Clinical effect of proprotein convertase subtilisin/kexin type 9 inhibition in patients undergoing coronary artery bypass surgery

Giuseppe Nasso, MD, PhD,[a,b] Alfredo Marchese, PhD,[a] Giuseppe Santarpino, PhD,[c,d,e] Walter Vignaroli, MD,[f] Vincenzo Calabrese, MD,[g] Giovanni Taverna, MD,[h] Claudio Larosa, MD,[i] Francesco Bartolomucci, MD,[i] Flavio Fiore, MD,[a] Mario Siro Brigiani, MD,[a] Gaetano Contegiacomo, MD,[a] Ernesto Greco, PhD,[j] and Giuseppe Speziale, PhD[a]

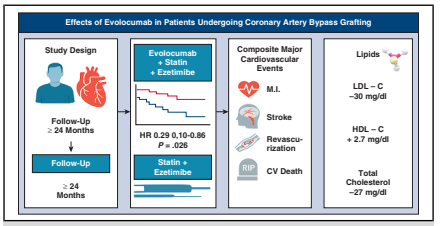
ABSTRACT

Objectives: To evaluate whether adding evolocumab to statin plus ezetimibe in patients undergoing coronary artery bypass grafting improves lipid control and reduces clinical events.

Methods: This retrospective study included 254 patients with dyslipidemia undergoing coronary artery bypass grafting. Of these, 111 received statin + ezetimibe plus evolocumab, whereas 143 received only statin + ezetimibe. The 2 groups were compared for lipid levels and cardiovascular outcomes. Cox regression analysis identified significant predictors of events, including treatment group, hypertension, European System for Cardiac Operative Risk Evaluation II, and previous stroke.

Results: Mean follow-up was 70 ± 20 months in the evolocumab group and 48 ± 18 months in the control group, with a minimum follow-up of 24 months for all enrolled patients. Evolocumab treatment showed a protective effect on composite hard major cardiovascular events (primary end point): cardiovascular death, myocardial infarction, cerebrovascular events, and repeat coronary revascularization (percutaneous coronary intervention/coronary artery bypass grafting) with a hazard ratio of 0.29 (95% CI, 0.10-0.86, $P = .026$) in the time-to-first-event analysis administratively censored at 24 months. Recurrent angina, a secondary end point, did not significantly differ between groups. Cholesterol levels decreased more rapidly in the evolocumab group, with a mean total cholesterol reduction of 27 mg/dL ($P < .01$), low-density lipoprotein by 30 mg/dL ($P < .001$), triglycerides by 18.77 mg/dL ($P < .001$), and a high-density lipoprotein increase of 2.7 mg/dL ($P < .001$), compared to the control group.

Conclusions: Evolocumab added early to standard therapy after coronary artery bypass grafting achieved greater lipid lowering and was associated with fewer hard cardiovascular events during midterm follow-up. (JTCVS Open 2026;30:101684)



MACE, Major adverse cardiovascular events.

CENTRAL MESSAGE

Early evolocumab + statin ± ezetimibe after CABG reduced major cardiovascular events and improved lipid control over mid-term follow-up, supporting perioperative PCSK9 inhibition in high-risk patients.

PERSPECTIVE

Prospective multicenter randomized trials in patients with dyslipidemia post-CABG treated with evolocumab are needed, targeting hard clinical end points. Priorities include defining optimal therapy timing, using biomarkers (LDL-C, Lp(a), hs-CRP), assessing atheroma with advanced imaging, evaluating long-term efficacy, and testing combinations with anti-inflammatory or cardiometabolic agents.

From the [a]Department of Cardiac Surgery, Anthea Hospital and Santa Maria Hospital GVM Care & Research, Bari, Italy; [b]Department of Medicine and Surgery, LUM University, Casamassima, Bari, Italy; [c]Department of Cardiac Surgery, Città di Lecce Hospital, GVM Care & Research, Lecce, Italy; [d]Department of Clinical and Experimental Medicine, Magna Graecia University, Catanzaro, Italy; [e]Department of Cardiac Surgery, Paracelsus Medical University, Nuremberg, Germany; [f]Department of Cardiac Surgery, San Carlo di Nancy Hospital GVM Care & Research, Rome, Italy; [g]Department of Nephrology, Kore University, Enna, Italy; [h]Department of Cardiology, University of Messina, Messina, Italy; [i]Department of Cardiology Azienda Ospedaliera B.A.T., Bonomo Hospital, Andria, Italy; and [j]Department of Health and Life Sciences European University of Rome, Rome Italy.

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Address for reprints: Giuseppe Nasso, MD, PhD, Santa Maria Hospital - GVM Care & Research and LUM University, Via A. De Ferrariis, Bari 70124, Italy (E-mail: gnasso@gvmnet.it).

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Abbreviations and Acronyms

ACS = acute coronary syndrome
ALT = alanine aminotransferase
CABG = coronary artery bypass grafting
HDL-C = high-density lipoprotein cholesterol
HR = hazard ratio
LDL-C = low-density lipoprotein cholesterol
PCI = percutaneous coronary intervention
PCSK9 = proprotein convertase subtilisin/kexin type 9
PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor
SMD = standardized mean difference
SVG = saphenous vein graft

Monoclonal antibodies that inhibit proprotein convertase subtilisin-kexin type 9 (PCSK9) are emerging as a new class of drugs to lower low-density lipoprotein cholesterol (LDL-C) levels[1] especially after an acute coronary syndrome (ACS).[2] The basis of this effect is genetic: the carriage of PCSK9 loss-of-function alleles is linked to lower LDL-C levels, reducing the risk of myocardial infarction.[3,4]

In particular, patients with ACS are at increased risk of recurrent ischemic events[5] and evolocumab has been shown to reduce major cardiovascular events in secondary prevention.[6-9] Indeed, an early and strong strategy to lipid-lowering using proprotein convertase subtilisin-kexin type 9 inhibitors (PCSK9i) in patients with ACS is safe and effective in clinical practice.[10] However, the LDL-C−lowering efficacy of PCSK9 antibody treatment during ACS in patients who undergo coronary artery bypass surgery (CABG) is unknown. Previously, we analyzed the short-term effect of evolocumab in this cohort.[11] The CABG population is difficult to analyze and understand: ischemic and reperfusion myocardial injury is often reported in patients who undergo CABG[12,13] despite substantial advancements in cardiopulmonary support devices and surgical techniques.[14,15,16] To date, clinical outcomes of PCSK9i in patients who undergo CABG remain limited.

Given the potential cardioprotective effects of PCSK9i, we hypothesized that evolocumab could improve clinical outcomes after CABG. Although randomized evidence in this setting is still emerging[17] we combined ACS and -elective CABG cohorts and extended follow-up to assess the clinical impact of early evolocumab in addition to statin + ezetimibe.

The NEWTON-CABG CardioLink-5[18] randomized trial evaluated early evolocumab initiation after CABG, focusing on anatomical end points of saphenous vein graft (SVG) disease at 24 months. The trial reported no significant difference in graft patency between evolocumab and placebo despite marked LDL-C reduction, and it was not designed or powered to assess clinical outcomes. We hypothesized that early PCSK9 inhibition with evolocumab in patients undergoing CABG would improve lipid control and translate into fewer adverse clinical events during follow-up compared with the use of standard lipid-lowering therapy alone.

METHODS

From January 2017 to June 2022, all patients who underwent CABG as a result of chronic coronary artery disease or ACS were retrospectively analyzed. Of these, all patients affected by dyslipidemia (defined as LDL-C concentration ≥70 mg/dL), or patients already in preoperative treatment with statin + ezetimibe alone or with statin + ezetimibe plus evolocumab, met the criteria to be enrolled in the retrospective analysis.

This retrospective observational study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement; the completed Strengthening the Reporting of Observational Studies in Epidemiology checklist is provided as Online Data Supplement.

The evolocumab group included all patients with dyslipidemia who underwent CABG and were treated with subcutaneous PCSK9i plus statin + ezetimibe. The standard group comprised patients who underwent CABG and were treated only with statin + ezetimibe.

Until December 2019, optimized lipid-lowering therapy included a high- or moderate-intensity statin with or without ezetimibe to obtain an LDL-C concentration ≤70 mg/dL. Since January 2020, once evolocumab treatment was deemed usable according to Italian legislation in patients with high LDL-C values (≥70 mg/dL), in all patients meeting these LDL-C values and the same baseline characteristics described above, a subcutaneous PCSK9 inhibitor was added to background statin therapy (with or without ezetimibe) at a dose of 140 mg every 2 weeks.

Evolocumab was administered at baseline as early as possible, usually before coronary angiography or at the end of the procedure when CABG treatment was proposed to the patient or immediately after surgery. All patients were followed up for clinical end points and laboratory levels (every 3 months), and the results were compared between the 2 groups. The follow-up period for this study was set at a minimum of 24 months for all enrolled patients (last enrollment in June 2022), enabling midterm comparative analyses. Follow-up time was measured from the date of the index CABG (time zero) to the earliest of first occurrence of the primary composite end point or last clinical contact; patients without events were censored at their last documented visit. Scheduled assessments were planned every 3 months (clinic visit or structured telephone contact), with verification of events through hospital electronic

medical records, discharge summaries, procedural/angiographic reports and communication with referring cardiologists when needed. The observed mean follow-up was 70 ± 20 months in the evolocumab group and 48 ± 18 months in the control group; the minimum follow-up was ≥24 months for all patients. Differences in individual follow-up duration were managed using time-to-event methods as specified herein. To ensure homogeneous observation across groups and reduce the risk of bias attributable to differing follow-up lengths, the primary event analysis was administratively censored at 24 months, thereby providing a common time window for all patients.

The primary clinical end point was time to first hard major cardiovascular event, defined as a composite of cardiovascular death, myocardial infarction, cerebrovascular events (stroke/transient ischemic attack), and repeat coronary revascularization (percutaneous coronary intervention [PCI] or CABG). Recurrent angina was evaluated as a secondary end point.

Laboratory end points included serial measurements of total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides, and alanine aminotransferase (ALT) at baseline, 3 months, and final follow-up.

Ethics, Data, and Material Availability

The data used and analyzed in this study are available upon reasonable request from the corresponding author. All methodologic details, including patient selection criteria, treatment procedures, and statistical analyses, are described herein. Any additional data or supplementary materials can be provided upon request, in compliance with ethical regulations and patient privacy policies. The present study conforms to the Declaration of Helsinki. It was approved by our institutional review board (Anthea Hospital and Santa Maria Hospital GVM Care & Research) for human research for retrospective studies with 2 different protocols for elective (Prot. No. 001.06.96, study number 7815) and "acute coronary syndrome" patients (Prot. No. 22.01.24, study number 7809) approved by local ethics committee on February 6, 2024, and March 13, 2024, respectively. Patients gave consent to use their clinical data for research purposes and permission for the publication of deidentified study data.

Statistical Analysis

Data are presented as mean ± standard deviation, median (interquartile range), or number (percentage), as appropriate; distributions assessed graphically and with formal normality testing when needed. No missing data were identified. There were 111 patients in the evolocumab group and 143 in the standard group (standard lipid-lowering therapy without PCSK9i). Comparisons were made using the Student t test or Mann-Whitney U test (continuous variables) and the Pearson χ^2 or Fisher exact test (categorical). Baseline balance/confounding by indication: standardized mean differences (SMDs; |SMD|<.10 adequate) plus hypothesis testing.

Time-to-event was determined by Cox proportional hazards models (hazard ratios [HRs], 95% CIs). Because follow-up differed, primary analyses used administrative censoring at 24 months (follow-up truncated at 24 months); time zero CABG; Kaplan-Meier curves/log-rank; Cox HRs. The adjusted model included clinical judgment plus penalized (ridge) Cox regularization/variable selection; variables with relative importance above the median were retained and entered into multivariable Cox with clinically relevant covariates. For sensitivity analysis, we estimated propensity scores (logistic regression with baseline covariates related to allocation/outcomes: ACS presentation, age, sex, body mass index, diabetes and insulin-treated diabetes, current smoking, previous myocardial infarction, previous PCI, previous CABG, peripheral vascular disease, previous stroke, previous transient ischemic attack, malignancy, hypertension, European System for Cardiac Operative Risk Evaluation II, number of bypass grafts) and used these scores to construct inverse probability of treatment weighting with stabilized weights; balance was reassessed by SMDs; primary Cox was repeated in the weighted pseudo-population with robust standard errors; and balance before/after weighting was calculated as shown in Table E1. For longitudinal total cholesterol, LDL-C, HDL-C, triglycerides, and ALT, generalized linear models for repeated measures with group-by-time interaction to estimate differences in slopes were created. Given the retrospective nature of the study, we did not perform an a priori sample size calculation; the sample size was fixed by the number of eligible patients, and infrequent events may result in limited power and imprecise estimates (ie, wider confidence intervals), which should be considered when interpreting the observed effect.

RESULTS

A total of 254 patients with dyslipidemia undergoing CABG were included in the analysis. Of these, 111 patients (the evolocumab group) received statin plus ezetimibe in combination with evolocumab—31 presenting with ACS and 80 with chronic coronary artery disease—initiated before surgery or immediately thereafter.

The remaining 143 patients (the standard therapy group) were treated with statin plus ezetimibe alone; among them, 43 had ACS and 100 had chronic coronary artery disease. Treatment timing was comparable between groups (Figure 1).

Patients were aged 68 years (63-73 years), there were 190 male patients (75%), and the body mass index was 27 (24-29) kg/m^2. In total, 126 (50%) had arterial hypertension, 70 (28%) had diabetes, and 73 (29%) were current smokers.

At baseline, the 2 groups differed only in HDL-C ($P = .017$), triglycerides ($P = .040$), and ALT ($P < .001$). No significant differences were found in age ($P = .063$),

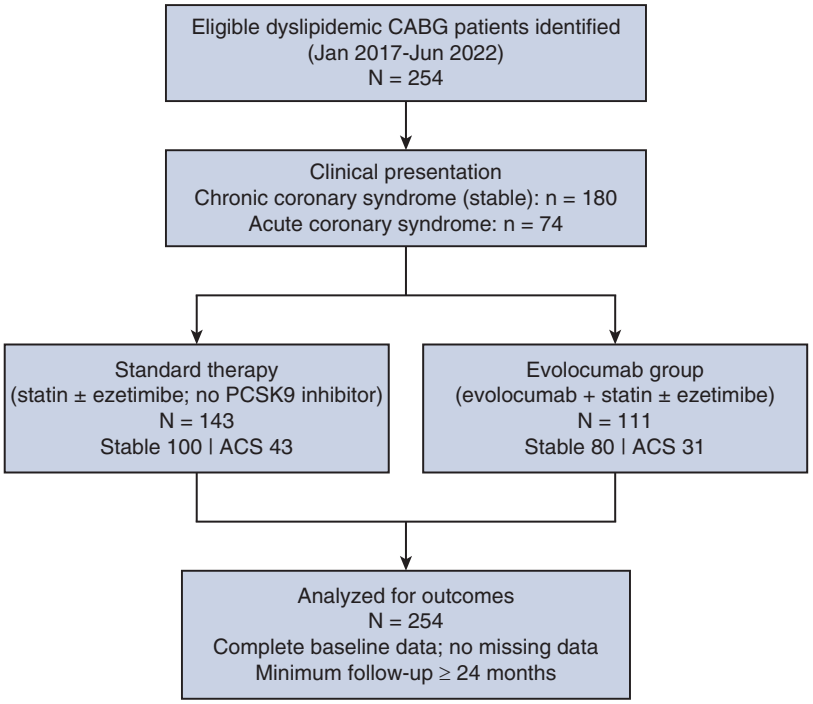

FIGURE 1. Eligible dyslipidemic CABG patients identified between January 2017 and June 2022 (N = 254), stratified by clinical presentation (stable vs acute coronary syndrome) and allocated to evolocumab + statin ± ezetimibe (n = 111) or standard therapy without PCSK9 inhibition (n = 143). All patients had complete baseline data and a minimum follow-up of 24 months. *CABG*, Coronary artery bypass grafting; *PCSK9*, proprotein convertase subtilisin/kexin type 9; *ACS*, acute coronary syndrome.

body mass index ($P = .199$), presence of hypertension ($P = .200$), or LDL-C ($P = .743$). HDL-C and ALT levels were greater in the evolocumab group, whereas other clinical and biochemical parameters were comparable between groups. The mean follow-up was 70 ± 20 months in the evolocumab group and 48 ± 18 months in the control group; the minimum follow-up was 24 months for all enrolled patients; 39 patients (15%) manifested cumulative events (hard major cardiovascular events plus recurrent angina), 7 (6%) in the evolocumab group and 32 (22%) in the control group ($P < .001$). The following clinical events were observed: (1) In the evolocumab group, 7 events were observed: 3 patients experienced recurrent angina, 3 patients required reintervention (PCI), and 1 patient died of cardiovascular causes. In the control group, 32 events were observed: 5 patients presented with recurrent angina, 4 patients experienced myocardial infarction, 1 patient had a cerebrovascular event, and 15 patients required reintervention (14 PCI and 1 CABG). Seven patients died of cardiovascular causes.

Table 1 shows the preoperative characteristics of the 2 groups (standard and evolocumab). After inverse probability of treatment weighting, the covariate balance was adequate with all absolute SMDs <0.10 (Table E1).

In detail, hard major cardiovascular events occurred in 4 of 111 (3.6%) patients in the evolocumab group and 27 of 143 (18.9%) in the standard group. In the time-to-first-event analysis administratively censored at 24 months, evolocumab was associated with a lower risk of the hard composite end point (HR, 0.29; 95% CI, 0.10-0.86; $P = .026$).

Within 24 months, hard events occurred in 4 of 111 versus 17 of 143 patients, respectively ($P < .05$). Recurrent angina, evaluated as a secondary end point, occurred in 3 of 111 (2.7%) versus 5 of 143 (3.5%) patients and did not significantly differ between groups. On multivariable analysis, PCSK9 inhibition remained independently associated with a lower risk of the composite clinical end point (Table 2).

Kaplan-Meier analysis confirmed a significantly lower incidence of the hard composite clinical end point in patients treated with PCSK9 inhibition compared with controls (Figure 2).

Furthermore, cholesterol levels decreased more quickly over time in the evolocumab-treated group than in the conventional group, with an average difference of 27 mg/dL ($P < .01$). Similarly, LDL-C decreased by approximately 30 mg/dL ($P < .001$), triglycerides by approximately 18.77 mg/dL ($P < .001$), whereas HDL-C increased by an average of 2.7 mg/dL more than in the conventional therapy ($P < .001$) (Table 3).

Regarding safety, no serious adverse events related to evolocumab administration were reported during the study

TABLE 1. Preoperative characteristics of the study population

Variable	Group 0 (n = 143)	Group 1 (n = 111)	Overall (n = 254)	*P* value
Male sex, n (%)	104 (73)	86 (77)	190 (75)	.387
Age, y	63.0/68.0/73.0	61.5/67.0/72.0	63.0/68.0/73.0	.063
Body mass index, kg/m^2	24.0/26.0/28.5	24.5/27.0/29.0	24.0/27.0/29.0	.199
Diabetes mellitus, n (%)	38 (27)	32 (29)	70 (28)	.690
Current smoker, n (%)	37 (26)	36 (32)	73 (29)	.252
Previous myocardial infarction, n (%)	20 (14)	16 (14)	36 (14)	.923
Previous PTCA, n (%)	24 (17)	19 (17)	43 (17)	.944
Previous CABG, n (%)	2 (1)	1 (1)	3 (1)	.716
PVD, n (%)	8 (6)	6 (5)	14 (6)	.948
Previous stroke, n (%)	4 (3)	2 (2)	6 (2)	.604
Previous TIA, n (%)	6 (4)	5 (5)	11 (4)	.905
History of cancer, n (%)	10 (7)	8 (7)	18 (7)	.947
EuroSCORE II, %	1.20/1.60/2.05	1.10/1.70/2.15	1.20/1.60/2.10	.596
Hypertension, n (%)	76 (53)	50 (45)	126 (50)	.200
Number of bypass grafts	2/3/4	2/3/4	2/3/4	.974
Total cholesterol at baseline, mg/dL	156.5/180.0/199.0	124.0/189.0/206.0	155.0/187.0/200.0	.991
LDL cholesterol at baseline, mg/dL	120.5/145.0/165.0	78.0/150.0/165.0	120.0/145.0/165.0	.743
HDL cholesterol at baseline, mg/dL	33.0/36.0/39.0	34.0/38.0/40.0	33.0/37.0/40.0	.017
Triglycerides at baseline, mg/dL	173 ± 16	178 ± 17	176 ± 16	.040
ALT at baseline, U/L	32.0/37.0/41.0	36.0/40.0/44.0	33.0/38.5/43.0	<.001

Baseline characteristics of patients treated with PCSK9 inhibition plus statin + ezetimibe (group 1) and statin + ezetimibe alone (group 0). Categorical variables are reported as n (%). Continuous variables are reported as median (25th/50th/75th percentile) or mean ± standard deviation, as appropriate. *P* values refer to between-group comparisons. *PTCA*, Percutaneous transluminal coronary angioplasty; *CABG*, coronary artery bypass grafting; *PVD*, peripheral vascular disease; *TIA*, transient ischemic attack; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *LDL*, low-density lipoprotein; *HDL*, high-density lipoprotein; *ALT*, alanine aminotransferase.

period. Liver enzyme levels (ALT) remained within normal ranges across both groups, with no treatment discontinuation due to drug intolerance. These findings confirm the favorable tolerability profile of evolocumab previously demonstrated in broader cardiovascular populations.

DISCUSSION

We previously demonstrated that evolocumab treatment is able to reduce total cholesterol and LDL-C levels after cardiac surgery in elective patients[19] and in patients with ACS.[11] Given the potential cardioprotective effects of evolocumab, it may be hypothesized that this therapy could be beneficial in patients undergoing cardiovascular surgery. In the present study, patients undergoing CABG who were treated with evolocumab experienced fewer cardiac events—defined as a composite of myocardial infarction, cerebrovascular events, repeat coronary revascularization (PCI or CABG), and cardiovascular death—compared with patients receiving standard therapy with statin plus ezetimibe alone.

To date, the clinical efficacy of PCSK9i in the setting of cardiovascular surgery has not been clearly established. In this study, we present our preliminary results investigating the efficacy of the PCSK9i evolocumab in reducing ischemic and reperfusion-related myocardial injury in patients with multivessel coronary artery disease undergoing elective or urgent/emergent CABG.

Importantly, because overall follow-up differed between groups (mean 70 ± 20 vs 48 ± 18 months; minimum 24 months for all), the primary end point was performed using a standardized 24-month time-to-first-event window with administrative censoring at 24 months, to ensure a common observation period.

Due to these clinical consequences, our findings are consistent with the Fourier trial[6] in the cardiac surgery field: these authors found that the addition of evolocumab to statin therapy significantly reduced the risk of cardiovascular events, with a 15% reduction in the risk of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. In our study, the addition of evolocumab to statin therapy reduced cardiovascular events. In particular, within a common 24-month observation window and using a hard composite end point, cumulative hard events (myocardial infarction, cerebrovascular events, coronary artery reangioplasty/rebypass, and cardiac death) occurred in 17 of 143 (11.9%) patients receiving standard therapy and 4 of 111 (3.6%) receiving

TABLE 2. Multivariable analysis for the composite clinical end point

Variable	Hazard ratio	95% CI	*P* value
PCSK9 inhibition (group 1)	0.28	0.13-0.61	<.001
Age (per 1-y increase)	1.04	1.01-1.07	.009
Diabetes mellitus	1.78	1.02-3.11	.041
Baseline LDL cholesterol (per 10 mg/dL increase)	1.12	1.03-1.22	.008

Multivariable Cox proportional hazards regression analysis for the composite clinical end point. Only variables retaining statistical significance in the final model are shown. Hazard ratios are reported with 95% CIs. *LDL*, Low-density lipoprotein.

evolocumab, corresponding to an absolute risk reduction of 8.3 percentage points and a relative risk reduction of 69.7%.

Across the entire follow-up, we observed 32 cumulative adverse events in the standard therapy group (22%) and 7 events in the evolocumab group (6.3%) a reduction of 15.7%. However, given the unequal mean follow-up duration between groups, these cumulative rates should be interpreted as descriptive and supportive, whereas the primary inference is based on the standardized 24-month time-to-event analysis. These positive effects of the addition of evolocumab are, however, probably still only partially known, given that the midterm results of the therapy in patients at cardiovascular risk have also been published, demonstrating that the long-term LDL-C lowering with evolocumab was associated with persistently low rates of adverse events that did not exceed those observed in the original placebo arm.[16]

Therefore, also in support of our study, it appears important to underline the early intake of the drug itself as proposed by us in our approach immediately, ie, 1 month after the surgical revascularization procedure. In contrast, an early start is a hypothesis on which our study is based

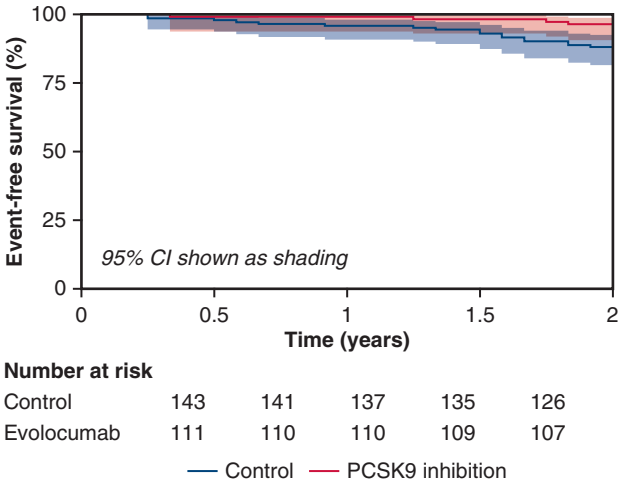

FIGURE 2. Kaplan–Meier estimates of event-free survival (%) over 2 years after CABG comparing Control (*blue*) versus PCSK9 inhibition (evolocumab) (*red*). Shaded areas indicate 95% confidence intervals. Numbers at risk are shown below the x-axis. *CABG*, Coronary artery bypass grafting; *PCSK9*, proprotein convertase subtilisin/kexin type 9.

and has had clear bibliographical support for several years. In fact, a delay between the onset of LDL-C lowering and the emergence of the full clinical benefit of the intervention in terms of clinical risk reduction has been well documented in many trials.[6,20-23] The benefit of decreasing LDL-C levels therefore remains indisputable, given that even studies before the use of evolocumab showed significant reductions in major cardiovascular events using statins alone in the Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction (PROVE IT–TIMI) and Treating to New Targets (TNT) trials.[24,25]

This study provides clinical and laboratory evidence on in-hospital initiation of evolocumab in patients undergoing CABG, showing a cardioprotective association together with a substantially greater reduction in LDL-C levels. Our results build upon previous studies in ACS[26] patients who are statin-intolerant[27] familial hypercholesterolemia[28] and stable ischemic heart disease.[6,29] In our previous work, we did not observe an early clinical benefit[19]; however, with longer follow-up, we observed an association between PCSK9 inhibition and fewer adverse cardiovascular events.

Recently, the NEWTON-CABG CardioLink-5 randomized trial evaluated early initiation of evolocumab after CABG using an anatomical primary end point—SVG disease at 24 months assessed by computed tomography or invasive angiography—and found no reduction in SVG disease despite robust LDL-C lowering; clinical outcomes were not powered and did not differ significantly between groups. By design, NEWTON-CABG focused on early graft dysfunction, a process predominantly driven by thrombosis and vein remodeling (intimal hyperplasia) rather than by classic atherosclerotic mechanisms. Accordingly, the end points and time horizons are nonoverlapping—SVG patency at 24 months versus clinical major adverse cardiovascular events over a substantially longer period—so the neutral graft-patency result does not inform (nor refute) the clinical risk reduction we observed. Our findings therefore provide the clinical counterpart that NEWTON-CABG did not test and support the role of PCSK9 inhibition in reducing atherothrombotic events after CABG despite neutral effects on early vein-graft disease.

Evidence from the Fourier program helps contextualize our results. In a dedicated analysis, Oyama and colleagues reported that evolocumab was associated with fewer events

TABLE 3. Lipid profile and biochemical parameters during follow-up

Variable	Group 0 (n = 143)	Group 1 (n = 111)	Overall (n = 254)	*P* value
Total cholesterol at 3 mo, mg/dL	141.0/151.0/151.0	97.0/105.0/118.0	105.0/137.0/151.0	<.001
Total cholesterol at last follow-up, mg/dL	121.5/135.0/138.0	90.0/94.0/97.0	94.0/114.0/135.0	<.001
LDL cholesterol at 3 mo, mg/dL	93.0/111.0/111.0	47.5/65.0/80.0	65.0/88.0/111.0	<.001
LDL cholesterol at last follow-up, mg/dL	70.0/85.0/100.0	38.0/41.0/46.0	42.0/65.0/88.0	<.001
HDL cholesterol at 3 mo, mg/dL	38.0/40.0/41.0	38.0/40.0/45.0	38.0/40.0/43.0	.355
HDL cholesterol at last follow-up, mg/dL	41.0/45.0/55.0	44.5/55.0/55.0	44.0/51.0/55.0	<.001
Triglycerides at 3 mo, mg/dL	153 ± 17	159 ± 17	156 ± 17	<.001
Triglycerides at last follow-up, mg/dL	168.0/173.0/180.0	110.0/140.0/144.0	140.0/155.5/175.0	<.001
ALT at 3 mo, U/L	41.0/44.0/54.0	40.0/45.0/55.0	41.0/44.0/55.0	.125
ALT at last follow-up, U/L	44.0/45.0/58.0	44.0/55.0/88.0	44.0/54.5/73.8	.021

Lipid and biochemical parameters assessed during follow-up in patients treated with PCSK9 inhibition plus statin + ezetimibe (group 1) and statin + ezetimibe alone (group 0). Continuous variables are reported as median (25th/50th/75th percentile) or mean ± standard deviation, as appropriate. *P* values refer to between-group comparisons. *LDL*, Low-density lipoprotein; *HDL*, high-density lipoprotein; *ALT*, alanine aminotransferase.

related to complex coronary disease requiring revascularization, supporting the concept that intensive LDL-C lowering may reduce repeat coronary procedures in high-risk patients.[30] Similarly, Furtado and colleagues showed consistent benefit of evolocumab in patients with prior PCI, including reductions in revascularization-related outcomes.[31] Finally, the EVOCABG randomized trial protocol highlights the growing interest in evaluating evolocumab specifically in CABG candidates, complementing our real-world postoperative cohort.[17]

Limitations

Its retrospective, single-center design may introduce selection bias and, despite multivariate and machine-learning adjustments, residual confounding may remain. The study period spanned both before and after evolocumab became commercially available, which may have influenced prescribing patterns. We also lacked consistent inflammatory marker data and atherosclerotic imaging, limiting mechanistic interpretation. Finally, the small number of events reduces statistical power for subgroup and mortality analyses.

CONCLUSIONS

In patients with dyslipidemia undergoing CABG, early evolocumab added to standard lipid-lowering therapy was associated with fewer hard major cardiovascular events in a standardized 24-month time-to-event analysis and more favorable lipid trajectories. These findings support further prospective, adequately powered randomized trials focused on hard clinical end points to confirm efficacy and guide optimal timing and patient selection.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: dyslipidemia, cardiac surgery, PCSK9

TABLE E1. Baseline covariate balance before and after inverse probability of treatment weighting (IPTW)

Variable	Standard unweighted (n = 143)	Evolocumab unweighted (n = 111)	|SMD| unweighted	Standard IPTW	Evolocumab IPTW	|SMD| IPTW
ACS presentation	43 (30.1%)	31 (27.9%)	0.047	28.9%	28.2%	0.015
Age, y	67.50 ± 7.78	65.58 ± 7.64	0.250	66.69 ± 8.25	66.87 ± 7.20	0.023
Male sex	102 (71.3%)	86 (77.5%)	0.141	73.6%	72.7%	0.019
BMI, kg/m^2	26.14 ± 2.93	26.67 ± 3.05	0.175	26.33 ± 2.93	26.35 ± 3.14	0.005
Diabetes	71 (49.7%)	51 (45.9%)	0.076	47.3%	47.0%	0.006
Insulin-treated diabetes	30 (21.0%)	17 (15.3%)	0.147	18.6%	18.3%	0.008
Current smoker	36 (25.2%)	43 (38.7%)	0.293	29.7%	30.0%	0.006
Previous myocardial infarction	44 (30.8%)	32 (28.8%)	0.044	29.4%	29.1%	0.007
Previous PCI	27 (18.9%)	19 (17.1%)	0.046	18.3%	18.0%	0.008
Previous CABG	3 (2.1%)	2 (1.8%)	0.018	1.3%	1.8%	0.042
Peripheral vascular disease	13 (9.1%)	10 (9.0%)	0.003	9.1%	9.1%	0.001
Previous stroke	6 (4.2%)	6 (5.4%)	0.057	4.7%	4.7%	0.001
Previous TIA	11 (7.7%)	9 (8.1%)	0.016	7.9%	7.9%	0.001
Malignancy	12 (8.4%)	10 (9.0%)	0.021	8.6%	8.6%	0.001
EuroSCORE II	1.60 ± 0.52	1.60 ± 0.52	0.004	1.61 ± 0.49	1.61 ± 0.49	0.010
Hypertension	102 (71.3%)	73 (65.8%)	0.119	68.1%	68.1%	0.000
Number of bypass grafts	3.24 ± 0.95	3.19 ± 0.90	0.057	3.31 ± 0.95	3.30 ± 0.89	0.016

Unweighted values are shown as mean ± SD for continuous variables and n (%) for categorical variables. IPTW columns report weighted means ± SD or weighted proportions (%) using stabilized inverse probability of treatment weights. values <0.10 indicate adequate balance. Propensity scores were estimated using logistic regression including ACS presentation, age, sex, BMI, diabetes, insulin treatment, current smoking, previous myocardial infarction, previous PCI, previous CABG, peripheral vascular disease, previous stroke, previous TIA, malignancy, hypertension, EuroSCORE II, and number of bypass grafts. |SMD|, Absolute standardized mean difference; *ACS*, acute coronary syndrome; *BMI*, body mass index; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *TIA*, transient ischemic attack; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation II; *SD*, standard deviation.