Duplex ultrasound in the early diagnosis of acute mesenteric ischemia: a longitudinal cohort multicentric study

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Objective **Acute mesenteric ischemia (AMI) is a life-threatening condition requiring time-dependent treatment; thus, early recognition may improve outcomes. We hypothesized that clinician-performed mesenteric vessels duplex ultrasound (DUS) could facilitate early identification of patients with AMI in high-risk patients presenting with abdominal pain.**

Methods **This was a single-operator, observational, prospective cohort study. Patients aged at least 65 presenting to Emergency Departments with acute abdominal pain and no clear diagnosis after an initial work-up were enrolled. All patients underwent multidetector computed tomography and these findings provided the reference standard in this study. DUS of the celiac artery and superior mesenteric artery (SMA) were obtained to measure the peak systolic velocity (PSV) and were performed within 24 h of admission. PSVs outside the normal range were considered to indicate AMI.**

Results **Of 49 patients identified, 47 were consented to enrollment and diagnostic images were obtained in 45 (96%). Fifteen patients (33%) had AMI (six occlusive, nine nonocclusive disease). Among these, 12 (80%) had abnormal DUS velocities. SMA PSV showed a sensitivity of 78.57% [95% confidence interval (CI): 49.2–95.34], a specificity of 64.52% (95% CI: 45.37–80.77), a positive predictive value of 50% (95% CI: 28.22–71.78), and a negative predictive value of 86.96% (95% CI: 66.41–97.22) for AMI. DUS had a sensitivity of 100%, a specificity of 64%, and a negative predictive value of 100% for occlusive AMI. Assessment of celiac artery PSV did not improve diagnostic performance.**

Conclusion **In this single-operator pilot study, mesenteric vessel DUS was performed successfully in the Emergency Department, with a high proportion of diagnostic images obtained. A normal SMA PSV was associated with a low risk of occlusive AMI.** ***European Journal of Emergency Medicine*** **00:000–000 Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.**

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Introduction

Acute mesenteric ischemia (AMI) occurs in around one in 1000 patients presenting to the Emergency Department (ED) [1,2] and accounts for ~ 1% of hospitalizations with acute abdomen pain [3,4]. The incidence of AMI ranges from 4.5 to 44 cases per 100 000 persons per year, but is increased in elderly and patients with cardiovascular disease [5,6].

AMI is considered a vascular emergency [7] with a high time-dependent death rate (40–70%) [8,9].

AMI may be subdivided into occlusive mesenteric ischemia (OMI), characterized by arterial occlusion (acute thrombosis or embolism) or venous thrombosis, and nonocclusive mesenteric ischemia (NOMI), determined by reduced blood and oxygen supply relative to requirements (for example in shock or associated with vasopressor therapy) [10]. Early diagnosis is challenging as presenting symptoms are often nonspecific. These include abdominal pain in 96% of cases, which is often out of proportion to the examination findings, vomiting, nausea, and diarrhea [11]. The initial assessment includes plain radiography and blood tests, which are frequently nondiagnostic, although an elevated lactate may suggest the diagnosis [12,13]. Multidetector computed tomography (MDCT) and computed tomography (CT) angiography are considered the gold-standard imaging techniques to confirm the diagnosis as catheter angiography is invasive, costly, and not available in all facilities [14,15]. Early open or endovascular treatment strategies may restore blood flow in cases of OMI [16,17], whereas the treatment of NOMI is supportive, with resuscitation, anticoagulant therapy, and occasionally intra-arterial papaverine infusion [18,19].

Duplex ultrasound (DUS) of the mesenteric vessels and bowel wall ultrasound evaluation have been shown to be a reliable tool in detecting AMI [20–22]. To the best of our knowledge, its use has not been described in an ED performed by emergency physicians.

We therefore aimed to evaluate the performance of an emergency physician performing DUS of the celiac artery

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(CA) and the superior mesenteric artery (SMA) to detect AMI in the ED compared with the reference standard of MDCT ± angiography.

Methods

This observational prospective cohort study was carried out in two closely located hospitals in Tuscany (Italy) between October 2012 and April 2014. Both EDs were provided with a 24 h/day radiology service performing standard abdomen ultrasound and an ED-staffed 24–48 h observational unit. Every time a patient suitable for the study was identified, the ED staff contacted the investigator, an emergency physician, who performed all DUS exams.

The investigator was trained in basic ultrasound (point-of-care thoracic ultrasound, echocardiography, and abdominal ultrasound) with additional training in peripheral vascular Doppler studies. This was supplemented by further training from a one-day dedicated course on mesenteric vessel ultrasound. Before the study, consolidation experience was gained by the evaluation of 30 patients under the supervision of an expert gastroenterologist sonographer.

Patients presenting to ED with abdominal pain and/or alteration of bowel habit were subjected to laboratory tests (full blood count, electrolyte, renal and liver function, amylase, D-dimer, lactic dehydrogenase, creatine kinase, myoglobin, lactate), abdominal radiographs, and an abdominal ultrasound (performed by a radiologist) as their initial work-up. If this assessment offered no specific diagnosis, the operator was contacted to assess eligibility for the study and to perform DUS. The protocol was identical for both hospitals.

Patients

Patients were eligible for the study if they fulfilled all the following criteria: age at least 65; acute abdominal pain with onset less than 24 h of presentation and/or altered bowel habit; history of atrial fibrillation and/or atherosclerosis in any vascular territory (cerebral vascular disease, carotid atherosclerosis, ischemic heart disease, peripheral arterial disease); and no diagnosis after initial work-up.

Patients with a clear diagnosis after initial assessment, such as those with gallstones, pancreatitis, hepatitis, appendicitis, perforation, bowel obstruction, or renal colic, were excluded. Any of the following was also considered an exclusion criterion: history of trauma, clinical diagnosis of gynecologic pathology, and bowel disturbance as a consequence of drug use or intoxication.

Entry to the study did not delay any participants from undergoing diagnostic MDCT imaging, but the investigator was blinded to the results of this when performed before inclusion in the study. The study thus included a convenience sample; however, all patients identified as eligible for the study were approached for participation. All DUS were performed in the ED or the observation unit.

Ethical review

The study was carried out in accordance with the Declaration of Helsinki and approved by our local ethical committee. Written informed consent was obtained from all patients. The study was registered by the Local Ethical Committee of the University Hospital of Siena (reference code CE 25_09_12–1).

Duplex ultrasound evaluation

All DUS examinations were performed as soon as possible and always within 24 h of hospital presentation; the operator was blinded to all clinical information and imaging. DUS was performed using an Esaote MyLab70 (Esaote SpA, Caciolle, Italy) using standard abdominal software and a curvilinear phased array transducer (4.5–6 MHz). Duplex assessment consisted of peak systolic velocity (PSV) evaluation of both the CA and the SMA with a beam angle between 40° and 60° and a 1.5 mm gate [23].

The SMA was evaluated in the sagittal plane with the duplex gate placed within 2 cm of the aorta [24]. The CA was evaluated in the transverse view, where the main branches (common hepatic, splenic, and left gastric arteries) are best visualized, with the duplex gate placed within 1 cm of the aorta [25]. We considered normal PSV values to be 90–190 cm/s for the CA and 80–200 cm/s for the SMA [26]. Thus, PSV abnormal velocities were considered less than 90 cm/s or greater than 190 cm/s for CA and less than 80 cm/s or greater than 200 cm/s for SMA. High velocities are an indication of stenosis greater than 30%, whereas a reduced or absent flow speed represents subtotal occlusion/occlusion pattern [22,27].

MDCT and CT angiography diagnostic criteria

An abdominal MDCT was performed in all patients in the ED as dictated by clinical assessment. The timings and decision for MDCT were independent of the study. A plain CT was enhanced with contrast medium for CT angiography (including arterial, venous, and portal phase) unless contraindicated. Contrast medium was not infused if there was renal impairment (defined as creatinine > 1.5 mg/dl/ > 150 μmol/l) and/or known contrast allergy. OMI was diagnosed by the presence of emboli or thrombi visualized as filling defects in the lumen of CA, superior, or inferior mesenteric artery. NOMI was diagnosed by the finding of a patent arterial system with a reduction in enhancement and thickening of the bowel wall.

Statistical analysis

Abnormally high or low PSV values obtained in either the CA or the SMA were considered indicative of AMI. If both arteries had normal blood flow on DUS, AMI was assumed not to be present. Sensitivity (SE), specificity (SP), positive and negative predictive value (PPV and NPV, respectively), and likelihood ratios were calculated against the reference standard of MDCT. The Hosmer–Lemeshow goodness-of-fit test was used to evaluate model calibration.

The Student *t*-test or the Fisher exact test was used to compare quantitative Gaussian or non-Gaussian variables, respectively, to assess the differences between patients with and without AMI. The Kolmogorov–Smirnov statistical test was used to verify the normality of data distribution. A statistical comparison between diagnostic tests was performed by evaluating the 95% confidence interval of sample estimates using a bootstrap approach [28].

The SPSS software v.21 (IBM Software, Amonk, New York, USA), held by the University of Siena Inc., and Matlab v.5 (The MathWorks, Inc., Natick, USA) package were used for statistical computations and score model design, respectively.

Results

Over an 18-month period, 49 patients were found to be eligible for the study, but two withdrew consent. Among the 47 study participants, we obtained diagnostic DUS images in 45 (in which the PSV CA was unidentifiable in one patient). Demographic, clinical, and diagnostic test results are reported in Table 1. Final diagnoses on the basis of CT abdomen findings are reported in Table 2. Eight patients did not receive contrast medium for CT angiography acquisition on the basis of the criteria discussed above. The mean time to MDCT was 8 h (± 7 h), whereas the mean time to DUS was 4 h (± 8 h).

MDCTs were reported as showing AMI in 15/45 patients. A total of 6/15 patients were reported to have OMI: four because of SMA occlusion (one during new-onset atrial fibrillation, three presumed thrombosis), one involving the celiac trunk, and one involving the inferior mesenteric artery. A total of 9/15 had NOMI: ischemic changes were observed in the descending and sigmoid colon – rectal wall in seven patients (78%), the duodenum in one patient, and the ascending colon in one patient.

Abnormal PSVs in either the SMA or the CA were found in 27 patients, 12 of whom had AMI on the basis of the MDCT criteria. Of the remaining 18 patients with normal SMA and CA PSV values, three had AMI on the basis of the MDCT criteria.

Normal and abnormal PSV frequencies for both SMA and CA divided into AMI and non-AMI patients are reported in Table 3.

Abnormal CA PSV values were identified in 23/44 cases. We found high PSV (>190 cm/s) in 21 of these and two had a PSV below the defined normal range (< 90 cm/s). Abnormal SMA PSV values were obtained in 22/45 patients. These were elevated (PSV > 200 cm/s) in 19 patients and three patients had low PSV (< 80 cm/s) values.

For each of SMA PSV, CA PSV, and a combination of both SMA and CA PSV, we evaluated the performance of DUS in identifying patients with AMI. The results of SE, SP, positive and negative likelihood ratio, PPV, and NPV are reported in Table 4. The performances of SMA PSV alone in diagnosing AMI, OMI, and NOMI are reported in Table 5.

Discussion

To our knowledge, this is the first study to investigate the usefulness of emergency physician performed DUS

Table 1 Demographic, clinical, and diagnostic test results of the population studied (*N* = 45)

Age	81 ± 8.7				
Sex					
Male	12 (27)				
Female	33 (73)				
Comorbidities					
AF	11 (24)				
Carotid atherosclerosis	11 (24)				
Coronary atherosclerosis	16 (36)				
Cerebral vascular disease	15 (33)				
Peripheral arterial disease	4 (8)				
Presentation symtoms					
Abdominal pain	36 (80)				
Change in Bowel habit	12 (27)				
	AMI (*n* = 15)		Non-AMI (*n* = 30)		
Laboratory	Mean	SD	Mean	SD	*P* value
Lactate dehydrogenase	163	48.4	184	51.4	0.25
Creatine kinase	53	35.9	125.67	166.8	0.98
Myoglobin	289.2	412.1	135.3	82.4	0.81
Lactate	3.01	2.53	0.9	0.08	0.19
D-Dimer	1.3	0.8	1.5	0.9	0.75

AMI, acute mesenteric ischemia.

Table 2 Final diagnosis on the basis of MDCT (*N* = 45)

Acute mesenteric ischemia	15 (33)	Incarcerated hernia	2 (5)
Occlusive	6/15	Volvulus	2 (5)
Nonocclusive	9/15	Ureteric colic	1 (2)
Diverticulitis	8 (18)	Bowel perforation	1 (2)
Neoplasm	3 (7)	Pleural effusion	1 (2)
Biliary colic	3 (7)	No abnormality found	9 (20)

Values are represented as *n* (%).
MDCT, multidetector computed tomography.

Table 3 Normal and abnormal peak systolic velocities for the superior mesenteric artery and/or the celiac artery versus diagnosis of acute mesenteric ischemia

	AMI group	Non-AMI group
PSV SMA or CA abnormal	12	15
PSV SMA or CA normal	3	15
PSV SMA and CA abnormal	8	10
PSV SMA and CA normal	7	20
PSV SMA abnormal	11	11
PSV SMA normal	3	20
PSV CA[a] abnormal	9	14
PSV CA[a] normal	6	15

We report the number of patients with normal/abnormal PSV SMA or CA, PSV SMA, and CA, only PSV SMA and PSV CA divided into AMI and non-AMI.
AMI, acute mesenteric ischemia; CA, celiac artery; PSV, peak systolic velocity; SMA, superior mesenteric artery.
[a]CA PSV is missing one patient (44 instead of 45) as a diagnostic view could not be obtained.

Table 4 Comparison of the performances of duplex ultrasound normal or abnormal peak systolic velocity of the superior mesenteric artery and celiac artery combined or in isolation to identify acute mesenteric ischemia

	DUS performances to detect AMI			
	Abnormal (SMA and CA) PSV	Abnormal (SMA or CA) PSV	Abnormal SMA PSV	Abnormal CA PSV
Sensitivity (95% CI)	53.33% (26.65–78.66)	80% (51.91–95.43)	78.57% (49.2–95.34)	60.00% (32.33–83.57)
Specificity (95% CI)	66.67% (47.19–82.69)	50% (31.31–68.69)	64.52% (45.37–80.77)	51.72% (32.54–70.54)
Positive LR (95% CI)	1.60 (0.80–3.20)	1.60 (1.03–2.48)	2.21 (1.28–3.83)	1.24 (0.71–2.17)
Negative LR (95% CI)	0.70 (0.39–1.27)	0.40 (0.14–1.17)	0.33 (0.12–0.94)	0.77 (0.38–1.58)
PPV (95% CI)	44.44% (21.58–69.21)	44.44% (25.50–64.66)	50.00% (28.22–71.78)	39.13% (19.74–61.45)
NPV (95% CI)	74.07% (53.71–88.84)	88.33% (58.56–96.23)	86.96% (66.41–97.22)	71.43% (47.83–88.65)

In this study, SMA PSV performed better than CA PSV.
AMI, acute mesenteric ischemia; CA, celiac artery; CI, confidence interval; DUS, duplex ultrasound; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; PSV, peak systolic velocity; SMA, superior mesenteric artery.

in the evaluation of patients with abdominal pain. The investigator obtained PSV readings for the SMA in 45/47 patients (96%) and for the CA in 44/47 patients (94%). In two cases, DUS was not possible because of high BMI and consistent air interposition, difficulties that have been reported in previous studies [29,30].

Fifteen of 45 patients (33%) had a final diagnosis of AMI. A normal DUS (in both the CA and the SMA) had a reasonable NPV (88.33%), suggesting the diagnosis of AMI to be unlikely (Table 4). However, a normal DUS does not exclude the diagnosis and will miss around one in 8.5 presentations. As PPV and SP were low (44.44 and 66.67%, respectively), an abnormal PSV suggests that DUS offers little to confirm the diagnosis (negative likelihood ratio = 0.70). Thus, a positive DUS may be useful to emergency physicians in identifying a population at high risk of AMI for immediate MDCT ± angiography. As AMI has a low prevalence in the ED compared with our selected study population, PPV may be an overestimate if applied to a broader ED population [2,31,32].

The SE and SP of DUS in identifying patients with AMI reported here are in agreement with previous work [20,33]. These studies were carried out in an ambulatory care setting on high-risk preoperative patients and were performed by sonographers or vascular surgeons; thus, these data cannot be generalized to the ED population. Nonetheless, this study suggests that a suitably trained emergency physician performing DUS in the ED can potentially obtain diagnostic information. If these findings are reproducible in a larger study involving a broader spectrum of emergency physicians, then DUS may play a role in risk stratification of patients with possible AMI.

Overall SMA PSV values were abnormal and most frequently increased in patients with AMI ($P < 0.05$). SMA PSVs offered superior diagnostic performances (SE: 78%, SP: 64%, PPV: 50%, NPV: 86%) compared with CA PSVs (SE: 60%, SP: 51%, PPV: 39%, NPV: 71%) in diagnosing AMI. The anatomy of the CA makes DUS evaluation more technically challenging than for the SMA [34]. Furthermore, CA PSVs offered little additional diagnostic benefit when added to SMA PSVs in this study (Table 4). Future studies should be focused on the SMA alone, so seeing the DUS performed more simply and more rapidly.

The SE of DUS for AMI was higher for patients with OMI compared with NOMI and abnormal SMA PSV velocities found in all patients with OMI (Table 5). Hence, a normal SMA PSV makes the diagnosis of OMI very unlikely and consequently the requirement for urgent reperfusion strategies is rarely required. Its diagnostic performance for NOMI was less robust, with a SE of 66% and an NPV of 88%. These findings may be expected from the underlying physiopathology of the two diseases: OMI occurs because of an acute occlusion of the main arterial branches (both embolic and thrombotic) and DUS can easily detect blood flow abnormalities at this level; NOMI occurs because of ischemic bowel wall insult as a consequence of hypotension and/or microcirculatory vasoconstriction. The latter is associated with less intense arterial flow changes at the origin of the splanchnic arteries [35]. Other duplex flow indices have been found to be altered during NOMI, such as the early diastolic peak flow velocity. These were not explored in the study reported here and may be difficult to measure in acute settings [36]. However, even in the absence of a

Table 5 SMA PSV performance to diagnose AMI, OMI, and NOMI

	AMI ($n = 15$) $P = 0.0028$	OMI ($n = 6$) $P = 0.005$	NOMI ($n = 9$) $P = 0.13$
Sensitivity	78.57% (95% CI = 49–95%)	100% (95% CI = 54–100%)	66% (95% CI = 57–79%)
Specificity	64.52% (95% CI = 45–80%)	64% (95% CI = 64–78%)	63% (95% CI = 48–81%)
PPV	50% (95% CI = 28–71%)	30% (95% CI = 12–54%)	31% (95% CI = 9–59%)
NPV	86.9% (95% CI = 66–97%)	100% (95% CI = 86–100%)	88% (95% CI = 78–97%)

AMI, acute mesenteric ischemia; CI, confidence interval; NOMI, nonocclusive mesenteric ischemia; NPV, negative predictive value; OMI, occlusive mesenteric ischemia; PPV, positive predictive value; PSV, peak systolic velocity; SMA, superior mesenteric artery.

vascular obstruction of the main arteries, high SMA PSV values were found among NOMI patients. This supports the hypothesis proposed by van Petersen *et al.* [37] that a compensatory mesenteric perfusion reflex leads to increased flow velocities because of the ischemic insult.

The inferior mesenteric artery is not well visualized by DUS and AMI in this arterial distribution will be missed by DUS. Consequently, it was not evaluated in this study.

The incidence of AMI (33%) in this study is high compared with that found in the overall population presenting to ED with abdominal pain, but is in line with previous findings on the basis of high-risk patient groups and similar to those identified by our inclusion criteria (age $\geq$65 and history of cardiovascular disease) [38,39]. However, a direct comparison cannot be made with these studies as they were not carried out in the ED, involved different populations (one held in North Europe, the other two in North America), and DUS was not performed by emergency physicians.

In our study, the incidence of NOMI was greater than OMI, which is in contrast to previous work [28,40]. This may reflect the small sample size, but could also be related to the fact that eight patients did not undergo CT angiography and were imaged using MDCT without contrast medium. Two of these eight patients were diagnosed with NOMI, two with diverticulitis, one with biliary colic, one with ureteric colic, and two had no abnormal findings reported. Noncontrast MDCT provides no direct diagnostic information on arterial blood flow and the diagnosis of AMI is suggested by bowel wall appearance. Consequently, the two patients with NOMI and the two with normal findings could potentially have had arterial branch occlusion, increasing the rate of OMI cases. Three of these four patients had abnormal PSV values and consequently the finding of arterial occlusion would have a significant effect on the findings reported here.

Clinical signs and laboratory markers showed limited usefulness in differentiating between AMI and non-AMI patients, in agreement with previous work [41]. Lactate was increased in the AMI group, but not significantly in this study ($P=0.19$). Lactate and D-dimer have been investigated previously as early markers of ischemia and thrombosis, respectively. These have been shown to have 80–90% SE for AMI; thus, normal values make the diagnosis unlikely [42]. Positive likelihood ratios of 3 for lactate and 1.6 for D-dimer are reported, but their usefulness is hampered by poor SP (40–45% for both) [43]. If the findings of this study are replicated in larger series, then a normal SMA PSV may suggest that an elevated lactate is not a consequence of OMI.

MDCT angiography remains the gold standard for the diagnosis of AMI and offers a wide range of alternative diagnoses that are not readily identified by ultrasound or DUS (Table 2). Diagnostic information is provided even when intravenous contrast medium is not administered and six of the eight who did not receive it had a specific diagnosis offered.

Limitations

There are several limitations to this work. It is a feasibility study by a single sonographer in two EDs. The results are not generalizable and do not clarify whether DUS may be performed by emergency physician sonographers and also do not report interobserver reliability. The study was observational and thus lacked a control group, further limiting clinical application. Inclusion criteria and initial work may not be reproducible in other settings. We also do not report the operative findings, where applicable, or clinical outcomes that may offer a more comprehensive reference standard. Participants represented a convenience sample and were recruited within 24 h of arrival in ED; earlier and standardized DUS evaluation time would have been desirable, but limited by the operator availability. Furthermore, we do not know how many eligible patients have been missed. Our study was also carried out in a high-risk cohort and these results may not be applicable to the wider population presenting with abdominal pain. Indeed, abdominal pain is the third most common ED presentation in the at least 65 years old population [44]. This study also involved no intervention or change in care and therefore there is no evaluation of whether clinician-performed DUS impacts on any outcomes. Finally, the DUS findings were not reviewed by a more experienced operator; thus, the findings were not confirmed and the interobserver reliability was not assessed.

Conclusion

We have shown that a suitably trained emergency physician can perform DUS in the ED setting and obtain PSV readings in a high proportion of patients with possible AMI. A normal DUS suggests that the diagnosis of AMI, particularly OMI, is unlikely, but will miss around one in 8.5 patients with the disease. OMI requires time-dependent revascularization treatment, whereas NOMI usually requires supportive care (6.46). However, half of our patients with abnormal DUS findings were found not to have AMI on MDCT $\pm$ angiography. SMA PSV alone performed similar to CA PSV and SMA PSV combined and, if supported by future work, suggests that a more simple DUS protocol than that used in our study may be applied. If our findings are reproduced in a larger study involving a wider range of emergency physicians, DUS may play a role as a risk stratification tool in identifying patients who require immediate MDCT $\pm$ angiography. This may be of particular use in EDs with more limited access to advanced imaging.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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