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Comparison of Fractional Flow Reserve-Guided Revascularization Strategies in Isolated Proximal Left Anterior Descending Coronary Artery Disease

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Abstract

The data about FFR-guided revascularization in isolated proximal LAD disease are limited and studies comparing long-term outcomes of FFR-guided PCI versus FFR-guided CABG in single-vessel proximal LAD disease are lacking. We aimed to assess the 4-year long-term safety and effectiveness of fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) and FFR-guided coronary artery bypass graft surgery (CABG) for the treatment of proximal left anterior descending (LAD) lesions. The study included 129 patients with functionally significant (FFR ≤ 0.80) isolated proximal LAD stenosis (PCI, 88 patients vs. CABG, 41). Clinical endpoints were assessed by Kaplan-Meier method and compared by the log-rank test. At a mean follow-up time of 47 ± 12 months, a higher incidence of myocardial infarction in the PCI group (PCI: 32% vs. CABG: 15%; p = 0.003) and a higher incidence of stroke in the CABG group (CABG: 3 (7%) vs. PCI 0 (0%); p = 0.031) were observed. However, there were no significant differences in the primary composite endpoint, death and target vessel revascularization between PCI and CABG groups. The PCI and CABG in isolated proximal LAD lesions yielded similar long-term outcomes regarding the primary composite clinical endpoints. However, stroke was more frequent in the CABG group than in the PCI group.

Keywords

Coronary Artery Bypass Grafting, Fractional Flow Reserve, Percutaneous Coronary Intervention

1. Introduction

The presence of a significant obstructive coronary lesion of the proximal left anterior descending coronary artery (LAD) is a commonly approved indication for treatment by either percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) [1] [2] [3]. Few small trials had been done using these modalities of revascularization in patients with single-vessel LAD disease [4] [5] [6].

The gold-standard method to detect coronary artery disease is still coronary angiography. Although coronary angiography has been used to determine lesion severity, in moderate coronary artery stenosis (50% - 70%), the presence of ischemia is uncertain. Therefore, coronary flow reserve and fractional flow reserve (FFR) are developed in order to assess hemodynamically important coronary artery stenosis. FFR is a pressure-wire-based index that is utilized during coronary angiography to evaluate the coronary artery stenosis severity by inducing myocardial ischemia [7] [8] [9]. It is shown that, if there is an increase in microvascular resistance in the coronary artery, the ratio of FFR is decreased.

Compared to angiography-guided alone either FFR-guided PCI or FFR-guided CABG is recommended in multi-vessel coronary disease due to the reliable clinical outcome data [10] [11] [12] [13] [14]. However, the data about FFR-guided revascularization in isolated proximal LAD disease are limited [15]. Furthermore, studies comparing long-term outcomes of FFR-guided PCI versus FFR-guided CABG in single-vessel proximal LAD disease are lacking. Hence, the aim of this trial was to determine long-term outcomes associated with FFR-guided revascularization modalities of PCI versus CABG in single-vessel proximal LAD.

2. Materials and Methods

2.1. Patient Selection

In this retrospective study, patients who had an intermediate stenosis of the LAD artery at coronary angiography and subsequently underwent FFR measurement in between February 2007 and October 2013 were included (n = 129). Inclusion criteria were having LAD disease defined as the >50% diameter stenosis and FFR value less than 0.80 with no other stenosis more than 30% in the other coronary arteries. Exclusion criteria were having additional valvular heart disease requiring treatment, overt congestive heart failure, other significant coronary lesions, atrial fibrillation, atrial flutter, severe bradycardia, severe left ventricular hypertrophy (>15 mm in any segment of the left ventricle) and presenting with an acute coronary syndrome. Patients were divided into two groups FFR-guided PCI and FFR-guided CABG. Patients with long coronary lesions with severe tortuosity, heavy calcification, ostial location, bifurcation/trifurcation feature and diffusely diseased distal segments that were not favorable for PCI were in the CABG group. Follow-up was assessed by telephone interview and medical record for every patient was reviewed. Major cardiac events were defined as the overall death, target vessel revascularization (TVR), cerebrovascular accident

(CVA) and myocardial infarction (MI). The TVR was defined as any percutaneous or surgical revascularization performed at the follow-up either to the index study vessel or the related vascular graft conduit.CVA was defined as ischemic or hemorrhagic stroke with a transient or a permanent neurological deficit. MI was defined as Type 1 (spontaneous MI), Type 2 (MI secondary to an ischemic imbalance), Type 3 (MI resulting in death when biomarker values are unavailable), Type 4 (MI related to PCI) and Type 5 (MI related to CABG) according to the previously published Third universal definition of myocardial infarction [16]. In all patients, a high-resolution B-mode ultrasonography was performed to detect stenosis of the common carotid arteries using an instrument generating a wide-band ultrasonic pulse with a middle frequency of 7.5 MHz (Siemens Elegra Ultrasonography Systems, Tokyo, Japan). Significant carotid artery disease was defined as any stenosis over 70% in the internal carotid artery without any symptoms. The study protocol was approved by the local ethics committee of our hospital.

2.2. Coronary Angiography

Coronary angiography was performed by a standard percutaneous femoral or radial approach with 6 F or 7 F diagnostic or guiding catheters. After administration of intravenous heparin 100 IU/kg, a 0.014-inch sensor tipped PCI guide wire (Pressure Wire, St. Jude Medical, and Uppsala, Sweden) was calibrated and introduced into the guiding catheter. The wire was introduced up to the tip of the guiding catheter, and it was confirmed that the pressure measured by the pressure monitoring guide wire was equal to the pressure measured by the guiding catheter. Next, the wire was advanced into the LAD until the pressure sensor was positioned in the mid to the distal part of the LAD. Adenosine was given to induce maximum hyperemia, either intravenously (140 mcg/kg/min) or by intracoronary bolus (150 - 220 mcg). Fractional flow reserve was defined as the ratio between mean distal coronary pressure and mean aortic pressure; both measured simultaneously at maximal hyperemia.

2.3. Coronary Artery Bypass Graft Procedure

All patients had received left internal mammary artery graft for isolated significant LAD disease that was performed on-pump with conventional cardioplegic methods by the experienced surgeons.

2.4. Statistical Analysis

All analyzes were performed with Statistical Package for the Social Sciences (SPSS) version 16 (SPSS Inc., Chicago, IL). Continuous variables are expressed as mean ± SD. Categorical variables are reported as frequencies and percentages. Normal distribution was assessed by the Kolmogorov-Smirnov test. The student t-test was used to compare continuous variables. Comparisons between categorical variables were evaluated using the 2-tailed Fisher exact test or Pearson χ^2

test, as appropriate. Clinical end points were assessed by Kaplan-Meier method and compared by the log-rank test. A probability value of 0.05 was considered statistically significant.

3. Results

Of the 129 patients included in the study, 41 (31.8%) patients had undergone CABG and 88 (68.2%) patients PCI. The mean follow-up was 47 ± 12 months. Baseline clinical characteristics are summarized in Table 1. Among baseline demographic characteristics except for hypertension, smoking and creatinine levels, there were no differences between the CABG and PCI groups.

In the PCI group, the percentage of the patients with hypertension was significantly higher than the CABG group (75% vs. 54%, p = 0.015). In the CABG group, creatinine levels were statistically greater than the PCI group (1.03 ± 0.24 mg/dl vs. 0.91 ± 0.24 mg/dl, p = 0.002). In the CABG group, the percentage of the current smokers was significantly higher than the PCI group (68% vs. 48.9 %, p = 0.039). In the PCI group, 18 (20.4%) patients received drug-eluting stents while 70 (79.6%) patients received bare-metal stents. Based on the lesion characteristics, in the CABG group 13 (31%) patients had bifurcation lesions

Table 1. Baseline clinical characteristics.

Variables	FFR-guided CABG (n = 41)	FFR-guided PCI (n = 88)	P value
Age	63.20 ± 10.94	62.93 ± 7.96	0.877
Female/Male Sex (*n*)	7/34	24/64	0.207
Glucose	116.52 ± 32.19	138.41 ± 75.07	0.410
Creatinine	1.03 ± 0.24	0.91 ± 0.24	0.002
Total Cholesterol	183.34 ± 49.85	189.02 ± 54.36	0.561
LDL Cholesterol	115.02 ± 42.29	116.29 ± 43.04	0.879
HDL Cholesterol	40.88 ± 12.35	40.93 ± 12.35	0.574
Triglycerides	154.29 ± 99.90	153.82 ± 78.32	0.838
Hypertension	22 (54%)	66 (75%)	0.015
Diabetes Mellitus	14 (34%)	41 (47%)	0.183
Smoking	28 (68%)	43 (48.9%)	0.039
Carotid artery disease	4 (9.8%)	8 (6.8%)	0.754
Aspirin	40 (97.6%)	88 (100%)	0.318
Clopidogrel	8 (19.5%)	88 (100%)	<0.001
B-blocker	35 (85.4%)	73 (83%)	0.730
ACEI/ARB	25 (61%)	48 (54.5%)	0.493
Statin	33 (80.5%)	74 (84.1%)	0.612

ACEI: Angiotensin-Converting Enzyme Inhibitor, ARB: Angiotensin Receptor II Blocker, CABG: Coronary Artery Bypass Grafting, PCI: Percutaneous Coronary İntervention, LDL: Low-Density Lipoprotein, HDL: High-Density Lipoprotein.

(4 with heavy calcified lesions), 3 had trifurcation lesions, 9 had ostial LAD lesions (3 with distal disease, 2 with long calcified lesions), 6 patients had long calcified lesions (4 with long lesion length, 3 with bifurcation), 10 patients had tortuous lesions (2 with bifurcation).

During a mean follow-up of 47 ± 12 months, the rate of MI and CVA differed between the two groups: Of the 88 patients in the PCI group, 28 (32%) had MI while in the CABG group 6 (15%) had MI. The difference was statistically significant (p = 0.003). 8 patients in the PCI group and 1 patient in the CABG group were considered as post-procedural MI. The other MIs occurred during the outpatient follow-up. Of the 88 patients in the PCI group, none (0%) experienced CVA while in the CABG group 3 (7%) had CVA (p = 0.031). Of the patients who experienced CVA, one was a transient ischemic attack while the others had permanent neurological dysfunction. The type of the CVA was thromboembolic, and all of them happened within three days after the procedure. Neither the rate of overall death nor the TVR rate differed between the groups (Table 2).

Subgroup analysis of the patients with hypertension showed that creatinine levels were statistically higher in the CABG group than the PCI group (1.07 ± 0.28 mg/dl vs. 0.91 ± 0.27 mg/dl, p = 0.006) and the number of current smokers was also higher in the CABG group than PCI group (14 (64%) vs. 26 (40%), p = 0.048). Moreover, there was a significant difference between the two groups regarding prior MI (PCI 25 (38%) vs. CABG 3 (14%); p = 0.034), and CVA occurred only in the CABG group (3, 14%). All combined endpoints except for CVA and death did not differ between the two groups. CVA and death showed a statistically significant difference favoring the CABG arm (CABG 7 (32%) vs. PCI 6 (9%), p = 0.016).

The Kaplan-Meier survival analysis for the CVA is shown in Figure 1. The incidence of CVA was significantly higher in the CABG arm.

Table 2. Clinical events at follow-up.

	FFR-guided CABG	FFR-guided PCI	P value
TVR	4 (10%)	18 (21%)	0.132
Death	6 (15%)	7 (8%)	0.345
Stroke	3 (7%)	0 (0%)	0.031
MACEs	0 (0%)	2 (2%)	1.000
Death/MI	11 (27%)	31 (35%)	0.343
Death/MI/CVA	13 (32%)	31 (35%)	0.695
MI/Death/CVA/TVR	13 (32%)	31 (35%)	0.695
Death/CVA	8 (20%)	7 (8%)	0.076
MI/CVA	9 (22%)	28 (32%)	0.249

FFR: Fractional Flow Reserve, MACEs: Major Adverse Cardiovascular Event, MI: Myocardial Infarction, TVR: Target Vessel Revascularization, CVA: Cerebrovascular Accident, CABG: Coronary Artery Bypass Grafting, PCI: Percutaneous Coronary İntervention.

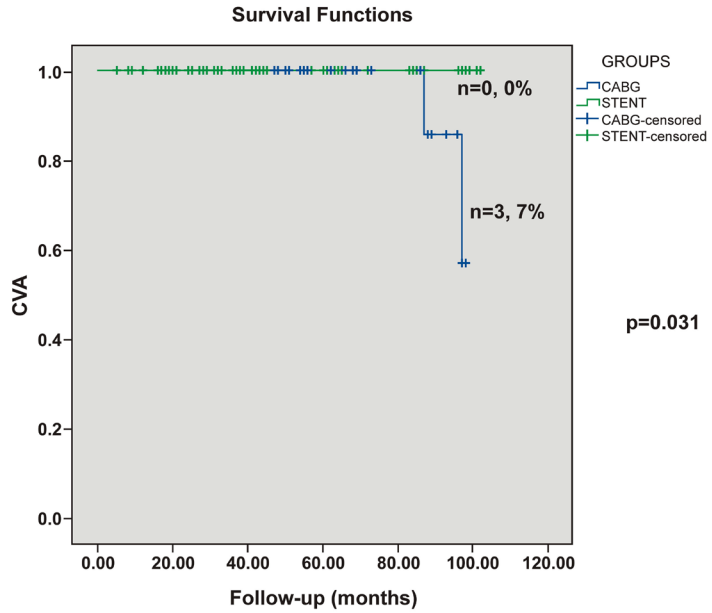

Figure 1. The Kaplan-Meier survival analysis for the Cerebrovascular accident.

Evaluation of all the combined clinical endpoints showed that the incidence of CVA and death was higher in the CABG group when compared to PCI group, however, this was not statistically significant (CABG 20%, versus PCI 8%, p = 0.076).

4. Discussion

In this study, the rate of stroke was higher in the CABG group than in the PCI group, but the rate of myocardial infarction was higher in the PCI group than in the CABG group. Based on survival rates, the present study did not reveal any superiority of PCI over CABG treatment in patients with isolated proximal LAD coronary artery disease because the survival rate free of major adverse cardiac events (MACE) (all-cause mortality, myocardial infarction, stroke and target vessel revascularization) were similar in both groups.

In the present study, most of the patients received bare metal stents (BMS) (79.6%) and the adverse event rate was 8% in the PCI group and 20% in the CABG group. In the literature, several studies have compared the long-term clinical outcomes of PCI with CABG, either BMS or drug-eluting stents (DES) and without FFR, for patients with isolated proximal LAD coronary artery disease [17] [18] [19]. The SIMA (Stenting versus Internal Mammary Artery Grafting) Trial demonstrated higher rates of TVR in the BMS group and the rate of any adverse cardiac event was significantly higher in the PCI group compared to CABG group. However, during the follow-up period similar mortality and MI rates were observed [17]. Different from that study, we did not observe any significant difference in TVR rate between the groups; however, higher incidence of MI was found in the PCI group. The possible reasons for the higher rate of MI were that the percentage of the current smokers and the number of the patients

with hypertension were significantly higher in the PCI group than the CABG group. According to our results, even in the preference of BMS FFR-guided stenting for isolated proximal LAD coronary artery lesions may provide lower TVR rates by avoiding revascularization of hemodynamically non-significant stenosis. However, we observed relatively higher event rate in the CABG group (20%) compared to SIMA trial (17%) that we included stroke in the combined endpoint definition, which may explain the higher event rate in the CABG group. Also in the CABG group, creatinine levels were higher, and there were more complex coronary lesions, including heavy calcified lesions. Therefore, we can conclude that concomitant presence of calcified lesions in the ascending aorta and higher creatinine levels may have led to higher incidence of stroke in the CABG group even though the presence of severe carotid artery disease did not reach statistical significance between the PCI and CABG groups. In multi-vessel disease, low SYNTAX scores make PCI as an acceptable alternative to CABG; however, present data supports that CABG is the preferred therapy due to the lower rates of adverse events compared to PCI [20], especially in the diabetic population [21]. Among patients having isolated stenosis of the LAD coronary artery, in the studies comparing DES with CABG, similar rates of adverse events including death, MI and TVR were observed [5] [18]. Although in our study patients mainly received BMS, FFR-tailored therapy might have resulted in a lack of relevant differences between groups. This explanation would align with the above-mentioned DES studies with long-term follow-up concerning MACE by revascularization for functionally significant stenosis only.

In the present study, during 4-years follow-up, we did not observe any difference in the survival rate free of MACE for patients in the PCI group, which was 65% and 68% in the CABG group. Botman *et al.* compared FFR-guided PCI versus FFR-guided CABG in multi-vessel coronary artery disease [13]. During 2-years follow-up patients with multi-vessel disease treated either PCI or CABG yielded similar event-free survival rates (80.9% in the PCI group vs. 81.6% in the CABG group), which was lesser than our event-free survival rates. However, in our study, the follow-up time was longer than the follow-up of the study mentioned above that might have directly affected MACE rates. After searching the literature, we found only one study utilizing FFR for isolated proximal LAD coronary artery disease [15]. Along with our study comparing revascularization strategies, Muller *et al.* compared the long-term clinical outcomes of age- and sex-matched controls to patients with isolated LAD stenosis [15]. These patients deferred PCI or CABG revascularization based on (FFR ≥ 0.80). The study showed a similar 5-year survival estimate in both medical and control groups. However, it must be noted that the study was not designed to determine the superiority of either FFR-guided CABG or FFR-guided PCI for all patients with isolated proximal LAD disease. Nonetheless, the study is important because its cohort included 166 patients who underwent a revascularization procedure when FFR was <0.80. In that study, only 25% of patients received drug-eluting stents. At 5 years, the Kaplan-Meier percent survival free of death, myocardial

infarction, or target vessel revascularization estimate was 89.7% in the medical group versus 68.5% in the revascularization group (PCI and CABG both). Also, the study's survival rate free of MACE for the revascularization group paralleled our findings.

The present study has several limitations. It was a retrospective, single-center, nonrandomized study; treatment assignment was based on coronary pressure measurements. The number of patients was small particularly a special subpopulation of isolated proximal LAD patients. This was unavoidable, however, as the intent of the study was not to compare PCI to CABG but to evaluate an FFR-guided approach to treating patients with proximal LAD disease.

5. Conclusion

This retrospective study has demonstrated that performing FFR-guided revascularization in proximal LAD disease, using either PCI or CABG, yielded similar favorable outcomes concerning survival. However, the results indicated a higher incidence of MI in the PCI group and a higher incidence of CVA in the CABG group.

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Conflict of Interests

We declare no conflicts of interests.

References

[1] Fox, K., Garcia, M.A., Ardissino, D., Buszman, P., Camici, P.G., Crea, F., *et al.* (2006) Guidelines on the Management of Stable Angina Pectoris: Executive Summary: The Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology. *European Heart Journal*, **27**, 1341-1381. https://doi.org/10.1093/eurheartj/ehl001

[2] Klein, L.W., Weintraub, W.S., Agarwal, J.B., Schneider, R.M., Seelaus, P.A., Katz, R.I., *et al.* (1986) Prognostic Significance of Severe Narrowing of the Proximal Portion of the Left Anterior Descending Coronary Artery. *American Journal of Cardiology*, **58**, 42-46. https://doi.org/10.1016/0002-9149(86)90238-9

[3] Yusuf, S., Zucker, D., Peduzzi, P., Fisher, L.D., Takaro, T., Kennedy, J.W., *et al.* (1994) Effect of Coronary Artery Bypass Graft Surgery on Survival: Overview of 10-Year Results from Randomized Trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet*, **344**, 563-570. https://doi.org/10.1016/S0140-6736(94)91963-1

[4] Toutouzas, K., Patsa, C., Vaina, S., Tsiamis, E., Vavuranakis, M., Stefanadi, E., *et al.* (2007) Drug Eluting Stents versus Coronary Artery Bypass Surgery in Patients with Isolated Proximal Lesion in Left Anterior Descending Artery Suffering from Chronic Stable Angina. *Catheterization Cardiovascular Interventions*, **70**, 832-837. https://doi.org/10.1002/ccd.21246

[5] Thiele, H., Neumann-Schniedewind, P., Jacobs, S., Boudriot, E., Walther, T., Mohr, F.W., *et al.* (2009) Randomized Comparison of Minimally Invasive Direct Coronary Artery Bypass Surgery versus Sirolimus-Eluting Stenting in Isolated Proximal Left Anterior Descending Coronary Artery Stenosis. *American College of Cardiology*, **53**, 2324-2331. https://doi.org/10.1016/j.jacc.2009.03.032

[6] Drenth, D.J., Veeger, N.J., Winter, J.B., Grandjean, J.G., Mariani, M.A., van Boven, A.J., *et al.* (2002) A Prospective Randomized Trial Comparing Stenting with Off-Pump Coronary Surgery for High-Grade Stenosis in the Proximal Left Anterior Descending Coronary Artery: Three-Year Follow-Up. *American College of Cardiology*, **40**, 1955-1960. https://doi.org/10.1016/S0735-1097(02)02536-6

[7] Pijls, N.H., De Bruyne, B., Peels, K., Van Der Voort, P.H., Bonnier, H.J., Bartunek, J., *et al.* (1996) Measurement of Fractional Flow Reserve to Assess the Functional Severity of Coronaryartery Stenoses. *New England Journal of Medicine*, **334**, 1703-1708. https://doi.org/10.1056/NEJM199606273342604

[8] De Bruyne, B., Pijls, N.H., Bartunek, J., Kulecki, K., Bech, J.W., De Winter, H., *et al.* (2001) Fractional Flow Reserve in Patients with Prior Myocardial Infarction. *Circulation*, **104**, 157-162.

[9] Pijls, N.H., Van Gelder, B., Van der Voort, P., Peels, K., Bracke, F.A., Bonnier, H.J., *et al.* (1995) Fractional Flow Reserve: A Useful Index to Evaluate the Influence of an Epicardial Coronary Stenosis on Myocardial Blood Flow. *Circulation*, **92**, 3183-3193.

[10] Hamilos, M., Muller, O., Cuisset, T., Ntalianis, A., Chlouverakis, G., Sarno, G., *et al.* (2009) Long-Term Clinical Outcome after Fractional Flow Reserve-Guided Treatment in Patients with Angiographically Equivocal Left Main Coronary Artery Stenosis. *Circulation*, **120**, 1505-1512. https://doi.org/10.1161/CIRCULATIONAHA.109.850073

[11] Puymirat, E., Peace, A., Mangiacapra, F., Conte, M., Ntarladimas, Y., Bartunek, J., *et al.* (2012) Long-Term Clinical Outcome after Fractional Flow Reserve-Guided Percutaneous Coronary Revascularization in Patients with Small-Vessel Disease. *Circulation*: *Cardiovascular Interventions*, **5**, 62-68. https://doi.org/10.1161/CIRCINTERVENTIONS.111.966937

[12] De Bruyne, B., Pijls, N.H., Kalesan, B., Barbato, E., Tonino, P.A., Piroth, Z., *et al.* (2012) Fractional Flow Reserve-Guided PCI versus Medical Therapy in Stable Coronary Disease. *New England Journal of Medicine*, **13**, 991-1001. https://doi.org/10.1056/NEJMoa1205361

[13] Botman, K.J., Pijls, N.H., Bech, J.W., Aarnoudse, W., Peels, K., van Straten, B., *et al.* (2004) Percutaneous Coronary Intervention or Bypass Surgery in Multivessel Disease? A Tailored Approach Based on Coronary Pressure Measurement. *Catheterization Cardiovascular Interventions*, **63**, 184-191. https://doi.org/10.1002/ccd.20175

[14] Toth, G., De DeBruyne, B., Casselman, F., De Vroey, F., Pyxaras, S., Di Serafino, L., *et al.* (2013) Fractional Flow Reserve-Guided versus Angiography-Guided Coronary Artery Bypass Graft Surgery. *Circulation*, **128**, 1405-1411. https://doi.org/10.1161/CIRCULATIONAHA.113.002740

[15] Muller, O., Mangiacapra, F., Ntalianis, A., Verhamme, K.M., Trana, C., Hamilos, M., *et al.* (2011) Long-Term Follow-Up after Fractional Flow Reserve-Guided Treatment Strategy in Patients with an Isolated Proximal Left Anterior Descending Coronary Artery Stenosis. *JACC Cardiovascular Interventions*, **4**, 1175-1182. https://doi.org/10.1016/j.jcin.2011.09.007

[16] Thygesen, K., Alpert, J.S., Jaffe, A.S., Simoons, M.L., Chaitman, B.R., White, H.D., *et al.* (2012) Third Universal Definition of Myocardial Infarction. *Circulation*, **126**,

2020-2035. https://doi.org/10.1161/CIR.0b013e31826e1058

[17] Goy, J.J., Kaufmann, U., Hurni, M., Cook, S., Versaci, F., Ruchat, P., *et al.* (2008) 10-Year Follow-Up of a Prospective Randomized Trial Comparing Bare-Metal Stenting with Internal Mammary Artery Grafting for Proximal, Isolated de novo Left Anterior Coronary Artery Stenosis the SIMA (Stenting versus Internal Mammary Artery Grafting) Trial. *American College of Cardiology*, **52**, 815-817. https://doi.org/10.1016/j.jacc.2008.05.037

[18] Hong, S.J., Lim, D.S., Seo, H.S., Kim, Y.H., Shim, W.J., Park, C.G., *et al.* (2005) Percutaneous Coronary Intervention with Drug-Eluting Stent Implantation vs. Minimally Invasive Direct Coronary Artery Bypass (MIDCAB) in Patients with Left Anterior Descending Coronary Artery Stenosis. *Catheterization Cardiovascular Interventions*, **64**, 75-81. https://doi.org/10.1002/ccd.20238

[19] Blazek, S., Holzhey, D., Jungert, C., Borger, M.A., Fuernau, G., Desch, S., *et al.* (2013) Comparison of Bare-Metal Stenting with Minimally Invasive Bypass Surgery for Stenosis of the Left Anterior Descending Coronary Artery: 10-Year Follow-Up of a Randomized Trial. *JACC Cardiovascular Interventions*, **6**, 20-26. https://doi.org/10.1016/j.jcin.2012.09.008

[20] Mohr, F.W., Morice, M.C., Kappetein, A.P., Feldman, T.E., Ståhle, E., Colombo, A., *et al.* (2013) Coronary Artery Bypass Graft Surgery versus Percutaneous Coronary Intervention in Patients with Three-Vessel Disease and Left Main Coronary Disease: 5-Year Follow-Up of the Randomised, Clinical SYNTAX Trial. *Lancet*, **381**, 629-638. https://doi.org/10.1016/S0140-6736(13)60141-5

[21] Farkouh, M.E., Domanski, M., Sleeper, L.A., Siami, F.S., Dangas, G., Mack, M., *et al.* (2012) Strategies for Multivessel Revascularization in Patients with Diabetes. *New England Journal of Medicine*, **367**, 2375-2384. https://doi.org/10.1056/NEJMoa1211585

Appendix

Guideline of the telephone interview: Telephone interviews were done for every patient to obtain post-procedural adverse events. Patients who continued to our hospital for follow-up visits were also reached. If the subject was not reached during the follow-up interview, an official death registry review was used to confirm the death and the reason for the death.