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Effects of Atrial Ischemia on Left Atrial Remodeling in Patients with ST-Segment Elevation Myocardial Infarction

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Background: Adverse left atrial (LA) remodeling after ST-segment elevation myocardial infarction (STEMI) has been associated with poor prognosis. Flow impairment in the dominant coronary atrial branch (CAB) may affect large areas of LA myocardium, potentially leading to adverse LA remodeling during follow-up. The aim of this study was to assess echocardiographic LA remodeling in patients with STEMI with impaired coronary flow in the dominant CAB.

Methods: Of 897 patients with STEMI, 69 patients (mean age, 62 ± 11 years; 83% men) with impaired coronary flow in the dominant CAB (defined as Thrombolysis In Myocardial Infarction flow grade < 3) were retrospectively compared with an age- and sex-matched control group of 138 patients with normal dominant CAB coronary flow.

Results: Patients with dominant CAB-impaired flow had higher peak troponin T (3.9 μg/L [interquartile range, 2.2-8.2 μg/L] vs 3.2 μg/L [interquartile range, 1.5-5.6 μg/L], $P = .009$). No differences in left ventricular ejection fraction or mitral regurgitation were observed between groups at baseline or at follow-up. LA remodeling assessment included maximum LA volume, speckle-tracking echocardiography–derived LA strain, and total atrial conduction time assessed on Doppler tissue imaging at baseline, 6 months, and 12 months. Patients with dominant CAB-impaired flow presented larger LA maximal volumes (26.9 ± 10.9 vs 18.1 ± 7.1 mL/m^2, $P < .001$) and longer total atrial conduction time (150 ± 23 vs 124 ± 22 msec, $P < .001$) at 6 months, remaining unchanged at 12 months. However, all LA strain parameters were significantly lower from baseline (reservoir, 20.3 ± 10.1% vs 27.1 ± 14.5% [$P < .001$]; conduit, 9.1 ± 5.6% vs 12.8 ± 8% [$P < .001$]; booster, 9.1 ± 5.6% vs 12.8 ± 8% [$P < .001$]), these differences being sustained at 6- and 12-month follow-up.

Conclusions: Atrial ischemia resulting from impaired coronary flow in the dominant CAB in patients with STEMI is associated with LA adverse anatomic and functional remodeling. Reduced LA strain preceded LA anatomic remodeling in early phases after STEMI. (J Am Soc Echocardiogr 2023;36:163-71.)

Keywords: Myocardial infarction, Primary percutaneous coronary intervention, Atrial ischemia, Left atrial strain

The left atrium may exhibit anatomic and functional remodeling after ST-segment elevation myocardial infarction (STEMI), which is a strong predictor of mortality and cardiovascular morbidity.[1,2] Left atrial (LA) remodeling after STEMI results from the interaction of different pathophysiologic mechanisms, such as increased left ventricular (LV) filling pressures, ischemic mitral regurgitation (MR), and atrial ischemia. Particularly, atrial ischemia resulting from coronary flow interruption in a coronary atrial branch (CAB) has been linked to anatomic and functional LA remodeling, with extensive fibrosis present from early phases after acute myocardial infarction.[3] Atrial infarction is not infrequent in patients with STEMI and has been detected in up to 17% of cases in postmortem studies.[4] However, the

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Abbreviations

CAB = Coronary atrial branch

LA = Left atrial

LCx = Left circumflex coronary artery

LV = Left ventricular

LVEF = Left ventricular ejection fraction

MR = Mitral regurgitation

PA-DTI = Total atrial conduction time assessed on Doppler tissue imaging

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

contribution of atrial ischemia or infarction to LA remodeling after STEMI is still poorly understood. In addition, the anatomic variability of CABs in humans[5,6] may hamper the evaluation of the impact of atrial ischemia on LA remodeling, as this may vary on the basis of the amount of jeopardized LA myocardium. Coronary flow impairment in the dominant CAB, defined as the largest CAB on coronary angiography, may affect large areas of LA myocardium, with important clinical consequences.

In the present study we analyzed the association of coronary flow impairment in the dominant CAB in patients presenting with STEMI and echocardiographic parameters of LA remodeling, both anatomic (LA volume and total atrial conduction time assessed on Doppler tissue imaging [PA-DTI], a surrogate marker of atrial fibrosis[7]) and functional (on the basis of LA myocardial strain measurements), at baseline (<48 hours after admission) and at 6- and 12-month follow-up.

METHODS

Study Population

Patients with STEMI referred to the Leiden University Medical Center for primary percutaneous coronary intervention between February 2004 and May 2013 were considered for inclusion. Only patients presenting with culprit lesions located in the right coronary artery or the left circumflex coronary artery (LCx) were included in the analysis, as the CABs originate from these vessels. During index hospitalization, patients underwent echocardiography within 48 hours of admission. At discharge, all patients were systematically followed for ≥1 year according to the institutional clinical care track for patients with STEMI,[8,9] which includes transthoracic echocardiography at 6 and 12 months. Baseline clinical characteristics were obtained from the departmental electronic patient information system (EPD-Vision, Leiden University Medical Center). Exclusion criteria have been previously described,[10] and included patients with incomplete coronary angiographic data for analysis of CAB flow, prior coronary artery bypass grafting, or conservative medical treatment during index coronary angiography and those lost to follow-up. The control group consisted of 138 age- and sex-matched subjects with STEMI involving either the right coronary artery or LCx with normal coronary flow at the dominant CAB on coronary angiography performed before, during, and after primary percutaneous coronary intervention. The control group was extracted from the same institutional STEMI database. This retrospective analysis of prospectively clinically acquired data was approved by the internal review board, which waived the need to obtain written informed consent.

Angiographic Evaluation

Coronary angiograms were retrospectively assessed by an experienced interventional cardiologist. The angiographic anatomic definitions of the different CABs have been described.[9] As previously reported, the angiographic anatomy of all visible CABs was systematically evaluated and characterized on the basis of the type of CAB, coronary artery, and segment of origin and CAB course (Figure 1). The dominant CAB was defined as the largest CAB.[10] Coronary flow at the dominant CAB was evaluated both after initial diagnostic angiography and at the end of the procedure and was graded on the basis of the Thrombolysis In Myocardial Infarction (TIMI) frame count method. We defined coronary flow impairment in the

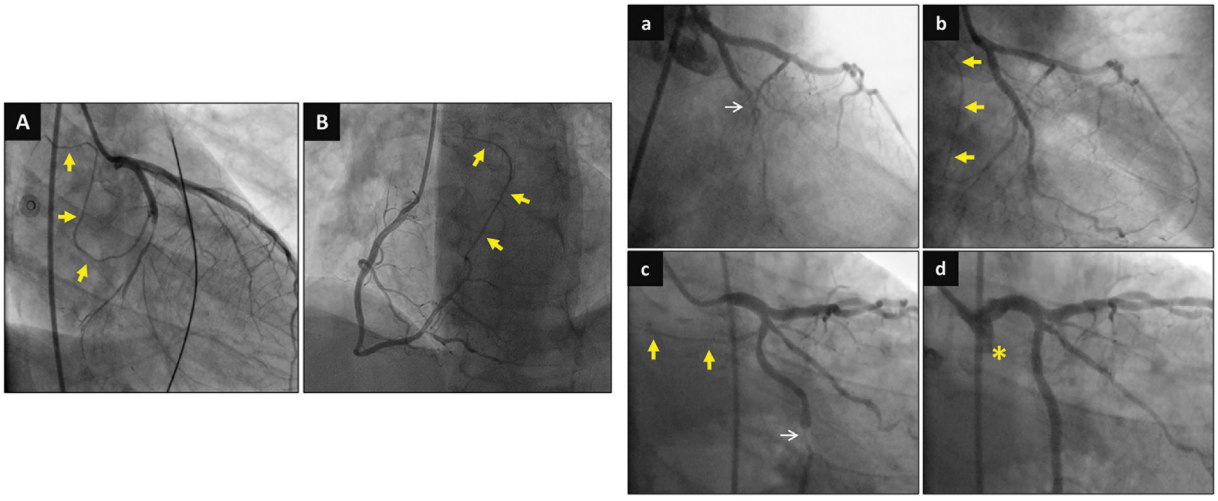

Figure 1 **(A, B)** Examples of dominant CABs *(arrows)* corresponding to a sinus node artery arising from the LCx **(A)** and to a sinus node artery arising from the posterolateral branch of the right coronary artery **(B)**. **(a-d)** Impaired coronary flow at the dominant CAB. Occlusion of the mid-LCx (**a**, *white arrow*) and result after treatment of the culprit lesion showing reperfusion of a previously occluded dominant CAB (**b**, *yellow arrows*). Dominant CAB arising from the proximal LCx (**c**, *yellow arrows*) with culprit lesion located at mid-LCx (**c**, *white arrow*), and subsequent occlusion of the dominant CAB (**d**, *asterisk*) after the implantation of stents up to the proximal segment of the LCx.

HIGHLIGHTS

- Flow impairment in dominant CABs may occur in patients with STEMI.
- The resulting atrial ischemia leads to LA anatomic and functional remodeling.
- Functional remodeling precedes structural remodeling in early phases after STEMI.
- These effects are independent of LVEF, significant MR, or LV diastolic dysfunction.

dominant CAB as a TIMI flow grade <3 at any time of the index percutaneous coronary intervention.[10]

Echocardiography Evaluation

Transthoracic echocardiography was performed with patients in the left lateral decubitus position using commercially available systems. Parasternal, apical, and subcostal views were acquired using 3.5-MHz or M5S transducers. Standard two-dimensional, M-mode, and Doppler data were digitally stored for offline analysis (EchoPAC version 201.0.0; GE Vingmed Ultrasound). Offline analysis of echocardiographic images was blinded to angiographic findings. LV ejection fraction (LVEF) was calculated using the Simpson biplane method.[11] MR severity was evaluated according to current recommendations[12] and graded as mild, moderate, or severe. Moderate and severe MR were considered as significant MR. LA maximal volume was measured at end-systole before mitral valve opening in the apical views according to the Simpson method and indexed to body surface area.[11] LV diastolic function was assessed by measuring early diastolic peak velocity (E) and late diastolic peak velocity (A) on pulsed-wave Doppler of mitral inflow, with subsequent calculation of the E/A ratio. Septal and lateral peak early diastolic mitral annular velocities were measured in the apical four-chamber view on Doppler tissue imaging.[13] LV filling pressures were assessed by the ratio of early diastolic transmitral peak flow velocity to early diastolic mitral annular tissue peak velocity.

Strain Imaging

LA reservoir, conduit, and booster pump functions were evaluated by using two-dimensional speckle-tracking echocardiography in the apical four-chamber view, with special attention to avoid images with LA foreshortening (Figure 2). The LA endocardial border was manually traced, and the region of interest was adjusted to include the LA wall. Pulmonary veins and the LA appendage were excluded. The electrocardiogram was adjusted to the onset of the QRS complex (R-R gated). LA reservoir strain was defined as the peak positive longitudinal strain during ventricular systole. LA conduit and booster pump functions were obtained at early and late diastole, respectively.[14] The intra- and interobserver variability for LA strain analysis in our institution has been previously reported.[15]

Atrial Tissue Doppler Imaging

Color-coded Doppler tissue imaging was used to calculate the total atrial conduction time. An atrial tissue Doppler tracing was obtained by placing the sample volume on the lateral wall of the left atrium above the mitral annulus in a four-chamber apical view (Figure 2).

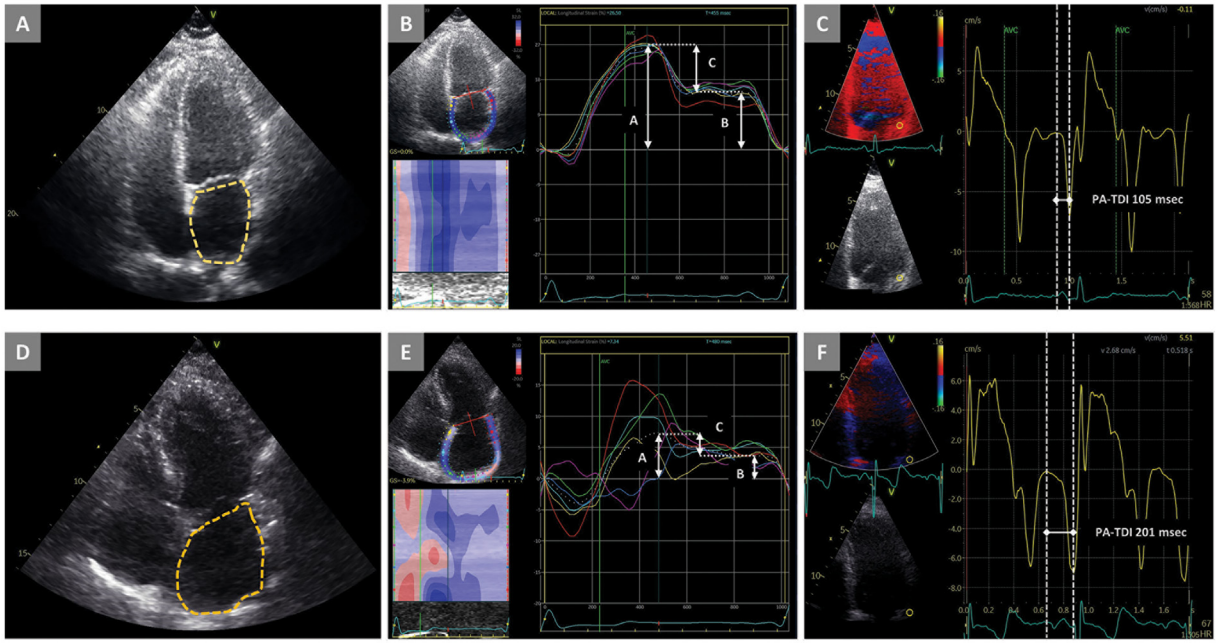

Figure 2 Example of measurement of LA maximal volume **(A, D)**, strain **(B, E)**, and PA-DTI **(C, F)** in two patients with STEMI with normal coronary flow in the dominant CAB *(top row)* and impaired coronary flow in the dominant CAB *(bottom row)*. In contrast to the patient with preserved coronary flow, the patient with impaired coronary flow in the dominant CAB shows an enlarged left atrium, markedly reduced LA strain reservoir function (**B** and **E**, *arrow A*), booster pump function (**B** and **E**, *arrow B*), and conduit function (**B** and **E**, *arrow C*) and a prolonged PA-DTI (201 vs 105 msec; **C** and **F**).

Table 1 Baseline characteristics

	Overall population (n = 207)	Impaired flow in the dominant atrial branch (n = 69)	Normal flow in the dominant atrial branch (n = 138)	P
Age, y	62 ± 11	62 ± 11	62 ± 11	.816
Male	171 (82)	57 (83)	114 (83)	1.000
Hypertension	75 (36)	25 (36)	50 (36)	1.000
Hypercholesterolemia	48 (23)	10 (14)	38 (26)	.037
Family history of CAD	77 (37)	27 (39)	50 (36)	.878
Diabetes	22 (10)	8 (12)	14 (10)	.812
Smoking history	128 (62)	42 (61)	86 (62)	.876
Previous MI	21 (10)	6 (9)	15 (11)	.808
Previous stroke	9 (4)	3 (4)	6 (1)	1.000
Peripheral vascular disease	11 (5)	1 (1)	10 (7)	.104
BSA, kg/m^2	2 ± 0.2	1.9 ± 0.2	2 ± 0.2	.275
SBP at admission, mm Hg	132.9 ± 27.1	126.8 ± 27.6	136.1 ± 26.4	**.025**
DBP at admission, mm Hg	79.3 ± 17.5	75.6 ± 18.7	81.3 ± 16.6	**.035**
Killip class ≥ 2	12 (6)	6 (9)	6 (4)	.220
Peak CK, U/L	1,329 (765-2,179)	1,422 (822-2,583)	1,217 (735-1,694)	.084
Peak TnT, μg/L	3.4 (1.6-6.4)	3.9 (2.2-8.2)	3.2 (1.5-5.6)	**.009**
eGFR, mL/min/1.73 m^2	100.3 ± 36.6	91.3 ± 35.1	105.1 ± 36.8	.051
Glucose, mmol/L	72.6 ± 39.7	75.5 ± 40.9	71.2 ± 39.2	.472
Aspirin at discharge	203 (98)	68 (99)	135 (98)	.778
P2Y$_{12}$ inhibitor at discharge	206 (99)	68 (98)	137 (99)	.335
ACE inhibitor/ARB at discharge	197 (95)	67 (98)	130 (95)	.721
β-blocker at discharge	192 (93)	63 (91)	129 (93)	.558
Statin at discharge	206 (99)	69 (100)	137 (99)	1.000

Data are expressed as mean ± SD, number (percentage), or median (interquartile range). *P* values in boldface type denote statistical significance. Hypertension was defined as office blood pressure ≥ 140/90 mm Hg or previous pharmacologic treatment. Hypercholesterolemia was defined as total cholesterol ≥ 190 mg/dL or previous pharmacologic treatment. Diabetes mellitus was defined as fasting blood glucose ≥ 7.0 mmol/L, glucose ≥ 11.1 mmol/L on 2-hour oral glucose tolerance test, or previous pharmacologic treatment.
ACE, Angiotensin-converting enzyme; *ARB*, angiotensin II receptor blocker; *BSA*, body surface area; *CAD*, coronary artery disease; *CK*, creatine kinase; *DBP*, diastolic blood pressure; *eGFR*, glomerular filtration rate (Cockcroft-Gault formula); *MI*, myocardial infarction; *SBP*, systolic blood pressure; *TnT*, troponin T.

The PA-DTI duration, an echocardiography-derived parameter of total atrial electrical conduction time, was defined as the time delay from the onset of the P wave on surface electrocardiography to the peak of the A′ wave on the Doppler tissue imaging tracing.[16]

Follow-Up and Data Collection

Patients were followed up at 6 and 12 months, and transthoracic echocardiography was performed at each follow-up visit. Changes in LA volume and PA-DTI (anatomic remodeling) and changes in reservoir, conduit, and booster pump strain (functional remodeling) were assessed over time.

Statistical Analysis

Continuous variables are presented as mean ± SD or median (interquartile range), as appropriate. Continuous variables were compared using the unpaired Student's *t* test if normally distributed and the Mann-Whitney *U* test if not normally distributed. Categorical data are summarized as frequencies and percentages and were compared using the χ^2 or Fisher exact test as appropriate. Changes in LA volume, LA strain parameters, and PA-DTI during echocardiographic follow-up were compared using two-way repeated-measure analysis of variance with appropriate interaction terms. Post hoc analysis (Bonferroni correction) was performed if statistical significance ($P \leq .05$) was achieved. Statistical analysis was performed with SPSS version 23.0 (IBM). A two-tailed P value $<.05$ was considered statistically significant.

RESULTS

Of 897 patients with STEMI, 69 (mean age, 62 ± 11 years; 83% men) with impaired coronary flow in the dominant CAB were matched and compared with 138 control subjects. Coronary flow impairment in the dominant CAB at the moment of diagnostic coronary angiography was reported as follows: TIMI flow grade 0 in 39 patients, TIMI flow grade 1 in 16, and TIMI flow grade 2 in four. At the end of the procedure, coronary flow in the dominant CAB was fully restored in 50 patients (72%), whereas 19 patients (28%) showed persistent impaired coronary flow (TIMI flow grade 0 in 11 patients, TIMI flow grade 1 in five, and TIMI flow grade 2 in six). Baseline clinical characteristics are summarized in Table 1. Of note, patients with impaired flow in the dominant CAB showed significantly higher troponin T peak values

Table 2 Angiographic findings

	Overall population (*n* = 207)	Impaired flow in the dominant atrial branch (*n* = 69)	Normal flow in the dominant atrial branch (*n* = 138)	*P*
Dominant CAB type				
Sinus node branch	194 (94)	62 (90)	132 (96)	.131
Others	13 (66)	7 (10)	6 (4)	
Dominant CAB vessel of origin				
Right coronary artery	125 (60)	58 (84)	67 (49)	<.001
LCx	82 (40)	11 (16)	71 (51)	
Right coronary dominancy	198 (96)	66 (96)	132 (96)	1.000
Multivessel coronary artery disease	92 (44)	28 (41)	64 (46)	.461
Culprit vessel right coronary artery	155 (75)	58 (84)	97 (70)	.041
Culprit lesion ACC/AHA type B2/C	162 (78)	60 (87)	102 (74)	.033
Visible thrombus	186 (90)	65 (94)	121 (88)	.221
Thrombus grade	2.3 ± 1.2	2.6 ± 1.2	2.1 ± 1.2	.010
Culprit vessel TIMI flow pre-PCI	0.7 ± 1.2	0.4 ± 0.8	0.9 ± 1.2	.002
Culprit vessel TIMI flow grade 0 or 1 post-PCI	5 (2)	1 (1)	4 (3)	.667
Door-to-balloon time, min	51 (36-75)	50 (31-79)	50 (35-75)	.478

Data are expressed as number (percentage), mean ± SD, or median (interquartile range). Bold values are statistically significant.
ACC, American College of Cardiology; *AHA*, American Heart Association.

compared with control subjects (3.9 μg/L [interquartile range, 2.2-8.2 μg/L] vs 3.2μg/L [interquartile range, 1.5-5.6 μg/L]; $P = .009$).

Coronary angiographic findings are summarized in Table 2. Compared with control subjects, patients with impaired flow in the dominant CAB more often had complex coronary culprit lesions (87% vs 74%, $P = .033$) and higher thrombus burden (mean TIMI thrombus grade, 2.6 ± 1.2 vs 2.1 ± 1.2; $P = .010$).

Echocardiography was available in 192 patients (93%) at baseline, in 190 (92%) at 6-month follow-up, and in 191 (92%) at 12-month follow-up. Baseline echocardiographic characteristics are displayed in Table 3. There were no differences in LVEF and frequency of significant MR between groups throughout follow-up. LA maximal volume, PA-DTI, and LA strain parameters are summarized in Table 3. LA maximal volume was similar in both groups at baseline. However, patients with impaired flow in the dominant CAB exhibited larger LA volumes at 6 months compared with their counterparts, and the difference was sustained at 12-month follow-up. Similarly, mean PA-DTI times were similar in both groups at baseline, whereas significantly longer PA-DTI times were observed in patients with impaired flow in the dominant CAB at both 6- and 12-month follow-up. All LA strain parameters (LA reservoir, conduit, and booster pump functions) were significantly lower in patients with impaired vs normal flow in the dominant CAB at baseline, remaining significantly impaired during at both 6- and 12-month follow-up (Table 4).

Repeated-measures analysis of variance showed a statistically significant effect of time on LA maximal volume ($F_{1.8,\ 267} = 41.3$, $P < .001$), PA-DTI ($F_{1.7,\ 275} = 17.1$, $P < .001$), LA strain reservoir function ($F_{1.5,\ 253} = 12.7$, $P < .001$), LA strain conduit function ($F_{1.7,\ 278} = 8.2$, $P < .001$), and LA strain booster pump function ($F_{1.7,\ 273} = 9.1$, $P < .001$; Figure 3). Post hoc testing revealed significant differences between patients with impaired versus normal flow in the dominant CAB in all evaluated parameters: LA maximal index volume ($F_{1,\ 145} = 23.7$, $P < .001$; corrected by LVEF and E/E′ ratio), PA-DTI ($F_{1,\ 156} = 21.7$, $P < .001$), LA strain reservoir function ($F_{1,\ 160} = 80.7$, $P < .001$), LA strain conduit function ($F_{1,\ 160} = 45.8$, $P < .001$), and LA strain booster pump function ($F_{1,\ 160} = 63.8$, $P < .001$).

DISCUSSION

The main conclusions of this study are as follows: (1) atrial ischemia resulting from coronary flow impairment in the dominant CAB in patients with STEMI was associated with significant LA anatomic remodeling, expressed as a larger LA maximal volume and a longer PA-DTI, present at 6-month follow-up and maintained at 12 months; (2) LA functional remodeling, expressed as impaired LA strain parameters, resulting from coronary flow limitation in the dominant CAB was observed at baseline and remained impaired both at 6- and 12-month follow-up; and (3) there were no significant differences in LVEF, significant MR, or LV diastolic dysfunction parameters between groups at any time point of the evaluation.

Atrial Coronary Anatomy, LA Coronary Perfusion Phenotype, and Atrial Ischemia

It has been postulated that coronary perfusion of the left atrium relies solely on CABs arising from the LCx. In a study conducted by Aguero *et al.*[3] in a swine model, an LA infarction was induced

Table 3 Echocardiographic findings

	Overall population (n = 207)	Impaired flow in the dominant atrial branch (n = 69)	Normal flow in the dominant atrial branch (n = 138)	P
Baseline				
LV end-systolic diameter, mm	32.5 ± 6.7	31.6 ± 6.6	32.8 ± 6.7	.266
LV end-diastolic diameter, mm	48.2 ± 6.4	47.2 ± 7.3	48.6 ± 6	.183
LV interventricular septum diameter, mm	11.5 ± 2.1	11.9 ± 2.4	11.3 ± 2	.096
LV posterior wall diameter, mm	11.3 ± 2.1	11.6 ± 2.4	11.1 ± 2	.179
LV mass, indexed, g/m^2	105.1 ± 28.3	107.5 ± 32.8	104.1 ± 26	.457
LV end-systolic volume, mL	54.6 ± 21.7	53.9 ± 24.9	55 ± 19.9	.758
LV end-diastolic volume, mL	103.7 ± 33	99.2 ± 33.2	106 ± 32.8	.189
LVEF, %	48.6 ± 9.2	48.1 ± 11.2	48.9 ± 8	.613
E/A ratio	2.1 ± 11.4	4.5 ± 19.7	0.9 ± 0.3	.167
E′, cm/sec	6.1 ± 2	6.5 ± 2.3	5.8 ± 1.8	.043
E/E′ ratio	12.2 ± 6.5	11.2 ± 4.9	12.7 ± 7.3	.148
Significant MR grade ≥ 2	15 (7)	8 (12)	7 (5)	.084
6 mo				
LV end-systolic volume, mL	48.1 ± 19.9	45.4 ± 18.3	49.3 ± 20.6	.257
LV end-diastolic volume, mL	104 ± 31.3	98.1 ± 30	106.7 ± 31.7	.114
LVEF, %	50.8 ± 6.9	51.5 ± 7.1	50.5 ± 6.8	.370
E/A ratio	0.8 ± 0.2	0.8 ± 0.2	0.8 ± 0.3	.549
E′, cm/sec	5.9 ± 1.8	5.9 ± 2	5.9 ± 1.7	.879
E/E′ ratio	11.7 ± 5.1	11.9 ± 6.8	11.5 ± 4.2	.686
Significant MR grade ≥ 2	8 (4)	5 (7)	3 (2)	.052
12 mo				
LV end-systolic volume, mL	46.7 ± 19.7	43.9 ± 16.1	47.9 ± 21.1	.245
LV end-diastolic volume, mL	102.1 ± 34.1	95.8 ± 27	104.9 ± 36.6	.127
LVEF, %	51.7 ± 7.1	51.8 ± 6.5	51.7 ± 7.3	.869
E/A ratio	0.9 ± 0.2	0.8 ± 0.2	0.9 ± 0.3	.147
E′, cm/sec	5.8 ± 1.8	5.7 ± 1.8	5.9 ± 1.8	.615
E/E′ ratio	14 ± 26	12.5 ± 5.2	14.7 ± 31.8	.647
Significant MR grade ≥ 2	8 (4)	3 (4)	5 (4)	.694

Data are expressed as mean ± SD or number (percentage). Echocardiograms were available for 192 of 207 patients at baseline, 190 of 207 patients at 6-month follow-up, and 191 of 207 patients at 12-month follow-up.

by occluding a CAB arising from the proximal LCx, which led to structural and functional LA remodeling. Similarly, occlusion of the proximal LCx artery in a sheep model led to significant electrophysiologic changes in the left atrium compared with animals with left anterior descending coronary artery infarctions.[17] However, it has been shown that LA coronary perfusion is complex and results from a variable contribution of the left and right CABs. In a sheep model, Yamazaki *et al.*[18] described three well-differentiated LA perfusion patterns: left-dominant (relying on the left proximal CAB), balanced double-vessel (left proximal and right CABs), and triple-vessel (right CAB and left proximal and distal CABs) perfusion. In most of the specimens, a double-vessel LA perfusion pattern was identified. Because of the similar distribution of CABs in sheep and human hearts,[19] it can be speculated that similar interspecimen variability of LA perfusion may also exist in the human heart. In the present study, the dominant CAB emerged from the right coronary artery in 84% of patients with impaired flow, and those patients showed LA remodeling at follow-up. In contrast, flow limitation in dominant CABs emerging from the LCx was not associated with greater LA structural and functional impairment. These findings strongly suggest the existence of, at least, a double-vessel LA perfusion pattern in a high proportion of patients.

Atrial Ischemia and LA Anatomic and Functional Remodeling

Atrial remodeling, defined as a permanent change in LA size and function, is a complex pathophysiologic process, especially after myocardial infarction.[20] However, isolated atrial infarction has been

Table 4 LA echocardiographic findings

	Overall population (n = 207)	Impaired flow in the dominant atrial branch (n = 69)	Normal flow in the dominant atrial branch (n = 138)	P
LA maximal indexed volume, mL/m^2				
Baseline	20.82 ± 6.2	20.5 ± 5.3	20.9 ± 6.7	.639
6 mo	20.7 ± 9.2	26.9 ± 10.9	18.1 ± 7.02	**<.001**
12 mo	20.9 ± 8.6	27.7 ± 9.1	18 ± 6.6	**<.001**
LA strain (reservoir), %				
Baseline	24.9 ± 13.6	20.3 ± 10.1	27.1 ± 14.5	**.001**
6 mo	33.3 ± 15.4	19.1 ± 6.8	39 ± 14.2	**<.001**
12 mo	31.7 ± 15	20 ± 7.6	36.8 ± 14.6	**<.001**
LA strain (conduit), %				
Baseline	13.3 ± 9	11.4 ± 7.6	14.3 ± 9.4	**.036**
6 mo	16 ± 9.5	8.8 ± 4.4	19 ± 9.5	**<.001**
12 mo	15 ± 9.5	9 ± 4.8	17.6 ± 10	**<.001**
LA strain (booster), %				
Baseline	11.6 ± 7.6	9.1 ± 5.6	12.8 ± 8	**.001**
6 mo	17.2 ± 8.3	10.3 ± 4	20 ± 8	**<.001**
12 mo	16.7 ± 8.1	11 ± 5.1	19.2 ± 7.9	**<.001**
PA-DTI, msec				
Baseline	125.9 ± 28	125 ± 30.7	126.3 ± 26.7	.781
6 mo	131.5 ± 25.3	150.1 ± 23.3	124 ± 22.1	**<.001**
12 mo	131.1 ± 25.7	144.8 ± 24.9	124.9 ± 23.6	**<.001**

Data are expressed as mean ± SD. Echocardiograms were available for 192 of 207 patients at baseline, 190 of 207 patients at 6-month follow-up, and 191 of 207 at 12 month follow-up. Bold values are statistically significant.

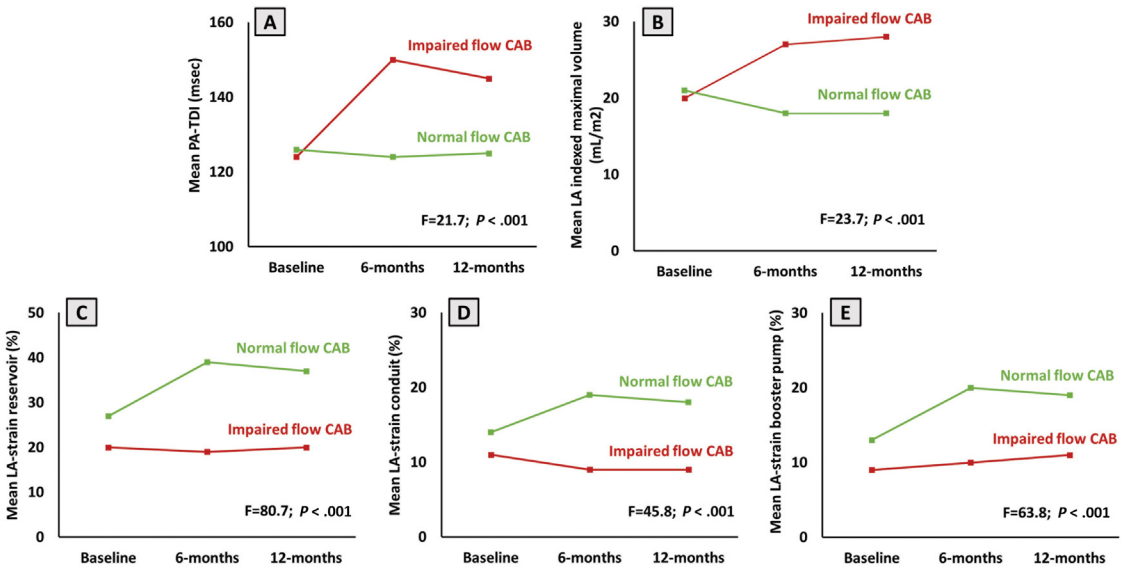

Figure 3 Two-way repeated-measures analysis of variance performed on LA echocardiographic variables assessed at baseline and 6- and 12-month follow-up, evaluating differences between patients with impaired (red) versus normal (green) coronary flow in the dominant CAB. The results (change at each time point) are plotted as mean values. Patients with impaired flow in the dominant CAB showed larger LA maximal index volumes **(A)** and longer PA-DTI **(B)** at 6 and 12 months. Additionally, they showed lower LA strain reservoir function **(C)**, conduit **(D)**, and booster pump function **(E)** in all measurements compared with patients with preserved flow at the dominant CAB.

recently recognized as a trigger of atrial fibrosis. Extensive atrial scarring with diffuse interstitial accumulation of collagen was observed 2 months after ischemic injury in an animal model.[3] Because of the thin myocardial wall of the atrium (2-3 mm), even limited ischemic injury may lead to significant structural impairment.[21,22] In clinical practice, noninvasive quantification of atrial fibrosis remains challenging. However, several echocardiography-based techniques have proved to be a reliable surrogate of atrial fibrosis. Prolongation of the PA-DTI, which measures the total atrial conduction time, shows a linear relationship with the degree of atrial fibrosis.[7] Likewise, atrial fibrosis may result in reduced LA compliance, represented by impaired LA reservoir strain.[23] A distorted structural and functional atrial substrate ultimately results in dilatation of the atria.[20] As demonstrated in other clinical scenarios, LA functional impairment often precedes LA anatomic changes.[24,25] In the present study, marked impairment of atrial function was evident shortly after ischemia. Far from transient, this effect remained unchanged throughout follow-up. However, significant changes in atrial structure, expressed as longer PA-DTI (a surrogate of atrial fibrosis) and larger LA volume, were observed from 6 months onward. Our observations are in line with experimental swine models of atrial ischemia,[3] in which markedly reduced LA reservoir and booster pump function were present shortly after LA ischemia and remained depressed at 2 months. In addition, specimens with atrial infarction presented with larger LA dilatation at 2 months as a result of extensive postischemic fibrosis. The maintenance of these structural changes over time, despite optimal medical therapy after STEMI, indicate the presence of extensive ischemia-related injury. Importantly, these findings were independent of LVEF or the presence of significant MR.

In recent years, the term *atrial cardiomyopathy* has been introduced to describe any structural and/or functional change in the atria leading to clinical consequences.[26] Although recognized as a potential cause of atrial myopathy,[27] ischemic atrial disease is not fully recognized as a clinical entity. The present study provides an "in vivo model" of the effect of atrial ischemia complicating STEMI and defines the time course of both structural and functional changes of the left atrium induced by atrial ischemia during 1-year follow-up. Our findings will help understand this often underdiagnosed problem and to define the potential clinical effects associated.

Study Limitations

Several limitations should be acknowledged. This was a retrospective, observational study of patients referred to a tertiary center, and therefore selection bias cannot be excluded. The dominant CAB was defined as the largest visible CAB. Therefore, dominant CAB with flush ostial occlusion may have been overlooked during coronary angiography, although this is highly unlikely, as previously reported in a subset of patients from this cohort who underwent follow-up coronary angiography.[9] In addition, there might be important variability in the total amount of supplied myocardium by a given dominant CAB. Because of the nature of the study, there was no objective quantification of the extension of the ischemia-induced atrial myocardial damage. Exact timing of changes in LA structure and function could not be determined, as the study was retrospective and the echocardiograms were obtained at specific time points during follow-up. Nevertheless, this objective was beyond the scope of the present study. Although the rate of previous MI is rather low, whether this could have induced preexisting atrial remodeling in these patients and therefore affected the observed results cannot be excluded.

CONCLUSION

Impaired coronary flow in the dominant CAB in patients with STEMI is associated with LA adverse anatomic and functional LA remodeling. Functional remodeling, assessed by LA strain, preceded anatomic structural remodeling in early phases after STEMI.

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