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ORIGINAL RESEARCH

Assessment of Transserosal Microcirculation with Visible Light Spectroscopy and Laser Doppler Flowmetry in Patients with Median Arcuate Ligament Syndrome and Chronic Mesenteric Ischemia

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Introduction: Previous studies with visible light spectroscopy (VLS) and laser Doppler flowmetry (LDF) have shown reduced mucosal circulation of the stomach and duodenal wall in patients with median arcuate ligament syndrome (MALS) and chronic mesenteric ischemia (CMI). However, transserosal microcirculatory assessment during the operative treatment of patients with these conditions has not yet been performed. We aimed to investigate if laparoscopic decompression for MALS and aortomesenteric bypass in CMI can result in immediate measurable increase in the microcirculation in stomach and duodenum.

Patients and Methods: In a single center, prospective comparative cohort study, twenty-eight patients suspected of MALS, and eleven with CMI underwent assessment of transserosal microcirculation of stomach and duodenum with Visible Light Spectroscopy (VLS) and Laser Doppler flowmetry (LDF), during surgery. Patients with computed tomography angiography (CTA) verified stenosis grade ≥50% in MALS and ≥70% in CMI were included in the study. Duplex ultrasound (DUS) was performed before and after the surgical treatment. The changes in the pre- and postoperative microcirculation were calculated with paired sample *t*-test.

Results: VLS showed significant increase in the transserosal relative hemoglobin concentration (rHb) after laparoscopic decompression in patients with MALS (Stomach, before: 58AU±13, after: 62AU±14, p = 0.017) and (Duodenum, before: 62AU±15, after:70AU ±15, p = 0.004). Furthermore, a significantly increased blood flow was found in duodenum (Before: 276AU±89, After: 315AU±93, p = 0.015). However, the SaO2 was decreased significantly in the stomach (Before: 86AU±10, After: 82AU±14, p = 0.015), but remained unchanged in the duodenal serosa.The study did not find any increase in the microcirculation of the CMI patients after revascularization. The baseline transserosal microcirculation was indifferent between the groups.

Conclusion: Laparoscopic decompression leads to enhanced transserosal microcirculation in stomach and duodenum in the patients with MALS. The baseline transserosal microcirculation in stomach and duodenum is indifferent in the MALS and CMI.

Keywords: laparoscopy, mesenteric ischemia, spectroscopy, laser, MALS, flowmetry

Introduction

Median arcuate ligament compression was first described in 1912, and later by Dunbar et al in a case series of the surgical treatment of median arcuate ligament syndrome (MALS) in 1965.[1,2] Controversies regarding its pathophysiology persist to this day, and even its very existence has been questioned.[3] Both neurogenic and ischemic etiologies have been proposed in the literature.[4–7] Studies have suggested that ischemia may be the underlying cause of MALS.[8–11]

The classic symptoms of MALS are post-prandial abdominal pain, and changes in food intake pattern with smaller meals, which ultimately leads to weight loss.[12–15] In worst cases, some patients complain of a constant abdominal pain

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with further aggravation after food intake or physical activity.[16] The symptoms of MALS resemble more common abdominal diseases, making it a diagnosis of exclusion.[14] A definite diagnosis of MALS is made when symptoms are relieved after surgery.[11] Recently, a single-center study has identified high plasma alpha glutathione S transferase (αGST) levels, a biomarker of enterocyte ischemia in patients with MALS.[17] Earlier studies, utilizing gastroscopy-assisted visible light spectroscopy (VLS) and laser Doppler flowmetry (LDF), have found reduced transmucosal microcirculation in the stomach and duodenum, not only in the patients with MALS, but also in those diagnosed with chronic mesenteric ischemia (CMI).[11,18]

Earlier, transserosal microcirculation assessment has been performed during colonic surgery and gastric tube construction.[19–23] To the best of our knowledge, intraoperative transserosal microcirculation assessment of the stomach and duodenum has not been performed earlier in patients with MALS. Therefore, in this study, we aimed to perform a microcirculation assessment of the stomach and duodenal wall by transserosal application of the VLS and LDF during laparoscopic surgery for MALS. We hypothesized that the microcirculatory parameters would show an increase in transserosalt circulation of both the stomach and duodenum after release of the CA in this study. Since earlier studies have shown reduced transmucosal microcirculation in the stomach and duodenum of patients with CMI, we also aimed to include CMI patients as a control group, expecting an increase in microcirculation after revascularization.[11,18]

Method and Materials

Study Design

This study is a single-center, prospective comparative cohort study conducted between November 2016 and April 2023 at the Department of Vascular Surgery, Oslo University Hospital, Aker and Ullevål, Norway.

Primary health care centers and other hospitals referred patients suspected of having MALS to the Vascular Department. The included patients went through a prior extensive investigations excluding more common causes of their symptoms, like peptic ulcer disease, cholelithiasis, pancreatitis, inflammatory bowel disease, and malignancy. The consensus diagnosis of MALS was based on the presence of post-prandial abdominal pain, weight loss, changes in eating habits, and computed tomography angiography (CTA) verified ≥50% stenosis of celiac artery (CA) caused by the median arcuate ligament.[16] Written informed consent was obtained from all the eligible participants prior to commencement. Patients with gallstone disease, CTA verified <50% stenosis of CA or unable to obtain consent were excluded.

An experienced physiologist performed duplex ultrasound (DUS) on all patients. Peak systolic velocity (PSV) ≥ 200 m/s was considered a sign of significant stenosis. Turbulence or increase in the PSV of the CA during deep expiration was considered due to external compression of median arcuate ligament. DUS findings were not used as a diagnostic criterion but as a supportive investigation modality to the CTA findings. The preoperative DUS findings were used as reference values for DUS at the follow-up.

A definitive diagnosis of MALS was based on a complete or partial relief of symptoms after the surgical procedure. A multidisciplinary panel comprising vascular surgeons and interventional radiologists evaluated and suggested the surgical treatment of MALS.

The patients with CMI had a CTA verified ≥70% atherosclerotic stenosis or occlusion in one or more mesenteric arteries. The patients were scheduled for an open bypass to the CA, the superior mesenteric artery (SMA), or both arteries from either supra-coeliac or infra-renal aorta. The microcirculatory findings were not used to change the preplanned surgical treatment of the patients in either study groups.

All included patients underwent laparoscopic decompression of the CA. The operative technique is described elsewhere.[16]

Measurements

Transabdominal Ultrasound

DUS examination was performed preoperatively and postoperatively with a GE Vivid E95 ultrasound scanner and a GE C1-6 curve array probe (GE Healthcare, Chicago, IL, USA). The same experienced physiologist performed all DUS examinations. The patients were examined in the dorsal decubitus position and, if necessary, in a sitting position.

Conventional B-mode and color Doppler were used to evaluate the vascular anatomy, identifying stenosis and turbulence. Hemodynamic variables such as PSV, end-diastolic velocity (EDV), and turbulence of the mesenteric arteries were measured in the inspiratory and expiratory phases was examined with spectral Doppler. Harmonic imaging was utilized to minimize artifacts. An effort was made to get the insonation angle $<60^\circ$ precisely corrected. All patients had overnight fasting, and the examination was before noon.

Intraoperative Transserosal Microcirculation Assessment

Patients with MALS

Under general anesthesia, transabdominal trocars (1 × 12 mm and 3 × 5 mm) were placed through the abdominal wall, and pneumoperitoneum was achieved with CO_2 insufflation. The insufflation pressure was kept at 12 mmHg or lower if a safe working peritoneal space was achieved. Transserosal measurements were performed by using a 2.6 mm "Oxygen-to-See (O2C) microprobe, LSX-43 (O2C, LEA Medizintechnik, Giessen, Germany). Figure 1 gives a schematic illustration of the working principles of the O2C machine. The O2C method is an optical measurement technique that utilizes LDF and VLS to make simultaneous measurements of flow, velocity, combined venous and arterial saturation of capillary hemoglobin (μHb_{SO2}), and a relative hemoglobin amount concentration (μHb_{con}). Light emitted from a broadband light source and light from a laser source penetrates the tissue. The sensor measures the light reflected from the tissue. The μHb_{SO2} and μHb_{con} is determined from the white light source spectrum in the wavelength range of 500–850 nm. In contrast, the laser light wavelength of 830 nm is used to determine blood flow and velocity.[24] While the penetration depth of the light depends on the tissue, an estimate is set to be about 0.78 mm.

The probe was placed through the trocar and carefully applied to the serosa of the predefined regions of the stomach (fundus, greater curvature, antrum, lesser curvature) and duodenum (duodenal bulb, pars descendants). Figure 2 illustrates the areas of the microcirculation measurements performed on both the stomach and duodenum. The measurement areas were carefully chosen, considering the vascular supply of the stomach and the duodenal regions by the CA

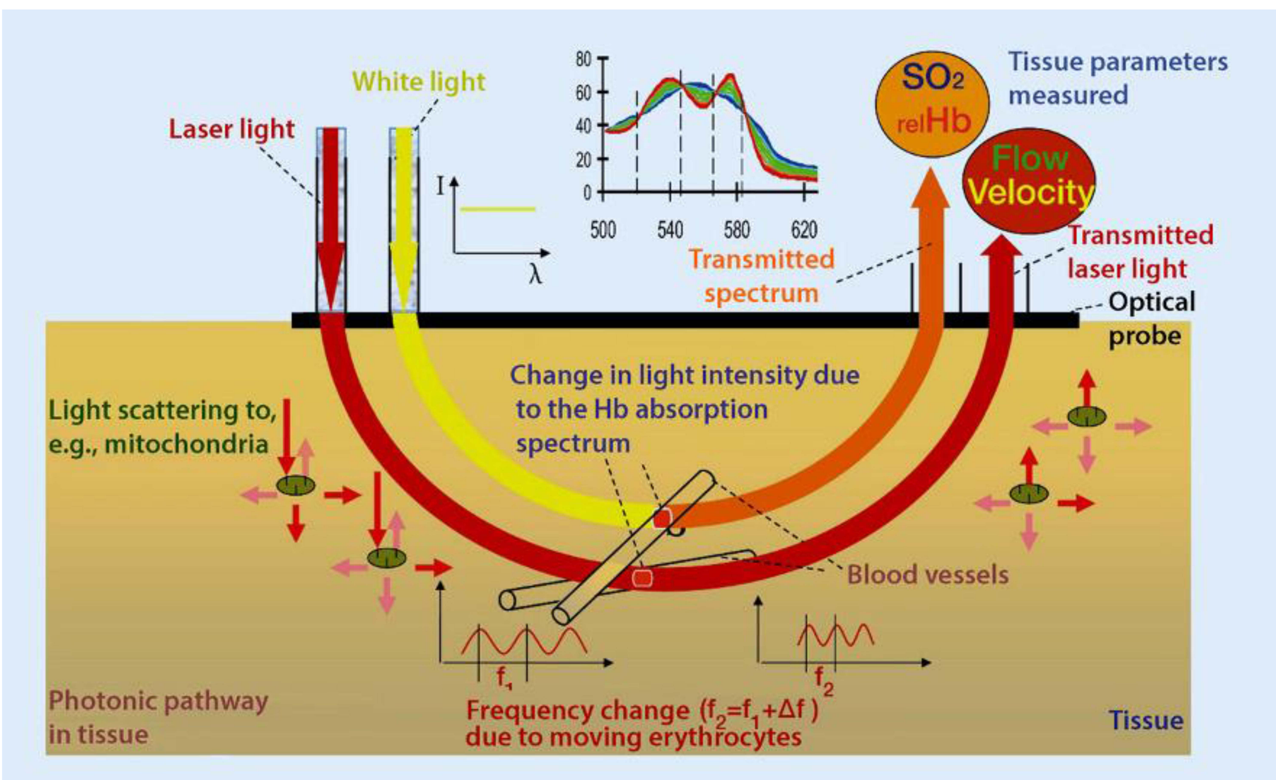

Figure 1 Measurement principles for Visible light spectroscopy (VLS) and laser Doppler flowmetry (LDF) in O2C machine. VLS measures oxygen saturation SO2 and relative hemoglobin concentration in the tissue, while LDF measures flow and velocity.(used with permission from the company LEA Medizintechnik GmbH).

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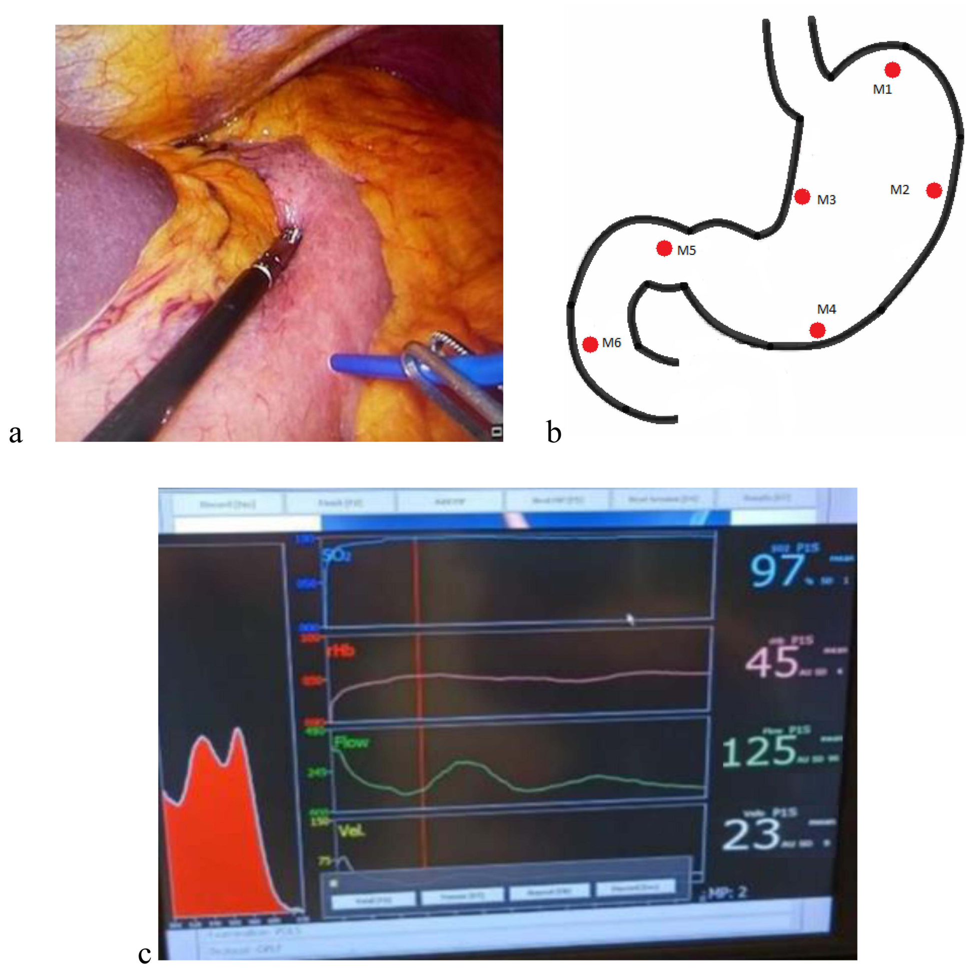

Figure 2 (**a**) Transserosal microcirculation assessment with the O2C probe on stomach surface; (**b**) schematic presentation of transserosal measuring locations on the surface of stomach and duodenum; (**c**) O2C machine; LCD screen shows Visible light spectroscopy (VLS) parameter, SaO2 in %, rHb concentration in AU, and laser Doppler flowmetry (LDF) parameters, Flow and Velocity in AU. Real-time quantitative and graphical presentation of the VLS and LDF data.

and SMA. Care was taken not to apply too much pressure on the serosa during the measurements. The O2C machine is sensitive to movement and pressure, and recordings that visually fluctuated or were unstable were discarded, and the measurements repeated. We kept the absorption spectra of oxyhemoglobin well above 50% of the arbitrary unit scale for each measurement. We generated a measurement protocol to perform 10 seconds of continuous measurements at each anatomical position. Mean measurements from the chosen areas were calculated. The O2C collects flow data 40 times per second, while SaO2 is collected thrice per second. Within 5–10 minutes after decompression of CA, the microcirculatory measurements were repeated at the same anatomic localizations.

Patients with CMI

The patients with CMI scheduled for mesenteric bypass were operated in general anesthesia and through a midline laparotomy. Microcirculatory measurements of both the stomach and duodenum were performed as described above. Depending upon the type of bypass, the supra-celiac or infrarenal aorta was dissected. In case of CA stenosis or occlusion, the common hepatic artery was prepared for end-to-side-anastomosis. The SMA was dissected approximately 2 cm distal to its origin from the aorta. Treitz's ligament was divided, and pars ascendens duodeni was mobilized to approach the periphery of the SMA and its branches. Intravenous Heparin was given before cross-clamping of the arteries. Polytetrafluoroethylene 8 mm graft with rings was used in all patients. All anastomoses were constructed end-to-side on a longitudinal arteriotomy on the aorta and the mesenteric arteries. Microcirculatory measurements of both stomach and duodenum were repeated within 5–10 minutes after the completion of the bypass procedure. Noradrenaline infusion was stopped two minutes before and during the measurements. Peripheral oxygen saturation was kept above 97% during measurements.

The patients were followed up with DUS and clinical examination at 3, 6, and 12 months and yearly. The clinical success of the surgical treatment was defined as an improvement in at least one of the symptoms of MALS or CMI at the follow-up.

Ethics and Trial Registration

Informed written consent was obtained from all patients. Before commencement, the study protocol was approved by the Regional Ethical Committee for Medical and Health Research Ethics in the South–Eastern region of Norway (REK reference no. 2016/682). The study was registered in the ClinicalTrials.gov Protocol Registration and Results System (NCT02914912). The study was conducted according to the principles of the Declaration of Helsinki.

Statistical Analysis

For continuous variables, mean values with standard deviations or median values with ranges are given unless otherwise specified. One sample *t*-test, Wilcoxon rank-sum test, and Pearson Chi-square test were used to compare patient's characteristics. A paired sample *t*-test was done to compare the microcirculation before and after intervention. The statistical significance was set at 5% ($p < 0.05$). Statistical analysis was performed using IBM SPSS Statistics version 29 (IBM Corp. Armonk, NY).

Results

Baseline Characteristics

From November 2016 until April 2023, twenty-eight patients with a consensus diagnosis of MALS and eleven consecutive patients with CMI were included in the study. The median age of the patients with MALS was significantly younger than in the CMI group ($p = 0.010$). Table 1 summarizes the patients' baseline characteristics.

Twenty-six (93%) patients with MALS had abdominal pain. Eighteen (64%) patients reported changes in eating habits and weight loss. The median weight loss in MALS patients was 6.5 ± 6.9 kg. All study patients underwent successful laparoscopic decompression. Twenty-seven (96%) MALS patients were followed-up postoperatively, and twenty (74%) of the patients reported relief from at least one of the preoperative symptoms.

All patients with CMI had post-prandial abdominal pain; ten (n = 10) patients (91%) reported changes in food intake patterns, and nine (n = 9) patients (82%) reported weight loss. The median weight loss was 10±3.6kg. All patients with CMI had retrograde bypasses from the infrarenal aorta or left common iliac artery, except one with a bypass from the supra-coeliac aorta. Eight patients received a single bypass to SMA, one patient received a bypass to both the common hepatic artery and the SMA, and two patients received distal anastomosis at the splenic artery. All patients in the CMI group reported symptom relief, 3 months after the mesenteric bypass surgery.

Transserosal Measurements Results

In the patients with MALS, the sum of all VLS measurements at the stomach showed a significant increase in rHb after laparoscopic decompression of the CA (Table 2). The sum of transserosal SaO_2 measurements at the stomach showed a significant reduction in SaO_2 as compared with the baseline SaO_2 measurements. At the two locations on the duodenum, the patients with MALS had significantly increased rHb, flow, and velocity after the laparoscopic release of the celiac artery but had no change in the SaO2 (Table 2).

In the patients with CMI, the sum of all the measurements on the stomach showed a significant decrease in SaO_2 after revascularization (Before 86%; After 80%, $p = 0.01$). After bypass measurements showed increased flow and velocity, but statistical significance was achieved only in the latter at the stomach (32AU and 36AU, $p = 0.016$). No significant change was found in the microcirculation of the duodenum in the patients with CMI after bypass operations.

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Table 1 Baseline Characteristics and Comorbidities of Patients with Median Arcuate Ligament Syndrome (MALS) and Chronic Mesenteric Ischemia (CMI)

Variable	MALS n=28	CMI n=11	P-value
Age in years (%)	47±19	64±10	0.010
Female Gender (%)	16 (57)	10 (91)	0.04[a]
Height (cm)	174±8	167±8	0.257
Weight (kg)	69±14	57±15	0.298
Current Smoking (%)	6 (21)	8 (73)	0.003
Estimated GFR (mL/min/1,73m$^{2)}$	94±22	91±14	0.192
Creatinine (μmol/L)	75±18	61±14	0.220
IBD (%)	2 (7)	0	0.363
Kidney failure (%)	1 (4)	0	0.525
IHD (%)	2 (7)	1 (9)	0.837
Stroke/TIA (%)	0	1 (9)	0.106
Diabetes mellitus (%)	2 (7)	1 (9)	0.837
Hypertension (%)	5 (18)	2 (18)	0.987
COPD (%)	2 (7)	2 (18)	0.307
PAD (%)	0	4 (36)	0.001
Cancer (%)	1 (3.6)	2 (18)	0.123
Weight loss (kg)	6.5±6.9	10±3.6	0.045[b]
Abdominal pain (%)	26 (93)	11 (100)	0.363
Debut <30 minutes after a meal (%)	3 (11)	1 (9)	0.880
Debut >30 minutes after a meal (%)	13 (46)	5 (45)	0.956
Duration of abdominal pain > 60 min (%)	8 (28)	1 (9)	0.194
Diarrhea/constipation /nausea (%)	5 (18)	0	0.133
Changes in eating habits (%)	18 (64)	10 (91)	0.096

Notes: Single-sample *t*-test; Descriptive analysis with descriptives. [a] Pearson Chi Square test; [b] Wilcoxon rank-sum test.
Abbreviations: NS, not significant; GFR, glomerular filtration rate; IBD, Inflammatory bowel disease; IHD, Ischemic heart disease; TIA, Transient ischemic attack; COPD, Chronic obstructive pulmonary disease; PAD, peripheral arterial disease.

Table 2 Mean Values of Transserosal Microcirculation Measured at Stomach and Duodenal Wall, Before and After Revascularization in Patients with Median Arcuate Ligament Syndrome (MALS) and Chronic Mesenteric Ischemia (CMI). SaO_2 and rHb are Measured with Visible Light Spectroscopy (VLS), While Flow and Velocity are Measured with Laser Doppler Flowmetry (LDF)

	SaO2 (%) Before	After	p-value	rHb (AU) Before	After	p-value	Flow (AU) Before	After	p-value	Velocity (AU) Before	After	p-value
MALS												
Stomach	86±10	82±14	0.015	58±13	62±14	0.017	275±76	275±90	0.984	33±8	34±7	0.570
Duodenum	81±14	81±12	0.920	62±15	70±15	0.004	276±89	315±93	0.015	33±9	38±10	0.007
CMI												
Stomach	86±11	80±13	0.01	59±14	60±18	0.664	263±171	284±112	0.316	32± 7	36±9	0.016
Duodenum	81±13	81±14	0.942	61±14	58±18	0.600	206±104	235±109	0.320	27±8	28±7	0.808

Notes: Used paired samples statistics to calculate mean and standard deviation. P-value is calculated by using Paired sample test.
Abbreviations: SaO_2, Oxygen saturation; rHb, relative hemoglobin; AU, arbitrary unit.

The baseline transserosal mean values and their standard deviation for all the baseline measurements on stomach and duodenum in the patients with MALS were SaO2 88±8, rHb 54±12, Flow 261±82 and Velocity 32±6, whereas, in CMI patients, SaO2 87±11, rHb 57±15, Flow 253±166 and Velocity 32±7. There was no statistically significant difference between the baseline transserosal microcirculation measurements between MALS and CMI patients.

Table 3 Pre-and 3 Months Post-Operative Transabdominal Ultrasound in Patients with MALS

TA-DUS (n=11)	Pre op. m/s ± std.	Post op. m/s ± std.	p-value
PSV	2.8±0.8	1.5±0.2	<0.001
EDV	1.0±0.4	0.4±0.1	0.002

Notes: Paired samples statistics to calculate mean and standard deviation (std). P-value is calculated by using Paired samples test.
Abbreviations: MALS Median arcuate ligament syndrome; TA-DUS (Transabdominal Duplex ultrasound); PSV (Peak systolic velocity); EDV (end diastolic velocity).

Duplex Ultrasound Results

Preoperative DUS was performed in thirteen (46%) patients with MALS and was technically unsuccessful in two patients. Pre- and postoperative DUS was performed successfully on eleven patients with MALS and showed a significant reduction in the PSV of the CA after laparoscopic decompression ($p < 0.001$) (Table 3).

Discussion

This study has shown that patients with MALS have reduced transserosal microcirculation prior to surgery. After laparoscopic decompression of the celiac artery, we found a significant increase in rHb on the measurement sites on both the stomach and duodenum, and a significant increase in flow and velocity at the duodenum.

Previous studies have shown that an increase in rHb concentration results from venous congestion, which again is caused by venous resection during dissection.[19–22] However, laparoscopic decompression of the celiac artery is a minimally invasive procedure, and the tissue dissection is limited and far beyond the sites of transserosal microcirculatory measurements on the stomach and the duodenum. The increase in rHb detected in this study cannot be explained by venous congestion but rather due to an increase in the transserosal blood flow. After laparoscopic CA decompression, a significant increase in flow and velocity was found at the duodenum. A small sample size could be an explanation for the lack of significant change in flow and velocity in the stomach. In our previous study, we found a significantly increased microcirculation of the stomach and duodenum mucosa SaO_2 and rHb in patients with MALS within 3 months after laparoscopic decompression of the CA.[11] However, in the present study, we found a decrease in transserosal $SaO_{2,}$ which was unexpected. A possible explanation could be due to increased oxygen consumption/ extraction by the chronic ischemic mucosa.[25]

In patients with CMI, the main location of ischemic changes is expected in the intestine. However, in case of severe stenosis or occlusion of CA, the duodenum and stomach get their blood supply from the SMA through its branches and collaterals. All CMI patients in the study had either stenosis or occlusion of the CA in addition to stenosis or occlusion of the SMA and inferior mesenteric artery. In the patients with CMI, increased blood flow through the mesenteric vessels and the bypass was confirmed with transit time flow measurement (TTFM) ultrasound probes after the completion of the anastomoses. However, a significant decrease in the transserosal SaO_2 was found in the stomach after the revascularization procedure. Oxygen extraction by the mucosa can explain this decrease in SaO2. In the CMI patients, increased transserosal flow was measured at the stomach and duodenum measuring sites. However, the increase was not statistically significant, probably due to the small sample size. Aortic as well as the mesenteric/ celiac artery cross-clamping for anastomoses construction, and traction and compression of stomach and intestine from the retractors during the operation, could have contributed to mucosal ischemia and affected the transserosal microcirculatory measurements. Although TTFM confirmed flow rates, representative of open bypass and a good run-off, an immediate assessment of the transserosal microcirculation, ie, within 5–10 minutes after anastomosis, was probably too early to capture the expected increase in microcirculation in the patients with CMI. If the measurements had been taken later, the results might have been different in the patients with CMI. Likewise, it is interesting that the baseline transserosal VLS and LDF values are statistically indifferent in patients with MALS and CMI. Including another control group of healthy individuals could have provided useful comparative information for the baseline transserosal microcirculatory status for MALS and CMI patients.

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The limitation of this study is its small sample size. Besides, no macro blood flow measurements were performed before and after the laparoscopic decompression of the celiac artery during the laparoscopic decompression. However, postoperative DUS at the follow-up confirmed improved blood flow through the CA. The patients did not have turbulence or an increase in the PSV during expiration at the follow-up, and they also reported symptom relief. Another limitation of VLS and LDF is that they only provide information on the measurement sites. In future studies, the number of measuring sites can be increased to include a larger area of the stomach and duodenum for a comprehensive microcirculatory assessment. Moreover, the measurement protocol can also be shortened to 2–3 seconds. The microcirculation data from this small study is limited, and further studies are required to standardize the transserosalt microcirculation values in patients with MALS and CMI.

The measurements performed could have been affected by the pressure artifacts and persistent effect of the systemic noradrenaline. However, the same methodology was followed at both measuring time points.

Conclusion

This study shows that patients with MALS show immediate improvement in transserosal microcirculation after laparoscopic decompression. The baseline transserosal microcirculation is similar in this study's patients with MALS and CMI.

Data Sharing Statement

De-identified data can be shared with investigators whose proposed use of the data has been approved by an independent review committee identified for this purpose. The proposal should be directed to the project leader, Syed Sajid Hussain Kazmi, at sshkazmi@gmail.com. Data requestors will need to sign a data access agreement to gain access.

Author Contributions

All authors made a significant contribution to the work reported, whether that is the conception, study design, execution of data, analysis, interpretation, drafting, revising, or critically reviewing the article; gave final approval of the version to be published with the Journal of Vascular Health and Risk Management. All authors agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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