Received: 4 October 2021 | Accepted: 16 October 2021

DOI: 10.1002/ajmg.c.31949

REVIEW ARTICLE

AMERICAN JOURNAL OF medical genetics PART C Seminars in Medical Genetics WILEY

Surgical treatment of abdominal compression syndromes: The significance of hypermobility-related disorders

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Abstract

Case reports and systematic studies of the most common hypermobility-related disorders, hypermobile Ehlers–Danlos syndrome (hEDS), and hypermobility spectrum disorder (HSD) typically describe gastroenterological symptoms and complaints attributed to structural malfunction, autonomic dysfunction, or inflammation of the gastrointestinal tract. However, abdominal compression syndromes (CS) may also contribute to pain and dysfunction in these individuals and be the leading pathology given symptoms significantly reduce or cease after decompressive surgery. Arising not only in the abdomen and causing pain (median arcuate ligament syndrome [MALS] and superior mesenteric artery syndrome [SMAS]), CS also occur in the retroperitoneum and the pelvis (nutcracker syndrome and May–Thurner syndrome), these latter conditions causing chronic pelvic congestion syndrome (PCS). Here, we report primarily on our experience of the assessment and management of MALS and SMAS in a cohort of cases with a surprising prevalence of HSD and hEDS. To our knowledge, this is the first cohort report of its kind in hEDS, HSD, and CS. We recommend that CS are considered in hEDS and HSD individuals with gastrointestinal and other painful complaints within the "belt" area. These CS can be identified using functional ultrasound duplex examination in experienced hands, and in appropriate cases stabilizing surgery can substantially improve quality of life.

KEYWORDS
hypermobile Ehlers–Danlos syndrome, median arcuate ligament syndrome (Dunbar), superior mesenteric artery syndrome (Wilkie)

1 | INTRODUCTION

Individuals affected by hypermobile Ehlers–Danlos syndrome (hEDS) or hypermobility spectrum syndrome disorder (HSD) often present with abdominal and/or pelvic pain with radiation into the groin and the back. It has been well documented that these individuals suffer from dysfunction of their autonomic nervous system (Hakim et al., 2017), multiple neurogastrointestinal concerns (Fikree, Chelimsky, Collins, Kovacic, & Aziz, 2017), and psychiatric comorbidities (Bulbena et al., 2017). Similar complex presentations are seen in individuals who present with compression syndromes (CS) such as median arcuate ligament syndrome (MALS), superior mesenteric artery syndrome (SMAS), nutcracker syndrome (NCS), and May–Thurner syndrome (MTS) (Huynh et al., 2019; Skelly et al., 2018). Depending on the structure that is compressed, a variety of symptoms are reported including early satiety, postprandial nausea, vomiting, and acute abdominal pain (Grotemeyer et al., 2009; Krzanowski et al., 2019; Pourhassan, Grotemeyer, Fürst, Rudolph, & Sandmann, 2008; Velasquez, Saeyeldin, Zafar, Brownstein, &

This article is an extension of either a plenary guest speaker lecture or an abstract presented at the EDS ECHO Conference on the Ehlers–Danlos syndromes held on October 2–3, 2020. The Editors-in-Chief of this journal affirm that this article was evaluated editorially and rigorously edited by the expert Guest Editors for this issue, Dr. Hakim, Dr. Francomano, and Dr. Tinkle and was not anonymously peer reviewed.

Erben, 2018). If more than one CS is present, which in the authors' experience is not uncommon in hypermobile patients, the differential diagnosis is challenging, and patients undergo a battery of classical gastrointestinal (GI) tests without any pathological finding prior to a CS being considered (if considered at all). Many patients lose weight, and some become cachectic and refuse to eat due to pain. Often the diagnostic odyssey can last years. Without any apparent conventional disease/disorder these mainly female individuals can find themselves in psychiatry and pain clinic services; a phrase often reported being "your pain is not in the belly, it is in your head." Skelly et al. (2018) reported that 28% of patients operated for MALS were initially described as having psychiatric morbidities.

1.1 | Why are individuals with hEDS and HSD at risk of missed diagnosis?

First, hEDS is considered rare, although recent studies have shown that the combined prevalence of hEDS and HSD is much more common than previously thought and in the order of 1 in 500 of the general population (Demmler et al., 2019).

Second, many practitioners are not aware of the diagnosis of hEDS or of CS and their complications.

Third, the mechanical effect of "compression = squeezing" may seem to be a rather too simplistic reason for symptoms or explanation of such a complex pathology in comparison to sophisticated neuro - gastrointestinal explanations.

Fourth, problems outside of the mainstream of clinical practice are often disregarded, it being difficult to find/access the expertise, and the work up for the differential diagnosis is time consuming and potentially difficult to fund.

Fifth, hemodynamics such as pressure, flow, and resistance (which can be safely and repeatedly measured by ultrasound duplex [USD] applied while the patient is examined in various postures and in combination with a test meal/drink to diagnose MALS and SMAS), are believed to be less reliable or precise compared to other imaging methods and too dependent on the examiner.

Sixth, standing in an upright position requires that that part of the body between the thorax and the hips (the "belt" region) is stable. Individuals affected by hEDS or HSD are often highly flexible and have a weak core and instability at the spine. CS may in part be a consequence of this instability (authors' opinion), and more readily demonstrated in the upright position. Interestingly, Doppler ultrasound techniques were only accepted as an alternative to other radiological imaging after intravenous ultrasound catheter studies demonstrated that compression sites and the degree of compression could be seen much better in various body positions by this technique (Krzanowski et al., 2019).

Finally, to date CS have been mainly described as monosyndromic. Individuals who continue to complain of symptoms after seemingly successful surgery of only one CS are not understood nor believed regarding their remaining painful symptoms. The literature shows a great number of case reports with clinically interesting mono-compressions and in metanalyses searching for the best diagnostic measure and the preferred therapy only mono-compressions have been evaluated (Ananthan, Onida, & Davies, 2017; Erben et al., 2015; Goodall et al., 2020). Yet, some individuals have more than one CS present.

Why these compressions develop and whether there is an etiology such as tissue laxity underlying them has not been considered to date. Although one author (W.S.) has gained considerable experience with surgery for congenital aorto-arterial and venous replacement in children and adolescents (Sandmann et al., 2014), it was thought that CS were just another congenital anomaly. At first, it was not noted that tissue hyperlaxity and hypermobility may play an important role as an underlying etiology.

Here, we report primarily on our experience of the assessment and management of MALS and SMAS, in what is, to our knowledge, the first cohort report of its kind in hEDS, HSD, and CS.

2 | METHODS

An observational study was undertaken on 169 patients who underwent 196 open operations for CS between 2010 and 2020 in our unit. Data were collected on gender, age, nature of CS, presence of hypermobility, hyperlordosis, a diagnosis of hEDS, or HSD (or joint hypermobility syndrome [JHS] prior to the 2017 criteria changes), and outcome of surgery.

The presence of generalized joint hypermobility was determined by applying the Beighton score (Beighton, & Horan, 1969). The diagnosis of JHS, hEDS, or HSD was determined by applying the relevant diagnostic criteria pre- and post-2017 (Tinkle et al., 2017). This information was determined prospectively in patients returning for a second operation because of another CS, or evaluated by telehealth interview at follow-up, or from records of managing physicians.

To assess hyperlordosis as part of the etiology in the development of abdominal, retroperitoneal, and pelvic CS (Scholbach, 2007, 2009), the degree of lumbar lordosis was assessed by transabdominal sonography in the supine position. The minimal distance from the ventral surface of the most prominent lumbar vertebra to the inner lining of the abdominal wall was measured. No normal values for the distance between the ventral surface of the apex of the lumbar spine and the abdominal wall for healthy adults could be retrieved in public medical databases (PubMed, Google Scholar, Mendeley Data). However, a distance less than 25 mm as an exaggerated lordotic curvature since 25 mm is the normal distension of a filled small bowel loop (Haworth et al., 1967). Many patients suffer from intermittent compressions of prespinal venous segments due to filling bowel loops. Such an effect can be directly observed in real time during functional postprandial ultrasound. If the distance is less the 25 mm, then a spatial conflict of filling bowel and left renal and left common iliac vein becomes likely.

We paid special attention to the actual effect of this hyperlordosis on the individual compression site of vessels and parts of the intestinal tract and the effect of changing body posture on the

location and degree of the compression. That's why we recommended physical exercises and favorable postures to reduce the lordosis, sometimes with very helpful clinical effects.

We developed a sixfold measurement of the effect of the compression:

1. As diameter reduction and its changes.
2. As flow acceleration and its changes.
3. As changed and changing flow directions in feeding vessels.
4. As changed and changing flow volumes in the compressed vessel and its feeders.
5. As changed and changing flow volumes in three consecutive parenchymal layers in both kidneys by the PixelFlux technique.
6. As changed and changing flow volume ratio of left to right kidney.

Here, the word changed refers to the effect of the compression itself and changing refers to the different effects of various body postures.

In our opinion from our observation of many cases over the years, patients with connective tissue disorders not only suffer from a higher compressibility of tubular organs but also substantially from their increased distensibility, we measured the effects of gravity on their circulating arterial blood volumes.

The sonographically determined aortic flow volume, peak velocity, and heart rate immediately cranially to the diaphragm in a supine and standing position were compared. The drop of circulating volume while standing was used to gauge the pooling venous volume which was trapped in the legs and pelvic vessels. In addition, pelvic and femoral vessel flow volumes, directions, and diameters plus the changing cross section area of the vena cava inferior at its compression site by manual tracing of its contour were measured.

As there were no data in the literature to rely on, we used these parameters to compare the separate effects of the pure genetic component of the connective tissue disorder and the additional effect of the compressions in order to estimate the chances of symptom relief by a decompression operation.

Our surgical approach was always open exposure via a midline incision. The surgical technique was not changed during the observation period of the study and consisted for MALS of partial resection of the median arcuate ligament (including scar and remaining fibers in cases with recurrence but preserving as much nervous fibers from the celiac plexus as technically feasible) and for SMAS of transposition of the SMA from its suprarenal origin into the infrarenal aorta.

If a compression of the duodenum was seen in the fasting patient, the relevance of this finding was confirmed by observing the duodenal peristalsis and concomitant symptoms after ingestion of solid food and liquids. Moreover, a compression and upstream dilation of the stomach was looked for. Then, attention was paid to the additional compressive effect of the enlarging stomach onto the precompressed left renal vein and subsequent flow changes as described in points 1 to 6 earlier. This was done to discriminate the postprandial symptoms of MALS, SMAS, and lordotic left renal vein compression. This is crucial for prioritizing the extent and sequence and synchronicity of the various decompression operations. All three compressed structures can, depending on the extent, the time of onset, and the chronicity, cause overlapping and radiating pain. So, following the acuity of pain while giving test meal/drink and study continuously with duplex ultrasound helps the differential diagnosis and decision making as to which CS should be treated at first (if not two or all three at the same time), because entering the same anatomy days, weeks or even months later is surgically demanding.

In many cases, the compressions were not found exactly in the midline. The hyperlordosis regularly produced a scoliosis and a concomitant shift of the aorta to the left side of the spine, the concavity of its lumbar scoliosis. This produced a clockwise twist of the aorta from a causal perspective with a subsequent anterior course of the right renal artery. Its curvature is the compression site.

It is possible that the scoliosis may be a clinical marker and warrants further assessment.

3 | RESULTS

3.1 | Demographics and CS diagnosis

Out of 169 patients with CS, 132 (78.1%) were female, 37 (21.9%) were male. The mean age was 31.36 years (female 33.82 years, male 29.44 years) regarding geographical origin, 85 (50.3%) patients came from Germany, 59 (34.9%) from other European countries, and 25 (14.8%) from outside Europe (Table 1).

The majority ($n = 123$, 72.8%) of 169 patients presented with multiple types of CS. In 66 (39.1%) cases, 2 types of CS were diagnosed; in 37 (21.9%) cases, 3 types of CS were diagnosed; and in 20 (11.8%) cases, 4 types of CS were demonstrated and decompressed. Ninety-five (77.9%) presented with MALS as one of multiple CS, most often in combination with NCS ($n = 85$). Of 46 (27.6%) cases with a mono-compression, 27 (58.7%) had MALS (Table 2).

Forty-four (26%, female $n = 36$, male $n = 8$) of the cohort were admitted because of recurrence after previous surgery for CS elsewhere. Of these, 41 (93%) were affected by hEDS or HSD (82.9% female $n = 34$, and 17.1% male $n = 7$). The recurrence rate within each gender group was not significantly different (female 94.4% compared to male 87.5%) (Table 3).

A total of 122 of the 169 cases had a co-existing hypermobility related disorder with a diagnosis of either JHS, hEDS, or HSD; 41 within the recurrence cohort described above (Table 4). The Beighton score varied between 4/9 and 9/9.

Eighty-one (66.4%) of the 122 patients were operated for primary or recurrence of MALS, that is 47.9% of the total number of patients undergoing surgery for abdominal-retroperitoneal and pelvic (mean age 29.45 years; female 30.61 years, male 25.14 years). Twelve (9.5%) patients demonstrated maximum Beighton scores (9/9) and had histories of dislocations at shoulder or patellofemoral joint. Sixty-nine (54.9%) presented with Beighton scores of 4 or 5 out of 9. In addition, 20 patients with isolated (3 NCS and 2 MTS) or combined NCS and MTS showed signs of hypermobility with Beighton scores of 4/9 and below.

Patients	N	%	%	
	169	100		
Female	132	78.1		
Male	37	21.9		
Mean age: 29.98				
Geographical origin				
Germany	85	50.3		
Europe	59	34.9		
Overseas	25	14.8		
Operations total	196		100	
Incomplete decompression/recurrence	51	26.0	100	
From outside	36	18.4	70.6	
Own	13	6.6	25.5	
Re-recurrence	2		0.1	3.9

TABLE 1 Overview of all patients with compression syndromes in the abdomen, retroperitoneum, and pelvis (ARPCS) operated within a 15-year time period by the senior author (W.S)

TABLE 2 Forty-four patients (26.0%) were readmitted for recompression, out of which 34 (94.4%) were affected by hEDS/HSD

							Mortality	
	N	%	♀	%	♂	%	N	%
Patients (total)	169	100	102	78.1	37	21.9	2 (♀)	1
Patients after	44	26.0	36	81.8	8	18.2	1	
Previous surgery for ARPCS								
Patients with hypermobility	41	23.2	34	94.4 (82.9)	7	87.5 (17.1)	1 (♀)	2.9 (♀)
Leading diagnosis for previous surgery								
Patients								
NCS	13	29.5	10	76.9	3	23.1		
MALS	12	27.3	9	75.0	3	25.0		
SMAS	10	22.7	8	80.0	2	20.0		
MTS	1	2.3	1	100.0				
PCS	2	4.6	2	100.0				
Combined	6	13.6	6	100.0			1 (♀)	16.7 (♀)

Note: Obviously the tissue in patients with hypermobility tends to restabilize the structures by building scar, especially after laparoscopic approach.
Abbreviations: ARPCS, Abdominal-Retroperitoneal-Pelvic Compression Syndromes; hEDS, hypermobile Ehlers–Danlos syndrome; HSD, hypermobility spectrum disorder; MALS, median arcuate ligament syndrome; MTS, May–Thurner syndrome; NCS, nutcracker syndrome; PCS, pelvic congestion syndrome; SMAS, superior mesenteric artery syndrome.

Hyperlordosis was identified in 90% of female patients, accounting for 78.1% of all the patients. In male patients the lordotic posture in the presence of CS was found in 65%.

3.2 | Surgical outcomes

Not every CS was treated at the same operation, the focus being on treating the most painful ones. Some patients developed pain and complaints from compressions already present but not painful at the time of the first operation and underwent a second or third operation months or even years later. As a result, the overall number of surgeries in the cohort was 196.

Hundred and twenty-two patients with either MALS as a mono-lesion or in combination with other CS underwent partial resection of the MAL. Those with recurrences after previous laparoscopic approach elsewhere were more challenging to expose, but in all except four patients, the typical complaints of substernal pain, painful eating, feeling of restricted breathing, bloating, and constipation disappeared or had improved significantly 2–3 weeks later at the time of dismission.

All except four patients being operated for MALS and SMAS reported significant improvement 3 months after surgery as evidenced by pain-free eating, gaining weight, returning to work or studies, sports activities, and so on. In three patients, the celiac trunk had to be replaced, because after resection of the MAL, the trunk had

TABLE 3 The literature usually reports concern cases with monocompressions

Monocompressions			Multicompressions		
Total	***N***	**%**		***N***	**%**
	46	27.2		123	72.8
Types					
MALS	27	58.7	MALS + NCS	34	27.6
SMAS	14	30.4	MALS + MTS	2	
NCS	3	6.5	MALS + SMAS	7	
MTS	2	4.3	MALS + NCS + MTS	21	17.1
			MALS + NCS + SMAS	10	8.2
			MALS + MTS + SMAS		1
			SMAS + NCS	2	
			SMAS + MTS	1	
			NCS + MTS	20	16.3
			SMAS + NCS + MTS	5	
			MALS + SMAS + NCS + MTS	20	16.3
Simultaneous compressions					
		N			**%**
Two		66			39.1
Three		37			21.9
Four		20			11.8

Note: Only recently, it is described that an individual patient, especially those with hEDS can suffer from two or more compression syndromes. May be due to admittance practice we encountered patients with even four syndromes(11.8%) present, which raises the question whether each single syndrome should be operated separately, amounting probably to four laparotomies and building most probably constricting adhesions or all of which should be decompressed in one operation, as it is our preferred approach.
Abbreviations: hEDS, hypermobile Ehlers–Danlos syndrome; MALS, median arcuate ligament syndrome; MTS, May–Thurner syndrome; NCS, nutcracker syndrome; SMAS, superior mesenteric artery syndrome.

TABLE 4 The presence of hEDS/HSD in patients with APRCS was established elsewhere in 40 (23.7%) patients before admission

Patients	***N***		**%**	
Total	169		100	
Admitted with hypermobility syndromes	40		23.7	
Frequency of ARPCS per patient				
	I	II	III	IV
	2	9	23	6
With or with suspected hypermobility syndromes	81		47.9	
Frequency of ARPCS per patient				
	I	II	III	IV
	12	25	31	13

Note: As in earlier years, we were not aware that there might exist in many cases that underlying etiology we retrospectively evaluated our material and suspect that almost half (47.9%) of the cases suffered from hypermobility (a prospective study has been initiated).
Abbreviation: ARPCS, Abdominal-Retroperitoneal-Pelvic Compression Syndromes.

remained severely stenosed and the patients continued to have severe pain and vomiting while trying to eat. All three patients had hEDS. One graft had a small diameter and thrombosed shortly after surgery with intermittent mesenteric ischemia but required no further intervention. However, the patient also suffers from SMAS and needs to be reoperated soon. The two other grafts remained patent. One patient regained normal weight, the other was extremely weak (body mass index [BMI] below 13) but is improving continuously at 7 months after surgery.

One female patient (aged 33 years, BMI 13) who suffered from weakness, mast cell activation syndrome, small fiber neuropathy, and hEDS and refused preoperative feeding expired 1 hr after extubation.

The cause of death was suspected to be bleeding, but at autopsy no hematoma was found, and the final diagnosis was respiratory failure due to volume overload from crystalloids. This was the only early postoperative death in our total patient material of 196 operations.

A subgroup of 43 (25.4%) patients (female $n = 36$, mean age 25.8 years; male $n = 7$, mean age 23.3 years) underwent superior mesenteric artery transposition (SMATX) from suprarenal into the infrarenal aorta for treatment of SMAS (Figure 1). Before admission all patients had been exposed to innumerable endoscopies and a battery of other gastrointestinal tests elsewhere. All patients had lost between 15 and 35% of body weight, some much more, and refused to eat because of pain. Five (11.8%) patients had arrived tube fed, three (7%) had central lines, i.v. lines, or port for parenteral feeding, and nine (20.9%) had undergone gastrojejunostomy/duodenojejunostomy without substantial weight gain or pain relief and had returned to parenteral feeding.

Regardless of previous examinations, our own diagnostic work up (T.S.) consisted of functional USD examination together with a test meal/liquid to assess the diameter of the duodenum and the efficiency of peristalsis at the third part of the duodenum. USD was used also to detect or exclude simultaneous MALS and NCS. In patients with previous surgery and suspicion of more than one CS, computed tomography angiography (CTA) or magnetic resonance angiography (MRA) was performed if not recently done outside. In all patients a transposition of the SMA from its suprarenal origin into the infrarenal aorta (SMATX) was successfully performed.

Thirty-eight (90.5%) patients in this SMAS subgroup having undergone SMASTX reported pain-free eating and weight gain within 6 months postoperation. In all women who suffered from amenorrhea, menstruation returned within 2 years with one exception. Of this cohort of 43 cases, 23 (63.5%) of 36 women and 4 (57%) men were diagnosed with hypermobility spectrum disorder or hEDS. Five (11.6%) patients, all female with hEDS, suffered from gastroparesis. One underwent classical duodenojejunostomy 2 years later and has less eating problems and improved; one had undergone port implantation for intravenous nutrition but remains very weak; and one had a stomach pacemaker implanted, the wires of which were accidentally cut while undergoing renal autotransplant elsewhere but is stable with little eating and i.v. nutrition via a port and; one improved slightly, worsened again and did not respond to nonsurgical treatment, and is being considered for a small bowel transplant. The follow up of one is not known except that the patient underwent autotransplant of the left kidney and reports to be in pain. None of them suffered presurgery from narcotic bowel syndrome, but all of them from severe constipation.

Finally, interestingly, we have had several members from six families admitted for decompression surgery and affected by hypermobility-related disorders, out of which we have operated successfully on more than one member, mostly for MALS but also because of SMAS, NCS, and MTS. We could not determine a dominant clinical pattern connected to familial relationships and genetic testing is currently being undertaken, but the mother was usually the main carrier.

4 | DISCUSSION

Individuals with generalized laxity may develop spontaneous or posture dependent abdominal pelvic or left flank pain, postprandial pain, and suprainguinal pain due to CS and subsequent venous congestion. These patients have often lost a significant amount of weight by the time a CS is considered as the cause, many having been diagnosed with various types of nutritional intolerances before surgery, which did not improve after dietary exclusion. Many patients had already undergone multiple gastroscopies and other investigations without any findings. When these tests show that everything is normal, but

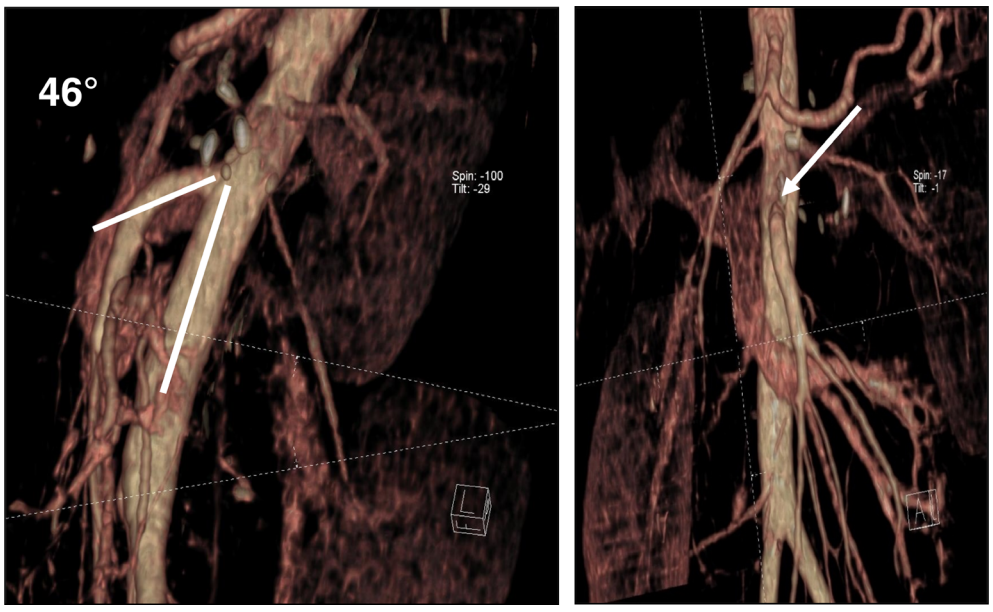

FIGURE 1 Angiography after transposition of the superior mesenteric artery (SMA). From its suprarenal origin into the infrarenal aorta. The transposed SMA arises with an angle greater than 40°. There is no further compression of the duodenum

the patient continues to have much pain, the term "irritable bowel" is often used. This is a replacement diagnosis for symptoms which may not yet be understood. CS are missed.

It is noteworthy that SMAS cannot be diagnosed with high probability by endoscopy. Insufflation of air under pressure, which allows one to examine the mucosa within the stomach and duodenum dilates these tube-like structures often so much that compression from outside as in SMAS is overlooked.

We have observed a tendency to claim a psychosomatic explanation for the symptoms of CS in many patients with hEDS and similar disorders without even considering CS. But with the knowledge of the numerous interrelationships of CS and their remote effects due to far-reaching collateral circuits very often most if not all of the apparently unrelated symptoms can be explained and even cured.

Once the term "irritated bowel syndrome" has been applied as a diagnosis there is a tendency to stop further diagnostic investigation and conditions such as CS get missed, leaving patients coping with marked symptoms that have a significant impact on their quality of life. (For example, we operated on a 70-year-old patient who had been treated as irritable-bowel for 35 years. She struggled to control diarrhea and to keep weight on and vomited two or more times per day. Significant MALS and NCS were identified on USD examination, and she was very hypermobile even for her age. After an uneventful resection of MAL and protecting the left renal vein by external stenting, she started a new life with horse-riding and normal eating.)

Imaging (CTA, MRA, digital subtraction angiography [DS], venography) has prominence within the majority of publications related to CS. Such imaging is helpful in patients having been treated intra-abdominally for other causes and after failed attempts at treating CS, but in our experience, these forms of imaging are less sensitive and no more specific in identifying CS compared to USD examination in experienced hands. Also, they do not provide information about the grade of compression related to various body positions, which USD can.

Based on our experience, we recommend classical clinical examination including auscultation first. Secondly, a functional, quantitative, and trigger focused color Doppler sonography should be performed (Scholbach, 2007; Scholbach, Dimos, & Scholbach, 2004; Scholbach, Girelli, & Scholbach, 2005; Scholbach, Scholbach, & Di Martino, 2008). If compressions are obvious and consistent regarding the symptoms and Complaints, further imaging is only required if needed to decide which treatment procedure should be selected in cases who have already undergone previous surgery. If other causes for the reported complaints cannot be excluded or the patient has undergone surgery for other abdominal pathologies or for previous CS surgery, CTA should be requested.

MRA is less specific than CTA for detection of CS because it overestimates the degree of stenosis and was developed originally to assess tissue disorders. DSA is outdated for the diagnosis of CS but was intentionally used by others in patients previously treated elsewhere to stent the celiac trunk if laparoscopically applied dissection of MAL had failed and further surgery to replace the celiac trunk was felt to be too risky. In our cohort, some patients in which a stent had been placed elsewhere had not experienced a positive effect because the compressive force by the MAL could not be released. We replaced the celiac trunk with autologous GSV or with the deep profunda vein. The small angle with which the SMA arises from the suprarenal aorta in patients affected by SMAS can be easily, and importantly noninvasively and repeatedly measured by USD. Also, the peristalsis of the duodenum working against the stenosis between the SMA and the aorta in patients with SMAS can be demonstrated noninvasively by functional USD, especially if a test meal/drink is given to the patient.

4.1 | Surgical methods and strategies

The compression of the celiac trunk and open surgical treatment by dividing and cutting of the MAL was described by Harjola (1963). The radiological appearance of not only compression but also deviation was shown by Dunbar, Molnar, Beman, and Marable (1965). Open surgery was considered the regular approach. Although the laparoscopic approach was initially felt to be suitable for treatment of MALS, we saw 44 patients admitted for recurrence of MALS after laparoscopic surgery. From our point of view, the laparoscopic approach has two disadvantages: (i) The MAL being too close to the aorta and to the celiac trunk so that the instrumentation and electric current can cause bleeding, which can be challenging and dangerous and (ii) being too cautious to avoid these complication may leave patent MAL fibers behind, so that the decompression remains incomplete. Just dividing but not resecting a segment of the MAL can cause recurrence due to strong scar tissue, something we saw in 25 cases, the greater majority of whom were female and hypermobile. Early reapproach, although through laparotomy, is challenging because the scar remains in black color due to burned tissues and does not allow safe anatomical exposure, and recurrent surgery has to be postponed. In any case, in our experience the safest way is open surgery.

SMAS was first described by von Rokitansky (1862) in the fourth edition of his textbook of pathology. Wilkie (1921, 1927) described the clinical finding of SMAS as high ileus due to a compression of the third part of the duodenum between the aorta and the SMA. It was considered to be a gastrointestinal problem and treatment was gastrojejunostomy or duodenojejunostomy by visceral surgeons. However, the compression remained after this approach and quite regularly the pain also persists.

We prefer the SMATX method, introduced in 2006 (W.S), and published by our group in 2008 (Pourhassan et al., 2008). This technique is not new in reconstructive aorto-arterial surgery but new for this indication. It is a constructive but not a reconstructive method and changes the small angle from the suprarenal aorta into an open angle.

In patients who suffer from NCS in addition to MALS, there is another method to open that angle. We use a modified technique of Barnes et al. (1988), who described external stenting of the left renal vein, to protect the vein against compression. A ring enforced expanded polytetrafluorethylen tube with appropriate diameter is incised longitudinally and positioned around the left renal vein and readapted and suture fixed to the SMA, the IVC, the aorta and the

LRV itself. This tube being within the "nutcracker" space (but not within the vein) spreads the angle with which the SMA arises from the aorta. In less severe cases of SMAS and combined NCS this technique presents a less invasive and an effective solution.

5 | CONCLUSION

The differential diagnosis of abdominal and pelvic pain and associated symptoms can be difficult. In our experience, CS within the abdomen, the retroperitoneum and the pelvis are over-looked. Many cases have hypermobility-related disorders for which other causes of pain have been considered, and when nothing is found, labeled as IBS when a CS is present. In addition, in our experience more than one CS can be present in this particular group of patients.

This report primarily concerns patients with MALS and SMAS, but the principles are as relevant in patients who suffer from venous compressions also (NCS, MTS, pelvic congestion syndrome [PCS]).

We have learned that several proposed surgical and endovascular techniques for MALS and SMAS cannot produce a durable result in hEDS and HSD patients because the anatomic and mechanical system in which we operate is hyperelastic tissue and therefore unstable. Adaptive operative methods are required to stabilize the functional instability at the compressed sites. The techniques used and outcomes warrant further exploration.

ACKNOWLEDGMENTS

We thank Dr. Alan Hakim for the scientific discussion and support to prepare the manuscript; Sabrina Jacobi, CTA, without her meticoulos documentation of the patients files and follow-up this paper and future research could not have been elaborated and Prof. Dr. Karl Kremer, surgical teacher, and mentor of Wilhelm Sandmann, which taught to be open minded and without prejudgment in patients which present with rare and complex syndromes.

CONFLICT OF INTEREST

Thomas Scholbach developed the software PixelFlux together with his son and holds shares on Chameleon software. Wilhelm Sandmann and Konstantinos Verginis have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions. The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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How to cite this article: Sandmann, W., Scholbach, T., & Verginis, K. (2021). Surgical treatment of abdominal compression syndromes: The significance of hypermobility-related disorders. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*, 1–9. https://doi.org/10.1002/ajmg.c.31949