Indian Heart Journal xxx (xxxx) xxx

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Editorial

Long-term clinical outcomes after kissing balloon inflation in patients with coronary bifurcation lesions treated with provisional stenting technique. Results from the real-world multicenter registry

Keywords:
Coronary bifurcation
Kissing-dilatation
Provisional stenting
Percutaneous coronary interventions
Left main

A B S T R A C T

Objective: There is a lack of data regarding the long-term clinical efficacy of the kissing balloon inflation (KBI) after provisional stenting of coronary bifurcation lesions. The aim of this study was to analyze the impact of KBI on long-term clinical outcomes in patients undergoing provisional stenting for the coronary bifurcation lesions in a large real-world population.

Methods: A total of 873 patients who underwent percutaneous coronary interventions (PCI) with provisional stenting and had clinical follow up were analyzed. Patients treated with 2-stent strategy were excluded. To reduce the effect of potential confounding factors in this observational study, propensity score matching was conducted.

Results: KBI was performed in 325 patients (37.2%). The median follow-up duration was 37.3 months. Patients treated with KBI more often had a previous PCI (48.6% vs. 42.5% SMD = 0.123). Patients in non-kissing group had more complex coronary disease with higher prevalence of calcification (14.8% vs. 21.4% SMD = 0.172), thrombosis (2.8% vs. 5.8% SMD = 0.152) and longer side branch lesions (8.3% vs. 11.7% SMD = 0.113). There were no significant differences in the major adverse cardiac events including death, myocardial infarction, target lesion revascularization after KBI versus no KBI (15.4% vs. 15.7%, $p = 0.28$), in total cohort or in matched patients (17.1% vs. 15.8%, adjusted HR 1.01, 95% CI: 0.65−1.65, $p = 0.95$). The lack of effect of KBI on clinical outcomes was consistent across various subgroups including left main disease.

Conclusion: In this multicenter real-world registry, KBI did not improve long-term clinical outcomes in patients with coronary bifurcation lesions treated with provisional stenting technique.

1. Introduction

Coronary bifurcations represent one of the most challenging lesions in interventional cardiology, accounting for 15−20% of all lesions undergoing percutaneous coronary interventions (PCI).[1,2] Such procedures are complex and are often associated with a higher restenosis rate and worse clinical outcome. Although kissing balloon inflation (KBI) has been thought to restore native tubular geometry and coronary flow according to vascular branching law as well as to open the stent struts overlying the side branch (SB) ostium, some studies have suggested that KBI could induce stent elliptical deformation, which may increase the risk of adverse events.[3–5] Furthermore, only limited data regarding the clinical efficacy of the KBI technique are available, especially in European population.[6] Therefore, the objective of this study was to analyze the impact of KBI on long-term clinical outcomes in patients undergoing provisional stenting for the coronary bifurcation lesions in a large real-world population.

2. Methods

2.1. Study design and population

The IBS (International Bifurcation Study) is a prospective, multicenter, real-world registry of patients undergoing PCI for coronary bifurcation lesions (NCT03450577). Between February 2018 and August 2020, a total of 1900 patients were consecutively enrolled, of which 873 patients, included in the analysis, underwent PCI with provisional stenting of single bifurcation lesion and had clinical follow up. Patients treated with planned 2-stent strategy, as well as patients with bail-out two-stent strategy after failed provisional approach (a total of 45 patients) were excluded from study. We compared the clinical, technical, and procedural characteristics, and long-term clinical outcomes between patients with and without kissing balloon inflation after provisional stenting. The study was carried out in accordance with the Helsinki declaration and was approved by the institutional review board.

https://doi.org/10.1016/j.ihj.2023.05.003

Abbreviations

PCI	percutaneous coronary interventions
KBI	kissing balloon inflation
MI	myocardial infarction
MACE	major adverse cardiac events
TVR	target vessel repeat revascularization
SD	standard deviation
LM −	left main
MLD	minimum lumen diameter
RVD	reference vessel diameter
HR −	hazard ratio

2.2. Percutaneous coronary intervention procedure and kissing balloon technique

Coronary interventions were performed in accordance with the relevant standard guidelines at the time of each procedure. All patients received loading doses of aspirin (300 mg) and P2Y12 inhibitors (clopidogrel 300–600 mg, prasugrel 60 mg, or ticagrelor 180 mg) before the PCI unless they had previously received these antiplatelet medications. Anticoagulation was performed using unfractionated heparin 100 units/kg. All patients underwent provisional stenting approach in which the coronary stent was implanted in the main vessel across the side branch (an 'A technique' (A for across the SB) of the Main, Across, Distal, Side (MADS) classification). The treatment strategies, such as direction of stent implantation, proximal optimization technique, final kissing inflation, access site, type of stents, use of intravascular imaging or an invasive physiologic assessment were all left to the operator's discretion. After the PCI, 100 mg of aspirin was continued indefinitely, and the maintenance duration of clopidogrel (75 mg/day), was at the cardiologist discretion.

2.3. Data collection and quantitative coronary angiographic analysis

All information about the patient, including demographics, medications, laboratory data, angiographic data, procedural data, outcomes was collected using a web-based REDCap system.

Bifurcation lesions were classified according to the Medina classification and divided into 3 segments for a quantative coronary angiography analysis: proximal main branch (MB), distal MB, and SB. True bifurcation lesions were defined as Medina classification types 1.1.1, 1.0.1, and 0.1.1. For both the pre- and post-procedures, the minimum lumen diameter (MLD), reference vessel diameter (RVD), and lesion length for each vessel were measured, and the percent diameter stenosis for each vessel was calculated as: 100 × (RVD - MLD)/RVD.

2.4. Follow-up

Follow-up was performed either via direct phone contact with the patient or during a visit of the patient to the hospital.

2.5. Outcomes and definitions

The primary clinical outcome was a major adverse cardiac events (MACE) - the composite endpoint of death, non-fatal myocardial infarction (MI), target lesion revascularization (TLR).

Death was considered as having a cardiac cause unless an unequivocal noncardiac cause could be established.

MI was defined according to Fourth universal definition of myocardial infarction.[7]

In all patients including to this registry, CK/CKMB was measured routinely before and 6–12 h after the procedure (6–12 h after the procedure) according to local standards of care. Additionally, troponin was measured in patients with acute coronary syndrome and in cases of: 1) acute onset of ischemic symptoms during/after procedure; 2) new electrocardiographic changes suggestive of acute ischemia; 3) side branch flow impairment after main branch stenting.

The dissection was graded according to the National Heart, Lung, and Blood Institute classification.[8]

Technical success was defined as a residual stenosis less than 30% and TIMI 3 flow at the end of the procedure and was evaluated in the MB and SB respectively. Procedural success was defined as technical success without any in-hospital MACE.

Procedural success was defined as a residual stenosis less than 30% and TIMI 3 flow in the MB at the end of the procedure with no in-hospital serious adverse events including death, MI, urgent repeat revascularization or pericardiocentesis.

2.6. Statistical analysis

Data was analyzed using IBM SPSS v24.0, R 4.12 package. Data are presented as means ± standard deviations (±SDs) or medians and interquartile range (IQR) for continuous variables, and numbers and proportions for categorical variables. Missing preoperative data (<1% for all variables) were imputed using multiple imputations via MICE package. The balance between groups was assessed using standardized mean difference.

To reduce the effect of potential confounding factors in this observational study, propensity score matching was conducted. The propensity score matching was performed using Matchit package. Matching success was determined by a standardized mean difference <0.1 on variables following the match.

Patients from the kissing group were matched to those from the non-kissing group according to the propensity score using the greedy nearest neighborhood matching algorithm with caliper width of the 0.1 SD of the logit of propensity score.

We also did a survival analysis between the kissing group and the non-kissing group in both unmatched and matched cohorts by using Cox regression models. To compare survival rates between groups under study we used Cox regression models with a cluster-robust estimator to account for the matched design. Subgroup analysis was conducted using forestplot package in R.

3. Results

Among the 873 eligible patients, KBI was performed in 325 patients (37.2%). Baseline characteristics are shown in Table 1. Patients treated with KBI were younger (62.7 ± 8.7 vs. 63.8 ± 9.2 SMD = 0.124) and less likely to have chronic obstructive pulmonary disease (4.3% vs. 6.9% SMD = 0.114) and dyslipidemia (34.8% vs. 43.2% SMD = 0.174). Furthermore, those patients were more likely presented chronic coronary disease and more often had a previous PCI (48.6% vs. 42.5% SMD = 0.123).

3.1. Angiographic characteristics

Angiographic data are presented in Table 2. LM disease was more often present in KBI patients (36.9% vs. 12.0% SMD = 0.604). In addition, patients in the KBI group had a significantly larger proximal (3.55 mm ± 0.54 vs. 3.31 mm ± 0.61 SMD = 0.417) as well as distal diameter of MB (2.99 mm ± 0.36 vs. 2.85 mm ± 0.40 SMD = 0.370) and an accordingly larger diameter

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Table 1
Demographic and clinical characteristics of the study patients.

Variable		Total cohort		SMD	*P* value	Matched patients		SMD	*P* value
		non-kissing group (n = 548)	kissing group (n = 325)			non-kissing group (n = 234)	kissing group (n = 234)		
age (mean (SD))		63.85 (9.3)	62.74 (8.8)	0.124	0.080	62.7 (9.8)	63.1 (8.3)	0.04	0.685
female (%)		140 (25.5)	78 (24.0)	0.036	0.667	61 (26.1)	61 (26.1)	<0.001	1.000
hypertension (%)		517 (94.3)	302 (92.9)	0.058	0.486	219 (93.6)	217 (92.7)	0.034	0.855
diabet (%)		137 (25.0)	73 (22.5)	0.060	0.443	51 (21.8)	49 (20.9)	0.021	0.910
dyslipidemia (%)		237 (43.2)	113 (34.8)	0.174	0.016	93 (39.7)	87 (37.2)	0.053	0.635
smoking (%)		119 (21.7)	71 (21.8)	0.003	1.000	47 (20.1)	47 (20.1)	<0.001	1.000
previous PCI (%)		233 (42.5)	158 (48.6)	0.123	0.093	98 (41.9)	106 (45.3)	0.069	0.514
previous CABG (%)		25 (4.6)	14 (4.3)	0.012	0.995	9 (3.8)	10 (4.3)	0.022	1.000
MI history (%)		267 (48.7)	154 (47.4)	0.027	0.755	112 (47.9)	105 (44.9)	0.060	0.578
cerebrovascular disease (%)		64 (11.7)	43 (13.2)	0.047	0.569	27 (11.5)	29 (12.4)	0.026	0.887
copd (%)		38 (6.9)	14 (4.3)	0.114	0.151	10 (4.3)	9 (3.8)	0.022	1.000
BMI (mean (SD))		30.3 (5.1)	30.1 (5.3)	0.043	0.538	30.7 (5.0)	30.3 (5.4)	0.081	0.380
anemia (%)		22 (4.0)	8 (2.5)	0.088	0.305	6 (2.6)	6 (2.6)	<0.001	1.000
atrial fibrilation (%)		65 (11.9)	43 (13.2)	0.041	0.626	29 (12.4)	32 (13.7)	0.038	0.784
currently on dialysis (%)		5 (0.9)	1 (0.3)	0.078	0.534	1 (0.4)	1 (0.4)	<0.001	1.000
OAC (%)		45 (8.2)	23 (7.1)	0.043	0.635	16 (6.8)	19 (8.1)	0.049	0.725
peripheral artery disease (%)		34 (6.2)	34 (10.5)	0.154	0.032	18 (7.7)	22 (9.4)	0.061	0.620
EF, % (mean (SD))		56.5 (10)	57 (10.3)	0.050	0.473	56.1 (10.1)	56.9 (9.8)	0.080	0.388
clinical presentation (%)	Stable angina	319 (58.2)	207 (63.7)	0.182	0.113	138 (59.0)	147 (62.8)	0.205	0.300
	Unstable angina	98 (17.9)	58 (17.8)			46 (19.7)	40 (17.1)		
	STEMI	52 (9.5)	20 (6.2)			20 (8.5)	15 (6.4)		
	Silent ischemia	28 (5.1)	21 (6.5)			9 (3.8)	17 (7.3)		
	NSTEMI	51 (9.3)	19 (5.8)			21 (9.0)	15 (6.4)		

PCI = percutaneous coronary interventions, CABG = coronary artery bypass grafting, MI = myocardial infarction, COPD = chronic obstructive pulmonary disease, BMI = body mass index, OAC = oral anticoagulant, EF = ejection fraction, CTO = chronic total occlusion, SD = standard deviation, SMD = standardized mean difference, STEMI = ST elevation myocardial infarction.

Table 2
Angiographic characteristics of the study patients.

Variable		Total cohort		SMD	*P* value	Matched patients		SMD	*P* value
		non-kissing group (n = 548)	kissing group (n = 325)			non-kissing group (n = 234)	kissing group (n = 234)		
bifurcation location (%)	Left main	66 (12.0)	120 (36.9)	0.642	<0.001	59 (25.2)	57 (24.4)	0.004	0.65
	LAD/DA	306 (55.8)	119 (36.6)			107 (45.7)	104 (44.4)		
	LCX/OM	103 (18.8)	57 (17.5)			38 (16.2)	49 (20.9)		
	RCA bifurcation	53 (9.7)	25 (7.7)			26 (11.1)	21 (9.0)		
	LAD/Septal	14 (2.6)	1 (0.3)			3 (1.3)	1 (0.4)		
	Other location	6 (1.1)	3 (0.9)			1 (0.4)	2 (0.9)		
Left main bifurcation (%)		66 (12.0)	120 (36.9)	0.604	<0.001	59 (25.2)	57 (24.4)	0.020	0.91
trifurcation (%)		17 (3.1)	23 (7.1)	0.182	0.01	10 (4.3)	10 (4.3)	<0.001	0.99
angle (mean (SD))		57 (21)	55 (11)	0.090	0.20	55 (21)	54 (19)	0.040	0.67
calcification (%)		117 (21.4)	48 (14.8)	0.172	0.02	41 (17.5)	42 (17.9)	0.011	0.99
trombosis (%)		32 (5.8)	9 (2.8)	0.152	0.06	10 (4.3)	9 (3.8)	0.022	0.99
CTO (%)		54 (9.9)	26 (8.0)	0.065	0.43	23 (9.8)	23 (9.8)	<0.001	0.99
Medina classification (%)	0.0.1	41 (7.5)	37 (11.4)	0.218	0.14	18 (7.7)	26 (11.1)	0.031	0.40
	0.1.0	143 (26.1)	95 (29.2)			72 (30.8)	62 (26.5)		
	0.1.1	40 (7.3)	25 (7.7)			14 (6.0)	19 (8.1)		
	1.0.0	99 (18.1)	60 (18.5)			49 (20.9)	42 (17.9)		
	1.0.1	45 (8.2)	29 (8.9)			12 (5.1)	21 (9.0)		
	1.1.0	100 (18.2)	46 (14.2)			39 (16.7)	38 (16.2)		
	1.1.1	80 (14.6)	33 (10.2)			30 (12.8)	26 (11.1)		
True bifurcation (%)		120 (21.9)	58 (17.8)	0.102	0.18	44 (18.8)	45 (19.2)	0.011	0.99
SB lesion length ≥10 mm (%)		64 (11.7)	27 (8.3)	0.113	0.14	21 (9.0)	22 (9.4)	0.015	0.99
Proximal MB diameter (mean (SD))		3.31 (0.6)	3.55 (0.5)	0.417	<0.001	3.48 (0.6)	3.45 (0.5)	0.053	0.56
Side branch diameter (mean (SD))		2.38 (0.5)	2.71 (0.5)	0.708	<0.001	2.61 (0.5)	2.59 (0.4)	0.057	0.53
Distal MB diameter (mean (SD))		2.85 (0.4)	2.99 (0.4)	0.370	<0.001	2.93 (0.4)	2.93 (0.4)	0.010	0.92
SB 2.75 mm and less (%)		447 (81.6)	181 (55.7)	0.581	<0.001	153 (65.4)	159 (67.9)	0.054	0.62
SB 2.5 mm and less (%)		381 (69.5)	118 (36.3)	0.706	<0.001	105 (44.9)	112 (47.9)	0.060	0.58

CTO = chronic total occlusion, DA = diagonal artery, LAD = left anterior descending artery, RCA = right coronary artery, LCX = left circumflex artery, MB = main branch, OM = obtuse marginal branch, SB = side branch, SD = standard deviation, SMD = standardized mean difference.

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of SB (2.71 mm ± 0.45 vs. 2.38 mm ± 0.47 SMD = 0.708). While patients in non-kissing group had more complex coronary disease with higher prevalence of calcification (14.8% vs. 21.4% SMD = 0.172), thrombosis (2.8% vs. 5.8% SMD = 0.152) and longer side branch lesions (8.3% vs. 11.7% SMD = 0.113).

After propensity score matching, 234 pairs were compared and those differences between the groups were adjusted among all variables.

3.2. Procedural outcomes

Procedural and clinical outcomes are summarized in Table 3. In unmatched cohort's patients in the kissing group had a higher technical success in side branch (73.8% vs. 57.8% $p = 0.04$). Furthermore, these patients more often had a residual dissection in the side branch (5.8% vs. 2.6%, $p = 0.002$), but more rarely TIMI 0–1 flow in the side branch (7.1% vs. 3.7%, $p = 0.03$). However, there were no significant differences in technical success, procedural success, residual stenosis as well as in-hospital MACE (1.3% vs. 0.4% $p = 0.40$) in either matched group.

3.3. Clinical outcomes

The median follow-up duration was 37.3 (interquartile range, 26.0–51.8) months. Survival curves for MACE, all-cause death, cardiac death, MI, and target lesion revascularization are shown in Figs. 1 and 2. There were no significant differences in the MACE after KBI versus no KBI (15.4% vs. 15.7%, adjusted HR 0.82, 95% CI: 0.58–1.17, $p = 0.28$), in total cohort or in matched patients (17.1% vs. 15.8%, adjusted HR 1.01, 95% CI: 0.65–1.65, $p = 0.95$). Additional subgroup analyses in all patients are shown in Fig. 3. The lack of effect of KBI on clinical outcomes was consistent across various subgroups, including LM disease (adjusted HR 0.76, 95% CI: 0.30–1.94, $p = 0.57$) (Table 4).

4. Discussion

The main results of our study are the following: a) the incidence of the KBI after provisional stenting in the multicenter all-comer registry was 37,2%; b) KBI didn't improve clinical outcomes in patients treated with 1-stent technique; c) the lack of effect of KBI on clinical outcomes was consistent across various subgroups including left main bifurcation; d) Patients in non-kissing group had more complex SB stenosis with higher prevalence of calcification, thrombosis and longer side branch lesions.

The provisional stenting technique remains the preferred strategy in the majority of coronary bifurcation lesions. Several optimization techniques were proposed to achieve better proximal stent apposition and improve angiographic and clinical outcomes.[9,10] While proximal optimization technique considered as a mandatory step of the provisional stenting, efficacy of KBI is still questioned due to controversial data.[11–13] Although European consensus recommends KBI only in cases of sub-optimal result in the SB, so far, the definitions are not clear enough.[14] All these factors led to significant decrease of the usage of a KBI after 1-stent procedures. Thus, in the study of Lee et al for the past decade the use of KBI decreased from 49,1% to 30,7%.[15] In our study the rate of KBI was 37,2%, which is slightly higher than that in Asian population and comparable with results of e-ULTIMASTER registry (36,5%).[16] Meanwhile, usage of KBI is much higher in patients with left main disease. In the 2-center registry, which include 1832 patients who underwent stent implantation for LM bifurcation lesions KBI was performed in 76% of cases.[17] Which is consistent with results of our study (64,5%). This could be due to the fact that the SBs of LM bifurcations are always considered prognostically relevant. However, long term efficacy of KBI has recently been questioned in patients with LM bifurcation lesions. Thus, in the EXCEL trial, KBI after PCI of LM bifurcation lesions was not associated with improved four-year clinical outcomes (composite of death, MI and stroke) regardless of whether one stent (17.5% after KBI vs.15.9% no-KBI (adjusted HR 1.12, 95% CI: 0.68–1.84, $p = 0.65$)) or ≥2 stents (19.8% after KBI vs. 25.8% no-KBI (adjusted HR 0.65, 95% CI: 0.38–1.10, $p = 0.11$)) were implanted.[18] Same results were demonstrated in a large registry of LM PCI, in which MACE rates were similar between the KBI and no-KBI groups (15.1% vs. 15.5%; $p = 0.967$), independent of the use of imaging or proximal optimization.[19] The only factor which associated with a lower rate of target lesion revascularization was short overlap KBI (<3 mm), which underline that quality of KBI could have significant influence on results of SB opening.[19]

While it is well known that suboptimal coronary flow (TIMI<3) has been associated with poor prognosis in STEMI patients, it remains unclear whether coronary flow after PCI is related with outcomes in bifurcation lesions, especially in the SB. In the study of Poorhosseini et al it was showed that gaining TIMI-III flow in a SB could be an indicator for terminating the procedure.[20] However, to our knowledge, no previous studies have examined the effect

Table 3
Procedural outcomes and in-hospital MACE in kissing group compared with non-kissing group.

Outcomes		Total cohort			Matched patients		
		non-kissing group (n = 548)	kissing group (n = 325)	*P* value	non-kissing group (n = 234)	kissing group (n = 234)	*P* value
Technical success in main branch		524 (95.6)	319 (98.2)	0.18	225 (96.2)	229 (97.9)	0.30
Technical success in side branch		317 (57.8)	240 (73.8)	0.04	156 (66.7)	168 (71.8)	0.23
Residual stenosis in main branch		74 (13.5)	39 (12.0)	0.88	27 (11.5)	30 (12.8)	0.57
Residual stenosis in side branch		269 (49.1)	120 (36.9)	0.38	93 (39.7)	94 (40.2)	0.99
Residual dissection in main branch		74 (13.5)	39 (12.0)	**0.04**	5 (2.1)	0	**0.03**
Residual dissection in side branch		14 (2.6)	19 (5.8)	**0.002**	3 (1.3)	15 (6.4)	**0.003**
Proximal optimization		32 (5.8)	48 (14.8)	0.297	25 (10.7)	31 (13.2)	0.08
Procedural success		515 (94.0)	316 (97.2)	0.35	225 (96.2)	226 (96.6)	0.81
TIMI flow in side branch	0	26 (4.7)	7 (2.2)	0.85	6 (2.6)	6 (2.6)	0.83
grade	1	13 (2.4)	5 (1.5)		5 (2.1)	4 (1.7)	
	2	13 (2.4)	11 (3.4)		4 (1.7)	9 (3.8)	
	3	496 (90.5)	302 (92.9)		219 (93.6)	215 (91.9)	
Side branch compromise		54 (9.9)	24 (7.4)	0.43	17 (7.3)	19 (8.1)	0.66
In-hospital MACE		10 (1.8)	3 (0.9)	0.9	1 (0.4)	3 (1.3)	0.40

MACE = major adverse cardiovascular events.

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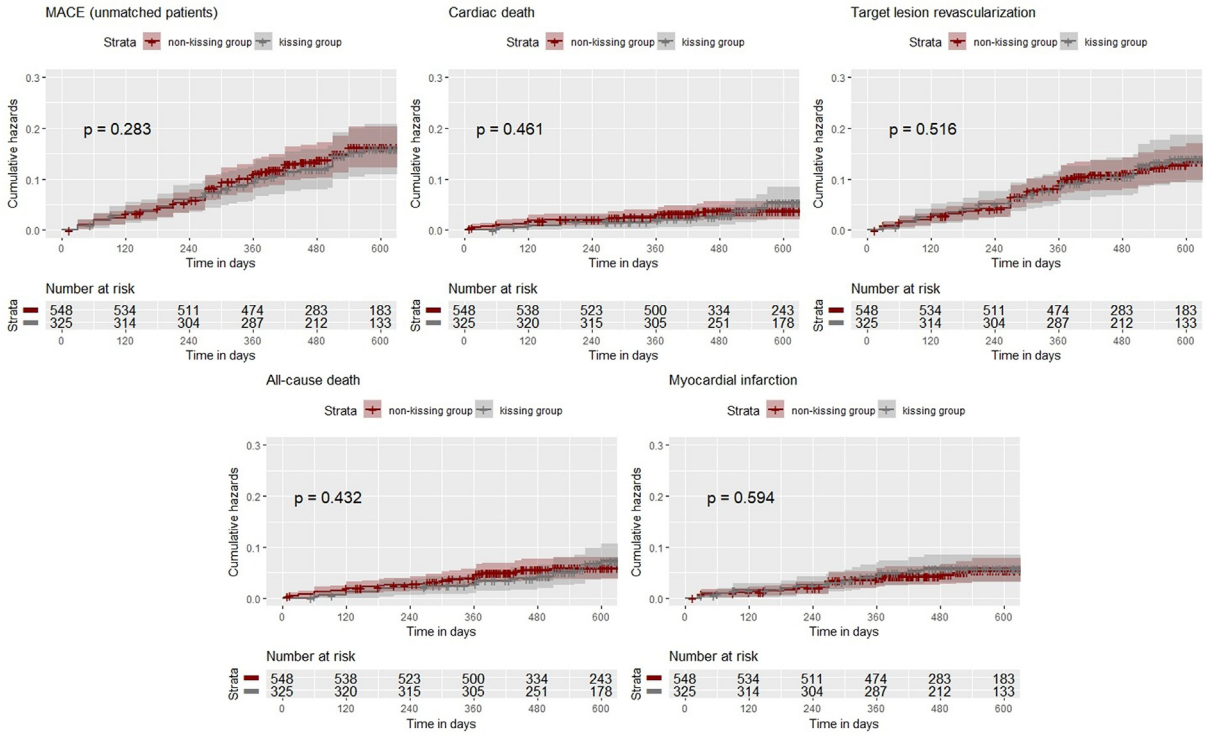

Fig. 1. The Kaplan–Meier curves of clinical events in entire population. Legend (A) Cumulative incidence of MACE (B) Cumulative incidence of cardiac death (C) Cumulative incidence of target lesion revascularization (D) Cumulative incidence of all-cause death (E) Cumulative incidence of myocardial infarction.

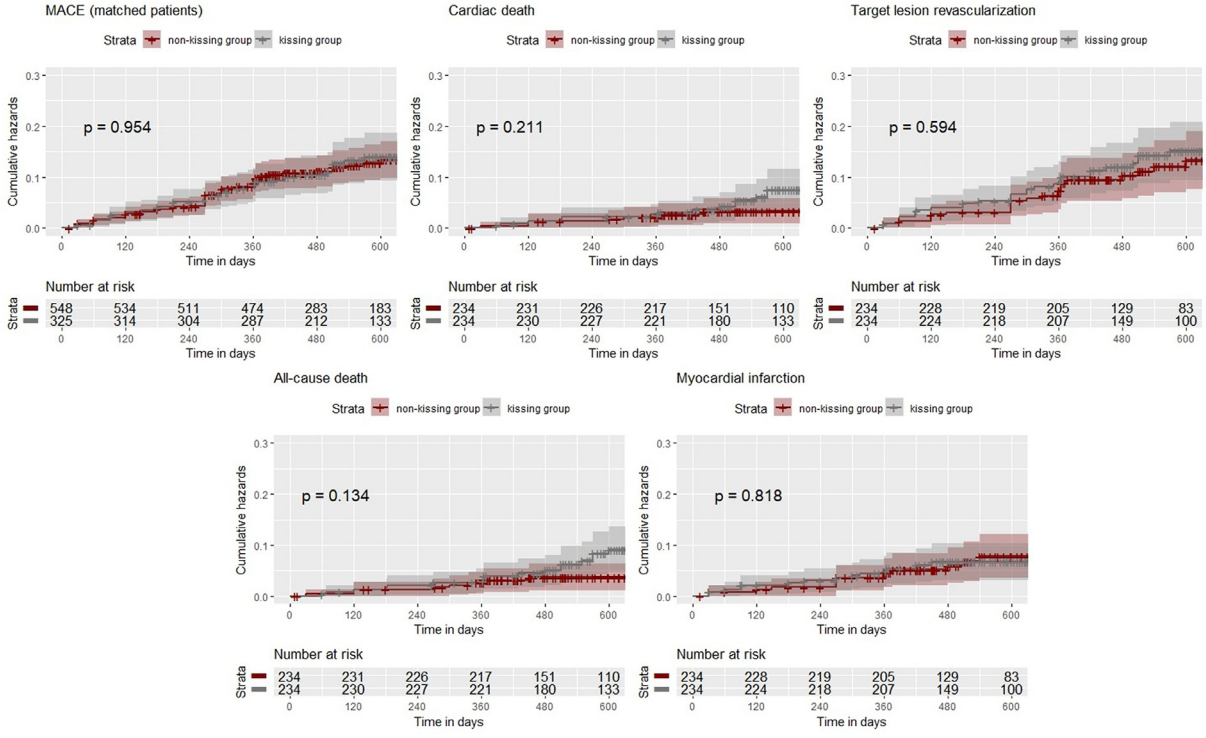

Fig. 2. The Kaplan–Meier curves of clinical events in adjusted population. Legend (A) Cumulative incidence of MACE (B) Cumulative incidence of cardiac death (C) Cumulative incidence of target lesion revascularization (D) Cumulative incidence of all-cause death (E) Cumulative incidence of myocardial infarction.

of reduced coronary flow on long-term prognosis after bifurcation PCI. According to the results of our study the number of patients with TIMI 0/1 flow in the side branch were lower in the kissing group, but it was not associated with worse clinical outcomes. The similar results were demonstrated by Niemela et al in the

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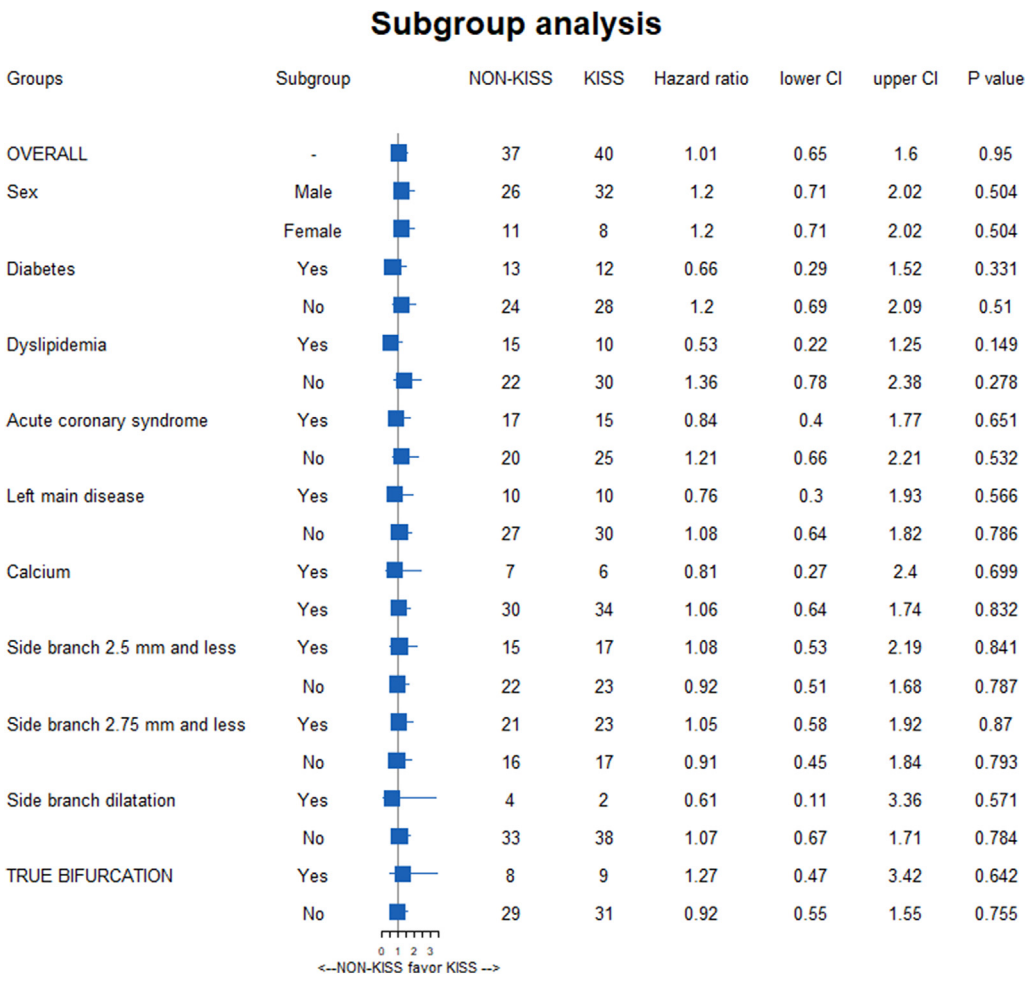

Fig. 3. Title: Hazard ratios for major adverse cardiac events.

Table 4
Clinical outcomes in Kissing group compared with Non-kissing group during follow-up period.

Outcomes	Total cohort				Matched patients			
	non-kissing group (n = 548)	kissing group (n = 325)	Hazard ratio (95%CI)	*P* value	non-kissing group (n = 234)	kissing group (n = 234)	Hazard ratio (95%CI)	*P* value
MACE	86 (15.7)	50 (15.4)	0.82 (0.58–1.17)	0.28	37 (15.8)	40 (17.1)	1.01 (0.65–1.60)	0.95
TLR	73 (13.3)	46 (14.1)	0.88 (0.61–1.29)	0.52	29 (12.4)	36 (15.4)	1.16 (0.70–1.90)	0.56
All-cause death	32 (5.8)	20 (6.1)	0.98 (0.56–1.72)	0.95	9 (3.8)	18 (7.6)	1.86 (0.84–4.15)	0.13
Cardiac death	21 (3.8)	15 (4.6)	1.11 (0.57–2.16)	0.75	8 (3.4)	15 (6.4)	1.74 (0.74–4.10)	0.21
Myocardial infarction	35 (6.4)	25 (7.7)	0.86 (0.51–1.48)	0.60	19 (8.1)	19 (8.1)	0.92 (0.48–1.76)	0.80
	Left main subgroup							
	Total cohort				Matched patients			
	non-kissing group (n = 66)	kissing group (n = 120)	Hazard ratio (95%CI)	*P* value	non-kissing group (n = 59)	kissing group (n = 57)	Hazard ratio (95%CI)	*P* value
MACE	12 (18.2)	18 (15)	0.69 (0.32–1.45)	0.33	10 (17)	10 (17.5)	0.76 (0.30–1.94)	0.57
TLR	9 (13.6)	16 (13.3)	0.80 (0.35–1.85)	0.60	3 (5.1)	5 (8.7)	1.39 (0.34–5.70)	0.64
All-cause death	5 (7.6)	7 (5.8)	0.63 (0.20–2.01)	0.43	3 (5.1)	4 (7)	1.08 (0.25–4.65)	0.91
Cardiac death	3 (4.5)	4 (3.3)	0.56 (0.12–2.58)	0.46	4 (6.8)	4 (7)	0.67 (0.15–2.96)	0.60
Myocardial infarction	4 (6)	7 (5.8)	0.75 (0.21–2.68)	0.66	7 (11.8)	9 (15.8)	0.94 (0.33–2.69)	0.91

MACE = major adverse cardiovascular events, TLR = target lesion revascularization, CI = confidence intervals.

NORDIC III study. It was showed that provisional stenting with and without KBI was associated with similar clinical outcomes.[6]

In contrast to our study, in a large multicenter registry COBIS II patients in the KBI group had a lower incidence of MACE (adjusted HR: 0.50, 95% CI: 0.30 to 0.85; $p = 0.01$), driven by target lesion revascularization in the main vessel (adjusted HR: 0.51, 95% CI: 0.28 to 0.93; $p = 0.03$).[21] Meanwhile there were no significant differences between the groups in terms of the rates of cardiac death,

Please cite this article as: D. Khelimskii, I. Bessonov, M. Kashtanov *et al.*, Long-term clinical outcomes after kissing balloon inflation in patients with coronary bifurcation lesions treated with provisional stenting technique. Results from the real-world multicenter registry, Indian Heart Journal, https://doi.org/10.1016/j.ihj.2023.05.003

MI, or stent thrombosis.[21] In the study from large COBIS III registry Lee and co-authors examined the outcomes of bifurcation lesions treated with a provisional stenting strategy with or without additional balloon side-branch opening in 2194 patients.[22] Of note, 509 patients who underwent balloon side-branch opening initially had a more complex bifurcation lesion, including true bifurcations, distal left main lesions, and longer lesion length which eventually could answer the question why the operator decided to open the side branch. However, at 5 years, there were no significant differences in the primary composite endpoint of target lesion failure between groups, even in "complex" subgroups such as left main bifurcations, true bifurcations etc. At the same time, in our study, the rate of KBI in complex bifurcation lesions was lower, which, on the one hand, fits with the general trend towards a decrease of the usage of a KBI after 1-stent procedures, and, on the other hand, reflects the results of studies that did not demonstrate the benefits of additional side branch modifications. As a result, when achieving a good blood flow through side branch after stent implantation, the operator prefers to avoid additional dilatation of side branch giving a higher risk of complications and conversion to a two-stent techniques. Conflicting results between studies could be also explained that KBI is very operator dependent technique, and its optimal result depends on multiple factors such as a size of balloons, number and consequence of inflations, location of the wire re-crossing. However, these results suggest that the most SBs may not have a significant impact in clinical outcomes and even its restenosis/residual stenosis doesn't translate into ischemia-driven revascularization. Determining the clinical relevance of SB is the key point that significantly influences treatment strategy. But most criteria's used in real practice are surrogates of SB-related myocardial mass and not validated in large clinical studies.

5. Conclusions

In this multicenter real-world registry, KBI did not improve long-term clinical outcomes in patients with coronary bifurcation lesions treated with provisional stenting technique.

Study limitations

Our study has several limitations. First, it was an observational study with all inherent limitations of such studies. Angiographic characteristics were not analyzed in a core lab but provided by local investigators from participating centers. Second, several baseline characteristics were significantly different between groups. The decision to perform KBI as well as proximal optimization in each patient was made at the operator's discretion. Third, follow-up was not available in all registry patients. Fourth, the bifurcation lesions included in this analysis were not all the lesions diagnosed but those in which PCI was performed.

Funding

No funding.

Ethics committee approval

The study was carried out in accordance with the Helsinki declaration and was approved by the Institutional Review Board (№ 21 from 13 December 2017) and registered at ClinicalTrials.gov under NCT03450577.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools. REDCap is a secure, web-based application designed to support data capture for research studies, providing: (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources.

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29 March 2023
Available online xxx

Please cite this article as: D. Khelimskii, I. Bessonov, M. Kashtanov *et al.*, Long-term clinical outcomes after kissing balloon inflation in patients with coronary bifurcation lesions treated with provisional stenting technique. Results from the real-world multicenter registry, Indian Heart Journal, https://doi.org/10.1016/j.ihj.2023.05.003