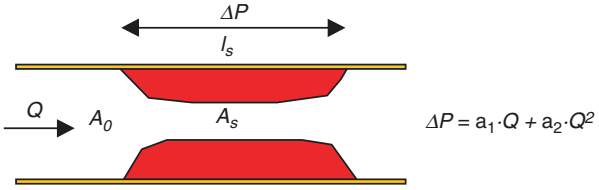
Chapter 5
Arterial Stenosis



Aortic coarctation and arterial stenosis is a localized narrowing of the arterial lumen, typically as a result of atherosclerosis. A stenosis is quantified by the ratio A_s/A_0, called the area ratio, often expressed as % area occlusion, given as $(1 - A_s/A_0)\cdot 100$. The relation between pressure drop across the stenosis, ΔP, and flow, Q, is quadratic, which means that stenotic resistance increases with flow. The linear term in the pressure drop-flow equation accounts for the viscous losses within the stenosis, whereas the quadratic term accounts for losses due to turbulence. In severe stenoses (area occlusion more than 85%), turbulent losses dominate and the pressure drop is proportional to flow squared. Severe stenoses add significant resistance to flow and can be potentially harmful by preventing adequate blood supply to distal beds.

5.1 Description

Stenosis, from the Greek word for 'narrowing', is a medical term used to describe a localized constriction in an artery. Stenoses are usually caused by the development of atheromatous plaques in the sub intimal layer of the arterial wall, which subsequently protrude into the lumen of the artery, thus causing a narrowing and limiting the free passage of blood.

A coarctation or arterial stenosis consists of a converging section, a narrow section, with the minimal luminal section defining the degree of stenosis, and a diverging

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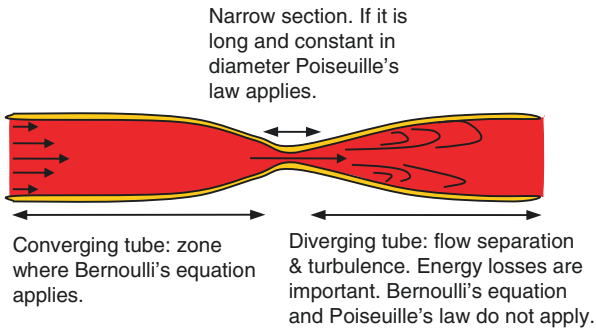

Fig. 5.1 A coarctation consists of a converging section, a narrow section and a diverging section, each with their particular pressure-flow relations

section (Fig. 5.1). In the converging section, Bernoulli's equation holds (see Chap. 3). In the narrow section Poiseuille's law is assumed to apply, provided that this narrow section is long enough with approximately constant diameter. In the diverging section flow separates and is often turbulent with significant viscous losses, which means that in this region neither Bernoulli's nor Poiseuille's law applies.

The severity of a stenosis can be expressed as % area $(1 - A_s/A_o)\cdot 100$ or percentage of the normal diameter as $(1 - D_s/D_o)\cdot 100$, with subscripts s and o denoting stenotic and unstenosed vessel segments, respectively (Figure in the Box). Pressure losses over a coarctation can be treated through semi-empirical relations. Such a relationship was developed by Young & Tsai [1] who performed a series of experiments of steady and pulsatile flows in models of concentric and eccentric stenoses. Young and Tsai found that the pressure across a stenosis, ΔP, can be related to flow, Q, by the following relation:

$$\Delta P = \frac{8\pi \cdot \eta \cdot l_s}{A_s^{\,2}} \cdot Q + \frac{K_t \cdot \rho}{2A_0^{\,2}} \cdot \left[A_0 / A_s - 1\right]^2 \cdot Q^2 = a_1 Q + a_2 Q^2$$

where A_0 is the unobstructed cross-sectional lumen area and A_s the minimal free cross-sectional lumen area (see Box Figure). The first term of the stenosis equation accounts for the viscous losses (Poiseuille's law) as blood flows through the narrow coarctation lumen. The second term accounts for the pressure losses distal to the stenosis and it is derived from the mechanics of flow in a tube with an abrupt expansion. The K_t is an empirical coefficient approximately equal to 1.5, but strongly depending on the shape of the stenosis, smoother return to distal area corresponds with a smaller K_t. The equation is derived for steady flow, but for oscillatory pressure-flow relations a qualitatively similar equation holds [2].

5.1.1 Post Stenotic Dilatation

The arterial diameter distal of a stenoses is often increased, a phenomenon called post stenotic dilatation. The mechanism causing the dilatation is still not clear. It may be due to abnormal shear stress and turbulent flow downstream of the stenosis,

leading to extracellular matrix remodeling in the vessel wall. It has also been suggested that vessel wall vibrations distal to the stenosis cause the dilatation [3] Another possible mechanism of post-stenotic dilatation is the effect of increased shear stress within the stenosis upon platelets which become activated and release the serotonin from their dense granules. Serotonin acts upon endothelial $5HT_1$ receptors to release nitric oxide which relaxes the vascular smooth muscle to produce dilatation.

5.2 Physiological and Clinical Relevance

The best way to characterize a stenosis is by constructing the relation between flow through and pressure across the stenosis (See Fig. 5.2).

The empirical formula for the pressure drop across a stenosis shows that both flow and area appear as quadratic terms. This is an important aspect of the hemodynamics of a coarctation. To illustrate the significance of the quadratic terms, let us assume that the stenosis length, l_s, is very small so that the first term in the equation above, $a_1 \cdot Q$, is negligible. The pressure drop is then proportional to the flow squared. Suppose that a patient with a mild coarctation in the femoral artery has, at rest, a pressure gradient over the narrowed section of 10 mmHg. When the patient starts walking, and the peripheral bed dilates to allow for more perfusion flow through the microcirculation, the gradient in pressure increases. When flow needs to increase by a factor three the pressure gradient should be $10 \cdot 3^2 = 90$ mmHg. This is clearly impossible and vasodilation, the decrease in peripheral resistance of the leg, does not help to increase flow sufficiently.

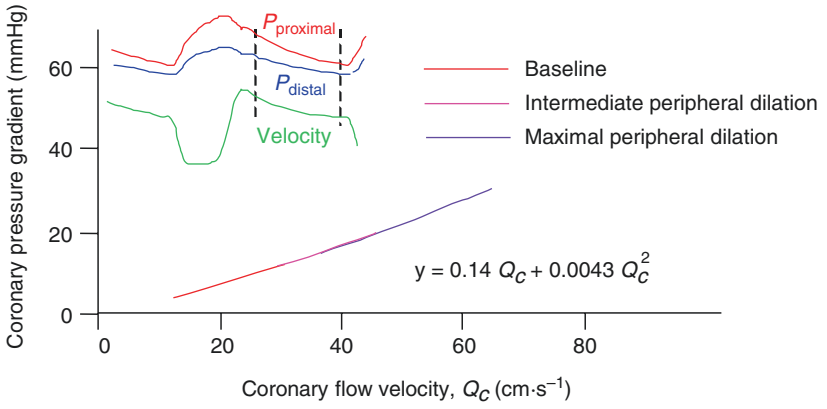

Fig. 5.2 Pressure drop over a coronary stenosis, as a function of blood flow velocity during diastole to minimize the effect of cardiac muscle contraction on the vasculature. The range of velocities is obtained by vasodilation of the distal vessels. The quadratic expression can be applied. (Adapted from Ref. [4], used by permission)

The pressure drop is inversely related to the square of the cross-sectional area in the stenosis. For an 80% area stenosis, the factor $(A_0/A_s - 1)^2$ equals $(1/0.2 - 1)^2 = 16$, whereas for a 90% stenosis this factor increases to 81. Thus a 90% stenosis is 81/16 or about 5 times more severe in terms of pressure drop than an 80% stenosis for a similar flow, i.e., it increases from 10 to 50 mmHg. This strongly nonlinear effect implies that complaints from ischemia will arise 'suddenly' when the narrowing becomes more severe, typically for a stenosis of >70%. Measurement from angiography is often not accurate enough to distinguish the small differences in area reduction.

From Bernoulli's equation it follows that at high velocity in a stenosis the pressure is low (Chap. 3). This implies that, as is the case during vasodilation, when flow and thus velocity is increases, the transmural pressure in the narrow section may decrease to low values. For compliant stenoses, (compliant wall) the decrease in transmural pressure may lead to extra narrowing, thereby worsening the situation.

5.2.1 Flow Reserve

Angiographic data often do not give accurate information about the functional hemodynamic aspects of a stenosis or coarctation. This has led several investigators to propose methods to obtain a quantitative description in terms of pressure-flow relations. One approach is the determination of flow reserve. The, absolute, flow reserve is defined as the ratio of flow during maximal (pharmacologic) dilatation and flow during control (Q_{max}/Q_{contr}). In Fig. 5.3, pressure distal to a stenosis, P_d, is plotted as a function of flow, while proximal (aortic) pressure is assumed to be constant. It is apparent that when the periphery is strongly dilated, i.e., the peripheral resistance decreases from R_{contr} to R_{min} the flow increases. However, in the presence of a severe stenosis (lower curve in Fig. 5.3), the flow increase is limited and distal pressure greatly decreases. In control conditions, at rest, flow may be hardly affected by the presence of the stenosis, since peripheral (physiological) dilation may compensate for the stenosis 'resistance', i.e., Q_{contr} depends on stenosis severity and on microvascular resistance. At maximal vasodilation a severe stenosis limits maximal flow Q_{max} considerably, but the peripheral resistance remains playing a role. Thus, in presence of a stenosis, flows are not determined by the stenosis alone, but by both the stenosis and the microvascular resistance. In other words, the flow reserve (Q_{max}/Q_{contr}) is not determined by the severity of a stenosis alone.

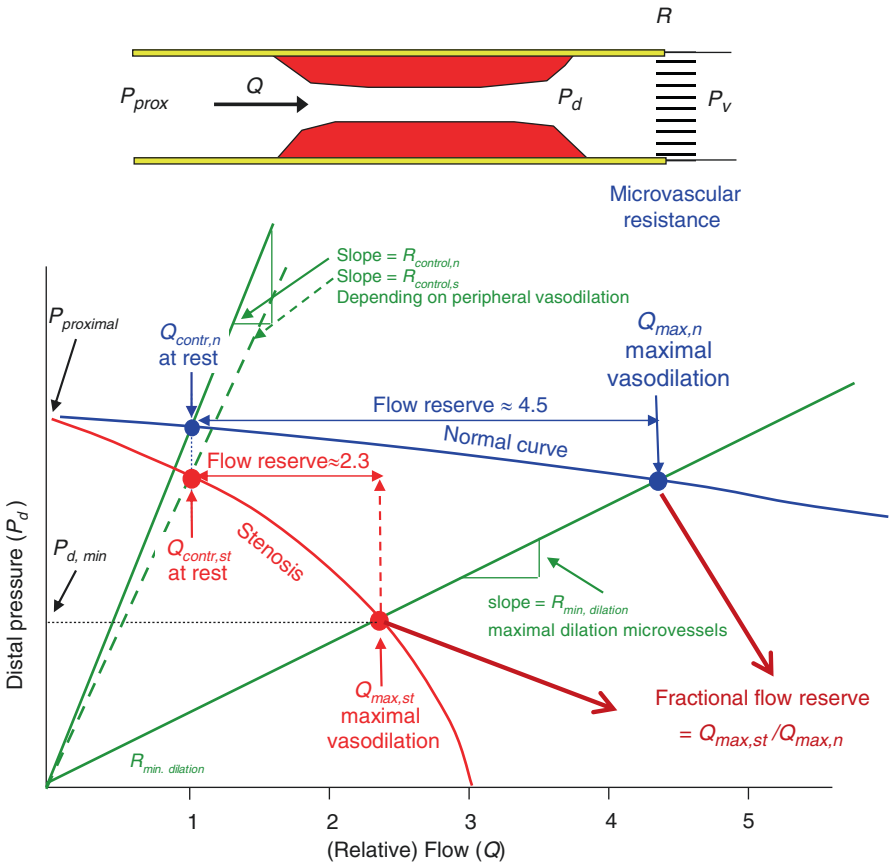

Fig. 5.3 In this figure pressure (distal of a stenosis) is plotted as a function of flow. Flow reserve is defined as the ratio of flow during maximal vasodilation and flow during control. Without stenosis the $Q_{max,n}/Q_{contr,n}$ is much larger than with a stenosis present, $Q_{max,st}/Q_{contr,s}$. With the stenosis the microcirculation may dilate to result in similar flow at rest (indicated by green). When the peripheral bed is maximally vasodilated, peripheral resistance decreases from R_{contr} to $R_{min,dilation}$ and flow increases, but distal pressure decreases. The decrease in distal pressure limits the maximal flow under vasodilation, thereby reducing the flow reserve. Thus, the flow reserve depends on the stenosis severity and microvascular resistance both in control and after maximal dilation. The Fractional Flow Reserve, FFR, is the ratio of the maximal flow with the stenosis present and maximal flow in the unaffected bed, $Q_{max,st}/Q_{max,n}$. The FFR depends on the stenosis severity and also on how much the distal bed can dilate. The FFR is close to the ratio of the distal pressure during dilation and the proximal pressure, $P_{distal,min}/P_{prox}$, if the maximally dilated bed distal to the stenosis is "normal". The, nonlinear, relation between pressure drop over the stenosis and flow through it, $(P_{prox} - P_{dmin})/Q$, depends on the stenosis severity only

5.2.2 *Fractional Flow Reserve*

Another estimate of stenosis severity is the Fractional Flow Reserve, FFR, which is the ratio of the maximal (pharmacologically induced) flow, $Q_{max,st}$ in the bed perfused by the stenosed artery and the maximal flow in a normal, not stenosed bed, $Q_{max,n}$. The FFR is thus

$$FFR = Q_{\max,st} / Q_{\max,n} = [(P_d - P_v) / R_{st,\min}] / [(P_{prox} - P_v) / R_{contr,\min}]$$
$$\cong P_d / P_{prox} \cong P_d / P_{aorta}$$

with P_d being the distal pressure during maximal dilation, and P_{prox} the proximal (aorta) pressure, and P_v venous or intercept pressure (Chap. 6). For coronary stenoses the proximal pressure equals aortic pressure. Under the assumption that the microvascular bed of the stenosed area has the same resistance as the bed of the normal area, $R_{st} = R_n$, and assuming that P_v is small with respect to P_d it holds that the FFR is close to the ratio P_d/P_{aorta} [5].

Although a normal periphery and the periphery distal to a stenosis may not have similar resistance, the FFR appears a workable parameter. The cut-off value of the FFR is 0.74, i.e. for values higher than 0.74 the stenosis is not considered functionally important. For segmented stenoses, i.e., stenoses severity changes over the vessel's length, and for multiple stenoses P_d should be measured distal of the last lesion.

Spaan et al. [6] have reviewed the principles and limitations of flow reserve.

References

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