Role of the Left Atrium

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Introduction

There is currently a general consensus in the literature about the definitions of diastolic dysfunction and diastolic failure, even though these concepts have only relatively recently been introduced into the clinical arena. The key to their definitions, as discussed in other chapters, is the central and predominant role played by the ventricular chamber in terms of its ability to accommodate adequate filling volume at reasonably low pressure through its capacity to rapidly relax while maintaining chamber elastic properties. More marginal, if not completely neglected, is the role of the atrial chamber within the clinical scenario of diastolic dysfunction and failure. Recently, however, several studies have demonstrated how the left atrium plays a primary role not only in modulating ventricular filling and function through the atrioventricular interaction mechanism but also in providing important prognostic clues for the risk stratification of patients with diastolic dysfunction.

Basic Mechanical Function of the Left Atrium

The main function of the left atrium is to connect the pulmonary circulation with the left ventricle, acting as a reservoir during atrial filling when the mitral valve is closed or as a booster when the atrial contraction ensues, but especially acting as a conduit during diastasis. Accordingly, the atrial cavity has at times been assigned the minimal role of being a “transit chamber” devoted exclusively to collecting and redirecting the reflux blood from the pulmonary district toward the systemic circulation. It would be wrong to deduce from this “pipeline” function that the left atrium is a passive player in the complex scenario of the cardiac cycle; on the contrary, it performs multiple tasks either in direct interaction with the underlying ventricle, or by paracrine modulation of the systemic circulation.

Its interaction with the ventricular cavity, which is not restricted to the ventricular filling phase in diastole, is discussed later. It should be emphasized at the outset, however, that, in addition to this relation with the underlying chamber, the left atrium can also interact with general systemic homeostasis, acting as a true “control” center. It is now well known, in fact, that the left (as well as the right) atrium also acts as a volume sensor.

The Atrium as a Control Center

Blood Volume Regulation

The control of flow volume is effected by the left atrium through the production of neurohormonal substances. Among these substances, a major role is played by the natriuretic peptides, including atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) of predominantly ventricular origin, and endothelial peptide (C-type natriuretic peptide [CNP]), which also has a regulatory function in the renin-angiotensin-aldosterone system.
Whenever a load of volume, salts or vasoconstricting drugs, stimulates the atrial mechanoreceptors, ANP performs its vasodilatory action either directly or indirectly, inhibiting sympathetic activity.\textsuperscript{6} It also induces natriuresis, inhibits the renin-angiotensin-aldosterone system, increases capillary permeability, and antagonizes the proliferation of smooth muscle cells.\textsuperscript{7} With the progression of cardiac insufficiency, plasmatic concentration of this peptide increases in proportion to the severity of the pathology.\textsuperscript{8} In patients with cardiac disorders, then, ANP may be produced not only by the atrium but also by the ventricle, a typical feature of the fetal heart that is lost in adult life.\textsuperscript{9} Brain natriuretic peptide has a structure similar to that of ANP, but BNP is secreted mostly by the ventricles when they dilate, even though small quantities are released at the atrial level.\textsuperscript{10} For BNP, as for ANP, there is a correlation between the severity of the disorder and the amount of peptide produced.\textsuperscript{11}

Because of the presence of ANP and BNP in the serum of patients suffering from asymptomatic left ventricular (LV) dysfunction, natriuretic peptides have been proposed as markers targeted to an early diagnosis of ventricular dysfunction.\textsuperscript{12} There is evidence that in the advanced stages of diastolic dysfunction the negative reshaping of the atrial cavity can cause, over time, increased concentrations of natriuretic peptides mostly ascribed to ANP.\textsuperscript{13,14} In addition to the stimulus that follows stretching of the walls, the atrium may also react to other stimuli, such as levels of angiotensin II\textsuperscript{15} and endothelin\textsuperscript{16} by secreting ANP.

### Mechanoreceptors and Signaling Mechanisms

A second mechanism of interaction between the atrial cavity and the cardiovascular system is due to the presence of receptors for the afferent paths of various reflexes.\textsuperscript{17,18} Among the most important of these receptors are the mechanoreceptors disseminated throughout the atrial walls: in case of increased venous backflow (such as during physical stress), the relaxation of the walls causes the activation of these receptors, with the final consequence of accelerating the discharge frequency of the cells of the sinus node (stress-induced tachycardia, the Bainbridge reflex).\textsuperscript{19}

### Structural Characteristics

To analyze the role played by the left atrium in the various progressive stages of diastolic dysfunction, it is obviously necessary to consider, last but not least, the histologic and structural properties of this chamber. Both atria show, in fact, peculiar morphologic and structural characteristics different, to some extent, from those characterizing the ventricular cavities. These include peculiar reactions and behaviors of the atrial wall in response to hemodynamic alterations associated with the progressive dysfunction of the underlying cavity. At the histologic level, the atrial chambers show myocytes of smaller dimensions than those of the corresponding ventricular myocytes and are characterized by the presence of chains of myosin with fetal type expressions (in the case of both light and heavy chains), which are associated with a shorter duration of the action potential.\textsuperscript{20}

As mentioned earlier, we know that the atrium is particularly sensitive not only to the physical stretching of its walls but also to surrounding levels of angiotensin II. This is explained by the fact that the atrium depends largely on phosphatidylinositol for signal translation,\textsuperscript{21} and this dependence may explain why the positive inotropic angiotensin-mediated effect is sensibly greater at the atrial than at the ventricular level.\textsuperscript{22}

These peculiar histologic and physiologic features may derive, in part, from the fact that the atrial chambers do not need to exert a particularly strong contractile activity, as they do not have to generate high intracavity pressures, although they must be capable of responding, rather quickly, to changes in the surrounding volume while maintaining a pumping capacity able to guarantee adequate ventricular filling.

### How the Atrium Interacts with Ventricular Filling

Left atrial function is intimately related to ventricular function throughout the whole cardiac cycle.\textsuperscript{21} During ventricular systole, longitudinal fiber shortening forces the descent of the cardiac