Influence of coronary artery dominance on long-term outcome in patients with non-obstructive coronary artery disease

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Abstract

Aim: Coronary arterial dominance is described on the basis of artery that feeds the posterior descending artery (PDA) and posterolateral branches. The literature lacks any data on long-term influence of coronary arterial dominance on non-obstructive coronary artery disease (CAD). This research therefore aims to study the influence of coronary dominance on long-term mortality in patients with non-obstructive CAD.

Material and Methods: This retrospective research involved 592 patients who had been subjected to elective coronary angiography. On the basis of coronary artery dominance pattern, the subjects were categorized into two groups i.e. left dominance group (n=84) and right dominance group (n=508). Patients demonstrating co-dominance were placed in the left dominance group. All-cause mortality was considered to be the primary endpoint of the research.

Results: Most (65%, 382) of the patients included in the study were male. Average age of subjects was 60±9.7 years. Right coronary dominance was demonstrated by 85.8% patients while left coronary dominance was demonstrated by 14.2% patients. 42 deaths occurred as per the recordings made in a follow-up of 48±12.9 months. In case of right dominance group, mortality rate was 6.1% and in case of left dominance group, it was 13.1% (p=0.021). Findings of a multivariate regression analysis indicated that diabetes mellitus (HR: 2.008, 95% CI:1.034−3.902, p=0.04) and left dominance (HR:1.55, 95%CI: 1.094−2.200, p=0.014) can serve as independent predictors of mortality in these patients.

Conclusion: Left dominance has been found to be associated with higher rates of mortality in non-obstructive CAD patients during a long-term follow up.

Keywords: Coronary dominance; non-obstructive coronary artery disease; prognosis

INTRODUCTION

The coronary arterial dominance is described on the basis of the artery which is responsible for giving rise to posterior descending artery and the posterolateral branches. It can also be described as the blood supplying left ventricle's diaphragmatic face. Coronary arterial dominance includes right dominance (RD), left dominance (LD) and co-dominance (CD) (1,2). Researchers have reported variable relative frequencies of coronary artery dominance for different populations. In general, right dominance has proven to be the most common coronary circulation pattern. In particular, 82-89% persons demonstrate right dominance. On the other hand only 7-8% persons demonstrate LD and only 3-7% persons demonstrate CD (3,4).

In case of persons demonstrating left dominance, the left coronary system is responsible for providing the left ventricular blood supply as well as feeding. It has recently been shown that coronary dominance can serve as independent predictor of mortality in hospitalized patients who are subjected to percutaneous coronary intervention following acute coronary syndrome (5,6). It has also been recently demonstrated that left dominance patients having acute coronary syndrome and coronary artery disease (CAD) demonstrate increased rates of mortality (7,8). At present, literature lacks any comprehensive research which has investigated the association of coronary dominance and prognosis in non-obstructive CAD patients following long-term follow-up.

This research is aimed at investigation of the association between pattern of coronary artery dominance and long-term prognosis in patients having non-obstructive coronary artery disease following elective coronary angiography.

MATERIAL and METHODS

This retrospective study involved 592 consecutive patients who had been subjected to elective coronary angiography and were diagnosed with non-obstructive coronary artery disease during the period between 2013 and 2015. An individual is said to have non-obstructive CAD when the luminal narrowing is <50% in at least one epicardial coronary artery (9,10). Exclusion criteria included a) recent acute coronary syndromes, b) detection of systemic disorders like chronic liver failure, chronic renal failure or cancer) c) atrial fibrillation, d) obstructive coronary artery disease (detected with stenosis severity over 50%) and e) established ischemic heart disease (past myocardial infarction, history of coronary revascularization). Two expert invasive cardiologists categorized the patients in two groups on the basis of coronary dominance. Patients having right coronary artery (RCA) as the dominant artery were categorized as group 1 and remaining subjects were categorized as group 2. Origin of PDA as well as posterolateral ventricular arteries was considered for determining coronary dominance. Individuals demonstrating co-dominance were categorized in group 2. Approval from the local ethics committee was approved for the method of trial. Moreover, the research was in agreement with the declaration of Helsinki. Demographic variables and baseline characteristics of the subjects were noted. The methods suggested by the American Society of Echocardiography (ASE) were used for obtaining echocardiographic images in the four standard patterns i.e. four-chamber apical, two-chamber apical, short-axis parasternal and long-axis parasternal. Left ventricular ejection fraction was calculated from apical 4 chamber views by manually tracing end-diastolic and end-systolic endocardial borders, using Simpson's method (11). All-cause mortality was considered to be the primary clinical endpoint for the research. All subjects involved in the research were retrospectively followed up. Minimum time period for follow up was 3 years and maximum time period for follow up was 5 years.

Coronary angiography

Invasive coronary angiography was made using Shimadzu Digitex 2400 and Philips Allura Xper FD 10 x-ray systems. Coronary angiography was performed as Judgkins method and 4 images were obtained for the left coronary system(left anterior oblique cranial and left anterior oblique caudal, anteroposterior cranial, right anterior oblique cranial and right anterior oblique caudal) and 2 images were obtained for right coronary artery (left and right oblique). Each image was stored in a digital archive. Images of the coronary angiography were assessed by two experienced invasive cardiologists who are blinded to study protocol and patient's clinical data. The interobserver concordance rate in detection of coronary dominance was 96%. In case of disagreement, the final diagnosis was achieved by mutual agreement. The intraobserver concordance rate was 98%.

Statistical analysis

All statistical tests were conducted using the Statistical Package for the Social Sciences 19.0 for Windows (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to analyze the normality of the data. Continuous data were expressed as mean ± SD, and categorical data were expressed as percentages. Fisher Exact or/and Chi-square test were used to assess differences in categorical variables between groups. Student's t-test or Mann Whitney U test was used to compare unpaired samples as needed. Univariate and multivariate Cox regression analysis was used to identify independent variables associated with mortality. Independent variables in univariate analysis were sex, age, diabetes mellitus (DM), hypertension (HT), hyperlipidemia, smoking status, left ventricular ejection fraction (LVEF), creatinine and RCA dominant. After performing univariate analysis, statistically significant variables were selected into the multivariate Cox regression analysis with the stepwise method. Cumulative survival curves were derived according to the Kaplan-Meier method and differences between curves were analyzed on log-rank statistics. Significance was assumed at a 2-sided $p<0.05$.

RESULTS

Average time period for the follow up was 48 ± 12.9 months. Table 1 presents the clinical and demographic characteristics of the patients included in the study. Majority of the patients were male (382, 65%). Three hundred twenty-five (64%) of the patients with dominant RCA were male and similarly, 57 (68%) of the patients with left dominant were male. Average age in the left dominance group and in the RCA group was 60.8 ± 9.2 years and 59.2 ± 10.3 years, respectively.

Significant difference was not detected between the two studied groups in context of hyperlipidemia, diabetes mellitus and hypertension. Same was the case with observed values for hemoglobin and creatinine as they were statistically same for the two groups. Also, the EF of the two groups did not demonstrate any statistically significant difference (dominant RCA vs non-dominant RCA, 54.2 ± 6.9 vs 52.9 ± 7.9, p = 0.124).

During the follow-up period of the patients, 42 patients died. In particular, 31 (6.1%) patients of the RCA dominant group died and 11 (13.1%) patients demonstrating non-dominant RCA died during the follow up (p = 0.021). All-cause deaths recorded during four years for the two groups included in the study were compared. Upon comparison it was found that the cumulative incidence of all cause deaths in patients having a LD coronary artery system was 13.5%. On the other hand, in case of patients having RD coronary systems, it was 5.6%. Survival analysis for the groups was carried out through log-rank test. Kaplan-Meier curves were used to evaluate the survival rates and differences among the two groups were found to be statistically significant (log-rank p = 0.011) as shown in Figure 1.

Table 1. Baseline characteristics of study groups

	Dominant RCA, n=508	Non-dominant RCA, n=84	p
Age, y (mean ± SD)	59.2 ± 10.3	60.8 ± 9.2	0.184
Male, n(%)	325 (64%)	57 (68%)	0.535
Smoking, n(%)	243 (48%)	45 (54%)	0.307
Hypertension, n(%)	314 (62%)	46 (55%)	0.183
Diabetes mellitus, n(%)	182 (36%)	38 (45%)	0.106
Hyperlipidemia, n(%)	254 (50%)	41 (49%)	0.683
LVEF (%)	54.2 ± 6.9	52.9 ± 7.9	0.124
Creatinine, mg/dL	0.88 ± 0.2	0.86 ± 0.2	0.487
Hemoglobin, g/dl	13.5 ± 1.7	13.4 ± 1.9	0.710
Death, n(%)	31 (6.1%)	11 (13.1%)	**0.021**

RCA: Right Coronary Artery; SD: Standard Deviation;
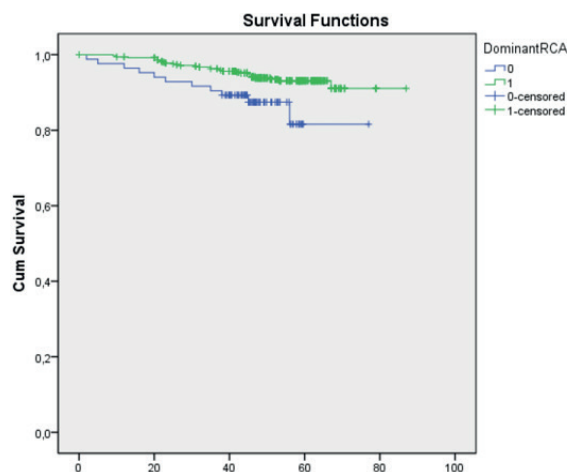LVEF: Left Ventricular Ejection Fraction

Figure 1. Kaplan−Meier curve for all-cause mortality in patients with a right dominant and left dominant coronary artery system (log-rank p , 0.011)

Table 2. Univariate and multivariate regression analysis of predictors of death

Variable	Univariate			Multivariate		
	HR	95%CI	p	HR	95%CI	p
Gender	0.794	0.413-1.528	0.490			
Age	0.996	0.968-1.026	0.794			
Diabetes mellitus	2.536	1.369-4.698	**0.003**	2.008	1.034-3.902	**0.040**
Hypertension	1.540	1.064-2.227	**0.022**	0.718	0.483-1.068	0.102
Hyperlipidemia	1.194	0.712-2.001	0.501			
Smoking	0.770	0.524-1.132	0.184			
LVEF	0.980	0.942-1.020	0.319			
Creatinine	0.567	0.113-2.837	0.490			
Non-RCA dominant	1.549	1.095-2.189	**0.013**	1.552	1.094-2.200	**0.014**

LVEF: Left Ventricular Ejection Fraction; RCA: Right Coronary Artery

Table 2 presents the univariate as well as multivariate Cox regression analysis performed for the predictors of mortality for the subjects included in the study. Diabetes mellitus (HR: 2.008, 95% CI: 1.034−3.902, p = 0.040) and non-RCA dominance (HR: 1.55, 95% CI: 1.094−2.200, p = 0.014) proved to be independent predictors of mortality.

DISCUSSION

The potential association between pattern of coronary dominance and long term prognosis in patients who had undergone elective coronary angiography and were diagnosed with non-obstructive CAD was studied during this research. It was found upon long-term follow up of patients that rate of mortality was higher in patients with left dominance in comparison to those with right dominance (13.1% vs. 6.1%, log-rank p, 0.011) as shown in Figure 1. Findings of the Cox regression analysis indicated that diabetes mellitus and left dominance can serve as predictors of mortality (p = 0.04 and p = 0.014, respectively).

Cardiovascular disorders, especially CAD, have turned into the most prominent cause of mortality in males and females all around the world (1). On time diagnosis of CAD is of crucial importance particularly for lowering down the rates of morbidity and mortality caused by CAD. It has been reported in the past that coronary arterial dominance is capable of influencing the mortality caused by cardiovascular disorders. Coronary arterial dominance is described on the basis of vessel which is responsible for giving rise to the PDA that supplies blood to interventricular septum (3,4).

Influence of coronary dominance on rates of mortality has been studied in the past as well. 1425 patients subjected to coronary computed tomography angiography were included in a Dutch research. The patients were followed up for a period of 24 months and all-cause mortality rates as well as non-fatal myocardial infarction were recorded. It was found that these rates were higher in individuals with significant CAD as per the findings of computed

tomography angiography (HR, 3.20; 95% CI, 1.67−6.13; p < 0.001) (12). Goldberg et al., carried out a research involving 27289 patients and found that mortality rates were higher in case patients demonstrating left dominance and experiencing coronary angiography for acute coronary syndrome. Following a follow-up of 3.5 years, left dominance proved to be the independent predictor of long-term mortality in studied subjects (HR, 1.13; 95% CI, 1.00−1.28)(7). 207,926 patients subjected to percutaneous coronary intervention in order to manage acute coronary syndrome were included in the Cath PCI registry research. Increased rates of in-hospital mortality were recorded for patients demonstrating left dominance (OR=1.19, 95% CI, 1.06−1.34) and co-dominance (OR=1.16, 95% CI, 1.01−1.34) (5). Veltman et al., carried out a research study that involved 1132 patients subjected to coronary angiography for ST-elevation myocardial infarction (STEMI). A follow-up of five years revealed that rate of all-cause mortality was considerably higher in patients demonstrating left dominance in comparison to those with right dominance (log-rank p = 0.013). The researchers declared left dominance as the independent predictor for one month mortality (OR 2.25, 95% CI 1.09-4.61, p = 0.028) (13). During another research conducted by Kuno et al., 4873 patients who were subjected to percutaneous coronary intervention for acute coronary syndrome were included. Considerably worse in-hospital clinical outcomes were demonstrated by patients with left dominance in comparison to those with right dominance. Similarly, symptoms of cardiopulmonary arrest (p = 0.003), cardiogenic shock (p = 0.021) and heart failure (p = 0.025) were considerably more prominent in the group of left dominance as compared to the group of right dominance. Just like earlier studies, left dominance proved to be an independent predictor of in-hospital mortality in patients with acute coronary syndrome (OR 1.75; 95% CI 1.06-2.89; p = 0.030) (6). Omerbasic et al., performed a study involving 100 patients who experienced coronary artery bypass surgery for coronary artery disease. Rates of negative clinical outcomes were higher in case of left dominance patients as compared to right dominance patients. Significant difference was not found in terms of neurological, renal, respiratory and surgical complications; however, the stay in hospital was found to be lengthier in case of left dominance patients (p = 0.003) (14).

In a retrospective study, Emad Abu-Assi et al. investigated the effect of pattern of coronary dominance on long-term prognosis. The study involved 767 STEMI patients subjected to primary percutaneous coronary intervention. A follow-up of 40.8 months revealed that individuals with left dominance are at greater mortality risk as compared to those with right dominance (p < 0.001). The researchers carried out multivariate analysis and detected a correlation between left dominance and reinfarction (HR = 2.06; p = 0.01) mortality (HR = 1.76; p = 0.02) (15). Liyuan Peng et al., carried out a research to study how coronary dominance affected the 3-vessel coronary artery disease. The study involved 2225 patients who were subjected to coronary angiography. Rate of 3-vessel CAD was found to be higher in patients demonstrating right dominance (36.6% vs 27.3%, p = 0.008). Similarly, the patients with right dominance demonstrated higher rates of stenosis of right coronary artery (40.5% vs 29.2%, p = 0.001). Logistic regression analysis revealed an association between 3-vessel disease and right dominance (OR 1.768, 95% CI 1.057−2.956, p = 0.030) (16). The association between pattern of coronary dominance and severity of coronary artery disorder has also been studied by BinYan et al. The researchers analyzed 1654 patients who were subjected to coronary angiography. Patients with right dominance demonstrated greater Gensini score as compared to left dominance patients (42.3 ± 33.6 vs 36.3 ± 29.8; p = 0.033). As per the findings of multivariate linear regression, right dominance proved to be an independent predictor indicating severity of coronary artery disorder (β=6.699, 95% CI 1.193 to 12.205, p = 0.017) (17). Unlike these studies, Catherine Gebhard et al., detected no significant difference in survival rates on computed tomography angiography demonstrated by left and right dominance 6,382 patients during a follow up of 60 months (18).

CONCLUSION

In our study, we found a high mortality rate after long-term follow-up in patients with left dominance (13.1% vs 6.1%, log-rank p = 0.011; Figure 1). After cox regression analyses revealed that left dominant was found to a predictor of death (HR: 1.55, 95% CI: 1.094−2.200, p = 0.014). This may be explained by the effect of a greater amount of myocardium after myocardial infarction due to left coronary artery occlusion in patients with left dominance. A normal coronary angiography excludes epicardial coronary artery disease, but microvascular disease may be responsible for cardiac death in this group of patients. The difference of our study from other previous studies is that it was performed in patients with patients with non-obstructive coronary artery disease. To the best of our knowledge, there are no studies published about the association of coronary dominance and prognosis in non-obstructive CAD patients following long-term follow-up. Our findings suggested that the prognosis of patients with non-obstructive coronary artery disease may be related to coronary artery dominance. We found that the mortality rate is significantly different with left coronary arterial dominancy as compared to the right pattern. However, the reasons for these relationships are not clear. In case of non-obstructive CAD patients, individuals with left coronary artery dominance are at higher risk of mortality.

LIMITATIONS

Due to small proportion of left and codominant coronary arterial system in the general population our findings should be confirmed with larger and sufficiently studies. The deaths in our study were performed in different hospitals, the death records were taken from the death notification system and the causes of death could not be determined. The major limitation of our study is regarding the number of patients. To increase the statistical strength of this study, more patients should be included.

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