

Predictors of Well Developed Coronary Collateral Circulation in Patients with Stable Angina Pectoris

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Abstract

Objective: We aimed to demonstrate the predictors of Coronary Collateral Development (CCD) in patients with Stable Angina Pectoris (SAP).

Methods: We prospectively enrolled 52 patients with at least 90% coronary stenosis. Their demographic, anthropometric and clinical data as well as hematological and biochemical parameters, medications, Ejection Fraction (EF) and perfusion index values and angiographic findings were used for determining the predictors for CCD. The Rentrop score (between 0 and 3) was used for the angiographic categorization and patients in Rentrop grades 0 and 1 were classified as poor CCD, and patients in Rentrop grades 2 and 3 were classified as well CCD.

Results: We found moderate negative correlation between the Rentrop score and ejection fraction ($r=-0.469$, $p<0.001$). There was also positive correlation between the Gensini score (GS) and the Rentrop score ($r=0.627$, $p<0.001$). We made Classification and Regression Tree Model (C&RT) to define best predictors of CCD and found that EF (cut off 55%) and GS (cut off 41%) together constitute a useful prediction algorithm. Furthermore an advanced research was conducted to develop another algorithm to forecast coronary collateral development prior to angiography. The analysis was repeated after the extraction of angiographic data from the first C&RT model. It was concluded that EF (cut off 55%) and mean platelet volume (MPV) (cut off 9 fl) can be used in the second algorithm.

Conclusions: CCD is negatively related to EF and positively related to GS. EF and MPV together constitute a simple and cost effective algorithm to predict the CCD before the angiography. However, GS and EF seem to be the best predictors of CCD among the whole variables.

Keywords: Coronary collateral; Coronary artery disease; Ejection fraction; Mean platelet volume; Gensini score

Introduction

Coronary Collaterals (CC) are present at birth, with wide inter-individual variation in their functional capacity. In the absence of stenosis, it has been assumed that coronary arteries are functional end-arteries [1]. However, they may develop further in response to obstruction of epicardial coronary arteries to protect jeopardized myocardium to restore blood flow to ischemia territories. The human Coronary Collateral Circulation (CCC) meets myocardial demands during a brief coronary occlusion in 1/4 to 1/3 of individuals [2]. In the course of acute obstruction, a flow of 20% to 25% is sufficient to provide blood supply at rest. However it is generally not sufficient to meet myocardial demands during exercises [3].

The number of collaterals and the extent of their coverage are associated with improved survival in patients with coronary heart disease. There have been numerous studies that show a protective role of well-developed vs. poor-developed collateral arteries demonstrating smaller infarcts, less ventricular aneurysm formation, reduction in post infarct ventricular dilatation, reduced future cardiovascular events and reduced QT prolongation during myocardial ischemia [4-6]. And finally it was shown that, in patients with chronic stable Coronary Artery Disease (CAD), a well-developed CC might reduce mortality [2,7]. In addition, Berry et al. underlined the prognostic importance of collateral circulation and suggested that therapeutic augmentation of collaterals with emerging biological therapies may represent a desirable goal for treating Coronary Heart Disease (CHD) patients [8].

The value of a well-developed CC to predict the prognosis in patients with CHD, have been leading the researchers to examine the

demographic and biochemical determinants of CCC. Previous studies found a positive correlation between a well-developed CC and male gender, smoking, hyperlipidemia, calcium channel blocker usage, statin usage, higher serum CRP and lipoprotein associated phospholipase A2 level, paraoxanase activity and asymmetric dimethylarginine level [9-14]. On the other hand, diabetes mellitus demonstrates a relation to poor Coronary Collateral Development (CCD) [11]. Finally, some hematological parameters such as high Mean Platelet Volume (MPV), neutrophil/lymphocyte (N/L) ratio and Red Blood Cell Distribution width (RDW) levels also demonstrate a relation to poor CCD [15,16].

There are reports indicating close relation between the endothelial dysfunction and the CCD [17,18]. Moreover, it has been reported that elevated MPV values are associated with the extent of atherosclerosis in coronary tree and arterial stiffness, which is accepted as a marker of endothelial dysfunction [19,20]. There are also some reports demonstrating that there is a close relation with the endothelial function and the left ventricular function [21,22].

Accordingly, in the current study, we investigated the role of

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hematological parameters, Gensini score and Ejection Fraction (EF) which all seem to have close relation with endothelial function that is known to play a major role in the CC development. We also aimed to investigate the relations of demographic, anthropometric and clinical data, as well as biochemical variables with CCD.

Methods

Between April and September 2013 a total of 52 consecutive patients, who were admitted to our hospital for coronary angiography procedure with stable angina pectoris with greater than/or equal to 90% stenosis, were prospectively enrolled to this study and evaluated. All patients had stable anginal symptoms and/or positive stress test or myocardial perfusion scintigraphy results or electrocardiographic changes indicating ischemia. Clinical information including age, weight, gender, and any data known to influence development of collaterals such as current medications, history of hypertension and diabetes mellitus, complete blood count, serum creatinine and cholesterol levels were documented. Patients were excluded if they had a recent history (i.e. a history of less than one month) of acute coronary syndrome, previous coronary intervention, NYHA class III-IV heart failure, atrial fibrillation, severe valvular heart disease, presence of co-existent inflammatory disease (e.g. rheumatoid arthritis), severe renal failure, severe hepatic diseases, active malignancy, malnutrition, chronic obstructive pulmonary disease, or pregnancy. The study was approved by the regional Ethics Committee, and all the patients signed a written informed consent.

Definitions

Patients were defined as hypertensive if their blood pressure was $\geq 140/90$ mmHg, or if they were taking any anti-hypertensive medications. Diabetes mellitus was defined as the presence of a history of anti-diabetic medication usage, or a fasting glucose level above 126 mg/dL. Patients were considered to have hyperlipidemia if their total cholesterol was ≥ 200 mg/dL, or if they were taking lipid-lowering medication. Smoking behavior was ascertained by participant self-report. Subjects were allocated to 1 of 3 categories: active smokers, ex-smokers (abstinence from smoking for >30 days), or nonsmokers (<100 cigarettes in the past lifetime and no regular smoking in the weeks before the baseline and follow-up evaluation) [23]. To define the duration of symptoms suggestive of ischemia, patients were asked to describe the monthly time from the onset of ischemic symptoms (typical angina or angina equivalent symptoms like shortness of breath (dyspnea), diaphoresis or extreme fatigue) to the day of angiography procedure. Anamnesis of patients was taken by the same cardiologist just before the angiography procedures.

Laboratory analysis

In all cases, blood samples were drawn at admission before starting any further medication. For assessment of hematological parameters, blood samples were taken and put into tubes containing tripotassium ethylene-diaminetetraacetic acid before clopidogrel, heparin, or tirofiban administration and studied within 30 min. Blood samples were measured using an auto analyzer (A Sysmex XE-2100 (Sysmex, Kobe, Japan)). Serum creatinine, triglyceride, total-cholesterol, Low-Density Lipoprotein (LDL)-cholesterol and High-Density Lipoprotein (HDL)-cholesterol levels were also measured before the angiography procedure.

Coronary angiography and grading of coronary collaterals

Selective coronary angiography was performed in multiple

orthogonal projections using the Judkins technique. Angiograms were reviewed by two experienced angiographers who were blind to clinical knowledge of patients. Intracoronary nitrates infusion was performed in case of significant lesion (stenosis or total occlusion). The severity of coronary stenosis was evaluated by measuring the percent reduction in lumen diameter from the cineangiogram. Presence of ≥ 50 luminal atheromatous stenosis at least in one coronary artery was considered coronary artery disease. Significant coronary narrowing was defined as stenosis $>70\%$ in at least one main branch of the coronary arteries. The coronary collateral vessels were graded according to the Rentrop scoring system: 0=no filling; 1=filling of the small side branches; 2=partial filling of the epicardial artery by collateral vessels; 3=complete filling of the epicardial artery by collateral vessels [24]. Patients in Rentrop grades 0 and 1 were classified as Group 1 (poor coronary collateral development), and patients in Rentrop grade 2 and 3 were classified as Group 2 (well coronary collateral development).

The extensiveness of coronary artery disease was evaluated using angiographic Gensini score (GS) [25]. Based on lumen stenosis, according to this scoring the following scoring was made primarily: lumen stenosis 1%-25%: 1 point, 26%-50%: 2 points, 51%-75%: 4 points, 76%-90%: 8 points, 91%-99%: 16 points and complete stenosis: 32 points. Subsequently, these scores were multiplied by certain coefficients according to the importance of the coronary vessel and the segment in which stenosis was present. For example, a coefficient of 5 was used for the left main coronary artery, a coefficient of 2,5 was used for the left anterior descending and proximal part of the circumflex coronary artery and a coefficient of 1 was used for the proximal right coronary artery. To obtain the total GS of the patient the score found for each luminal stenosis and the coefficients were added.

Perfusion Index

The Perfusion Index (PI) is the ratio of the pulsatile blood flow to the non-pulsatile or static blood in peripheral tissue. Perfusion Index thus represents a noninvasive measure of peripheral perfusion that can be continuously and noninvasively obtained from a pulse oximeter. In this study we also aimed to demonstrate any relation with PI and CC development. PFI was measured by using the Masimo Radical® with Masimo SET® pulse oximetry, under the same conditions for all patients in the catheterization laboratory, just before the angiography procedure.

Echocardiography

Before the coronary angiography procedure, echocardiographic assessment was performed with the Philips HD11 XE ultrasound system (Philips Healthcare, Andover, MA, USA), and the Left Ventricular Ejection Fraction (LVEF) was determined using the modified Simpson's rule.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of numeric variables. For the numeric variables that were normally distributed, comparison between two groups was made by independent sample t test and descriptive statistics were presented as mean \pm standard deviation. For the numeric variables that were not normally distributed, comparison between two groups was made by Mann-Whitney U test and descriptive statistics were presented as median (25-75 percentiles). To analyze the categorical data, a chi-square test was used and descriptive statistics were presented as frequency (%).

The Spearman's rho correlation analysis was used to determine the correlation between the numeric variables. The p values below 0.05 were considered statistically significant.

Classification and Regression Tree (C&RT)

C&RT is a recursive partitioning method to be used both for regression and classification. C&RT is constructed by splitting subsets of the data set using all predictor variables to create two child nodes repeatedly, beginning with the entire data set. The best predictor is chosen using a variety of impurity or diversity measures. The goal is to produce subsets of the data, which are as homogeneous as possible with respect to the target variable [26]. In our study, we used the C&RT method in order to choose the best predictor for CCD.

Results

The study population consisted of 52 patients. 7 patients (13.4%) had Rentrop grade 0, 17 patients had grade 1 (32.6%), 14 patients had grade 2 (26.9%) and 14 patients (26.9%) had grade 3 collateral circulation. The

Variables	All patients (n=52)	Coronary collateral circulation		p
		Well developed (n=27) 48.1%	Poor developed (n=25) 51.9%	
Baseline characteristics				
Mean age, years	64.6 ± 10.4	65.3 ± 9.5	63.9 ± 11.4	0.639
Male gender, n (%)	40 (77)	22 (81.5)	18 (72)	0.630
Height, cm	170.8 ± 6.9	171 ± 6.8	170 ± 7.2	0.839
Weight, kg	79.5 ± 7.8	80.2 ± 7.9	78.8 ± 7.7	0.530
Body mass index, kg/m ²	27.1 ± 1.66	27.3 ± 1.8	27 ± 1.47	0.457
Hypertension, n (%)	13 (25)	10 (37)	3 (12)	0.078
Diabetes Mellitus, n (%)	15 (28.8)	9 (33.3)	6 (24)	0.663
Smoking status				
Active smokers	32 (61.5)	16 (59.3)	16 (64)	1.000
Non-smokers	17 (32.7)	9 (33.3)	8 (32)	
Ex-smokers	3 (5.8)	2 (7.4)	1 (4)	
Ejection fraction, %	60 (44-66)	44 (40-62)	66 (60-68.5)	<0.001
Perfusion Index	6.2 ± 3.1	5.8 ± 3.1	6.7 ± 3	0.327
Systolic blood pressure, mmHg	110 (100-120)	110 (100-125)	110 (105-110)	0.410
Diastolic blood pressure, mmHg	60 (61.2-73.7)	70 (60-75)	70 (62.5-72.5)	0.436
Duration of ischemic symptoms	8.01 ± 3.56	7.44 ± 3.04	8.8 ± 3.98	0.173
Laboratory findings				
Total cholesterol, mg/dL	198.3 ± 43.7	199.8 ± 46.7	196.7 ± 41.1	0.802
LDL, mg/dL	118.4 ± 34.5	118.4 ± 39.4	118.4 ± 28.9	0.997
HDL, mg/dL	36 (33-40)	37 (31-40)	35 (33-41.5)	0.876
Triglyceride, mg/dL	160 (120-246.7)	180 (120-287)	133 (114-225)	0.394
Creatinine, mg/dl	0.9 (0.7-1.1)	0.9 (0.7-1.2)	0.9 (0.7-1.1)	0.447
Hemoglobin, mg/dl	13 ± 2	13.1 ± 2.1	12.8 ± 2	0.660
Hematocrit, %	39.3 ± 5.4	39.5 ± 5.1	39.1 ± 5.9	0.788
MCV, fl	85.3 ± 6.3	85.1 ± 5.5	85.5 ± 7.2	0.814
RDW, %	14.9 ± 1.1	14.8 ± 1	15 ± 1.3	0.572
MPV, fl	9.4 ± 1	9.4 ± 1.1	9.3 ± 0.9	0.913
PDW, %	45.6 (16.2-51.3)	47 (16.5-52.8)	9.2 (8.7-10.2)	0.148
N/L ratio	2.3 (1.9-3.2)	2.3 (1.9-3.1)	2.3 (1.9-3.5)	0.798

Table 1: Baseline characteristics of the study patients; and their comparisons.

Variables	Coronary collateral development		p
	Poor n (%)	Well n (%)	
Number of diseased vessels			0.834
1 vessel disease	7 (28%)	8 (29.6%)	
2 vessel disease	13 (52%)	12 (44.4%)	
3 vessel disease	5 (20%)	7 (25.9%)	
Significant RCA disease	21 (84%)	16 (59.3%)	0.097
Significant LAD disease	14 (56%)	21 (77.8%)	0.169
Significant Cx disease	13 (52%)	16 (59.3%)	0.805
Total Gensini score	32 (24-42)	48 (42-84)	<0.001

Table 2: Angiographic characteristics in patients with poor and well collaterals CAD: coronary artery disease; RCA: Right coronary artery; LAD: Left anterior descending artery; Cx: Circumflex artery.

Variables	All patients (n=52)	Coronary collateral circulation		p
		Well developed (n=27) 48.1%	Poor developed (n=25) 51.9%	
ACE inhibitors/ARB, n (%)	10 (19.2)	7 (25.9)	3 (12)	0.296
Beta blocker, n (%)	12 (23.1)	6 (22.2)	6 (24)	1.000
Statin, n (%)	17 (32.7)	6 (22.2)	11 (44)	0.169
Fibrate, n (%)	6 (11.5)	3 (11.1)	3 (12)	1.000
Nitrate, n (%)	5 (9.6)	4 (14.8)	1 (4)	0.352
Calcium channel blockers, n (%)	5 (9.6)	3 (11.1)	2 (8)	1.000
Acetyl salicylic acid, n (%)	24 (46.2)	11 (40.7)	13 (52)	0.592

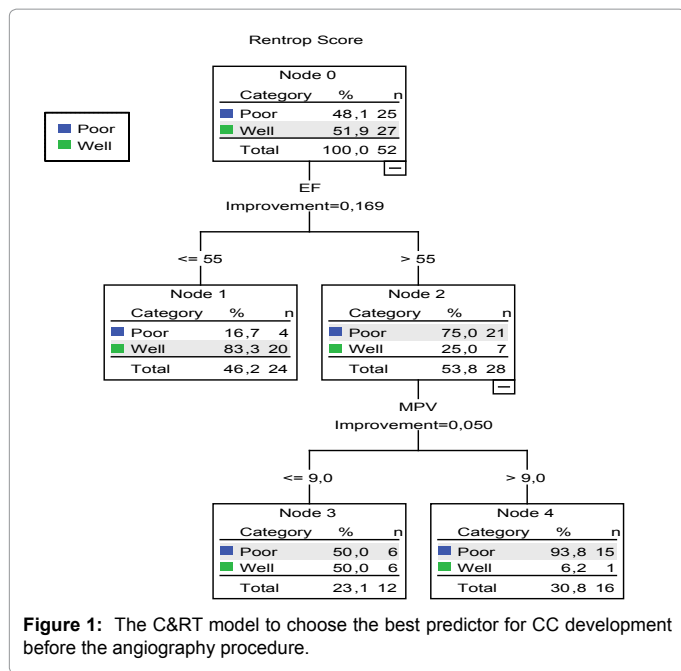
Table 3: Baseline medicine characteristics of the study patients and their comparisons.

clinical characteristics and hematological and biochemical parameters of the patients in the well and poor CC groups are summarized in Table 1. There were no statistically significant differences between the two groups with respect to age, sex, weight, height, Body Mass Index (BMI), Presence Of Hypertension (HT), Diabetes Mellitus (DM), smoking status, and creatinine, total cholesterol, Triglyceride (TG), Low-Density Lipoprotein Cholesterol (LDL) and High-Density Lipoprotein Cholesterol (HDL) levels and hematological parameters like hemogram, hematocrit, Red Blood Cell Distribution width (RDW), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Neutrophil to Lymphocyte ratio (N/L). However, well CC group had significantly lower ejection fraction (EF) values as compared to the poor CC group (44 (40-62) versus 66 (60-68.5) respectively, p<0.001). There was also no difference between the groups by means of systolic and diastolic blood pressures and Perfusion Index values (PI). There wasn't any significant difference between the groups with respect to the duration of ischemic symptoms (p=0.173) (Table 2).

With respect to the number of diseased coronary vessels, we didn't see significant difference between the groups (p=0,834) (Table 2). We didn't also see significant difference between the groups by means of particular diseased vessels (left anterior descending, circumflex and right coronary arteries) (Table 2). However, we found that there was significant difference between the groups with respect to GS (p<0.001). The GS was higher among the well-developed CC group (32 (24-42) versus 48 (42-84)).

There was no statistically significant difference between the groups with respect to the medications of the patients like Angiotensin Converting Enzyme (ACE) inhibitors, Angiotensin Receptor Blockers (ARB), acetyl salicylic acid, beta blockers, statin, fibrate, oral nitrate and calcium channel blockers (Table 3).

The correlation analysis revealed moderate negative correlation



between the Rentrop score and ejection fraction ($r=-0,469$, $p<0,001$). There was also strong positive correlation between the GS and the Rentrop score ($r=0,627$, $p<0,001$). We also found a positive weak correlation between the Rentrop score and the PDW values ($r=0,283$, $p=0,042$). We didn't find a correlation between the Rentrop score and the duration of ischemic symptoms and number of the significantly diseased vessels.

We performed classification and regression tree (C&RT) model in order to choose the best predictor for CC development (Figure 1). In the first model, we did not put angiographic variables into the model. We wanted this model to be helpful for clinicians to predict CC development before the angiography procedure. In that model, patients were first divided into two branches according to their EF values (cut off value of EF was 55%) for the prediction of CC. According to this model, patients that had EF values below 55% had better CCD (83.3% versus 16.7%). However the patients who had EF value over 55% were shown to have worst CCD (75% versus 25%).

This first model then further divided the patients who had EF over 55%. It divided them into two branches according to their MPV values (cut off value was 9 fl). The model had no predication to determine CC development for the patients who had MPV under 9 (50% had well CC where 50% had poor CC). However, for the patients who had MPV over 9, the model is signing to worst CC development (93.8% had poor CC where 6.2% had well CC).

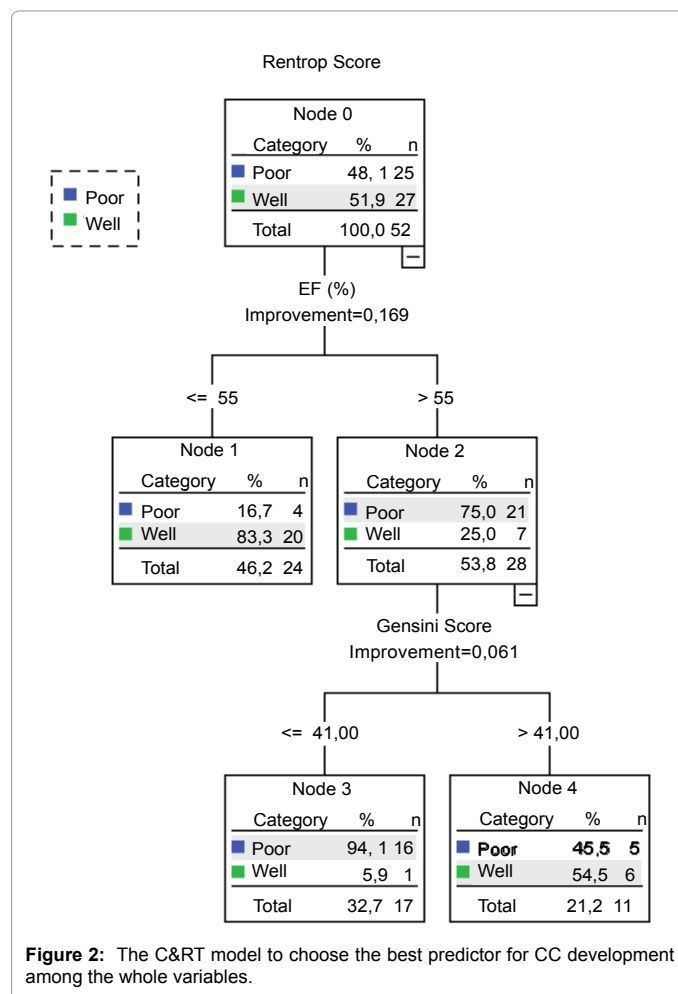
In the second C&RT model, we added angiographic variables to the model in order to describe the roles of all factors effecting CC development. In that second model, patients were first divided into two branches according to their EF values (cut off value of EF was 55%) for the prediction of CC. According to this model, patients that have EF values below 55% had better CCD (83.3% versus 16.7%). However, the patients who had EF value over 55% were shown to have worst CCD (75% versus 25%) (Figure 2).

This second model then further divided the patients who had

EF over 55%. It divided them into two branches according to their GS values (cut off value was 41). The model had poor predication to determine CC development for the patients who had GS over 41 (54.5% had well CC where 45.5% had poor CC). However, for the patients who had GS under 41, the model is signing to worst CC development (94.1% had poor CC where 5.9% had well CC). The model also listed the whole variables of the study according to their importance to predict CCD (Figure 3). This model has a sensitivity of 64%, specificity of 96.3% and accuracy of 80.8% to detect those who had poor CC development.

Discussion

The most prominent finding of our study is to be able to demonstrate significant difference between the well and poor CC groups with respect to EF and PDW. Our study is unique to establish the relation between the demographic, anthropometric, clinical, hematological and biochemical variables as well as Ejection Fraction (EF) and Perfusion Index (PI) all together with CCD. First we wanted to find the best predictors of CCD to help clinicians before the angiography procedure. Thus, we put all the variables, except angiographic findings, to the C&RT model. According to this model, the first dividing patients with respect to their EF values, and then performing further division with respect to patients' MPV levels (for the patients who had EF>55%) can be used in an algorithm for predicting CCD in patients with stable angina pectoris before the angiography procedure. Then we wanted to define the best predictors of CCD, including angiographic findings.



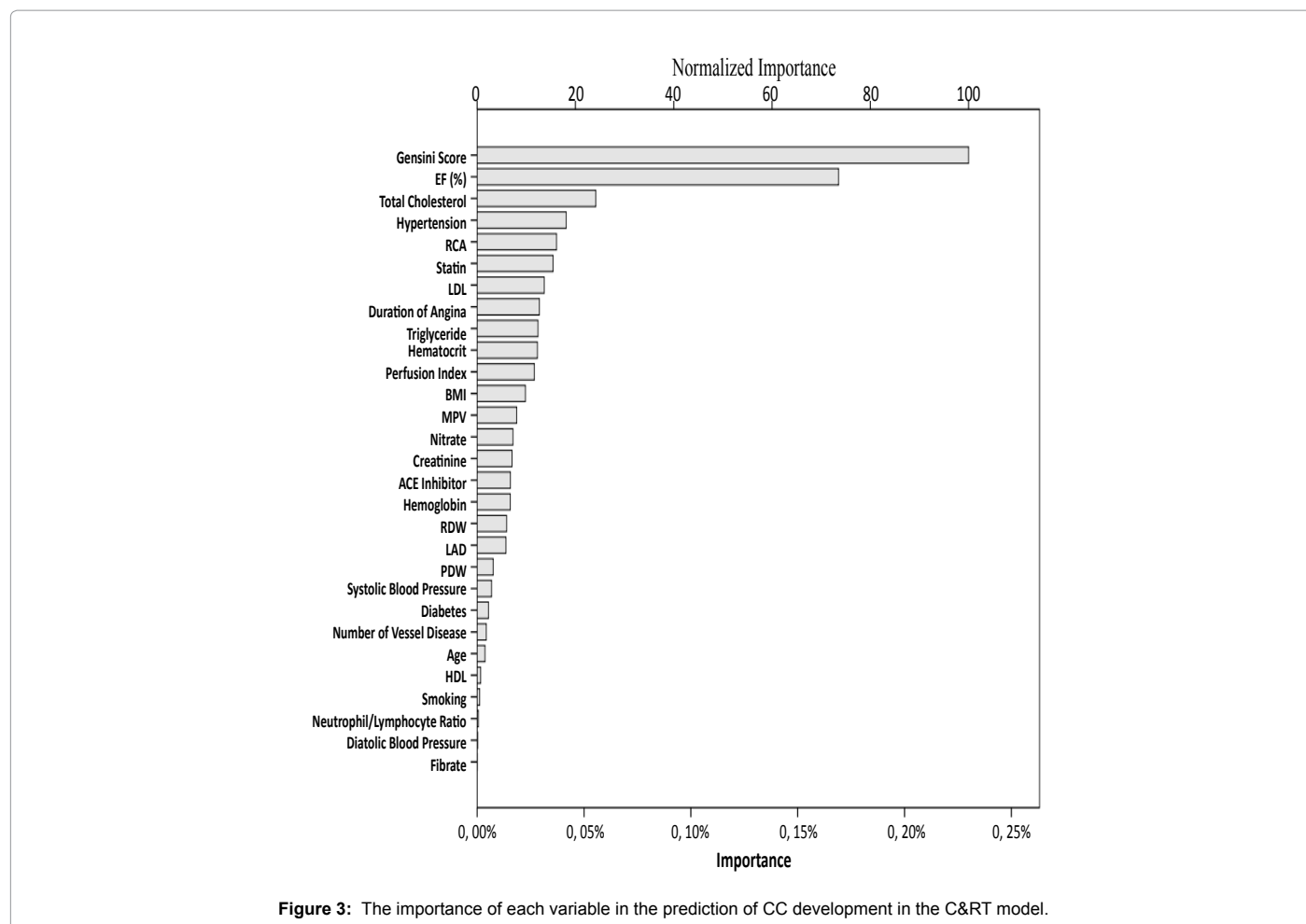


Figure 3: The importance of each variable in the prediction of CC development in the C&RT model.

So, we added angiographic findings to the previous C&RT model and found out that MPV becomes less important but GS becomes more important for the further division of groups to determine CCD. In this study, with the help of the C&RT model, we also put all the variables in order, according to their priority of importance for the determination of CCD.

We found a negative correlation between the Rentrop score and the EF values of the patients with stable angina pectoris. It is known that, in patients with obstructive CAD, left ventricular regional contractility and relaxation are influenced by collateral blood flow [27]. Furthermore, in angina, the presence of regional myocardial contractile dysfunction can be related to inadequate blood flow in collateral artery-dependent territories [28]. In other words, inadequate blood supply in collateral dependent myocardium may lead to ventricular dysfunction [8].

A different way of explaining the relationship between the EF and the CCD is to focus on the phenomenon known as “coronary steal” phenomenon. This phenomenon causes a regional myocardial hypo-perfusion because of the alteration of circulation patterns of the coronary bed. Coronary steal may also be mediated by the collateral arteries. In other words, coronary steal phenomenon through a well-developed CC may result in the myocardial regional wall dysfunction. Werner et al. suggested in their hypothesis that steals could explain regional wall motion abnormalities in patients who have chronic total coronary occlusions without a history of previous myocardial infarction [29].

We found that GS has a positive correlation with the Rentrop scores of the stable angina pectoris patients. The C&RT model revealed that a value of GS below 41 is very helpful to detect those who had poor CCD and have EF>55%. We found that GS, which is reflecting the severity of atherosclerosis in the whole coronary tree, may be related to the CCD. A possible explanation of this finding may lie under the relation of more severe atherosclerosis and resultant intermittent myocardial ischemia. There may be a provoking effect of intermittent ischemia on CCD. Of interest, Takeshita et al. previously suggested that coronary collaterals develop in response to intermittent myocardial ischemia and that these collaterals are preserved even if they are closed at rest, in order to offer immediately function on acute coronary artery occlusion, after recruitment [30].

On the other hand, Herlitz et al. demonstrated that the patients with chronic angina pectoris before an acute MI had smaller infarcts compared with the patients with angina pectoris of short duration before an acute MI [31]. They had, however, a higher 1-year mortality rate and a higher risk of re-infarction. This probably reflects more extensive CAD in these patients, with a higher risk of death.

We also demonstrated that PDW has a weak positive correlation with the Rentrop scores of the stable angina pectoris patients. Of interest, a recent study demonstrated a close relation with PDW and Chronic Total Occlusions (CTO) [32]. Moreover, they suggested that PDW can be used to predict CTO in patients with CAD. To the best

of our knowledge, our study is the first to demonstrate a significant relationship between CCD and PDW. And we suggest that PDW can also be used to predict CCD before angiography procedure.

In contrast to previous studies, we didn't find any relationship between RDW and CCD (16). In the literature, there is also a controversy about the correlation analysis data between the hematological parameter MPV and CCD [33,34]. In this particular study, we didn't find any correlation between the CCD and the MPV. However, we found that in the subgroup of study population who has EF<55%, MPV can be used in an algorithm for the prediction of CCD before the angiography procedure. In that subgroup, we didn't find MPV to have predictive value for the ones who had MPV<9 fl, however we demonstrated that patients who had MPV>9 fl had poor CCD.

In contrast with other researches, we didn't find any relation with the statin therapy and the development of collateral circulation [35].

Although many study results have suggested that angiotensin-converting enzyme inhibitors (ACE-I), beta-blockers, and nitrates may promote CCD, clinical study results are generally lacking [36-38]. We also did not find any relationship between CCD and use of this group of drugs.

Our data show that diabetes is not, as shown in the study of Zbinden et al. an independent predictor for coronary collaterals [39]. We also didn't find a relationship between diastolic blood pressure and CCD in contrast to the recent study of Shu et al. [40].

Conclusion

Before the angiography procedure, the presence of coronary collaterals can be predicted with the help of ejection fraction and hematological parameters like PDW. Patients with lower EF and higher PDW levels seem to have better CCD. Moreover, MPV > 9 fl can be helpful in further determination of CCD in the subgroup of the patients who has EF>55%. We can say that EF and MPV together constitute a simple, important, effortless, and cost effective algorithm to predict the CCD in patients with stable angina pectoris before the angiography procedure. However, in conclusion, considering all data including angiographic findings together, EF and GS together raise to be the best predictors of CCD.

Limitations

First of all, the prominent limitation of that study is the relatively small number of patients. Secondly, an important clinical data, the duration of symptoms was missing. Also, angiographic details such as the involving vessels, lesions proximity, and severity of CAD were also missing. Furthermore, the classification of the Rentrop score was made without occluding the contralateral vessels, as it was suggested in the original manuscript about that subject. This visual method also has some other limitations: it is not a very objective method as it may be influenced by blood pressure, and the force of contrast injection as well as the duration of filming. And it should also be remembered that arterioles <100 qm are invisible to the naked eyes and visible collaterals typically have diameter of ≥0.5 mm.

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