The value of exercise SPET for the detection of coronary artery steal syndrome secondary to unligated major side branch of left internal mammary artery

Osman Beton[1] MD,
Hakki Kaya[1] MD,
Ozan Kandemir[2] MD,
Buket Alibazoglu[3] MD,
Haluk Alibazoglu[3,4] MD,
Ercan Karabey[1] RT,
Okan Onur Turgut[1] MD,
Mehmet Birhan Yilmaz[1] MD

1. Department of Cardiology, Heart Center, Cumhuriyet University, Sivas, Turkey.
2. Department of Nuclear Medicine, Numune State Hospital, Sivas, Turkey
3. CardioCheck Nuclear Imaging Center, Ankara, Turkey.
4. Department of Nuclear Medicine, Imaging Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates.

Abstract

Objective: The clinical significance of unligated major left internal mammary artery (LIMA)-side branches (SB) remains controversial in patients with previous coronary artery bypass graft (CABG) surgery. The aim of this study was to investigate the clinical significance of unligated major LIMA-SB by using exercise myocardial perfusion imaging (MPI) with single-photon emission tomography. **Subjects and Methods:** We conducted a retrospective analysis of 2819 consecutive patients who underwent diagnostic angiography. There were 407 CABG patients with LIMA graft. The demographic, laboratory, pre-angiographic stress test and angiographic data of these patients were collected. A subgroup of patients with unligated major LIMA-SB who were referred to angiography with the diagnosis of stable angina pectoris and positive exercise MPI was identified and divided into two groups for comparison: anterior wall vs non-anterior wall ischemia groups. **Results:** Among 407 patients with LIMA graft, 112 (27.5%) patients were found to have unligated major LIMA-SB. In a subgroup of patients (n=45) with positive exercise MPI and patent LAD-LIMA system with unligated major LIMA-SB, the median values of diameter and length of unligated major LIMA-SB were statistically higher in anterior wall ischemia group (n=24) compared to non-anterior wall ischemia group (1.8mm vs 0.6mm, $P<0.001$ and 17.0cm vs 8.0cm, $P<0.001$, respectively). The cut-off values of unligated major LIMA-SB length and diameter were 11cm and 1.3mm respectively. Unligated major LIMA-SB with a length of ≥11.0cm and a diameter of >1.3cm had 95.8% of sensitivity and 100% of specificity for predicting anterior wall ischemia on exercise MPI. In patients with anterior wall ischemia, summed stress score and summed difference score were improved after percutaneous coil embolization of large unligated major LIMA-SB with ≥11.0cm length and >1.3mm diameter. **Conclusion:** Large unligated major LIMA-SB with ≥11.0cm length and >1.3mm diameter seems to be a potential source of ischemia in CABG patients. We suggest that exercise MPI might be a first option noninvasive test in evaluating the clinical significance of unligated major LIMA-SB and the effectiveness of embolization therapy.

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Corresponding author:
Osman Beton MD,
Department of Cardiology,
Heart Center, Cumhuriyet University,
PC 58140, Sivas, Turkey
Tel: +90-346-258-1833,
Fax: +90-346-219-1268
obeton@cumhuriyet.edu.tr

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Introduction

The left internal mammary artery (LIMA) which is also known as the internal thoracic artery, is the gold-standard graft for surgical revascularization of left anterior descending artery (LAD) due to high long-term patency rates and favorable prognosis compared to vein grafts [1-2]. Myocardial ischemia after coronary artery bypass grafting (CABG) surgery can occur due to numerous reasons [3-4]. The coronary artery steal syndrome secondary to unligated major side branches (SB) of LIMA (LIMA-SB) is one of the possible reasons for myocardial ischemia after CABG [3-4]. The major LIMA-SB is lateral costal artery which is also known as the first large intercostal artery, lateral internal mammary artery or lateral internal thoracic artery which is found in 15%-30% of the population [5-6]. It has been assumed that a large unligated major LIMA-SB can divert blood flow from LIMA and cause myocardial ischemia (anterior wall) [7].

Angiographic studies revealed that the incidence of unligated major LIMA-SB is 9% to 30% in patients with prior CABG surgery [8-10]. Doppler studies demonstrated that the steal of blood flow from LIMA graft by a SB feeding intercostal muscles is unlikely based on physiologic principles, because the arterial flow to the intercostal muscle is predominantly systolic whereas it is predominantly diastolic in LAD [11-13]. However, these studies did not definitively conclude that coronary artery steal syndrome secondary to unligated major LIMA-SB cannot occur. On the contrary, there are increasing numbers of case reports supporting the concept of coronary artery steal syndrome secondary to large unligated major LIMA-SB by demonstrating the reversal of the anterior wall myocardial ischemia after occlusion of large unligated major LIMA-SB [13-16]. In patients with large unligated major LIMA-SB, angina might occur especially during exercise because of simultaneous increase in oxygen demand by both myocardium and intercostal muscles. Myocardial perfusion imaging (MPI) with single-photon emission tomography (SPET) in particular is a well-established technique to evaluate the hemodynamic significance of a stenosis [17, 18]. Myocardial perfusion imaging with SPET is also a useful noninvasive test to detect the recurrence of myocardial ischemia after CABG [19]. Additionally, it was found that SPET is valuable for functional evaluation of stenosis in coronary artery bypass grafts [20]. Exercise stress MPI with SPET might be a useful non-invasive test method for the detection of coronary artery steal syndrome secondary to unligated major LIMA-SB.

The purpose of our study was to investigate the clinical significance of unligated major LIMA-SB by using exercise stress MPI with SPET and to determine the angiographic features of unligated major LIMA-SB leading to coronary artery steal syndrome.

Subjects and Methods

Study cohort

We conducted a retrospective analysis of 2819 consecutive patients who underwent diagnostic coronary angiography (CAG) between July 2013 and July 2015 at Cumhuriyet University Hospital. Among these 2819 patients, there were 459 patients with prior CABG. Among these 459 patients, 407 patients had LIMA graft distally anastomosed to LAD (no complex LIMA graft: H or Y or T grafting) and none of them had critical stenosis at left subclavian artery. Hence, our study cohort consisted of 407 patients with LIMA graft. All patients gave their informed consent. The study was performed in accordance with the Declaration of Helsinki for Human Research.

Data collection

Data of 407 CABG patients with LIMA graft were retrospectively collected from patients' medical files and computer based database system. Demographic features, details about previous CABG surgery, laboratory data and echocardiographic data were recorded. During echocardiographic evaluation, left ventricular ejection fraction was routinely calculated with modified Simpson's method [21].

Angiographic analyses of LIMA grafts

All 407 patients with LIMA grafts who had no left subclavian artery stenosis were included in detailed angiographic analyses. Diagnostic coronary angiography (CAG) records were assessed retrospectively via two experienced cardiologists, blinded to study plan, with special attention to unligated LIMA-SB. The LIMA was visually divided into three parts. Quantitative angiography was utilized for the remaining measurements. The diameter of LIMA was measured from distal one-third of LIMA before anastomosis. The presence of LIMA stenosis, its location and percent diameter stenosis were recorded. In case of multiple stenoses, stenosis with maximal lumen narrowing was considered for the analyses. The presence or absence of unligated major LIMA-SB was recorded. In the presence of unligated major LIMA-SB, its origin according to intercostal space and destination features was noted. The diameter of unligated major LIMA-SB was measured from the first 1cm distal to the origin. The length of unligated major LIMA-SB was measured from the origin to the end of the artery. Features of native LAD after LIMA anastomosis were also noted and the diameter of native LAD was measured from the first 1cm distal to the LIMA anastomosis. Left anterior oblique (5° to 30°) view was used for measurements of LIMA, LAD and unligated major LIMA-SB. Stenosis with <50% luminal narrowing was accepted as non-critical.

Subgroup of patients with unligated major LIMA-SB and ischemia on exercise SPET

One hundred and twelve patients with unligated major LIMA-SB (or lateral costal artery) were included initially in the subgroup analyses (please refer to flow chart in Figure 1). Clinical exclusion criteria of acute coronary syndromes, stable angina pectoris (SAP) without positive stress test and stress tests other than exercise stress MPI with SPET were applied (Figure 1). Am-ong the remaining 62 SAP patients with exercise stress MPI with SPET, 21 had non-anterior wall ischemia (Group 1) and 41 had anterior wall ischemia. In patients with anterior wall ischemia, 17 patients were excluded according to angio-graphic exclusion criteria: 8 patients with critical stenosis at native LAD distal to LIMA anastomosis, 2 patients with small calibrated native LAD (<1.5mm) distal to LIMA anastomosis, 4 patients with LIMA diameter <2.0mm or LIMA stenosis, and 3 patients with totally occluded LIMA distal to major LIMA-SB. Anterior wall ischemia group was consisted of the remaining 24 patients (group 2). Demographic, clinical, laboratory and angiographic features were compared in these groups.

Myocardial perfusion imaging technique and test interpretation

All subgroup patients underwent a symptom-limited treadmill exercise test using Bruce protocol and monitoring with a 12-lead electrocardiogram, heart rate and blood pressure during stress and recovery. Using the same day rest-stress imaging protocol, we performed technetium-99m methoxyisobutylisonitrile (^{99m}Tc-MIBI) gated SPET imaging at rest 45 minutes after intravenous (i.v.) injection of 370-555MBq ^{99m}Tc-MIBI. Stress imaging was performed 3 to 5 hours later (mean 3.5hrs), 10-15 minutes after the i.v. injection of 370-555MBq ^{99m}Tc-MIBI, at peak exercise. All images were acquired in the supine position using a Siemens Symbia S gamma camera (Siemens Healthcare, Illinois, USA) and a low energy high resolution collimator. Additionally, post-stress images were acquired in both the supine and prone position in order to identify attenuation artifacts due to breast and/or

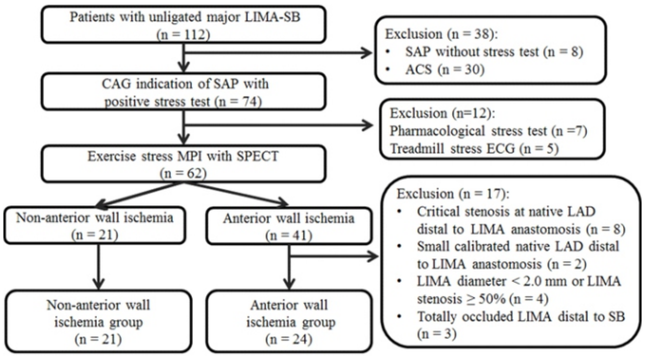


Figure 1. Flow chart of the patients who participated in the subgroup. ACS: acute coronary syndromes; CAG: coronary angiography; ECG: electrocardiography; LAD: left anterior descending artery; LIMA: left internal mammary artery; MPI: myocardial perfusion imaging; SAP: stable angina pectoris; SB: side branch.

excessive lateral chest-wall fat [22]. Each imaging set was acquired over a 180 degrees arc starting from 45 degrees right anterior oblique to 45 degrees left posterior oblique, 64 projections in circular orbit, 64 by 64 matrix size, 25 seconds per projection for stress and 20 seconds per projection for rest. All images were processed using a low-pass Butterworth filter, with a cut-off frequency at the range of 0.35-0.45 and an order of 5. Interpretation of myocardial perfusion images was performed by two experienced nuclear medicine specialists certified by the American Board of Nuclear Cardiology and the American Board of Nuclear Medicine, blind to any clinical information or patients' identity. A standard 17-segment model and semiquantitative scoring system was used for grading perfusion and function [23]. For the assessment of myocardial perfusion on stress and rest imaging, each segment was scored on a scale of 0 to 4 (0= normal activity, 1=mild, 2=moderate, 3=severe reduction in photon activity, 4=complete absence of photon activity). For each image, a summed stress score (SSS) and a summed rest score (SRS) was calculated by adding the segment scores. A summed difference score (SDS) was derived for each image by subtracting the SRS from the SSS.

Percutaneous coil embolization technique

The percutaneous coil embolization intervention was performed under local anesthesia, via a 6Fr right femoral artery puncture, in the angiography room. During the intervention, patients received a bolus of 100 IU/kg of i.v. heparin to achieve an activated clotting time >300 to 350 seconds. No specific sedation or prophylactic antibiotic treatment was administered. A 6 French LIMA guiding catheter was placed via the femoral artery. A micro-catheter was advanced over a 0.014" guidewire into the large unligated LIMA-SB through guiding catheter and placed distally to the one-third proximal SB artery. Pushable fibered platinum micro coils with 2-3mm diameter were delivered and deployed through the micro-catheter by using 0.018" coil pusher guidewire. A number of micro coils were deployed until full occlusion of the unligated major LIMA-SB artery (or lateral costal artery) was achieved (Figure 2). A control exercise stress MPI with SPET was performed in subgroup patients with anterior wall ischemia 3 months after the intervention (Figure 2).

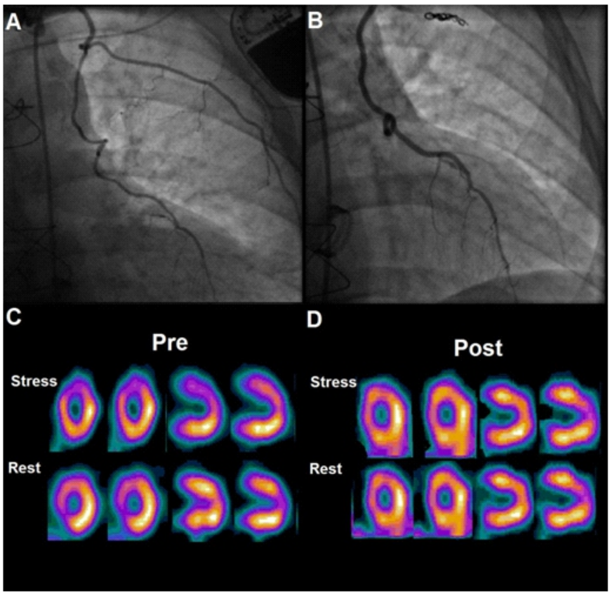


Figure 2. An example of percutaneous embolization of unligated major LIMA-SB in a patient who had persistent exercise angina for five years after CABG surgery. LIMA angiogram before embolization of major LIMA-SB (A). LIMA angiogram after coil embolization of major LIMA-SB (B). Exercise MPI before embolization of major LIMA-SB (C). Exercise MPI after coil embolization of major LIMA-SB (D). CABG: coronary artery bypass grafting; LAD: left anterior descending artery; LIMA: left internal mammary artery; MPI: myocardial perfusion imaging; SB: side branch.

Statistical analysis

The variables were investigated using analytical method (Kolmogorov-Smirnov test) to determine whether or not they were normally distributed. Continuous variables were expressed as mean±standard deviation or median (min-max) in the presence of abnormal distribution, and categorical variables as percentages. Comparisons between groups of patients were made by use of a χ^2 test for categorical variables, independent samples T test for normally distributed continuous variables, and Mann-Whitney U test when the distribution was skewed. Paired sample t test was used to compare means of SRS, SSS and SDS pre and post embolization procedure. All statistical analyses were performed using SPSS software version 22.0 (SPSS Inc., Chicago, IL) except sensitivity and specificity analyses which were performed by using MedCalc software version 15.11.4 [MedCalc inc, Mariakerke, Belgium (personal license of MBY)]. A P value of 0.05 was considered as statistically significant.

Results

Characteristics of study population

Baseline characteristics of 407 patients with LIMA graft to LAD are presented in Table 1. The median age of patients was 68 (41-89) years with 294 males (72.2%). The median left ventricular ejection fraction (EF) was 40% (20%-62%). Median time after the CABG was 10 (1-21) years. Stable angina pectoris with positive stress test was the diagnostic CAG indication in 46.7% of patients and acute coronary syndromes in 40.8% of patients.

Table 1. *Baseline characteristics of study population*

Variables	All patients (n=407)
Age, years	68 (41-89)
Male gender, n (%)	294 (72.2)
Body mass index, kg/m^2	27.6±5.2
Hypertension, n (%)	298 (73.2)
Diabetes mellitus, n (%)	147 (36.1)
Obesity, n (%)	118 (29.0)
Hyperlipidemia (%)	301 (74.0)
Smoking, n (%)	150 (36.9)
Alcohol, n (%)	39 (9.6)
COPD, n (%)	42 (10.3)
Prior stroke or TIA, n (%)	48 (11.8)
Heart valve prosthesis, n (%)	14 (3.4)
Pacemaker/ICD, n (%)	75 (18.4)
Atrial fibrillation, n (%)	96 (23.6)
LV ejection fraction,%	40 (20-62)
BUN, mg/dL	31.6 (22-80)
Creatinine, mg/dL	1.0 (0.6-2.8)
Hemoglobin, gr/dL	12.1 (7.0-14.5)
LDL cholesterol, mg/dL	131 (72-222)
Time passed after CABG surgery, year	10.0 (1.0-21.0)
Indication for CAG	
SAP without stress test, n (%)	51 (12.5)
SAP with positive stress test, n (%)	190 (46.7)
Acute coronary syndrome-NSTEMI, n (%)	151 (37.1)
Acute coronary syndrome-STEMI, n (%)	15 (3.7)

BUN: blood urea nitrogen; CABG: coronary artery bypass grafting; CAG: coronary angiography; COPD: chronic obstructive lung disease; ICD: implantable cardioverter defibrillator; LDL: low density lipoprotein; LV: left ventricle; NSTEMI: non ST elevation myocardial infarction; SAP: Stable angina pectoris; STEMI: ST elevation myocardial infarction; TIA: transient ischemic attack

Angiographic characteristics of LIMA graft and major LIMA-SB

Angiographic features of LIMA graft and unligated major LIMA-SB are presented in Table 2. Three hundred and twenty five (79.9%) patients had LIMA with diameter ≥2.0mm and stenosis <50%. The LIMA graft was totally occluded in 51 (12.5%) patients. Unligated major LIMA-SB was found in 112 (27.5%) patients. The median diameter and length of unligated major LIMA-SB was 0.9 (0.5-3.0)cm and 10.8 (4.0-24.1)cm, respectively. A positive correlation was found between diameter and length of major LIMA-SB (Spearman's rho=0.804, P<0.001).

Control exercise stress MPI with SPET after percutaneous coil embolization

Seventeen patients in anterior wall ischemia group were underwent percutaneous coil embolization of unligated major LIMA-SB. Procedure was successful in all these patients without any complication. Exercise capacity of these patients was improved after the embolization procedure. None of these patients had prior anterior MI. All patients were studied 4.0±1.0 months after the embolization procedure. Summed rest score, SSS and SDS were calculated for LAD related 7 segments in the standard 17-segment model

Table 2. *Angiographic features of LIMA grafts and major LIMA-SB*

Variables	All patients (n=407)
Patent LIMA-diameter ⩾2.0mm with stenosis <%50, n (%)	325 (79.9)
Patent LIMA-diameter ⩾2.0mm with stenosis ⩾%50, n (%)	16 (3.9)
Patent LIMA-diameter < 2.0mm with stenosis <%50, n (%)	8 (2.0)
Patent LIMA-diameter < 2.0mm with stenosis ⩾%50, n (%)	7 (1.7)
Totally occluded LIMA, n (%)	51 (12.5)
LIMA with major SB, n (%)	112 (27.5)
Diameter of major LIMA-SB, mm	0.9 (0.5-3.0)
Length of major LIMA-SB, cm	10.8 (4.0-24.1)

LIMA: left internal mammary artery; SB: side branch.

Table 3. *Characteristics of patients in subgroup*

Variables	Non-anterior wall ischemia group (n=21)	Anterior wall ischemia group (n=24)	P
Demographic			
Age, years	60±5	61±7	0.811
Male gender, n (%)	17 (81.0)	19 (79.2)	1.0
Body mass index, kg/m^2	26.5±5.0	29.3±6.2	0.106
Hypertension, n (%)	16 (76.2)	20 (83.3)	0.713
Diabetes mellitus, n (%)	7 (33.3)	11 (45.8)	0.583
Obesity, n (%)	4 (19.0)	9 (37.5)	0.302
Hyperlipidemia, n (%)	15 (71.4)	18 (75.0)	1.0
Smoking, n (%)	13 (61.5)	9 (37.5)	0.182
LV ejection fraction,%	46.7±9.8	44.5±6.0	0.615
Creatinine, mg/dL	1.1±0.4	0.92±0.3	0.105
Hemoglobin, gr/dL	11.7 ±1.6	12.1±1.7	0.408
Time passed after CABG surgery, years	2.8±0.8	3.5±1.2	0.242
Prior anterior MI, n (%)	4 (19.0)	3 (12.5)	0.689
Angiographic			
Diameter of major LIMA-SB, mm	0.6 (0.5-1.3)	1.8 (1.0-3.0)	<0.001
Length of major LIMA-SB, cm	8.0 (4.0-11.0)	17.0 (11.0-24.1)	<0.001
LIMA diameter, mm	2.8±0.7	2.6±0.7	0.428
LIMA to major LIMA-SB diameter ratio	4.3±1.7	1.5±0.6	<0.001
LAD diameter, mm	2.1±0.4	2.1±0.3	0.822

CABG: coronary artery bypass grafting; LAD, left anterior descending artery; LIMA: left internal mammary artery; LV: left ventricle; SB: side branch; MI, myocardial infraction.

before and after the embolization in these patients. Summed rest score was not different between pre and post embolization procedure (5.2±3.4 vs 5.2±3.1, P=1.0, respectively). Summed stress score and SDS decreased significantly after the embolization procedure (11.3±3.0 vs 6.5±2.7, P< 0.001 and 6.1±2.9 vs 1.3±1.2, P<0.001, respectively).

Discussion

To our knowledge, this is the first study investigating the dimensional features of unligated major LIMA-SB leading coronary steal syndrome which was demonstrated by exercise MPI with SPET. Also, this is the first study investigating the usefulness of exercise MPI with SPET not only for the detection of coronary steal syndrome secondary to unligated major LIMA-SB but also for the demonstrating the effectiveness of coil embolization procedure. We demonstrated that large unligated major LIMA-SB with ⩾11.0cm length and >1.3mm diameter has very high sensitivity and specificity for the prediction of anterior wall ischemia on exercise MPI. Furthermore, we showed that percutaneous coil embolization of large unligated major LIMA-SB causing anterior wall ischemia can improve SSS and SDS on MPI.

Angiographic studies found that the incidence of unligated major LIMA-SB is 9% to 30% in patients with prior CABG surgery [8-10]. Consistent with these studies, it was 27.5% in our study. None of these studies investigated the angiographic size of unligated major LIMA-SB and its dimensional relationship with coronary steal syndrome.

Coronary steal syndrome secondary to unligated major LIMA-SB is controversial according to Doppler flow based clinical [11] and experimental [12, 13, 24] studies. However, in the recent years, there are increasing numbers of case reports with coronary steal syndrome secondary to unligated major LIMA-SB who was successfully treated by embolization and the reversal of the ischemia was demonstrated after the embolization procedure [13-16]. Beside this debatable issue, surgeons prefer to ligate all SB of LIMA during classic CABG operation with sternotomy [6, 25]. Sometimes, SB can be left unligated because of access problems during operation. Side branches originating from more proximal parts of the LIMA are more prone to be left unligated. On the other hand, LIMA may not be harvested in its full length during minimally invasive direct CABG (MIDCABG) using old endoscopic harvesting techniques with minithoracotomy or ministernotomy and the proximal SBs of LIMA could be left unligated in most cases during MIDCABG [24, 26]. So, determining the characteristics of unligated major LIMA-SB which has potential to cause ischemia is clinically important because of relatively high prevalence in angiographic studies [8-10].

Up to now, various invasive and noninvasive tests were used to determine clinical significance of unligated LIMA SB. Invasive intracoronary Doppler studies evaluating distal LIMA flow at rest and after administration of intracoronary adenosine or left arm exercise during SB balloon occlusion demonstrated insignificant change in LIMA coronary flow reserve (CFR) [13]. Conversely, significant LIMA CFR increase was reported after adenosine administration with or without forced ventilation exercise during SB occlusion [27, 28]. Noninvasively, treadmill stress electrocardiography test was used to determine ischemia [13]. However, it is not able to locate ischemia, so have limited value for accessing LAD steal syndrome secondary to unligated major LIMA-SB. Stress MPI was used with capability of locating anterior ischemia secondary to large unligated major LIMA-SB and accessing improvement after SB occlusion procedure [13, 14]. Recently, MRI and dobutamine stress echocardiography were tried to determine ischemia due to unligated major LIMA-SB in some case reports [15, 29]. Up to date, we recorded that our patients with unligated major LIMA-SB have anginal complaints mostly during exercise. So, we hypothesized that increased oxygen demand of both myocardium and intercostal muscle should be present simultaneously in order to access clinical significance of LIMA SB. On the other hand, of 42 patients with anterior wall ischemia on exercise MPI, 17 (41.5%) patients were excluded from the subgroup analyses because of the presence of LAD (native LAD after LIMA anastomosis) or LIMA stenosis or small calibrated LAD or LIMA which can affect the result of exercise MPI. Also, not all unligated major LIMA-SB causes coronary steal syndrome. Exercise MPI with SPET seems to be helpful in differentiation of ischemia causing unligated major LIMA-SB from non-ischemia causing unligated major LIMA-SB, while exercise MPI cannot differentiate the ischemia due to coronary steal syndrome secondary to unligated major LIMA-SB from the ischemia due to real stenosis of LAD or LIMA.

From pathophysiological aspects towards coronary artery steal syndrome secondary to unligated major LIMA-SB, it is theoretically possible when large SB divert the flow away from the LIMA and compromise flow to the coronary bed, because of its relatively lower resistance as compared to a higher resistance of coronary bed [11, 13, 27]. However, previous studies postulated that in the presence of well-constructed LIMA graft to LAD anastomosis, LAD flow is mainly diastolic and unligated LIMA-SB (or intercostal artery branches of lateral costal artery) flow is mainly systolic, so the intercostal muscular and coronary territories do not share the same amount of flow because their hemodynamic phases are different and steal is not possible [11, 13]. These studies also postulated that coronary artery steal syndrome secondary to unligated LIMA-SB is possible in the presence of excessive selective muscular vasodilatation or technical imperfections of surgery or poor anatomical quality (small sized) of LIMA or LAD [11, 13]. Although these factors were not present in anterior wall ischemia group of our study, they had anginal complaints and demonstrated ischemia on exercise MPI. This might be explained by exercise response: during muscular activity oxygen demand increase in myocardium and intercostal muscle (due to ventilation), as a consequence combined systemic and coronary vasodilatation occurs leading an increase in both systolic and diastolic flow [11]. Additionally, it is well known that diastolic time decreases during exercise more markedly than systolic and experimental studies demonstrated that systolic to diastolic coronary blood flow ratio may increase during exercise [29, 30]. It is demonstrated that intercostal muscle blood flow increases linearly up to 90 minute ventilation (lmin-1) with the work of breathing during hyperpnoea [31]. Briefly, both diastolic and systolic flow might be needed for adequate perfusion of LAD area from LIMA during exercise. So, combined effect of decreased diastolic perfusion time of LAD during exercise and increased blood flow of intercostal muscle during hyperpnoea (due to exercise) might be the triggering mechanism of coronary artery steal syndrome secondary to large unligated major LIMA-SB.

Besides controversies over coronary artery steal syndrome secondary to unligated major LIMA-SB, there is a clear evidence supporting this syndrome which is reversal of the documented ischemia and improved anginal complaints after occlusion of these SB. Additionally, it is clear that not all unligated major LIMA-SB cause steal syndrome and a noninvasive method might be needed for evaluating the clinical significance of a unligated major LIMA-SB recorded during CAG. So, a simple and clinically valuable method such as exercise stress MPI with SPET might be useful in both detection of clinically significant unligated major LIMA-SB and assessment of their occlusion treat-ment. Eight (33.3%) patients in anterior ischemia subgroup had dipyridamole stress MPI with SPET (after CABG surgery) within the previous two years in which ischemia was not detected. Furthermore, exertional angina complaints of these patients were wrongly attributed to extra-cardiac causes after non-ischemic results of dipyridamole stress MPI. Exertional angina complaint of these patients were continued, and within 3 months after dipyridamole stress MPI, 5 of them underwent CAG which showed patent LIMA to LAD system with unligated major LIMA-SB, patent additional grafts (vein or radial) and ungrafted native coronary arteries (RCA or LAD) without critical stenosis. No treatment was planned to angiographically demonstrated unligated major LIMA-SB. After detection of anterior wall ischemia on exercise stress MPI, percutaneous coil embolization was performed to unligated major LIMA-SB of these patients at our clinic and exertional angina complaints of these patients were improved after the procedure. These findings seem to be a clear evidence for supporting the usefulness of exercise stress MPI with SPET in coronary artery steal syndrome secondary to unligated major LIMA-SB.

Coronary artery steal syndrome can occur not only secondary to unligated major LIMA-SB but also secondary to subclavian artery stenosis in CABG patients with LIMA graft [32]. Georgoulias et al reported a patient with coronary steal syndrome secondary to subclavian artery stenosis who had ischemia negative exercise MPI (SPET) using a Bruce protocol [32]. Because of patient's typical angina symptoms, stress MPI in combination with exercise of left arm was repeated and extensive myocardial ischemia was recorded [32]. Left arm exercise stress during MPI might be also helpful in diagnosing coronary artery steal syndrome secondary to unligated major LIMA-SB. So, a prospective study is needed to investigate the value of left arm exercise stress during MPI in patients with steal syndrome secondary to unligated major LIMA-SB.

Study limitations

Several limitations of this study should be acknowledged. Firstly, it was a retrospective study which is susceptible to bias in data selection. Secondly, sample size of our study was small, especially in subgroup. Thirdly, it was a single center study and large scaled multicenter studies are needed to support our findings. Fourth, it is well known that exercise MPI with SPET have a fair margin of error with false positive and negative results. Last but not least, although MPI is a quite valid technique for the evaluation of myocardial ischemia, it cannot differentiate between myocardial ischemia due to coronary artery stenosis and to coronary steal syndrome secondary to unligated major LIMA-SB.

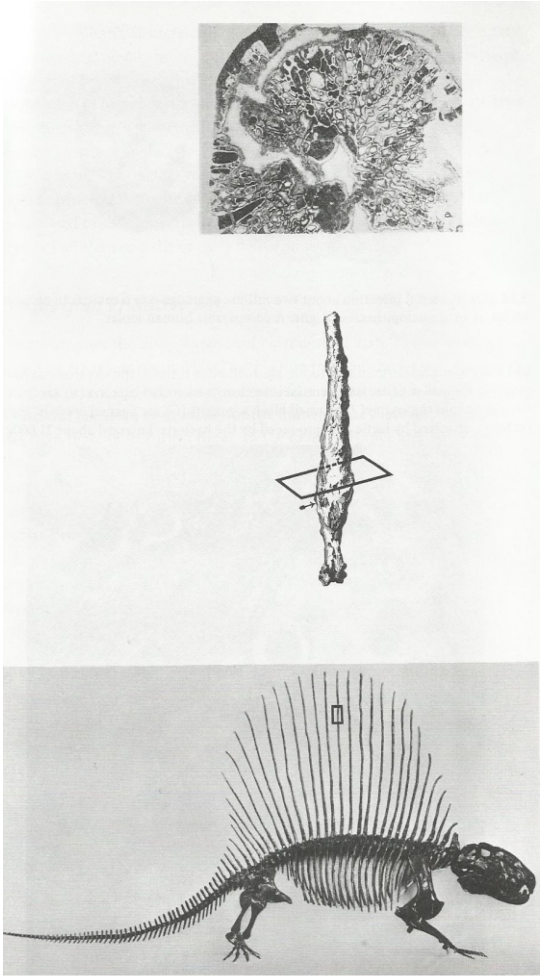
In conclusion, large unligated major LIMA-SB might be a potential source of ischemia in CABG patients. We suggest that exercise stress MPI with SPET may be a first option noninvasive test in evaluating the clinical significance of unligated major LIMA-SB and the effectiveness of percutaneous coil embolization therapy of these SB.

Bibliography

1. Loop FD, Lytle BW, Cosgrove DM et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med* 1986; 314: 1-6.
2. Cameron A, Kemp HG, Green GE. Bypass surgery with the internal mammary artery graft: 15 year follow-up. *Circulation* 1986; 74: 30-6.
3. Tönz M, von Segesser L, Carrel T et al. Steal syndrome after internal mammary artery bypass grafting--an entity with increasing significance. *Thorac Cardiovasc Surg* 1993; 41: 112-7.
4. Horowitz MD, Oh CJ, Jacobs JP et al. Coronary-subclavian steal: a cause of recurrent myocardial ischemia. *Ann Vasc Surg* 1993; 7: 452-6.
5. Barberini F, Cavallini A, Carpino G et al. Lateral costal artery: accessory thoracic vessel of clinical interest. *Clin Anat* 2004; 17: 218-26.
6. Seevanayagam S, Buxton B. Surgical techniques for internal thoracic artery grafting. In: He GW. Eds. *Arterial Grafting for Coronary Artery Bypass Surgery*. 2nd edn. Berlin: Springer Verlag 2006: 97-104.
7. Kern MJ. Does a LIMA side branch ever need occlusion?. *Cathet Cardiovasc Diagn* 1998; 45: 307-9.
8. Bauer EP, Bino MC, von Segesser LK et al. Internal mammary artery anomalies. *Thorac Cardiovasc Surg* 1990; 38: 312-5.
9. Singh RN, Sosa JA. Internal mammary artery-coronary artery anastomosis. Influence of the side branches on surgical result. *J Thorac Cardiovasc Surg* 1981; 82: 909-14.
10. Sutherland FW, Desai JB. Incidence and size of lateral costal artery in 103 patients. *Ann Thorac Surg* 2000; 69: 1865-6.
11. Gaudino M, Serricchio M, Glieca F et al. Steal phenomenon from mammary side branches: when does it occur? *Ann Thorac Surg* 1998; 66: 2056-62.
12. Gaudino M, Serricchio M, Tondi P et al. Do internal mammary artery side-branches have the potential for haemodynamically significant flow steal? *Eur J Cardiothorac Surg* 1999; 15: 251-4.
13. Guzon OJ, Klatte K, Moyer A et al. Fallacy of thoracic side-branch steal from the internal mammary artery: analysis of left internal mammary artery coronary flow during thoracic side-branch occlusion with pharmacologic and exercise-induced hyperemia. *Catheter Cardiovasc Interv* 2004; 61: 20-8.
14. Abdo N, Curran PJ, Kumar V, Tobis JM. Coronary steal syndrome with coil embolization of a large LIMA side branch: radionuclide evidence for reversible ischemia. *Catheter Cardiovasc Interv* 2005; 66: 360-3.
15. Firstenberg MS, Guy G, Bush C, Raman SV. Impaired myocardial perfusion from persistent mammary side branches: a role for functional imaging and embolization. *Cardiol Res Pract* 2010 Sep 13; 2010. pii: 203459. doi: 10.4061/2010/203459.
16. Akilli A, Duygu H, Erturk U et al. Transbrachial coil occlusion of unligated thoracic side branch of arterial graft of internal mammary artery leading to silent ischemia in a diabetic patient. *Int J Cardiol* 2006; 113: 16-8.
17. Mahmarian JJ, Boyce TM, Goldberg RK et al. Quantitative exercise thallium-201 single photon emission computed tomography for the enhanced diagnosis of ischemic heart disease. *J Am Coll Cardiol* 1990; 15: 318-29.
18. Lakkis NM, Mahmarian JJ, Verani MS. Exercise thallium-201 single photon emission computed tomography for evaluation of coronary artery bypass graft patency. *Am J Cardiol* 1995; 76: 107-11.
19. Mahenthiran J, Ghumman W, Jacob S et al. Detection of early postoperative internal mammary artery atherosclerosis using Tc-99m myocardial perfusion SPECT imaging. *J Nucl Cardiol* 2004; 11: E1-E3.
20. Salm LP, Bax JJ, Vliegen HW et al. Functional significance of stenoses in coronary artery bypass grafts. Evaluation by single-photon emission computed tomography perfusion imaging, cardiovascular magnetic resonance, and angiography. *J Am Coll Cardiol* 2004; 44: 1877-82.
21. Lang RM, Bierig M, Devereux RB et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography. *J Am Soc Echocardiogr* 2005; 18: 1440-63.
22. Holly TA, Abbott BG, Al-Mallah M et al; American Society of Nuclear Cardiology imaging guidelines for nuclear cardiology procedures. Single photon-emission computed tomography. *J Nucl*

Cardiol 2010; 17: 941-73.

23. Cerqueira MD, Weissman NJ, Dilsizian V et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Int J Cardiovasc Imaging* 2002; 18: 539-42.
24. Pragliola C, Gaudino M, Bombardieri G et al. Patent side branches do not affect coronary blood flow in internal thoracic artery-left anterior descending anastomosis: an experimental study. *J Thorac Cardiovasc Surg* 1999; 118: 66-70.
25. Cheng K, Rehman SM, Taggart DP. A Review of Differing Techniques of Mammary Artery Harvesting on Sternal Perfusion: Time for a Randomized Study? *Ann Thorac Surg 2015*; 100: 1942-53.
26. Pagni S, Bousamra M 2nd, Shirley MW, Spence PA. Successful VATS ligation of a large anomalous branch producing IMA steal syndrome after MIDCAB. *Ann Thorac Surg* 2001; 71: 1681-2.
27. Morocutti G, Gasparini D, Spedicato L et al. Functional evaluation of steal by unligated first intercostal branch before transcatheter embolization in recurrent angina after a LIMA-LAD graft. *Catheter Cardiovasc Interv* 2002; 56: 373-6.
28. Raval NY, O'Meallie LP, Diez JG. Doppler evaluation and coil embolization of left internal mammary artery bypass graft side branch. *J Invasive Cardiol* 2005; 17: 180-2.
29. Duncker DJ, Bache RJ. Regulation of coronary blood flow during exercise. *Physiol Rev* 2008; 88: 1009-86.
30. Khouri EM, Gregg DE, Rayford CR. Effect of exercise on cardiac output, left coronary flow and myocardial metabolism in the unanesthetized dog. *Circ Res* 1965; 17: 427-37.
31. Vogiatzis I, Athanasopoulos D, Habazettl H et al. Intercostal muscle blood flow limitation in athletes during maximal exercise. *J Physiol* 2009; 587: 3665-77.
32. Georgoulias P, Demakopoulos N, Xaplanteris P, Mortzos G. Tc-99m tetrofosmin myocardial SPECT combined with a modified exercise protocol in an unusual case of steal phenomenon. C*lin Nucl Med* 2003; 28: 762-3.



Ancient reptile with a trauma in the dorsal spine. The oldest trauma, $2*10^8$ years ago found in Texas.