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ORIGINAL ARTICLE

Study comparing the double kissing (DK) crush with classical crush for the treatment of coronary bifurcation lesions: the DKCRUSH-1 Bifurcation Study with drug-eluting stents

S. L. Chen*, J. J. Zhang*, F. Ye*, Y. D. Chen†, T. Patel‡, K. Kawajiri§, M. Lee¶, T. W. Kwan**, G. Mintz†† and H. C. Tan‡‡

*Nanjing First Hospital of Nanjing Medical University, Nanjing, China, †Beijing Anzhen Hospital of Capital Medical University, Beijing, China, ‡Krishina Heart Institute, Ahmedabad, India, §Tokushio Hospital, Osaka, Japan, ¶Queen Mary Hospital, Hong Kong, China, **Beth Israel Hospital, New York, USA, ††Cardiac Research Foundation, Columbia University, New York, USA, ‡‡National University Hospital, Singapore

ABSTRACT

Background Classical crush has a lower rate of final kissing balloon inflation (FKBI) immediately after percutaneous coronary intervention (PCI). The double kissing (DK) crush technique has the potential to increase the FKBI rate, and no prospective studies on the comparison of classical with DK crush techniques have been reported.

Materials and methods Three hundred and eleven patients with true bifurcation lesions were randomly divided into classical (n = 156) and DK crush (n = 155) groups. Clinical and angiographic details at follow-up at 8 months were indexed. The primary end point was major adverse cardiac events (MACE) including myocardial infarction, cardiac death and target lesion revascularization (TLR) at 8 months.

Results FKBI was 76% in the classical crush group and 100% in the DK group ($P < 0{\cdot}001$). The incidence of stent thrombosis was 3·2% in the classical crush group (5·1% in without- and 1·7% in with-FKBI) and 1·3% in the DK crush group. Cumulative 8 month MACE was 24·4% in the classical crush group and 11·4% in the DK crush group ($P = 0{\cdot}02$). The TLR-free survival rate was 75·4% in the classical crush group and 89·5% in the DK crush group ($P = 0{\cdot}002$).

Conclusions DK crush technique has the potential of increasing FKBI rate and reducing stent thrombosis, with a further reduction of TLR and cumulative MACE rate at 8 months.

Keywords Coronary bifurcation lesions, DK crush, final kissing balloon inflation.

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Introduction

The percutaneous treatment of coronary bifurcation lesions is still limited by technical challenges and both restenosis and stent thrombosis even in the era of drug-eluting stents (DES) [1–6]. During DES implantation, in order to improve ostial side branch coverage without compromising access to the side branch, the classical crush technique was developed [7]. Studies reported that final kissing balloon inflation (FKBI) after classical crush was mandatory to improve outcomes [8,9]. In a previously published pilot study we modified the classical crush technique by developing 'double kissing (DK) double crush' bifurcation stenting [10]. To study this technique in comparison to the classical crush technique, we organized a prospective, multicentre, randomized DKCRUSH-1 trial. In particular, we sought to determine the differences in rates of FKBIs as well as long term clinical outcomes.

Materials and methods

Study population and randomization

From April 2005 to May 2006, 312 patients scheduled for percutaneous coronary intervention (PCI) of a true coronary bifurcation lesion (Lefevre Classification) [3] in eight centres from China, Singapore, India, Japan and the USA were randomized to classical crush versus DK crush techniques. Demographic and procedural characteristics were entered into a dedicated database. Randomization was performed in blocks for each participating centre with the ratio of 1 : 1 by computerized assignment. Patients were randomized before the wiring of any vessel. This project was approved by Ethical Committees in all participating centres, and all patients gave their formal written consent. All members had full access to the database and participated in the interpretation of data. A stent thrombosis rate of ≥ 5% in any group would necessitate premature termination of the trial.

Inclusion criteria

Inclusion criteria included main vessel ≥ 2·5 mm and side branch diameter ≥ 2·0 mm by visual estimation. Lesions in the main vessel had to be completely covered by two overlapped stents. Two or more bifurcation lesions were eligible as long as there was only one bifurcation lesion per vessel, and each lesion had to be treated by the strategy assigned at randomization. Patients with another single lesion in a different target vessel that could be covered by a single DES were also included.

Exclusion criteria

Patients were excluded if expected clinical survival was < 1 year or in the presence of concomitant liver dysfunction, plasma levels of creatinine > 200 Umol L^{-1}, a cerebrovascular event within 6 months, a history of previous coronary artery bypass grafting (CABG), or allergy to aspirin, clopidogrel and DES.

Implantation of DES

Paclitaxel-eluting stent (Boston Scientific, Natick, MA, USA) and sirolimus-eluting stents (Cardis, Johnson & Johnson, Miami Lakes, FL, USA) were used. Deployment of additional DES to completely cover a dissection proximal or distal to a previous stent was allowed. Bare metal stents were not allowed. The procedural time was defined from 'guide wire in' to 'guiding catheter out'.

Classical and DK crush techniques have been described previously [7,10]. Briefly, the classical crush technique involves first delivering the side branch stent with 3–5 mm protruding proximally into the main vessel, and then crushing the proximal portion of the side branch stent with the main vessel stent. The DK crush technique differes from the classical crush technique in that the part of the side branch stent protruding into the main vessel was first crushed with a balloon in the main vessel, then a first kissing balloon inflation was performed, next the main vessel was stented, and at the end a final kissing balloon inflation was performed.

Activated clotting time (ACT) > 280 s during the procedure was maintained using unfractionated heparin. Glycoprotein (GP) IIb/IIIa inhibitors were administered at the discretion of the operator. Clopidogrel (75 mg d^{-1}) was taken for at least 12 months and aspirin (100 mg d^{-1}) was recommended for life.

End points

The primary end point was major adverse cardiac events (MACE) at 8 months, including myocardial infarction, cardiac death, target lesion revascularization (TLR) by either PCI or CABG. Secondary end points included binary angiographic restenosis and late loss in both the main vessel and side branch after 8 months.

Myocardial infarction (MI) was defined as creatine kinase-MB (CK-MB) enzyme elevation ≥ 3 times the upper limit of the normal value, either with (Q wave MI) or without (non-Q wave MI), and new Q waves in at least two contiguous leads on electrocardiogram. TLR was defined as repeat revascularization with a diameter stenosis ≥ 50% within the stent or in the 5 mm distal or proximal segments adjacent to the stent. Target vessel revascularization (TVR) was defined as repeat revascularization within the treated vessel. Stent thrombosis was defined as an acute coronary syndrome with angiographic documentation of either vessel occlusion or thrombus within or adjacent to a previously successfully implanted stent, or in the absence of angiographic confirmation, either acute MI in the distribution of the treated vessel or death not clearly attributable to other causes. Stent thrombosis was categorized, according to the timing of the event, into: early (≤ 1 month after the procedure) and late (1 month to 1 year after the procedure).

Plasma level of creatinine, CK-MB and troponin I was monitored before, immediately after and at 8 h and 24 h post-PCI. All patients were contacted by telephone or seen at a clinic review every month.

Quantitative angiographic analysis (QCA) and angiographic follow-up

Angiographic follow-up was scheduled at 8 months after the procedure unless clinically indicated earlier. QCA was performed at the Nanjing Heart Centre core laboratory (Nanjing, China) by observers who were blind to the treatment assignment. A validated computer-based edge detection system (CAAS II 4·1·1, Pie Medical Imaging, The Netherlands) was used to analyse QCA. Views were matched pre-procedural, post-procedural and at 8 month follow-up.

Vessels involved in the bifurcation lesion were divided into 3 segments: pre-bifurcation segment of main vessel (Proximal-MV), post-bifurcation segment of main vessel (Distal-MV), and side branch. Proximal-MV segment included the stented segment and 5 mm proximal to the stented segment. Distal-MV and side branch

Table 1 Baseline Clinical Characteristics

	Classical Crush				
	Overall	Without final kissing balloon	With final kissing balloon	DK crush	*P* Overall Classical vs. DK Crush
No. of patients (n)	156	39	117	155	> 1·0
Age (years)	63·9 ± 8·6	64·1 ± 7·7	63·7 ± 8·9	63·8 ± 9·2	0·9
Males (%)	70·0	67·7	73·7	76·2	0·5
Hypertension (%)	76·6	77·4	76·4	76·2	1·0
Hyperlipidaemia (%)	62·6	60·6	68·4	68·6	0·4
Diabetes mellitus (%)	8·4	12·9	6·6	27·0	0·03
Current smoking (%)	62·6	58·1	64·5	63·8	0·9
Previous PCI (%)	11·2	9·7	11·8	11·5	0·8
Previous MI (%)	12·1	6·5	14·5	8·6	0·5
Unstable angina (%)	70·1	67·7	71·1	69·5	1·0
Acute MI (%)	16·8	19·4	15·8	15·2	0·9
LVEF (%)	62·7 ± 13·2	61·0 ± 9·9	64·2 ± 5·8	61·6 ± 11·2	0·9

Abbreviations: LVEF, left ventricular ejection fraction; MI, myocardial infarction, PCI, percutaneous coronary intervention, DK, double kissing.

segments included the stented segment and 5 mm distal to the stent segment. Bifurcation angle was defined as the angle between the axis of the post-bifurcation segments of the main vessel and the side branch origin.

Angiographic success was defined as a residual stenosis < 30% with Thrombolysis in Myocardial Infarction (TIMI) flow 3 in both branches. Procedural success was defined as angiographic success in the absence of any in-hospital MACE. The final kissing balloon inflation was classified as 'satisfied' (no waist at the side branch ostium) or 'unsatisfied' (≥ 20% diameter stenosis waist at the side branch ostium).

Statistics and data management

We assumed a cumulative incidence of 8-month MACE in classical crush cohorts of 25% and predicted that MACE in the DK crush group would be ≤ 12%. Therefore, 129 patients would be needed in each group with > 80% power using two-sided Fisher's exact test. Because of the uncertainty of follow-up, the sample size was expanded by 20%; therefore, a total of 312 patients were needed.

Continuous variables are expressed as mean ± 1SD and compared using P-P plot and ANOVA test. Categorical variables (as frequencies or percentages) were compared with chi-square statistics or Fisher's exact test. The primary end points were analysed by the Kaplan–Meier method and log-rank test. Cox regression models were used to identify the predictors of TLR at 8 months. A *P*-value of < 0·05 was considered statistically significant. All data were analysed with SPSS version 11·5 (SPSS Inc., Chicago, IL).

Because of the previously reported importance of final kissing balloon inflations on long term success of bifurcation intervention, we also analysed patients with-, versus without-, final kissing balloon inflations.

Results

Baseline characteristics

A total of 311patients with 324 bifurcation lesions (156 patients with 163 lesions in the classical crush group, and 155 patients with 161 lesions in the DK crush group) were enrolled into this study, one patient in the classical crush group was excluded because of implantation of a bare-metal stent.

The two groups were matched regarding baseline clinical characteristics with the exception of diabetes mellitus (Table 1); more patients with diabetes were randomized to DK crush than classical crush ($P = 0·03$). Patients were admitted mainly due to unstable symptoms.

Lesions and procedural characteristics

Bifurcation lesions most commonly involved left anterior descending (LAD) and diagonal (Table 2). Final kissing balloon inflations were performed in 76% of the classical stent crush group and in 100% of the DK crush group ($P < 0·001$, Table 1 and Table 2). Patients in the classical crush group who did not have final kissing balloon inflations had several typical features: smaller bifurcation angle, shorter lesions, shorter stent length in the main vessel, fewer distal left main trunk lesions, more left circumflex-obtuse marginal

Table 2 Baseline lesion and procedural characteristics

	Classical crush				
	Overall	**Without final kissing balloon**	**With final kissing balloon**	**DK crush**	***P* Overall classical vs. DK crush**
No. of lesions	163	39	124	161	> 1·0
Lesion characteristics					
Thrombus	5	3	2	4	0·9
Severe calcification	0	0	0	1	0·7
Tortuous	20	6	14	14	0·6
Restenotic	5	1	4	5	
Chronic occlusion	3	0	3	7	0·3
Lesion location (%)					
LAD-diagonal	61·7	61·3	61·8	65·7	0·9
Distal LM	15·9	3·2	21·2	15·3	0·9
LCX-marginal	14·0	22·6	10·5	11·3	1·0
Distal RCA	8·4	12·9	6·6	7·6	0·9
Angle (°)	52·8 ± 23·0	46·2 ± 13·9	55·6 ± 25·4	53·8 ± 22·8	0·8
Guiding catheter (Fr)	7·1 ± 0·5	7·2 ± 0·4	7·1 ± 0·3	6·5 ± 0·5	< 0·001
GP IIb/IIIa use (#)	14	5	9	13	0·4
Balloons (#)	2·2 ± 0·8	2·1 ± 0·7	2·2 ± 0·9	2·5 ± 0·7	< 0·01
Contrast volume (ml)	108·4 ± 71·5	87·9 ± 59·8	117·1 ± 74·6	130·3 ± 78·5	0·04
Procedure time (min)	34·9 ± 18·4	34·9 ± 18·3	33·9 ± 18·5	46·5 ± 24·2	< 0·001
Cypher stents (%)	29	17	22	20	0·11
No of stents					
Main vessel	1·1 ± 0·4	1·0 ± 0·2	1·2 ± 0·4	1·2 ± 0·4	0·4
Side branch	1·2 ± 0·4	1·0 ± 0·2	1·1 ± 0·3	1·0 ± 0·1	0·06
Overlapping stents (%)					
Main vessel	10·4	4·4	13·3	17·3	0·14
Side branch	4·7	0	6·7	6·9	0·6
Max pressure (atm)					
Main vessel	16·9 ± 2·8	17·0 ± 2·7	17·0 ± 2·8	16·7 ± 2·7	0·6
Side branch	16·0 ± 2·7	15·9 ± 2·7	16·0 ± 2·7	16·0 ± 2·7	0·9
Lesion length (mm)					
Main vessel	20·0 ± 9·7	16·7 ± 5·5	21·4 ± 10·7	21·3 ± 11·3	0·4
Side branch	10·5 ± 7·5	10·2 ± 7·6	10·6 ± 7·5	10·3 ± 6·3	0·8
Stent length (mm)					
Main vessel	25·0 ± 12·7	28·1 ± 5·4	22·0 ± 14·3	22·2 ± 12·5	0·5
Side branch	17·9 ± 7·0	15·4 ± 3·1	18·8 ± 8·0	17·4 ± 5·6	0·6
Stent diameter (mm)					
Main vessel	3·39 ± 0·54	3·37 ± 0·55	3·42 ± 0·54	3·44 ± 0·35	0·8
Side branch	2·78 ± 0·39	2·59 ± 0·33	2·84 ± 0·39	2·71 ± 0·44	0·2
Unsatisfactory final kissing balloon inflation (%)			27·6	6·3	< 0·01

Abbreviations: LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery; GP, glycoprotein; DK, double kissing.

Table 3 Quantative angiographic analysis of the pre-bifurcation main vessel (Proximal-MV) segment

	Classical crush				
	Overall	Without final kissing balloon	With final kissing balloon	DK crush	*P* Overall classical vs. DK crush
No. of lesions	135	30	105	130	0·9
Baseline					
RVD (mm)	2·86 ± 0·63	2·87 ± 0·62	2·84 ± 0·58	2·85 ± 0·53	0·5
MLD (mm)	0·94 ± 0·57	0·96 ± 0·56	0·92 ± 0·49	0·93 ± 0·49	0·16
DS (%)	64·5 ± 13·9	65·9 ± 14·2	63·7 ± 14·5	64·8 ± 13·2	0·13
Post-PCI					
RVD (mm)	3·44 ± 0·54	3·26 ± 0·56	3·48 ± 0·45	3·48 ± 0·51	0·6
MLD (mm)	2·94 ± 0·55	2·81 ± 0·59	2·98 ± 0·46	3·02 ± 0·52	0·6
DS (%)	12·8 ± 7·1	12·0 ± 6·3	13·1 ± 7·4	14·6 ± 8·0	0·3
Acute gain (mm)	1·88 ± 0·58	1·80 ± 0·59	1·91 ± 0·55	1·96 ± 0·56	0·9
8-month follow-up					
RVD (mm)	3·38 ± 0·63	3·30 ± 0·71	3·38 ± 0·59	3·38 ± 0·54	0·6
MLD (mm)	2·58 ± 0·76	2·59 ± 0·81*	2·72 ± 0·85	2·89 ± 0·86	0·01
DS (%)	22·6 ± 24·2	25·4 ± 21·5	18·7 ± 15·9	19·6 ± 16·6	0·8
Late loss (mm)	0·38 ± 0·12	0·42 ± 0·15*	0·35 ± 0·11	0·32 ± 0·15	0·05
Restenosis (%)					
Overall	8·9	20·0	5·7	6·2	0·6
Edge	2·9	6·6	1·9	1·5	0·8
In-stent	5·9	13·3	3·8	4·7	0·6

Abbreviations: RVD, reference vessel diameter; MLD, minimum lumen diameter; DS, diameter stenosis; DK, double kissing.
*$P < 0·05$ comparing classical crush without final kissing inflations to both classical crush with final kissing inflations as well as DK crush.

lesions, and shorter stent length and smaller stent diameter in the side branch. Independent factors for final kissing balloon inflation were lesion location (OR = 0·58, 95% CI 0·36–0·92, $P = 0·020$), main vessel stent length (OR = 1·08, 95% CI 1·02–1·14, $P = 0·012$), post-PCI side branch minimum lumen diameter (OR = 6·97, 95% CI 1·07–45·78, $P = 0·003$), and bifurcation angle (OR = 1·02, 95% CI 1·00–1·04, $P = 0·043$).

The DK crush procedure was characterized by more contrast use ($P = 0·04$), more balloons ($P < 0·01$), longer procedural times ($P < 0·001$), and a lower rate of unsatisfactory final kissing balloon inflations (27·63% vs. 6·3%, $P < 0·01$).

QCA analysis

QCA analysis of the Proximal-MV segment is shown in Table 3. There were no significant differences between the two groups (classical vs. DK crush) pre-PCI or immediately post-PCI. However, at follow-up, late lumen loss was significantly greater and minimum lumen diameter was significantly smaller in the classical crush group. This difference was primarily attributable to the patients in the classical crush group who did not have final kissing balloon inflations and in whom restenosis in the body of the Proximal-MV stented segment was the most common pattern.

Analysis of the Distal-MV segment is shown in Table 4. There were no significant differences between the two groups (classical vs. DK crush).

Analysis of the side branch is shown in Table 5. Smaller acute gain and greater final diameter stenosis were found in the classical crush vs. the DK crush branches primarily due to differences in lesions not undergoing final kissing balloon inflations. At follow-up late loss was greater, minimal lumen diameter (MLD) was smaller, final diameter stenosis was also greater, and restenosis was more common in the classical crush group compared to the DK crush group again, primarily due to the difference in lesions not undergoing final kissing balloon inflations. The ostial side branch was the common site of the MLD both post-PCI and at 8 month follow-up in lesions treated with the classical crush technique, but without final kissing balloon inflations; the restenosis rate at this site was 33·3%.

Table 4 Quantitative angiographic analysis of the post-bifurcation main vessel (Distal-MV) segment

	Classical crush				
	Overall	**Without final kissing balloon**	**With final kissing balloon**	**DK crush**	***P* Overall classical vs. DK crush**
No. of lesions	135	30	105	130	
Baseline					
RVD (mm)	2·56 ± 0·49	2·57 ± 0·46	2·51 ± 0·42	2·53 ± 0·41	0·4
MLD (mm)	0·62 ± 0·25	0·65 ± 0·22	0·62 ± 0·23	0·65 ± 0·25	0·7
DS (%)	62·1 ± 11·7	64·3 ± 13·8	61·7 ± 18·5	65·6 ± 19·7	0·4
Post-PCI					
RVD (mm)	3·15 ± 0·57	3·24 ± 0·59	3·23 ± 0·55	3·26 ± 0·55	0·7
MLD (mm)	2·67 ± 0·56	2·69 ± 0·60	2·67 ± 0·54	2·96 ± 0·57	0·8
DS (%)	14·3 ± 6·4	14·7 ± 5·4	13·1 ± 4·6	13·5 ± 5·9	0·11
Acute gain (mm)	1·55 ± 0·42	1·43 ± 0·44	1·56 ± 0·47	1·58 ± 0·46	0·8
8-month follow-up					
RVD (mm)	2·98 ± 0·46	2·89 ± 0·43	3·02 ± 0·45	2·92 ± 0·47	0·6
MLD (mm)	2·46 ± 0·47	2·47 ± 0·44	2·41 ± 0·39	2·48 ± 0·36	0·7
DS (%)	23·8 ± 19·4	24·3 ± 21·5	19·6 ± 17·8	18·5 ± 16·3	0·9
Late loss (mm)	0·36 ± 0·11	0·34 ± 0·16	0·33 ± 0·13	0·31 ± 0·11	0·7
Restenosis (%)					
Overall	3·7	10·0	1·8	2·3	0·5
Edge	1·5	3·3	0·9	0·8	0·5
In-stent	2·2	6·6	0·9	1·5	0·3

Abbreviations: RVD, reference vessel diameter; MLD, minimum lumen diameter; DS, diameter stenosis; DK, double kissing.

Comparison of restenosis rate is shown in Fig. 1. The overall restenosis rate (defined by any one of 3 segments analysed having restenosis) was 32·3% in classical crush and 20·3% in the DK crush groups ($P = 0·01$). This difference was mainly attributable to patients in the classical crush group who did not undergo final kissing inflation.

Clinical outcomes

Clinical results are shown in Table 6. Procedural success was 91·1% in the classical crush group (87·2% in classical crush without final kissing balloon inflations and 92·3% in classical crush with final kissing balloon inflations); it was 96·1% in DK crush. Although there was one intraprocedural stent thrombosis in the DK crush group, there was no difference in in-hospital MACE between treated groups.

Clinical follow-up was available in 100% of patients, and angiographic follow-up was available in 82% of patients (overall, 257 patients with 265 lesions) at a mean period of 246 ± 17 days after procedure. Cumulative 8 month MACE was 24·4% in the classical crush group (35·9% in patients without final kissing balloon inflations and 19·7% in patients with final kissing balloon inflations), significantly greater than in the DK crush group (11·4%, $P = 0·02$, Table 6). This was primarily attributed to a much higher rate of revascularization in the classical crush treated bifurcation lesions that did not include final kissing balloon inflations. There was one death from acute inferior wall infarction 5 months after treatment of an LAD-diagonal lesion in the DK crush group. Two patients in the classical crush group (one with and one without final kissing balloon inflations) died from acute MI in the distribution of the treated vessels. The incidence of stent thrombosis was 3·2% in the classical crush group (5·1% in 'without' and 1·7% in 'with' final kissing balloon inflations) and 1·3% in the DK crush group. The TLR-free survival rate was 75·4% in the classical crush group (71·2% in 'without' and 77·6% in 'with' final kissing balloon inflations) vs. 89·5% in the DK crush group ($P = 0·002$, Figs 2 and 3).

Lack of final kissing balloon inflations was the only independent predictor of post-procedural stent thrombosis (OR = 1·60, 95% CI 1·63–4·756, $P = 0·035$). By Cox regression analysis, side branch minimal lumen diameter (HR = 16·57, 95% CI 3·39–11·20,

Table 5 Quantitative angiographic analysis of the side branch

	Classical crush				
	Overall	**Without final kissing balloon**	**With final kissing balloon**	**DK crush**	***P* Overall classical vs. DK crush**
No. of lesions	135	30	105	130	
Baseline					
RVD (mm)	2·45 ± 0·45	2·45 ± 0·33	2·49 ± 0·48	2·46 ± 0·54	0·5
MLD (mm)	0·84 ± 0·51	0·83 ± 0·55	0·85 ± 0·59	0·84 ± 0·58	0·4
DS (%)	65·7 ± 18·9	62·4 ± 17·5	66·3 ± 19·2	65·4 ± 19·8	0·3
Post-PCI					
RVD (mm)	2·85 ± 0·39	2·85 ± 0·36	2·86 ± 0·39	2·88 ± 0·40	0·13
MLD (mm)	2·56 ± 0·42	2·18 ± 0·46	2·59 ± 0·49	2·59 ± 0·45	0·8
DS (%)	19·4 ± 8·7	22·6 ± 9·2	15·5 ± 9·1	14·6 ± 8·7	0·04
Acute gain (mm)	1·45 ± 0·59	1·37 ± 0·57*	1·64 ± 0·55	1·69 ± 0·64	0·01
8-month follow-up					
RVD (mm)	2·81 ± 0·41	2·80 ± 0·37	2·83 ± 0·42	2·82 ± 0·54	0·7
MLD (mm)	1·95 ± 0·45	1·52 ± 0·50*	2·24 ± 0·52	2·29 ± 0·71	0·8
DS (%)	38·6 ± 17·5	39·4 ± 17·7*	23·9 ± 14·6	21·2 ± 14·5	0·03
Late loss (mm)	0·48 ± 0·28	0·51 ± 0·39*	0·34 ± 0·23	0·33 ± 0·25	0·04
Restenosis (%)					
Overall	24·4	36·6	20·9**	12·3	0·01
Edge†	17·8	33·3	13·3	7·7	0·01
In-stent	6·6	3·3	7·6	4·6	0·08

Abbreviations: RVD, reference vessel diameter; MLD, minimum lumen diameter; DS, diameter stenosis; DK, double kissing.
*$P < 0·001$ comparing classical crush without final kissing inflations to both classical crush with final kissing inflations as well as DK crush.
**$P = 0·01$ comparing classical crush with final kissing inflations to DK crush.
†indicates the restenosis at ostial side branch (within 5 mm proximal to side stent).

$P = 0·001$) and lack of DK crush technique (HR 24·68, 95% CI 4·15–23·55, $P = 0·001$) were two independent predictors of MACE. Independent predictors of TLR were an unsatisfactory final kissing balloon inflation (HR = 12·21, 95% CI 0·01–0·34, $P = 0·002$) and lack of DK crush technique (HR = 16·05, 95% CI 1·01–4·83, $P = 0·001$).

Discussion

The DKCRUSH-1 study is the first large prospective, multicentre randomized trial to compare the two different crush stenting techniques in patients with coronary bifurcation lesions. Previous studies [11] suggested that the clinical outcome was similar between the single stent and the double stent groups in an international randomized trial for bifurcation lesions. The MACE at 6 months was very low but the restenosis rate (19·2%) of the side branch was still high when utilizing the single stent strategy. Hoye [12] *et al*. reported in their study of 231 patients after classical crush stent with a survival free TLR rate of 90·3%, survival free of MACE of 83·5%, possible stent thrombosis of 4·3%, and a restenosis rate of the side branch of 25·3% at 9 months. Another prospective registry by Moussa *et al*. [9] revealed that TLR at 6 months after classical crush stenting using sirolimus-eluting stents was 11·3% but FKBI was performed in 87·5% patients. The most effective strategy to treat bifurcation lesions is still unknown [13,14]. Our study showed a remarkable 100% FKBI rate, a stent thrombosis rate of 1·3%, side-branch restenosis rate of 12·3%, and a survival free TLR rate of 89·5% at 8 months in the DK crush group. Since this is a randomized study, superiority to the classical crush stent strategy is noted.

Effect of randomization on results

Diabetic patients were at high risk for restenosis and MACE after PCI [15,16], and a predictor of TLR after the classical crush technique. [17] In the current study there was no

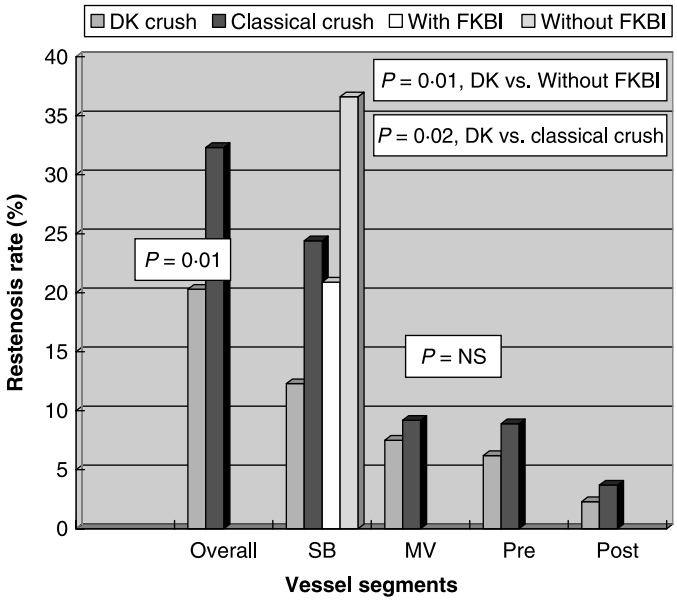

Figure 1 The comparison of restenosis rate at 3 segments between two groups: classical crush vs. double kissing (DK) crush. Overall, as indicated, any one of 3 analysed segments had restenosis. Proximal-MV, pre-bifurcation segment of main vessel; Distal-MV, post-bifurcation segment of main vessel; MV, both pre- and post-bifurcation segments of main vessel; SB, side branch; With FKBI, with final kissing balloon inflation; Without FKBI, without final kissing balloon inflation.

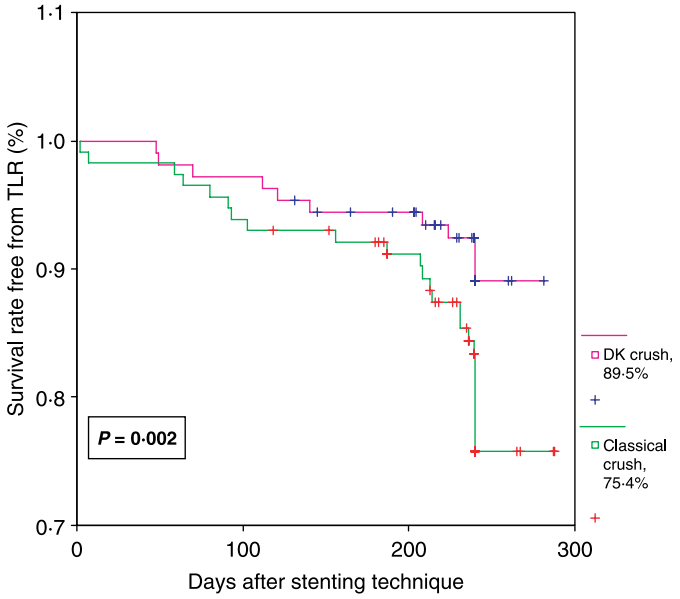

Figure 2 Cumulative survival rate free from target lesion revascularization (TLR) at 8 month follow-up by Kaplan-Meier method. DK, double kissing.

sub-randomization of diabetic patients, and more diabetic patients were randomized to the DK crush than to the classical crush technique. This, if anything, minimized the effectiveness of the DK crush technique.

We previously reported that the DK crush technique was superior to classical crush regarding procedural time, balloons used and contrast volume [17]. However, these advantages were lost in this current randomized study. Of note, smaller guiding catheters were used in DK crush treated patients.

Mechanisms and importance of optimal final kissing balloon inflations

Previous studies have reported that FKBI were necessary to optimize clinical outcomes [8,9,17]. One study reported that a narrow distal left main artery bifurcation angle was associated with less ostial left circumflex (LCX) stent expansion [18]. Dzavik *et al*. concluded that a bifurcation angle ≥ 50° was an independent predictor of MACE after classical crush [19]. Ormiston *et al*. demonstrated that a kissing balloon inflation did not achieve full expansion of the side branch stent with a bifurcation angle of 80° [20]. Conversely, in the current study the bifurcation angle in classical crush without final kissing balloon inflations was lower than that in the other two groups.

Distorted side stent geometry and irregularity in overlapped stent strut layers at the carina of bifurcation are two common geographic characteristics immediately after the classical crush technique. In addition to technical pitfalls i.e. the guide wire is commonly advanced under the side branch stent rather than into the true stent lumen, [10] less expanded side branch stents with irregular and small stent cells after classical crush do not allow for easy advancement of post-dilation balloons. Similar to the present study, previous studies demonstrate that the post-stent MLD is commonly seen at the ostial side branch [20,21]. The main difference between classical and DK crush was the introduction of a first kissing balloon inflation prior to implanting the second stent. This suggests that the first kissing inflation not only repaired the distorted geometry, but also enlarged the cells of the side branch stent allowing easier performance of FKBI. The finding in the current study that left main bifurcation lesions had the highest rate of final kissing balloon inflations supports this concept.

We also found an influence of main vessel stent length and lesion site on FKBI. Explanations include [1] careless overlapping of two main vessel stents at the level of carina and [2] longer main vessel stents may be associated with stent-vessel wall malapposition, resulting in incorrect advancement of the guide wire [20,21]. From subgroup analysis, we found that the success of rate of final kissing inflation was lower when lesions were located at distal right

Table 6 Major adverse cardiac events

	Classical crush				
	Overall	Without final kissing balloon	With final kissing balloon	DK crush	*P* Overall classical vs. DK crush
No. of lesions	156	39	117	155	
Angiographic success (%)	97·4	94·9	98·3	100	0·9
Procedural success (%)	91·1	87·2	92·3	96·1	0·3
In hospital MACE (%)	6·4	7·7	5·9	4·1	0·9
Cardiac death	0	0	0	0	
Q wave MI	0	0	0	0	
Non-Q MI	5·8	7·7	5·9	4·1	0·5
TLR	0·6	2·6	0	0	0·5
TVR	0·6	2·6	0	0	0·5
Stent thrombosis	0·6	2·6	0	0·7	0·7
8-month MACE (%)					
Cumulative	24·4	35·9*	19·7	11·4**	0·02
Cardiac death	1·7	2·5	2·5	0·6	0·5
Q wave MI	3·5	5·1	0·9	1·2	0·7
Non-Q MI	11·1	10·2	8·1	9·1	0·9
TLR	18·9	22·6*	17·8	9·0	0·03
TVR	21·9	26·5*	20·0	10·3	0·03
Stent thrombosis	3·2	5·1	1·7	1·3	1·0

Abbreviations: MACE, major adverse cardiac events; MI, myocardial infarction; TLR, target lesion revascularization; TVR, target vessel revascularization; DK, double kissing.
*$P < 0·01$ comparing classical crush without final kissing inflations to both classical crush with final kissing inflations as well as DK crush.
**$P < 0·05$ comparing classical crush with final kissing inflations to DK crush.

coronary or LCX, compared to lesions involved LAD-D, or distal left main. However, this finding was not included in this manuscript (unpublished data).

Restenosis is highest at the side branch ostium after bifurcation stenting; however, its mechanism is not entirely known. Ge *et al*. proposed that polymer rupture and uneven distribution of stent struts were two possible factors contributing to this phenomenon [17]. Murasato *et al*. reported that final kissing balloon inflations improved the apposition of the stent to the vessel wall; however, the narrowed side branch stent at the overlapping site, and a metal mass limited the complete side branch balloon expansion resulting in severe stent strut malapposition [21,22].

Part of the reason that DK crush stenting can improve the clinical outcomes is by achieving a 100% final kissing balloon inflation and also reducing the unsatisfactory kissing. In the present study unsatisfactory kissing balloon inflation was an independent predictor of TLR. This appeared to have been alleviated by the initial kissing balloon inflation that is part of the DK procedure. Furthermore, unsatisfactory kissing balloon inflations not only affected the side branch ostium, but also increased the restenosis rate in Proximal-MV segment in this study. The mechanisms are yet unknown.

Pathological studies have suggested that bifurcation stenting is associated with increased DES thrombosis [12,23–25]. The cause of DES late stent thrombosis is multifactorial with delayed healing in combination with other clinical and procedural risk factors playing a role. In the current study the only independent predictor of stent thrombosis was the lack of final kissing balloon inflations suggesting that optimal final kissing balloon inflations have the potential to minimize the risks of stent thrombosis within the first year.

Clinical implications

The current observations have important clinical implications. With the introduction of the DK crush stenting technique, a paradigm shift occurs in the crush stenting strategy, displacing the classical crush stenting by the DK crush stenting when treating patients with bifurcation lesions. According to the present results,

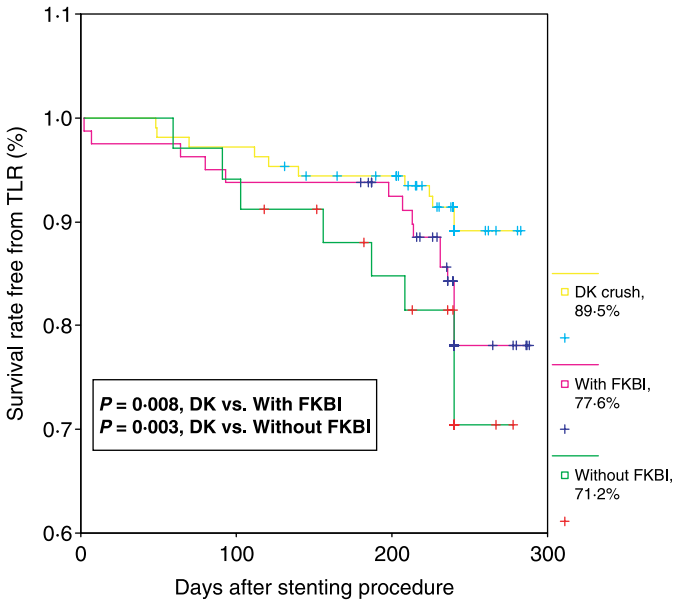

Figure 3 Cumulative survival rate free from target lesion revascularization (TLR) at 8 month follow-up by Kaplan–Meier method. With FKBI, with final kissing balloon inflation; Without FKBI, without final kissing balloon inflation.

the DK crush stenting has reduced the unfavourable outcome, reducing clinical and angiographic restenosis rate. Percutaneous intervention with the use of the DK crush stenting technique seems to be the preferred strategy.

Limitations

The present study was a randomized one but it had an open study design. The operators were aware of the technique used. Operators' experience on procedure times, contrast volumes, balloons used, and how to control the quality of kissing balloon inflations may all have an effect to the outcomes. On the other hand, GP IIbIIIa and IVUS were not used routinely. The data on clinical outcome might be improved. In addition, this was only a randomized trial between the two different crush stents techniques; other strategies, e.g. SKS (simultaneous kissing stents), T stents, V-stents, Y-stents or Culotte stents, etc. were not studied. There is no information to address other stenting techniques.

Conclusions

The DK crush technique for bifurcation DES stenting appears to improve outcome by allowing 100% FKBI and optimizing acute procedural results.

Address

Nanjing First Hospital of Nanjing Medical University, Nanjing, China (S. L. Chen, J. J. Zhang, F. Ye); Beijing Anzhen Hospital of Capital Medical University, Beijing, China (Y. D. Chen); Krishna Heart Institute, India (T. Patel); Tokushio Hospital, Osaka, Japan (K. Kawajiri); Queen Mary Hospital, Hong Kong, China (M. Lee); Beth Israel Hospital, New York, USA (T. W. Kwan); Cardiac Research Foundation, Columbia University, New York, USA (G. Mintz); National University Hospital, Singapore (H. C. Tan).
Correspondence to: Dr S. L. Chen, Cardiological Department, Nanjing First Hospital of Nanjing Medical University, Nanjing 210006, China. Tel./fax: 25-52208048, e-mail: chmengx@126.com; and Dr G. Mintz, Cardiac Research Foundation, Columbia University, New York, USA. e-mail: gsm18439@aol.com

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