Bifurcation Functional Significance Score as Predictor of Mortality

Dobrin Vassilev

"Alexandrovska" University Hospital, Medical University Sofia

Niya Mileva (✉ nmileva91@gmail.com)

"Alexandrovska" University Hospital, Medical University Sofia

Carlos Collet

Onze Lieve Vrouweziekenhuis Hospital

Pavel Nikolov

"Alexandrovska" University Hospital, Medical University Sofia

Katerina Sokolova

"Alexandrovska" University Hospital, Medical University Sofia

Kiril Karamfiloff

"Alexandrovska" University Hospital, Medical University Sofia

Vladimir Naunov

"Alexandrovska" University Hospital, Medical University Sofia

Jeroen Sonck

Onze Lieve Vrouweziekenhuis Hospital

Gianluca Rigatelli

Rovigo General Hospital

Ghassan S. Kassab

California Medical Innovations Institute

Robert J. Gil

Central Clinical Hospital of the Ministry of Interior

Research Article

Keywords: Bifurcation functional significance score, predictor, mortality, coronary bifurcation stenosis, procedural and clinical outcomes

Posted Date: July 23rd, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-702610/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Considerable progress has been made in the treatment of coronary bifurcation stenosis. Anatomical characteristics of the vessel and lesion, however, fail to give information about the functional significance of the bifurcation stenosis. To the best of our knowledge, there is no study that systematically establishes the baseline functional significance of coronary stenosis and its effect on procedural and clinical outcomes.

Methods: Patients with significant angiographic bifurcation lesions defined as diameter stenosis $> 50\%$ in main vessel and/or side branch were included. FFR was performed in main vessel (MV) and side branch (SB) before and after percutaneous coronary intervention (PCI). 169 patients from Fiesta study (derivation cohort) and 555 patients from prospective bifurcation registry (test cohort) were analyzed to validate angiographic prediction score (BFSS) used to determine the potentially functional significance of coronary bifurcation stenosis.

Results: Bifurcation functional significance score (including the following parameters - SYNTAX ≥ 11 , SB/MB BARI score, MV %DS $\geq 55\%$, MB %DS $\geq 65\%$, lesion length $\geq 25\text{mm}$) with a maximum value of 11 was developed. A cut-off value of 8.5 was shown to give the best discriminatory ability – with accuracy 87% (sensitivity 77%, specificity 96%, $p < .001$). There was also a significant difference in all-cause mortality between patients with $\text{BFSS} \geq 8.5$ vs. $\text{BFSS} < 8.5$ – 17.8% vs. 13.4%, log-rank $p = .006$, as well as cardiac mortality: $\text{BFSS} \geq 8.5$ vs. $\text{BFSS} < 8.5$ – 14.6% vs. 12.5%, log-rank ($p = .042$). The cardiac mortality was significantly lower in patients with smaller absolute SB territory, $p = 0.023$.

Conclusion: An angiographic score (BFSS) with good discriminatory ability to determine the functional significance of coronary bifurcation stenosis was developed. The value for $\text{BFSS} \geq 8.5$ can be used as a discriminator to define groups with higher risk for all-cause and cardiac mortality. Also, we found that the smaller side branches pose greater mortality risk.

Introduction

Considerable progress has been made in the treatment of coronary bifurcation stenosis¹. Currently, we have increasing knowledge on how to achieve optimal flow dynamics in coronary bifurcation lesions. Several estimates of lesion and vessel significance, however, are highly subjective. The historical Medina classification is a simple tool used to describe the location of angiographically significant stenosis. It fails to give detailed anatomical information with a potential impact on functional significance (e.g., lesion length in main and side branches). Percutaneous coronary intervention (PCI) of functionally non-significant lesions will fail to provide clinical benefit and would expose the patient to unnecessary risk of periprocedural complications²⁻⁴. To the best of our knowledge, insights in functional significance of bifurcation lesions *before* PCI are lacking. Available data focused on fractional flow reserve (FFR) measurements of residual side branch ostial stenosis significance *after* main vessel stenting^{5,6}. No study

systematically evaluated baseline functional lesion significance and its effect on procedural and clinical outcomes.

We previously determined the rates of functionally significant stenoses at the ostium of side branches after main vessel stenting, which correlated with changes on intracoronary electrocardiogram⁷. One surprising finding was the high rate of angiographically significant bifurcation stenoses, which were not functionally significant when measured with FFR. Therefore, we decided to extend recruitment of patients to confirm or reject our initial observations.

Methods

Patient selection All patients with coronary bifurcation lesions were included in an observational registry from July 2014. Patients included in the FIESTA study⁷ were used to form the derivation cohort. In general, these were patients with angiographic bifurcation lesions in a native coronary artery with diameter ≥ 2.5 mm and ≤ 4.5 mm and SB diameter ≥ 2.0 mm and percentage diameter stenosis $> 50\%$ in the main vessel. Patients with left main coronary artery stenosis, total occlusion before occurrence of the SB, lesion of interest located in an infarct-related artery, subjects with LVEF $\leq 30\%$, subjects with moderate or severe degree of valvular heart disease or primary cardiomyopathy were excluded. The data from the FIESTA study were used to extract variables predictive of functional significance of bifurcation lesions and to create a prediction score for functional significance (bifurcation functional significance score; BFSS). The remaining patients from the registry formed the test cohort for the score. These are patients with same inclusion criteria as patients in FIESTA group. Figure 1 illustrates the flow chart of patient selection.

Definition of endpoints

A functionally significant bifurcation lesion was defined by the presence of a stenosis in the main vessel (MV) and/or side branch (SB) with FFR < 0.80 in accordance with the latest recommendations⁸. A main branch (MB) functionally significant lesion was considered a stenosis in the MV with an FFR measured distally from the bifurcation. Patients in both the derivation and test cohorts were followed up by telephone contact and/or clinical visit at 30 days and then monthly for vital status through their insurance number in the National Insurance Institute. Cardiovascular death was defined as death with clearly determined cardiac origin or death from unknown reason. Myocardial infarction after hospitalization was diagnosed according to the Fourth definition of myocardial infarction⁹; i.e., as any rise in troponin or creatine-kinase MB more than 99th percentile of normal values in association with symptoms and/or documented ECG changes.

Procedures

Initial FFR of MV and SB was performed using the PrimeWire or PrimeWire Prestige (Volcano Corp., USA). For all FFR measurements, intracoronary adenosine was given in increasing doses of 60 mcg, 120 mcg, and 240 mcg. A check for drift was performed before every measurement and at the end of the procedure.

PCI was performed according to the current guidelines^{10,11}. Provisional stenting was the default strategy in all patients. Pre-dilatation of MV was mandatory. After stenting and proximal optimization balloon inflation (left on operator discretion) FFR were measured in main and side branches. It was recommended that in case of SB FFR < 0.80, a balloon dilatation of SB should be performed. The SB was stented in case of TIMI flow less than 3, when visual diameter stenosis at ostium was more than 70%, despite kissing balloon inflation (KBI), and when the patient was symptomatic (i.e., with chest pain). If none of the above was present and FFR > 0.80, the SB was left untreated. Final KBI or sequential balloon inflation were performed at the discretion of the operator. All lesions were stented with second generation DES. Angiographic success was defined as the end procedural MV percent diameter stenosis (%DS) < 20% and SB stenosis < 70% without significant dissection nor flow impairment. Procedural success included angiographic success in the absence of in-hospital MACE (death, stroke, and myocardial infarction). All patients received double antiplatelet therapy with aspirin and P2Y2 inhibitor. All procedures were carried out in accordance with the standard of clinical practice and regulations

Angiographic Analysis

Dedicated bifurcation quantitative coronary angiography (QCA) analysis was performed according to the recommendation of the consensus on QCA methods for bifurcation lesions¹². True bifurcation lesions were defined as visual percent diameter stenosis (%DS) > 50% at the SB. The minimal luminal diameter (MLD), reference vessel diameter (RVD) and %DS were measured for every segment of the bifurcation (i.e., proximal, and distal MV and SB) pre- and post-intervention. Lesion length was measured from proximal MV to distal MB (i.e., we considered beginning and ending points where hypothetically the stent will be implanted). SB lesion length was measured from the ostium to the first normal appearing part of the vessel. All analyses were performed by two investigators (P.N. and V.N) and in case of disagreement, a consensus was formed with additional analysis from the first author (D.V.). All the analyses were performed with dedicated General Electric QCA software and additionally with MicroDicom QCA software. For the test cohort a visual angiographic analysis was performed from the same authors. For assessment of territory at risk and relative contribution of bifurcation lesion to all territory at risk adapted Bypass Angioplasty Revascularization Investigation Myocardial Jeopardy Index (BARI) score was calculated [17, 18].

Statistical Analysis

Differences between groups were examined with paired or unpaired t-tests as appropriate, with normal distributions. Otherwise, the Wilcoxon sign-ranked test and Mann-Whitney U-tests were used. Chi-square tests were applied for qualitative data. The area under the receiving operating characteristics curve (AUC) was used to assess the diagnostic accuracy of the test. Correlation analysis was performed (Pearson or Spearman test depending on type of data) between FFR values and possible predictors. Multiple logistic regression analysis was performed to identify independent predictors of functionally significant bifurcation lesion, as well as functionally significant stenoses in main branch and side branch directions. Multivariate Cox regression analysis was performed for identification of independent predictors of all-

cause death and cardiovascular death. Mortality rate in the two groups with functionally significant and non-significant bifurcation stenoses were compared. The study was investigator initiated, funded by the local institution ("Alexandrovska" University Hospital, Sofia, Bulgaria). The local ethics committee (Medical University of Sofia, Sofia, Bulgaria) approved the study and patients signed informed consent for participation into registry. All statistical calculations were performed via SPSS version 23 (SPSS, USA).

Results

Derivation cohort: Final derivation cohort consisted of 169 patients (65% male). Flow chart of patient's selection is shown in **Figure 1**. Almost half had positive (FFR<0.80) measurements in the MB (81/169, 48%), 28% (44/166) had FFR<0.80 in both SB and MB. In only two patients a SB FFR of less than 0.80 was measured and decision for treatment was taken based on the large SB diameter. Lastly, in 3 patients it was impossible to measure FFR in the SB at baseline due to a tight ostial stenosis and/or steep angulation. The left ventricular ejection fraction (EF) overall was 58%±7% and was not different between functionally significant and non-significant groups. The differences in demographic characteristics and angiographic factors are presented in Table 1. LAD was the dominant vessel under investigation (81%, n=137/169). Angiographically, patients with a positive FFR(<0.80) had a more severe stenoses at any bifurcation segment with longer lesion length in the main vessel, but not in the SB. It is noteworthy that lesions with significant FFR had larger SB territories, but equal main branch areas at risk in comparison with non-significant functionally bifurcation lesions. It is also interesting, that functional significance depends on the length of the SB (reflected by SBBARI score) but not the diameter. On univariate regression analysis factors associated with positive FFR results were proximal main vessel %DS, distal main branch %DS, SB %DS, main branch reference diameter, lesion length, SYNTAX score, number of diseased vessels, SB to MB reference vessel diameter ratio, SB BARI risk score (absolute side branch territory at risk) and ratio of SBBARI score to MBBARI score (relative side branch territory at risk). On multivariate logistic regression analysis for identification of predictors of functionally significant bifurcation stenosis, the following factors were identified: MB %DS (OR=9.138, CI 2.809-29.725, p<.001), MV %DS (OR=7.227, CI 2.325-22.464, p=.001), lesion length (OR=14.937, CI 4.663-47.851, p<.001), SYNTAX score (OR=3.577, CI 1.276 – 10.028, p=.014), ratio of SBBARI to MBBARI scores (OR=4.994, CI 1.020 – 23.976, p=.047).

For ROC analysis, the following cut-off values were defined: MB %DS $\geq$ 65%, c-statistics 0.879 (CI 0.825-0.932, p<.001; sensitivity= 73%, specificity=88%), MV %DS $\geq$ 55%, c-statistic 0.830 (CI 0.766 - 0.894, p<.001; sensitivity= 75%, specificity= 86%), lesion length $\geq$ 25 mm, c-statistic 0.898 (CI .849 - .947, p<.001; sensitivity= 86%, specificity=74%), SYNTAX score $\geq$ 11, c-statistic .819 (CI .752 - .886, p<.001; sensitivity=75%, specificity= 85%), ratio SBBARI/MBBARI $\geq$ 50%, c-statistic 0.600 (CI 0.516 - 0.687, p = 0.023; sensitivity=52%, specificity=58%). On basis of the above parameters with their relative weight in prediction of significant value of FFR, we developed a score (Table 2). The score had a maximum value of 11, with a significant difference between the groups with functionally significant and non-significant

stenoses - 9 ± 2 vs. 3 ± 2 , $p<0.001$. By ROC analysis, we determined a cut-off value of 8.5 that gave the best discriminatory ability with accuracy 95% (sensitivity 77%, specificity 96%, $p<0.001$; **Figure 2**)

Test cohort: The testing cohort consisted of 555 patients followed-up for more than 6 months from index PCI. The differences between two groups are presented in Table 3. There were no significant differences in the risk factors rate between the two groups that underwent PCI. The frequency of LAD as a target vessel was significantly higher in the derivation than in the test cohort – 80% vs 69%, $p=0.013$. The two groups had similar sized vessels and degrees of stenosis, despite higher rate of multivessel disease in the test group. Those patients also had shorter lesions and smaller SB territories. The frequency of “true” bifurcation stenosis (side branch ostial stenosis more than 50%) was similar in the test group and stented group from the derivation cohort (63%, $n=348$ and 60%, $n=53$, respectively). The rates of SB stenting were non-significantly different between groups – 24% ($n=20/81$, from initially $FFR<0.80$ patients) in derivation group vs. 18% ($n=100$), as were rates of POT (73% vs. 69%, $p=0.309$) and kissing balloon inflation (35%, $n=31$ vs. 42%, $n=191$, $p=0.531$). In regard to the bifurcation functional significance score (BFSS), the patients in test group had lower mean score in comparison with derivation group. In total 382 patients (69%) had a $BFSS\geq 6$, meaning that with 86% probability those patients had functionally significant coronary bifurcation stenoses.

Clinical outcomes: All patients were followed-up for vital status. To be included in this analysis, at least 6 months follow-up following the PCI procedure was required. In case of patient death, family members or family physicians were interrogated to define the cause of death. The mean follow-up time was 38 ± 18 months (median 40, IQR 23-55 months). For patients in the FIESTA registry, the all-cause mortality was numerically lower: 8.5% ($n=7/82$) in the non-stent group and 12.6% in the stented group ($n=11/76$; these includes patients not initially treated but receiving a stent in other institutions within 3 months from initial the procedure), $p=0.387$. The cardiac mortality was also numerically lower, but statistically non-significantly different (9.8%, $n=8/82$ vs. 11.5%, $n=10/88$, $p=0.714$). The all-cause mortality among patients in the test cohort was not significantly different in comparison with the stented cohort from the derivation cohort patients receiving a stent – 15.9%, $n=88/555$, $p=.561$; the same was true for cardiac mortality – 13.7%, $n=76/555$, $p=0.702$ (**Figure 3**). Factors associated with mortality are illustrated in tables 4 and 5.

Role of side branch territory for functional significance of coronary bifurcation stenosis and

prognosis: We analyzed the impact of the absolute and relative side branch territory size on the functional significance of bifurcation stenosis and mortality. On ROC analysis ($c=0.612$, $p=0.032$) the $SBBARI\geq 12\%$ had a 75% sensitivity and 52% specificity to detect functionally significant bifurcation stenosis. If the cut-off of the SB territory at risk was set at 10% (the traditional value for territory at risk requiring revascularization) the sensitivity increase to 92%, but with extremely low specificity of 29%. There was no relation between SB reference diameter and bifurcation stenosis functional significance. Regarding the risk of death, there was a significant difference in cardiac mortality with values of SBBARI starting from 10% (Figure 1). The cardiac mortality was significantly *lower* in patients with smaller absolute SB territory – $p=0.023$. The same was true for relative SB territory – a larger SBBARI/MBBARI

ratio was related with numerically lower all-cause mortality and statistically significantly lower cardiac death. There was also a significant difference in all-cause mortality between patients with $\text{BFSS} \geq 8.5$ vs. $\text{BFSS} < 8.5$ – 17.8% vs. 13.4%, log-rank $p=0.006$, as well as cardiac mortality: $\text{BFSS} \geq 8.5$ vs. $\text{BFSS} < 8.5$ – 14.6% vs. 12.5%, log-rank $p=0.042$. Thus, the BFSS, which incorporates relative side branch territory, has a high discriminatory ability to select patients at risk of death.

Discussion

There are several new findings in our study: First, an angiographic score (BFSS), which can predict functional significance of coronary bifurcation lesions with reasonable accuracy ($>85\%$) was developed. The variables forming the score were not related to the bifurcation only, but also considering the overall disease severity and territory supplied by MB and SB. Second, we estimated a proportion of patients with functionally significant bifurcation stenoses and explored the rates of mortality among those patients based on BFSS values. The frequency of probably functionally significant bifurcation stenoses estimated by $\text{BFSS} \geq 6$ was around 2/3 of whole examined population and if we consider 85% accuracy of our score, then 57% of patients would be with $\text{FFR} < 0.80$. We chose the value for $\text{BFSS} \geq 8.5$ as the one with best discrimination ability in all-cause and cardiac mortalities. This value gave 99% sensitivity, but only 54% specificity in our test group and would reclassify probably functionally significant bifurcation stenosis up to 80%. Overall, there is a high probability that at the time of PCI between 20%-40% of the patients had probably borderline functional significance bifurcation stenosis. This confirms our earlier observation from FIESTA study ⁷. Finally, for the first time, we determined the role of SB territory in relation to mortality in patients with stented coronary bifurcation stenoses. An unexpected finding was that the smaller the absolute and relative territory supplied by the side branches, the greater mortality risk they pose.

BARI risk score is a useful tool, that can be used in every catheterization laboratory and does not require any specific equipment or software for calculation ^{13,14}. Not unexpectedly, larger side branches, with a larger absolute and relative territory were more frequently associated with $\text{FFR} < 0.80$. It is interesting that the ratio of SB and MB vessel diameter also correlated with functional significance but was not independently related with $\text{FFR} < 0.80$. The possible explanation is that diffuse disease precludes adequate assessment of vessel sizes and its relation to myocardial mass, especially when assessed with coronary angiography ¹⁵. Calculation of absolute SB territory (SB BARI score) requires a high-quality angiogram, including a good visualization of the length of every coronary artery branch with a diameter more than 1 millimeter. The SBBARI/MBBARI ratio is dimensionless, does not require visualization of the whole coronary artery tree and is easy to apply in every patient. Our data could not be directly compared with previous studies on this topic as they included patients with left main stenosis, as well as completely normal bifurcations, assessed with computer tomography ^{16,17}. The major advantage of our method is the ease of use and applicability in daily practice.

There is a general belief that larger side branches have higher impact on patient prognosis. One speculation is that smaller SBs are associated with larger main branches, supplying larger myocardial territory and in case of stent-related event, the fatality rate would be higher. There was no statistically

significant difference between MBBARI scores in groups with smaller or larger SB territories. Another possible explanation is that larger side branches give a better collateral supply to a neighbor territory and in case of event in main branch, the SB could ensure a minimum supply and limit possible myocardial necrosis, thus improving patient prognosis. This hypothesis deserves further investigation.

The frequency of all-cause and cardiac death in our population is higher than reported in previous studies^{18,19}. We could not confirm the data published previously, that periprocedural increase in troponin is associated with higher mortality risk^{20,21}. We tested different levels of increase in postprocedural troponin values (up to 70xUNL) for its association with mortality, but neither was significant. However, the baseline concentration of troponin was related with outcome and the cut-off value associated with mortality was *below* the currently accepted upper normal limit for high-sensitivity troponin (UNL<0.012 ng/ml; the value in our study related with increase in death is 0.010 ng/ml). This raises question about the baseline risk stratification and current reference standards, especially for the patients with complex coronary artery disease. From multivariate analysis, we did not observe any effect on mortality of side branch compromise (diameter stenosis more than 50% after stenting main vessel), SB stenting, type of pre- or post-dilatation, as well as number of stents or total stent length, despite that each of these factors were univariately associated with mortality rates.

Conclusion

An angiographic score (BFSS) with good discriminatory ability to determine the potential functional significance of coronary bifurcation stenosis was validated. The value for BFSS ≥ 8.5 can be used as discriminator to define groups with higher risk for all-cause and cardiac mortality. Also, our analysis showed that the smaller as an absolute and relative territory side branches pose greater mortality risk.

Declarations

Funding statement: The study was investigator initiated, funded from the local institution ("Alexandrovska" University Hospital, Sofia, Bulgaria).

Conflict of Interest: Carlos Collet reports receiving research grants from Biosensor, Coroventis Research, Medis Medical Imaging, Pie Medical Imaging, Cathworks, Boston Scientific, Siemens, HeartFlow Inc. and Abbott Vascular; and consultancy fees from Heart Flow Inc, Opsens, Abbott Vascular and Philips Volcano

References

1. Grundeken, M. J. *et al.* First generation versus second generation drug-eluting stents for the treatment of bifurcations: 5-year follow-up of the LEADERS all-comers randomized trial. *Catheter Cardiovasc Interv***87**, E248-260, doi:10.1002/ccd.26344 (2016).
2. Tonino, P. A. *et al.* Angiographic versus functional severity of coronary artery stenoses in the FAME study fractional flow reserve versus angiography in multivessel evaluation. *J Am Coll Cardiol***55**, 2816-

2821, doi:10.1016/j.jacc.2009.11.096 (2010).

3. De Bruyne, B. *et al.* Fractional flow reserve-guided PCI for stable coronary artery disease. *N Engl J Med***371**, 1208-1217, doi:10.1056/NEJMoa1408758 (2014).

4. van Nunen, L. X. *et al.* Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. *Lancet***386**, 1853-1860, doi:10.1016/s0140-6736(15)00057-4 (2015).

5. Koo, B. K. *et al.* Physiologic assessment of jailed side branch lesions using fractional flow reserve. *J Am Coll Cardiol***46**, 633-637, doi:10.1016/j.jacc.2005.04.054 (2005).

6. Koo, B. K. *et al.* Physiological evaluation of the provisional side-branch intervention strategy for bifurcation lesions using fractional flow reserve. *Eur Heart J***29**, 726-732, doi:10.1093/eurheartj/ehn045 (2008).

7. Vassilev, D. *et al.* Intracoronary electrocardiogram to guide percutaneous interventions in coronary bifurcations - a proof of concept: the FIESTA (Ffr vs. IcEcGSTA) study. *EuroIntervention***14**, e530-e537, doi:10.4244/eij-d-17-00189 (2018).

8. Knuuti, J. *et al.* 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J***41**, 407-477, doi:10.1093/eurheartj/ehz425 (2020).

9 Thygesen, K. *et al.* Fourth universal definition of myocardial infarction (2018). *European Heart Journal***40**, 237-269, doi:10.1093/eurheartj/ehy462 (2018).

10. Burzotta, F. *et al.* European Bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. *Catheter Cardiovasc Interv***96**, 1067-1079, doi:10.1002/ccd.29071 (2020).

11. Burzotta, F. *et al.* Percutaneous Coronary Intervention For Bifurcation Coronary Lesions. The 15th Consensus Document from the European Bifurcation Club. *EuroIntervention*, doi:10.4244/eij-d-20-00169 (2020).

12. Collet, C. *et al.* Quantitative angiography methods for bifurcation lesions: a consensus statement update from the European Bifurcation Club. *EuroIntervention***13**, 115-123, doi:10.4244/eij-d-16-00932 (2017).

13. Ortiz-Pérez, J. T. *et al.* Angiographic estimates of myocardium at risk during acute myocardial infarction: validation study using cardiac magnetic resonance imaging. *Eur Heart J***28**, 1750-1758, doi:10.1093/eurheartj/ehm212 (2007).

14. Alderman, E. L. *et al.* Native coronary disease progression exceeds failed revascularization as cause of angina after five years in the Bypass Angioplasty Revascularization Investigation (BARI). *J Am Coll*

*Cardiol***44**, 766-774, doi:10.1016/j.jacc.2004.05.041 (2004).

15. Kassab, G. S., Bhatt, D. L., Lefèvre, T. & Louvard, Y. Relation of angiographic side branch calibre to myocardial mass: a proof of concept myocardial infarct index. *EuroIntervention***8**, 1461-1463, doi:10.4244/eijv8i12a220 (2013).

16. Kim, H. Y. *et al.* Identification of Coronary Artery Side Branch Supplying Myocardial Mass That May Benefit From Revascularization. *JACC Cardiovasc Interv***10**, 571-581, doi:10.1016/j.jcin.2016.11.033 (2017).

17. Jeon, W. K. *et al.* Anatomical attributes of clinically relevant diagonal branches in patients with left anterior descending coronary artery bifurcation lesions. *EuroIntervention***16**, e715-e723, doi:10.4244/eij-d-19-00534 (2020).

18. Zimarino, M. *et al.* Mid-term outcomes after percutaneous interventions in coronary bifurcations. *Int J Cardiol***283**, 78-83, doi:10.1016/j.ijcard.2018.11.139 (2019).

19. Ferenc, M. *et al.* Long-term outcomes of routine versus provisional T-stenting for de novo coronary bifurcation lesions: five-year results of the Bifurcations Bad Krozingen I study. *EuroIntervention***11**, 856-859, doi:10.4244/eijv11i8a175 (2015).

20. Kini, A. S. *et al.* Correlation of postpercutaneous coronary intervention creatine kinase-MB and troponin I elevation in predicting mid-term mortality. *Am J Cardiol***93**, 18-23, doi:10.1016/j.amjcard.2003.09.006 (2004).

21. Prasad, M. *et al.* Coronary microvascular endothelial dysfunction is an independent predictor of development of osteoporosis in postmenopausal women. *Vasc Health Risk Manag***10**, 533-538, doi:10.2147/vhrm.s63580 (2014).

Tables

Due to technical limitations, table 1-5 is only available as a download in the Supplemental Files section.

Figures

Figure 1

Patient selection flow chart

Figure 2

ROC curve analysis for the discriminatory ability of potential functional significant coronary bifurcation lesions. A cut-off value of BFSS of had 95% accuracy (sensitivity 77%, specificity 96%, $p < 0.001$). ROC – receiver operator's curve; BFSS – bifurcation functional significance score.

Figure 3

Kaplan-Meier curves: A. All-cause mortality in patients with SBBARI score $\geq 10\%$ and $< 10\%$. B. Cardiac mortality in patients with SBBARI score $\geq 10\%$ and $< 10\%$. C. All-cause mortality in patients with SBBARI/MBBARI $\geq 50\%$ and less $< 50\%$; D. Cardiac mortality in patients with SBBARI/MBBARI $\geq 50\%$ and less $< 50\%$

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Tables.pdf](#)