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Original Article

Internal mammary artery graft failure: Clinical features, management, and long-term outcomes

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ABSTRACT

Objective: Data on long-term outcomes after internal mammary artery (IMA) coronary graft failure are scarce. Our objective was to describe the clinical characteristics, management, and prognosis after angiographically confirmed IMA graft failure following coronary revascularization.
Methods: A three-hospital retrospective registry, observational and descriptive, with prospective follow-up of all consecutive cases of IMA graft failure between 2004 and 2014 was conducted. After treatment, clinical and procedural features were compared between those with and without cardiovascular events.
Results: Fifty-seven patients were included (89% male, mean age: 62 years, at surgery) in the registry. Most patients underwent an IMA angioplasty (percutaneous coronary intervention [PCI], 74%). In nine cases, the PCI failed at the graft level, and seven underwent a native vessel revascularization. Native vessel treatment was performed in 20% of the study subjects, all with stents. Finally, medical management was decided in three cases. Events after treatment for IMA graft failure were frequent (50.8%), during a median follow-up of 7.5 years. Acute presentation (hazard ratio$_{MACE}$ = 1.35; 95% confidence interval (CI): 1.12–3.00, $p < 0.01$), age of the patient (hazard ratio$_{MACE}$ = 1.85, 95% CI: 1.17–2.11, $p < 0.01$), presence of diabetes mellitus (hazard ratio$_{MACE}$ = 2.75, 95% CI: 1.13–6.69, $p = 0.02$), and the management modality used (IMA-simple angioplasty VS IMA-stenting: hazard ratio$_{MACE}$ = 5.5, 95% CI: 1.40–21.15, $p = 0.01$) displayed prognostic relevance on multivariate analysis. All-cause mortality occurred in 21.1% and presentation as infarction (hazard ratio$_{DEATH}$ = 1.05, 95% CI: 1.01–2.17, $p = 0.01$), age (hazard ratio$_{DEATH}$ = 9.08, 95% CI: 2.52–32.69, $p < 0.01$), and left ventricular ejection fraction (hazard ratio$_{DEATH}$ = 3.68, 95% CI: 1.65–8.18, $p < 0.01$) were independent predictors of the same.
Conclusions: In this long-term registry, most patients presented with an acute condition (myocardial infarction, progressive angina) within 12 months after surgery. Acute presentation, age, diabetes mellitus, reduced left ventricular ejection fraction, IMA graft failure segment affected, and the management strategy were related with long-term prognosis.

1. Introduction

Coronary artery disease is still the leading cause of death in the developed world. Regarding its management, internal mammary artery (IMA) coronary grafting is a classical surgical approach being currently considered the gold standard for this condition.[1] Thus, the European Society of Cardiology guidelines on myocardial revascularization (2014) strongly support its use in most patients undergoing surgery, even suggesting the use of bilateral IMA grafting.[1] The main reason is the high long-term patency rates reported for IMA grafts: 88–95% for left IMA at 10 years and 65–90% for right IMA at 10 years.[1] Several data on saphenous vein grafts failure have

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been previously published, showing worse results (32–71% patency at 10 years).[2–4]

Unfortunately, sometimes, because of technical or patient-related reasons, these excellent conduits fail too. However, data regarding management or long-term prognosis after a confirmed IMA graft failure is scarce.

The aim of this study was to describe the clinical characteristics of patients with angiographically confirmed IMA graft failure, the management chosen, and the long-term outcomes after this event. We considered as main outcome a major adverse combined event (MACE) composed by all-cause death or readmission because unstable angina, myocardial infarction (MI), heart failure (HF), or stroke. All the other events were considered separately as secondary end points.

2. Methods

We performed a retrospective registry, through a multipurpose prospective database with data between 2004 and December 2014, involving three centers functioning as an interventional cardiology network. The study was observational and descriptive. All patients with angiographically confirmed IMA graft failure, considered as severe stenosis (>70%) or total occlusion, were eligible. A total of 57 consecutive patients were identified. All cases were thoroughly reviewed by two operators (I.J.N.G. and E.A.) before inclusion. Clinical, surgical, and interventional details were reviewed. Therapeutic strategy was decided by the attending physician. Discharge medications were reviewed in all surviving patients. Long-term follow-up was performed through office visits or directly contacting the patient or family by telephone. The last follow-up was conducted in July 2015.

The study population, patients with an established mammary artery graft failure diagnosis, was divided in two groups: those with and those without a subsequent combined MACE during follow-up.

For statistical purposes and data processing the SPSS software, v20.0 (SPSS, USA) and multimedia package OFFICE 2013 (Microsoft, USA) were used. The baseline characteristics of the patients are depicted as mean (±standard deviation), or as median (interquartile range) for continuous variables, and categorical variables as an absolute figure (percentage). Between-group comparisons were performed using Pearson χ^2 for qualitative variables and Student *t* test or Mann–Whitney *U* test for continuous variables, as indicated by the dispersion of data. Long-term survival curves of the different groups were performed using the Kaplan–Meier method, and comparisons were obtained using the Log-rank or the Breslow test. The MACE was considered including: all-cause death or HF, unstable angina, MI, readmissions, or stroke. In patients with multiple events, only the first one was included in the primary analysis. The Cox proportional hazard regression model was used to analyze and select the variables independently associated with the appearance of long-term events. An excessive number of variables in the multivariate analysis were avoided by reducing their number using a prespecified model that included those deemed to be associated with prognosis, after the univariate approach ($p \leq 0.20$). Thus, several multivariate models were explored. In brief, age (quartiles: <55, 55–59.9, 60–70.5 and > 70.5 years), diabetes mellitus (yes/no), peripheral artery disease (yes/no), MI or ventricular tachycardia as reason to the diagnosis (yes/no), left ventricular ejection fraction (LVEF; strata: normal > 55%, mild 45–55, moderate 35–44 or severely depressed <35%), dual antiplatelet duration (months), number of grafts (categorical: 1–2 or 3–4 grafts), final technique used to revascularize the IMA graft (IMA simple percutaneous transluminal coronary angioplasty (PTCA), IMA stenting, native coronary artery stenting or medical management), and other coronary lesions revascularized (yes/no) were included as covariates in the final models and several clinical events as dependent variables. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated by backward stepwise regression analysis (Wald). The null hypothesis was rejected—no statistically significant differences—using a two-tail *p* value < 0.05 as cutoff. The study was conducted in compliance with human studies guidelines and approved by an institutional review board.

3. Results

A total of 57 patients with angiographically definite IMA graft failure were identified after a median time of 29.5 months after their initial CABG. The group included mainly males (89%), with a median age of 62 years (at the time of index surgery) and presenting with several cardiovascular risk factors. The main reason for index surgery was multivessel disease (98.2%) in a stable angina context (70.2%). All but one (diagonal branch) left IMA grafts were linked to the left anterior descending artery.

Demographics and clinical features are depicted in Table 1. During follow-up, at least one MACE occurred in 29 (50.9%) patients (12 deaths, 28 acute coronary syndromes, 2 strokes and 8 HF readmissions). Both study cohorts, patients with MACE events (MACE +) and without (MACE -), were clinically pretty similar except for the fact that MACE + patients tended to be older, more frequently diabetic, with peripheral artery disease, and with lower LVEF (54% vs 63%, $p = 0.03$). Initial surgical technique and antithrombotic management are compared in Table 1.

Table 2 shows the cardiac catheterization data and the IMA graft failure management details. Most of the failures were diagnosed (65%) during the first year after the surgery, mainly because of an acute coronary syndrome. The IMA problem was detected mostly at or near the distal anastomotic area, (Fig. 1). Most of the patients underwent an IMA PCI (74%). However, in 9 cases, the PCI failed at the IMA level, and then most those patients underwent a native vessel revascularization (7; 77.8%). All native vessel PCIs included stenting, usually drug-eluting stents (DESs), excepting one case (bare-metal stent (BMS) at the left main because of size availability issues).

Comparing the IMA segments involved, those different from the distal anastomosis displayed a higher probability for a failed PCI (3/7, 42.9% Vs 6/50, 12.0%; $p = 0.03$). Acute patients, considered as those with a MI/ventricular tachycardia, displayed clearly a worse long-term prognosis in terms of MACE ($p < 0.01$).

Appendix Fig. 1 shows the overall Kaplan–Meier curves on main events.

The in-hospital mortality was 5.2% (Table 3), and the total any-cause mortality reached the 21.1%, during a median follow-up of 7.5 years after the IMA failure diagnosis (median total follow-up after surgery 114 months). Table 3 displays other adverse events during follow-up. Table 4 depicts MACE events regarding the IMA management technique finally used. Respecting MACE occurrence, multivariate models pointed out age (HR 1.85; 95% CI: 1.17–2.11; per year/quartile), diabetes mellitus (HR 2.75; 95% CI: 1.13–6.69), clinical presentation, other lesions revascularized (HR: 0.8; 95% CI: 0.15–0.96), and the treatment strategy of the IMA failure (stenting HR: 5.5; 95% CI: 1.40–21.15) as independent prognostic factors. Table 5 shows the most significant variables related to MACE and death during follow-up.

Appendix Fig. 2 displays MACE and death-free survival curves regarding age, diabetes, and LVEF. On the other hand, age, low LVEF, MI as the reason for IMA failure diagnosis, and the previous number of grafts were the variables linked to all-cause death development. Fig. 2 shows the influence of working diagnosis (infarction or not), stenotic IMA segment, and management technique on Kaplan Meier curves in relation to the primary event, i.e. MACE.

Table 1
Epidemiological and surgical features.

Clinical features	Overall ($n = 57$)	MACE + ($n = 29$)	MACE − ($n = 28$)	p
Gender/male (%)	49 (89.0%)	24 (82.8%)	25 (89.3%)	0.70
Age[+] (mean ± SD)	62.2 ± 10.4	64.3 ± 10.8	60.1 ± 4.8	0.13
Weight (mean ± SD), kg	75.3 ± 11.3	75.9 ± 10.6	74.7 ± 12.1	0.69
Height (mean ± SD), cm	166.3 ± 8.9	166.2 ± 6.9	166.6 ± 10.8	0.85
Hypertension (%)	44 (77.2%)	23 (79.3%)	23 (82.1%)	0.76
Dyslipidemia (%)	46 (80.7%)	23 (79.3%)	23 (82.1%)	0.78
Diabetes mellitus (%)	27 (47.3%)	18 (62.0%)	9 (32.1%)	0.03
Smoking habit (%)	36 (63.2%)	16 (55.2%)	20 (71.4%)	0.27
CAD family history (%)	4 (7.0%)	2 (6.9%)	2 (7.1%)	1
Known allergies (%)	6 (10.5%)	3 (10.3%)	3 (10.7%)	1
Renal failure/CrCl<30 (%)	8 (14.0%)	5 (17.2%)	3 (10.7%)	0.70
Peripheral vascular disease (%)	9 (15.8%)	7 (24.1%)	2 (7.1%)	0.14
Working diagnosis (%)				0.29
- Chest pain.	2 (3.5%)	1 (3.5%)	1 (3.6%)	
- Stable angina	40 (70.2%)	17 (58.6%)	23 (82.1%)	
- NSTEMI	6 (10.6%)	3 (10.3%)	3 (10.7%)	
- STEMI	8 (14.0%)	7 (24.1%)	1 (3.6%)	
- Ventricular tachycardia/fibrillation	1 (1.7%)	1 (3.5%)	0	
Right dominance (%)	49 (86.0%)	25 (86.2%)	24 (85.7%)	0.99
Coronary artery disease, number of vessels (%)	2.84 ± 0.41	2.79 ± 0.49	2.89 ± 0.31	0.36
- 1	1 (1.7%)	1 (3.5%)	0	
- 2	7 (12.3%)	4 (13.8%)	3 (10.7%)	
- 3	49 (86.0%)	24 (82.7%)	25 (89.3%)	0.56
Left ventricular ejection fraction (mean ± SD), %	58.9 ± 15.0%	54.6 ± 14.7%	63.3 ± 14.7%	0.03
Surgical considerations				
Coronary artery bypass grafting timing (%)				
- Elective	57 (100%)	29 (100%)	28 (100%)	1
Pump surgery procedure (%)				0.62
- Off pump (OPCAB)	37 (64.9%)	18 (62.1%)	19 (67.8%)	
- On pump	11 (19.3%)	7 (24.1%)	4 (14.3%)	
- Unknown	9 (15.8%)	4 (13.8%)	5 (17.9%)	
Associated (valve) procedures	1 (1.8%)	1 (100%)	0	-
Number of grafts (mean ± SD)	2.26 ± 0.91	2.1 ± 0.8	2.43 ± 0.9	0.18
- 1 (%)	10 (17.6%)	6 (20.7%)	4 (14.3%)	
- 2 (%)	30 (52.6%)	16 (55.2%)	14 (50.0%)	
- 3 (%)	9 (15.8%)	5 (17.2%)	4 (14.3%)	
- 4 (%)	8 (14.0%)	2 (6.9%)	6 (21.4%)	
Type of conduits (%)				0.33
- Left internal mammary artery	57 (100%)+++	29 (100%)	28 (100%)	
- Right internal mammary artery	7 (12.2%)	3 (10.3%)	4 (14.3%)	
- Radial artery	7 (12.2%)	1 (3.4%)	6 (21.4%)	
- Saphenous vein.	35 (61.4%)	20 (68.9%)	15 (53.5%)	
Antithrombotic therapy				
Aspirin (%)	56 (98.2%)	29 (100%)	27 (96.4%)	0.30
Clopidogrel/others (%)[++]	15 (26.3%)	6 (20.7%)	10 (35.7%)	0.20
Anticoagulation (%)	5 (8.8%)	2 (6.9%)	3 (10.7%)	0.61
Discharge dual antiplatelet therapy (%)	14 (24.6%)	7 (24.1%)	11 (39.2%)	0.21
- 3 months	1 (1.8%)	0	1 (3.5%)	
- 4 months	1 (1.8%)	1 (3.4%)	0	
- ≥12 months	12 (21.0%)	6 (20.7%)	10 (35.7%)	
Surgery to last follow-up, time				0.23
- Mean ± SD, months	112.2 ± 59.7	102.9 ± 60.3	121.8 ± 58.7	
- Median (q1-q3), months	113.9 (78.0–131.9)	112.2 (59.9–134.4)	118.6 (98.3–130.7)	

MACE -during follow-up- subgroups are displayed.
+Age, when underwent cardiac surgery; ++, one patient on prasugrel; +++ 5 cases, sequential AMI anastomosis.
NSTEMI, non ST elevation myocardial infarction; MACE: major adverse combined events; STEMI, ST elevation myocardial infarction; SD, standard deviation.
In only one case the right mammary was sequential. Usually mammary conduits are skeletonized.
Significant $p < 0.05$.

4. Discussion

We present here a three-hospital retrospective registry, with prospective follow-up of 57 consecutive cases of IMA graft failure between 2004 and 2014. After treatment, clinical and procedural features are provided. This series is, to the best of our knowledge, one of the largest with the longest follow-up after its treatment, aiming to describe the natural history of the whole process on this dreadful situation.

Considering our data, some circumstances pointed out a worse prognosis once an IMA failure is diagnosed: age, diabetes, low LVEF, acute clinical presentation, and more importantly certain management issues. Same way that CABG patients with previous PCI would display worse outcomes, we present the outcomes after the diagnosis and management of a complex situation, an IMA graft failure.

IMA makes an excellent graft with a low failure rate.[1,5,6] Thus, IMA grafts markedly reduce the risk of occlusion or stenosis as frequently seen with vein grafts,[2,3,7,8] with improved clinical end points.[1–3,8,9] Although some patients do not present symptoms after surgery, potential consequences of loss of graft patency include angor pectoris, HF, re-infarction, or cardiac death.[4]

Table 2
Diagnostic cardiac catheterization features, when IMA graft failure was made, and its management.

	Overall ($n = 57$)	MACE + ($n = 29$)	MACE − ($n = 28$)	p
Main index-cath indication (%)				0.46
- Dyspnea	2 (3.5%)	1 (3.4%)	1 (3.5%)	
- Ventricular tachycardia	1 (1.8%)	1 (3.4%)	0	
- Presurgical (asymptomatic)	1 (1.8%)	0	1 (3.5%)	
- Heart failure	1 (1.8%)	0	1 (3.5%)	
- Silent ischemia	3 (5.3%)	0	3 (10.7%)	
- Stable angina	3 (5.3%)	2 (6.9%)	1 (3.5%)	
- Progressive angina/NSTEMI	26 (45.6%)	14 (48.2%)	12 (42.9%)	
- STEMI	20 (35.1%)	11 (37.9%)	9 (32.1%)	
- STEMI/Shock + Killip IV	6[b] (10.5%)	4 (13.8%)	2 (7.1%)	0.41
Myocardial Infarction/VT as new-cath indication (%)	33 (57.9%)	22 (75.9%)	11 (39.3%)	<0.01
Surgery to index catheterization time				0.70
- Mean ± SD, months	29.5 ± 54.4	32.3 ± 54.8	26.7 ± 54.9	
- Median (q1-q3), months	5.4 (0.14–29.0)	5.4 (0.09–44.1)	5.4 (0.24–24.0)	
IMA failure timing				0.64
- Acute/early (<1 month)	18 (31.6%)	10 (34.5%)	8 (28.6%)	
- Late (1–12 months)	19 (33.3%)	8 (27.6%)	11 (39.3%)	
- Very late (>12 months)	20 (35.1%)	11 (37.9%)	9 (32.1%)	
Management				
IMA PCI failure	9 (15.8%)	3 (10.3%)	6 (21.4%)	0.25
Final Technique				0.13
- IMA, PTCA	25 (43.9%)	11 (37.9%)	14 (50.0%)	
- IMA, drug eluting stent[a]	17 (19.2%)	13 (44.8%)	4 (14.3%)	
- Native vessel, stenting+	12 (19.3%)	3 (10.3%)	8 + (28.6%)	
- Medical management	3 (7.0%)	1 (3.4%)	2 (7.1%)	
Stenosis IMA location				0.17
- Distal anastomosis	50 (87.7%)	28 (96.6%)	22 (78.6%)	
- IMA body.	3 (5.3%)	0	3 (10.7%)	
- IMA origin.	3 (5.3%)	1 (3.4%)	2 (7.1%)	
- Diffuse disease.	1 (1.8%)	0	1 (3.6%)	
Other coronary lesions revascularized	32 (56.1%)	13 (44.8%)	19 (67.9%)	0.08
Antithrombotic therapy				
Aspirin (%)	56 (98.2%)	29 (100%)	27 (96.4%)	0.30
Clopidogrel (%)	48 (84.2%)	24 (82.8%)	24 (85.7%)	0.76
Anticoagulation (%)	6 (10.5%)	2 (6.9%)	4 (14.3%)	0.36
Discharge dual antiplatelet therapy (%)				0.15
- 2 months	2 (3.5%)	0	2 (7.1%)	
- 3 months	5 (8.8%)	3 (10.3%)	2 (7.1%)	
- 4–8 months	2 (3.5%)	2 (6.9%)	0	
- 12 months	33 (57.9%)	16 (55.2%)	17 (60.7%)	
- ≥24 months[c]	7 (12.2%)	3 (10.3%)	4 (14.3%)	
- Mean ± SD, months	14.3 ± 20.9	10.4 ± 9.4	18.3 ± 27.9	0.16

+ In one case a BMS (bare-metal stent) was used, all the remaining patients received DES (drug eluting stents).
IMA, internal mammary artery graft; MACE, major adverse combined event; NSTEMI, non ST-elevation myocardial infarction; PTCI, percutaneous transluminal coronary angioplasty; SD: standard deviation; STEMI, ST elevation myocardial infarction.
Significant $p < 0.05$.
[a] In 1 case, the graft treated was a right IMA.
[b] Over 6 cardiogenic shocks, 4 were acute and 2 late I MA failures.
[c] Four patients are on dual antiplatelet therapy indefinitely.

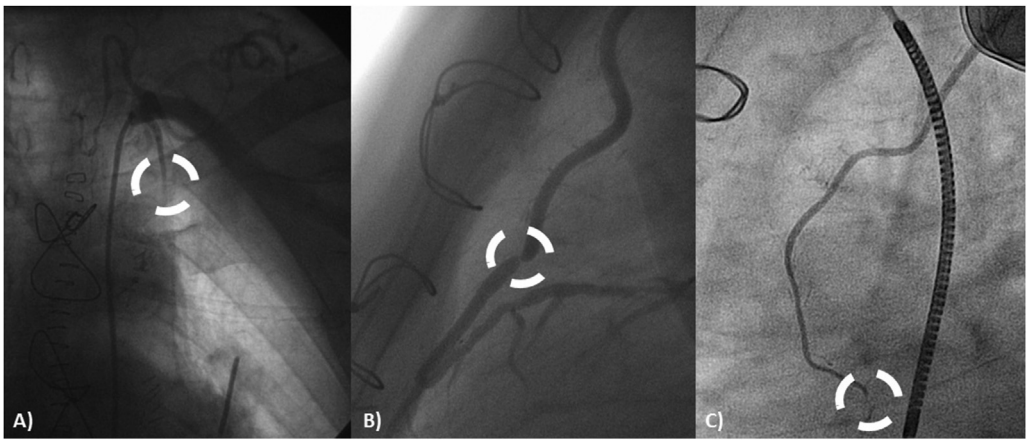


Fig. 1. Coronary angiography. Areas of internal mammary artery stenosis (white circle). Because mammary atherosclerosis is rarely seen, lesions usually are related with technical factors. A) Proximal involvement. This lesion supposed a failed percutaneous coronary angioplasty (PCI). B) Body stenosis. PCI with stent achieved good result with good long-term evolution. C) Anastomotic lesion. The most common problem. A) Anteroposterior view. B) and C) are lateral views.

Table 3
Long-term follow-up and outcomes, after IMA graft failure diagnosis was made.

	Overall ($n = 57$)
Follow up after the new catheterization[+]	
- Median (q1-q3), months	89.7 (56.0–117.5)
Heart failure[++] (%)	8 (14.0%)
Unstable angina[++] (%)	13 (22.8%)
Acute myocardial infarction[++] (%)	15 (26.3%)
Bleeding[+++] (%)	7 (12.3%)
Embolism (pulmonary embolism) (%)	1 (1.8%)
Stroke[++] (%)	2 (3.5%)
New IMA TLR	8 (14.0%)
New IMA TVR	12 (21.0%)
Other vessel revascularization	12 (21.0%)
Any new revascularization	26 (48.1%)
Death[++] (%)/In-hospital Death (%)	12 (21.1%)/3 (5.2%)
- Cardiac	8 (14.0%)
- Stroke	1 (1.7%)
- Multiorganic failure	2 (3.5%)
- Sepsis	1 (1.7%)

+, the moment the IMA graft failure is confirmed; ++, variables included in MACE definition; +++, considering BARC bleedings type 3 to 5.
IMA, internal mammary artery graft; SD, standard deviation; TVR; target vessel revascularization; TLR, target lesion revascularization.

Several factors could lead to an IMA graft failure. Some studies have focused on surgical experience, volume, technique, and cardiopulmonary bypass use (off-pump, with all the issues associated with anastomoses on the beating heart, vs on-pump CABG with cardioplegia and arrest) as a factor for higher long-term patency regarding vein grafts.[4,10,11]

In our series, the precise management was decided by the attending physician, sometimes after a careful "heart team" evaluation. However, the official recommendations are vague, and because it is an infrequent problem the expertise is, for most groups, limited. In addition, some patients could course asymptomatic, making it difficult to discover the problem.[9] Nonetheless, our patients, usually after an acute presentation, frequently showed cardiac symptoms, something typical in other previously published series.[12]

Nowadays, an interventional approach is feasible for most cases and generally is the first option chosen by the attending team.[1] Repeat CABG is not optimal because patients are older, more frail, and technically challenging, sometimes lacking of conduits and because of an increased operative morbidity/mortality risk, with up to threefold to fourfold increase in the risk of death.[13,14]

Furthermore, patients with an acute presentation could have a worse prognosis. In this setting, it is probably a good idea to revascularize the most when and where possible (complete vs incomplete revascularization). Native vessel treatment is probably preferable, if feasible.[1] We know the long-term PCI results and outcomes after PCI for vein grafts stenosis are worse than in native vessels.[15] When we decide to treat the IMA, one has to accept a high rate of failed PCIs (15.8%, 9/57 in our series). Interestingly, our patients did better after stenting the native vessels than stenting the IMA grafts. Also, the IMA segment affected matters. On one hand, anastomotic problems are sometimes more feasible to successful percutaneous treatment than body or origin lesions, if the vessel displays a reduced flow. On the other hand, occluded IMAs usually

Table 4
MACE regarding the IMA final management (simple PTCA, PCI with drug eluting stenting or native PCI).

Events[+]	IMA-PTCA ($n = 25$)	IMA stenting ($n = 17$)	Native stenting[++] ($n = 12$)	p
Heart failure (%)	2 (8.0%)	5 (29.4%)	1 (8%)	0.18
Unstable angina (%)	3 (12.0%)	7 (41.2%)	2 (16.0%)	0.15
Reinfarction (%)	5 (20.0%)	7 (41.2%)	3 (25.0%)	0.31
Any cause death (%)	5 (20.0%)	5 (29.4%)	2 (16.0%)	0.64
MACE (%)	11 (44.0%)	13 (76.5%)	4 (33.3%)	0.08
Bleeding (%)	1 (4.0%)	3 (17.6%)	3 (25.0%)	0.23
Embolic events (%)	1 (4.0%)	0	0	0.73
Stroke (%)	1 (4.0%)	1 (0.06%)	0	0.84
IMA-TVR (%)/IMA-TLR (%)	3 (12.0%)/2 (8.0%)	5 (29.4%)/3 (17.6%)	3 (25.0%)/2 (16.6%)	0.60/0.70

+n = 54, 3 patients were excluded for this table, because they only received medical treatment. ++ No native vessel simple PCI was performed.
IMA, internal mammary artery graft; MACE, major adverse combined event; PCI: percutaneous coronary intervention; PTCA: percutaneous transluminal coronary angioplasty; TLR, target lesion revascularization; TVR, target vessel revascularization.
Significant $p < 0.05$.

Table 5
Multivariate analysis on major adverse combined events (MACE) and all cause death.

Multivariate analysis			
	Hazard ratio	95%, Confidence interval	p
MACE			
Age (increasing quartile)	1.68	1.12–2.53	0.01
Diabetes Mellitus	2.79	1.09–6.32	0.02
Infarction/VT as index-cath indication	3.16	1.31–7.63	0.01
Other coronary lesion treated	0.34	0.13–0.84	0.02
Final technique (IMA stenting)	2,79	1.19–6.55	0.02
All cause death			
Age (increasing quartile)	9.08	2.52–32.69	<0.01
Infarction/VT as index-cath indication	1.05	1.01–2.17	0.01
Number of grafts (3–4)	0.07	0.01–0.50	<0.01
LVEF (decreasing LVEF strata)	3.68	1.65–8.18	<0.01

Multivariate models (Cox regression/Backward Wald), including variables with $p \leq 0.20$ in the univariate analysis for MACE (Major adverse combined events): age (quartiles), diabetes mellitus (yes/no), peripheral artery disease (yes/no), myocardial infarction, or ventricular tachycardia as reason to the diagnostic (yes/no), LVEF (left ventricular ejection fraction strata: normal, mild, moderate o severely depressed), dual antiplatelet duration (months), number of grafts (categorical: 1–2 or 3–4 grafts), final technique used to revascularize (categorical: IMA stenting or not), other coronary lesions revascularized (yes/no) were included as covariates (as depicted in Table 3). Remaining variables in the equation are displayed.
Significant $p < 0.05$.

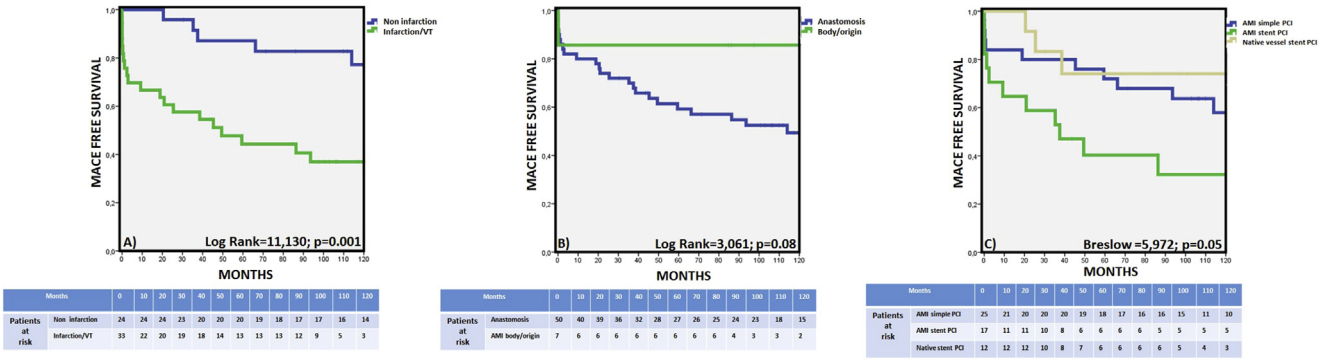


Fig. 2. Major adverse combined event-free survival Kaplan–Meier curves stratified by clinical diagnosis leading to the demonstration of the internal mammary artery failure (acute myocardial infarction or ventricular tachycardia or not) A), internal mammary artery segment involved (anastomosis or not) B) and final internal mammary artery interventional treatment modality C), over 120 months, respectively. Time = 0; internal mammary artery graft failure diagnostic cardiac catheterization. Significant $p < 0.05$.

begets a failed PCI, so in that case, is probably better to go directly for the native vessel.

Regarding "conduit treatment" technical aspects, it is known that stented vein grafts displayed lower rates of restenosis[16–18] than those managed with simple PCI. Currently, DES has been deemed to be the first choice because its lower rates of in stent restenosis, compared with BMS.[19,20] Recently, a 27-center registry by Lozano et al on the use of DES in 268 patients with a failed mammary graft, reported good long-term results.[21]

This report only included patients who had already received, at least, a DES in the IMA graft. However, our series reflects a more wide "real-life" assessment, reviewing all management strategies. In addition, we found better results with PTCA at the anastomosis level. This makes sense because the mechanistic could be different than for other territories (surgical technique here vs neoatherosclerosis-thrombosis issues regarding the regular coronary stenosis). Gruberg et al reported a higher use of simple PCI for distal lesions (anastomotic), while ostial lesions were managed more frequently with stents), with good clinical results up to 12 months.[22] Overall, this retrospective study reported higher target lesion revascularization rate for stenting (15.4%) compared with simple PCI (5.4%), at one year.[21]

With these limited data, it would be wise to be cautious with the use of drug-eluting balloons for recent anastomosis because the drug could impair the healing process in a sutured area.

Of note, some cases warranted redo surgery. Probably, we need to consider it for very early graft failures (fresh anastomosis, complex anatomies, risky antithrombotic treatment). Other grounds should include kinked grafts because its percutaneous treatment could displace the kink, risking the graft itself and the distal segments, or even other grafts if a sequential anastomosis is present (see Fig. 3).

Last, but not least, probably a good antithrombotic treatment is of paramount importance both before and after an IMA dysfunction is found. In fact, the 2015 American heart Association statement on "Secondary Prevention after Coronary Artery Bypass Graft Surgery" recommended the addition of clopidogrel to aspirin for 1 year in patients who receive off-pump surgery.[23] Our data suggest the same thing. A prolonged dual antiplatelet therapy could decrease ischemic events. A recent analysis of the PREVENT IV trial reviewing predictors of IMA graft failure, pointed out that IMA graft failure is not so uncommon and associated with higher rates of repeat revascularization, raising concerns about competitive flow and disputing the appropriateness of using IMA grafts in some stenosis without functional evidence of ischemia.[24]

4.1. Limitations

The study presents the boundaries of an observational and retrospective study with a small number of patients and events.

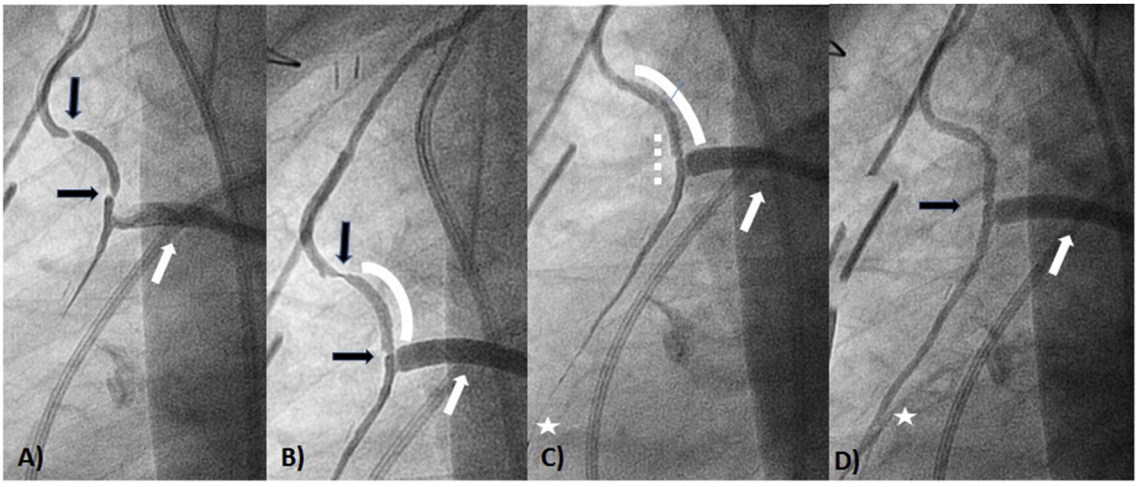


Fig. 3. Coronary angiography. An example of a "kinked" graft (black arrows). The patent received 3 grafts hours before. Two sequential saphenous vein grafts, "T"-shaped (white arrow), emerged from the internal mammary artery (IMA), which was destined to the left anterior descending artery (star), A). The "successful" stenting lead to a distal displacement of the kinked area, B) after one stent, and C) after the second stent (white lines). Because the anastomosis with the vein was involved a simple percutaneous coronary angioplasty (PCI) was performed (dash line), improving the flow but with a remaining anastomotic stenosis (black arrow), D). Finally, a native multivessel revascularization was needed. All pictures are lateral views.

Thus, therapeutic recommendations should be interpreted with caution. In fact, probably a competitive risk would be a more appropriate analysis to deal with the studied outcomes, but the small sample size, together with its limited statistical power could pose some issues. Notwithstanding, a condition with such infrequent diagnosis per se, makes it difficult to use other study designs. Hence, the data presented are possibly very close to real life current clinical practice.

5. Conclusion

In this long-term registry on IMA graft failure, most patients presented with acute symptoms (MI or progressive angina) within the first 12 months after surgery. The acute presentation together with increasing age, diabetes, low LVEF, IMA graft failure, segment affected, and the management strategy seem to be related with the long-term prognosis and the development of evolutive complications, which are frequent for this problem.

Conflicts of interest statement

All authors have none to declare.

Funding

None.

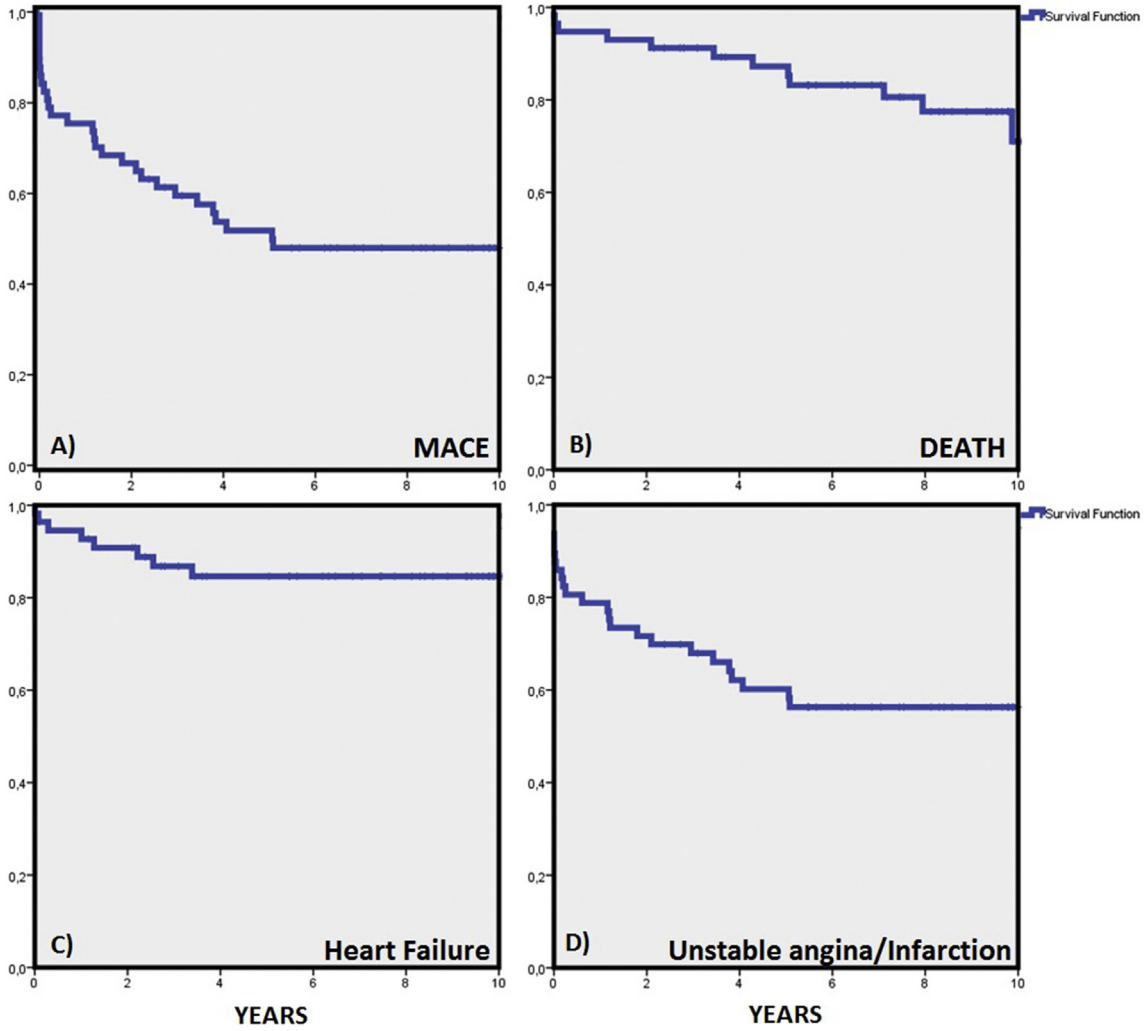
Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

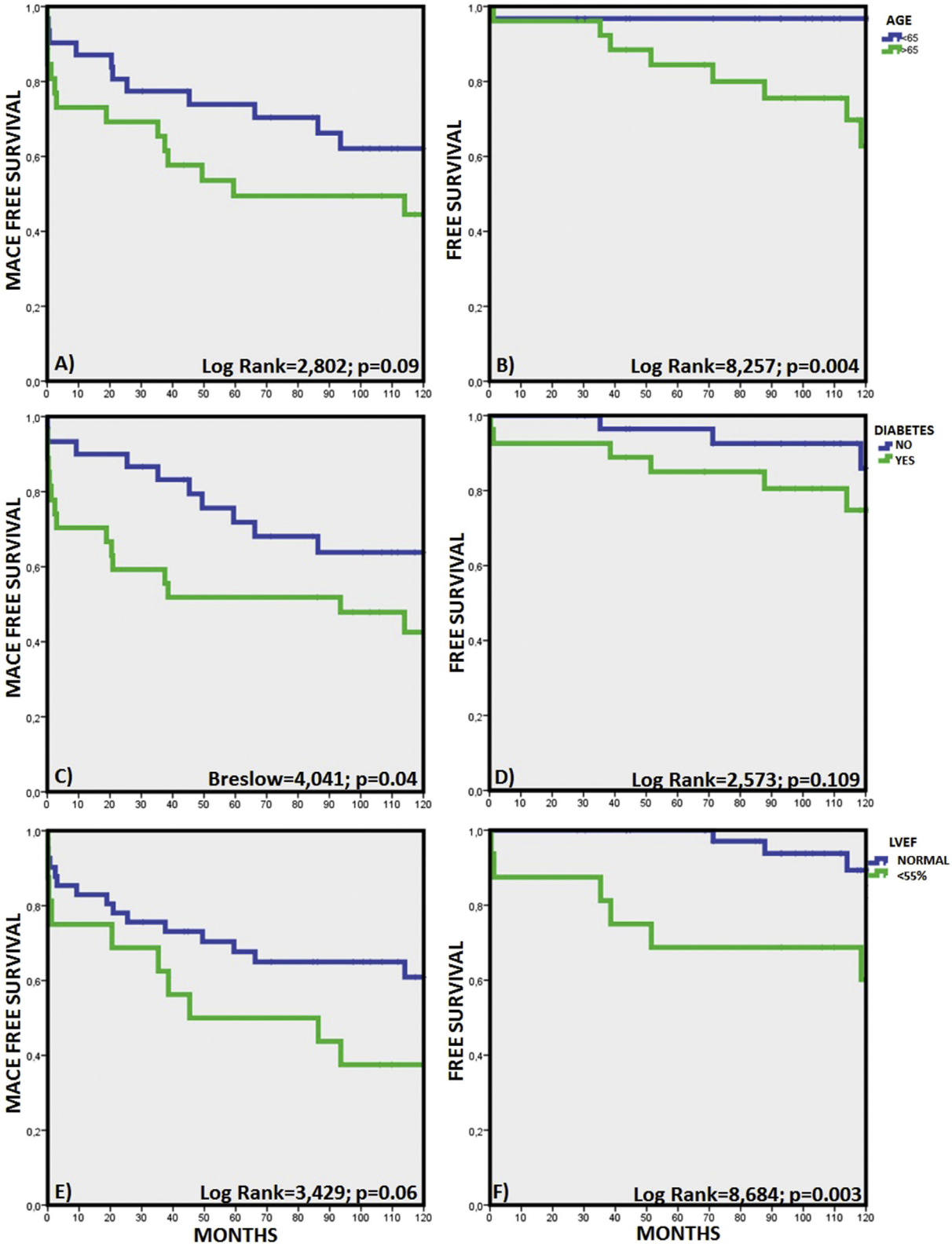
Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Appendix



Appendix Fig. 1. Kaplan–Meier curves showing time to major adverse combined event (MACE) A), all-cause mortality B), heart failure C), unstable angina, or reinfarction D), over a 10-year period. Most events happened the first years. Time = 0; internal mammary artery graft failure diagnostic cardiac catheterization. Significant $p < 0.05$.



Appendix Fig. 2. Kaplan–Meier curves stratified by age (<or >65 years) A and B), diabetes status C and D) and ejection fraction E and F) (normal or depressed) regarding Major adverse combined event (MACE) and all-cause mortality, respectively. Time = 0; internal mammary artery graft failure diagnostic cardiac catheterization. Significant $p < 0.05$.

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