

Echocardiographic changes and quality of life after surgical unroofing of myocardial bridges

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Abstract

Objective: To examine the echocardiographic changes and quality of life (QoL) after surgical unroofing of myocardial bridges (MBs) involving the left anterior descending (LAD) coronary artery compared with optimal medical therapy (OMT).

Methods: Twenty-two patients (median age, 24 years; interquartile range, 16–40 years) with MBs of the LAD artery and exertional angina from 2018 to 2019 were retrospectively analyzed. Twelve patients underwent OMT and 10 underwent surgery. Both groups underwent clinical and echocardiographic examinations during hospitalization and follow-up (mean, 1.0 ± 0.8 years). QoL was assessed with the Seattle Angina Questionnaire, short version (SAQ-7).

Results: Surgery resulted in significantly better QoL than OMT, with a significant improvement in left ventricular global longitudinal strain (GLS) [mean (standard error): 19% (0.19) to 22% (0.34) and 19% (0.15) to 20% (0.24), respectively; delta-change (delta-GLS) of 0.15 vs. 0.067]. In the

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univariate and multivariable analyses, delta-GLS was positively correlated with the SAQ-7 score and MB length ($\rho = 0.64$ and 0.71 , respectively), with a significant interaction between MB length and surgical treatment (beta coefficient, 1.95 ; 95% confidence interval, $0.14-3.77$).

Conclusions: MB unroofing surgery provided benefits in terms of QoL and left ventricular GLS improvement compared with 1 year of OMT.

Keywords

Myocardial bridge, quality of life, unroofing procedure, global longitudinal strain, myocardial function, echocardiography, Seattle Angina Questionnaire, optimal medical therapy

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Introduction

A myocardial bridge (MB) is a congenital abnormality defined as a muscle bridge overlying a segment of an epicardial coronary artery.¹ MBs primarily involve the left anterior descending (LAD) branch of the left coronary artery, resulting in a tunneled artery course beneath the myocardium.^{1,2} The incidence of MBs varies from 5% to 16% depending on the diagnostic imaging technique used [angiography or coronary computed tomography (CT)].³ Autopsy series have revealed a prevalence of approximately 25%.⁴

An MB produces reiterated systolic compression of the tunneled artery and persistent compression in mid to late diastole with a relative phase of non-compression during early diastole, during which time coronary arteries are mainly perfused.^{5,6} For this reason, MBs were traditionally considered as incidental and free of clinical implications.¹ Despite this belief, MBs have often been associated with angina, myocardial ischemia, and sudden cardiac death.^{3,7} Left ventricular (LV) dysfunction, myocardial stunning, and exercise-induced ventricular tachycardia may also be documented in patients with MBs.^{2,8,9}

A resting electrocardiogram (ECG) is frequently normal, while stress tests may induce nonspecific signs of ischemia or arrhythmias.³ Evaluation of myocardial ischemia can be particularly challenging in this context; perfusion defects are not usual and can be detected by myocardial scintigraphy.^{1,2} However, intracoronary hemodynamic assessment with dobutamine infusion as well as fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) quantification have demonstrated abnormalities in patients with hemodynamically relevant MBs.¹⁰⁻¹²

Because MBs are anatomical abnormalities, medical treatment is typically palliative, and therapy cessation may result in symptom reactivation.¹³ First-line therapy for angina-like symptoms consists of beta blockers, calcium channel blockers, or nitrates.^{14,15} Conversely, patients with MBs that are refractory to medical treatment (both adult and pediatric patients) may benefit from surgical unroofing.^{13,16}

Given these premises, this study was performed to examine the echocardiographic changes and quality of life (QoL) status in patients with MBs refractory to optimal medical therapy (OMT) after LAD unroofing surgery compared with patients who underwent OMT.

Methods

Study design and population

In this multicenter, retrospective, cross-sectional study, we used the databases of our Institutes (“Ospedali Riuniti” of Ancona and “SS. Annunziata” of Chieti) to select 22 patients [median age, 24 years; interquartile range (IQR), 16–40 years; all male] who had been referred for exertional angina with Canadian Cardiovascular Society (CCS) class II (IQR, class II–III) angina pectoris and who showed an MB of the LAD artery on CT from 2018 to 2019.

In our cohort, 12 patients (median age, 46 years; IQR, 40–52 years) were successfully treated with beta blockers or calcium channel blockers for symptomatic relief.¹⁴ Despite OMT, 10 patients (median age, 20 years; IQR, 18–22 years; 3 adolescents and 7 adults) underwent surgical unroofing because of refractory angina (continued reported episodes for ≥ 3 months after OMT titration)¹⁷ and the demonstration of hemodynamically significant MBs on angiographic FFR/iFR evaluation ($\leq 0.80/0.89$, respectively).

All patients in both the surgery and OMT groups underwent clinical and echocardiographic examinations before treatment (at hospitalization) and after treatment (follow-up), including two-dimensional speckle-tracking echocardiography. Pre- and post-treatment echocardiographic and clinical data were obtained from the stored images and clinical records in our databases, and additional data were collected through telephone calls. The mean duration of follow-up was 1.0 ± 0.8 years.

In agreement with the Declaration of Helsinki, all patients enrolled in this study provided written informed consent at the time of their evaluation, stating that their data and images may be subsequently

used for research purposes. For participants aged <16 years, a parent and/or legal guardian provided informed consent. Given the retrospective nature of the study, ethical committee approval was not required; however, our Institutional Board (Ospedali Riuniti Ancona – SOD CCPC) approved the study protocol (Ref. CCPC-001/18). All procedures were conducted in accordance with relevant international guidelines^{3,18} and our institutional regulations. The protocol was registered on ClinicalTrials.org.

Definitions of variables

The patients were divided into a surgery group and OMT group. The latter comprised all patients who presented with exertional angina and were successfully treated with beta blockers or calcium channel blockers.

Bisoprolol was administered at a starting dosage of 1.25 mg/day and increased each week; the dosage did not exceed 10 mg/day. Metoprolol was administered at a starting dosage of 100 mg/day divided every 12 hours; the dosage was increased each week and did not exceed 400 mg/day. Diltiazem was used only in patients aged >18 years; the dosage increased from 30 mg every 6 hours to 180 to 360 mg/day and did not exceed 360 mg/day. All medications were orally administered.

The surgery group included all patients with MBs who underwent surgical unroofing of the LAD coronary artery. Medical therapy was administered to these patients for a mean period of 2.0 ± 0.5 years (from 2016 to 2018) and titrated at the maximal dose tolerated without the onset of bradycardia or hypotension. All unroofing procedures were performed under cardiopulmonary bypass (mean extracorporeal circulation time, 105 ± 47 minutes; mean temperature, $32^\circ\text{C} \pm 3^\circ\text{C}$). No major

complications occurred during the postoperative period. No medications (beta blockers or calcium channel blockers) were used during postsurgical follow-up.

CT examinations

Coronary CT imaging revealed MBs in all patients. A tunneled myocardial segment of the LAD artery, presenting as a muscular bridge overlying the coronary artery, was considered positive for MBs (Figure 1).

All CT examinations were performed using a 384 (192 × 2)-slice third-generation scanner (SOMATOM Force CT; Siemens Healthineers, Erlangen, Germany) with patients in the supine position and the feet pointed toward the gantry. Images were acquired at an isotropic resolution of 0.5 to 0.75 mm in a 25-cm field of view. Patients received a nonionic low-osmolality contrast agent (iodixanol; GE Healthcare Life Sciences, Chalfont, United Kingdom) with a volume of 30 to 120 mL

(1.0–1.5 mL/kg) and flow injection rate of 3 to 5 mL/s, followed by saline injection administered intravenously using a power injector at the same volume and velocity.

The scanning area began from the upper limit of the sternum to 1 cm below the diaphragm in the superior-to-inferior direction. The scans were acquired with a 70- to 120-kV tube voltage using an automatic tube current modulation technique (CARE Dose technology; Siemens Healthineers). A prospective ECG-triggered axial coronary protocol was applied in a step-and-shoot scan mode, and the exposure time was adjusted between 40% and 70% of the cardiac cycle. Bolus triggering was used for scan initiation.

Coronary angiography

All patients underwent coronary angiography after CT examinations. The catheterization procedures were performed from either a radial or femoral arterial access

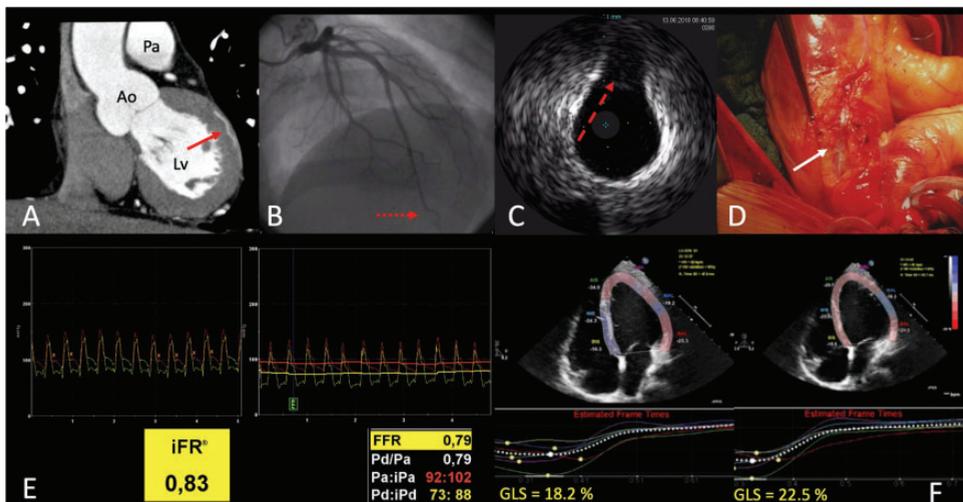


Figure 1. Multimodality imaging evaluation of a patient with an MB who underwent surgical unroofing. (a) Computed tomography. The arrow indicates the MB. (b) Coronary angiography. The dotted arrow indicates the MB. (c) Intravascular ultrasound. The dashed arrow indicates the half-moon sign. (d) Intraoperative picture of the unroofed MB (arrow). (e) FFR and iFR intravascular evaluation. (f) Two-dimensional speckle-tracking left ventricular global longitudinal strain analysis. MB, myocardial bridge; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio.

depending on the patients' age and vascular access availability. All patients received 5000 IU (for adults) or 100 IU/kg (for adolescents) of unfractionated heparin¹⁹ and 200 µg (for adults) or 3 µg/kg (for adolescents) of nitrates²⁰ before insertion of the guidewire to control the vasomotor tone.²¹

Basal angiography was obtained in different angiographic views for optimal visualization and characterization of the MBs. Intravascular ultrasound using a 40-MHz mechanical catheter (Atlantis SR Pro2; Boston Scientific, Marlborough, MA, USA) was performed to determine the presence of the MB, visualizing the characteristic half-moon sign (Figure 1), then to measure the length and thickness of the MB. Recordings were obtained during an automated pullback at 0.5 mm/s after the intravascular ultrasound catheter had been placed distally in the LAD artery.

The FFR and iFR measurements were obtained with the use of a coronary pressure guidewire (Philips/Volcano, San Diego, CA, USA). A threshold level of ≤ 0.80 for FFR and ≤ 0.89 for iFR was considered positive for hemodynamically relevant MBs. Both measurements were performed in basal conditions and after intravenous administration of dobutamine for inotropic stimulation. The infusion started at 10 µg/kg per minute and then increased by 5 µg/kg per minute every 5 minutes, up to 20 µg/kg per minute or until the patient developed symptoms. If patients did not develop symptoms or ischemia with 20 µg/kg per minute of dobutamine infusion, they were considered negative and did not require further evaluation.

Traditional and speckle-tracking echocardiography

All echocardiographic studies were performed using a commercially available Philips iE33 ultrasound system (Philips

Medical Systems, Amsterdam, the Netherlands), utilizing a 2.5- or 3.5-MHz transducer as appropriate. Images were acquired at a frame rate of >60 frames/s, applying a standard conventional two-dimensional gray-scale echocardiographic view. Images of three consecutive heart cycles were collected from the two-, three-, and four-chamber views. Pulsed-wave Doppler and tissue Doppler imaging of the mitral inflow was also acquired.

According to our internal protocol, all preoperative and postoperative echocardiographic images were stored and were available in the core laboratory of our institutes for further analysis. The echocardiographic images selected for postoperative and OMT evaluations were those acquired during the last available visit within 1 year of follow-up. QLab software (Philips Medical Systems) was used for offline retrospective strain analysis (Figure 1).

Two independent physicians (E.B. and V. B.), both experts in echocardiography and speckle-tracking analysis, reviewed and reanalyzed the stored images in a double-blind fashion (diagnosis and groups).

QoL assessment

During follow-up, all patients were asked to respond to a three-domain form questionnaire, the Seattle Angina Questionnaire, short version (SAQ-7), through telephone calls. This form comprises seven questions grouped in three main domains for QoL, physical limitation, and angina frequency assessment.^{22,23} The SAQ-7 is valid, reproducible, and sensitive to changes,²³ and it has been largely validated in the context of angina due to both coronary artery diseases and MBs.¹³

Statistical analysis

To the best of our knowledge, the largest study to date that evaluated the effects of

unroofing surgery in patients with symptomatic MBs enrolled only 14 participants.¹³ Therefore, we determined a sample size of 15 participants to gain sufficient statistical power at the 95% confidence interval (CI) and precision of 0.05.

Categorical variables are expressed as percentages, and continuous variables are presented as mean \pm standard deviation or median (IQR), as appropriate. Mean values of echocardiographic parameters and their corresponding standard errors are presented according to the defined groups after adjustment for age and body surface area. Adjustments derived from linear regression models, in which the variables were weighted for their regression coefficient, were computed to standardize the sample from differences derived from a different age and body surface area distribution. LV global longitudinal strain (GLS) was entered into the models as the absolute value.

Differences in continuous variables were assessed using Student's t-test, and differences in categorical variables were assessed using the chi-square test. Spearman's rho coefficient was calculated to determine the linear relationships between variables and the absolute LV GLS change before and after unroofing (delta-GLS). The latter was normalized for the basal value according to the following formula: (presurgical LV GLS – postsurgical LV GLS)/presurgical LV GLS.

A multivariable linear regression model was used to determine the beta coefficients for delta-GLS. According to the Kolmogorov–Smirnov test, variables with a non-normal distribution were logarithmically transformed before entering them into the multivariable analysis. Because of the small size of the study cohort, the model was tested only for age, body surface area, MB length and thickness, SAQ-7 score, and therapeutic strategy without further

adjustments. The latter should be considered explorative.

The interobserver agreement for the adjudicated double-blinded retrospective diagnosis was assessed by means of the kappa (k) statistic coefficient. A k of 1 indicated perfect agreement, a k of 0 indicated poor agreement, and the associated significance of the P-value indicated that the estimated k was not caused by chance alone.

A two-tailed P-value of 0.05 was considered statistically significant. All statistical analyses were performed with Stata v14.1 (StataCorp, College Station, TX, USA) and Prism 8.0 (GraphPad Software, La Jolla, CA, USA).

Results

General characteristics

Pretreatment clinical characteristics, relevant diagnostic data, and medications in the surgery and OMT groups are presented in Table 1. No statistically significant differences in the demographic and anthropometric characteristics, ECG findings, or previous medication regimens were found between the two groups. No differences in symptoms were found between adults and younger patients with the exception of the youngest patient (16 years of age), in whom angina was initially misinterpreted as palpitations.

No major complications occurred during hospitalization. After discharge, no patients in the surgery group required cardiac support or medications, and all patients were discharged without complications. After a mean follow-up of 1.0 ± 0.8 years, all patients in both the surgery and OMT groups were alive with CCS class I (IQR, I–II) angina pectoris. In the surgery group, only one patient developed post-pericardiotomy syndrome, which was effectively treated with ibuprofen therapy at 600 mg every 8 hours for 2 weeks with

Table 1. General characteristics of patients in surgery and OMT groups.

Anthropometric characteristics	Total N = 22	Surgery n = 10	OMT n = 12	P value
Age, years	25.9 ± 14.8	20.5 ± 3.0	26.7 ± 15.3	0.50
Weight, kg	67.3 ± 19.5	76.6 ± 13.8	67.3 ± 21.2	0.47
Systolic blood pressure, mmHg	122.4 ± 15.4	130.1 ± 16.1	122.4 ± 12.2	0.38
Diastolic blood pressure, mmHg	73.4 ± 8.8	81.2 ± 9.6	71.9 ± 10.1	0.06
Body surface area, m ²	1.7 ± 0.3	1.8 ± 0.1	1.7 ± 0.3	0.52
MB characteristics				
Length, mm	31 ± 12	41 ± 10	23 ± 6	<0.001
Thickness, mm	4 ± 1	3.5 ± 0.8	4 ± 1	0.35
Right coronary dominance	11 (50%)	4 (40%)	7 (60%)	0.73
FFR	0.81 ± 0.02	0.79 ± 0.01	0.83 ± 0.01	<0.001
iFR	0.90 ± 0.03	0.87 ± 0.01	0.93 ± 0.02	<0.001
ECG findings				
Bradycardia	5 (22%)	1 (10%)	2 (17%)	0.93
LVH	9 (39%)	5 (50%)	5 (42%)	0.69
RBBB	2 (9%)	1 (10%)	1 (8%)	0.89
TWI	7 (30%)	3 (30%)	4 (33%)	0.86
Stress tests				
Scintigraphy	11 (50%)	6 (60%)	5 (42%)	0.39
Ergometric stress test	7 (32%)	3 (30%)	4 (33%)	0.86
Echo stress	4 (18%)	1 (10%)	3 (25%)	0.36
Positive stress test	7 (30%)	3 (30%)	4 (33%)	0.86
Medications*				
Bisoprolol	10 (37%)	5 (50%)	5 (42%)	0.69
Dose, mg	10 (5–10)	5 (2.5–10)	10 (5–10)	0.37
Metoprolol	7 (45%)	2 (20%)	5 (42%)	0.27
Dose, mg	150 (150–200)	150 (150–200)	175 (150–200)	0.36
Diltiazem	5 (23%)	3 (30%)	2 (17%)	0.45
Dose, mg	180 (300–360)	330 (180–360)	330 (300–360)	0.52

Data are presented as mean ± standard deviation or median (interquartile range) for quantitative variables and as count (proportion) for categorical variables.

*Medication regimen before the unroofing procedure in the surgery group.

Boldface P values are statistically significant.

OMT, optimal medial therapy; MB, myocardial bridge; ECG, electrocardiogram; LVH, left ventricular hypertrophy; TWI, T-wave inversion; RBBB, right bundle branch block; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio.

subsequent tapering by 200 mg per day every 2 weeks.²⁴

Characteristics of MBs

The characteristics of MBs derived from the angiographic evaluations in the surgery and OMT groups are listed in Table 1. All MBs exhibited a systolic milking sign, while half of the entire sample exhibited right

coronary dominance (11/22, 50%). The MBs in the surgery group were longer than those in the OMT group (41 ± 10 vs. 23 ± 6 mm, respectively; P < 0.001). No statistically significant difference was found in MB thickness.

The invasive angiographic assessment after intracoronary dobutamine infusion demonstrated hemodynamic significance of the MBs subsequently assigned to the surgery

group: mean FFR of 0.79 ± 0.01 for surgery versus 0.83 ± 0.01 for OMT ($P < 0.001$) and mean iFR of 0.87 ± 0.01 for surgery versus 0.93 ± 0.02 for OMT ($P < 0.001$).

Echocardiographic characteristics and speckle-tracking analysis

The mean echocardiographic parameters after adjustment in the surgery and OMT groups are presented in Table 2.

In all patients, the Simpson's biplane echocardiographic LV ejection fraction, linear dimensions, and volumes were within the normal ranges in the pretreatment evaluation.²⁵ No patients exhibited ventricular hypertrophy, systolic anterior

movement of the mitral valve, or intraventricular gradients.

During follow-up in the surgery group, we found significant increases in the LV volume in both diastole and systole [mean (standard error): 57 (0.5) to 65 (0.5) mL/m², $P < 0.001$ and 20 (0.04) to 22 (0.5) mL/m², $P = 0.006$, respectively] and LV ejection fraction [64% (0.4) to 66% (0.4), $P = 0.002$]. One year after OMT, the LV linear dimensions and volumes showed no significant variations; however, the LV ejection fraction was significantly increased from 60% (0.4) to 62% (0.5) ($P = 0.005$).

With respect to diastolic function, septal e' changed from 12 (1.1) to 8 (0.9) in the surgery group with statistical significance ($P = 0.010$) and from 11 (1.1) to 9 (1) in

Table 2. Adjusted mean echocardiographic characteristics in surgery and OMT groups.

	Pre-Surgery		P value	Post-Surgery		P value	Pre-OMT		Post-OMT	P value
	n = 10			n = 12						
LV linear dimensions										
LV indexed end-diastolic diameter, mm/m ²	26 (0.9)	27 (1)	0.46	26 (0.8)	26 (1.2)	0.99				
LV indexed end-systolic diameter, mm/m ²	14 (0.8)	16 (0.9)	0.11	13 (1)	14 (1.5)	0.58				
Interventricular septum, mm	9 (0.6)	8 (0.7)	0.29	8 (0.6)	7 (0.8)	0.33				
Posterior wall, mm	9 (0.4)	9 (0.5)	0.99	8 (0.3)	8 (0.4)	0.99				
Relative wall thickness	0.38 (0.01)	0.37 (0.01)	0.49	0.36 (0.01)	0.36 (0.01)	0.99				
LV mass indexed, g/m ²	79 (0.5)	78 (0.8)	0.31	63 (1)	58 (1.1)	0.003				
LV volumes and function										
LV indexed end-diastolic volume, mL/m ²	57 (0.5)	65 (0.5)	<0.001	50 (0.6)	50 (0.5)	0.99				
LV indexed end-systolic volume, mL/m ²	20 (0.4)	22 (0.5)	0.006	20 (0.4)	19 (0.7)	0.23				
Ejection fraction, %	64 (0.4)	66 (0.4)	0.002	60 (0.4)	62 (0.5)	0.005				
Diastolic function										
E/A ratio	0.6 (0.3)	1.2 (0.2)	0.11	0.7 (0.3)	1.5 (0.3)	0.07				
Septal e' , cm/s	12 (1.1)	8 (0.9)	0.010	12 (1.1)	9 (1.0)	0.06				
Two-dimensional speckle-tracking analysis										
LV global longitudinal strain, %	19 (0.19)	22 (0.37)	0.0002	19 (0.15)	20 (0.18)	0.0012				

Data are presented as mean (standard error). Data are adjusted for age and body surface area.

Post-Surgery and post-OMT refer to follow-up; the latter lasted 1 year (1.0 ± 0.8 years).

Boldface P values are statistically significant.

OMT, optimal medical therapy; LV, left ventricular; E, mitral inflow E wave; A, mitral inflow A wave; E/A, E/A wave ratio.

the OMT group but without statistical significance. The E/A ratio improved from the pretreatment to post-treatment period in both groups, but without statistical significance.

Before treatment, the LV GLS was 19% (0.19) in the surgery group and 19% (0.15) in the OMT group. After 1 year, the LV GLS had significantly improved to 22% (0.37) in the surgery group ($P=0.0002$) and to 20% (0.24) in the OMT group ($P=0.0012$) (Figure 2), with an absolute delta-GLS of 0.15 vs. 0.067 ($P=0.007$).

Finally, we found good interobserver agreement between the two physicians in the LV GLS analysis (95%, $k=0.87$, $P<0.001$).

SAQ-7

A detailed representation of the SAQ-7 results is presented in Figure 3. After 1 year of follow-up, QoL was significantly better in the surgery than OMT group, with an overall SAQ-7 score of 95.2 versus

77.8, respectively ($P<0.001$). Patients in the surgery group reported less physical limitation ($P<0.001$) and lower angina frequency ($P=0.045$) than those in the OMT group, despite the fact that all patients (adult and pediatric) had post-treatment CCS class I angina pectoris according to their medical records.

Outcomes analysis

In the univariate analysis, the delta-GLS was positively associated with the MB length ($\rho=0.71$, $P<0.001$) and SAQ-7 score ($\rho=0.64$, $P<0.001$) (Figure 4). The univariate analysis showed no further correlations between variables.

The results of the multivariable analysis are shown in Table 3. The delta-GLS was positively correlated with the SAQ-7 score (beta coefficient, 0.76; 95% CI, 0.065–1.46; $P=0.035$), MB length (beta coefficient, 0.024, 95% CI, 0.002–0.047; $P=0.036$), and surgical unroofing strategy (beta coefficient, 5.38; 95% CI, 1.01–6.1; $P=0.031$). Additionally, a significant interaction was

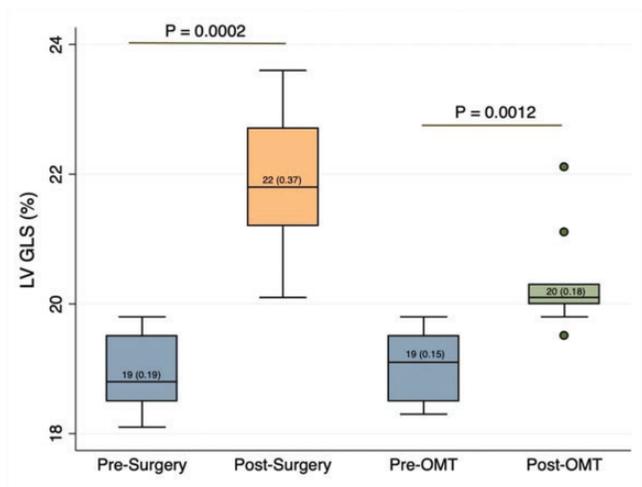


Figure 2. Differences in left ventricular two-dimensional speckle-tracking strain analysis before and after treatment: surgery and OMT. Post-Surgery and post-OMT refer to follow-up (1.0 ± 0.8 years). OMT, optimal medical therapy; LV GLS, left ventricular global longitudinal strain.

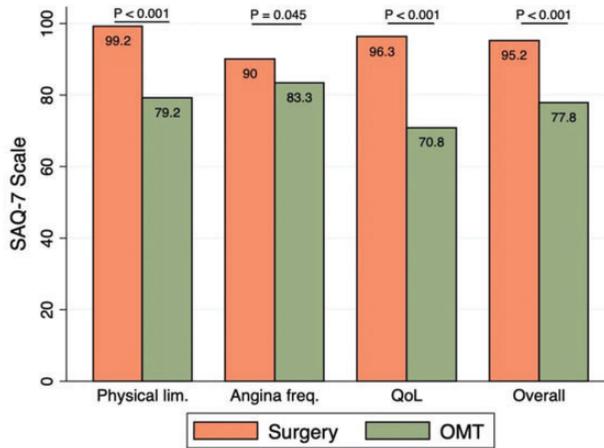


Figure 3. Differences in SAQ-7 scores before and after unroofing.

SAQ-7, Seattle Angina Questionnaire, short version; QoL, quality of life; OMT, optimal medical therapy; lim., limitation; freq., frequency.

found between MB length and surgery (beta coefficient, 1.95; 95% CI, 0.14–3.77; $P = 0.038$). MB thickness was not correlated with delta-GLS ($\rho = 0.094$, $P = 0.67$).

Discussion

In this small cohort of patients with symptomatic MBs characterized by angina and refractoriness to OMT, we observed basal LV GLS impairment that was nominally less than 20% to 22%.²⁶ After unroofing surgery, both adolescents and adults benefitted from the procedure in terms of symptomatic relief without major complications. Accordingly, the surgery group demonstrated significant improvement in QoL, with less physical limitation and lower angina frequency; these results were superior to those in the OMT group. The mean preoperative LV GLS increased during follow-up (19% to 22% vs. 19% to 20% in surgery vs. OMT group, respectively). The absolute change in the LV GLS was positively and independently associated with the MB length and surgical treatment.

Notably, this is the first study to confirm that a subtle form of myocardial contractility impairment may be found in patients with MBs,⁸ even in the presence of apparently normal cardiac function and OMT. We also demonstrated that surgical unroofing of MBs provides better QoL with less physical limitation and a lower angina frequency than does OMT in adults and adolescents. Moreover, the present study adds to the previous literature by providing 1-year follow-up outcomes in terms of QoL and angina relief; in fact, to the best of our knowledge, previous reports were limited only to pediatric populations with a 6-month follow-up.¹³ In addition, we demonstrated that the MB length may play a significant role in LV GLS improvement. The change in myocardial contractility, expressed as delta-GLS, was found to be positively and independently correlated with the MB length, with a significant interaction between MB length and surgical treatment in the multivariable analysis. These findings suggest that as the portion of the bridge affected by the muscular tunnel increases, the LV contractile

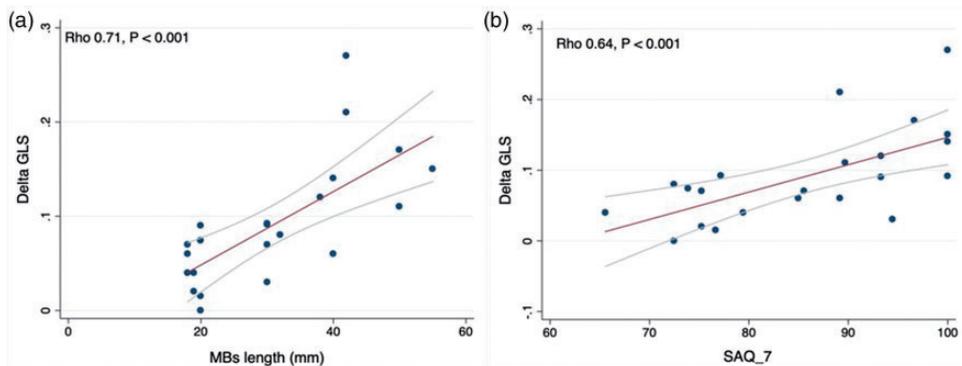


Figure 4. Linear relationships of delta-GLS with MB length and SAQ-7 score.

SAQ-7, Seattle Angina Questionnaire, short version; GLS, global longitudinal strain; Delta-GLS, absolute change between presurgical and postsurgical global longitudinal strain.

impairment worsens; therefore, a greater length of coronary unroofing is associated with greater benefit in terms of the change in LV GLS.

For many years, MBs were considered free of clinical implications despite reports of symptoms and events attributed to MBs. The latter is partially true; in fact, neither proximal stenosis of the MB nor systolic compression of the tunneled coronary segment can sufficiently explain an acute coronary syndrome. In contrast, experimental models of coronary occlusion that mimic the bridge pathophysiology suggest a dual mechanism of myocardial ischemia/hypoxia: systolic bridge compression and reduced diastolic perfusion time during tachycardia, exercise, or stress situations.^{2,5}

Coronary artery occlusion that is limited to systole produces phasic coronary blood flow in the whole length of the bridge. After the occlusion, the distal coronary pressure resumes with considerable delay during diastole, especially in the presence of tachycardia but also in all situations in which there is a reduced total diastolic time. This contributes to an increase in the coronary sinus lactate concentration and presumably to the development of conditions of chronic myocardial ischemia.² In the

above-described models, continuous systolic compression followed by increased compensatory diastolic flow results in a significant reduction in the mean coronary artery blood flow during the whole cardiac cycle. This continuous process of hypoxia and increased lactate may also lead to myocardial stunning, chronic reduction in myocardial contractility, and the development of symptoms.^{6,27,28}

Our findings suggest that MB length, more than thickness, may be associated with the development of myocardial ischemia/hypoxia. In fact, despite the presence of exertional angina, OMT resulted in normal iFR/FFR values and a shorter MB length. The angina was effectively treated with medications active for both cardiac frequency and catecholamine release. It is reasonable to argue that MBs are more prone to produce chronic myocardial injuries (with angina as the epiphenomenon) than acute events, probably supported by multiple stressors as tachycardia, increased catecholamines, or increased adrenergic tone. If these factors coexist, they may produce symptoms.^{3,5,7}

In the presence of a greater MB length, OMT may be not sufficient for symptom relief. The myocardial ischemia produced

Table 3. Correlates of LV GLS post-surgery increment (delta-GLS).

	Beta Coef.	95% confidence interval	P value
Age (per year)	0.05	0.47–0.57	0.830
BSA (per m ²)	0.39	0.86–16.5	0.491
Bridge thickness (per mm)	0.016	0.01–0.043	0.20
SAQ-7 overall score (per unit)	0.76	0.065–1.46	0.035
Bridge length (per mm)	0.024	0.002–0.047	0.036
Unroofing surgery (yes/no)	5.38	1.01–6.1	0.031

Boldface P values are statistically significant.

LV GLS, left ventricular global longitudinal strain; Coef., coefficient; BSA, body surface area; SAQ-7, Seattle Angina Questionnaire, short version.

by the MB may be enhanced by a greater MB length and greater hemodynamic relevance detected by the iFR/FFR investigation. The heterogeneity of the reports regarding patients with MBs can thus justify all these suggestions, although these phenomena were not demonstrated in the present study.^{3,5,7} More studies involving larger cohorts of patients with MBs are needed to test these hypotheses.

Limitations and strengths

The main limitations of this study are the small study sample and the cross-sectional design. Additionally, although we adjusted the analysis for age and body surface area, we cannot exclude residual confounders.

Rigorous patient selection was performed using our databases, and the SAQ-7 data were collected using telephone calls, providing a detailed and comprehensive evaluation of patients with MBs who were medically and surgically treated. This report could serve as a baseline for further investigations in this field.

Conclusions

Surgical unroofing of MBs can be safely accomplished in adolescents and young adult patients. In symptomatic patients whose condition is refractory to OMT, surgery seems to provide symptom relief and

benefits in terms of QoL and myocardial performance as assessed with two-dimensional speckle-tracking echocardiography. If confirmed in larger cohorts, these data suggest a potential role of surgery in this population.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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