From the Society for Vascular Surgery

Factors associated with successful median arcuate ligament release in an international, multi-institutional cohort

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ABSTRACT

Objective: Prior research on median arcuate ligament syndrome has been limited to institutional case series, making the optimal approach to median arcuate ligament release (MALR) and resulting outcomes unclear. In the present study, we compared the outcomes of different approaches to MALR and determined the predictors of long-term treatment failure.

Methods: The Vascular Low Frequency Disease Consortium is an international, multi-institutional research consortium. Data on open, laparoscopic, and robotic MALR performed from 2000 to 2020 were gathered. The primary outcome was treatment failure, defined as no improvement in median arcuate ligament syndrome symptoms after MALR or symptom recurrence between MALR and the last clinical follow-up.

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Results: For 516 patients treated at 24 institutions, open, laparoscopic, and robotic MALR had been performed in 227 (44.0%), 235 (45.5%), and 54 (10.5%) patients, respectively. Perioperative complications (ileus, cardiac, and wound complications; readmissions; unplanned procedures) occurred in 19.2% (open, 30.0%; laparoscopic, 8.9%; robotic, 18.5%; $P <$ .001). The median follow-up was 1.59 years (interquartile range, 0.38-4.35 years). For the 488 patients with follow-up data available, 287 (58.8%) had had full relief, 119 (24.4%) had had partial relief, and 82 (16.8%) had derived no benefit from MALR. The 1- and 3-year freedom from treatment failure for the overall cohort was 63.8% (95% confidence interval [CI], 59.0%-68.3%) and 51.9% (95% CI, 46.1%-57.3%), respectively. The factors associated with an increased hazard of treatment failure on multivariable analysis included robotic MALR (hazard ratio [HR], 1.73; 95% CI, 1.16-2.59; $P =$ .007), a history of gastroparesis (HR, 1.83; 95% CI, 1.09-3.09; $P =$ .023), abdominal cancer (HR, 10.3; 95% CI, 3.06-34.6; $P <$ .001), dysphagia and/or odynophagia (HR, 2.44; 95% CI, 1.27-4.69; $P =$ .008), no relief from a celiac plexus block (HR, 2.18; 95% CI, 1.00-4.72; $P =$ .049), and an increasing number of preoperative pain locations (HR, 1.12 per location; 95% CI, 1.00-1.25; $P =$ .042). The factors associated with a lower hazard included increasing age (HR, 0.99 per increasing year; 95% CI, 0.98-1.0; $P =$ .012) and an increasing number of preoperative diagnostic gastrointestinal studies (HR, 0.84 per study; 95% CI, 0.74-0.96; $P =$ .012) Open and laparoscopic MALR resulted in similar long-term freedom from treatment failure. No radiographic parameters were associated with differences in treatment failure.

Conclusions: No difference was found in long-term failure after open vs laparoscopic MALR; however, open release was associated with higher perioperative morbidity. These results support the use of a preoperative celiac plexus block to aid in patient selection. Operative candidates for MALR should be counseled regarding the factors associated with treatment failure and the relatively high overall rate of treatment failure. (J Vasc Surg 2022;■:1-11.)

Keywords: MALS; Median arcuate ligament release; Median arcuate ligament syndrome; Vascular Low Frequency Disease Consortium; VLFDC

Asymptomatic celiac artery compression affects ≤24% of the population. However, median arcuate ligament syndrome (MALS) is an exceptionally rare syndrome with a reported incidence of 2 per 100,000 persons.[1-3] As a result of its uncommon nature and unclear diagnostic criteria, MALS has remained a controversial and elusive diagnosis. The underlying pathophysiology of MALS remains unknown; however, the symptoms have classically been thought to have resulted from foregut ischemia in the setting of severe celiac stenosis. Many believe that the pain associated with MALS is neurogenic and the result of chronic compression and overstimulation of the celiac plexus.[4,5]

Median arcuate ligament release (MALR) was first described as a treatment of MALS in the 1960s, >50 years ago.[6,7] However, because of the rarity of the syndrome, the existing evidence for the treatment of MALS has been limited to small, single-center series subject to institutional selection, referral, and treatment biases.[5,8-11] Thus, the predictors of treatment success and failure have not yet been well-established for this patient population. Although open, laparoscopic, and, most recently, robot-assisted laparoscopic approaches have all been described as effective techniques for MALR, few series have directly compared the MALR techniques to identify the optimal approach.[12-14] Furthermore, it is unknown whether specific radiographic parameters are associated with treatment failure.

In the present study, we sought to determine (1) whether a difference exists in long-term treatment failure between open, laparoscopic, and robot-assisted laparoscopic MALR; (2) what patient factors, if any, are associated with treatment failure after MALR; and (3) whether any radiographic parameters associated with long-term symptom outcomes after MALR can be identified in a large, multicenter, international cohort of patients who had undergone MALR for MALS.

METHODS

Vascular Low Frequency Disease Consortium and database management. Given the low incidence of MALS, we used the Vascular Low Frequency Disease Consortium (VLFDC) database to analyze the international MALR outcomes for patients with presumed MALS. The method of the VLFDC process has been described previously.[15-17] The institutional review board at each participating institution approved the study and waived the requirement for patient informed consent for inclusion owing to the minimal risk and retrospective nature of the present study.

Data source, patient factors, and outcomes of interest. Patients who had undergone MALR for presumed MALS from 2000 to 2020 were included in the present study. The patients were identified using preexisting investigator databases and the following: International Classification of Diseases, 9th revision, code 447.4, and International Classification of Diseases, 10th revision, code I77.4 (celiac artery compression syndrome).

The patients were divided into three groups according to the operative technique: open, laparoscopic, or robotic MALR. The laparoscopic and robotic cases that had required conversion to open MALR were included in the open MALR group. The participating institutions contributed data for patient demographics and comorbidities, presenting symptoms, preoperative diagnostic studies, intraoperative variables, perioperative complications (≤30 days after MALR), and long-term outcomes (between MALR and the last follow-up). The variable definitions are listed in Supplementary Table I (online only).

The primary outcome of interest was long-term treatment failure after MALR. Treatment failure was defined as no relief after primary MALR or symptom recurrence after initial symptom relief during long-term follow-up. However, arterial, graft, or stent stenosis recognized at symptom recurrence, with reintervention to correct the stenosis, which resulted in partial or complete symptom relief, was not categorized as treatment failure. Partial relief of symptoms after MALR, without recurrence, was included as treatment success. This binary outcome was chosen owing to the retrospective nature of the study, which precluded a standardized, quantifiable assessment of symptoms. The secondary outcomes of interest were reinterventions and postoperative complications. Follow-up was defined as the period between MALR and the last known clinical encounter.

Prespecified analyses were performed in subgroups to determine whether specific radiologic cutoffs were associated with a higher or lower hazard of treatment failure for patients with available imaging studies. The variables tested for a univariable association with symptom relief after MALR and the need for reintervention included the following:

1. Difference between the preoperative expiratory and inspiratory peak systolic velocities (PSVs)
2. A preoperative expiratory PSV >200 cm/s
3. A preoperative expiratory PSV >350 cm/s
4. A resting preoperative PSV >200 cm/s
5. A resting preoperative PSV >350 cm/s
6. An increase in expiratory PSV after MALR (ie, postoperative expiratory PSV greater than the preoperative expiratory PSV)
7. Degree of compression found on preoperative angiography, magnetic resonance angiography (MRA), or computed tomography angiography (CTA), expressed by the aortoceliac angle, defined as the angle between the anterior border of the aorta and inferior border of the proximal celiac artery and analyzed as a continuous variable

A cutoff of 200 cm/s was chosen in accordance with the PSV criteria for >70% stenosis. A cutoff of 350 cm/s was chosen in accordance with prior literature.[18]

Statistical analysis. Statistical analyses were performed using STATA, version 15.1 (StataCorp, College Station, TX). A *P* value of < .05 was considered to indicate statistical significance. Differences between groups were analyzed using the χ^2 test, *t* test, and Kruskal-Wallis test, as appropriate. The long-term freedom from treatment failure and reintervention was determined using Kaplan-Meier analysis. The predictors of treatment failure were determined using a Cox proportional hazards model. Model development was performed using augmented backward elimination, for which we used $P < .20$ in an empty Cox model as the threshold for model inclusion; the exit criterion was $P > .10$.[19] The outcome for the subgroup analyses was estimated using Kaplan-Meier analysis, and the groups were compared using the log-rank test.

ARTICLE HIGHLIGHTS

- **Type of Research:** A retrospective review of a multicenter, international database (Vascular Low Frequency Disease Consortium) of patients with median arcuate ligament syndrome who had undergone median arcuate ligament release (MALR)
- **Key Findings:** Of 516 patients treated at 24 institutions, 227 (44.0%), 235 (45.5%), and 54 (10.5%) had undergone open, laparoscopic, and robotic MALR, respectively. Of the 488 patients (94.6%) with follow-up data available, 287 (58.8%) had had full relief, 119 (24.4%) had had partial relief, and 82 (16.8%) had derived no benefit from MALR. The 3 -year freedom from treatment failure for the overall cohort was 51.9% (95% confidence interval, 46.1%-57.3%). The factors associated with an increased hazard of treatment failure included robotic MALR, a history of gastroparesis, a history of abdominal cancer, dysphagia or odynophagia, no relief from a celiac plexus block, and the number of pain locations. Age and an increasing number of preoperative diagnostic gastrointestinal studies were associated with a lower hazard of failure. No radiographic parameters were associated with differences in treatment failure.
- **Take Home Message:** We found no difference in long-term failure after open vs laparoscopic release; however, open release was associated with higher perioperative morbidity. The overall rate of treatment failure was high, and operative candidates for MALR should be counseled regarding the factors associated with treatment failure.

RESULTS

Patient demographics and comorbidities. A total of 24 institutions in seven countries had contributed data from 522 patients with MALS. Of the 522 patients, 6 had not met the inclusion criteria. MALR had been performed in conjunction with liver transplantation for two patients, mesenteric bypass had been performed for atherosclerotic occlusive disease in three patients, and mesenteric aneurysm repair had been performed in one patient. Hence, 516 patients were included in the present analysis. Open MALR had been performed in 227 patients (44.0%; 8 converted from laparoscopic and 1 from robotic MALR),

Table I. Patient baseline demographics and comorbidities

Variable	Entire cohort (N = 516)	MALR Open (n = 227)	MALR Laparoscopic (n = 235)	MALR Robotic (n = 54)	*P* value
Age, years	39.5 ± 16.0	40.5 ± 16.3	39.1 ± 15.8	37.7 ± 16.1	.44
Female gender	406 (78.7)	173 (76.2)	186 (79.1)	47 (87.0)	.21
Race					.002
Non-Hispanic White	487 (94.4)	215 (94.7)	227 (96.6)	45 (83.3)	
Black	7 (1.4)	4 (1.8)	2 (0.9)	1 (1.9)	
Hispanic	10 (1.9)	2 (0.9)	3 (1.3)	5 (9.3)	
Asian	2 (0.4)	1 (0.4)	0 (0.0)	1 (1.9)	
Other	10 (1.9)	5 (2.2)	3 (1.3)	2 (3.7)	
Psychiatric disorder	142 (27.5)	85 (37.4)	38 (16.2)	19 (35.2)	<.001
Mood disorder[a]	94 (18.2)	50 (22.0)	32 (13.6)	12 (22.2)	.047
Anxiety disorder	64 (12.4)	47 (20.7)	8 (3.4)	9 (16.7)	<.001
Personality disorder	4 (0.8)	2 (0.9)	2 (0.9)	0 (0.0)	.79
Psychotic disorder	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)	.53
Eating disorder	8 (1.6)	5 (2.2)	2 (0.9)	1 (1.9)	.49
Other disorder	15 (2.9)	6 (2.6)	5 (2.1)	4 (7.4)	.11
Fibromyalgia	27 (5.2)	17 (7.5)	7 (3.0)	3 (5.6)	.093
Alcohol abuse	5 (3.8)	0 (0)	4 (4)	1 (14)	.17
Substance abuse	5 (1.0)	2 (0.9)	2 (0.9)	1 (1.9)	.78
Preoperative opioid pain medication					.31
None	430 (83.3)	193 (85.0)	197 (83.8)	40 (74.1)	
Yes, for abdominal pain	71 (13.8)	27 (11.9)	33 (14.0)	11 (20.4)	
Yes, for pain other than abdominal	15 (2.9)	7 (3.1)	5 (2.1)	3 (5.6)	
Chronic pain	49 (9.5)	29 (12.8)	15 (6.4)	5 (9.3)	.064
Autonomic dysfunction	26 (5.0)	24 (10.6)	0 (0.0)	2 (3.7)	<.001
Competing diagnosis	217 (42.1)	120 (52.9)	63 (26.8)	34 (63.0)	<.001
GERD	128 (24.8)	74 (32.6)	33 (14.0)	21 (38.9)	<.001
Gastroparesis	30 (5.8)	20 (8.8)	5 (2.1)	5 (9.3)	.005
Irritable bowel syndrome	50 (9.7)	23 (10.1)	23 (9.8)	4 (7.4)	.83
Inflammatory bowel disease	6 (1.2)	4 (1.8)	1 (0.4)	1 (1.9)	.36
Other competing diagnosis	107 (20.7)	65 (28.6)	22 (9.4)	20 (37.0)	<.001
Abdominal cancer	3 (0.6)	2 (0.9)	1 (0.4)	0 (0.0)	.68
Other cancer	18 (3.5)	12 (5.3)	2 (0.9)	4 (7.4)	.009
Migraine	53 (10.3)	30 (13.2)	17 (7.2)	6 (11.1)	.10
Hypertension	89 (17.2)	56 (24.7)	25 (10.6)	8 (14.8)	<.001
Diabetes mellitus	23 (4.5)	16 (7.0)	5 (2.1)	2 (3.7)	.036
Any history of smoking	166 (32.2)	68 (30.0)	88 (37.4)	10 (18.5)	.017
Active smoking	81 (15.7)	28 (12.3)	49 (20.9)	4 (7.4)	.009
Congestive heart failure	9 (1.7)	7 (3.1)	2 (0.9)	0 (0.0)	.11
Coronary artery disease	22 (4.3)	16 (7.0)	5 (2.1)	1 (1.9)	.021
Chronic kidney disease	7 (1.4)	1 (0.4)	6 (2.6)	0 (0.0)	.096

GERD, Gastroesophageal reflux disease; *MALR,* median arcuate ligament release.
Data presented as mean ± standard deviation or number (%).
[a]Depression or bipolar disorder.

laparoscopic MALR in 235 patients (45.5%), and robotic MALR in 54 patients (10.5%). The mean age of the cohort was 39.5 ± 16.0 years, and 78.7% of the cohort were women (Table I). Most of the cohort was White. Of the 516 patients, 142 (27.5%) had a history of a psychiatric disorder, which was less common in the laparoscopic

MALR group. A competing diagnosis (concurrent abdominal condition that could also explain the patient's symptoms) was present in 42.1% of the cohort and was significantly more common in the open and robotic MALR groups than in the laparoscopic MALR group ($P <$ .001). The most common competing diagnoses were gastroesophageal reflux disease, followed by irritable bowel syndrome, and gastroparesis.

Presenting signs and symptoms. The median symptom duration before MALR was 18 months (Table II). The most common presenting symptom was pain (96.9%). Pain had most commonly affected the epigastrium, although less often in the laparoscopic MALR group. Postprandial pain was common, with 86.4% of patients having postprandial pain or both postprandial and non–postprandial pain. Weight loss, nausea/vomiting, and diarrhea were other common symptoms. Dysphagia or odynophagia had affected 3.1% of the cohort. Of the 516 patients, 71 (13.8%) had undergone a preoperative celiac plexus block. Of these 71 patients, 42 (59.2%) had experienced total symptom relief, 19 (26.8%) partial relief, and 10 (14.1%) no relief.

Subgroup analyses examining anatomic and physiologic data from radiology studies. The number of patients with specific radiographic parameters and the mean values of those parameters are listed in Supplementary Table II (online only). Preoperatively, 356 patients (69.0%) had undergone duplex ultrasound, 317 (61.4%) had undergone CTA, 172 (33.3%) had undergone MRA, and 211 (40.9%) had undergone angiography. None of the prespecified radiology parameters were significantly associated with relief from MALR or symptom recurrence. No preoperative radiologic variables were associated with the need for postoperative reintervention. The difference between the preoperative expiratory and inspiratory PSV was measured in 224 patients (45.9%) and was not associated with the outcomes (symptom relief, $P = .39$; reintervention, $P = .24$). For the same 224 patients, neither a preoperative expiratory PSV >200 cm/s (symptom relief, $P = .12$; reintervention, $P = .86$) nor a preoperative expiratory PSV >350 cm/s (symptom relief, $P = .08$; reintervention, $P = .71$) was associated with the outcomes. The resting PSV was measured for 156 patients (32.0% of patients with follow-up data available), and neither a cutoff of 200 cm/s (symptom relief, $P = .76$; reintervention, $P = .72$) nor a cutoff of 350 cm/s (symptom relief, $P = .56$; reintervention, $P = .78$) affected the subgroup analysis outcomes. A difference between the postoperative and preoperative expiratory PSV was measured in 172 patients. However, an increase in the expiratory PSV postoperatively was not associated with the primary outcome (symptom relief, $P = .06$). The preoperative aortoceliac angle was not associated with the subgroup analysis outcome (symptom relief, $P = .86$; reintervention, $P = .78$). The aortoceliac angle showed a minimal correlation with the preoperative expiratory PSV ($r = 0.03$).

Operative variables and perioperative complications. Of the cohort, 11% had undergone a simultaneous planned vascular intervention (Table III). A planned simultaneous endovascular intervention (ie, balloon angioplasty or stenting, or both) had occurred with a similar frequency between the operative groups. However, mesenteric bypass and patch angioplasty had been more frequently performed with open MALR. Vascular surgeons had been involved in most cases (89.7%) but were involved in only 55.6% of the robotic MALR cases ($P < .001$). General surgeons had been involved in 18.4% of cases, and multiple specialties had participated in 15.1% of the cases. Intraoperative vascular and visceral injuries had occurred with a similar frequency between operative groups; however, other intraoperative complications had occurred more often with laparoscopic MALR (laparoscopic, 4.7%; open, 0.9%; robotic, 1.9%; $P =$ .039). These included pneumothorax, chylous leak, and one case of asystole requiring cardiopulmonary resuscitation.

Complications at 30-days postoperatively were most common after open MALR and least common after laparoscopic MALR. The most common complication was postoperative ileus, which had occurred in 7.7% of the cohort, most often after open MALR (open, 14.1%; laparoscopic, 2.1%; robotic, 5.6%; $P < .001$). Severe complications such as bleeding, myocardial infarction, pulmonary embolism, mesenteric ischemia, and acute kidney injury had occurred infrequently and only after open MALR (open, 2.3%; laparoscopic, 0%; robotic, 0%; $P = .040$). The patients who had undergone open MALR had had a significantly longer median postoperative length of stay.

Long-term outcomes and multivariable model. Of the 516 patients 28 (5.4%) had been lost to follow-up and were excluded from the long-term analysis. The median follow-up for the included patients was 1.59 years (interquartile range, 0.38-4.35 years). The initial results after MALR were a full relief of symptoms for 287 patients (58.8%), partial relief for 119 (24.4%), and no benefit for 82 (16.8%). The 1- and 3-year freedom from treatment failure for the overall cohort was 63.8% (95% confidence interval [CI], 59.0%-68.3%) and 51.9% (95% CI, 46.1%-57.3%), respectively.

On the unadjusted analysis, laparoscopic MALR was associated with the lowest incidence of treatment failure. The 3-year freedom from treatment failure was 62.4% (95% CI, 54.3%-69.5%) for laparoscopic MALR, 43.9% (95% CI, 34.9%-52.5%) for open MALR, and 37.7% (95% CI, 23.6%-51.8%) for robotic MALR (log-rank $P <$ .001; Fig 1). The 3-year freedom from reintervention was

Table II. Presenting signs and symptoms attributed to median arcuate ligament syndrome (MALR)

Variable	Entire cohort (N = 516)	MALR Open (n = 227)	MALR Laparoscopic (n = 235)	MALR Robotic (n = 54)	*P* value
Symptom duration, months	18.0 (8.0-48.0)	18.0 (7.0-48.0)	18.0 (8.0-48.0)	18.0 (9.0-84.0)	.76
Pain	500 (96.9)	221 (97.4)	227 (96.6)	52 (96.3)	.86
Location					
Epigastrium	379 (75.8)	184 (83.3)	151 (66.5)	44 (84.6)	<.001
Upper quadrant					
Right	143 (28.6)	66 (29.9)	66 (29.1)	11 (21.2)	.45
Left	140 (28.0)	55 (24.9)	76 (33.5)	9 (17.3)	.025
Lower quadrant					
Right	85 (17.0)	34 (15.4)	42 (18.5)	9 (17.3)	.68
Left	78 (15.6)	35 (15.8)	34 (15.0)	9 (17.3)	.91
Back	34 (6.8)	22 (10.0)	9 (4.0)	3 (5.8)	.040
Chest	16 (3.2)	10 (4.5)	6 (2.6)	0 (0.0)	.20
Inguinal region	10 (2.0)	5 (2.3)	2 (0.9)	3 (5.8)	.071
Quality					
Cramping	78 (15.6)	12 (5.4)	50 (22.0)	16 (30.8)	<.001
Dull	36 (7.2)	17 (7.7)	15 (6.6)	4 (7.7)	.90
Sharp	88 (17.6)	31 (14.0)	45 (19.8)	12 (23.1)	.15
Burning	28 (5.6)	12 (5.4)	13 (5.7)	3 (5.8)	.99
Deep	25 (5.0)	7 (3.2)	18 (7.9)	0 (0.0)	.015
Spasmodic	18 (3.6)	3 (1.4)	14 (6.2)	1 (1.9)	.019
Pressure	101 (20.2)	17 (7.7)	74 (32.6)	10 (19.2)	<.001
Discomfort	74 (14.8)	15 (6.8)	51 (22.5)	8 (15.4)	<.001
Other	30 (6.0)	16 (7.2)	9 (4.0)	5 (9.6)	.18
Unknown	179 (35.8)	125 (56.6)	35 (15.4)	19 (36.5)	<.001
Postprandial pain					.006
Exclusively	184 (36.8)	88 (39.8)	84 (37.0)	12 (23.1)	
Not postprandial pain but worse with eating	248 (49.6)	99 (44.8)	122 (53.7)	27 (51.9)	
Food intake does not affect pain	49 (9.8)	26 (11.8)	16 (7.0)	7 (13.5)	
Unknown	19 (3.8)	8 (3.6)	5 (2.2)	6 (11.5)	
Positional change in pain					<.001
No	301 (60.2)	110 (49.8)	169 (74.4)	22 (42.3)	
Yes	50 (10.0)	22 (10.0)	23 (10.1)	5 (9.6)	
Unknown	149 (29.8)	89 (40.3)	35 (15.4)	25 (48.1)	
Food fear					<.001
No	303 (58.7)	99 (43.6)	186 (79.1)	18 (33.3)	
Yes	145 (28.1)	90 (39.6)	37 (15.7)	18 (33.3)	
Unknown	68 (13.2)	38 (16.7)	12 (5.1)	18 (33.3)	
Nausea and/or vomiting	287 (55.6)	141 (62.1)	119 (50.6)	27 (50.0)	.031
Diarrhea	158 (30.6)	47 (20.7)	95 (40.4)	16 (29.6)	<.001
Dysphagia or odynophagia	16 (3.1)	8 (3.5)	7 (3.0)	1 (1.9)	.81
Preoperative TPN	16 (3.1)	10 (4.4)	4 (1.7)	2 (3.7)	.24
Weight loss	341 (66.1)	143 (63.0)	171 (72.8)	27 (50.0)	.003
Weight loss >20 lb	152 (29.5)	72 (31.7)	73 (31.1)	7 (13.0)	.019
Bloating	17 (3.3)	15 (6.6)	1 (0.4)	1 (1.9)	<.001
Constipation	18 (3.5)	14 (6.2)	2 (0.9)	2 (3.7)	.008

Table II. Continued.

Variable	Entire cohort (N = 516)	MALR Open (n = 227)	MALR Laparoscopic (n = 235)	MALR Robotic (n = 54)	*P* value
Abdominal bruit					<.001
No	309 (59.9)	170 (74.9)	109 (46.4)	30 (55.6)	
Yes	27 (5.2)	9 (4.0)	17 (7.2)	1 (1.9)	
Unknown	180 (34.9)	48 (21.1)	109 (46.4)	23 (42.6)	

TPN, total parenteral nutrition.
Data presented as median (interquartile range) or number (%).

90.3% (95% CI, 84.4%-94.1%) for open MALR, 79.6% (95% CI, 70.7%-86.0%) for laparoscopic MALR, and 83.4% (95% CI, 67.5%-92.0%) for robotic MALR (log-rank $P = .046$; Fig 2). The most common reintervention was endovascular celiac artery angioplasty or stenting, performed in 49 patients (9.5%). Repeat MALR had been performed in six patients (1.2%). A total of 25 patients had undergone reintervention at recurrence, and 20 had experienced partial or full symptom relief—these patients were not included in the treatment failure group. These 25 reinterventions included 17 endovascular interventions (13 patients had experienced symptom improvement), 2 bypasses (both with symptom improvement), 1 ligament release (with symptom improvement), 1 combined endovascular intervention and ligament release (with symptom improvement), and 4 unspecified or unknown (3 with symptom improvement).

On multivariable analysis, the operative approach was categorized as a binary variable (robotic vs open/laparoscopic). The factors associated with an increased hazard of treatment failure included robotic MALR, a history of gastroparesis, a history of abdominal cancer, dysphagia or odynophagia as a presenting symptom, no relief from a preoperative celiac plexus block, and an increasing number of preoperative pain locations (Table IV). Increasing age and an increasing number of preoperative diagnostic gastrointestinal studies were associated with a lower hazard of treatment failure. The other variables did not meet the inclusion criteria for the model owing to a lack of statistical significance. When the variable for operative approach was categorized as a three-level categorical variable (open vs laparoscopic vs robotic with open MALR as the reference category), laparoscopic and open MALR had similar long-term outcomes (laparoscopic vs open: hazard ratio [HR], 0.82; 95% CI, 0.59-1.13; $P = .22$).

DISCUSSION

In the present international, multi-institutional experience of MALR for MALS, open and laparoscopic MALR were associated with similar rates of long-term success but robotic MALR had comparatively inferior results. Open MALR was associated with more perioperative complications than laparoscopic MALR but fewer long-term reinterventions. Uniquely, this analysis identified multiple patient factors associated with long-term freedom from treatment failure. Within this cohort, we were unable to identify any specific radiographic parameters that affected the long-term outcomes.

Compared with the traditional laparotomy used in the open approach, laparoscopy has been associated with fewer perioperative complications, a shorter length of stay, and faster recovery and has become the standard of care for most nonvascular abdominal operations.[20,21] The results from the present study have confirmed that laparoscopic MALR is associated with a lower incidence of perioperative complications and a shorter length of stay compared with open MALR, without compromising symptom relief. Laparoscopic MALR was associated with a slightly higher rate of long-term reintervention compared with open MALR. Consistent with the literature, the vast majority of these reinterventions were endovascular interventions that were generally well-tolerated and achieved favorable results.[9] Our analysis has shown that a laparoscopic-first approach to MALR is reasonable with the well-documented benefits of laparoscopic surgery. However, it is also reasonable to perform MALR in an open fashion, especially for patients who might benefit from simultaneous open revascularization.

Although some investigators have advocated for the liberal use of revascularization, no specific revascularization technique was associated with improved outcomes in our study.[22,23] However, we can postulate that the patients who had undergone revascularization as a part of their MALR procedure might have had anatomic differences not reflected in these data. It is reasonable to use revascularization as an adjunct for patients with severe residual celiac stenosis after MALR or associated celiac aneurysmal degeneration. Patients with persistent symptoms after MALR with residual celiac artery stenosis should undergo revascularization, and an endovascular-first approach in for such cases is reasonable.[9]

In our series, robotic MALR release had had an ~75% higher hazard of treatment failure compared with open

Table III. Operative variables and intraoperative and postoperative complications

Variable	Entire cohort (N = 516)	Open MALR (n = 227)	Laparoscopic MALR (n = 235)	Robotic MALR (n = 54)	*P* value
Planned endovascular intervention	23 (4.5)	9 (4.0)	13 (5.5)	1 (1.9)	.44
Celiac artery	20 (3.9)	7 (3.1)	12 (5.1)	1 (1.9)	.38
SMA	3 (0.6)	2 (0.9)	1 (0.4)	0 (0.0)	.68
Planned mesenteric bypass[a]	19 (3.7)	19 (8.4)	0 (0.0)	0 (0.0)	<.001
Celiac artery	18 (3.5)	18 (7.9)	0 (0.0)	0 (0.0)	<.001
SMA	2 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	.28
Planned patch angioplasty	8 (1.6)	7 (3.1)	1 (0.4)	0 (0.0)	.043
Other planned vascular intervention	7 (1.4)	7 (3.1)	0 (0.0)	0 (0.0)	.011
No planned vascular intervention	459 (89.0)	184 (81.1)	222 (94.5)	53 (98.1)	<.001
Specialty					
Vascular surgeon	463 (89.7)	222 (97.8)	211 (89.8)	30 (55.6)	<.001
General surgeon	95 (18.4)	22 (9.7)	40 (17.0)	33 (61.1)	<.001
Other	36 (7.0)	3 (1.3)	12 (5.1)	21 (38.9)	<.001
Multiple	78 (15.1)	20 (8.8)	28 (11.9)	30 (55.6)	<.001
Operative time,[b] minutes	140.7 ± 69.2	179.1 ± 78.7	107.5 ± 41.8	170.6 ± 54.3	<.001
Estimated blood loss,[c] mL	50.0 (50.0-100.0)	75.0 (50.0-200.0)	50.0 (50.0-50.0)	40.0 (20.0-100.0)	<.001
Intraoperative complications					
Vascular injury	13 (2.5)	8 (3.5)	2 (0.9)	3 (5.6)	.060
Visceral injury	1 (0.2)	0 (0.0)	1 (0.4)	0 (0.0)	.55
Other	14 (2.7)	2 (0.9)	11 (4.7)	1 (1.9)	.039
Perioperative (0-30 days) complications after MALR					
Any	99 (19.2)	68 (30.0)	21 (8.9)	10 (18.5)	<.001
Postoperative ileus					<.001
Yes, managed with nasogastric decompression	25 (4.8)	21 (9.3)	3 (1.3)	1 (1.9)	
Yes, managed without nasogastric decompression	15 (2.9)	11 (4.8)	2 (0.9)	2 (3.7)	
Return to operating room for bleeding	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)	.53
Myocardial infarction	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)	.53
Pulmonary embolism	0 (0)	0 (0)	0 (0)	0 (0)	–
Deep vein thrombosis	3 (0.6)	2 (0.9)	1 (0.4)	0 (0.0)	.68
No VTE	514 (99.6)	226 (99.6)	234 (99.6)	54 (100.0)	.89
Postoperative mesenteric ischemia	1 (0.2)	1 (0.4)	0 (0.0)	0 (0.0)	.53
Acute kidney injury	2 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	.28
Wound infection					.11
Medical treatment	5 (1.0)	5 (2.2)	0 (0.0)	0 (0.0)	
Operative intervention	1 (0.2)	0 (0.0)	1 (0.4)	0 (0.0)	
Other wound complication	14 (2.7)	7 (3.1)	7 (3.0)	0 (0.0)	.43
Postoperative length of stay, days	4.0 (2.0-5.0)	5.0 (4.0-7.0)	2.0 (2.0-4.0)	2.0 (1.0-3.0)	<.001
30-Day readmission					.004
Surgery service	21 (4.1)	13 (5.7)	7 (3.0)	1 (1.9)	
Medical or nonsurgical service	22 (4.3)	13 (5.7)	3 (1.3)	6 (11.1)	

MALR, Median arcuate ligament release; *SMA*, superior mesenteric artery; *VTE*, venous thromboembolism.
Data presented as number (%), mean ± standard deviation, or median (interquartile range).
[a]A total of 20 mesenteric vessels were revascularized in 19 patients.
[b]Missing data for 20.9%.
[c]Missing data for 15.5%.

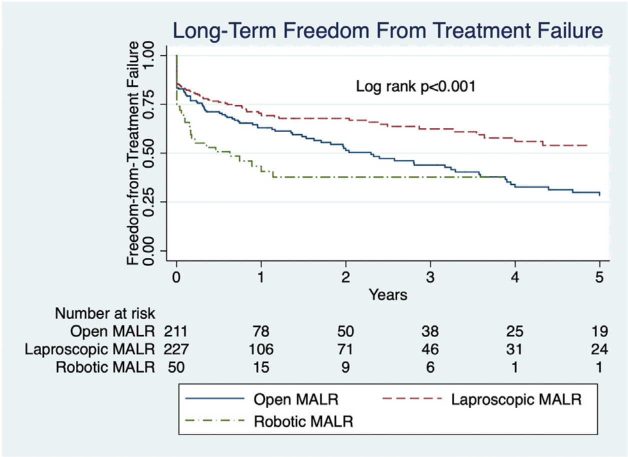

Fig 1. Kaplan-Meier curve for long-term freedom from treatment failure for open median arcuate ligament release (MALR; *solid blue line*), laparoscopic MALR (*dashed red line*), and robotic MALR (*green dot-dash line*). Standard error <10% for all available data.

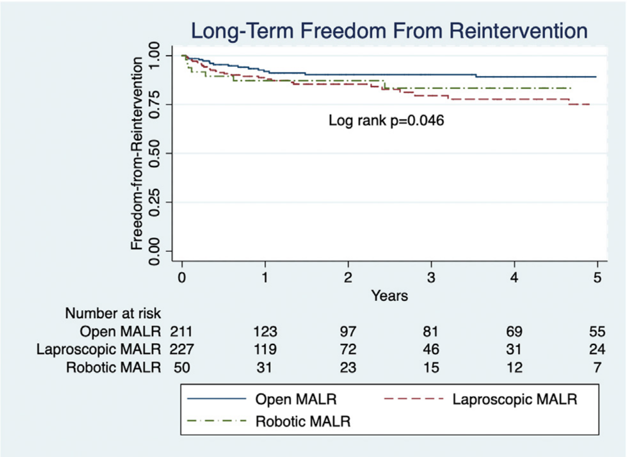

Fig 2. Kaplan-Meier curve for long-term freedom from reintervention for open median arcuate ligament release (MALR; *solid blue line*), laparoscopic MALR (*dashed red line*), and robotic-assisted laparoscopic MALR (*green dot-dash line*). Standard error <10% for all displayed data; standard error >10% after 8.3 years for laparoscopic MALR group.

and laparoscopic MALR when controlling for other factors. There is an overall paucity of data in the literature on robotic MALR. In a 2020 literature review, 62 cases were identified.[24] Complete and partial symptom relief had occurred 58.1% and 16.1% of the patients in the review, respectively. This rate of success was superior to our series. Of our patients who had undergone robotic MALR, only 37.7% had experienced complete or partial relief at 3 years after MALR. Direct comparisons between robotic MALR and other techniques have almost uniformly shown equivalence, with the caveat that the comparative groups had only included 5 to 30 patients per group.[12,25-27] The conclusion that robotic MALR is inferior should be interpreted with caution for three reasons. First, just as with the previously reported data, robotic MALR has been significantly underrepresented relative to open and laparoscopic MALR. Second, general surgeons have been significantly more invested in the robotic skill set but were underrepresented in this cohort compared with vascular surgeons. Finally, surgeons might still be overcoming the learning curve associated with performing MALR robotically, given that it is a relatively new technology. Further comparisons are necessary to determine the role of robotic MALR in treating MALS. However, the robotic cases had had a lower rate of vascular surgeon involvement in our cohort. We would advocate for involvement of vascular surgeons in the care of patients with MALS to manage celiac artery stenosis, assist in MALR and neurolysis, and prevent or address intraoperative arterial complications.

Few prior studies have had a sufficiently powered sample size to perform a robust multivariable analysis and identify the factors associated with long-term treatment failure. In terms of the predictors of failure, the response to a preoperative celiac plexus block can be used to predict the response to MALR for patients with MALS as described in a cohort from the Mayo Clinic. Of nine patients who had successfully undergone a celiac plexus block, all nine had achieved symptom relief after MALR.[28] However, little evidence has been reported to support this, and its use is not universal. Only 71 patients in our cohort had undergone a preoperative celiac plexus block. Our results support the celiac plexus block response as a prognostic modality to assist with patient selection and preoperative patient counseling. It is important to recognize that symptom relief after a celiac plexus block was not necessarily associated with success in our cohort—only a lack of symptom relief after a celiac plexus block was associated with a significantly higher treatment failure rate. In contrast, one patient who had not experienced symptom relief after the preoperative celiac plexus block had undergone MALR and achieved symptom relief. Thus, some degree of operator dependence undoubtedly exists with performance of the celiac plexus block, and the lack of symptom relief should not be considered an absolute contraindication to MALR, although such patients should be counseled regarding the higher risk of failure.

It has been widely accepted that other potential causes of abdominal pain should be excluded before MALR, and other investigators have incorporated nonvascular testing into diagnostic algorithms.[3,29] Our analysis has demonstrated that a more extensive workup will be associated with better symptomatic outcomes, suggesting that a complete diagnostic gastrointestinal evaluation is necessary before MALR. It can be difficult to

Table IV. Cox proportional hazards model for factors associated with treatment failure

Variable	HR	95% CI	*P* value
Robot-assisted laparoscopic MALR	1.73	1.16-2.59	.007
Age (per increasing year)	0.99	0.98-1.00	.012
Gastroparesis	1.83	1.09-3.09	.023
Abdominal cancer	10.3	3.06-34.6	<.001
Dysphagia or odynophagia	2.44	1.27-4.69	.008
No. of preoperative diagnostic gastrointestinal studies (per increasing No.)	0.84	0.74-0.96	.012
No relief from celiac plexus block	2.18	1.00-4.72	.049
No. of pain locations (per increasing No.)	1.12	1.00-1.25	.042

CI, Confidence interval; *HR*, hazard ratio; *MALR*, median arcuate ligament release.

parse out the symptoms of MALS from those of other known abdominal conditions. As such, a known history of gastroparesis or abdominal cancer, which can mimic the symptoms of MALS, has been associated with higher rates of treatment failure. Dysphagia/odynophagia and an increasing number of pain locations are atypical symptoms of MALS. However, it is important to remember that atypical presentations are possible and have been previously described.[30] Although prior studies have shown that a preoperative psychiatric diagnosis will be associated with inferior outcomes, psychiatric diagnoses were not associated with treatment failure in our cohort.[22,31] Each of these factors can be used to predict the potential response to MALR and guide an informed discussion with the patient about the risks and benefits of surgery preoperatively. Although patients with risk factors will have a higher hazard of treatment failure, MALR can still be successful for select patients. Thus, none of the risk factors we have identified should be considered a contraindication to MALR.

Celiac artery compression is a necessary component of a MALS diagnosis. As such, duplex ultrasound or angiography with breathing maneuvers, CTA, or MRA is a necessary part of the preoperative workup to confirm the presence of celiac artery compression.[3] However, no PSV or aortoceliac angle cutoff has correlated with symptom relief or reintervention after MALR. Although it might be tempting to suggest that some of the parameters showed a trend toward significance (eg, an increase in postoperative expiratory PSV, $P = .059$), it is important to remember that no correction for multiple testing was performed. As such, patients should not be considered to have a higher or lower risk of treatment failure or the need for postoperative reintervention from the imaging findings. Postoperative imaging studies to evaluate for residual celiac artery stenosis should also be used to guide reintervention in the setting of persistent symptoms.

Study limitations. Our study had some notable limitations. First, the VLFDC is a consortium primarily of vascular surgeons. Thus, general surgeons who perform MALR were underrepresented in our cohort, which might explain, in part, the inferior outcomes of robotic MALR. Ultimately, it remains unclear how a higher prevalence of general surgeons in the cohort might have affected the outcomes. Second, although the retrospective multicenter nature of our cohort enabled the compilation of a large sample size, details regarding the specific operative techniques such as the extent of neurolysis of the celiac plexus could not be reliably captured. Different degrees of ligament release and neurolysis could have contributed to the differences in outcomes. Similarly, we had limited data on the vascular anatomy and symptom response to reintervention after MALR. Accordingly, these limitations precluded determining whether MALS is a neurogenic or vascular problem. Third, the symptoms, including pain, could only be assessed qualitatively owing to the retrospective nature of our study. Other methods, such as objective quality of life surveys, might be more informative and quantifiable. Finally, the retrospective nature of the study left the data collectors completely reliant on the electronic medical records. It is possible that the symptoms were not comprehensively recorded in the medical documentation. Even with these limitations, the findings from our study are important, given the large, diverse cohort of patients compared with previous studies of this topic.

CONCLUSIONS

We found open and laparoscopic MALR were equally effective for long-term symptom relief and that robot-assisted laparoscopic MALR was associated with a higher hazard of treatment failure. However, the data for the latter modality remain limited. The factors associated with an increased hazard of treatment failure included robotic MALR, a history of gastroparesis, a history of abdominal cancer, dysphagia or odynophagia, no relief from a preoperative celiac plexus block, and an increasing number of pain locations. However, the use of an increasing number of preoperative diagnostic gastrointestinal studies was associated with a lower hazard of failure. The celiac plexus block is a useful modality for patient selection and prognostication. MALS remains a challenging entity to identify and treat, as indicated by the high rate of long-term treatment failure. Thus, continued studies to determine the etiology of MALS-related pain and optimal patient selection are needed.

AUTHOR CONTRIBUTIONS

Conception and design: CD, KW, PL, AD
Analysis and interpretation: CD, KW, PL, AD
Data collection: CD, KW, AP, RHG, AC, SY, GK, PH, MT, MBS, DG, BM, RD, PW, SI, VR, BA, LK, WS, KJ, RS, CA, GL, PB, MD, DM, MS, JY, RG, JL, DR, AG, PD, GC, FB, CW, MRS, BS, SH, ZS, EP, FS, NM, NJM, PL, AD
Writing the article: CD, AD
Critical revision of the article: CD, KW, AP, RHG, AC, SY, GK, PH, MT, MBS, DG, BM, RD, PW, SI, VR, BA, LK, WS, KJ, RS, CA, GL, PB, MD, DM, MS, JY, RG, JL, DR, AG, PD, GC, FB, CW, MRS, BS, SH, ZS, EP, FS, NM, NJM, PL, AD
Final approval of the article: CD, KW, AP, RHG, AC, SY, GK, PH, MT, MBS, DG, BM, RD, PW, SI, VR, BA, LK, WS, KJ, RS, CA, GL, PB, MD, DM, MS, JY, RG, JL, DR, AG, PD, GC, FB, CW, MRS, BS, SH, ZS, EP, FS, NM, NJM, PL, AD
Statistical analysis: CD, KW, PL, AD
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Overall responsibility: AD

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Additional material for this article may be found online at www.jvascsurg.org.

Supplementary Table I (online only). Variable definitions

Variable	Definition
Age	Age in years at surgery for median arcuate ligament release
Competing diagnosis	Another diagnosis that could potentially have caused the patient's symptoms, including GERD, gastroparesis, irritable bowel syndrome, inflammatory bowel disease, abdominal cancer, and other less common conditions that could have caused the symptoms
Psychiatric diagnosis	A documented psychiatric diagnosis from either the patient's PCP or a psychiatrist, including mood disorder (ie, depression, bipolar disorder), anxiety disorder, personality disorder, psychotic disorder, eating disorder, or other psychiatric disorder
Fibromyalgia	A documented diagnosis of fibromyalgia using the 2010 American College of Rheumatology diagnostic criteria for fibromyalgia
Alcohol use	Patient was consuming alcohol daily at preoperative evaluation
Substance abuse disorder	A documented diagnosis of substance abuse disorder, an ED visit for substance abuse disorder, or an inpatient visit for substance abuse disorder
Preoperative opioid use for pain	Patient actively taking opioid pain medications at preoperative evaluation
Chronic pain	A diagnosis of, or being treated for chronic pain located in any location other than the abdomen
Autonomic dysfunction	A documented diagnosis of autonomic dysfunction, including postural hypotension or orthostatic tachycardia syndrome
GERD	A documented diagnosis of GERD
Gastroparesis	A documented diagnosis of gastroparesis
Irritable bowel syndrome	A documented diagnosis of irritable bowel syndrome
Inflammatory bowel disease	A documented diagnosis of inflammatory bowel disease, including Crohn disease or ulcerative colitis
Migraines	A documented history of migraines
Cancer	A documented diagnosis of cancer

(Continued)

Supplementary Table I (online only). Continued.

Variable	Definition
Diabetes mellitus	A documented diagnosis of diabetes mellitus (type 1 or 2) using hemoglobin A1c, fasting plasma glucose, oral glucose tolerance test, or random plasma glucose test at any point during their lifetime (per American Diabetes Association guidelines)
Hypertension	A document diagnosis of hypertension (>130 mm Hg systolic or >80 mm Hg diastolic) from an average of ≥2 recordings from 2 separate visits
Active smoking	Patient engaging in use of cigarettes, pipes, or cigars on a daily basis ≤6 weeks of index median arcuate ligament release
Congestive heart failure	A documented diagnosis of heart failure classified using New York Heart Association guidelines as class III or class IV
Coronary artery disease	Coronary artery disease evidenced by findings on a stress test or coronary angiogram (≥50% stenosis), a formal diagnosis of coronary artery disease, previous myocardial infarction, or previous coronary revascularization (PCI or CABG)
Chronic kidney disease	A documented diagnosis of chronic kidney disease of stage ≥3 (eGFR <60 mL/min/1.73 m^2)
Dysphagia or odynophagia	Trouble or pain with swallowing, including sensation of food stuck in throat
Positional change of pain	Symptoms changing with change of position (pain improving in supine position and worsened by leaning forward)
Postoperative ileus	Oral intolerance for >48 hours postoperatively, nausea, and/or vomiting, prompting de-escalation of oral diet
Perioperative myocardial infarction	A documented diagnosis of myocardial infarction by a documented elevation of troponin, electrocardiographic changes, or coronary intervention between 0 and 30 days after median arcuate ligament release

Supplementary Table I (online only). Continued.

Variable	Definition
Perioperative acute venous thromboembolism	A documented diagnosis of DVT and/or PE between 0 and 30 days after median arcuate ligament release
Perioperative acute kidney injury or renal failure	A documented increase in serum creatinine of 0.3 mg/dL ≤48 hours or an increase in serum creatinine of ≥1.5 times the baseline (according to the Kidney Disease Improving Global Outcomes clinical practice guidelines)
Mesenteric ischemia	Signs and/or symptoms of mesenteric ischemia and/or an intervention required for acute mesenteric ischemia ≤30 days after index operation
Wound infection	Signs of wound infection (including, but not limited, to erythema, purulent drainage) present ≤30 days after index operation
Other wound issues	Any other wound issues that had occurred that were not an infection
Length of stay after median arcuate ligament release	Duration of hospital stay in days after median arcuate ligament release
Unplanned readmission ≤30 days postoperatively	An unplanned hospital readmission ≤30 days of index median arcuate ligament release
Severe complications	Composite of return to operating room for bleeding, myocardial infarction, pulmonary embolism, mesenteric ischemia, and/or acute kidney injury

CABG, Coronary artery bypass grafting; *DVT,* deep vein thrombosis; *ED,* emergency department; *eGFR,* estimated glomerular filtration rate; *GERD,* gastroesophageal reflux disease; *PCI,* percutaneous coronary intervention; *PCP,* primary care physician; *PE,* pulmonary embolism.

Supplementary Table II (online only). Data on radiographic studies parameters (N = 516)

Variable	Value
Patients with aortoceliac angle data on preoperative imaging	359 (69.6)
Aortoceliac angle on preoperative imaging, °	22.0° ± 15.7°
Patients with data on PSV with inspiration on preoperative duplex ultrasound	248 (48.1)
PSV with inspiration on preoperative duplex ultrasound, cm/s	261.4 ± 107.9
Patients with data on PSV with expiration on preoperative duplex ultrasound	234 (45.3)
PSV with expiration on preoperative duplex ultrasound, cm/s	320.2 ± 121.2
Patients with data on resting PSV on preoperative duplex ultrasound	158 (30.6)
Resting PSV on preoperative duplex ultrasound, cm/s	294.0 ± 121.3
Patients with aortoceliac angle data on postoperative imaging	142 (27.5)
Aortoceliac angle data on postoperative imaging, °	30.2° ± 15.2°
Patients with data on PSV with inspiration on postoperative duplex ultrasound	223 (43.2)
PSV with inspiration on postoperative duplex ultrasound, cm/s	219.7 ± 92.4
Patients with data on PSV with expiration on postoperative duplex ultrasound	227 (44.0)
PSV with expiration on postoperative duplex ultrasound, cm/s	246.5 ± 105.9
Patients with data on resting PSV on postoperative duplex ultrasound	28 (5.4)
Resting PSV on postoperative duplex ultrasound, cm/s	245.9 ± 130.0

PSV, Peak systolic velocity.
Data presented as number (%) or mean ± standard deviation.