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FFR guided PCI on long coronary lesions: 2-year clinical results with 2nd or newer generation DES

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Background. Despite improvements in drug-eluting stent (DES) technology, treatment strategies for long coronary artery lesions remain a controversial issue. The aim of our study was to evaluate the long-term clinical results after FFR guided PCI on long coronary lesions.

Materials and methods. A total of 74 consecutive patients with significant (mean FFR 0.61 ± 0.11) coronary artery lesions ≥30 mm in length were included in the prospective study. All patients were treated with FFR guided PCI implanting newer generation Biolimus, Everolimus or Zotarolimus eluting stents. Clinical endpoints – target vessel revascularization (TVR) and major adverse cardiac events (MACE) – were recorded at 1 and 2 years.

Results. 100% angiographic procedure success was achieved, the mean post procedural FFR was 0.88 ± 0.06. At 2-year follow-up, 6 (8.1%) patients had ischemia driven TVR, all within the first 12 months. There were no target vessel related acute coronary syndromes and definite stent thromboses in the study group. At 2 years, the total MACE rate was 29.7%. There was a trend towards a higher TVR rate in patients with overlapping DES vs single DES implanted (9.6 vs 4.5%, $p = 0.6$). On regression analysis, the total stent length had no influence on the TVR rate.

Conclusions. At 2 years after stenting long coronary lesions with newer generation DES the TVR rate was 8.1%, which is acceptable in the high cardiovascular risk population with diffuse coronary artery disease. The total stent length did not affect the long-term clinical outcomes.

Keywords: long coronary lesions, FFR guided PCI, drug-eluting stent

INTRODUCTION

There is still a controversy in the treatment of long coronary lesions. In the case of diffuse coronary artery disease the optimal extent of PCI is not well established and is usually operator dependent. Earlier data with bare metal stents (BMS) and first generation drug eluting stents (DES) indicate that the total stent length is associated with a risk of stent restenosis and thrombosis (1–3). The first generation DES have also been associated with the increased rates of very late (>1 year) stent thrombosis (4–5). The introduction of new generation DES has further reduced the rates of adverse clinical events and supports the opinion that the preferred strategy is to cover the entire lesion, because the residual plaque burden is known to be a predictor for stent edge restenosis (6). The large study comparing the first and new generation DES found the association between the stent length and long-term clinical outcomes

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only in the first generation DES group, concluding that the stent length might not be associated with clinical outcomes in the new generation DES era (7). The retrospective registry based study showed that the ultra-long (≥50 mm) second generation DES implantation is associated with higher target lesion revascularization (TLR) rates (8). Therefore we conducted a prospective study to evaluate the safety and clinical efficacy of the newer generation DES after stenting long coronary lesions.

MATERIALS AND METHODS

This was a prospective single center observational study of the clinical outcomes. The study protocol was approved by the local Ethics Committee, and all patients signed a written informed consent.

The inclusion criteria were as follows:

– Stable angina pectoris or acute coronary syndrome.

– At least one lesion ≥30 mm in length in major coronary artery ≥50% stenosis by visual assessment.

– FFR <0.8 in the target vessel distally to the lesion.

Patients with ST-elevation MI (STEMI), contraindication to long-term dual antiplatelet therapy, with an expected survival <1 year, or with an allergy to sirolimus, biolimus, everolimus or zotarolimus were not included. Chronic total occlusions (CTO) were also excluded from the study.

A conventional FFR guided PCI technique was used. The FFR was measured with a coronary pressure guidewire in the distal segment of the target vessel (PressureWire, St. Jude Medical, Uppsala, Sweden) at maximal hyperaemia, induced by an intravenous adenosine infusion at a rate of 140 μg/kg/min.

Stent implantation was performed according to current standard techniques. All patients were treated with Biolimus A9 (Biomatrix Flex, Biosensors, Newport Beach, California), Everolimus (Xience Xpedition, Abbott Vascular, IL) or Zotarolimus (Resolute Integrity, Medtronic Vascular, Santa Rosa, CA) eluting stents (Table 1). An angiographically successful procedure was defined as a final TIMI flow grade of 3 and residual angiographic diameter stenosis ≤20%.

All patients were on optimal medical therapy including dual antiplatelet agents for 12 months, statin, a beta blocker and an angiotensin-converting–enzime (ACE) inhibitor or an angiotensin II–receptor blocker.

Table 1. Stents used by type

Stent type	No. (%)
Biolimus A9 eluting with biodegradable polymer	107 (80.5%)
Zotarolimus eluting with durable polymer	16 (12.0%)
Everolimus eluting with durable polymer	10 (7.5%)

QCA was performed according to the standard procedure using the QAngio XA 7.3 (Medis Medical Imaging Systems) software.

Angiographic follow-up was scheduled at 9 months, clinical follow-up at one and two years.

Study end points and definitions

Target vessel revascularization (TVR) at one and two years was defined as any repeated PCI or surgical bypass of any segment of the target vessel (9).

Major adverse cardiac events (MACE) at 1 and 2 years were defined as a composite of all-cause death, myocardial infarction, target vessel and non-target vessel revascularization.

Late lumen loss (LLL) was defined as the difference in millimetres in the minimal luminal diameter of a stented segment immediately after the procedure and at follow-up.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), categorical variables were expressed as numbers or percentages. Continuous variables with a normal distribution were compared using a Student's t test, otherwise, nonparametric Wilcoxon's signed-rank tests were used. Categorical variables were compared by using χ^2 or a Fisher exact test. Binary logistic regression analysis was performed to assess the associations of dichotomous dependent variables and independent variables. P value <0.05 was considered significant. Statistical analysis was performed with SPSS version 21.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

In total, 74 patients with hemodynamically significant lesions in one of the major coronary arteries (FFR ≤ 0.8) were enrolled into the study. Baseline

clinical, lesion, and procedural characteristics are listed in tables 2, 3 and 4, respectively. The mean lesion length was 39.04 ± 14.11 mm. 1.80 ± 0.62 stents per lesion were implanted with a mean total stented segment length of 50.72 ± 14.6 mm. A successful angiographic result was achieved in all patients. A slight postprocedural elevation of cardiac biomarker values was observed in all cases, 5 (6.8%) of them were classified as a PCI related MI according to the consensus criteria (10). The mean post procedural FFR was 0.88 ± 0.06.

At 2-year follow-up, 6 (8.1%) of the patients had ischemia driven TVR, all within the first 12 months. There were no definite stent thromboses and target vessel related acute coronary syndromes in the study group. At 2 years, the total MACE rate was 29.7%. 3 (4.1%) cardiac deaths were reported, none of them was target vessel related (Table 5).

The angiographic in-stent late lumen loss was 0.24 ± 0.41.

The regression analysis was performed to evaluate the influence of the total stent length, reference vessel diameter, stent diameter and presence of diabetes on the clinical endpoints. There was no association between neither of these variables and MACE or TVR rates at 24 months. No independent predictors of TVR were identified (Table 6). There was a trend towards a higher TVR rate in patients with overlapping DES vs single DES implanted, though not statistically significant (9.6 vs 4.5%, $p = 0.6$).

Table 2. Baseline clinical characteristics

No. of patients	74
Age, y	67.8 ± 9.9
Male sex, No. (%)	54 (73.0)
Diabetes mellitus, No. (%)	16 (21.6)
Hypertension, No. (%)	67 (90.5)
Hyperlipidemia, No. (%)	60 (81.1)
Current smoker, No. (%)	14 (18.9)
Previous PCI, No. (%)	26 (35.1)
Previous CABG, No. (%)	2 (2.7)
Previous myocardial infarction, No. (%)	27 (36.5)
Multivessel disease	62 (83.8)
Clinical indication, No. (%)	
Stable angina	53 (71.6)
Unstable angina	17 (23.0)
NSTEMI	4 (5.4)

Table 3. Lesion characteristics

Target vessel, No. (%)	
Left anterior descending	61 (82.4)
Left circumflex	8 (10.8)
Right coronary	5 (6.8)
Bifurcation lesions, No. (%)	29 (39.2)
Severe calcification, No. (%)	17 (23.0)
Lesion length, mm	39.04 ± 14.11
Baseline FFR	0.61 ± 0.11

Table 4. Procedure characteristics

No. of stents used at the target lesion, No. (%)	
1 stent	22 (29.7)
2 stents	46 (62.2)
3 stents	5 (6.8)
4 stents	1 (1.3)
Mean	1.80 ± 0.62
Overlapping stents, No. of patients (%)	52 (70.3)
Length of stents used, mm	50.72 ± 14.6
Average stent diameter, mm	3.21 ± 0.36
Maximal implantation pressure, atm	14.49 ± 2.74
Direct stenting, No. (%)	5 (6.8)
Post-dilatation, No. (%)	61 (82.4)
Maximal post-dilatation pressure, atm	18.38 ± 3.67

DISCUSSION

In the present study with the newer generation DES we reported a 2-year TVR rate of 8.1%. All TVR occurred within the first 12 months and reached the peak in the period of scheduled angiographic follow up. There was no target vessel related events during the second year of follow up. The reported TVR rate in our study is higher than expected in general population, but is comparable to the rates reported by Honda et al. with the long DES (7.2% when the total stent length was 20–50 mm and 13.5% with the stents ≥50 mm) (8). In support to the most studies with newer generation DES and in contrast to the studies with the first generation DES and BMS (2, 3, 11), there was no association between the total stent length and TVR rate at follow up. Though, there was a trend towards a higher TVR rates in patients with overlapping DES implanted (9.6% vs 4.5%) (Fig. 1), suggesting that the double stent layer at the sites of stent overlap could possibly be related to a risk of DES restenosis. However, this difference was not statistically significant. The impact of overlapping first generation DES on clinical outcomes was analyzed by Raber et al., who reported higher rate of TVR, total MACE and late lumen loss in the overlapping first generation DES

Table 5. Clinical endpoints at follow up

Clinical endpoints (N = 74)	0–12 months	12–24 months	At 24 months
Death	2 (2.7%)	1 (1.3%)	3 (4.1%)
Cardiac, No. (%)	2 (2.7%)	1 (1.3%)	3 (4.1%)
Not cardiac, No. (%)	0 (0%)	0 (0%)	0 (0%)
Myocardial infarction	5 (6.8%)	2 (2.7%)	7 (9.5%)
Periprocedural MI, No. (%)	5 (6.8%)	NA	5 (6.8%)
Target vessel related MI, No. (%)	0 (0%)	0 (0%)	0 (0%)
Not target vessel related MI, No. (%)	0 (0%)	2 (2.7%)	2 (2.7%)
Definite stent thrombosis, No. (%)	0 (0%)	0 (0%)	0 (0%)
Target vessel revascularization, No. (%)	6 (8.1%)	0 (0%)	6 (8.1%)
Other vessel revascularization, No. (%)	5 (6.8%)	3 (4.0%)	8 (10.8%)
Major adverse cardiac events, No. (%)	18 (24.3%)	4 (5.4%)	22 (29.7%)

Table 6. Independent predictors of 2-year TVR

Variable	OR (95% CI)	*p* value
Total stent length (per 10-mm increase)	0.96 (0.86–1.01)	0.41
Overlapping stent	**2.23 (0.25–20.32)**	**0.48**
Bifurcation lesion	**3.44 (0.59–20.15)**	**0.17**
RVD (per 0.2-mm increase)	0.74 (0.03–18.04)	0.85
MLD (per 0.5-mm increase)	0.43 (0.02–8.96)	0.58
NSD (per 0.25-mm increase)	0.03 (0.00–4.63)	0.17
Diabetes Mellitus	**1.93 (0.32–11.62)**	**0.47**

RVD is reference vessel diameter; MLD is minimal luminal diameter; NSD is nominal stent diameter.

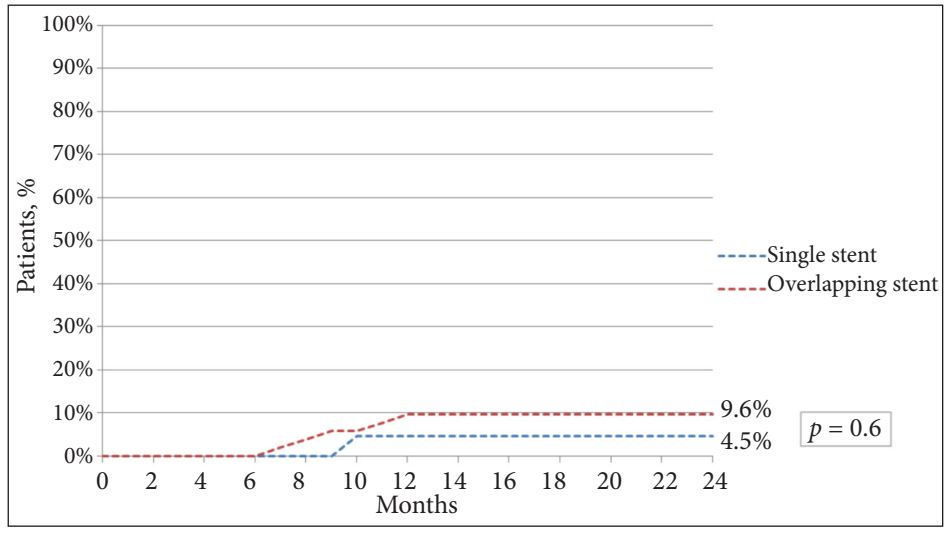

Fig. 1. TVR at follow up in single stent and overlapping stent groups

group (12). Kitabata et al. compared clinical endpoints in the first and second generation overlapping DES, concluding that stent overlap with EES was associated with lower rates of MACE and stent thrombosis than the first-generation DES. The reported TVR rates were 3.7 vs 9.1 vs 11.7% in the EES, SES and PES groups, respectively (13).

In contrast to the studies with the first generation DES, where the rate of the late stent thrombosis was >2% (14), there was no definite stent thrombosis reported in the current study. Considering the mean stent length >50 mm, we can assume that the total length of newer generation DES implanted does not affect the long-term patient safety.

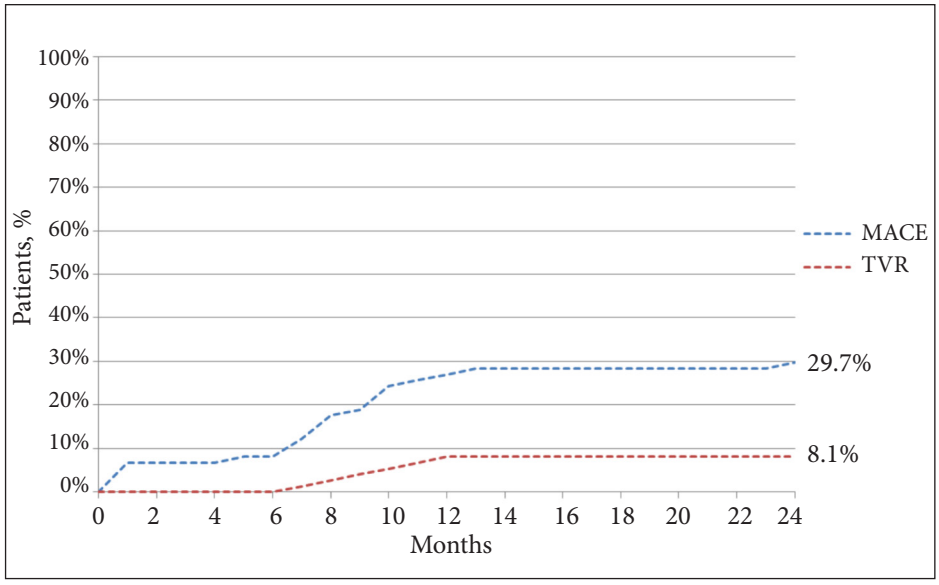

Fig. 2. MACE and TVR at follow up

In the current study the overall incidence of MACE at 2 years was high at a rate of 29.7% (Fig. 2), mostly driven by non-target vessel related events (revascularization, MI and cardiac death) (Table 5). This could be explained by the high complexity of the study population and high rate of comorbidities and multivessel disease (Table 2). We did not exclude severely ill patients from the inclusion to the study because they are common in daily practice and represent the greatest challenge of coronary revascularization. The results of the current study show that PCI of the long coronary lesions with a newer generation DES is a reasonable and safe option, especially in the high CABG risk patients with diffuse coronary atherosclerosis.

CONCLUSIONS

At 2 years after stenting long coronary lesions with newer generation DES the TVR rate was 8.1%, which is acceptable in the high cardiovascular risk population with diffuse coronary artery disease. The total stent length did not affect the long-term clinical outcomes.

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ILGŲ VAINIKINIŲ ARTERIJŲ SUSIAURĖJIMŲ PKI VADOVAUJANTIS FRAKCIJINIO TĖKMĖS REZERVO TYRIMU: DVEJŲ METŲ KLINIKINIAI REZULTATAI NAUDOJANT ANTROS IR NAUJESNĖS KARTOS VAISTAIS DENGTUS STENTUS

Santrauka

Darbo tikslas. Nors vaistais dengtų stentų (VDS) technologijos nuolatos tobulinamos, ilgų vainikinių arterijų pažeidimų gydymo taktika išlieka diskutuotina. Mūsų tyrimo tikslas – įvertinti ilgalaikius klinikinius rezultatus po ilgų vainikinių arterijų pažeidimų perkutaninės koronarinės intervencijos (PKI), atliktos vadovaujantis frakcinio tėkmės rezervo tyrimu (FTR).

Tyrimo medžiaga ir metodai. Iš viso 74 pacientai, kuriems nustatytas reikšmingas (vidutinis FTR 0,61 ± 0,11) vainikinės arterijos pažeidimas, ilgesnis nei 30 mm, buvo įtraukti į prospektyvinį tyrimą. Visiems pacientams implantuoti antros ir naujesnės kartos Biolimus, Everolimus ar Zotarolimus išskiriantys stentai. Stentuotos kraujagyslės pakartotina revaskuliarizacija (SKR) ir didieji nepageidaujami kardiovaskuliniai įvykiai buvo stebimi dvejus metus.

Rezultatai. Visiems pacientams atlikta sėkminga PKI, vidutinis FTR po procedūros buvo 0,88 ± 0,06. Per dvejų metų stebėjimo laikotarpį 6 (8,1 %) pacientams dėl išemijos buvo atlikta SKR (visiems per pirmus 12 mėn.). Tiriamųjų grupėje stentuotos kraujagyslės nulemtų ūminių koronarinių sindromų ir stento trombozės atvejų nenustatyta. Didžiųjų nepageidaujamų kardiovaskulinių įvykių dažnis per dvejų metų stebėjimo trukmę buvo 29,7 %. Stebėta dažnesnės SKR tendencija pacientams, kuriems implantuoti keli persidengiantys VDS, palyginti su pacientais, kuriems implantuotas vienas VDS (9,6 ir 4,5 %, $p = 0,6$). Atlikus logistinę regresinę analizę nustatėme, kad bendras stento ilgis neturėjo įtakos SKR dažniui.

Išvados. Pacientams, sergantiems toli pažengusia (difuzine) koronarine širdies liga su ilgais vainikinių arterijų pažeidimais, gydymas naujesnės kartos VDS yra saugi ir efektyvi gydymo alternatyva (SKR dažnis per dvejus metus siekė 8,1 %). Bendras implantuotų stentų ilgis neturėjo įtakos ilgalaikiams klinikiniams rezultatams.

Raktažodžiai: ilgi vainikinių arterijų pažeidimai, PKI, vaistais dengtas stentas