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RESEARCH ARTICLE

Intracoronary Electrocardiography-guided Strategy for the Treatment of Coronary Bifurcation Lesions

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Abstract

Introduction: Revascularization of bifurcation lesions remains an interventional challenge. Intracoronary electrocardiograms can predict the functional significance of side branch stenosis after bifurcation stenting.
Aim: This study was aimed at evaluating the effects of an intracoronary ECG electrocardiography (icECG)-guided revascularization strategy, compared with the currently accepted standard of care, on the clinical outcomes of patients after coronary bifurcation stenting.
Methods: Patients with coronary bifurcation lesions who underwent percutaneous revascularization were enrolled in a prospective all-comers' registry. Clinical outcomes were compared between patients who underwent icECG-guided revascularization versus the current standard of care (SOC), provisional stenting.
Results: A total of 768 patients were included in the analysis: 349 were treated with an icECG-guided strategy, and 419 received SOC. The overall all-cause death rate was 23.2%, and the cardiovascular death rate was 15.9%. Patients with icECG guidance had significantly lower all-cause mortality (20.3% vs. 25.5% for icECG vs. SOC, log-rank P=0.006) and cardiovascular mortality (12.6% vs. 18.6% for icECG vs. SOC, log-rank P=0.004). The decrease in mortality was most pronounced in patients with no increase or a moderate increase in troponin post-PCI, or with higher-than-normal baseline troponin concentrations.
Conclusion: An icECG-guided strategy for coronary bifurcation PCI led to lower patient mortality than the provisional stenting strategy.

Keywords: Coronary bifurcation; percutaneous coronary intervention; clinical outcomes

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Abbreviations: KBI, Kissing balloon inflation; POT, Proximal optimization technique; DES, Drug-eluting stents; MI, Myocardial infarction; icECG, Intracoronary electrocardiography; QCA, Quantitative coronary angiography.

Introduction

Revascularization of bifurcation lesions remains challenging in terms of both procedural success and long-term cardiovascular outcomes [1]. In recent years, substantial improvements have been made in the percutaneous treatment of coronary bifurcation stenoses. The introduction of kissing balloon inflation (KBI) and proximal optimization technique (POT) have significantly improved patient clinical outcomes [2].

Furthermore, the development of newer-generation drug-eluting stents (DES) has significantly decreased the rates of restenosis at the bifurcation region and, to a lesser degree, the rates of "hard" endpoints, such as all-cause death, cardiovascular death and spontaneous non-fatal myocardial infarction (MI). Compared with bare metal stents and first-generation DES, second-generation DES have been associated with lower risks of in-stent restenosis, stent thrombosis and MI [3, 4]. The most recent data have indicated relatively low rates of stent thrombosis (1.0%), target lesion failure (5.1%), cardiac death (1.8%) and all-cause death (1.8%) 1 year after bifurcation percutaneous coronary intervention (PCI) [5]. Previously, we hypothesized that these improved PCI results are partially associated with improvements in stent technology (platforms, drugs and drug carriers) [6]. With technological advances, interventional technical performance has improved, as clearly indicated by changes in the recommendations of the European Bifurcation Club over time [7, 8].

In addition, using intracoronary electrocardiography (icECG) guidance may be useful in predicting the functional significance of side branch (SB) stenosis after bifurcation stenting [9]. We have demonstrated that icECG can predict post-procedural increases in troponins after coronary bifurcation lesion stenting [10]. Moreover, icECG has a unique ability to locate possible sources of post-PCI rise in troponin, by detecting zones with ST-segment elevation on icECG at the end of the procedure. However, to our knowledge, the influence of icECG-guidance for bifurcation PCI on all-cause and cardiovascular mortality had not previously been analyzed.

The aim of the current analysis was to evaluate the influence of an icECG-guided revascularization strategy on the clinical outcomes of patients after coronary bifurcation stenting.

Methods

Patient selection

From July 2017 to December 2020, patients with coronary bifurcation stenoses referred for percutaneous revascularization were included in a prospective registry. In the current analysis, patients with acute coronary syndrome, left bundle branch block, left main stenosis, ST-elevation MI, hemodynamic instability and life expectancy <12 months were excluded. In addition, patients with in-hospital events were excluded. No other restrictions for patient inclusion were used.

Procedure

Patients were randomly assigned to receive one of two procedure types:

1) icECG-guided revascularization

The icECG-guided revascularization strategy was previously demonstrated in the FIESTA study [11]. After obtaining optimal projection, two standard workhorse PCI wires (Runthrough, Terumo, Japan; Sion Blue, Asahi, Japan; or BMW Universal II, Abbot Vascular, USA) were introduced into the main branch and SBs. The tips of the wires were ascertained to be freely moving, without any wedging into the myocardium. The outer ends of the wires were connected to unipolar ECG leads with alligator clips (Supplementary Video 1). The baseline recordings were made before the insertion of any other devices into the target artery. In some cases of interaction signals due to contacts between the wires, a pre-dilatation balloon was inserted to the position of the tip of the guiding catheter. In rare cases, the balloon was inserted into the tip of the bifurcation carina to divide crisscrossing wires. After the baseline signals were obtained, predilatation to the main branch, SB or both, was performed at the operator's discretion. After stent implantation, a second recording was made from both wires. Proximal optimization technique was recommended, but the decision was left to the surgeon. In cases of ST-segment elevation on icECG from an SB

wire, balloon dilatation of the SB ostium (KBI was highly recommended) was performed. Finally, after intracoronary nitroglycerine administration (100–200 mcg), another recording of icECG was made. If the ST-segment elevation persisted, the wire from the SB was slowly pulled back to the ostium of the side vessel, and the ECG was recorded through the whole vessel length. If ST-segment elevation was present only in the distal half of the vessel length, it was considered a result of distal embolization. If ST-segment elevation was also present in the proximal half of the vessel, it was considered a result of diffuse microcirculatory spasm in addition to microembolization. In both cases, patients received heparin and nitroglycerin intravenous infusions for the next 18–24 h. If there was any sign of vessel dissection, more than type B and icECG changes, a stent was implanted into the SB. After POT, if no icECG changes were observed, SBs were balloon dilated only in cases of ≥90% SB ostial diameter stenosis or TIMI flow <2. A case example is illustrated in Figure 1. A detailed description of the icECG analysis is included in the Supplementary Material.

2) Provisional T-stenting strategy

The provisional T-stenting strategy, also referred to as standard of care (SOC), followed the most recent European Bifurcation Club recommendations [8]. A detailed description of the provisional T-stenting technique is included in the Supplementary Material.

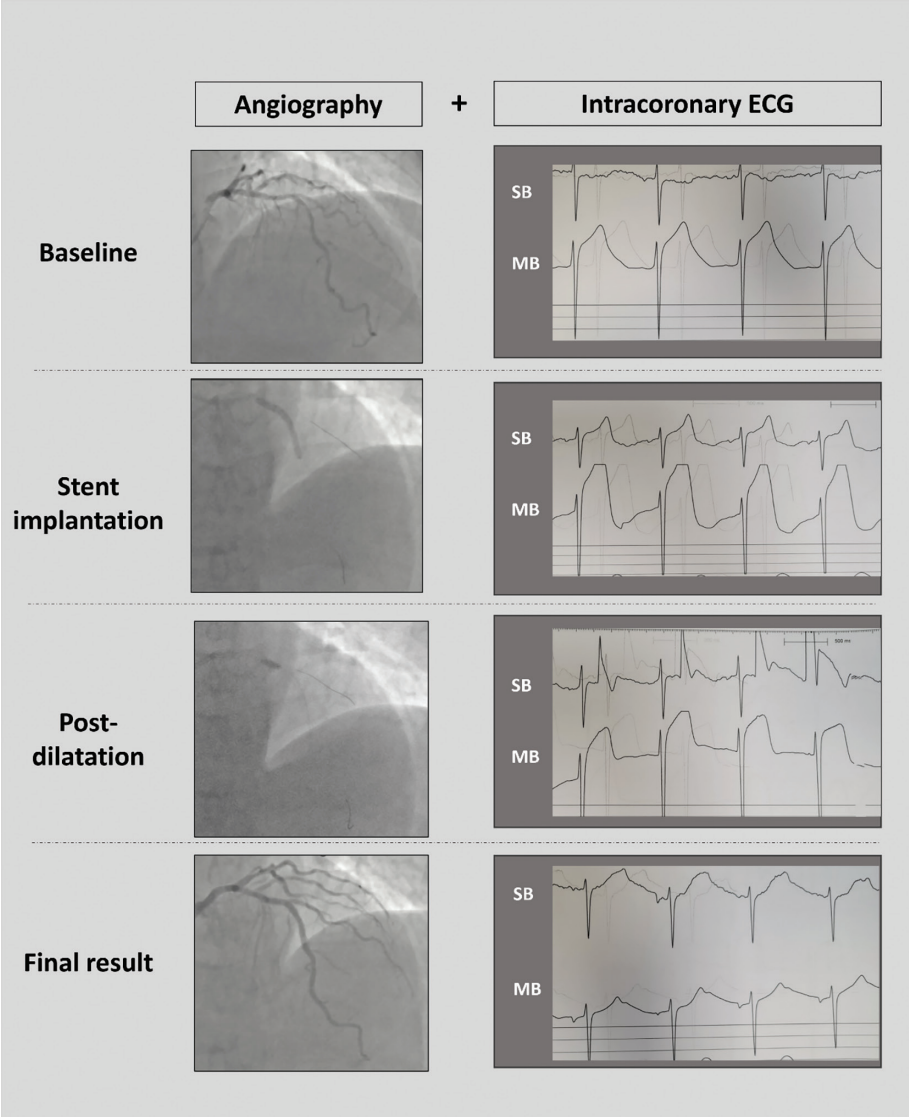

Figure 1 Case Example of a Patient Treated with an Intracoronary ECG Guided Strategy.

Angiographic analysis

Dedicated bifurcation quantitative coronary angiography (QCA) analysis was performed according to the recommendations of the consensus on QCA methods for bifurcation lesions using General Electric QCA software and MicroDicom QCA software [12]. Bifurcation lesions were classified according to the Medina classification [13]. True bifurcation lesions were defined by a visual percentage diameter stenosis (%DS) >50% at the SB with lesions at the proximal or distal main branch. The minimal luminal diameter, reference vessel diameter and %DS were measured for every segment of the bifurcation (i.e., proximal and distal MV and SB) pre- and post-intervention. Lesion length was measured from the proximal main vessel to the distal main branch (i.e., the beginning and end points where the stent would potentially be implanted). SB lesion length was measured from the ostium to the first normal-appearing part of the vessel. All analyses were performed by two investigators (N.M. and P.P.). In cases of disagreement, a consensus was reached according to additional analysis by the first author (D.V.).

Definition of endpoints

All patients were followed up by telephone contact and/or clinical visit at 30 days, and vital status was subsequently monitored monthly through the National Insurance Institute. Clinical outcomes were defined according to the current recommendations [12]. Cardiovascular death was defined as death due to a clearly determined cardiac origin or an unknown reason. MI after hospitalization was diagnosed according to the fourth definition of MI [14]. Major adverse cardiac events were a combination of cardiovascular death and MIs. Patient oriented cardiac events were a summary of major adverse cardiac events and target vessel failure rates. Target vessel failure was defined as any intervention in the target vessel.

Statistical analysis

All data are presented as means±standard deviation. Differences between groups were examined with paired or unpaired t-tests as appropriate, for data with a normal distribution. If the data distribution was not normal, Mann-Whitney U-tests were performed. Analysis of variance was used for multiple comparisons of data when parameters were distributed normally. Otherwise, Kruskal-Wallis test was performed. Cox–multiple regression analysis with a backward elimination process was used to identify predictors of death and cardiovascular death. All univariate predictors with $P<0.1$ were included in a multivariate model. Chi-square tests were applied for qualitative data. A P-value <0.05, with 85% power, was accepted as significant. All statistical calculations were performed in the SPSS package, version 25, USA. The study was approved by the local ethics committee.

RESULTS

Demographic and procedural characteristics

Among 1042 patients who underwent coronary bifurcation stenting, 768 were included in the current analysis. A total of 349 patients underwent an icECG-guided strategy, and 419 underwent SOC (Figure 2). The two groups had similar risk profiles (Table 1). The icECG-guided group, compared with the SOC group, had significantly more smokers (54% vs. 34%, P 0.001) and more patients with previous MIs, but a lower rate of chronic kidney disease (GFR 78±26 mL/kg/min vs. 71±23 mL/kg/min, respectively, $P<0.001$). Furthermore, the rate of atrial fibrillation was slightly lower in the icECG-guided group than the SOC group (18% vs. 24%, respectively, $P=0.024$). Interestingly, the patients with icECG guidance received statins less frequently (93% vs. 98%, $P=0.001$), and clopidogrel more frequently (88% vs. 82%, $P=0.019$), than those in the SOC group.

We specifically evaluated the differences in patient symptoms, left ventricular function and mitral regurgitation between groups. No difference was observed regarding angina (median CCS class 3, IQR, 2–4), but more patients had dyspnea in the SOC group (NYHA class II–III: 13% vs. 22%, icECG vs. SOC, $P=0.001$). Patients with icECG guidance had a higher left ventricular ejection fraction (57±8% vs. 55±10%, $P=0.009$) and lower rates of significant mitral regurgitation (14% vs. 23%, $P=0.001$).

The procedural and angiographic data are presented in Tables 2 and 3. The icECG-guided group

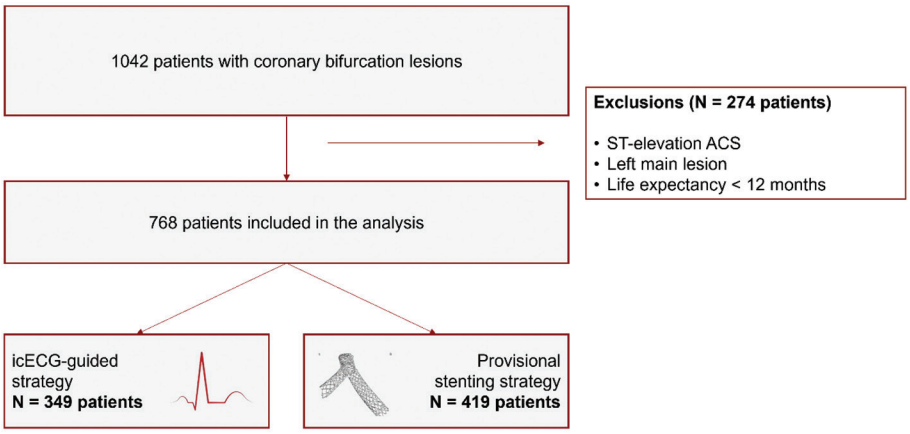

Figure 2 Flow Chart of Patient Selection and Enrollment.

Table 1 Demographic Characteristics.

Patient characteristics	icECG group	SOC group	P-value
Age (years)	66±10	68±10	0.001
Male sex, % (n)	31% (108)	31% (130)	0.998
Hypertension, % (n)	98% (342)	99% (414)	1.0
Hyperlipidemia, % (n)	93% (324)	94% (393)	0.932
Smoking, % (n)	54% (188)	34% (142)	0.001
Diabetes, % (n)	37% (129)	42% (175)	0.231
Renal failure, % (n)	25% (87)	37% (142)	0.001
Previous myocardial infarction, %(n)	29% (101)	23% (96)	0.039
Previous PCI, % (n)	48% (167)	49% (205)	0.978
Atrial fibrillation, % (n)	18% (62)	24% (100)	0.024
Peripheral artery disease, % (n)	9% (31)	11% (46)	0.763
Previous stroke or TIA, % (n)	14% (49)	18% (75)	0.121
Carotid artery disease, % (n)	5% (17)	8% (33)	0.781
COPD, % (n)	12% (42)	14% (58)	0.675
Cancer, % (n)	7% (24)	6% (25)	0.854
Aspirin treatment, % (n)	91% (318)	90.5 (381)	0.882
Clopidogrel treatment, % (n)	80.2% (280)	80% (336)	0.941
Prasugrel treatment, % (n)	12.8% (44.7)	12 (50)	0.792
Ticagrelor treatment, % (n)	7% (24)	8% (33.5)	0.602

Renal failure is defined as a glomerular filtration rate, calculated according to the Cockcroft–Gault formula, <60 mL/min.
Abbreviations: TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease.

included significantly fewer true bifurcation lesions (50% vs. 63%, P=0.001), thus probably explaining the higher prevalence of predilatation in the SOC group than the icECG group (83% vs. 76%, respectively, P=0.034). Although icECG-guidance resulted in a slightly longer procedural time, the X-ray time and the amount of contrast used did not exceed those in the SOC group. The icECG guidance strategy, compared with the PTS strategy, resulted in almost 50% less SB stenting and significantly fewer stents used per procedure overall (1.63±0.81 vs. 1.86±1.00, P=0.001). Consequently, the total stent length was significantly shorter in the icECG-guided group, regardless of the similar lesion length in the two groups. Importantly, the icECG guidance strategy resulted in higher final SB ostial stenosis (Table 3). The frequency of final SB ostial stenosis >50% was 68% in the icECG group and 38% in the

Table 2 Procedural Characteristics.

Procedure details	icECG group	SOC group	P-value
LAD/diagonal, %	75%	66%	0.001
LCX/marginal, %	20%	18%	
RCA PD/PL, %	6%	16%	
Multivessel disease, %	61%	69%	0.021
SYNTAX score (mean±SD)	11±5	12±6	0.065
Stent diameter, mm (mean±ds)	3.01±0.35	3.16±0.36	0.001
Stent length, mm (mean±SD)	38±22	49±27	0.001
Kissing balloon inflation,%	32%	30%	0.638
Main vessel POT, %	67%	63%	0.249
Second stent, %	12%	21%	0.001
Guidewires used, %	71%	72%	0.509
Microcatheters used, %	15%	17%	0.311
Procedural time, min (mean±SD)	90±34	82±38	0.003
Scopic time, min (mean±SD)	22.5±10.8	21.0±8.8	0.177
Contrast, mL (mean±SD)	194±105	204±120	0.265

Abbreviations: LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; PD, posterior descending artery; PL, postero-lateral branch artery.

Table 3 Angiographic Results.

	icECG	SOC	P-value
MV RVD, mm	3.38±0.39	3.30±0.44	0.014
MV %DS, %	55±30	56±30	0.670
MV %DS final, %	2±8	1±4	0.001
MB RVD, mm	3.09±1.82	3.13±1.49	0.897
MB %DS, %	69±23	65±24	0.009
MB %DS final, %	2±4	2±4	0.423
SB RVD, mm	2.33±0.36	2.39±0.98	0.332
SB %DS, %	47±30	50±31	0.164
SB %DS, post stenting, %	61±30	37±32	0.001
SB %DS, final, %	43±31	20±26	0.001
Total lesion length, mm	35±19	36±19	0.832

Abbreviations: icECG, intracoronary electrocardiography; SOC, standard of care; MV, main vessel before side branch, MB, main branch, after side branch, SB, side branch, %DS, percentage diameter stenosis, RVD, reference vessel diameter.

PTS group (P=0.001). Interestingly, this frequency was not associated with less KBI (Table 2) or any SB post dilatation with a balloon (icECG 53% vs. 50% PTS, P=0.638).

Periprocedural troponin dynamics

We specifically explored the periprocedural troponin dynamics. Twenty-eight percent of the patients in the icECG-guided group had a post-PCI troponin increase ≥5× the UNL, as compared with 37.5% of the patients in the SOC group (P=0.009). In addition, the troponin increase post-PCI was significantly lower (77%) in the icECG group than the SOC group (82%, P=0.046). No difference was observed in the frequency of periprocedural MIs between groups (P=0.582; Supplementary Table 1).

Clinical outcomes

The median follow-up time was 56 months [IQR 38–60 months]. The rate of all-cause mortality was

23.2% (178/768), and that of cardiovascular mortality was 15.9% (122/768). The type of interventional strategy significantly affected survival: patients with icECG guidance had significantly lower all-cause mortality (20.3% vs. 25.5%, log-rank P=0.006) and cardiovascular mortality (12.6% vs. 18.6% log-rank P=0.004, for icECG vs. SOC, respectively; Figure 3).

Because of the strong association observed between icECG guidance and troponin dynamics, we analyzed the effect of this strategy in three troponin strata: 1) normal vs. elevated at baseline; 2) more or less than 5× UNL post PCI; and 3) presence of absence of an increase post PCI. Kaplan-Meier curves (Figures 4 and 5, and Table 4) indicated that icECG guidance had a significant effect on patient survival, particularly in patients with elevated baseline troponin, those with myocardial injury (with troponin increases post-PCI not reaching the cut-off value for periprocedural infarction) and those without changes in baseline troponin. However, even in the remaining groups, the icECG-guided group had numerically better survival.

Multivariate Cox-regression analysis was performed to evaluate independent predictors of mortality (Table 5). In all models, the type of treatment retained in the model independently of the whole model result. A strong trend toward statistical significance was observed between icECG guidance of bifurcation stenting and lower cardiovascular death. Moreover, troponin dynamics strongly influenced survival, such that patients with high postprocedural troponin levels had better survival. In fact, the link between troponin dynamics and survival was observed only when icECG guidance was included in the multivariate model.

Discussion

Our analysis revealed several new findings (Figure 6), as follows: i) The icECG-guided strategy for coronary bifurcation revascularization was associated with lower mortality than SOC. ii) This lower mortality was probably associated with the baseline level of troponin and its dynamics during the intervention. The effect of decreased mortality was most pronounced in patients with no increase or a moderate increase in troponin post-PCI, as well as those with higher-than-normal concentrations. iii) icECG guidance was associated with the use of significantly fewer SB stents, thus leading to fewer total implanted stents and a shorter total stent length for lesions of similar length.

No difference was observed in the baseline risk profiles between patients receiving icECG guidance vs. SOC. A significant difference in patient age was observed between groups, and was higher in the SOC group, thus potentially explaining the different rates of CKD and atrial fibrillation.

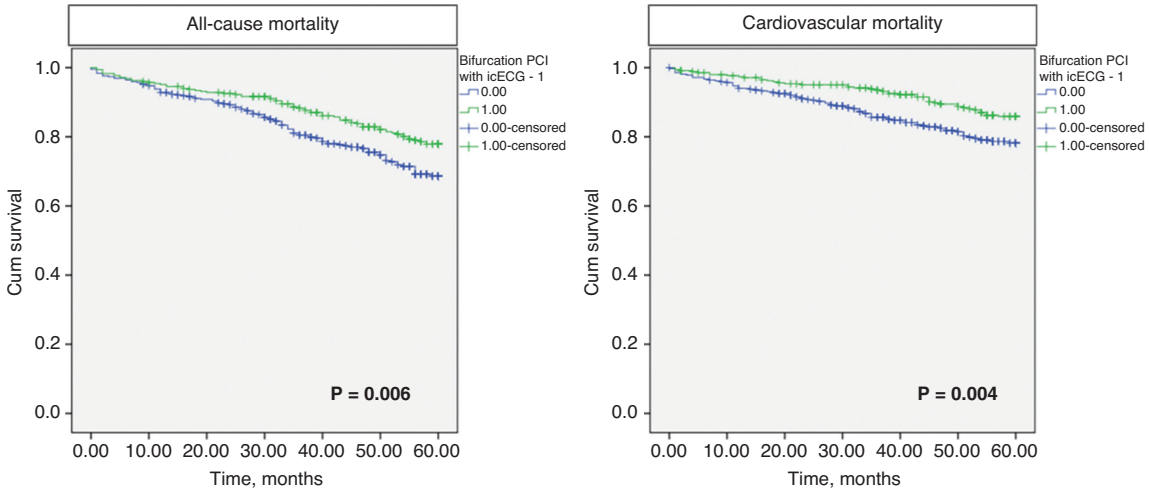

Figure 3 Kaplan-Meier Survival Curves For Events.
Green lines indicate the icECG guided group; blue lines indicate the standard of care (provisional stenting) group.

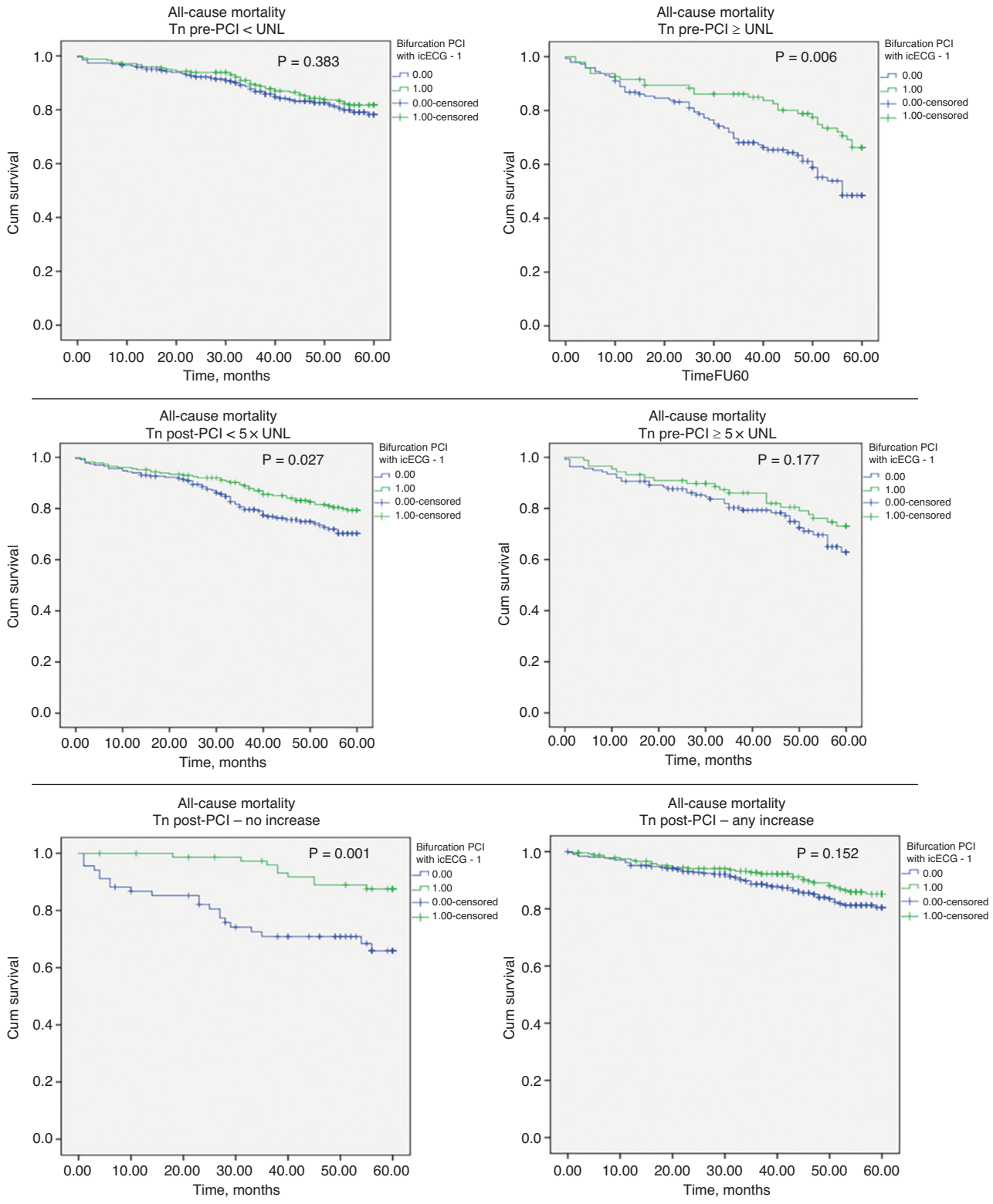

Figure 4 Kaplan-Meier Survival Curves Showing the Effects of an icECG Guided Strategy of Bifurcation Stenting vs. SOC in Different Strata of Troponin Dynamics on All-Cause Death.
Green lines indicate the icECG guided group; blue lines indicate the standard of care (provisional stenting) group.

However, to some extent, this difference was balanced by a higher smoking rate and higher rate of previous MI in the icECG guidance group.

One notable finding of our study was that patients with icECG guidance during bifurcation stenting had higher rates of angiographically

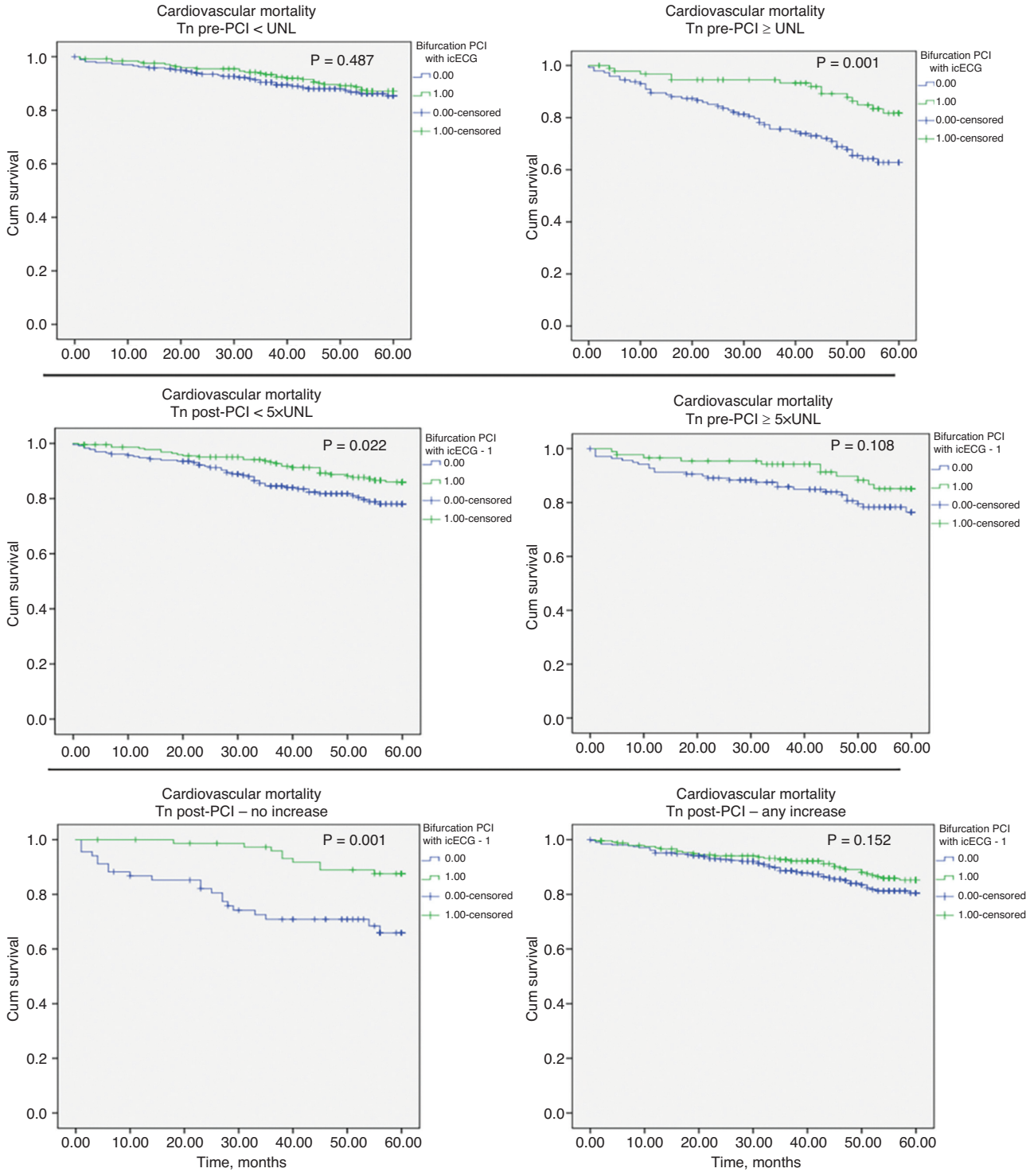

Figure 5 Kaplan-Meier Survival Curves Showing the Effects of an icECG Guided Strategy of Bifurcation Stenting vs. SOC in Different Strata of Troponin Dynamics on Cardiovascular Death.

significant stenoses in SBs after stenting and at the end of PCI, without an increase in mortality at 5 years. One stent strategy is well known to perform better for coronary bifurcations [8, 14, 15]. Notably, actual ischemia detected with icECG in the SB region is a different entity from a significant fractional flow reserve (FFR) value observed in the same region [11]. As we have demonstrated in the FIESTA study, an FFR ≤0.80 after bifurcation stenting is almost always associated with an

Table 4 Mortality Rates among Different Troponin Strata.

All-cause death			
	Bifurcation PCI strategy	**% (n)**	**P-value**
Baseline troponin			
≤UNL	SOC	17.4% (46/264)	0.383
	icECG	17.1% (42/246)	
>UNL	SOC	42.4% (61/144)	0.006
	icECG	29.5% (28/95)	
Troponin post-PCI			
≤5× UNL	SOC	25% (58/232)	0.022
	icECG	19.3% (44/228)	
>5× UNL	SOC	28.1% (39/139)	0.177
	icECG	23.6% (21/89)	
Any troponin increase post-PCI			
No	SOC	30.9% (21/68)	0.001
	icECG	11.7% (9/77)	
Cardiovascular death			
	Bifurcation PCI strategy	**% (n)**	**P-value**
Baseline troponin			
≤UNL	SOC	12.5% (33/264)	0.487
	icECG	11.8% (29/246)	
>UNL	SOC	31.2% (45/144)	0.001
	icECG	14.7% (14/95)	
Troponin post-PCI			
≤5× UNL	SOC	19% (44/232)	0.022
	icECG	12.7% (29/228)	
>5× UNL	SOC	19.4% (27/139)	0.108
	icECG	12.4% (11/89)	
Any troponin increase post-PCI			
No	SOC	30.9% (21/68)	0.001
	icECG	11.7% (9/77)	
Yes	SOC	15.9% (49/309)	0.152
	icECG	12.8% (31/242)	

Abbreviations: UNL, upper normal limit; PCI, percutaneous coronary intervention; SOC, standard of care; icECG, intracoronary electrocardiography.

Table 5 Predictors of Mortality in Cox Multivariate Analysis.

Factor	All-cause death		Cardiovascular death	
	HR (95% CI)	**P**	**HR (95% CI)**	**P-value**
icECG guidance	0.844 (0.612–1.163)	0.300	0.673 (0.466–1.041)	0.074
Age	1.036 (1.019–1.053)	0.001	1.036 (1.015–1.057)	0.001
Diabetes	1.435 (1.056–1.952)	0.021	1.724 (1.175–2.531)	0.005
Dyslipidemia	0.576 (0.348–0.953)	0.032	0.410 (0.228–0.737)	0.003
COPD	2.025 (1.400–2.929)	0.001	2.368 (1.515–3.700)	0.001
Serum creatinine, per mmol/l	1.004 (1.001–1.007)	0.022	1.002 (0.997–1.007)	0.404
Mitral regurgitation >1st degree	1.691 (1.191–2.402)	0.003	1.664 (1.060–2.613)	0.027
Dyspnea (NYHA ≥2 class)	1.395 (0.968–2.008)	0.074	1.335 (0.845–2.110)	0.215
Baseline troponin ≥UNL	1.552 (1.111–2.168)	0.010	1.543 (1.008–2.363)	0.046
Post PCI increase in troponin	1.411 (0.965–2.064)	0.076	0.640 (0.411–0.997)	0.048

Abbreviations: HR, hazard ratio; CI, confidence interval; icECG, intracoronary electrocardiography; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

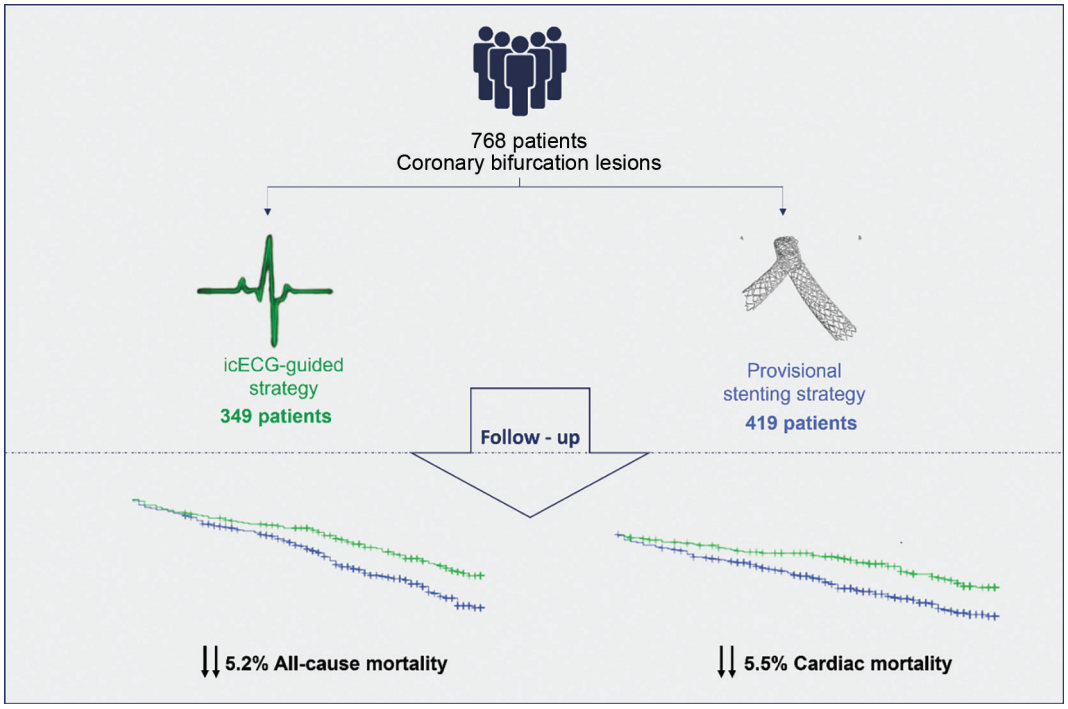

Figure 6 Summary of the Main Findings of the Study, Focusing on the Lower All-Cause and Cardiovascular Mortality in Patients with Intracoronary ECG-Guided Revascularization.
Abbreviation: icECG, intracoronary electrocardiography.

icECG ST-segment elevation but can also be associated with no icECG changes [16]. The lack of ECG changes may be associated with normal flow in the region. Furthermore, icECG demonstrated ST-segment elevation in cases without a significant decrease in FFR. The most probable explanation is that distal embolization led to active ischemia and increased peripheral resistance, thus "normalizing" the FFR values. This difference was detectable only with icECG. In addition, in main branches over the length of the vessel, use of a pull-back maneuver was able to detect or exclude active ischemia, thus avoiding unnecessary stenting, in an additional advantage of our method.

We specifically explored periprocedural troponin dynamics and found a relatively smaller increase in troponin post-PCI. These results are in accordance with our previously published findings indicating that icECG guidance decreases periprocedural myonecrosis in bifurcation PCI [10].

We hypothesize that a conservative approach regarding SB ostial stenoses not generating ischemia, and the opposite invasive strategy in stenosis causing ischemia on icECG, resulted in better patient outcomes. The standard approach at the end of a coronary intervention involves observation of patients for chest pain or ST-segment changes on surface ECG. However, surface ECG has been demonstrated to be less sensitive than intracoronary recordings [17]. icECG ischemic changes at the end of a PCI can alert physicians to potential complications that may require additional treatment. The latter could be a probable explanation for the observed effect of icECG guidance on survival.

Whereas functional assessment with FFR and non-hyperemic indexes has questionable value in assessing the ischemic potential of a lesion before PCI, icECG may have a substantial benefit in intraprocedural and post-PCI lesion assessment. This method does not increase the fluoroscopic time or the contrast volume; therefore, it can be used as a complement to FFR to avoid unnecessary interventions and benefit patients' clinical outcomes.

Limitations

The main limitation of our study is its observational design. In addition, this was a single-center study with no independent adjudication and some restrictions due

to cost limitations. However, we carefully selected patients, and, to our knowledge, this is the first study to assess the effects of icECG guidance on clinical outcomes in patients with bifurcation PCI.

Conclusion

An icECG-guided strategy for coronary bifurcation PCI led to lower patient mortality than the SOC. This effect was most pronounced in patients with no increase or a moderate increase in troponin post-PCI as well as in patients with baseline troponin concentrations higher than normal.

Data Availability Statement

The data that support the findings of this study are available upon request from the corresponding author.

Ethics Statement

All participants gave their informed consent for inclusion before participating in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee.

Author Contributions

DV made a substantial contribution to the concept and design of the study, and reviewed the manuscript and figures. NM made a substantial contribution to data collection and analysis, drafted the manuscript and prepared the figures. PP, KK, KY and NP contributed to data collection. CC, GR, RG and TN critically revised the design of the study and the manuscript, and contributed substantial intellectual input.

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Conflict of Interest

NM reports receiving speaker fees from Abbott Vascular. CC reports receiving research grants from Biosensor, Coroventis Research, Medis Medical Imaging, Pie Medical Imaging, Cathworks, Boston Scientific, Siemens, HeartFlow, Inc. and Abbott Vascular; and consultancy fees from Heart Flow Inc, Opsens, Abbott Vascular and Philips Volcano. The other authors have nothing to disclose.

Supplementary Material

Supplementary material for this paper is available from the following link: https://cvia-journal.org/wp-content/uploads/2023/08/CVIA_346-SUPPLEMENTAL_MATERIAL.pdf.

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