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Original article

Long-term prognostic impact of the left anterior descending coronary artery as the STEMI-related culprit vessel: subanalysis of the EXAMINATION-EXTEND trial

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ABSTRACT

Introduction and objectives: There is limited data on the impact of the culprit vessel on very long-term outcomes after ST-elevation myocardial infarction (STEMI). The aim was to analyze the impact of the left anterior descending coronary artery (LAD) as the culprit vessel of STEMI on very long-term outcomes.
Methods: We analyzed patients included in the EXAMINATION-EXTEND study (NCT04462315) treated with everolimus-eluting stents or bare-metal stents after STEMI (1498 patients) and stratified according to the culprit vessel (LAD vs other vessels). The primary endpoint was the patient-oriented composite endpoint (POCE), including all-cause mortality, myocardial infarction (MI) or revascularization at 10 years. Secondary endpoints were individual components of POCE, device-oriented composite endpoint and its individual components and stent thrombosis. We performed landmark analyses at 1 and 5 years. All endpoints were adjusted with multivariable Cox regression models.
Results: The LAD was the culprit vessel in 631 (42%) out of 1498 patients. The LAD-STEMI group had more smokers, advanced Killip class and worse left ventricular ejection fraction. Conversely, non-LAD-STEMI group showed more peripheral vascular disease, previous MI, or previous PCI. At 10 years, no differences were observed between groups regarding POCE (34.9% vs 35.4%; adjusted hazard ratio [HR], 0.95; 95% confidence interval [95%CI], 0.79-1.13; $P = .56$) or other endpoints. The all-cause mortality rate was higher in the LAD-STEMI group ($P = .041$) at 1-year.
Conclusions: In a contemporary cohort of STEMI patients, there were no differences in POCE between LAD as the STEMI-related culprit vessel and other vessels at 10 years follow-up. However, all-cause mortality was more common in the LAD-STEMI group within the first year after STEMI.

Keywords: Acute myocardial infarction. STEMI. Angiography. Coronary. Percutaneous coronary intervention.

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Impacto pronóstico a largo plazo de la arteria descendente anterior como vaso culpable del IAMCEST: subanálisis del estudio EXAMINATION-EXTEND

RESUMEN

Introducción y objetivos: Existen datos limitados sobre el impacto a muy largo plazo del vaso culpable después de un infarto de miocardio con elevación del segmento ST (IAMCEST). El objetivo fue analizar el efecto de la arteria descendente anterior (DA) como vaso culpable en el IAMCEST en los resultados a muy largo plazo.
Métodos: Se analizaron los pacientes incluidos en el estudio EXAMINATION-EXTEND (NCT04462315) que recibieron *stents* liberadores de everolimus o *stents* metálicos después de un IAMCEST (1.498 pacientes) y se estratificaron según el vaso culpable (DA frente a otros vasos). El objetivo primario fue el objetivo combinado orientado al paciente (POCE) que incluyó muerte por cualquier causa, infarto agudo de miocardio (IAM) o revascularización a los 10 años. Los objetivos secundarios fueron los componentes individuales del POCE, el evento compuesto orientado al dispositivo y sus componentes individuales, así como la trombosis del *stent*. Se realizaron análisis de puntos de referencia a 1 y 5 años. Todos los objetivos fueron ajustados mediante modelos de regresión de Cox multivariantes.
Resultados: De los 1.498 pacientes, la DA fue el vaso culpable en 631 (42%). El grupo IAMCEST-DA mostró mayor proporción de fumadores, una clase Killip más avanzada y una peor fracción de eyección del ventrículo izquierdo. En cambio, el grupo sin IAMCEST-DA mostró mayor prevalencia de enfermedad vascular periférica, IAM previo y angioplastia coronaria previa. A los 10 años no se observaron diferencias entre los grupos para el POCE (34,9 frente a 35,4%; *hazard ratio,* 0,95; intervalo de confianza del 95%, 0,79-1,13; p = 0,56) ni para otros objetivos. Hubo una mayor mortalidad por cualquier causa en el grupo IAMCEST-DA (p = 0,041) al primer año.
Conclusiones: En una cohorte contemporánea de pacientes con IAMCEST no hubo diferencias en cuanto al POCE entre la DA como vaso culpable en el IAMCEST y los otros vasos a los 10 años de seguimiento. Sin embargo, en el primer año después del IAMCEST, la mortalidad por cualquier causa fue más común en el grupo IAMCEST-DA.

Palabras clave: Infarto agudo de miocardio. IAMCEST. Angiografía. Coronaria. Intervención coronaria percutánea.

Abbreviations

LAD: left anterior descending coronary artery. **LVEF:** left ventricular ejection fraction. **MI:** myocardial infarction. **PCI:** percutaneous coronary intervention. **POCE:** patient-oriented composite endpoint. **STEMI:** ST – segment elevation myocardial infarction.

INTRODUCTION

Percutaneous coronary intervention (PCI) is the first-line therapy in patients with ST-segment-elevation myocardial infarction (STEMI).[1] The STEMI-related culprit vessel is usually considered as one of the most important prognostic factors in STEMI patients.[2,3] This assumption comes from previous studies –conducted in the pre-reperfusion or thrombolysis era– which showed that left anterior descending artery (LAD)-related STEMIs were associated with worse clinical outcomes compared with right coronary (RCA) and left circumflex artery (LCX)-related lesions.[4-9]

However, in the contemporary era of primary PCI there are limited data about the prognostic impact of LAD as the STEMI-related culprit vessel especially in a very long follow-up.[10,11]

Therefore, the aim of this study was to investigate the impact of the LAD as the STEMI-related culprit vessel on very long-term clinical outcomes in STEMI patients undergoing primary PCI enrolled in the EXAMINATION-EXTEND study (10-year follow-up of the EXAMINATION trial).

METHODS

Study design and patients

The EXAMINATION trial (NCT00828087) was an all-comer, multicenter, prospective, 1:1 randomized, 2-arm, single-blind, controlled trial conducted at 12 centers across 3 countries to assess the superiority of EES (Xience V) vs BMS (Multilink Vision, Abbott Vascular) in STEMI patients regarding the primary endpoint of all-cause mortality, any myocardial infarction, and any revascularization at 1 year. The study had broad inclusion criteria and few exclusion criteria to ensure an all-comer STEMI population representative of the routine clinical practice. The study outcomes have been reported up to the year 5.[12,13] After that, it was reinitiated as the EXAMINATION-EXTEND study to evaluate patient- and device-oriented composite endpoints at 10 years. The latter is registered at ClinicalTrials.gov (NCT04462315) as an investigator-driven extension of follow-up of the EXAMINATION trial. An independent study monitor (ADKNOMA, Barcelona, Spain) verified the adequacy of the extended follow-up and events reported. All events were adjudicated and classified by an independent event adjudication committee blinded to the therapy groups (Barcicore Lab, Barcelona, Spain). The 10-year primary endpoint results of the EXAMINATION-EXTEND study have been previously published.[14] For the aim of this study, baseline, procedural characteristics and outcomes were stratified according to the STEMI-related culprit vessel (LAD vs others). All centers participating in the EXAMINATION trial received the approval of their Medical Ethics Committee, and all enrolled patients who had already signed their written informed consent forms. Medical ethics committee approval for EXAMINATION-EXTEND was granted at the institutions of the principal investigators (Hospital Clínic and Hospital Bellvitge, Barcelona, Spain), and the requirement to obtain informed consent to gather information on 10- year events was waived. The study complied with the Declaration of Helsinki.

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Study endpoints

The primary endpoint of this study was the patient-oriented composite endpoint of all-cause mortality, any myocardial infarction, or any revascularization at 10 years. Secondary endpoints were each individual components of the primary endpoint, device-oriented composite endpoint (cardiac death, target-vessel myocardial infarction, target lesion revascularization), its individual components and stent thrombosis. Detailed descriptions of the study endpoints and definitions have been published previously.[15]

Statistical analysis

Continuous variables are expressed as median (interquartile range; IQR), and categorical variables as absolute and relative frequencies (percentages).

Baseline clinical, angiographic, and procedural characteristics were compared between the groups stratified by the STEMI-related artery (LAD vs other vessels) using the Wilcoxon rank sum test, the chi-square, or Fisher's exact test, where appropriate.

Time-to-event curves for POCE and all-cause death were plotted using the one minus the Kaplan-Meier estimate and the cumulative incidence function for other outcomes. The incidence of events at the follow-up was compared between groups using log-rank or Grey's test. Landmark analyses were also performed, setting landmark points at 1 and 5 years.

The association between LAD as a STEMI-related culprit vessel and events was analyzed in univariable and multivariable cause-specific Cox regression models. Covariates were added to the multivariable model in 2 blocks. The first model included all clinically relevant baseline characteristics variables with $P < .1$ in the between-groups comparison (LAD vs other vessels), i.e., sex, smoking status, peripheral vascular disease, previous PCI, previous CABG, previous MI, and Killip class. The second model (expanded adjustment) included both the baseline characteristics and the left ventricular ejection fraction (LVEF) at discharge.

Two-tailed P-value < .05 was considered statistically significant. All statistical analyses were performed using *R* (R Core Team (2022). R: a language for statistical computing. R Foundation for Statistical Computing, Austria) with the following packages: survival, tidycmprsk, jskm, and gtsummary.

RESULTS

Patient characteristics

In 631 (42%) out of the 1498 STEMI patients included in the EXAMINATION EXTEND trial, the LAD was the culprit vessel (LAD-STEMI group), whereas in 867 patients (58%) it was not (non-LAD-STEMI group). Patients' inclusion flowchart is shown in figure 1.

LAD-STEMI group had a higher incidence of active smokers, advanced Killip class and more depressed LVEF vs the non-LAD-STEMI group, which, however, exhibited a higher incidence of peripheral vascular disease, previous MI and previous PCI (table 1). Also, although non-statistically significant, the frequency of late comers and bailout PCI was numerically higher in the LAD-STEMI group.

Regarding procedural data, LAD-STEMI group received smaller stent diameter (3.12 mm vs 3.26 mm; $P = .001$) and had a lower incidence of ST-segment resolution than the non-LAD-STEMI group (73%, vs 50%; $P = .001$) (table 2). The use of GP IIb/IIIa inhibitors

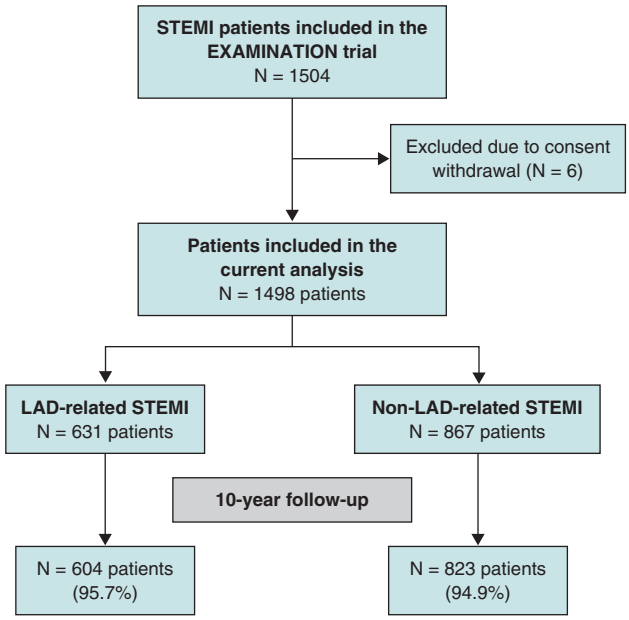

Figure 1. Study flowchart. A total of 1498 patients were initially recruited. At 10 years, clinical follow-up was obtained in 95.2% of the patients. LAD, left anterior descending artery; STEMI, ST-elevation myocardial infarction.

was numerically lower in the LAD-STEMI group, although the differences between groups were not statistically significant. Of note, almost half of the patients (46%) with LAD-STEMI had the lesion in the proximal LAD compared with 44% of them who had it in the mid/distal LAD.

Ten-year outcomes

At the 10-year follow-up, POCE did not differ between LAD-STEMI and non-LAD-STEMI group (adjusted HR, 0.95; 95%CI, 0.79-1.13; $P = .56$) (figure 2). Moreover, no differences were found in terms of each individual component of POCE (all-cause mortality, MI, any revascularization) (figure 3) and other secondary endpoints (figure 1 of the supplementary data). Furthermore, when the expanded adjustment was performed and LVEF was included in the multivariable analysis, there were no inter-group differences between (table 3).

Landmark analyses

POCE landmark analysis showed no differences between the 2 groups across different time points. (figure 4A). Looking specifically at the various POCE individual components, the LAD-STEMI group exhibited a higher rate of all-cause mortality within the first year vs the non-LAD-STEMI group (p = 0.041), but this difference disappeared thereafter (figure 4B). Between years 0 and 1, there was also a trend toward a lower rate of myocardial infarction in the LAD-STEMI group vs the non-LAD-STEMI group (p = 0.081), which disappeared after year 1 (figure 4C). No differences were ever found regarding any revascularization (figure 4D) or other secondary endpoints between the 2 groups (figure 2 of the supplementary data).

DISCUSSION

The main findings of this study can be summarized as follows: *a)* STEMI patients with LAD as the culprit vessel have a different

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Table 1. Baseline clinical characteristics

Clinical characteristics	Overall (N = 1498)[a]	LAD-STEMI (N = 631)[a]	Non-LAD-STEMI (N = 867)[a]	*P*[b]
Age (years)	61 [51-71]	61 [51-71]	61 [51-70]	.778
Sex (male)	1,244 (83%)	512 (81%)	732 (84%)	.094
Current smoker	415 (28%)	197 (31%)	218 (25%)	.009
Hyperlipidemia	655 (44%)	268 (43%)	387 (45%)	.419
Hypertension	725 (48%)	307 (49%)	418 (48%)	.843
Peripheral vascular disease	55 (3.7%)	14 (2.2%)	41 (4.7%)	.011
Previous stroke	31 (2.1%)	14 (2.2%)	17 (2.0%)	.726
Previous myocardial infarction	80 (5.3%)	23 (3.7%)	57 (6.6%)	.013
Previous PCI	61 (4.1%)	18 (2.9%)	43 (5.0%)	.042
Previous CABG	10 (0.7%)	1 (0.2%)	9 (1.0%)	.052
Clinical presentation				.126
PCI (< 12 h)	1,268 (85%)	520 (82%)	748 (86%)	
Bailout PCI	98 (6.5%)	51 (8.1%)	47 (5.4%)	
PCI after successful thrombolysis	34 (2.3%)	14 (2.2%)	20 (2.3%)	
Late comer (> 12 h and < 48 h)	97 (6.5%)	46 (7.3%)	51 (5.9%)	
Killip class				< .001
I	1,337 (90%)	525 (83%)	812 (94%)	
II	115 (7.7%)	76 (12%)	39 (4.5%)	
III	23 (1.5%)	20 (3.2%)	3 (0.3%)	
IV	18 (1.2%)	8 (1.3%)	10 (1.2%)	
In-hospital LVEF (%)	52 (45, 58)	46 [40-55]	55 [50-60]	< .001
Symptom onset to first medical contact time (hours)	1.38 (0.70, 3.00)	1.27 [0.67-3.00]	1.47 [0.75-3.00]	.353

CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.
[a] Median [interquartile range] or frequency (%).
[b] Wilcoxon rank sum test; Pearson's chi-squared test; Fisher's exact test.

baseline clinical profile vs STEMI patients with other culprit vessels; *b)* in the contemporary era of primary PCI, LAD as the STEMI-related culprit vessel did not bring worse very long-term outcomes compared with other coronary vessels; *c)* nevertheless, between years 0 and 1 the LAD-STEMI group exhibited a higher all-cause mortality rate, which disappeared thereafter compared with non-LAD-STEMI group.

Cardiology community knows (as reflected by the ESC guidelines on the management of acute coronary syndromes) that STEMI with LAD involvement as culprit vessel is a clinical marker of high risk of further events.[1] LAD-related STEMI represents, approximately, 40% up to 50% of all STEMIs,[12,16] and its worse prognosis has been related to the large myocardium covered by the LAD flow compared with the myocardium supplied by other coronary vessels. Of note, those studies were performed in the pre-reperfusion[4-7] and early thrombolysis/PCI era,[8,9] when PCIs were still not widely available. In the PCI era, there are very few studies (with short or mid-term follow-ups ranging from 1 to 3 years) reporting that LAD-STEMI is associated with an increased risk of stroke, heart failure, all-cause mortality[10,17] and cardiovascular death[11] after the PCI.

In our analysis, conducted in a cohort where the PCI was extensively performed, LAD as the STEMI culprit vessel did not appear to confer a worse prognosis to patients at the 1- or even 10-year follow-up. Of interest, LAD-STEMI patients exhibited the classical clinical features related to LAD, such as advanced Killip class at the time of presentation, lower ST-segment resolution and lower LVEF, which is similar to previous studies.[8-11,17] All these unfavorable clinical characteristics are indeed related to the large amount of myocardium damaged in a LAD-STEMI with subsequent heart failure and ventricular arrhythmias.[17-19] Nevertheless, this did not translate into a worse, very long-term clinical outcome. Significantly, even after accounting for variations in LVEF (which we addressed separately in our model due to its perceived role in the outcome cascade) the results showed no differences. This observation stands in contrast to earlier evidence, where the higher mortality rate in this cohort had been partially attributed to the subsequent decline in LVEF after STEMI.[9,10]

Several explanations may be claimed to understand our main finding. It may be hypothesized that worse outcome related to anterior STEMI may have been overcome by the introduction of

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Table 2. Angiographic and procedural characteristics

Procedural characteristics	Overall (N = 1498)[a]	LAD-related STEMI (N = 631)[a]	Non-LAD-related STEMI (N = 867)[a]	*P*[b]
STEMI-related culprit vessel				N/A
LAD	631 (42)	631 (100)	0 (0)	
LMCA	3 (0.2)	0 (0)	3 (0.3)	
RCA	650 (43)	0 (0)	650 (75)	
LCx	207 (14)	0 (0)	207 (24)	
SVG	7 (0.5)	0 (0)	7 (0.8)	
Multivessel disease	188 (13)	72 (11)	116 (13)	.256
Total ischemic time (hours)	3.9 [2.7-6.8]	4.0 [2.7-7.3]	3.9 [2.7-6.3]	.366
Manual thrombectomy	976 (65)	405 (64)	571 (66)	.502
Glycoprotein IIb/IIIa inhibitor	785 (52)	312 (49)	473 (55)	.051
Direct stenting	885 (60)	390 (63)	495 (59)	.113
Stent type				.312
DES	751 (50)	326 (52)	425 (49)	
BMS	747 (50)	305 (48)	442 (51)	
No. of stents	1.39 (0.65)	1.37 (0.63)	1.40 (0.66)	.428
Total stent length (mm)	23 (18-35)	23 (18-33)	23 (18-35)	.154
Maximal stent diameter (mm)	3.20 (0.45)	3.12 (0.40)	3.26 (0.47)	< .001
Post-dilatation	221 (15)	97 (15)	124 (14)	.564
TIMI flow after PCI				.607
0	26 (1.7)	9 (1.4)	17 (2.0)	
1	12 (0.8)	5 (0.8)	7 (0.8)	
2	59 (4.0)	29 (4.6)	30 (3.5)	
3	1396 (94)	584 (93)	812 (94)	
ST-segment resolution > 70%	852 (63)	285 (50)	567 (73)	< .001

BMS, bare metal stent; CABG, coronary artery bypass graft. DES, drug-eluting stent; LAD, left anterior descending coronary artery, LCx, left circumflex artery; LMCA, left main coronary artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI: ST-segment elevation myocardial infarction; SVG, saphenous venous graft; TIMI, thrombolysis in myocardial infarction.

[a] Median [interquartile range], mean (standard deviation) or frequency (%).

[b] Fisher's exact test; Pearson's chi-squared test; Wilcoxon rank sum test.

the PCI with quick myocardial reperfusion. Pharmacological treatment has been also improved from thrombolysis to the PCI era, not only in terms of antiplatelet agents, but also in terms of secondary prevention (high intensity statins and angiotensin converting enzyme inhibitors/angiotensin receptor blockers or angiotensin receptor/neprilysin inhibitors for left ventricular dysfunction).[20-23] Furthermore, in our study, the LAD-STEMI group had a higher proportion of active smokers. Smoking cessation remains the most critical preventive measure for coronary artery disease. The relationship between smoking and cardiovascular outcomes has been a matter of discussion, as some studies have suggested improved cardiovascular outcomes, even in the long term, among smokers who experienced STEMI.[24] However, many of these studies were observational registries conducted in the pre-PCI era. Recent evidence indicates that smoking is associated with more post-PCI long-term adverse outcomes.[25] Therefore, the so-called "smoker's paradox" might be better explained by factors such as younger age and a lower prevalence of other risk factors among smokers. Indeed, in our study, while the LAD-STEMI group had a higher proportion of smokers, they had a lower prevalence of other risk factors, such as peripheral vascular disease and a history of prior PCI or MI.

Last, but not least, in landmark analysis we found that between years 0 and 1, all-cause mortality was more common in the LAD-STEMI group. Notably, in this period, there was a numerically higher number of cardiac deaths (although not statistically significant, $P = .12$), a similar finding to other existing evidence that found a higher relatively short-term mortality in the LAD-STEMI group within the first 30 days. In these studies, the elevated short-term mortality was associated with acute sequelae, such as heart failure and was also speculated to be connected to other lethal complications, such as ventricular arrhythmias, cardiogenic shock or mechanical complications.[10,11] In our cohort, we found a trend towards a higher rate of reinfarction in the non-LAD-STEMI group ($P = .081$) that was largely unrelated to TLR, TVMI, or stent

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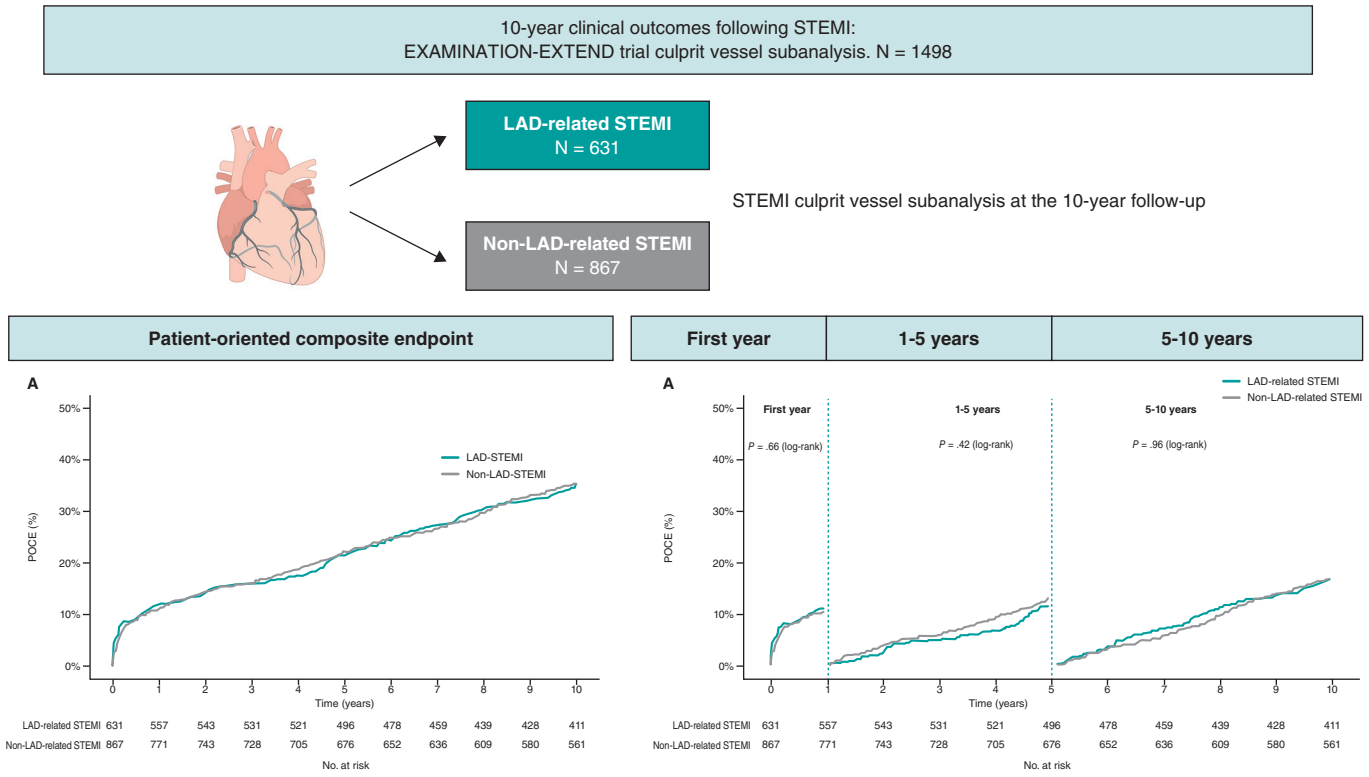

Figure 2. Central illustration. Outcomes of patients with ST-segment elevation myocardial infarction according to the culprit vessel at the 10-year follow-up. LAD, left anterior descending coronary artery; STEMI: ST-segment elevation myocardial infarction; POCE: patient-oriented composite endpoint.

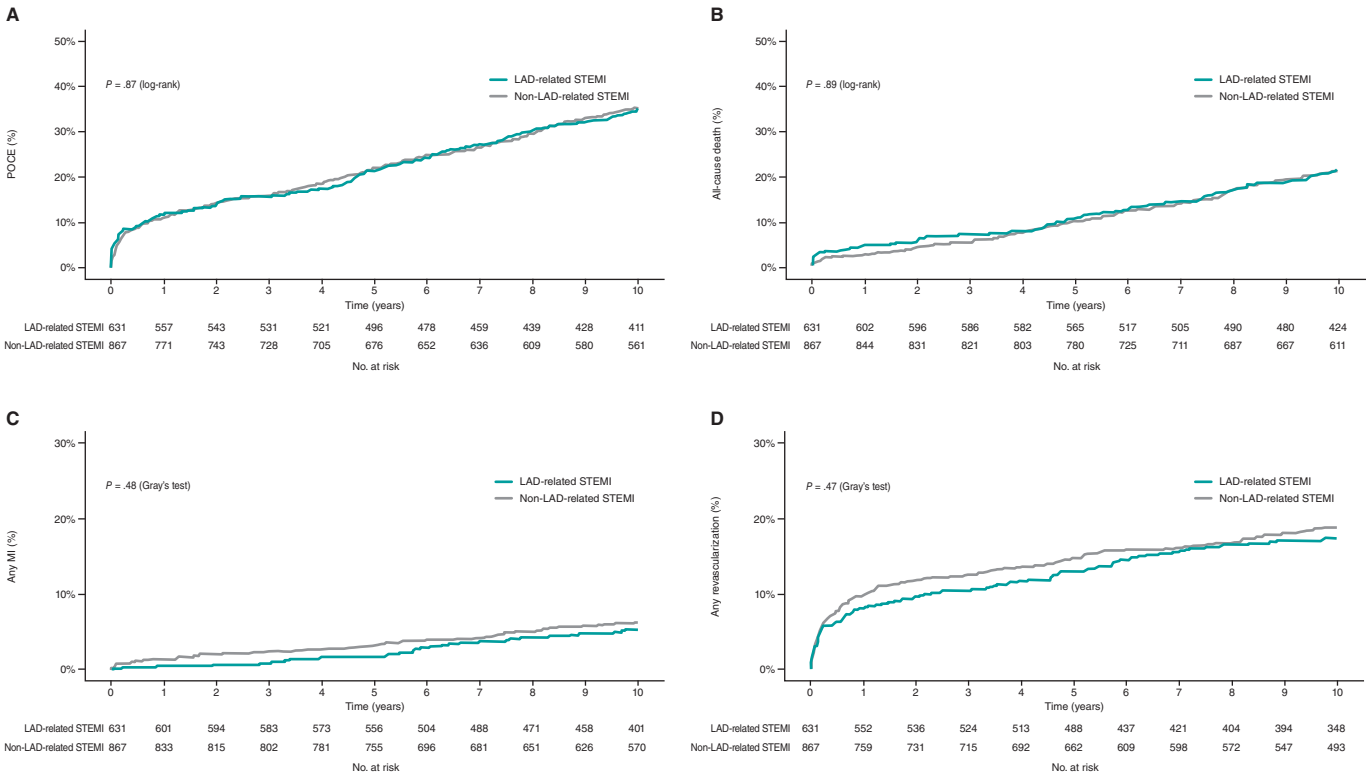

Figure 3. Time-to-event curves for the patient-oriented composite endpoint (A), all-cause mortality (B), myocardial infarction (C), and any revascularization (D) in patients stratified according to the culprit vessel. LAD, left anterior descending coronary artery; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; POCE, patient-oriented composite endpoint.

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Table 3. Ten-year outcomes

10-year outcomes	LAD-related STEMI (N = 631)	Non-LAD-related STEMI (N = 867)	Unadjusted HR (95%CI)	*P*	Adjusted HR (95%CI)	*P*[a]	Expanded adjusted HR (95%CI)	*P*[b]
Patient-oriented composite endpoint[c]	220 (34.9)	307 (35.4)	0.99 (0.83-1.17)	.87	0.95 (0.79-1.13)	.56	0.98 (0.78-1.23)	.86
All-cause mortality[d]	131 (21.6)	179 (21.2)	1.02 (0.82-1.28)	.84	0.93 (0.74-1.18)	.56	0.81 (0.59-1.09)	.17
Any myocardial infarction[e]	33 (5.5)	53 (6.3)	0.86 (0.56-1.33)	.50	0.93 (0.60-1.45)	.76	1.14 (0.67-1.93)	.61
Any revascularization	108 (17.4)	161 (18.8)	0.93 (0.73-1.18)	.55	0.96 (0.75-1.22)	.72	1.12 (0.83-1.52)	.45
Device-oriented composite endpoint[f]	94 (14.3)	132 (14.2)	0.98 (0.75-1.28)	.88	0.91 (0.70-1.20)	.50	0.95 (0.67-1.35)	.77
Cardiac death	72 (9.8)	95 (10.0)	1.06 (0.78- 1.44)	.71	0.89 (0.65- 1.23)	.49	0.71 (0.47-1.09)	.12
Target vessel myocardial infarction	16 (2.6)	36 (4.2)	0.62 (0.34-1.11)	.10	0.69 (0.38-1.25)	.22	0.87 (0.43-1.77)	.71
Target lesion revascularization	44 (7.0)	63 (7.3)	0.97 (0.66-1.43)	.89	1.01 (0.68-1.49)	.96	1.20 (0.76-1.93)	.43
Definite/probable stent thrombosis[g]	17 (2.7)	28 (3.3)	0.84 (0.46-1.54)	.57	0.83 (0.45-1.55)	.57	0.80 (0.38-1.73)	.58

95%CI, 95% confidence interval; HR, hazard ratio; LAD, left anterior descending artery, STEMI: ST-elevation myocardial infarction.
Data are expressed as no. (%).
[a] Cause-specific Cox regression model adjusted for sex, smoking status, peripheral vascular disease, previous percutaneous coronary intervention, previous coronary artery bypass graft, previous myocardial infarction, and Killip class.
[b] Cause-specific Cox regression expanded model, adjusted for baseline comorbidities and left ventricular ejection fraction at discharge.
[c] Composite endpoint of all-cause death, any recurrent myocardial infarction, and any revascularization.
[d] Death was adjudicated according to the Academic Research Consortium definition.
[e] Myocardial infarction was adjudicated according to the World Health Organization extended definition.
[f] Composite endpoint of cardiac death, target vessel myocardial infarction, target lesion revascularization, and stent thrombosis.
[g] Stent thrombosis was defined according to the Academic Research Consortium definition.

thrombosis. This observation contrasts with previous literature that reported a more common occurrence of reinfarction at the follow-up in patients with the SVG as the culprit vessel[26] as well as the LAD,[8] but not in LCx or the RCA.[9-11]

Our 10-year follow-up revealed similar clinical event rates between LAD-STEMI and non-LAD-STEMI group, indicating absence of long-term divergence. Previous studies showed a favorable post-acute phase prognosis for LAD-STEMI patients,[10,11] which is consistent with our findings. In fact, non-cardiac factors seem to impact long-term mortality more than infarct location does.[19] Thus, patients with STEMI should receive uniform management focused on secondary prevention strategies, regardless of the culprit vessel. Unfortunately, insufficient long-term data collection limits deeper insights into these outcomes (such as the presence of heart failure, optimal medical therapy, or other comorbidities).

Limitations

This study presents several limitations. First, this is a non-prespecified post-hoc analysis of the EXAMINATION-EXTEND study and therefore its conclusions must be considered only hypothesis generating. The association between infarction and outcomes may be driven by confounders which have not been recorded in the study. Then, several clinical and procedural characteristics were not available for the analysis, such as specified in-hospital or follow-up clinical data, like optimal medical treatment or compliance to medication at the follow-up.

CONCLUSIONS

In a contemporary cohort of STEMI patients, there were no differences in POCE between LAD as the STEMI-related culprit vessel and other vessels at the 10-year follow-up. However, within the first year after STEMI, all-cause death was more common in the LAD-STEMI group. Our results should be considered as hypothesis-generating. Further studies are needed to specifically assess the relationship between infarction location and outcomes in a contemporary setting where interventional and medical treatments are optimized.

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ETHICAL CONSIDERATIONS

The study fully complied with the Declaration of Helsinki and was approved by our Institutional Review Committee. All patients signed a written informed consent form before being included in this study. The clinical ethics committee gave its approval for the analysis of the data collected. In this work, SAGER guidelines regarding sex and gender bias have been followed.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence tools were used during the preparation of this work.

AUTHORS' CONTRIBUTIONS

The authors declare they meet the full criteria and requirements for authorship and have reviewed and agree with the content of

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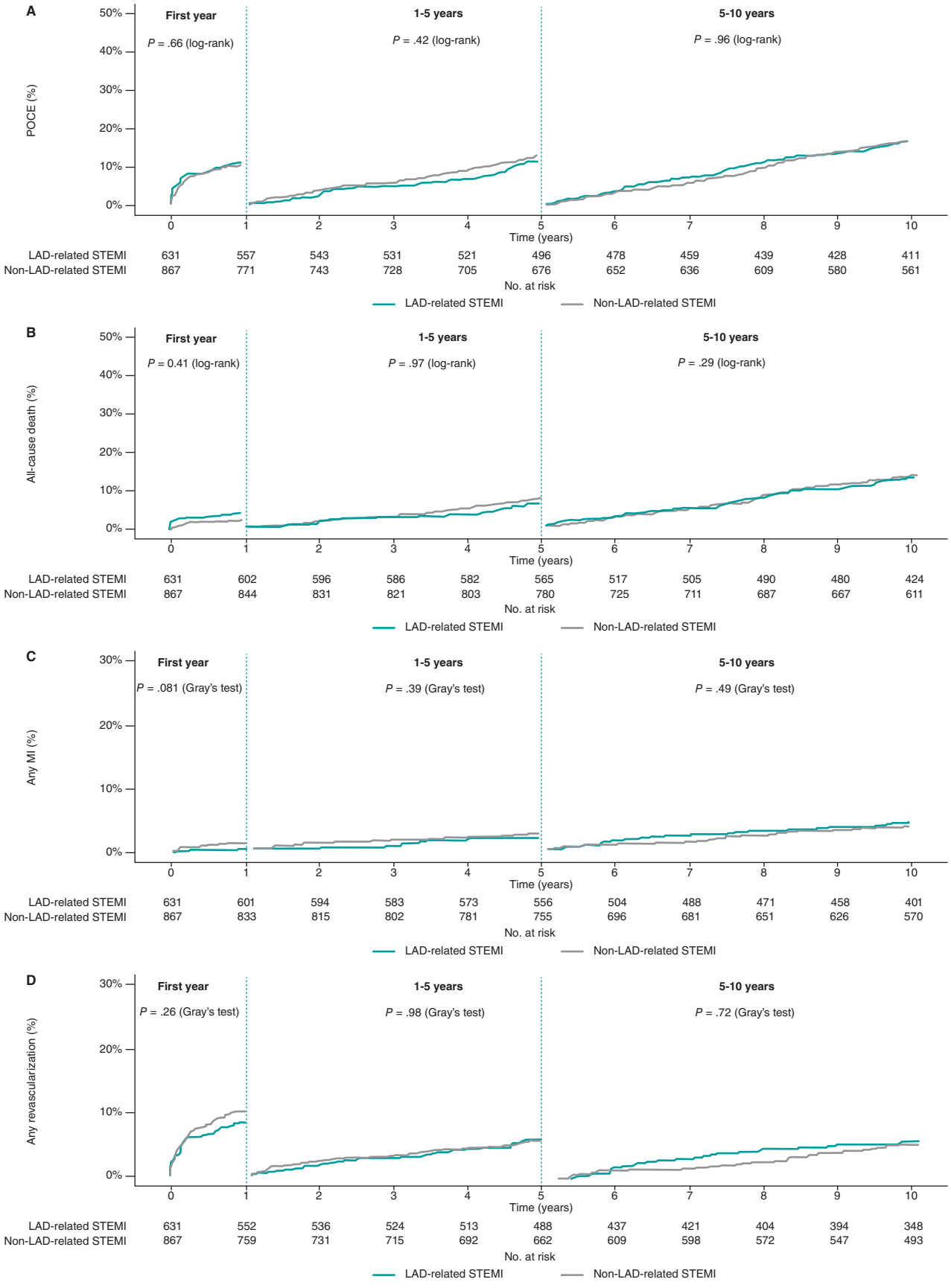

Figure 4. Landmark analysis for the patient-oriented composite endpoint (A), all-cause mortality (B), myocardial infarction (C), and any revascularization (D) in patients stratified according to the culprit vessel. LAD, left anterior descending coronary artery; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; POCE, patient-oriented composite endpoint.

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the article. P. Vidal Calés, K. Bujak, R. Rinaldi, A. Salazar Rodríguez, S. Brugaletta and M. Sabaté contributed to conceptualization, design, data analysis and drafting of the manuscript. L. Ortega-Paz, J. Gómez-Lara, V. Jiménez-Diaz, M. Jiménez, P. Jiménez-Quevedo, R. Diletti, P. Bordes, G. Campo, A. Silvestro, J. Maristany, X. Flores, A. De Miguel-Castro, A. Íñiguez, A. Ielasi, M. Tespili, M. Lenzen, N. Gonzalo, M. Tebaldi, S. Biscaglia, R. Romaguera, J.A. Gómez-Hospital and P. W. Serruys reviewed and edited the manuscript.

CONFLICTS OF INTEREST

M. Sabaté declares he has received consulting fees from Abbott Vascular and iVascular outside the submitted work. R. Romaguera is associate editor of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The rest of the authors declared no conflicts of interest whatsoever.

WHAT IS KNOWN ABOUT THIS TOPIC?

- In STEMI patients, the culprit vessel is often regarded as a crucial prognostic factor.
- This assumption is based on earlier studies conducted during the pre-reperfusion or thrombolysis era, which demonstrated that STEMIs involving the left anterior descending coronary artery (LAD) were linked to poorer clinical outcomes vs those involving other vessels.
- In the current PCI era, there is limited data on the long-term prognostic impact of the LAD as the culprit vessel in STEMI patients.

WHAT DOES THIS STUDY ADD?

- Patients with LAD as the STEMI-related culprit vessel have a higher all-cause mortality within the first year after STEMI.
- However, our study found that this difference did not persist beyond the initial year suggesting that the prognostic impact of the culprit vessel might pertain to the immediate post-STEMI period.
- Moreover, our results support that (irrespective of the location of the infarction) all STEMI patients should receive uniform medical care in the long-term focused on implementing secondary prevention strategies.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M24000488.

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