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Original Article



## Doppler ultrasound unveils splanchnic arteries ischemia allowing early successful revascularization in symptomatic systemic sclerosis patients

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## ABSTRACT

**Background:** Systemic sclerosis (SSc) is characterized by macro and microvasculopathy, including splanchnic circulation. Chronic mesenteric ischemia (CMI) is a potentially severe condition which can complicate SSc gastrointestinal vasculopathy. Doppler ultrasound (DUS) may be a non-invasive procedure for identifying CMI in symptomatic SSc patients.

**Objectives:** To investigate the capacity of DUS to detect early CMI and the effect of the endovascular approach on CMI-related symptoms.

**Methods:** DUS of splanchnic arteries was performed in symptomatic SSc patients, during routinary outpatient visits.

**Results:** In 6 out of 72 SSc symptomatic patients, DUS suggested a splanchnic vessels stenosis which was confirmed by computed tomography angiography (CTA). After multidisciplinary evaluation in 3 patients a revascularization was performed. Three-monthly clinical and DUS follow-up was negative in all patients.

**Conclusion:** CDU is a useful screening tool for CMI in SSc patients. Revascularization of stenotic mesenteric arteries seems to be a safe and effective procedure.

## 1. Introduction

Systemic sclerosis (SSc) is an autoimmune rheumatic disease where vasculopathy is one of the main hallmarks, and the gastrointestinal (GI) tract is one of the most affected systems [1,2]. In fact, SSc is characterized by esophageal dysfunction, gastro-esophageal reflux disease (GERD), visceral dysmotility, bowel distention and small intestinal bacterial overgrowth syndrome (SIBO), and complete loss of bowel motility [3]. Currently there are no standardized guidelines to assess and manage SSc-related GI involvement, however in recent years the understanding of SSc-related GI disease has grown both for an early diagnosis and management of its complications [4].

SSc pathogenesis is complex and not yet completely understood [5]. The hypothesis that vascular injury can be fundamental in the pathogenesis of SSc related complications is supported by numerous clinical and experimental studies [6]. It is well known that vasculopathy is an early event contributing to the pathogenesis and development of SSc. Endothelial injury is considered a central event in the pathogenesis of SSc vasculopathy; endothelium dysfunction results in vasoactive factors imbalance and dysregulation of various neurotransmitters finally leading to intimal thickening and tissue fibrosis [7]. Endothelial injury is also considered the very early event that, through a complex pathogenic cascade which includes fibroblast activation, neointima formation and vascular remodeling [8], leads to the formation of atherosclerotic

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plaques. In the last decade several evidence suggesting that accelerated atherosclerosis is a potential complication of many autoimmune diseases, including systemic sclerosis, has been published [9]. In this perspective, the early diagnosis and treatment of vascular-related SSc complications is fundamental for improving patients' prognosis.

Moreover, on top of several clinical complications due to vasculopathy, such as Raynaud's phenomenon, digital ulcers (DUs), pulmonary hypertension (PH) and scleroderma renal crisis (SRC), the attention has recently been focused on chronic mesenteric ischemia (CMI), which seems a rare clinical complication and could often be underestimated and undertreated. In fact, CMI is itself an underdiagnosed condition characterized by inadequate blood flow supply to the GI tract leading to long lasting ischemic symptoms prior diagnosis [10]. Therefore, a timely diagnosis of CMI is of paramount importance for a prompt intervention to prevent the development of acute ischemia, which is usually associated with high morbidity and mortality. The typical symptoms include a classic CMI triad characterized by postprandial abdominal pain, food aversion and weight loss. However, this clinical presentation is present in only 20 % of patients, while other atypical signs and symptoms, such as nausea, vomiting, bloating, constipation and diarrhea, are usually predominant [11]. For that reason, as well as for its rarity, the suspicion of CMI and consequently its diagnosis is challenging. In 90 % of cases, atherosclerosis of one or more mesenteric arteries is the main cause of CMI [12]. In SSc, an early and accelerated atherosclerosis has been described, and the underlying vasculopathy can lead to a vast blood flow impairment due to concurrent macro and microvascular involvement [13–16]. This process may involve all the main target organs (i.e. lung, heart, kidney), yet only recently the splanchnic circulation has become a matter of interest for the SSc community [17,18].

The GI tract can be investigated with Doppler Ultrasound (DUS), a non-invasive tool which is considered the first choice imaging examination for CMI screening and diagnosis [19]. Therefore, DUS evaluation of splanchnic vessels is a pivotal investigation in the evaluation of the multifaceted involvement of the GI system in SSc.

The aim of our work was to investigate the presence of CMI in symptomatic SSc patients and, when indicated, to refer the patient for multidisciplinary evaluation in order to assess the need for revascularization and its outcome on SSc patients.

## 2. Materials and methods

Consecutive SSc patients classified according to ACR EULAR 2013 criteria, underwent a GI DUS of the 3 main splanchnic vessels: the Celiac Trunk (CT), the Superior Mesenteric Artery (SMA) and the Inferior Mesenteric Artery (IMA). The DUS study was performed by two different expert operators (GB and GC), after a fasting state of at least 8 hours, with an Esaote Mylab 70 Twice using a 3.5–5 MHz Convex probe for a panoramic view of abdominal aorta and splanchnic arteries, and a 5–12 MHz Linear probe for the accurate measurement of caliber, thickness and echogenicity of the abdominal vessels. The caliber was measured 15 mm after the emergence from the abdominal aorta for CT, 25 mm for SMA and 15 mm for IMA. Doppler parameters were measured 15 mm after the emergence from the abdominal aorta for the three arteries. The position of the probe was adjusted to reach an angle of  $<60^\circ$  and the sample volume was corrected to include the entire inner diameter of the vessel. Peak systolic velocity (PSV) and end diastolic velocity (EDV) were recorder in the point of maximum stenosis identified aided by the aliasing artifact. Every measurement was the mean of three different examinations. For the identification of suspected splanchnic vessels stenosis previously validated criteria were used as reference values: for the SMA a PSV cut-off of 280 cm/sec was considered indicative of a stenosis  $> 50\%$ , instead for the CT a PSV cut-off of 200 cm/sec was considered indicative of a stenosis  $> 70\%$  [20,21].

When DUS revealed a hemodynamic stenosis of the artery in CT and/or SMA and/or IMA, a confirmatory computed tomography angiography (CTA) was performed, as indicated in the ESC and ESVS guidelines [19].

After a multidisciplinary consensus and patient's consent, the revascularization procedure was performed.

The outcome of the procedure was evaluated after one month during the following outpatient evaluation. DUs was performed in all patients after 1 month and then 3-monthly.

The research project was approved by local Ethical Committee (approval number: 23,805\_oss). All patients enrolled in the study gave their informed consent.

## 3. Results

Out of 72 SSc patients consecutively investigated with abdominal ultrasound for GI symptoms, 6 (8.3 %) patients were symptomatic for a suspected CMI (Table 1). None of them had the classic clinical CMI triad, whereas in all cases non-specific symptoms such as postprandial bloating, abdominal discomfort and nausea were present. One patient complained of at least two classic clinical symptoms like post prandial abdominal pain and recent significant weight loss. DUS showed a high PSV of SMA, indicating a stenosis of  $>50\%$  (PSV  $> 280$  cm/sec) in 4 out of 6 patients; in 3 of these 4 cases the stenosis was estimated to be  $>70\%$  because PSV was  $> 400$  cm/sec, with EDV  $> 80$  cm/sec and a mesenteric-aortic ratio (MAR) higher than 3.5. The other 2 patients had a suspected celiac trunk hemodynamic stenosis, since PSV was  $> 250$  cm/sec, indicating a stenosis  $> 70\%$ .

In these patients, the stenosis of the mesenteric and celiac trunk arteries were confirmed at CTA which showed the presence of atherosclerotic plaques; only one patient, the 73-year-old, former smoker with cardiovascular comorbidities, had SMA calcific hemodynamic plaques. She was not diabetic, nor she had chronic kidney failure.

These cases confirm the DUS high sensitivity and specificity when performed in specialized centers with skilled operators. A multidisciplinary discussion was carried out to focus on therapeutic options and only 3 (4.2 %) patients were sent to surgical evaluation for an endovascular procedure. All these patients underwent percutaneous endovascular treatment using a femoral approach under local anesthesia and conscious sedation.

In Fig. 1 the DUS (Fig. 1a) and CTA images (Fig. 1b) of a patient with SMA symptomatic stenosis are shown. The patient underwent balloon angioplasty of the superior mesenteric artery (Fig. 2). Through trans-brachial access, a catheterization of the SMA was achieved. Selective angiography documented the presence of stenosis at the origin of the SMA that was crossed by a catheter and a hydrophilic guidewire. A predilation of the stenosis was performed with a  $7 \times 40$  mm balloon (Abbott, Armada, Santa Clara, USA) (Fig. 2A,B), followed by a drug-eluting balloon of  $7 \times 40$  mm (Medtronic, Inpact, Minneapolis, USA) (Fig. 2C). The final angiography documented an excellent result with

**Table 1**  
Demographic and clinical characteristics of the patients with CMI.

	Pts 1*	Pts 2*	Pts 3*	Pts 4	Pts 5	Pts 6
Age (years)	56	50	74	51	60	73
Sex	Female	Female	Female	Female	Female	Female
Disease duration (years)	4	10	13	24	13	12
Disease subset	dcSSc	lcSSc	dcSSc	dcSSc	dcSSc	dcSSc
Autoantibodies	Scl70	ACA	Scl70	Scl70	Scl70	Scl70
Digital ulcers	No	Yes	No	Yes	Yes	No
Cardiovascular comorbidities	No	No	No	No	No	Yes
Cigarette smoking	No	Former	No	No	Active	Former
Postprandial pain	No	Yes	Yes	Yes	No	No
Food aversion	No	No	No	No	No	No
Weight loss	Yes	Yes	No	No	Yes	Yes
Other GI symptoms	Yes	Yes	Yes	Yes	Yes	Yes

\* patients who underwent endovascular treatment.

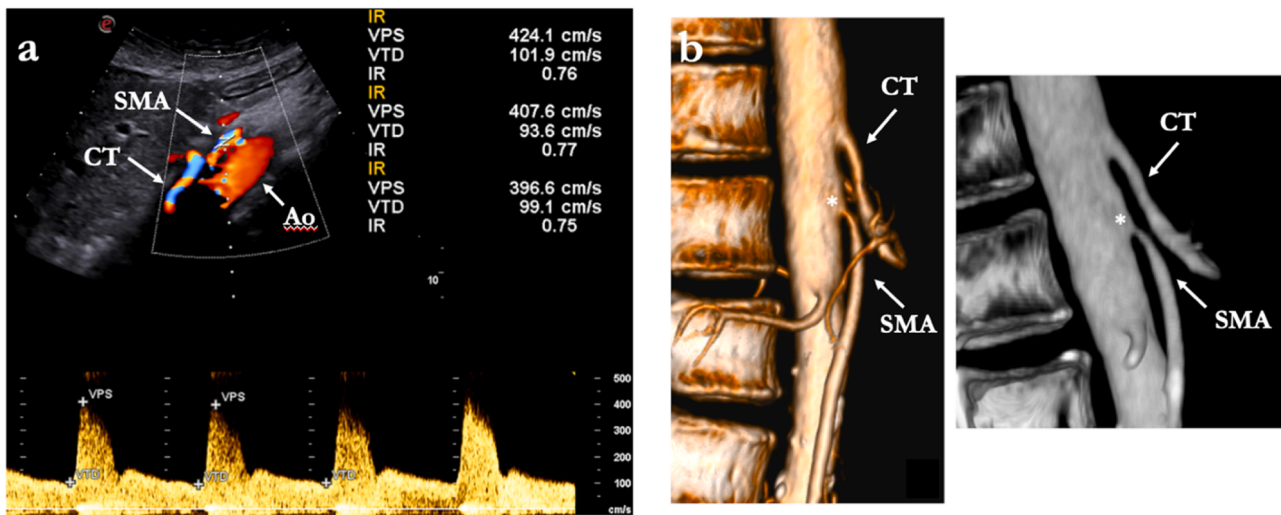


Fig. 1. DUS (Fig. 1a) and CTA (Fig. 1b) of a patient with superior mesenteric artery stenosis.

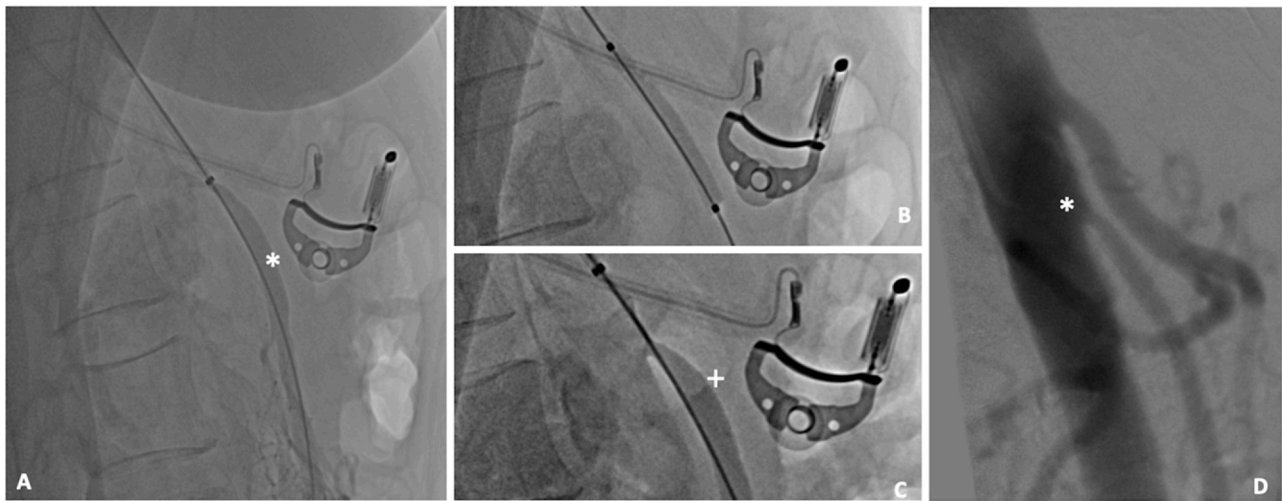


Fig. 2. Intraoperative angiography and angioplasty of a patient with systemic sclerosis and superior mesenteric artery stenosis. Selective angiography documented the presence of stenosis at the origin of the superior mesenteric artery, for which dilation was performed with an 7 × 40 mm balloon (Abbott, Armada, Santa Clara, USA) (Fig. 2A), followed by a drug-eluting balloon of 7 × 40 mm (Medtronic, Inpact, Minneapolis, USA) (Fig. 2B, C). The final angiography documented an excellent result with resolution of the stenosis (Fig. 2D).

resolution of the stenosis (Fig. 2D).

All the surgical procedures did not have any intra or post-operative complication and a dual antiplatelet maintenance therapy with aspirin and clopidogrel was continued for a minimum of three months thereafter.

A rigorous and tight control with outpatient follow-up, including DUS mesenteric flow every three months was performed; all patients reported a significant symptoms relief as early as the first month after surgery and at one year follow up no patients presented any symptoms indicating a recurrence or any DUS hemodynamic signs suggestive of CMI restenosis (Fig. 3).

#### 4. Discussion and conclusion

Our experience confirms that CMI is an insidious complication which may be present without specific symptoms, thus representing a dangerous clinical condition potentially leading to acute ischemia. This is particularly true for SSc patients, where the possible association between atherosclerotic lesions and specific vasculopathy may exponentially increase the risk of acute and chronic complications.

Furthermore, in SSc the presence of GI symptoms such as diarrhea, weight loss, bloating, constipation, and abdominal discomfort are aspecific and usually part of the clinical presentation of the GI involvement [4], thus making the clinical scenario treacherous and difficult for an early detection of a possible coexisting CMI.

The DUS of the splanchnic circulation is a non-invasive examination with good accuracy and reproducibility for the diagnosis of CMI. Today multiparametric ultrasound is useful to investigate the entire GI system and the DUS study of the splanchnic circulation is an essential completion of the ultrasound examination for the assessment and screening of GI SSc-related vasculopathy. Thus, DUS may warn the clinician for a possible macrovascular splanchnic involvement suggesting a further investigation with CTA and a prompt endovascular procedure. Furthermore, given the well-known characteristics of repeatability, non-invasiveness and low costs, DUS might be very useful even in the evaluation of asymptomatic SSc patients to disclose a splanchnic macrovascular involvement as early as possible in order to promptly treat them and prevent any possible chronic or acute irreversible damage. Finally, being a patient-friendly examination, DUS is an excellent tool not only for the diagnosis of CMI, but even for the



**Fig. 3.** Computed tomography angiogram demonstrate patency of the superior mesenteric artery over the follow-up.

follow up of both treated and untreated patients.

Revascularization is generally accepted in case of symptomatic multi-vessel stenosis and the presence of mesenteric collateral circulation is assumed to prevent single-vessel CMI. However, in the literature there is evidence for persistent symptom relief after endovascular treatment in patients with single-vessel CMI [22]. It must be considered also that the decision for an endovascular treatment of patients with a single vessel stenosis should be taken by a multidisciplinary consensus. Vascular injury is fundamental in the pathogenesis of SSC-related complications, and the complex microvascular involvement can lead to impaired angiogenesis and insufficient collateral vessels network development in case of macrovascular atherosclerosis damage. A recent retrospective study suggested that upper extremities percutaneous revascularization in patients with refractory digital ischemia and non-healing ulcers can facilitate healing of long-standing ulcers [23].

As per digital ulcers, even when considering GI vascular involvement, the awareness of the specific SSC underlying vasculopathy (macro and microvascular), potentially leading to an impaired ability to develop mesenteric collateral and compensatory blood flow [24], may guide the final decision for endovascular treatment.

Our report presents some limitations, especially regarding the small number of patients who underwent the endovascular treatment which makes it difficult to draw definitive conclusions concerning its real effectiveness.

In conclusion, our experience confirms the primary role of DUS as a fundamental non-invasive screening tool for the diagnosis of CMI also in SSC patients. Given the complex GI micro and macrovascular involvement of SSC patients, an early diagnosis and treatment of CMI can be of paramount importance not only to prevent a severe evolution to a critical GI ischemia but also to control the increasing burden of GI symptoms and progressive deterioration of patient's quality of life. Further and perspective studies are necessary to understand the real prevalence of CMI in SSC, its role in the complex pathogenesis of GI involvement and the real efficacy of the endovascular treatment.

#### Declarations of competing interest

All authors declare they have no conflict of interest.

#### Ethics approval

The study protocol was approved by local Ethical Committee (approval number: 23805\_oss).

#### Informed consent

All patients enrolled in the study signed informed consent.

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#### Data availability

Data are available, upon reasonable request, contacting the corresponding author.

#### References

- [1] Sjogren RW. Gastrointestinal features of scleroderma. *Curr. Opin. Rheumatol.* 1996;8:569–75.
- [2] Bandini G, et al. Significant gastrointestinal unmet needs in patients with Systemic Sclerosis: insights from a large international patient survey. *Rheumatol. Oxf. Engl.* 2024;63:e92–3.
- [3] Sjogren RW. Gastrointestinal motility disorders in scleroderma. *Arthritis Rheum.* 1994;37:1265–82.
- [4] Cheah JX, Khanna D, McMahan ZH. Management of scleroderma gastrointestinal disease: lights and shadows. *J. Scleroderma Relat. Disord.* 2022;7:85–97.
- [5] Varga J, Trojanowska M, Kuwana M. Pathogenesis of systemic sclerosis: recent insights of molecular and cellular mechanisms and therapeutic opportunities. *J. Scleroderma Relat. Disord.* 2017;2:137–52.
- [6] Matucci-Cerinic M, Kahaleh B, Wigley FM. Review: evidence that systemic sclerosis is a vascular disease. *Arthritis Rheum* 2013;65:1953–62.
- [7] Kahaleh MB. Vascular involvement in systemic sclerosis (SSc). *Clin. Exp. Rheumatol.* 2004;22:S19–23.
- [8] Sartore S, et al. Contribution of adventitial fibroblasts to neointima formation and vascular remodeling: from innocent bystander to active participant. *Circ. Res.* 2001;89:1111–21.
- [9] Blagojevic J, Matucci Cerinic M. Macrovascular involvement in systemic sclerosis: comorbidity or accelerated atherosclerosis? *Curr. Rheumatol. Rep.* 2007;9:181–2.
- [10] van Dijk LJ, et al. Clinical management of chronic mesenteric ischemia. *United Eur. Gastroenterol. J.* 2019;7:179–88.
- [11] Mensink PBF, et al. Clinical significance of splanchnic artery stenosis. *Br. J. Surg.* 2006;93:1377–82.
- [12] Clair DG, Beach JMMesenteric Ischemia. *N. Engl. J. Med.* 2016;374:959–68.
- [13] Zeng Y, et al. Macrovascular involvement in systemic sclerosis: evidence of correlation with disease activity. *Clin. Exp. Rheumatol.* 2012;30:S76–80.
- [14] Meiszterics Z, et al. Early morphologic and functional changes of atherosclerosis in systemic sclerosis—a systematic review and meta-analysis. *Rheumatol. Oxf. Engl.* 2016;55:2119–30.
- [15] Bartoli F, et al. Flow-mediated vasodilation and carotid intima-media thickness in systemic sclerosis. *Ann. NY Acad. Sci.* 2007;1108:283–90.
- [16] Au K, et al. Atherosclerosis in systemic sclerosis: a systematic review and meta-analysis. *Arthritis Rheum* 2011;63:2078–90.
- [17] Bandini G, et al. Ultrasound evaluation of bowel vasculopathy in systemic sclerosis. *Eur. J. Intern. Med.* 2022;100:62–8.
- [18] Bandini G, et al. Doppler ultrasound, a noninvasive tool for the study of mesenteric arterial flow in systemic sclerosis: a cross-sectional study of a patient cohort with review and meta-analysis of the literature. *Intern. Emerg. Med.* 2024. <https://doi.org/10.1007/s11739-024-03783-5>.
- [19] Aboyans V, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of peripheral arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). *Rev. Espanola Cardiol. Engl. Ed.* 2018;71:111.
- [20] Biri S, et al. Doppler ultrasonography criteria of superior mesenteric artery stenosis. *J. Clin. Ultrasound JCU* 2019;47:267–71.
- [21] Moneta GL, Lee RW, Yeager RA, Taylor LM, Porter JM. Mesenteric duplex scanning: a blinded prospective study. *J. Vasc. Surg.* 1993;17(79–84):85–6. discussion.
- [22] van Dijk LJD, et al. Persistent symptom relief after revascularization in patients with single-artery chronic mesenteric ischemia. *J. Vasc. Surg.* 2018;68:779–85.
- [23] Romero-Karam LA, Honan KA, Arain SA, Mayes MD. Percutaneous revascularization for the treatment of refractory digital ischemia in systemic sclerosis. *J. Scleroderma Relat. Disord.* 2023;8:36–42.
- [24] Kumar S, et al. Review article: pathogenesis and clinical manifestations of gastrointestinal involvement in systemic sclerosis. *Aliment. Pharmacol. Ther.* 2017;45:883–98.