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Antithrombotic Therapy for Patients with Left Ventricular Mural Thrombus

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Brief title: Left Ventricular Thrombus and Cardiovascular Events
Tweet: Left ventricular thrombus is associated with a very high risk of major cardiovascular events. Total thrombus regression can be obtained with different anticoagulants including DOACs and is a major determinant of improved clinical outcomes. @ActionCoeur @docjohanne
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ABSTRACT

Background: Contemporary data are lacking regarding the prognosis and management of left ventricular thrombus (LVT).

Objectives: To quantify the effect of anticoagulation therapy on LVT evolution using sequential imaging and to determine the impact of LVT regression on the incidence of thromboembolism, bleeding, and mortality.

Methods: From January 2011 to January 2018, a comprehensive computerized search of LVT was conducted using 90 065 consecutive echocardiogram reports. Only patients with a confirmed LVT were included after imaging review by two independent experts. Major adverse cardiovascular events (MACE), which included death, stroke, myocardial infarction or acute peripheral artery emboli were determined as well as major bleeding events (BARC ≥3) and all-cause mortality rates.

Results: There were 159 patients with a confirmed LVT. Patients were treated by vitamin K antagonists (VKA) (48.4%), parenteral heparins (27.7%) and direct oral anticoagulants (DOACs) (22.6%). Antiplatelet therapy was used in 67.9% of the population. A reduction of the LVT area from baseline was observed in 121 patients (76.1%) and total LVT regression occurred in 99 patients (62.3%) within a median time of 103 [32-392] days. The independent correlates of LVT regression were a non-ischemic cardiomyopathy (HR 2.74; 95%CI [1.43-5.26], p=0.002) and a smaller baseline thrombus area (HR 0.66; 95%CI [0.45-0.96], p=0.031). The frequency of MACE was 37.1%; mortality 18.9%; stroke 13.3%; and major bleeding 13.2%, during a median follow-up of 632 [187-1126] days. MACE occurred in 35.4% and 40.0% of patients with total LVT regression and those with persistent LVT (p=0.203). A reduced risk of mortality was observed among patients with total LVT regression (HR 0.48; 95%CI [0.23-0.98]; p=0.039) whereas an increased major bleeding risk was observed among patients with persistent LVT (9.1% vs. 12%; HR 0.34; 95%CI [0.14-0.82], p=0.011). A left ventricular ejection fraction ≥ 35% (HR 0.46; 95%CI [0.23-0.93], p=0.029) and anticoagulation therapy > 3 months (HR 0.42; 95%CI [0.20-0.88], p=0.021) were independently associated with less MACE.

Conclusion: The presence of LVT was associated with a very high risk of MACE and mortality. Total LVT regression, obtained with different anticoagulant regimens, was associated with reduced mortality.

Condensed abstract (100 words)

Left ventricular thrombus (LVT) has become a rare complication. In a large cohort, independent imaging review identified 159 patients with a confirmed LVT. A total LVT regression was obtained in 62.3% and was more frequent in patients with non-ischemic cardiomyopathy (HR 2.74; 95%CI [1.43-5.26], p=0.002) and smaller baseline thrombus area (HR 0.66; 95%CI [0.45-0.96], p=0.031). Clinical events were frequent with 37.1% of major adverse cardiovascular events, 18.9% of mortality and 13.2% of major bleeding. Total LVT regression, obtained with different anticoagulation regimens including direct oral anticoagulant, was associated with a reduced risk of mortality (HR 0.48; 95%CI [0.23-0.98]; p=0.039).

Keywords: Left ventricular thrombus, myocardial infarction, antithrombotic, thrombus regression, mortality, direct oral anticoagulant.

ABBREVIATIONS

ARVD: arrhythmogenic right ventricular dysplasia

BARC: bleeding academic research consortium
DOAC: direct oral anticoagulant
LEVF: left ejection ventricular fraction
LVT: left ventricular thrombus
MACE: major adverse cardiovascular events
MI: myocardial infarction
MRI: magnetic resonance imaging
STEMI: ST-segment elevation myocardial infarction
TIA: Transient Ischemic Attack
VKA: vitamin-K antagonist

Introduction

The advent of reperfusion therapy and the widespread use of primary percutaneous coronary intervention (PCI) have markedly reduced the incidence of post myocardial infarction (MI) left ventricular thrombus (LVT) over the last decades (1–3). Nevertheless, contemporary epidemiologic studies suggest that the incidence of LVT may remain as high as 15% to 25% in patients with ST-segment elevation MI (STEMI) (4–6) and up to 36% in the setting of dilated cardiomyopathy (7,8) when detected with optimal imaging modalities.

Despite adequate anticoagulation therapy, LVT remains a severe complication associated with a high risk of cerebral and peripheral arterial embolism and subsequent mortality (9–11). American and European Guidelines (12,13) recommend vitamin K antagonist (VKA) for at least 3 to 6 months. The duration must be individualized according to bleeding risk. The need for concomitant antiplatelet therapy may be considered. There is limited supportive evidence (14,15). The effect of anticoagulation on LVT regression as well as the optimal anticoagulation therapy duration and their potential impact on clinical outcomes are lacking. Moreover, no study has, to date, evaluated the efficacy and the safety of direct oral anticoagulants (DOACs) in this clinical setting.

The purposes of this study were, first, to describe the effect of anticoagulation therapy on LVT evolution and secondly, to identify the independent predictors of LVT regression and clinical outcomes.

METHODS

Study design and population

From January 2011 to December 2017, all reports of consecutive echocardiogram performed at the Institute of Cardiology, Pitié-Salpêtrière hospital (Paris, France), were analyzed

using a computerized case sensitive search. All patients with a reported LVT, regardless of the underlying disease, were screened and only patients with a confirmed LVT by two independent experts, were included. In case of discordance, an additional imaging modality was performed [i.e., contrast trans-thoracic echocardiography, cardiac computed tomography scan (CT scan) or cardiac magnetic resonance imaging (MRI)] and a third expert was requested to confirm the diagnosis. Patients with right ventricular thrombus and atrial thrombus were excluded from the study.

Thrombus evaluation

LVT was defined as an echodense mass adjacent to a hypokinetic or akinetic myocardial segment. To be distinguishable from the underlying myocardium, a clear thrombus–blood interface was required and LVT had to be visible at least on two views during all the cardiac cycle. LVT diameters (mm), area (mm^2) and volume (mm^3) were assessed for each trans-thoracic echocardiogram considering the mean of 3 measures to study LVT evolution over time (**Online Figure 1**). Mobility and location of LVT were also defined. LVT was considered mobile if thrombus had a pedunculated non-mural component. A calcified LVT was defined as a persistent left ventricular mural thrombus encapsulated by thickened and calcified endocardium. Left ventricular characteristics including left ventricular ejection fraction (LVEF), left ventricular volume, wall motion, cardiac output and potential mechanical complications were also collected. All echocardiograms were reviewed using the dedicated TOMTEC imaging system tools (TOMTEC, Unterschleissheim Germany).

Baseline and data collection

All patient baseline characteristics including cardiovascular risk factors, past medical history of major bleeding or ischemic event, underlying disease and long-term use of

anticoagulation therapy before the diagnosis of LVT were collected through medical reports. Special attention was given to the type (VKA, DOACs, low-molecular-weight heparin, unfractionated heparin) of anticoagulant used and duration of anticoagulation therapy and the association with antiplatelet therapy. Treatment duration was obtained through medical reviews of each hospital visit and by attending physician or patient interviews.

Study objectives

The objectives of this study were to evaluate LVT regression under anticoagulation therapy, the time needed for total LVT regression using sequential noninvasive imaging and the independent correlates associated with total LVT regression. The impact of LVT regression on thromboembolism, bleeding and mortality and factors associated with major cardiovascular adverse events were determined.

Endpoint definitions

Total LVT regression was defined by a complete disappearance of LVT on all echocardiography views at the last available follow-up. LVT persistence was classified as an increased thrombus dimension, a stable thrombus or a partial thrombus regression at the last available follow-up.

We collected the following clinical outcomes during the period of observation: major adverse cardiovascular events (MACE) defined as the composite of all cause death, ischemic stroke or transient ischemic attack (TIA), myocardial infarction (MI) or acute peripheral artery emboli., any embolic complications defined as the composite of ischemic stroke or TIA, acute coronary emboli or acute peripheral artery emboli (limb, renal or digestive arteries), all-cause death and bleeding events defined as clinically relevant bleeding events (BARC≥2) and major bleeding events (BARC≥3) according to the international Bleeding Academy Research

Consortium (BARC) (16).

Statistical analysis

All data were shown as means with standard deviations or medians with interquartile ranges for continuous variables and as numbers and percentages of patients for categorical variables. Non-Gaussian variables were compared with the use of the Mann–Whitney test. Chi-square testing was used for frequency comparisons. The 95% confidence interval (CI) for the hazard ratio (HR) is presented. The population was evaluated according to total LVT regression or incomplete regression during follow-up. Time to first clinical endpoints was estimated using the Kaplan-Meier method and differences between total LVT regression and persistent LVT were assessed with the log-rank test. Univariate and multivariate Cox regression analyses were used to identify independent correlates for total LVT regression. The following variables related to clinical outcomes in univariate analysis ($p<0.1$) were included in the first multivariate model : age, underlying disease (ischemic vs non-ischemic cardiomyopathy), LVEF, anticoagulation by DOACs or heparin (considering VKA treatment as reference), combined antithrombotic treatment by anticoagulant and antiplatelet therapy (in comparison to anticoagulation therapy alone), baseline thrombus area (defined as a continuous variable), history of atrial fibrillation, atrial fibrillation complication (occurring after thrombus diagnosis) and major bleeding (BARC≥3). A second multivariate Cox model, including the aforementioned variables with antithrombotic treatment duration and total LVT regression as additional variables, was performed to identify independent correlates of MACE, all-cause death and all embolic complications in this specific population of LVT patients. All tests had a two-sided significance level of 5% and were performed with the use of SAS software, version 9.2 (SAS Institute).

RESULTS

Characteristics of the patients and thrombus description

Of the 90,065 echocardiograms performed during the study period, a total of 174 patients had a reported LVT and 159 patients were definitively included in this analysis after imaging review by two independent experts (**Figure 1**). The baseline characteristics of the patients with confirmed LVT are described in **Table 1.** The population was relatively young (mean age of 58±13 years) with a high prevalence of cardiovascular risk factors leading to ischemic cardiomyopathy (78.6%, n=125) including STEMI in one out of three patients (35.2%, n=56). Severe left ventricular dysfunction was common (mean LVEF of 31.9±12.5%) with more than half of the population which had a mean cardiac output index of less than 2.6 L/min. The most frequent left ventricular wall motion abnormality was akinesis of the apical segments where LVT were predominantly located (98.1%). Left ventricular aneurysms were found in 15.1% (n=24) of patients. LVT were classified as mobile in 34.6% (n=55) of patients and calcified LVT were observed in 1.3% (n=2) of patients. The largest diameter, surface area and thrombus volume as well as the detailed baseline echocardiographic measurements are displayed in **Table 2**.

Antithrombotic therapy

Only two patients (1.2%) were treated with antiplatelet therapy alone due to high bleeding risk. The vast majority of the study population (98.8%) was exposed to anticoagulation therapy including VKA (48.4%, n=77) mostly fluindione (46.5%, n=74), DOACs (22.6%, n=36), low molecular weight heparin (23.3%, n=37) or unfractionated heparin (4.4%, n=7). Concomitant antiplatelet therapy was prescribed in 67.9% (n=108) of patients (**Table 3**). Median duration of anticoagulation therapy was 508 [115-986] days without significant difference regarding the anticoagulant drug administrated (**Online Table 1**).

Thrombus regression

A reduction of the thrombus area from the baseline echocardiography to the final echocardiography (median delay of 338 [38-907] days) was observed in 76.1% (n=121) of patients. The time-dependent cumulative total regression of LVT is represented in **Figure 2** showing a progressive decrease of thrombus area. Total LVT regression was achieved in 62.3% (n=99) of patients within a median time of 103 [32-392] days.

After multivariate adjustment, the presence of a non-ischemic cardiomyopathy (HR 2.74; 95%CI [1.43-5.26], p=0.002) and a smaller baseline thrombus area (HR 0.66; 95%CI [0.45-0.96], p=0.031) were independently associated with total LVT regression. A thrombus recurrence or an increase of thrombus area was observed in 14.5% (n=23) of patients. A review of medical records reported that recurrent or increased size of LVT was associated with poor treatment adherence, pro-thrombotic conditions such as active cancer, inflammatory, hematologic diseases or chronic renal failure (**Online Table 2**).

Cardiovascular events

MACE and embolic complications occurred in 37.1% (n=59) and 22.2% (n=35) of patients, respectively, within a median follow-up period of 632 [187-1126] days. All-cause mortality was 18.9% (n=30). Clinically relevant (BARC≥2) and major (BARC≥3) bleeding events occurred in 17% (n=27) and 13.2% (n=21) of patients, respectively. Reduced mortality was observed in patients with total LVT regression (15.2% vs. 25.0%; HR 0.48; 95%CI [0.23-0.98]; p=0.039) whereas an increased major bleeding risk was observed among patients with persistent LVT (9.1% vs. 12%; HR 0.34; 95%CI [0.14-0.82], p=0.011) (**Table 4, Figure 3**). MACE occurred more frequently in patients treated with a dual antithrombotic strategy (54%, n=30 for the association of single antiplatelet therapy and anticoagulant) than those treated with a triple antithrombotic strategy (29%, n=16 for the association of dual antiplatelet therapy and

anticoagulant) with similar rate of major bleedings being 14%, n=8 and 12.5%, n=7 respectively. After multivariate adjustment, a LVEF ≥35% (HR 0.46; 95%CI [0.23-0.93], p=0.029) and a prolonged anticoagulation therapy over 3 months (HR 0.42; 95%CI [0.20-0.88], p=0.021) were independently associated with a reduced risk of MACE (**Figure 4**). Moreover, a numerically lower rate of embolic complications was observed in patients treated by a prolonged anticoagulation therapy over 3 months (HR=0.46 [0.18-1.14]; p-value=0.093) (data not shown). It has to be noted that the type of anticoagulant therapy was not independently associated with cardiovascular events in our study (data not shown).

DISCUSSION

Although the incidence of LVT has decreased in modern times, it continues to complicate both ischemic and non-ischemic cardiomyopathies and is associated with poor outcomes. This analysis provides new insights from a large and well-characterized contemporary cohort of patients with LVT (**Central Illustration**). For patients with LVT, total regression was only achieved in two thirds of our population within 3 months for half of them using full anticoagulation. The use of antiplatelet agents was common. The independent correlates of total LVT regression were an underlying non-ischemic cardiomyopathy and a smaller baseline thrombus area. LVT patients had a very high risk of MACE, embolic or major bleeding complications and mortality. Most importantly, total LVT regression was associated with a reduced mortality and which was obtained with a full anticoagulation therapy using either heparin, VKA or DOACs.

Thrombus regression and suboptimal anticoagulation therapy

This study highlights that the current antithrombotic regimen needs to be improved since one third of patients did not achieve total LVT regression and remained exposed to a high risk of

clinical complications even when combining with antiplatelet agents. Consistent with our findings, a recent study screened more than 140,000 echocardiograms and found that LVT was a rare complication as 128 LVT patients were identified. Total LVT regression was reached in 71% of patients treated by anticoagulation therapy but, unfortunately, echocardiographic follow-up and data concerning LVT regression were not available for all of the patients (11). In a single cohort of 92 post-MI patients treated with VKA, the authors found that LVT regression was dependent on time in therapeutic range. Unlike our study, there was no experience using DOACs (9).

Left ventricular thrombus and clinical outcomes

The main result of the present study is the high rate of cardiovascular events as four out of ten patients had a MACE and one out of five patients died during the follow-up period, a dramatically higher case mortality than reported in STEMI patients without LVT (17, 18). These findings are here again difficult to compare with the few prior observational studies published so far (5, 14, 15, 19, 20) but are consistent with two recent studies (9, 11) and highlight the severity of this population and the need for more efficient therapeutic strategy to reverse such poor prognosis. Several approaches to improve the prognosis of LVT patients may be considered. One of them would be to refine the antithrombotic regimen to improve and accelerate LVT regression, a factor associated with lower mortality in our study. It could be argued that LVT regression could at least partially be the consequence of thrombus embolization. However, although we cannot exclude asymptomatic embolization, we did not find significant difference in embolic complications between patients with or without LVT regression. These embolic complications could occur at any time under antithrombotic therapy, as a consequence of thrombus fragmentation, quick thrombus regression or, on the contrary, persistence of the

thrombus. The achievement of total LVT regression seems to be a marker of morbidity and mortality of the patient more than the associated embolic risk. It should not be a predominant factor to shorten the antithrombotic treatment. Moreover, after adjustment for confounding factors, atrial fibrillation was not associated with a higher rate of clinical outcomes and our data support that thrombus regression is mostly due to the duration of antithrombotic therapy and the size of the LVT. Beyond the efficacy of each anticoagulant drug, the optimal treatment duration is a major clinical issue. In our study, we observed a lower occurrence of MACE among patients who were treated by an anticoagulation therapy for a longer duration than 3 months. We can hypothesize that a longer antithrombotic treatment could lead to a better prevention of embolic complications or myocardial infarction and prevent LVT recurrence. Such findings need to be confirmed by adequately sized randomized trials. However, any intensification of the antithrombotic treatment may be compromised by more frequent bleeding complications that are already reported in more than 10% of the patients in our study. Although not designed and powered for a direct comparison between DOACs versus VKA, our study suggests a similar rate of total LVT regression, MACE and bleeding complications with both anticoagulant strategies.

Limitations

We acknowledge several limitations. This was a retrospective study from a single centre albeit the largest volume centre in the Paris area. We also acknowledge that the diagnosis of LVT was mainly based on echocardiography which may have a lower sensitivity and specificity for the detection compared to other imaging modalities such as cardiac MRI (4, 19, 21). We also acknowledge that the comparison between the different antithrombotic drugs was limited by the small sample size and that our results should be considered exploratory rather than definitive. An individualized risk stratification based on the patient characteristics, the underlying disease and

the LVT evolution under antithrombotic treatment would be ideal to guide physician decision-making and to refine the management of LVT with the main objective of reducing the risk of clinical outcomes.

CONCLUSIONS

We conclude that the clinical prognosis of patients with LVT is poor with a very high risk of major cardiovascular events and mortality. Refinement in the antithrombotic management is needed to improve clinical outcomes of these relatively young patients. Total LVT regression can be obtained with different anticoagulation regimens including DOACs and thereby reduce mortality.

CLINICAL PERSPECTIVES

Competency in Patient Care: Left ventricular thrombus is an uncommon complication of ischemic and non-ischemic cardiomyopathies associated with a high risk of adverse events and mortality. Regression of thrombus is associated with lower mortality, but in about one-third of cases, thrombus does not resolve despite anticoagulation with or without antiplatelet therapy.

Translational Outlook: Randomized studies should assess the safety and efficacy of target-specific oral anticoagulants, clarify the optimum duration of treatment, and identify predictors of recurrence after thrombus resolution.

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FIGURE LEGENDS

Figure 1. **Study flow chart.** The figure represents the patients screened and included in the final analysis.

Figure 2. Time-dependent cumulative total left ventricular thrombus regression. Each point represents thrombus area of each patient at the different echocardiographic evaluation times. The red error bars represent the median interquartile ranges.

Figure 3. Time-to-event curves for major adverse cardiovascular events (A), all-cause death (B), embolic complications (C) and major bleeding events (D) according to left ventricular thrombus evolution on treatment. The red curve represents patients that reached to total thrombus regression on treatment during follow-up and the blue one represents patients with thrombus persistence at the end of follow-up.

Figure 4. Independent correlates of major adverse cardiovascular events. LVEF indicates Left Ventricular Ejection Fraction and MACE, Major Adverse Cardiovascular Events. * The baseline thrombus area is the thrombus area measured on the first echocardiography and the variable is presented as a continuous growing variable (unit=1cm²). †Atrial fibrillation was defined by the presence of permanent or paroxysmal atrial fibrillation.

Central Illustration. Clinical outcomes associated with left ventricular thrombus and impact of total thrombus regression on prognosis. VKA indicates Vitamin K Antagonist anticoagulant; DOAC, Direct oral anticoagulant and HR, Hazard Ratio. Major bleeding events were defined by Bleeding Academic Research Consortium types 3 or 5.

Table 1: Baseline clinical characteristics

Baseline characteristics	**Patients with LVT (n = 159)**
Age (years)	58 ±13
Female sex	28 (17.6)
Body Mass Index (kg/m^2)	25.0 (22.6 - 27.4)
Active smoking	73 (45.9)
Hypertension	57 (35.8)
Family history of cardiovascular disease	19 (11.9)
Diabetes mellitus	38 (23.9)
Dyslipidemia	65 (40.9)
Creatinine clearance < 60 ml/min	33 (20.8)
Prior coronary stenting	93 (58.5)
Prior coronary artery bypass graft	8 (5)
Peripheral artery disease	18 (11.3)
Prior stroke or transient ischemic attack	20 (12.6)
Prior atrial fibrillation	18 (11.3)
Prior major bleeding	8 (5)
Previous anticoagulant therapy	20 (12.6)
Vitamin K antagonist	14 (8.8)
Direct oral anticoagulants	6 (3.8)
Underlying disease	
Coronary artery disease	125 (78.6)
NSTEMI	18 (11.3)
STEMI	56 (35.2)
Successful revascularization	45 (80.3)
STEMI>24h	12 (21.4)
Dilated cardiomyopathy	23 (14.5)
Hypertrophic cardiomyopathy	2 (1.3)
Myocarditis	6 (3.8)
Tako-tsubo cardiomyopathy	2 (1.3)
ARVD with associated LV impairment	1 (0.6)

Variables are expressed in number (%) or mean ± interquartiles. ARVD indicates Arrhythmogenic Right Ventricular Dysplasia; NSTEMI, Non ST-segment Elevation Myocardial Infarction; LVT, Left Ventricular Thrombus and STEMI, ST-segment Elevation Myocardial Infarction.

Table 2. Baseline echocardiographic evaluation.

Baseline echocardiographic measurements	**Patients with LVT (n =159)**
Left ventricular ejection fraction (%)	31.9 ± 12.5
Cardiac output (l/min)	4.1 (3.0 - 4.9)
Left ventricular wall motion	
Akinesis in apical segments	130 (81.8)
Hypokinesis in apical segments	6 (3.8)
Global hypokinesis	23 (14.5)
Left Ventricular Thrombus	
Largest diameter (mm)	19 (13 - 24)
Area (cm^2)	1.34 (0.8 - 2.57)
Volume (mm^3)	1.06 (0.49 - 2.40)
Mobile thrombus	55 (34.6)
Apical thrombus	156 (98.1)
Left ventricular aneurysm	24 (15.1)
Other mechanical complication	1 (0.6)

Variables are expressed in number (%) or mean ± interquartiles.

LVT indicates Left Ventricular Thrombus

Table 3. Antithrombotic strategy following left ventricular thrombus diagnosis

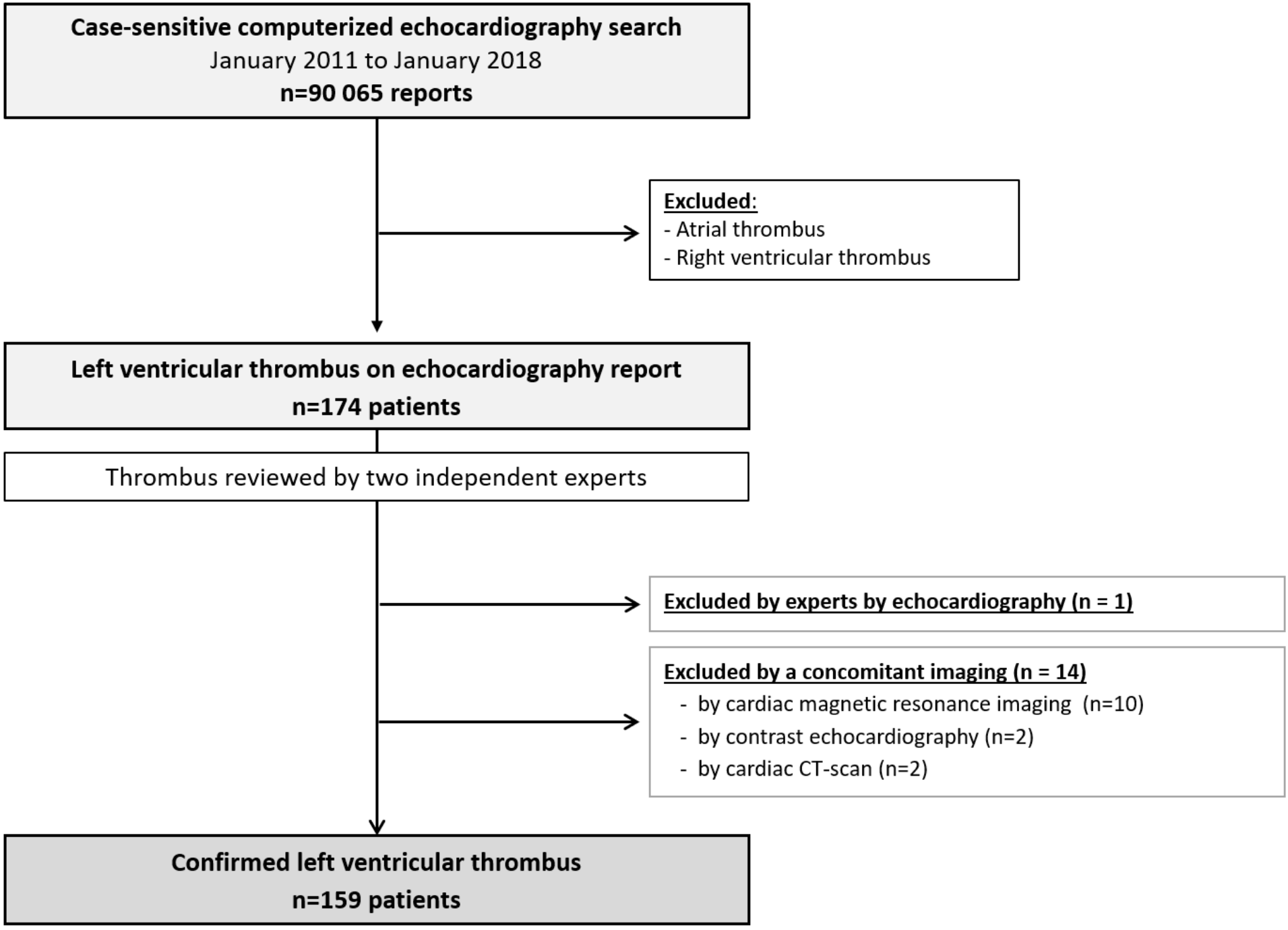
Antithrombotic strategy	Patients with LVT (n=159)
Antiplatelet therapy only	2 (1.2)
Anticoagulation only	45 (28.3)
Anticoagulation + Antiplatelet therapy	
Aspirin with anticoagulant	52 (32.7)
Clopidogrel with anticoagulant	3 (1.9)
Ticagrelor with anticoagulant	1 (0.6)
Anticoagulant + Dual Antiplatelet Therapy	56 (35.2)
Anticoagulation type	
Vitamin K Antagonist	77 (48.4)
Coumadin	3 (1.9)
Fluindione	74 (46.5)
Direct oral anticoagulant	36 (22.6)
Apixaban 2.5mg*2	9 (5.7)
Apixaban 5mg*2	9 (5.7)
Dabigatran 110mg*2	5 (3.1)
Dabigatran 150mg*2	0 (0)
Rivaxoraban 15mg	10 (6.3)
Rivaxoraban 20mg	3 (1.9)
Low Molecular Weight Heparin	37 (23.3)
Unfractionated Heparin	7 (4.4)

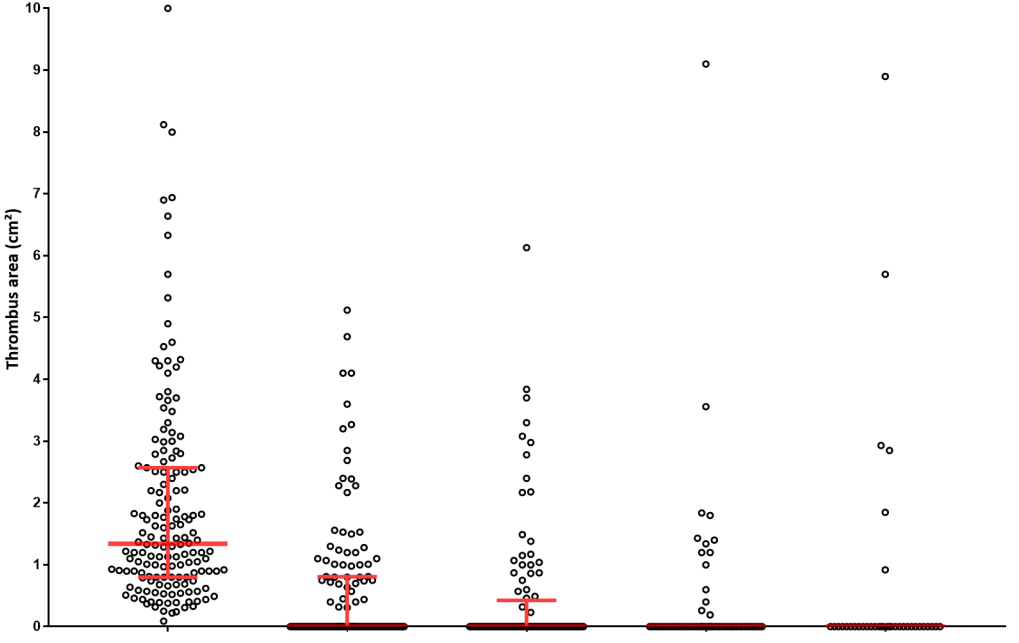
Variables are expressed in number (%). LVT indicates Left Ventricular Thrombus.

Table 4. Cardiovascular events in the whole population and according to the occurrence of a total thrombus regression

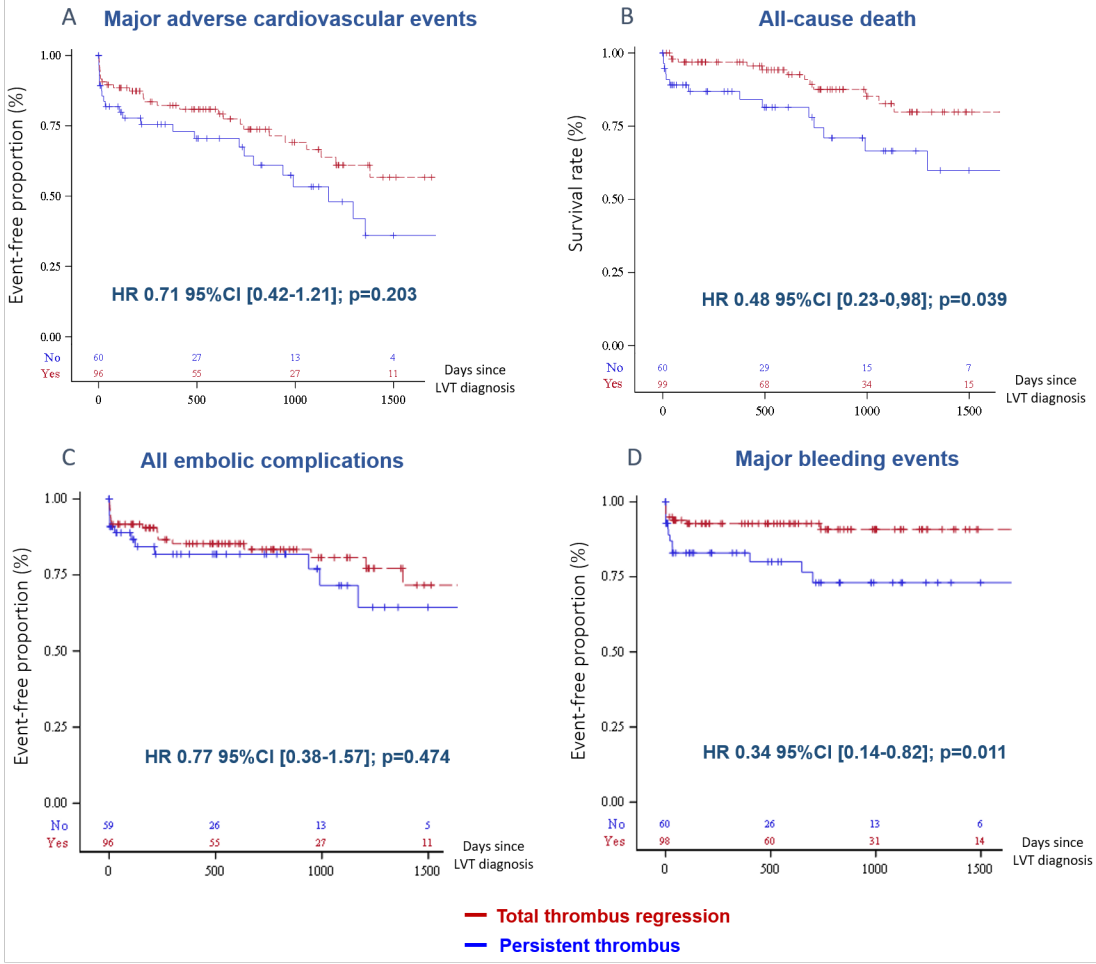
	All population (n=159)	Total thrombus regression (n=99)	Persistent thrombus (n=60)	Log-Rank test p value
Major Adverse Cardiovascular events: composite of all-cause death, ischemic stroke/TIA, MI or acute peripheral artery emboli	59 (37.1)	35 (35.4)	24 (40.0)	0.203
Composite of cardiovascular death, ischemic stroke/TIA, MI or acute peripheral artery emboli	46 (28.9)	29 (29.3)	17 (28.3)	0.524
Cardiovascular death	14 (8.8)	8 (8.1)	6 (10.0)	0.434
All-cause death	30 (18.9)	15 (15.2)	15 (25.0)	0.039
Stroke/TIA	21 (13.3)	14 (14.1)	7 (11.9)	0.871
Acute peripheral artery emboli	20 (12.7)	14 (14.1)	6 (10.2)	0.962
All embolic complications	35 (22.2)	22 (22.2)	13 (22.0)	0.474
BARC ≥ 2 bleeding	27 (17.0)	12 (12.1)	15 (25.0)	0.002
BARC ≥ 3 bleeding	21 (13.2)	9 (9.1)	12 (20.0)	0.011

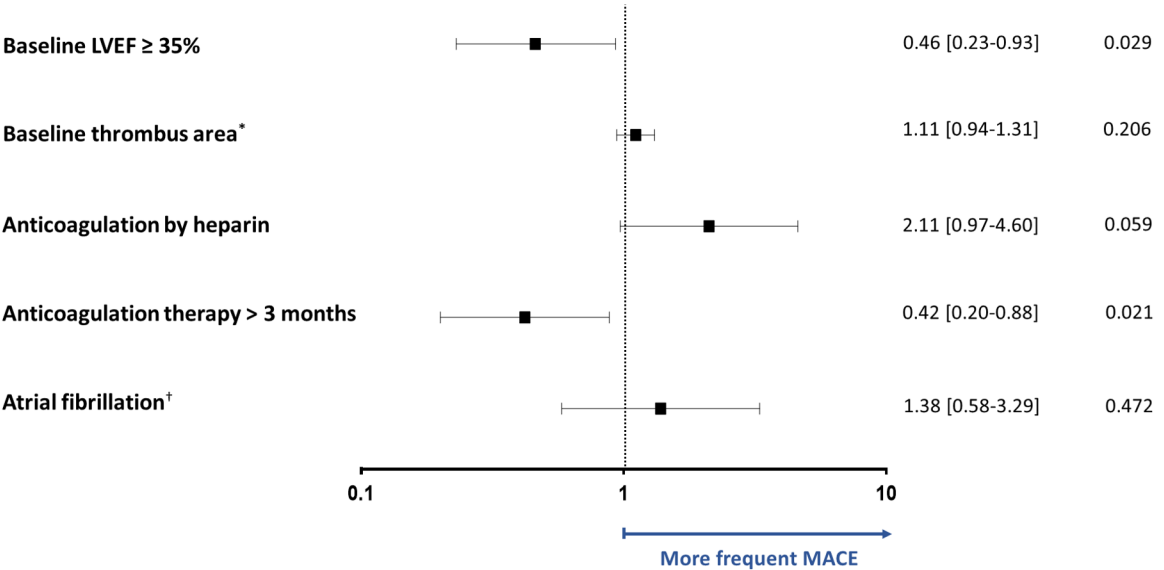
Variables are expressed in number (%). BARC indicates Bleeding Academic Research Consortium; MI, Myocardial Infarction and TIA, Transient Ischemic Attack


Case-sensitive computerized echocardiography search
January 2011 to January 2018
n=90 065 reports
Excluded:
- Atrial thrombus
- Right ventricular thrombus
Left ventricular thrombus on echocardiography report
n=174 patients
Thrombus reviewed by two independent experts
Excluded by experts by echocardiography (n = 1)
Excluded by a concomitant imaging (n = 14)
- by cardiac magnetic resonance imaging (n=10)
- by contrast echocardiography (n=2)
- by cardiac CT-scan (n=2)
Confirmed left ventricular thrombus
n=159 patients



Echocardiographic images	Index	2	3	4	5
Median time between echocardiograms		26 days	52 days	69 days	311 days
Cumulative total Thrombus regression		**43.4%** (n=69)	**50.5%** (n=93)	**61.0%** (n=97)	**62.3%** (n=99)


A
Major adverse cardiovascular events
Event-free proportion (%)
1.00
0.75
0.50
0.25
0.00
HR 0.71 95%CI [0.42-1.21]; p=0.203
No 60 27 13 4
Yes 96 55 27 11
0 500 1000 1500
Days since LVT diagnosis
B
All-cause death
Survival rate (%)
HR 0.48 95%CI [0.23-0,98]; p=0.039
No 60 29 15 7
Yes 99 68 34 15
Days since LVT diagnosis
C
All embolic complications
HR 0.77 95%CI [0.38-1.57]; p=0.474
No 59 26 13 5
Yes 96 55 27 11
Days since LVT diagnosis
D
Major bleeding events
HR 0.34 95%CI [0.14-0.82]; p=0.011
No 60 26 13 6
Yes 98 60 31 14
Days since LVT diagnosis
Total thrombus regression
Persistent thrombus


Adjusted HR [95%CI]
p-value
Baseline LVEF ≥ 35%
0.46 [0.23-0.93]
0.029
Baseline thrombus area*
1.11 [0.94-1.31]
0.206
Anticoagulation by heparin
2.11 [0.97-4.60]
0.059
Anticoagulation therapy > 3 months
0.42 [0.20-0.88]
0.021
Atrial fibrillation†
1.38 [0.58-3.29]
0.472
0.1
1
10
More frequent MACE