INTRODUCTION

Although atherosclerosis is a systemic disease affecting a variety of vascular beds in the body, the distribution of obstructive lesions is rather heterogeneous and asymmetric. Specific regions in the vasculature have been well recognised as more susceptible to the development of atheromatous plaques (brancing points, bifurcations, inner side of curvatures) probably owing to the local effect of flow-related haemodynamic forces (1-3).

The unique structural configuration of the human coronary arterial system presents considerable anatomic and physiologic differences between the left (LCA) and right (RCA) coronary artery. The effect of these differences in the prevalence, extent and severity of coronary lesions in the LCA versus RCA has come to the fore, as this may affect the clinical presentation and subsequent management of coronary artery disease.

The purpose of the present review is to summarise current evidence regarding differences in the localisation of coronary artery disease between LCA and RCA, describe their clinical implications, and provide a possible pathophysiologic explanation in relation to the flow-related risk factors for atherosclerosis.

ABSTRACT

Differences in the prevalence, extent and severity of atherosclerotic lesions in the left coronary artery (LCA) versus the right coronary artery (RCA) have come to the fore, as they may influence the clinical presentation, complications and subsequent management of coronary artery disease. Data from descriptive epidemiological studies suggest a higher susceptibility of the LCA for atherosclerosis in comparison to the RCA. Altered haemodynamics, as a result of the different forces exerted in LCA and RCA during the cardiac cycle, affect blood flow properties and favour the development of regions with low or oscillatory endothelial shear stress in the LCA, thereby promoting atherogenesis.

Increased wall stress in the LCA, as well as the complex three dimensional geometric configuration of the coronary arteries in combination with the divergent dynamic structural alterations they undergo during the cardiac cycle may also contribute to the above disparity in atherosclerosis susceptibility between RCA and LCA. Further analytical research in the above factors is warranted to elucidate the precise pathophysiologic mechanisms of coronary atherosclerosis.

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Left circumflex artery provides blood supply to the lateral wall of the left ventricle, the left atrium, a portion of the anterolateral mitral papillary muscle while in cases of left coronary dominance (10%) it is this vessel instead of the RCA which gives rise to a posterior descending artery, an atrioventricular branch and posterolateral branches (6). In 20% of cases the dominance is shared between the right and left coronary arterial system. With regards to the cardiac conduction system, the sinus node is supplied by the proximal RCA in 55% of cases and by the proximal left circumflex in the remainder. The atrioventricular node is supplied by the RCA in 90% of cases and by the left circumflex in 10%. The main left bundle of His has dual blood supply by the RCA and left circumflex coronary artery while the other parts of the His bundle are perfused by branches of the LCA (5).

Clinical manifestations of atherosclerosis in the LCA versus RCA

The clinical syndromes arising from lesions in the LCA show certain differences in their presentation and potential complications as compared to those coming from lesions in the RCA. Acute occlusions in the LCA manifest clinically as left ventricular infarction, while respective lesions in the RCA most commonly present as inferior or posterior wall infarctions in the setting of a right dominant coronary circulation, with a variable degree of right ventricular involvement depending on the exact site of obstruction.

With regards to complications, haemodynamic events including cardiogenic shock, ventricular septal rupture and free wall rupture are more common in cases of left ventricular infarctions, while electrical complications as bradycardia and heart block are more frequent in cases of inferoposterior infarctions but have a more benign prognosis than in the context of left anterior wall infarctions (5). In chronic coronary artery disease, lesions in the LCA more commonly cause exertional angina and left ventricular dysfunction and failure, while obstructions in the RCA may account for regional hypokinesis in the inferior left ventricular wall or the right ventricle which may not produce marked symptoms for a long time.

Epidemiology of atherosclerosis in the LCA versus RCA

A classic autopsy study of 600 women hearts revealed a higher prevalence of atherosclerosis in the LCA as opposed to the RCA. Notably this discrepancy was more pronounced with the progression of age (6). Another autopsy study in 600 men hearts also showed a greater degree of atherosclerosis in the proximal left anterior descending artery than in the other coronary segments but failed to demonstrate any differences in the pattern of atherosclerosis between LCA and RCA (7). Furthermore, histopathology data from 2,964 hearts showed a predilection of the left anterior descending artery for the development of atherosclerosis (8).

Moreover, an angiographic study in 302 patients showed the majority (73%) of lesions to be located in the LCA (9). Intravascular ultrasound (10) and computed tomography (11) data further confirm a higher prevalence of atherosclerosis in the LCA. In the largest angiographic registry published to date (n=17,305), coronary disease was more frequent in the LCA than in the RCA (odds ratio 5.37, p<0.001). Of note, men in this registry were less likely than women to have isolated LCA disease (odds ratio 0.75, p<0.001) and were instead more prone to present with widespread atherosclerosis involving both LCA and RCA (odds ratio 1.33, p<0.001) (12).

Haemodynamic differences between LCA and RCA

a) Effects of blood flow and endothelial shear stress (ESS)

Blood flow during the cardiac cycle exhibits considerable differences between LCA and RCA. Coronary flow in LCA follows a biphasic pattern being low during systole, rapidly rising at the onset of diastole and then progressively declining as the diastole continues. In total, 85% of the antegrade flow in the LCA occurs during diastole (13). On the other hand, blood flow in the RCA shows less phasic variation and is almost consistent during the cardiac cycle with a small systolic predominance (Figure 1) (13,14). However, in the RCA segments, which supply parts of the left ventricle, the same haemodynamic conditions with LCA prevail (13).

Figure 1: The flow patterns at the epicardial segments of the left (LCA, upper panel) and right coronary artery (RCA, lower panel) over the cardiac cycle.

The diastolic blood flow is less prominent in RCA than in LCA, whereas RCA has relatively systolic dominance in comparison to LCA (reprinted from Chatzizisis YS et al. Is left coronary system more susceptible to atherosclerosis than right?: A pathophysiological insight. Int J Cardiol 2007;116:7-13.)

The explanation of these variations lies on the definition of coronary flow. In principle, blood flow (Q) through an organ is determined by the pressure gradient (or perfusion pressure, DP) driving the flow divided by the resistance (R) to flow (16). In the coronary circulation, flow in the RCA and LCA is calculated as the quotient of the pressure gradient between the aortic root and the right or left ventricle, respectively, and the vascular resistance

\[ Q = \frac{\Delta P}{R} \]

In the case of the LCA, ΔP is much higher in diastole than in systole. This is because left ventricular end-diastolic pressure (normally ~10mmHg) is considerably lower than aortic end-diastolic pressure (normally ~80mmHg) while end-systolic pressures are fairly similar between left ventricle and ascending aorta (16).
RCA and LCA, which operate as low resistance distribution vessels, give off peripheral branches which submerge into the myocardium constituting the blood flow regulating microvascular resistance vessels \(^{(17)}\). The resistance to flow in these vessels which is transmitted to the LCA is reduced during diastole. Myocardial relaxation in diastole eliminates the mechanical systolic compression to the local coronary microvasculature by the contractile left ventricular myocardium, thus increasing arterial diameters and reducing resistance \(^{(18)}\). According to the Poisseuille’s equation, for any given vessel length (L), blood viscosity (\(\mu\)) and perfusion pressure (\(\Delta P\)), flow (Q) is proportional to the fourth power of the vascular radius (r):

\[
Q = \frac{\Delta P \times \pi \times r^4}{8 \times \mu \times L}
\]

As a result of these phenomena, coronary flow in the LCA is expected to be augmented during diastole.

In the case of RCA, systolic \(\Delta P\) is higher than in the LCA, as the right ventricular peak systolic pressure is much lower (normally \(~25mmHg\)) than aortic peak systolic pressure (normally \(~120mmHg\)), producing a net pressure gradient in the RCA during cardiac systole \(^{(16,19)}\). Furthermore, the mechanical compressive resistance imposed to the RCA endomyocardial branches by the relatively thin right ventricular wall is much lower than the resistance exerted to the LCA vasculature by the comparatively hypertrophied left ventricular myocardium. Thus, coronary flow in the RCA shows considerably less phasic variation than in the LCA containing a strong systolic component as well \(^{(15,20)}\).

ESS is the tangential force exerted on the vascular endothelial surface as a result of the friction caused by blood flow. ESS is equivalent to the product of the blood viscosity (\(\mu\)) and the radial gradient of axial blood velocity (dv/dy) at the endothelial surface:

\[
ESS = \mu \times \left(\frac{dv}{dy}\right)
\]

ESS is expressed in units of force per area i.e. N/m² or Pascal or dyne/cm² (1 N/m² = 1 Pascal = 10 dyne/cm²) \(^{(21)}\). ESS is a major modulator for the normal endothelial function and morphology. Low (approximately less than 10-12 dyne/cm²) and oscillatory (in time and space) ESS have been associated with the initiation and progression of atherosclerosis in specific coronary regions as well as with the development of vulnerable plaques \(^{(22-26)}\). Since ESS is directly proportional to the flow velocity gradient near the endothelium, it is conceivable that ESS variations during the cardiac cycle will follow the same pattern with blood flow \(^{(2,27)}\).

As a consequence of the previously described phasic differences in coronary flow between LCA and RCA, it is expected that ESS would exhibit greater oscillations in LCA than in RCA. Since an oscillatory ESS predisposes to atherogenesis, this ESS variation between the LCA and RCA may account for the increased susceptibility of LCA to atherosclerosis. A higher prevalence of atherosclerosis in the RCA which has been reported among patients suffering from chronic respiratory disease can be also explained in haemodynamic grounds \(^{(18,19)}\). In the setting of chronic respiratory disease, the ensuing pulmonary hypertension causes an increase in the right ventricular systolic pressure as well as right ventricular hypertrophy.

The latter leads to an increase in the compressive systolic myocardial resistance to blood flow, thereby limiting RCA flow in systole. In other words, fairly similar haemodynamic conditions with the left ventricular myocardium develop and a more oscillatory ESS is favoured in the RCA which would turn predispose to atherogenesis \(^{(13,19,20)}\).

Apart from ESS oscillations during cardiac cycle, static ESS values may differ between LCA and RCA. In a study of 17 three-dimensionally reconstructed coronary arteries, ESS was considerably lower in the RCA than in the LCA (\(p<0.001\), Figure 2a). In the first instance, this may seem contradictory to the higher preponderance of atherosclerosis in the LCA suggested by the epidemiological data, as low ESS favours atherosclerosis. However, in the same study a significant positive linear correlation between ESS and % luminal stenosis was found (\(r=0.457, p<0.001\), Figure 2b), and this was justified by the association of increasing ESS with constrictive arterial remodelling.

\[\text{Figure 2a: Endothelial shear stress (ESS) variation between left anterior descending (LAD) left circumflex (Cx) and right coronary artery (RCA).}\]

\[\text{ESS was significantly lower in RCA as compared to LAD and Cx.}\]

\[\text{Figure 2b: Linear correlation between ESS and % luminal stenosis.}\]

\[\text{ESS was positively correlated with % luminal stenosis (p<0.001).}\]

\[\text{Pa= Pascal}\]
In other words, while low ESS favours atherosclerosis, regions with higher ESS were found to elaborate a constrictive remodelling response to plaque growth. Such a response would cause an angiographic documentation of luminal stenosis. Thus, the higher ESS values found in the LCA were associated with lumen shrinkage and may account for the increased prevalence of angiographic lesions in the LCA as compared to the RCA (30).

The right and left coronary artery system differ not only in the prevalence, but also in the spatial distribution of plaque, particularly high-risk lesions. Rupture-prone thin-capped fibroatheromas cluster in the proximal left anterior descending coronary artery and left circumflex artery, whereas they are more uniformly distributed in the RCA, as evidenced by autopsy and in-vivo imaging studies. This longitudinal distribution of high-risk plaques co-localises with the proximal distribution of low ESS, which is more prominent in left compared to the right coronary system (1,23-33). These observations suggest that the RCA and LCA differ in the axial localisation of atherosclerotic lesions, a difference that fits well with the difference in the focal distribution of plaque-prone ESS conditions.

b) Effects of wall stress

Wall stress (WS) in the haemodynamic force exerted perpendicularly at the vascular wall as a result of the hydrostatic blood pressure divided by the product of intracoronary pressure (P) and vascular radius (r) divided by the arterial wall thickness (T): 

\[ WS = \frac{P 	imes r}{r} \]

Increased WS has been proposed as a factor promoting atherogenesis. In the left coronary arterial system, the sub-endocardial arteries experience retrograde flow during systole because of the mechanical compression exerted by the contractile myocardium. This longitudinal distribution of high-risk plaques co-localises with the proximal distribution of low ESS, which is more prominent in left compared to the right coronary system (1,23-33). These observations suggest that the RCA and LCA differ in the axial localisation of atherosclerotic lesions, a difference that fits well with the difference in the focal distribution of plaque-prone ESS conditions.

**REFERENCES**


**CONCLUSION**

Data from observational studies converge to the point that stenotic atherosclerotic lesions are more commonly found in the LCA than in the RCA. This may be attributed to the diverse haemodynamic conditions which prevail in the LCA versus RCA as a result of the variable forces exerted in each artery during the cardiac cycle. The complex three-dimensional geometric configuration of the coronary arteries in combination with the divergent dynamic structural alterations they undergo during the cardiac cycle also contribute to the above disparity in atherosclerosis susceptibility between RCA and LCA. Further analytical research in the above factors is warranted to elucidate the precise pathophysiological mechanisms of coronary atherosclerosis.


