

Chapter 5

Micro Flows in the Cardiopulmonary System: A Surgical Perspective

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Abstract Micro-flows in different organs—i.e., the flow of blood through the smallest vessels, the microcirculation—differ in a number of aspects from blood flow in larger vessels. Most prominently, the vessels of the microcirculation exhibit diameters which are comparable in diameter to the size of red blood cells. In addition to these hemorheological differences, the vessels of the microcirculation exhibit the largest fraction of the overall inner vessel surface which is covered by the endothelium. This chapter focuses on the heart and the lung addressing phenomena in the microcirculation, including the no reflow phenomenon, coronary microvascular dysfunction in the heart and the hypoxic pulmonary vasoconstriction in the lung.

5.1 The Heart

The blood flow is delivered to the heart through large epicardial conductance vessels (1–3 mm in size) and then into the myocardium by penetrating arteries leading a plexus of capillaries. The bulk of the resistance to coronary flow is in the penetrating arterioles (140 down to 20 μm in size). Because the heart is metabolically very active, there is a high density of capillaries such that there is approximately one capillary for every myocyte, with an intercapillary distance at rest of approximately 17 μm [22].

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Fig. 5.1 Coronary artery stents

Atherosclerotic disease primarily affects the large conductance vessels of the heart. The hemodynamic effect that a coronary artery stenosis has upon blood flow may be considered in terms of Poiseuille's law, which describes the resistance (R) of a viscous fluid to laminar flow through a cylindrical tube. Resistance is inversely proportional to the fourth power of the radius (r) and directly proportional to the length (L) of the narrowing, and viscosity of the fluid (μ). By Poiseuille's law a 1-cm, 80% stenosis has a resistance that is 16 times as high as the resistance of a 1-cm, 60% stenosis. Similarly, if this stenosis progresses to a 90% stenosis, the resistance is 256 times as great as the resistance of a 60% stenosis [6,10]

$$R = 8\mu L / \pi r^4$$

Placement of coronary artery stents (Figs. 5.1 and 5.2) or coronary artery bypass (Fig. 5.3) reestablish the coronary blood flow and decrease the probability of myocardial infarction. However, this approach is only addressing the patency of large vessels and there is increasing evidence that the microcirculation plays a very relevant role in the pathophysiology of myocardial perfusion states with increased flow resistance.



Fig. 5.2 Right coronary angiogram before (*left*) and after stent deployment (*right*)

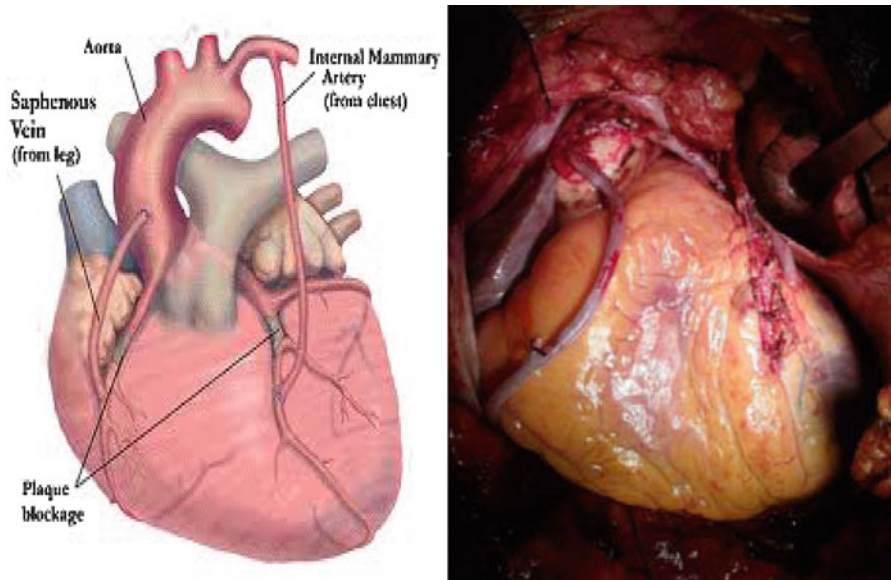


Fig. 5.3 Coronary artery bypass with left internal mammary artery to the left anterior descending coronary artery and saphenous vein graft to the right coronary artery

In a variable proportion of patients presenting with ST-segment elevation myocardial infarction, ranging from 5 to 50%, primary percutaneous coronary intervention (PCI) achieves epicardial coronary artery reperfusion but not myocardial reperfusion, a condition known as “no-reflow.” Of note, no-reflow is

associated with a worse prognosis at follow-up. The phenomenon has a multifactorial pathogenesis including: distal embolization, ischemia–reperfusion injury, and individual predisposition of coronary microcirculation to injury. Several therapeutic strategies have been tested for the prevention and treatment of no-reflow. In particular, thrombus aspiration before stent implantation prevents distal embolization during stent deployment and has been recently shown to improve myocardial perfusion and clinical outcome as compared with the standard procedure. However, it is conceivable that the relevance of each pathogenetic component of no-reflow is different in different patients, thus explaining the occurrence of no-reflow despite the use of mechanical thrombus aspiration [14].

Another term used to indicate reduced microvessel flow, commonly occurring following percutaneous coronary interventions (PCI), is Microvascular obstruction (MVO) which may lead to myocardial injury, and is an independent predictor of adverse outcome. Severe MVO may manifest angiographically as reduced flow in the patent upstream epicardial arteries, a situation that is termed, as mentioned above, “no-reflow.” Microvascular obstruction can be broadly categorized according to the duration of myocardial ischemia preceding PCI. In “interventional MVO” (e.g., elective PCI), obstruction typically involves myocardium that was not exposed to acute ischemia before PCI. Conversely “reperfusion MVO” (e.g., primary PCI for acute myocardial infarction) occurs within a myocardial territory that was ischemic before the coronary intervention. Interventional and reperfusion MVO have distinct pathophysiological mechanisms and may require individualized therapeutic approaches. Interventional MVO is triggered predominantly by downstream embolization of atherosclerotic material from the epicardial vessel wall into the distal microvasculature. Reperfusion MVO results from both distal embolization and ischemia–reperfusion injury within the subtended ischemic tissue. Management of MVO and no-reflow may be targeted at different levels: the epicardial artery, microvasculature, and tissue [8].

The no-reflow phenomenon, being inadequate myocardial perfusion of a given coronary segment, without angiographic evidence of mechanical vessel obstruction, after PCI, is difficult to understand and treat due to the large variability between patients and the experimental difficulties in assessing the different interacting processes at tissue level, such as ischemic injury, reperfusion injury, distal embolization, susceptibility of microcirculation to injury, which contribute to no reflow [15,18]. Increasingly, however, techniques to analyze microvascular function in experiments and in patients are developed [17]. For the clinical routine, approaches based on catheterization, including the index of microvascular resistance (IMR, a measure of microvascular function), and the fractional flow reserve (FFR, a measure of the epicardial component) have been introduced and used under different conditions [13].

The no-reflow phenomenon is a type of coronary microvascular dysfunction (CMD) occurring with an acute myocardial infarction [5]. The pathogenetic mechanisms of CMD include *structural*: luminal obstruction, vascular wall infiltration, perivascular fibrosis, *functional*: endothelial dysfunction, dysfunction of smooth-muscle cell, autonomic dysfunction *extravascular*: extramural compression. Research

aiming at a better understanding of the pathogenesis of CMD and the development of therapeutic principles is necessarily based on the knowledge of the physiological principles governing microvascular control of myocardial perfusion in healthy subjects.

A condition which is related to CMD is the observation of angina symptoms in patients with normal results in a coronary angiogram, often called coronary syndrome X [4,12]. Recent analyses have shown that this condition may have a significant negative influence on prognosis for cardiac events. This condition is specifically prevalent in women [21].

CMD is also linked to non cardiac diseases with well known microvascular implications. For example, diabetes mellitus (DM) strongly affects the microvascular system (arterioles, capillaries, venules). Also, the viscosity of the blood is increased in hyperglycemia, with concomitant increase in resistance of the microvasculature, leading to stasis and thrombosis of capillaries. Coronary heart disease events and mortality are greater in patients with DM.

5.2 The Lung

Airflow is delivered to the lungs through bronchi, into bronchioles and then into alveoli where the oxygen and carbon dioxide exchange takes place with the pulmonary capillaries. A mean number of 480 million alveoli with a mean diameter of 200 μm are found in human lungs [16]. The adequacy of gas exchange in the lungs is determined by the balance between pulmonary ventilation and capillary blood flow [3,7,11]. This balance is commonly expressed as the ventilation–perfusion (V/Q) ratio. A perfect match between ventilation and perfusion ($V/Q = 1$), which corresponds to normal arterial oxygenation, is the reference point for defining the abnormal patterns of gas exchange [1].

A V/Q ratio above 1.0 describes the condition where ventilation is excessive relative to capillary blood flow, with resultant hypoxemia and hypercapnia. The excess ventilation, known as *dead space ventilation*, does not participate in gas exchange with the blood [2]. Dead space ventilation increases when the alveolar–capillary interface architecture is destroyed such as in emphysema (Figs. 5.4 and 5.5)

A V/Q ratio below 1.0 describes the condition where capillary blood flow is excessive relative to ventilation. The excess blood flow, known as *intrapulmonary shunt*, does not participate in pulmonary gas exchange, with resultant also hypoxemia and hypercapnia [1]. The fraction of the cardiac output that represents intrapulmonary shunt is known as the *shunt fraction* [7,11,2]. Intrapulmonary shunt fraction increases when small airways are occluded, such as in asthma, when alveoli are filled with fluid, such as in acute respiratory distress syndrome (ARDS) (Figs. 5.6 and 5.7). The main functional mechanism to combat perfusion ventilation mismatch is the so-called hypoxic pulmonary vasoconstriction (HPV) [19], which leads vasoconstriction of arteriolar vessels supplying regions with low

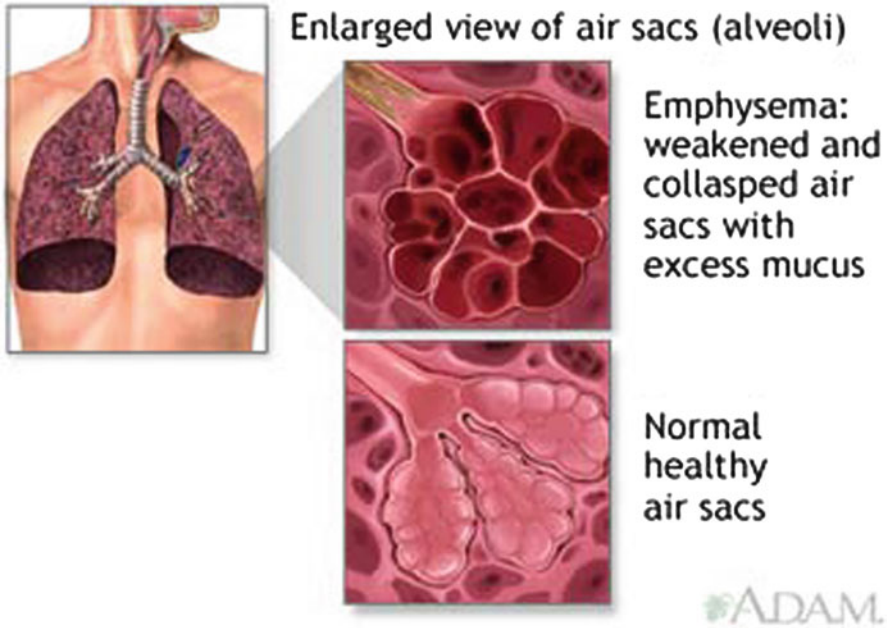


Fig. 5.4 Schematic of normal and emphysematous alveoli

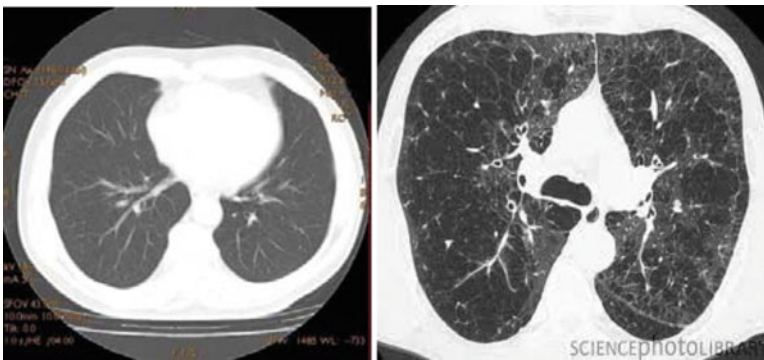


Fig. 5.5 Left: CT scan of lung with normal parenchyma. Right: CT scan of lung with emphysema

ventilation. Thus, local perfusion is matched to local ventilation. The assessment of such mechanisms and their relation to the microvascular flow properties in the living lung are still very difficult. However, major advances with respect to experimental approaches have been made [9,20] suggesting that the amount of information about pulmonary micro-flows and their clinical application will increase substantially in the near future.

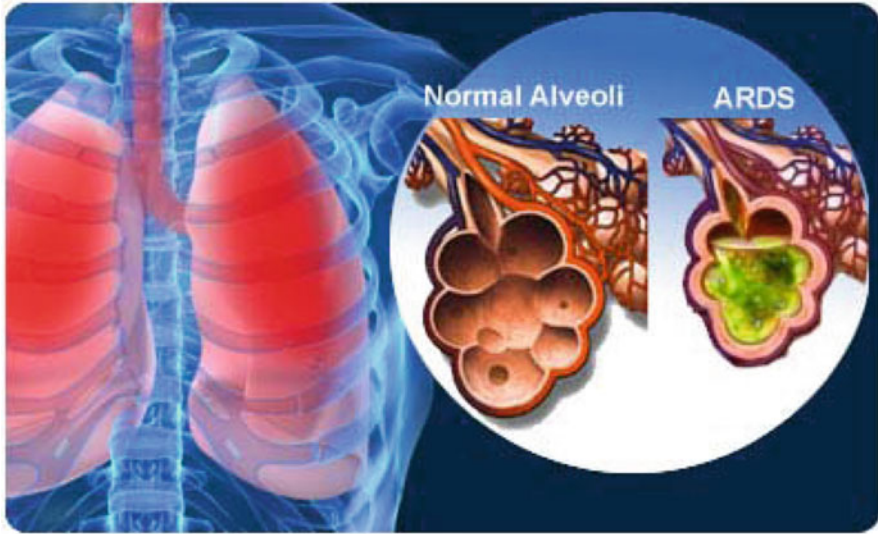


Fig. 5.6 Schematic of normal alveoli and ones filled with fluid due to ARDS



Fig. 5.7 *Left:* CT scan of lung with normal parenchyma. *Right:* CT scan of lung with fluid filled alveoli due to ARDS

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