Rev Esp Cardiol. 2018;71(10):801–810

Original article

Bifurcation Culprit Lesions in ST-segment Elevation Myocardial Infarction: Procedural Success and 5-year Outcome Compared With Nonbifurcation Lesions

Pablo Salinas,* Hernán Mejía-Rentería, Raúl Herrera-Nogueira, Pilar Jiménez-Quevedo, Luis Nombela-Franco, Iván Javier Núñez-Gil, Nieves Gonzalo, María del Trigo, María José Pérez-Vizcayno, Alicia Quirós, Javier Escaned, Carlos Macaya, and Antonio Fernández-Ortiz

Sección de Hemodinámica, Servicio de Cardiología, Hospital Clínico San Carlos, Madrid, Spain

Article history:
Received 19 February 2017
Accepted 14 June 2017
Available online 9 August 2017

Keywords:
ST-segment elevation myocardial infarction
Primary angioplasty
Coronary bifurcation
Propensity score

ABSTRACT

Introduction and objectives: We assessed short- and long-term outcomes of primary angioplasty in ST-segment elevation myocardial infarction by comparing bifurcation culprit lesions (BCL) with non-BCL.
Methods: Observational study with a propensity score matched control group. Among 2746 consecutive ST-segment elevation myocardial infarction patients, we found 274 (10%) patients with BCL. The primary outcome was a composite endpoint including all-cause death, myocardial infarction, coronary artery bypass grafting or target vessel revascularization, assessed at 30-days and 5-years.
Results: Baseline characteristics showed no differences after propensity matching (1:1). In the BCL group, the most frequent strategy was provisional stenting of the main branch (84%). Compared with the non-BCL group, the procedures were technically more complex in the BCL group in terms of need for balloon dilatation (71% BCL vs 59% non-BCL; $P = .003$), longer procedural time (70 ± 29 minutes BCL vs 62.8 ± 28.9 minutes non-BCL; $P = .004$) and contrast use (256.2 ± 87.9 mL BCL vs 221.1 ± 82.3 mL non-BCL; $P < .001$). Main branch angiographic success was similar (93.4% BCL vs 93.8% non-BCL; $P = .86$). Thirty-day all-cause mortality was similar between groups: 4.7% BCL vs 5.1% non-BCL; $P = .84$. At the 5-year follow-up, there were no differences in all-cause death (12% BCL vs 13% non-BCL; $P = .95$) or the combined event (22% BCL vs 21% non-BCL; $P = .43$).
Conclusions: Primary angioplasty of a BCL was technically more complex; however, main branch angiographic success was similar, and there were no differences in long-term prognosis compared with non-BCL patients.

Lesión culpable bifurcada en infarto agudo de miocardio con elevación del segmento ST: éxito del procedimiento y pronóstico a 5 años comparado con lesión no bifurcada

Palabras clave:
Infarto agudo de miocardio con elevación del segmento ST
Angioplastia primaria
Bifurcación coronaria
Puntuación de propensión

RESUMEN

Introducción y objetivos: En el infarto agudo de miocardio con elevación del segmento ST, se compararon los resultados a corto y largo plazo de la angioplastia primaria de lesiones culpables bifurcadas (LCB) y no bifurcadas (LCNB).
Métodos: Estudio observacional con grupo de control emparejado (1:1) por puntuación de propensión. En un total de 2.746 infartos agudos de miocardio con elevación del segmento ST consecutivos, se encontraron 274 casos de LCB (10%). El resultado principal es un combinado de muerte por cualquier causa, infarto, cirugía de revascularización coronaria o revascularización de vaso diana a 30 días y a 5 años.
Resultados: No había diferencias clínicas entre los grupos emparejados (1:1). En el grupo de LCB, el tratamiento predominante fue un *stent* en la rama principal (84%). Respecto al grupo de LCNB, los procedimientos fueron más complejos en cuanto a dilatación con balón (el 71% de las LCB frente al 59% de las LCNB; p = 0,003), duración del procedimiento (70 ± 29 frente a 62,8 ± 28,9 min; p = 0,004) y consumo de contraste (256,2 ± 87,9 frente a 221,1 ± 82,3 ml; p < 0,001). El éxito angiográfico en la rama principal fue similar (el 93,4 frente al 93,8%; p = 0,86). La mortalidad a 30 días fue similar (el 4,7 frente al 5,1%; p = 0,84).

SEE RELATED CONTENT:
http://dx.doi.org/10.1016/j.rec.2018.03.018

* Corresponding author: Sección de Hemodinámica, Servicio de Cardiología, Hospital Clínico San Carlos, Profesor Martín Lagos s/n, 28040 Madrid, Spain.
E-mail address: Salinas.pablo@gmail.com (P. Salinas).

http://dx.doi.org/10.1016/j.rec.2017.06.022
1885-5857/

A los 5 años de seguimiento, no había diferencias en mortalidad (el 12 frente al 13%; p = 0,95) ni en el objetivo combinado (el 22 frente al 21%; p = 0,43).
Conclusiones: La angioplastia primaria de las LCB fue técnicamente más compleja, pero el éxito en la rama principal fue similar y no se hallaron diferencias en el pronóstico a largo plazo respecto a las LCNB.

Abbreviations

BCL: bifurcation culprit lesion
BIF: bifurcation
MC: matched control
MI: myocardial infarction
PCI: percutaneous coronary intervention
STEMI: ST-segment elevation myocardial infarction

INTRODUCTION

Bifurcations are considered challenging lesions for percutaneous coronary intervention (PCI), and despite substantial improvements, bifurcation (BIF) PCI is associated with worse immediate results and clinical outcomes, mainly because of a higher revascularization rate.[1,2] In the last years, the growing body of BIF research has allowed a consensus regarding a simpler approach using 1 stent in the main vessel (provisional stenting) instead of 2-stent techniques or dedicated devices for most cases.[3] This approach simplifies the procedure but carries a greater risk of side branch (SB) closure that apparently is not associated with worse clinical outcomes.[4–6]

In acute ST-segment elevation myocardial infarction (STEMI), timely primary PCI is currently the standard treatment for most patients.[7] During a primary PCI, the operator must deal in an emergent situation with *ad hoc* intervention over thrombotic lesions in often unstable patients. Therefore, finding a BIF as the culprit lesion adds further complexity to primary PCI, which could potentially lead to worse short- and long-term outcomes. The purpose of this study was to evaluate the incidence of bifurcation culprit lesions (BCL) in acute STEMI, and to compare procedural characteristics and clinical outcomes between BCL STEMI patients and a matched control (MC) group of non-BCL STEMI patients.

METHODS

We designed an observational, analytical, retrospective cohort study, using propensity score matching to pair patients with and without a BCL in STEMI.

Patient Selection

Data from all cardiac catheterizations and hospital admissions were prospectively filled in a comprehensive database shared by a network of hospitals that includes 1 main tertiary center and 2 satellite centers. For the purpose of this study, we retrospectively selected from the database patients with STEMI treated with primary or rescue PCI $<$ 24 hours from symptom onset. Exclusion criteria were: normal coronary arteries or alternative diagnostics different from STEMI; other emergent indications for PCI different from STEMI (cardiac arrest or shock without suspected STEMI); culprit lesion located at left main or surgical grafts and facilitated PCI. From 2004 to 2015, a total of 2746 STEMI patients met the inclusion/exclusion criteria.

Lesion Selection

All cases with the culprit lesion coded as bifurcated in our database had their angiographies independently reviewed by 2 interventional cardiologists who were not involved in the analysis of the outcomes. The selection of BIF cases and controls is detailed in Figure 1 of the supplementary material and Table 1 of the supplementary material. The BIF group included 274 patients (10%) with lesions involving or adjacent ($\leq$ 5 mm) to a SB $\geq$ 2 mm by visual estimation or quantitative coronary angiography if there was disagreement.

Propensity Score Matching for Comparison Group

Propensity score matching was used to create an MC group for comparison and reduce differences in clinical characteristics.[8] The propensity score was estimated using logistic regression, entering only baseline (pre-PCI) covariates by statistical (differences with *P* value $<$ .1) and clinical criteria. The model was adjusted by date of the primary PCI, time from symptoms onset to PCI, culprit vessel, age, sex, rescue PCI, number of diseased vessels, previous myocardial infarction (MI), and diabetes. There were no interactions among variables, and the area under the curve was 0.66. Participants were matched using 1:1 nearest neighbor matching. A total of 274 patients from the BIF group were matched with 274 patients from the control group, from which 2189 were unmatched. The achieved balance was assessed with a Hotelling's T-square statistic (T^2, 0.56, df, 12,535; *P* = .876).[9]

Variables and Clinical Outcomes Definitions

The main outcome of this study was all-cause mortality and a combined endpoint (including all-cause death, recurrent MI, coronary artery bypass graft or target vessel revascularization) at 5 years.

Main branch (MB) angiographic success was defined as patent artery (Thrombolysis In Myocardial Infarction [TIMI] flow 2 or 3) with residual stenosis $\leq$ 30% (visual estimation). Side branch angiographic success was defined as TIMI flow 2 or 3. BCL global angiographic success was defined as MB and SB angiographic success. Death was analyzed as all-cause death. Medina BIF classification was evaluated when TIMI flow[10] 2 or 3 was obtained, and defined as previously described.[11] Recurrent MI (nonfatal) was considered as type 1 or 2 using the third universal definition.[12] Target vessel revascularization and target lesion revascularization (TLR) was defined as any revascularization within the culprit vessel or the culprit lesion (or 5 mm edge), respectively.

Data from the index cardiac catheterization, hospital admission, and 30-day follow-up was routinely and prospectively collected in all patients. Follow-up data were obtained (mainly from electronic clinical records, and telephone interview in patients with external clinical follow-up) for the BIF and MC cohort (n = 548) and updated until January 2016, then censored to a maximum of 5 years of follow-up. Censoring was done due to a wide inclusion timeframe (January 2004 to January 2015) and in order to ensure greater consistency in the follow-up data (≥ 1 year and up to 5 years). The mean follow-up was 42.9 ± 21.4 months.

Procedural Characteristics

All patients were premedicated with aspirin and tyenopiridine or ticagrelor with loading dose; no upstream glycoprotein IIb/IIIa inhibitors were used. Other treatments, the interventional technique and the BIF approach were decided by the operator. Secondary prevention drugs following current European guidelines and 12 months of dual antiplatelet therapy were recommended at discharge.[7]

Statistical Analysis

Continuous variables are expressed as mean values ± standard deviation and were compared by the Student *t* test if normally distributed. In the case of skewed distribution, we used median values with interquartile ranges and the data were compared by Wilcoxon Mann-Whitney test. Categorical variables are expressed as numbers and percentages and were compared using the chi-square or Fisher exact test, as deemed appropriate. Thirty-day events were compared

Table 1
Clinical and Anatomic Characteristics, Before and After Propensity Matching

Variable	Before matching				After matching		
	Total (n = 2746)	BIF group (n = 274)	Controls (n = 2472)	*P*	BIF group (n = 274)	MC group (n = 274)	*P*
Age[a]	63 ± 13	62 ± 14	63 ± 13	.83	62 ± 14	63 ± 13	.75
Female[a]	594 (22)	57 (21)	537 (22)	.76	57 (21)	57 (21)	1
BMI, kg/cm²	28 ± 5	28 ± 4	28 ± 5	.64	28 ± 4	27 ± 4	.72
Cardiovascular risk factors							
Obesity	653 (24)	69 (25)	584 (24)	.58	69 (25)	67 (25)	.84
Hypertension	1414 (52)	135 (49)	1279 (52)	.44	135 (49)	141 (51)	.61
Dyslipidemia	1166 (43)	114 (42)	1052 (43)	.76	114 (42)	116 (42)	.86
Diabetes[a]	572 (21)	50 (18)	522 (21)	.31	50 (18)	49 (18)	.91
Smoking history	1713 (64)	176 (64)	1537 (62)	.51	176 (64)	166 (60)	.29
Familial CAD history	120 (4)	11 (4)	109 (4)	.75	11 (4)	11 (4)	1
Previous history							
Previous stroke	100 (4)	8 (3)	92 (4)	.50	8 (3)	8 (3)	1
Peripheral vascular disease	115 (4)	7 (3)	108 (4)	.16	7 (3)	6 (2)	.78
Chronic kidney disease	103 (4)	8 (3)	95 (4)	.45	8 (3)	7 (3)	.79
Previous MI[a]	248 (9)	18 (7)	230 (9)	.13	18 (7)	13 (5)	.36
Previous PCI	230 (8)	20 (7)	210 (8)	.50	20 (7)	12 (4)	.15
Previous CABG	16 (0.6)	1 (0.4)	15 (0.6)	.62	1 (0.4)	1 (0.4)	1
Coronary anatomy							
Number of diseased vessels[a]				.68			.70
0[b]	80 (3)	8 (3)	72 (3)		8 (3)	7 (3)	
1	1472 (54)	147 (54)	1325 (54)		147 (54)	157 (57)	
2	803 (29)	86 (31)	717 (29)		86 (31)	74 (27)	
3	391 (14)	33 (12)	358 (15)		33 (12)	36 (13)	
Mean number of severely diseased vessels	1.35 ± 0.7	1.33 ± 0.7	1.35 ± 0.7	.67	1.33 ± 0.7	1.29 ± 0.6	.48
Dominance				.21			.72
Left	188 (7)	20 (7)	168 (7)		20 (7)	18 (7)	
Right	2323 (85)	223 (81)	2100 (85)		223 (81)	219 (80)	
Balanced	235 (31)	31 (11)	204 (8)		31 (11)	37 (14)	
Culprit vessel[a]				< .001			.59
LAD	1096 (40)	159 (58)	937 (38)		159 (58)	147 (54)	
LCx	324 (12)	39 (14)	285 (12)		39 (14)	53 (19)	
RCA	1107 (40)	50 (18)	1057 (43)		50 (18)	49 (18)	
Other	219 (8)	26 (9)	193 (8)		26 (9)	25 (9)	

BIF, bifurcation; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; LAD, left anterior descending artery; LCx, left circumflex; MC, matched control; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.
Data are expressed as mean ± standard deviation or No. (%).
[a] Indicates the variables included in the propensity score.
[b] Culprit lesion located in a secondary vessel.

with Cox regression analysis, providing survival probabilities and hazard ratios (HR) for comparison. Five-year all-cause mortality and the combined endpoint were compared with Cox regression analysis. Kaplan-Meier curves were built and then compared using the Breslow and log-rank tests. To adjust for the effect of concomitant all-cause mortality, the Fine and Gray competing risk proportional hazard regression was used to report the HRs for each component of the combined endpoint.[13] Crude HRs were adjusted by drug-eluting (vs bare metal) stent, aspiration thrombectomy, and use of IIb/IIIa inhibitors. *P* values below .05 were considered statistically significant. Propensity computations were performed with MatchIt package of R software (version 3.0.2), all other analyses with SPSS (version 21).

RESULTS

Baseline Characteristics

A total of 274 (10%) lesions were included in the BIF group, while all other lesions (2472) were considered non-BIF lesions (control group). Baseline clinical characteristics from the total population, BIF, control and MC groups are shown in Table 1. There were no significant differences in either cardiac risk factors or the extension of coronary disease between the BIF and control groups. The main difference before propensity matching was the infarct-related artery: in the BIF group, the left anterior descending artery was more frequently involved, and less frequently the right coronary artery (Figure 1A). Segments involved (Figure 1B) were also similar within left anterior descending artery or left circumflex infarcts (mainly proximal and midsegments). In contrast, in the right coronary artery the culprit lesion was found mainly in distal segments followed by midsegments in the BIF group, whereas it was found more frequently in proximal or midsegments in the control group. After propensity score matching, the infarct-related artery was well balanced between BIF and MC groups.

Angiographic Findings in the Bifurcation Group

Further anatomical data of the BIF group are shown in Table 2. The mean diameter of the SB was 2.16 ± 0.2 mm. More than half of the BIF (56%) were left anterior descending artery-diagonal (involving the first diagonal branch in 124 [45%] cases). The most frequent type of Medina classification was largely the 1.1.1 (64%), with the other

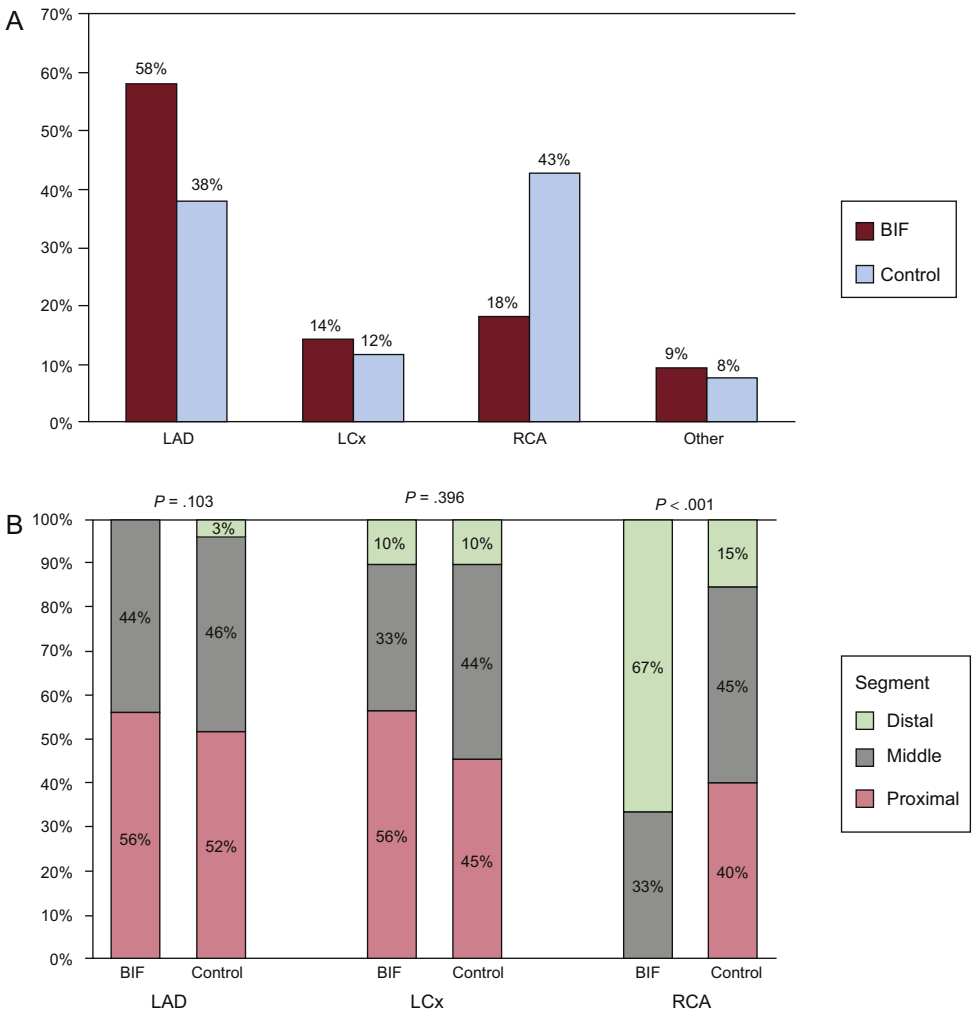

Figure 1. A: distribution of infarct-related artery between BIF (n = 274) and control (n = 2472) groups ($P < .001$). B: segment where the culprit lesion was found within each infarct-related artery. BIF, bifurcation; LAD, left anterior descending artery; LCx, left circumflex; RCA, right coronary artery.

Table 2
Coronary Anatomy and Angiographic Characteristics of the Bifurcation Group (n = 274)

Variable	No (%)
MB culprit vessel	
LAD	159 (58)
LCx	39 (14)
RCA	50 (18)
Others	26 (9)
SB involved	
Diagonal	153 (56)
Septal	6 (2)
Obtuse marginal/distal LCx	39 (14)
Acute marginal	12 (4)
Posterior descending artery	25 (9)
Posterolateral	25 (9)
Other subbranches	26 (9)
MB baseline TIMI flow	
0	170 (62)
1	25 (9)
2	50 (18)
3	29 (11)
SB baseline TIMI flow	
0	131 (48)
1	22 (8)
2	72 (26)
3	49 (18)
SB take-off angle	
< 45°	69 (25)
45 to 90°	164 (60)
> 90°	41 (15)
Medina classification	
1-0-0	24 (9)
0-1-0	18 (7)
0-0-1	8 (3)
1-1-0	17 (6)
0-1-1	18 (7)
1-0-1	14 (5)
1-1-1	175 (64)

LAD, left anterior descending artery; LCx, left circumflex; MB, main branch; RCA, right coronary artery; SB, side branch; TIMI, thrombolysis in myocardial infarction.

types were more or less evenly distributed. The type of lesion known as "true bifurcation" (1.1.1, 1.0.1, 0.1.1) was found in 207 (76%) patients.

Percutaneous Coronary Intervention Procedure

Comparative procedural and interventional data are shown in Table 3. Time from symptoms onset to PCI, a relevant prognostic factor in STEMI, was included in the propensity score and was similar in all groups. While it might be rather long (mean 281 and 298 minutes), it represents "real life" and decreased significantly over time (from a mean of 312 ± 275 minutes in the oldest quintile to 214 ± 169 minutes in the most recent (P = .003 for comparison among quintiles). The mean time from symptom onset to PCI was higher in the rescue PCI subgroup compared with the primary PCI subgroup (415 ± 243 vs 269 ± 230; P < .001); further differential procedural details between primary and rescue PCI are shown in Table 2 of the supplementary material and Table 3 of the supplementary material. The quintiles of procedural inclusion date (20% each 2 years), as well as the rate of rescue PCI (17.5% and 16.1%), were evenly distributed. After propensity score matching, the procedures in the BIF group were longer (70 ± 29 BIF vs 63 ± 30 minutes MC; P = .004), and required more fluoroscopy time (19 ± 13 minutes BIF vs 14 ± 7 minute MC; P < .001) and more contrast (256 ± 88 mL BIF vs 222 ± 81 mL MC; P < .001) compared with the MC group. The number of treated lesions were similar, but the procedures of the BIF group were technically more complex in terms of need for any balloon dilatation (71% BIF vs 59% MC; P = .003) and the number of different balloons used (1.64 ± 1.4 BIF vs 0.93 ± 1.1 MC; P < .001). After propensity score matching, the number of implanted stents per patient was similar between groups (1.23 ± 0.8 BIF vs 1.15 ± 0.7 MC; P = .14), but drug-eluting stents were more frequently implanted in the BIF group (64% BIF vs 54% MC; P = .04) and direct implantation was less frequently used (35% BIF vs 49% MC; P = .001).

Specific details of the PCI in the BIF group are depicted in Table 4. In two-thirds of the lesions, the SB was wired, and the preferred approach was a single, provisional stenting over the MB (84%). The SB was jailed in 81% but was patent in most cases at the end of the procedure (only 11% of TIMI flow 0 or 1). Main branch angiographic success was similar (93.4% BIF vs 93.8% MC; P = .86), although the global angiographic success was lower in the BIF group (84.7%).

Short and Long-term Clinical Outcome in the Paired Population

In the paired population (n = 574), in-hospital all-cause mortality and cardiac mortality were similar: 3.3% BIF vs 2.6% MC; P = .61 and 2.6% BIF vs 2.2% MC; P = .76, respectively. Thirty-day clinical events were similar with no differences in survival free from all-cause death (95.3% BIF vs 94.9% MC; P = .84; HR, 0.93; 95% confidence interval [95%CI], 0.44-1.97), survival free from cardiac mortality (96% BIF vs 95.6% MC; P = .83; HR, 0.91; 95%CI, 0.40-2.07) or survival free from recurrent MI (98.5% BIF vs 98.9% MC; P = .71, HR, 1.33; 95%CI, 0.30-5.95). Four patients underwent coronary artery bypass graft in the BIF group compared with 2 patients in MC group, but without statistical significance (survival free from coronary artery bypass grafting 98.5% BIF vs 99.3% MC; P = .42, HR, 2.01; 95%CI, 0.37-10.99).

At long-term follow-up, there were no differences in all-cause death or the composite endpoint (Figure 2 and Figure 2 of the supplementary material; Table 5 and Table 4 of the supplementary material). The individual components of the combined event were evenly distributed, with slightly higher numbers for target vessel revascularization and coronary artery bypass grafting in the BIF group (Table 5 and Figure 3). Target lesion revascularization occurred in 17 (6%) patients in the BIF group compared with 12 (4%) in the MC group; crude HR, 1.44; 95%CI, 0.69-3.02; P = .33 and adjusted HR, 1.47; 95%CI, 0.70-3.09; P = .31. There were 3 cases of definite stent thrombosis in each group, all of them were subacute in the BIF group, whereas 2 cases of thrombosis were subacute and the other one very late (17 months) in the MC group.

DISCUSSION

We present the second largest series of BCL in STEMI, the first with a propensity score matching control group and the longest follow-up. The main finding of the present study was the similar short- and long-term prognosis in patients with and without BCL in STEMI.

Table 3
Procedural Characteristics Before and After Propensity-matched Analysis

	Before matching				After matching		
Variable	Total (n = 2746)	BIF group (n = 274)	Controls (n = 2472)	*P*	BIF group (n = 274)	MC group (n = 274)	*P*
Inclusion date (quintile)[a]				.11			.26
1	550 (20)	45 (16)	505 (20)		45 (16)	47 (17)	
2	550 (20)	51 (19)	499 (20)		51 (19)	50 (18)	
3	548 (20)	69 (25)	479 (19)		69 (25)	87 (32)	
4	549 (20)	60 (22)	489 (20)		60 (22)	42 (15)	
5	549 (20)	49 (18)	500 (20)		49 (18)	48 (18)	
Symptoms to PCI[a]*, min*	291 ± 248	281 ± 240	292 ± 249	.47	281 ± 240	298 ± 240	.44
Rescue PCI[a]	410 (15)	48 (18)	362 (15)	.21	48 (18)	44 (16)	.65
Radial access	750 (30)	86 (31)	750 (30)	.72	86 (31)	83 (30)	.78
Contrast, mL	218 ± 78	256 ± 88	213 ± 76	< .001	256 ± 88	222 ± 81	< .001
Procedural time, min	61 ± 28	70 ± 29	60 ± 27	< .001	70 ± 29	63 ± 30	.004
Fluoroscopy time, min	15 ± 10	19 ± 13	15 ± 10	< .001	19 ± 13	14 ± 7	< .001
Number of treated lesions[b]	1.20 ± 0.5	1.21 ± 0.5	1.20 ± 0.5	.87	1.21 ± 0.5	1.18 ± 0.5	.55
IIb/IIIa glycoprotein inhibitors[b,c]	1126 (41)	125 (46)	1001 (41)	.10	125 (46)	112 (41)	.26
Any aspiration thrombectomy[b]	1279 (47)	129 (47)	1150 (47)	.86	129 (47)	130 (47)	.93
Any balloon dilatation[b]	1600 (42)	194 (71)	1406 (57)	< .001	194 (71)	161 (59)	.003
Number of different balloons[b]	0.97 ± 1.1	1.64 ± 1.4	0.90 ± 1.1	< .001	1.64 ± 1.4	0.93 ± 1.1	< .001
Any stent implantation[b]	2487 (91)	253 (92)	2233 (90)	.28	253 (92)	248 (91)	.45
Number of implanted stents[b]	1.15 ± 0.6	1.23 ± 0.8	1.14 ± 0.6	.03	1.23 ± 0.8	1.15 ± 0.7	.14
Direct stenting[d]	1251 (46)	96 (35)	1155 (47)	< .001	96 (35)	133 (49)	.001
Total stented length[d]	23.8 ± 12	24.4 ± 12	23.7 ± 12	.38	24.4 ± 12	23.0 ± 12	.19
At least 1 DES implanted[d]	1353 (49)	161 (64)	1192 (53)	.002	161 (64)	135 (54)	.04

BIF, bifurcation; DES, drug-eluting stent; MC, matched control; PCI, percutaneous coronary intervention.
Data are expressed as mean ± standard deviation or No. (%).
[a] Indicates the variables included in the propensity score.
[b] Per patient.
[c] All cases were downstream abciximab.
[d] Per patient with at least 1 stent implanted.

Angiographic Findings

In our study, the culprit lesion involved a BIF in 10% of STEMI. In the literature, this frequency ranges from 15% to 20% of all PCIs,[3] and in a few specific studies of BCL in STEMI between 10% and 23%.[14–17] Although there is no single anatomical feature that defines a SB as "significant" to consider the lesion as a BIF,[3] we used the 2-mm cutoff because it is common practice and was used in previous BIF studies.[18] Frangos et al.[16] and Kanei et al.[17] also selected patients with SB $\geq$ 2 and 2.25 mm, respectively, and found BCL rates of 10% and 14%.

The main difference between STEMI patients with and without a BCL was the infarct-related artery, with a predominance (56%) of left anterior descending artery-diagonal lesions within the BIF group and a majority (43%) of right coronary artery infarctions in non-BCL patients. This pattern was also found by Dudek et al.[15] and a probable explanation is that the proximal right coronary artery lacks significant branches, as shown in Figure 1B. Except for this peculiarity, the most frequently affected segments were proximal followed by middle, as previously reported.[19]

The classification of the BIF anatomy by Medina and all other classifications are troublesome in the setting of a STEMI because the angiographic appearance of the plaque or thrombus might be similar. Moreover, 62% of the MB and 48% of the SB had TIMI flow 0 at the baseline angiogram, and therefore we decided to assess the Medina classification when at least temporary TIMI flow 2 or 3 was obtained (after wire crossing and/or aspiration thrombectomy). Although the anatomy should be interpreted with caution, most BIF had a complex anatomy (64% 1.1.1; 76% "true bifurcation"). In contrast, previous authors classified the BIF before opening the infarct-related artery in STEMI but found discordant data.[14,16] In the stable setting, data from the large COBIS Registry II (non-left main BIF data) showed aggregate rates of 34% for 1.1.1 lesions and 56% for "true bifurcations".[20] Therefore, we might conclude that BCL in STEMI are at least as anatomically complex as in the stable setting.

Primary Percutaneous Coronary Intervention and Short-term Results

The PCI procedure in the BIF group was indeed longer (in terms of time, amount of contrast and radiation) and was also technically more complex. More patients in the BIF group underwent at least 1 balloon dilatation and predilatation before stenting. Conversely, there was no increase in the rate of aspiration thrombectomy or in the number of implanted stents. Many aspiration thrombectomy devices do not cross over a regular 6-Fr catheter if more than 1 wire has been inserted, which may explain the low rate of aspiration to both MB and SB (7%). The similar number of stents per patient is probably a result of the predominant single-stent approach, encouraged by the emergent setting. Moreover, the burden of

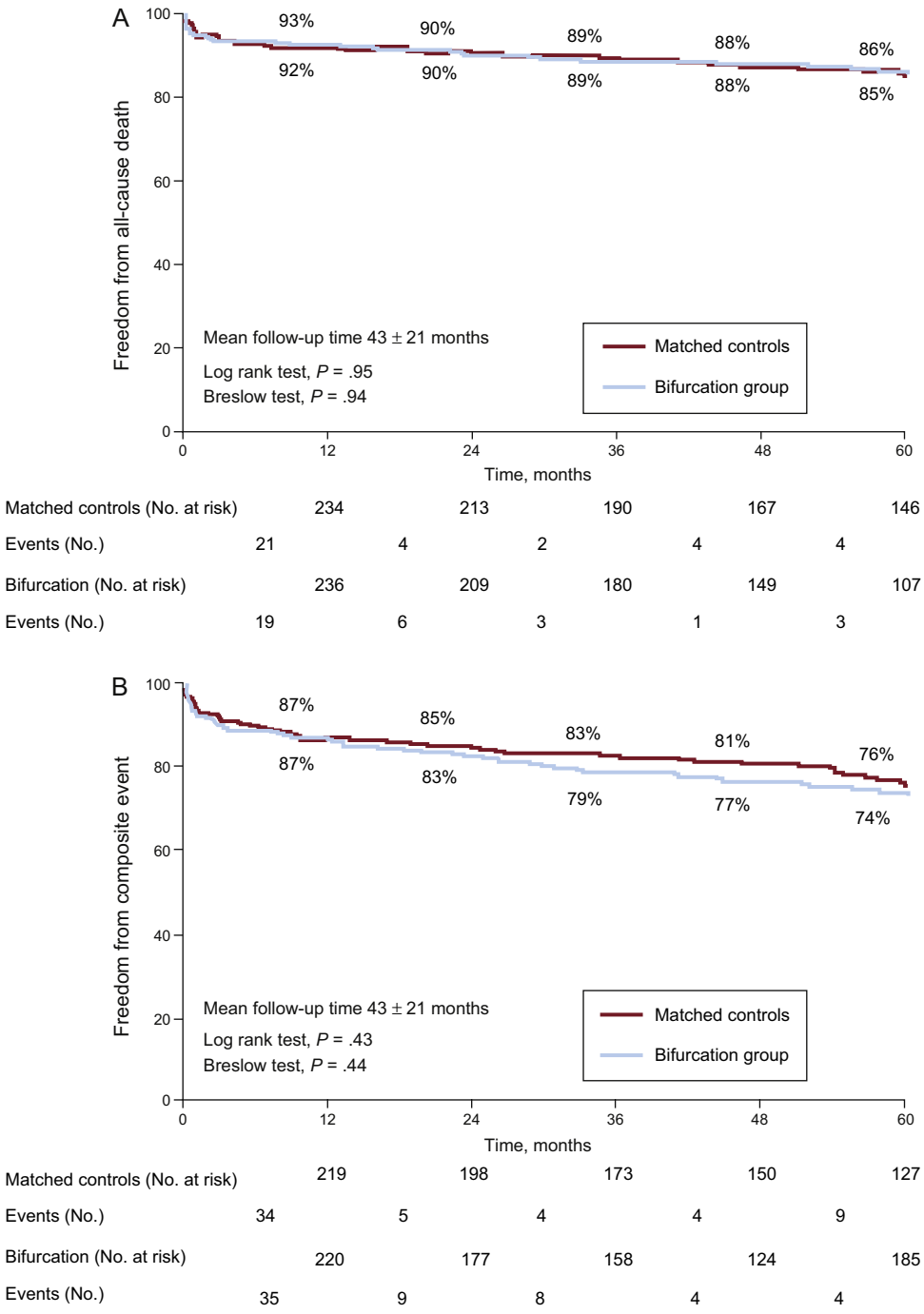

Figure 2. Kaplan-Meier curves. A: survival free from all-cause death. B: survival free from the composite event of death, recurrent myocardial infarction, coronary artery bypass graft or target vessel revascularization.

coronary disease in the patients with a BCL was also similar to that in the control group (similar number of diseased vessels, number of treated lesions, or total stented length).

The single-stent strategy chosen in 84% of the BCL patients (91% of patients who had at least 1 stent implanted) was consistent with that of many randomized studies showing similar or better outcomes with 1- vs 2-stent techniques (although most of them excluded STEMI patients).[4–6] Only the DKCRUSH II study included STEMI patients (n = 63) and found similar in-hospital or 1-year events comparing the provisional stenting and the double kissing double crush 2-stent technique.[21] On the other hand, higher rates of early and late stent thrombosis have been reported for STEMI patients,[22] and therefore provisional stenting seems reasonable in the emergent primary PCI setting.

Regarding the angiographic results, final TIMI flow was worse in the SB than in the MB, and global angiographic success was lacking in 15% of the BIF group. Nevertheless, MB angiographic success was similar in the BIF and MC groups, leading to similar clinical outcomes. These similar outcomes might be explained by the adjustment for other prognostic factors (time to reperfusion[23] or similar distribution of the infarct-related artery[24]) or the relatively low (15%) rate of "lost SBs". On the other hand, the SB occlusion

Table 4
Procedural Characteristics of Bifurcation Culprit Lesion

Variable	No. (%)
Sidebranch wiring	181 (66)
Sidebranch predilatation	86 (31)
Aspiration thrombectomy	
Any	129 (47)
Main branch	123 (45)
Side branch	24 (9)
Both branches	19 (7)
No stent implanted	20 (7)
1 stent strategy	230 (84)
Side branch jailed by main branch stent	222 (81)
2-stents strategy	24 (9)
T stenting	10 (4)
Crush	6 (2)
Other	8 (3)
Postdilatation at bifurcation	70 (25)
Sequential	40 (15)
Kissing balloon	30 (11)
Main branch final TIMI flow	
0	2 (1)
1	2 (1)
2	41 (15)
3	229 (83)
Side branch final TIMI flow	
0	16 (6)
1	13 (5)
2	36 (13)
3	209 (76)
Angiographic success	
Main branch	256 (93)
Side branch	245 (89)
Global	232 (85)

TIMI, Thrombolysis In Myocardial Infarction.

might be only temporary (spasm or thrombus that will resolve), and the subtended territory might be relatively small, making interventional efforts to preserve the patency of the SB clinically irrelevant or even deleterious (more contrast, procedure length, unnecessary manipulation of the MB stent). There is no available information on the fate of the SB in the setting of STEMI in the literature and it is unlikely that angiographic follow-up studies will be performed, and therefore this study might reassure a "keep it simple" approach focusing on provisional stenting and a good angiographic result of the MB.

Long-term Follow-up

The present study is the first that explores the clinical outcomes of a BCL in STEMI as long as 5 years after the index primary PCI, finding similar long-term prognosis in patients with and without BCL in STEMI. Two studies have compared clinical outcomes at follow-up in this setting: *a)* Abdel-Hakim et al.[14] studied an unselected population at 1-year, finding similar mortality (5% BCL vs 3% non-BCL; *P* = .15) but higher rates of a combined event (death, recurrent MI, and TLR) 23% BCL vs 20% non-BCL; *P* = .56 (at 1-year, we had 13% of the combined endpoint), and *b)* Dudek et al.,[15] in a substudy of the HORIZONS-AMI randomized trial (which excluded patients with an intended 2-stent strategy) showed lower mortality at 3 years: 6.1% BCL vs 6.7% non-BCL; *P* = .72 but similar rates of a combined event (death from any cause, stroke, recurrent MI and unplanned revascularization) at 3 years (22% BCL vs 22% non-BCL; *P* = .92); while our study found 11% mortality in both groups and composite endpoint rates of 21% BIF vs 17% MC at 3 years.

If we contrast our study to others in stable setting with 5-year follow-up, the Nordic BIF study reported 5.9% all-cause death in the single strategy against 10.4% in the double stent strategy (*P* = .16), and composite event rates (all-cause death, MI, target vessel revascularization, and definite stent thrombosis) of 12% (simple strategy) vs 28% (double stent); *P* = .03.[25] The 5-year results of the Bifurcations Bad Krozingen I study showed all-cause death of 7.9% (provisional T) vs 10% (routine T); *P* = .65; and composite event (all-cause death, MI, and TLR) rates occurring in 22.8% (provisional T) vs 22.9% (routine T); *P* = .91.[26] Although we did not compare any BIF strategies, these results compare favorably against our series of a predominant single-stent strategy. Moreover, our study did not show any relevant increase in clinically-driven TLR or target vessel revascularization, or stent thrombosis during follow-up in the BCL group. There are only a few contemporary randomized STEMI trials reporting 5-year all-cause death after primary PCI, which ranged between 9% and 16%.[27,28] Composite endpoints vary among studies, but the EXAMINATION trial reported a similar composite endpoint (all-cause death, recurrent MI or any revascularization) at 5 years (21% drug-eluting stent vs 26% bare metal stent).[27] All

Table 5
Events and Hazard Ratios at 5-year of Follow-up

	Events No. (%)		Crude HR		Adjusted HR[d]	
	BIF (n = 274)	MC (n = 274)	*P*	HR (95%CI)	*P*	HR (95%CI)
Death[a]	33 (12)	35 (13)	.95	0.98 (0.61-1.59)	.75	1.08 (0.67-1.75)
Cardiac death[a]	26 (9)	23 (8)	.59	1.17 (0.67-2.05)	.39	1.28 (0.73-2.25)
Combined event (death, CABG, AMI or TVR)[a]	61 (22)	56 (20)	.43	1.16 (0.80-1.66)	.36	1.20 (0.83-1.73)
Recurrent MI[b]	14 (5)	11 (4)	.49	1.32 (0.60-2.91)	.82	1.06 (0.66-1.69)
CABG[b,c]	8 (3)	3 (1)	.12	2.69 (0.72-10.16)	—	—
TVR[b]	23 (8)	14 (5)	.11	1.70 (0.87-3.30)	.33	1.55 (0.64-3.76)

95%CI, 95% confidence interval; AMI, acute myocardial infarction; BIF, bifurcation; CABG, coronary artery bypass graft; HR, hazard ratio; MC, matched control; MI, myocardial infarction; TVR, target vessel revascularization.
[a] Cox regression.
[b] Fine and Gray competing risk regression.
[c] No adjusted HR were obtained for CABG, as no patients with drug-eluting stent underwent CABG.
[d] Adjusted by drug-eluting (vs bare metal) stent, aspiration thrombectomy and use of IIb/IIIa inhibitors.

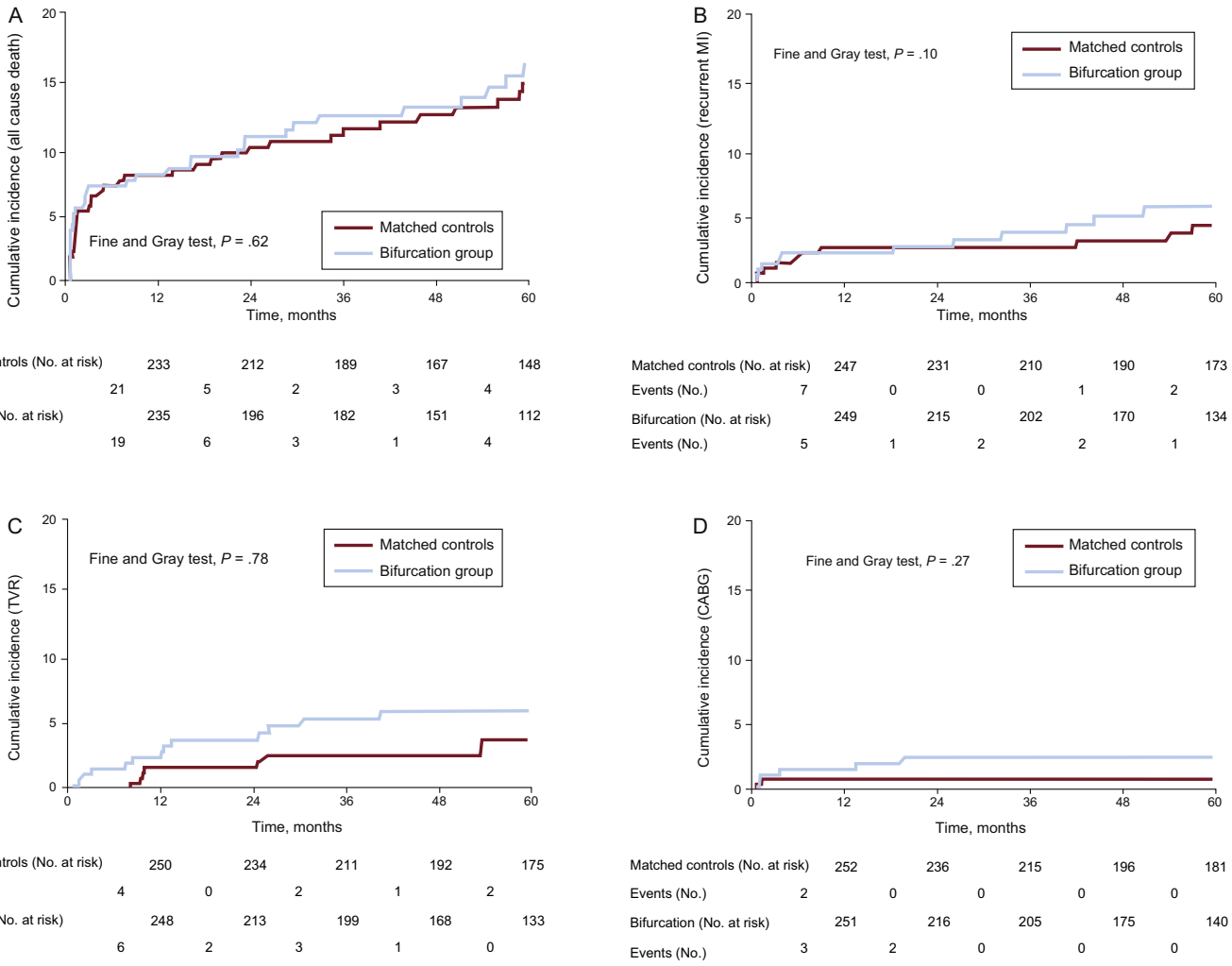

Figure 3. Cumulative incidence function plots. A: all-cause death. B: recurrent MI. C: TVR. D: CABG. CABG, coronary artery bypass graft; MI, myocardial infarction; TVR, target vessel revascularization.

these data are comparable to those in our study of an unselected population.

Limitations

This is an observational, nonrandomized study; therefore uncontrolled variables may have had an impact on the outcomes comparison between groups. However, propensity score matching was used to reduce disparities in clinical characteristics. We decided to exclude left main culprit lesions, a rare finding in primary PCI with large subtended territory at risk and different long-term prognosis. The interventional strategy for primary PCI and BIF treatment was not standardized and therefore no conclusions on specific BIF PCI techniques in the setting of a STEMI can be made. The data on Medina classification of BCL should be interpreted with caution as it was assessed when TIMI $\geq$ 2 was obtained, and therefore it could be modified by the maneuvers to restore coronary flow. We had no data on antithrombotic drug prescription after discharge, which could potentially influence outcomes such as stent thrombosis. The timeframe of the study was wide, with obvious changes in therapy throughout the years, although the study represents clinical practice and the controls were paired according to quintiles of the index procedure date.

CONCLUSIONS

A BCL can be found in 10% of primary or rescue PCI in STEMI patients, anatomically located mainly in left anterior descending artery-diagonal BIF. Primary PCI in this setting is technically more complex with increased procedural time and contrast use. However, compared with a propensity-matched cohort of non-BCL patients, a predominant single-stent strategy led to similar MB angiographic success, without differences in 30-day or 5-year clinical outcomes.

CONFLICTS OF INTEREST

None declared.

WHAT IS KNOWN ABOUT THE TOPIC?

- Bifurcated lesions represent 15% to 20% of all PCIs, with worse long-term results, especially in terms of need for new revascularization. In the setting of STEMI, there is a paucity of data regarding the incidence of BIF lesions, and only a few studies have explored BIF outcomes, with either short-term results or limitations in patient selection.

WHAT DOES THIS STUDY ADD?

- We present the second largest series of BCL in STEMI, the first with a propensity score matching control group, and the longest follow-up. A BCL was found in 10% of STEMI. The main finding of the present study was a similar short- and long-term prognosis in patients with and without BCL in STEMI.
- Bifurcation primary PCI was longer and technically more complex, with a lack of angiographic success in 15% of the BIF group. However, MB angiographic success was similar in both groups, leading to similar outcomes. This finding might reassure a "keep it simple" approach focusing on provisional stenting and a good angiographic result of the MB.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at http://dx.doi.org/10.1016/j.rec.2017.06.022.

REFERENCES

1. Lefevre T, Louvard Y, Morice MC, et al. Stenting of bifurcation lesions: classification, treatments, and results. *Catheter Cardiovasc Interv.* 2000;49:274–283.
2. Latib A, Colombo A. Bifurcation disease: what do we know, what should we do? *JACC Cardiovasc Interv.* 2008;1:218–226.
3. Lassen JF, Holm NR, Banning A, et al. Percutaneous coronary intervention for coronary bifurcation disease: 11th consensus document from the European Bifurcation Club. *EuroIntervention.* 2016;12:38–46.
4. Steigen TK, Maeng M, Wiseth R, et al. Randomized study on simple versus complex stenting of coronary artery bifurcation lesions: the Nordic bifurcation study. *Circulation.* 2006;114:1955–1961.
5. Colombo A, Bramucci E, Sacca S, et al. Randomized study of the crush technique versus provisional side-branch stenting in true coronary bifurcations: the CACTUS (Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-Eluting Stents) Study. *Circulation.* 2009;119:71–78.
6. Hildick-Smith D, De Belder AJ, Cooter N, et al. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British Bifurcation Coronary Study: old, new, and evolving strategies. *Circulation.* 2010;121:1235–1243.
7. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J.* 2012;33:2569–2619.
8. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika.* 1983;70:41–55.
9. Hotelling H. The Generalization of Student's Ratio. *Ann Math Stat.* 1931;2:360–378.
10. TIMI Study Group. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. *N Engl J Med.* 1985;312:932–936.
11. Medina A, Suárez de Lezo J, Pan M. A new classification of coronary bifurcation lesions. *Rev Esp Cardiol.* 2006;59:183.
12. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Eur Heart J.* 2012;33:2551–2567.
13. Pintilie M. An introduction to competing risks analysis. *Rev Esp Cardiol.* 2011;64:599–605.
14. Abdel-Hakim DE, Garot P, Champagne S, et al. Impact of bifurcation lesions on clinical outcome and prognosis of primary angioplasty in acute myocardial infarction. *EuroIntervention.* 2008;4:93–98.
15. Dudek D, Mehran R, Dziewierz A, et al. Impact of bifurcation target lesion on angiographic, electrocardiographic, and clinical outcomes of patients undergoing primary percutaneous coronary intervention (from the HORIZONS-AMI trial). *EuroIntervention.* 2013;9:817–823.
16. Frangos C, Noble S, Piazza N, et al. Impact of bifurcation lesions on angiographic characteristics and procedural success in primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. *Arch Cardiovasc Dis.* 2011;104:234–241.
17. Kanei Y, Nakra NC, Liou M, Singh J, Fox JT, Kwan TW. The importance of bifurcation lesions in patients undergoing percutaneous coronary interventions in ST-segment elevation myocardial infarction. *Cardiovasc Revasc Med.* 2013;14:81–83.
18. Pan M, Suarez de Lezo J, Medina A, et al. Simple and complex stent strategies for bifurcated coronary arterial stenosis involving the side branch origin. *Am J Cardiol.* 1999;83:1320–1325.
19. Wang JC, Normand SL, Mauri L, Kuntz RE. Coronary artery spatial distribution of acute myocardial infarction occlusions. *Circulation.* 2004;110:278–284.
20. Song YB, Hahn JY, Yang JH, et al. Differential prognostic impact of treatment strategy among patients with left main versus non-left main bifurcation lesions undergoing percutaneous coronary intervention: results from the Coronary Bifurcation Stenting Registry II. *JACC Cardiovasc Interv.* 2014;7:255–263.
21. Kwan TW, Gujja K, Liou MC, et al. Bifurcation stenting in patients with ST-segment elevation myocardial infarction: an analysis from DKCRUSH II randomized study. *Catheter Cardiovasc Interv.* 2013;82:E133–E137.
22. Kukreja N, Onuma Y, Garcia-Garcia HM, et al. The risk of stent thrombosis in patients with acute coronary syndromes treated with bare-metal and drug-eluting stents. *JACC Cardiovasc Interv.* 2009;2:534–541.
23. Guerchicoff A, Brener SJ, Maehara A, et al. Impact of delay to reperfusion on reperfusion success, infarct size, and clinical outcomes in patients with ST-segment elevation myocardial infarction: the INFUSE-AMI Trial. *JACC Cardiovasc Interv.* 2014;7:733–740.
24. Elsman P, Van't Hof AW, Hoorntje JC, et al. Effect of coronary occlusion site on angiographic and clinical outcome in acute myocardial infarction patients treated with early coronary intervention. *Am J Cardiol.* 2006;97:1137–1141.
25. Maeng M, Holm NR, Erglis A, et al. Long-term results after simple versus complex stenting of coronary artery bifurcation lesions: Nordic Bifurcation Study 5-year follow-up results. *J Am Coll Cardiol.* 2013;62:30–34.
26. Ferenc M, Ayoub M, Buttner HJ, et al. Long-term outcomes of routine versus provisional T-stenting for de novo coronary bifurcation lesions: five-year results of the Bifurcations Bad Krozingen I study. *EuroIntervention.* 2015;11:856–859.
27. Sabate M, Brugaletta S, Cequier A, et al. Clinical outcomes in patients with ST-segment elevation myocardial infarction treated with everolimus-eluting stents versus bare-metal stents: 5-year results of a randomised trial. *Lancet.* 2016;387:357–366.
28. Holmvang L, Kelbaek H, Kaltoft A, et al. Long-term outcome after drug-eluting versus bare-metal stent implantation in patients with ST-segment elevation myocardial infarction: 5 years follow-up from the randomized DEDICATION trial. *JACC Cardiovasc Interv.* 2013;6:548–553.