patients. Patient demographic information (age and sex), pre-existing disease, number of CT examinations during hospitalization, diagnostic proof and status at the time of discharge for the 20 patients are summarized in Table 1. Four patients were studied three times, with an interval time between the first and the second examination of 67, 237, 216 and 24 h, respectively, and between the second and third examinations of 174, 150, 69 and 144 h, respectively. In 12 out of 20 patients, pathological proof after surgery ($n = 11$) or autopsy ($n = 1$) demonstrated signs of reperfusion.

In all 20 patients with NOMI, no sign of SMA or SMV thrombosis or occlusion were found. The original axial and multiplanar reconstruction (MPR) images of all NOMI patients showed irregular narrowing of the SMA, spasms of the arcades of mesenteric arteries and impaired filling of intramural vessels.

None of the controls showed abnormal findings of SMA and its branches. The mean diameter of SMA and SMV of patients with NOMI was 4.6 ± 1.4 mm (range 2.2–7.4 mm) and 7.4 ± 2.4 mm (range 2.2–13 mm), respectively. The mean diameter of SMA and SMV of the controls was 7.3 ± 1.0 mm (range 5.4–9.2 mm) and 9.3 ± 1.8 mm (range 6.3–13.8 mm), respectively. By applying

the K-S test, a mean SMA diameter significantly smaller than that of the controlled cases was found for patients with NOMI (K-S test: $D = 0.75$, Prob = 3.7×10^{-8}). The SMA diameter of NOMI cases with a reperfusion event (mean value 5.0 ± 1.4 mm) and without (average 3.8 ± 1.1 mm) showed no statistical difference ($D = 0.40$, Prob = 0.21). No significant differences were found for

Table 3. Monovariate contingency tables and Fisher's exact test for categorical features and the reperfusion event

CT features	Reperfusion			<i>p</i> -value
Mesenteric features		Y (19)	N (9)	
Pale mesentery	Y (13)	7	6	0.22
	N (15)	12	3	
Fat stranding	Y (23)	18	5	0.026
	N (5)	1	4	
Bowel features		Y (19)	N (9)	
Paper thin	Y (17)	9	8	0.049
	N (11)	10	1	
Wall thickening	Y (16)	16	0	0.000032
	N (12)	3	9	
Pneumatosis	Y (9)	6	3	1.00
	N (19)	13	6	
HRI	Y (19)	15	4	0.097
	N (9)	4	5	
High attenuation of the wall on unenhanced CT images ^a		Y (18)	N (9)	0.00028
	Y (21)	18	3	
	N (6)	0	6	
Absent or diminished c.e. of the bowel wall ^b		Y (17)	N (9)	1.00
	Y (12)	8	4	
	N (14)	9	5	
Dilated colon ^c		Y (18)	N (9)	0.37
	Y (19)	12	7	
	N (7)	6	1	
Peritoneal features		Y (19)	N (9)	
Peritoneal fluid	Y (22)	15	7	1.00
	N (6)	4	2	
Free air	Y (2)	2	0	1.00
	N (26)	17	9	
Death	Y (15)	7	8	0.016
	N (13)	12	1	

c.e., contrast enhancement; HRI, hypotonic reflex ileus.

Capital Y and N stand for the occurrence or lack of the feature on 28 CT examinations, and values in parenthesis represent its frequency.

The results of the Fisher's exact tests (*p*-value) are two-sided.

Statistically significant results are highlighted in bold characters in the *p*-value column.

^aOne examination lacks the CT scan without contrast. Reperfusion is the corresponding event.

^bTwo examinations lack the CT scans with contrast. Absence of reperfusion is the corresponding event in both cases.

^cTwo examinations reported the bowel wall perforation. The corresponding event is reperfusion in one case and absence of reperfusion in the other one.

Table 4. Bivariate contingency tables and Fisher's exact test for categorical features and reperfusion event and for categorical features and patient survival

CT features		Reperfusion		p-value	Death		p-value
		Y (15)	N (7)		Y (11)	N (11)	
Pale mesentery + paper thin	Y (12)	6	6	0.074	8	4	0.20
	N (10)	9	1		3	7	
		Y (8)	N (6)		Y (8)	N (6)	
Fat stranding + paper thin	Y (13)	8	5	0.43	8	5	0.43
	N (1)	0	1		0	1	
		Y (15)	N (4)		Y (9)	N (10)	
Fat stranding + wall thickening	Y (15)	15	0	0.00026	6	9	0.3
	N (4)	0	4		3	1	
		Y(11)	N(6)		Y (11)	N (6)	
Normal m. vessels + wall thickening	Y (10)	10	0	0.00057	4	6	0.034
	N (7)	1	6		7	0	
		Y (6)	N (4)		Y (5)	N (5)	
Pale mesentery + fat stranding	Y (9)	6	3	0.40	6	3	0.40
	N (1)	0	1		0	1	
		Y (13)	N (5)		Y (6)	N (12)	
Normal mesentery + fat stranding	Y (14)	12	2	0.0044	6	8	0.58
	N (4)	1	3		3	1	

Annotations are as in Table 3.

Capital Y and N stand for the occurrence or lack of the feature on 28 CT examinations, and values in parenthesis represent its frequency.

The results of the Fisher's exact tests (p-value) are two-sided.

Statistically significant results are highlighted in bold characters in the column of p-value.

the SMV diameter in NOMI cases and controls ($D = 0.39$, Prob = 0.017). The percentage value of the other CT features (mesenteric, bowel and peritoneal features) in the 20 patients with NOMI (28 CT examinations) are summarized in Table 2. The correlation between CT features and the reperfusion event and survival in the 20 patients with NOMI (28 CT examinations) is reported in Tables 3 and 4. Fisher's exact test showed a strong connection between the presence of reperfusion and mesenteric fat stranding ($p = 0.026$), bowel wall thickening ($p = 3.2 \times 10^{-5}$) and high attenuation of the bowel wall on unenhanced CT images ($p = 2.8 \times 10^{-4}$) (Figure 2). A similar result was found by combining wall thickening plus fat stranding ($p = 2.6 \times 10^{-4}$) or plus normal mesenteric vessels ($p = 5.7 \times 10^{-4}$). We also found a strong link between the presence of reperfusion and the combination of normal mesenteric vessels and those with fat stranding ($p = 0.0044$). Furthermore, the occurrence of reperfusion was predominantly connected to the absence of paper thin bowel feature ($p = 0.049$). 11 of the 20 patients (55%) died during their hospital stay (10 males and 1 female; mean age of 73.26 years vs 74.05 years of the survivors). The reperfusion event was associated with a reduced mortality ($p = 0.016$) and in particular normal mesentery plus wall thickening; both signs of reperfusion were considerably connected with lower mortality ($p = 0.034$).

DISCUSSION

NOMI is reported for approximately 20% of AMI,¹ nevertheless its incidence in our study population was quite high. This is a consequence of an increase in the ageing of society and the dialysis population.^{2,3} NOMI prognosis is extremely low and its mortality rate has not changed in recent years. Many patients with NOMI could potentially have been misdiagnosed and consequently may have died as a result of not receiving the correct treatment. Early diagnosis has proven difficult, and moreover during the diagnostic process, the disease can slowly advance to an irreversible state with massive intestinal necrosis. Regarding pathogenesis, intestinal vasospasm due to consistent low perfusion is believed to be the cause of ischaemic disorder due to a reduction in the cardiac output and blood pressure.^{13,14} The main goal of current therapy for NOMI is reduction of spasm and improved perfusion of the mesenteric artery using vasodilators, and the role of surgery should be limited to the excision of irreversibly necrotized intestine. In cases of this type, the purpose of imaging in the diagnosis of NOMI is essential: firstly, for the earliest possible identification of this critical condition, to plan the most appropriate treatment that is based on a different approach from those of the occlusive forms of AMI,^{3,6} then to identify effective reperfusion. In fact, in NOMI, the primary injury as a result of ischaemia could be repaired by reperfusion, meaning the re-establishment of normal mesenteric

Figure 2. Imaging data of a patient with non-occlusive mesenteric ischaemia (male, 49 years old, Marfan Syndrome, Bentall for Type A aortic dissection, hypertension and obesity, cardiac failure during wedding party) with ineffective reperfusion. The axial CT images (a, b) of the first examination showed hypoperfusion phenomena involving the liver, spleen and left kidney; the reduction in calibre and number of mesenteric vessels (pale mesentery); and loop findings with paper thin and hypotonic reflex ileus. After 10 days of vasoactive therapy, the patient underwent another CT examination that showed mesentery findings with fat stranding reflecting the presence of vascular congestion and mesenteric fluid (c), thickened loops with high attenuation of the wall on unenhanced CT (d), with regular contrast enhancement (e). CT examination performed 6 days later because of worsening showed increase of intramural haemorrhage in the bowel wall and fluid in the peritoneal cavity (f), suggesting an ineffective reperfusion event. After intravenous administration of contrast media, there is no significant contrast enhancement of the bowel wall: 68 HU (g) vs 46 HU (f). Surgical intervention showed mesenteric petechiae and thickened bowel wall due to intramural haemorrhage (h). The patient died 3 days after surgical procedure. Adapted from Mazzei et al²⁴ with permission from Springer.

blood supply after an ischaemic event, more frequent than in an occlusive ischaemic condition. However, the event of reperfusion could be further worsened if the initial damage was caused by ischaemia, when it occurs in an advanced condition of ischaemia. This entity is known as ischaemia/reperfusion injury^{15,16} and, in many cases, can progress into shock, multiple organ failure and death.¹⁷ Some authors criticize the low sensitivity and specificity of MDCT when used to diagnose NOMI, because it may hinder the correct diagnosis especially in the early phases of NOMI.¹ However, Woodhams et al has recently published a study that shows the possibility of MDCT to be as equally useful as angiography in the diagnosis of NOMI by deciphering the morphological appearance and diameter of SMA.¹¹ In NOMI early phase, CT appearances concerning the abnormal

arterial findings are superimposable to angiography, demonstrating the narrowing of many subdivisions of SMA (the so called “string of sausage” sign: alternate dilatation and stenosis of the superior mesenteric arterial branches), the intestinal marginal artery spasm and the reduction of vein contrast enhancement in the muscular layer as signs of vasospasm associated with NOMI. In our case population, the average value of the SMA diameter was 4.6 ± 1.4 mm (range 2.2–7.4 mm), whereas it was 3.4 ± 1.1 mm in the study of Woodhams. There was a significant difference with controls in both studies, and the mean SMA diameter was consistent within the errors. We thus confirm the reduction of the SMA diameter in NOMI cases, but with much larger statistics (28 CT examinations vs 4 in Woodhams et al). Also, Mitsuyoshi et al suggests to perform MDCT instead

of angiography upon suspicion of NOMI, claiming that it provides vascular information comparable to that obtained in angiography.⁴ In any case, apart from the low number of patients described in the study of Woodhams (four), both studies are also restrictive regarding the ability of MDCT in diagnosing NOMI, because the authors consider the only possibility in the evaluation of vessel appearance at CT examination. On the contrary, the major advantage of MDCT when compared with angiography is the potential evaluation of mesenteric, bowel and peritoneal cavity findings, not only the vessels features.^{13,14} In our population, mesenteric, bowel and peritoneal CT features were identified in all CT examinations, varying from 7.14% (free air in peritoneal cavity) to 82.14% (mesenteric fat stranding) and many demonstrated a significant correlation with a reperfusion occurrence (mesenteric fat stranding, $p = 0.026$; bowel wall thickening, $p = 3.2 \times 10^{-5}$; and high attenuation of the bowel wall on unenhanced CT images, $p = 2.6 \times 10^{-4}$) representing CT signs useful for the diagnosis of NOMI and to recognize the reperfusion event. In case of reperfusion, an acute inflammatory reaction develops due to the production of reactive metabolites and activated neutrophils.¹⁸ Thickening of the bowel wall can occur in cases of reperfusion as a result of the superimposition of the reperfusion effects on the ischaemic damage caused by hypoperfusion. They are presented as oedema and thickening of the submucosa, signalled vascular congestion and granulation tissue. Inflammatory cells with numerous neutrophils and nuclear detritus developing pseudomembranes can also be present. The remaining epithelium demonstrates reconstructive changes with denudation of villi, crypts coated with hyperchromatic cells that proliferate the replacement of the destroyed epithelium.^{19,20} The superimposition of the reperfusion effects on the ischaemic injury distinguished by signalled vascular congestion could lead to an explanation of high attenuation of the bowel wall on unenhanced CT scans, which is usually associated with intramural haemorrhage and haemorrhagic infarction in literature.¹¹ The bivariate analysis also demonstrates a significant association between some CT signs (normal mesentery and thickening of

bowel wall) and mortality, suggesting the possible prognostic value of the CT features in NOMI. Finally, from a diagnostic point of view, it is important to note that owing to the possibility of the reperfusion event, NOMI can be a dynamic condition and its appearance upon imaging could be significantly different because of these reasons and at the time in which the CT examination is performed, as demonstrated by the analysis of the CT images of patients who underwent more CT examinations during their hospital stay in our case history. Some limitations of the present study should be outlined. Firstly, it is a retrospective study, although all CT examinations were re-evaluated in a prospective setting. In our series, there are a small number of patients and the obtained result should be confirmed in large prospective studies in order to assess the real clinical utility in the early diagnosis and treatment and to confirm the prognostic power in a clinical setting.

CONCLUSION

Among various mesenteric ischaemia presentations, the early phase of NOMI is not easy to diagnose *via* CT because it could reveal a different appearance at imaging dependant on the presence of reperfusion. Drawing a distinction between these two forms (NOMI with or without reperfusion), it is necessary to ensure the correct treatment (medical or surgical).^{3,4,21–24} The analysis of not only vessels features but also of mesenteric, bowel and peritoneal CT findings propose a potentially useful method to distinguish NOMI with reperfusion (absent or present) and, in addition, any possible prognostic value. Therefore, the introduction of MDCT in the decision tree of NOMI treatment may bring the benefit of a prompt diagnosis and subsequent early and efficient initiation of therapy in the emergency setting, which may improve the mortality rate.

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REFERENCES

1. Trompeter M, Brazda T, Remy CT, Vestring T, Reimer P. Non-occlusive mesenteric ischemia: etiology, diagnosis, and interventional therapy. *Eur Radiol* 2002; **12**: 1179–87. doi: <http://dx.doi.org/10.1007/s00330-001-1220-2>
2. Mazzei MA, Guerrini S, Cioffi Squitieri N, Imbriaco G, Mazzei FG, Volterrani L. Non-obstructive mesenteric ischemia after cardiovascular surgery: not so uncommon. *Ann Thorac Cardiovasc Surg* 2014; **20**: 253–5. doi: <http://dx.doi.org/10.5761/atcs.le.12.02154>
3. Woodhams R, Nishimaki H, Fujii K, Kakita S, Hayakawa K. Usefulness of multidetector-row CT (MDCT) for the diagnosis of non-occlusive mesenteric ischemia (NOMI): assessment of morphology and diameter of the superior mesenteric artery (SMA) on multi-planar reconstructed (MPR) images. *Eur J Radiol* 2010; **76**: 96–102. doi: <http://dx.doi.org/10.1016/j.ejrad.2009.05.012>
4. Kamimura K, Oosaki A, Sugahara S, Mori S. Survival of three nonocclusive mesenteric ischemia patients following early diagnosis by multidetector row computed tomography and prostaglandin E1 treatment. *Intern Med* 2008; **47**: 2001–6. doi: <http://dx.doi.org/10.2169/internalmedicine.47.1213>
5. Mitsuyoshi A, Obama K, Shinkura N, Ito T, Zaima M. Survival in nonocclusive mesenteric ischemia: early diagnosis by multidetector row computed tomography and early treatment with continuous intravenous high-dose prostaglandin E(1). *Ann Surg* 2007; **246**: 229–35. doi: <http://dx.doi.org/10.1097/01.sla.0000263157.59422.76>
6. Moschetta M, Stabile Ianora AA, Pedote P, Scardapane A, Angelelli G. Prognostic value of multidetector computed tomography in bowel infarction. *Radiol Med* 2009; **114**: 780–91. doi: <http://dx.doi.org/10.1007/s11547-009-0422-6>
7. Mazzei MA, Guerrini S, Cioffi Squitieri N, Genovese EA, Mazzei FG, Volterrani L. Diagnosis of acute mesenteric ischemia/infarction in the era of multislice CT [In Italian.] *Recenti Prog Med* 2012; **103**: 435–7. doi: <http://dx.doi.org/10.1701/1166.12884>
8. Ende N. Infarction of the bowel in cardiac failure. *N Engl J Med* 1958; **258**: 879–81. doi:

- <http://dx.doi.org/10.1056/NEJM195805012581804>
9. Siegelman SS; Sprayregen S, Boley SJ. Angiographic diagnosis of mesenteric arterial vasoconstriction. *Radiology* 1974; **112**: 533–42. doi: <http://dx.doi.org/10.1148/112.3.533>
 10. Nakamura Y, Urashima M, Toyota N, Ono C, Iida M, Fukumoto W, et al. Non-occlusive mesenteric ischemia (NOMI): utility of measuring the diameters of the superior mesenteric artery and superior mesenteric vein at multidetector CT. *Jpn J Radiol* 2013. [Epub ahead of print]
 11. Furukawa A, Kanasaki S, Kono N, Wakamiya M, Tanaka T, Takahashi M, et al. CT diagnosis of acute mesenteric ischemia from various causes. *AJR Am J Roentgenol* 2009; **192**: 408–16. doi: <http://dx.doi.org/10.2214/AJR.08.1138>
 12. Mazzei MA, Mazzei FG, Marrelli D, Imbriaco G, Guerrini S, Vindigni C, et al. Computed tomographic evaluation of mesentery: diagnostic value in acute mesenteric ischemia. *J Comput Assist Tomogr* 2012; **36**: 1–7. doi: <http://dx.doi.org/10.1097/RCT.0b013e31823b4465>.
 13. Bassiouny HS. Nonocclusive mesenteric ischemia. *Surg Clin North Am* 1997; **77**: 319–26.
 14. Bailey RW, Bulkley GB, Hamilton SR, Morris JB, Haglund UH. Protection of the small intestine from nonocclusive mesenteric ischemic injury due to cardiogenic shock. *Am J Surg*. 1987; **153**: 108–16. doi: [http://dx.doi.org/10.1016/0002-9610\(87\)90210-8](http://dx.doi.org/10.1016/0002-9610(87)90210-8)
 15. Mallick IH, Yang W, Winslet MC, Seifalian AM. Ischemia-reperfusion injury of the intestine and protective strategies against injury. *Dig Dis Sci* 2004; **49**: 1359–77. doi: <http://dx.doi.org/10.1023/B:DDAS.0000042232.98927.91>
 16. Cerqueira NF, Hussni CA, Yoshida WB. Pathophysiology of mesenteric ischemia/reperfusion: a review. *Acta Cir Bras* 2005; **20**: 336–43. doi: <http://dx.doi.org/S0102-86502005000400013>
 17. Pierro A, Eaton S. Intestinal ischemia reperfusion injury and multisystem organ failure. *Semin Pediatr Surg* 2004; **13**: 11–7. doi: <http://dx.doi.org/10.1053/j.sempedsurg.2003.09.003>
 18. Schoenberg MH, Fredholm BB, Haglund U, Jung H, Sellin D, Younes M, et al. Studies on the oxygen radical mechanism involved in the small intestinal reperfusion damage. *Acta Physiol Scand* 1985; **124**: 581–9. doi: <http://dx.doi.org/10.1111/j.1748-1716.1985.tb00051.x>
 19. Saba L, Berritto D, Iacobellis F, Scaglione M, Castaldo S, Cozzolino S, et al. Acute arterial mesenteric ischemia and reperfusion: macroscopic and MRI findings, preliminary report. *World J Gastroenterol* 2013; **19**: 6825–33. doi: <http://dx.doi.org/10.3748/wjg.v19.i40.6825>
 20. Noffsinger A, Fenoglio-Preiser C, Maru D, Gilinsky N. Gastrointestinal diseases. *Atlas of Nontumor pathology*. Washington: ARP Press; 2007.
 21. Liu S, Sun Q, Tao H, Sun X. Oral administration of mannitol may be an effective treatment for ischemia-reperfusion injury. *Med Hypotheses* 2010; **75**: 620–2. doi: <http://dx.doi.org/10.1016/j.mehy.2010.07.048>
 22. Takizawa Y, Kitazato T, Kishimoto H, Tomita M, Hayashi M. Effects of antioxidants on drug absorption *in vivo* intestinal ischemia/reperfusion. *Eur J Drug Metab Pharmacokinet* 2011; **35**: 89–95. doi: <http://dx.doi.org/10.1007/s13318-010-0020-y>
 23. Newton WB 3rd, Sagransky MJ, Andrews JS, Hansen KJ, Corriere MA, Goodney PP, et al. Outcomes of revascularized acute mesenteric ischemia in the American College of Surgeons National Surgical Quality Improvement Program database. *Am Surg* 2011; **77**: 832–8.
 24. Mazzei MA, Volterrani L. Nonocclusive mesenteric ischaemia: think about it. *Radiol Med* 2015; **120**: 85–95. doi: <http://dx.doi.org/10.1007/s11547-014-0460-6>