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REVIEW ARTICLE

Right Ventricle Health and Disease: A Prospective Review

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ABSTRACT
Even though there is a lot of information about how important right ventricular function is in many heart diseases, not much research has been done on the specific physiological features of the RV in both healthy and sick states. There is an increasing awareness of this deficiency in understanding. Hence, in our review, we have discussed RV in health and disease by discussing its normal structure, cell biology in health and disease, and the causes and mechanisms of RV and RHF.
Keywords: *RV, RHF, Health, Disease, Cell Biology, Cause, Mechanism.*

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INTRODUCTION

Studies also concluded that it has long been thought that the RV is dispensable. Additionally, a study found that Starr and colleagues' 1943 ablation of the RV in dogs resulted in no change in venous pressures and was compatible with life. [1] Accordingly, studies showed that Fontan and Baudet (F&B) created cavo-pulmonary anastomosis for the first time in 1971 as a palliative method for treating specific heart abnormalities. [2] Studies also concluded that people who have been diagnosed as "F" patients lead lives that are almost completely normal and inactive, despite not having RV for many decades. [3] On the other hand, studies also concluded that they experience a decrease in their ability for aerobic exercise of 30–50%. [4] In addition to this, studies concluded that this provides an indirect indication of the role that the RV plays in determining maximal CO. [4] Studies also came to the conclusion that any factor that raises pulmonary artery pressure (PAP) in people with FC may be the cause of CF. [3] As a result, the RV may be dispensable, but only in a calm, sedentary life with a normal CO and a low-resistance PC. Studies also concluded that RV is a crescent-shaped volume generator with thin walls that is seen in mammals and birds. It is further related to the systemic venous return on one side and the PC on the other side. [5] Researchers also found that when reptiles and amphibians change from poikilothermic to endothermic (warm-blooded) mammals and birds, their metabolic systems need more gas exchange to keep up. Only via an extraordinarily thin blood-gas barrier is it possible to exchange enough O and CO2. As a result, studies also revealed that it is shielded from the high systemic vascular pressure (HSVP) inside a distinct PC that has low resistance. [5]

NORMAL STRUCTURE

Studies also concluded that the normal RV has walls that are between 3 and 5 millimeters thick and a high degree of compliance, in comparison to its counterpart on the left side, which has walls that are thinner than 3 millimeters.[6] Studies concluded that "deoxygenated blood (DOB) is supplied into the lungs at a relatively low cost until the RV afterload is low during the resting state".[6] For instance, the LV removes roughly 75% of the oxygen (O2) provided by the coronary blood flow (CBF), while the RV removes roughly 50% of it.[6] Studies also concluded that, in response to an increase in the O demand of the LV, CBF increases. On the other hand, an increase in the oxygen demand of the RV may be addressed in either of two ways: either by increasing the CBF or by increasing the O2 extraction.[6] Studies also showed that the RV's CO (Qc) and myocardial energetics go up by almost four times from rest to maximal effort, and

some measures of the RV's systolic function are higher than those seen in the LV. This increase in RV output and myocardial energetics is due to the increase in RV contractility during maximal effort. [7]
According to different researchers, "the two most noticeable things about the RV's anatomy compared to the left are its complicated shape that defies simple geometric approximation and the fact that it has a relatively thin free wall".[8] Studies also showed that the "muscle fibers(MF) that make up the RV are usually thought to be split into two layers: a thin layer that runs around the RV and parallel to the AV groove, and a thick layer that runs from the top to the bottom".[8] Studies also showed that "the tricuspid annular plane systolic excursion (TAPSE), an ECG measure of RV systolic function, is what represents this later plane of shortening".[9] Studies also concluded that "TAPSE decreases in proportion to the degree to which RV shortening, or systolic function, improves. There are two layers of muscles that are not parallel to each other, separated by a circumferential MB. This allows the LV to contract in a complex way, including twisting, shortening, and thickening".[8,9] In addition, the studies revealed that "LV fibers are wrapped around the elliptical chamber in a manner that is more complex".[9] According to different researchers,RV is situated in the human heart, facing forward, slightly below the sternum. Studies also concluded that it sits between the annulus of the HV and the PV when there is no CHD.[8,10,11] The heart is stabilized by being split into the front, side, and bottom parts, as well as the base, middle, and top parts.[12]

PROPERTY [13]

S.NO.	PROPERTIES	RV	LV
1.	EDV, ml/m^3	75±13(49-100)	65±12(44-90)
2.	Mass, g/m^3	26±5(17-34)	87±12(64-110)
3.	Wall Thickness, mm	2-5	7-11
4.	VP ,mmHg	25/4 [(15-30)/(1-7)]	130/8[(90-140)/(5-12)]
5.	V E mmHg/ml	1.30±0.84	5.48±1.23
6.	Afterload (PVR & SVR)	70(20-130)	1100(700-1600)
7.	Accomodation to imposed load	Better in response to volume overload	Better in response to pressure overload

TABLE 1: LV v/s RV [13]

GENDER DIFFERENCE FOR RV

It has been well documented in numerous cases that there are significant differences in left ventricular mass and volume.[14,15] In a recent study, it was found that " men had a higher RV mass (8%), a larger RV end DV (10%), and a slightly lower RV ejection percentage (around 4%) compared to women".[16] It became evident when comparing the two genders. These differences can be observed in the left ventricle (LV) as well, with men generally exhibiting higher mass, volume, and ejection percentages compared to women [28, 30]. Another similar study where "3500 men and post-menopausal women found a correlation between higher testosterone levels, increased mass, and larger RV volumes".[17] In a similar vein, women with higher levels of DHEA exhibited larger mass and volume, indicating that androgens play a role in influencing the mass and volume of the RV. There is a positive correlation between higher levels of estradiol and a higher RVEF in women using hormone therapy.[13] It's interesting that this link stays the same even when different types of left ventricle function are taken into account. This shows that estradiol doesn't change the way the right ventricle works when it comes to systolic function.[13]

NORMAL BIOCHEMICAL PROPERTIES OF CELL IN RV

Studies have also concluded that the cellular differences (CD) that exist between RV cardiomyocytes (CM) and LVCM have not been the subject of a great deal of research, nor have they been thoroughly described. Several studies have shown that RV papillary muscle produces less force per unit mass than LV papillary muscle, even though the RV muscle shortens faster than the LV muscle when it is isolated.[18,19] Studies have also found that when RV and LV myocytes are tested separately, the maximal sarcomere shortening is much lower in RV myocytes than in LV myocytes from the same heart, even though the diastolic sarcomere length doesn't change.[20] Moreover, it has been shown that the mechanical differences between RV and LV are reflected in measurements of intracellular calcium transients. More specifically, the peak calcium transient in LV myocytes is much larger than in RV myocytes. This difference has been shown to be a reflection of the mechanical differences between RV and LV. This data shows that the dynamics of calcium may play a significant role in controlling the differences between different tissues. Researchers also found that the differences in contractile velocities seen between the RV and the LV are most likely caused by changes in the expression of myosin heavy chain isozyme (MHCI). In a study

conducted on rats[18] and rabbits [21], it was revealed that the RV has a noticeably higher concentration of the MHCI (V1) isozyme compared to the LV. Thus, studies have revealed in this context that an increase in ATPase activity has been linked to the presence of this isozyme.[13] In spite of the fact that shortening velocity was not measured, it is essential to point out that the Ca-ATPase activity was lower in the RV compared to the LV in the more recent experiment. Additionally, studies have shown that differences in the MHCI composition cannot adequately explain the fundamental differences in the quantity and velocity of shortening between RV and LV and that additional research is necessary to determine the cause of this phenomenon.[13]

RV IN DISEASE

Studies revealed that, as a consequence of the increased prevalence of conditions that put patients at risk for developing the illness, current clinical practice is seeing an uptick in the occurrence of a condition known as RHF, which is becoming an increasingly prevalent phenomenon.[22] The main cause of RVD in the overwhelming majority of patients is either an overload of pressure or volume, or a combination of the two.[22] A decreased RV contractility due to the primary loss of RV myocardium may potentially contribute to the development of RHF. Ischemia is the one condition that may cause RV myocardial damage, but other than that, the conditions that might cause this kind of injury are very rare and, in most cases, do not just affect the right heart. It is essential to take notice of the fact that up to 25 percent of critically ill patients who have acute lung injury and up to 50 percent of those who have sepsis may develop acute right heart failure while they are being treated in the intensive care unit due to a variety of factors.[Figure 1 &2][22]

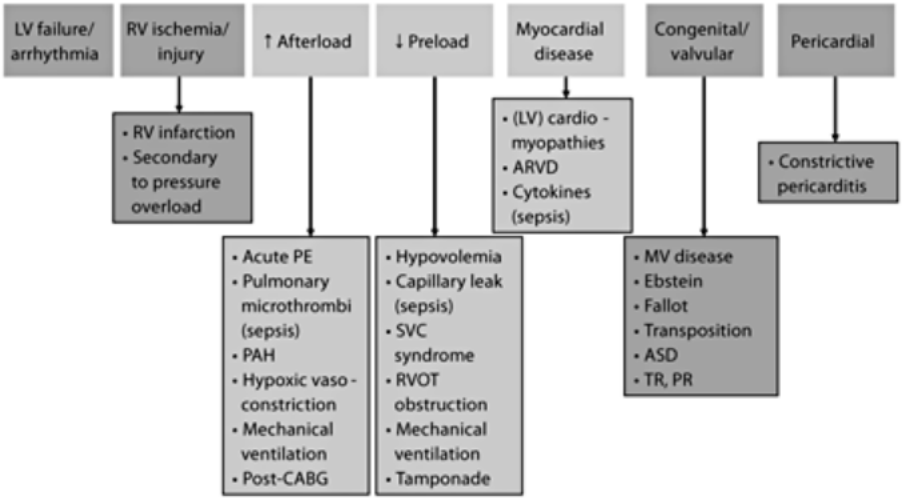

FIGURE 1: CAUSES & MECHNISM OF RV [22]

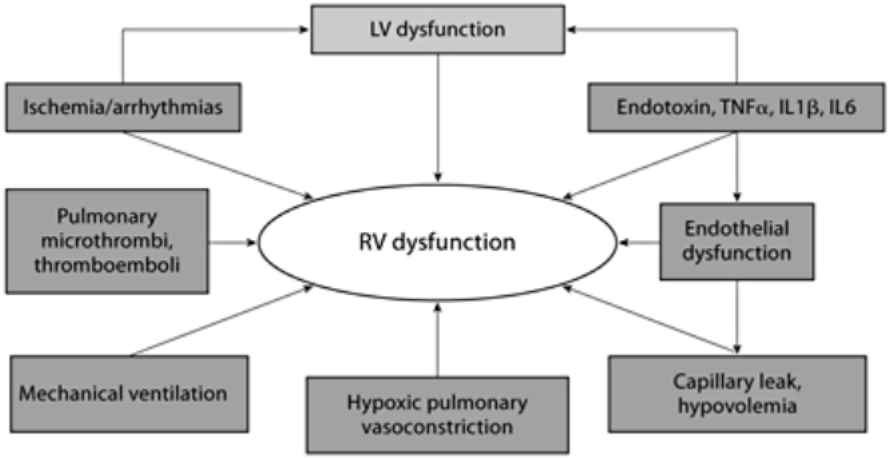

FIGURE 2:MECHANISM OF RHF [22]

CELL BIOLOGY ON RVF

Studies showed that the RV was very important in the early mechanical descriptions of total cardiac contractility. However, the exact nature of the functional shift in the failed myocyte remains unknown, and there is still ongoing debate about the process of this functional change. Some studies suggest a decrease in myofilament function, while others suggest an increase or no change. The function of RV myofilaments is decreased in RV trabeculae and in isolated skinned RV hypertrophic myocytes of rats that have experienced extensive LV infarctions along with LV failure.[23,24] Recent studies have shown a significant decrease in the force produced in intact RV strip preparations from rats with severe LV infarctions when exposed to either isoproterenol or calcium.[25]

Studies showed that the bulk of the altered proteins may be attributable to a switch from the metabolism of fatty acids to an increase in the metabolism of glucose. This switch may be the origin of many of the reported modifications in the proteins. Hypertrophy of the left ventricle (LV) is known to generate metabolic changes in the body[26,27], but hypertrophy of the right ventricle (RV) does not cause these changes.[28] There is a change in the way energy substrates are used in the hypertrophied LV, and there are similar changes in the proteome of the hypertrophied RV, with fewer oxidation enzymes and more glycolytic enzymes.[29] It has been thought for a long time that changes in substrate consumption and the possible switch from energy-efficient mitochondrial-mediated oxidative metabolism to limiting glycolysis may play a part in RV dysfunction under pressure overload. Recent studies concluded that cutting-edge research in pressure-overloaded RVs utilizing FDG PET scanning has shown that glycolysis is increased and that mitochondrial activity is aberrant.[30,31] These findings and others like them have sparked the intriguing possibility that mitochondrial dysfunction might be a problem that can be addressed in the therapy of RV pressure overload. A number of research organizations have already started examining this possibility, which is a good sign.[31,32,33] Studies have also concluded that dichloroacetate reduces PDH phosphorylation and improves glucose oxidation in the failing RV. In another similar study, RV dysfunction may have an underlying pressure overload component, which is another characteristic of the pressure-overloaded RV and its relationship to autoimmune illnesses.[34,35,36] Studies also found that people with PHT caused by scleroderma or other inflammatory lung diseases have a much worse outlook, and it seems to have a worse impact on the RV than people with other types of PHT. In addition to this, studies revealed that the dysfunction of the LV, remodeling of the LV, and production of pro-inflammatory cytokines such as TNF- and IL-6 have all been shown to have a direct and causal relationship with one another in a number of studies.[37,38] This relationship has been shown to be the source of LVD as well as remodeling. This association has been shown to have a direct cause-and-effect relationship with one another. .Researchers found that in almost all of the well-studied animal models of RV dysfunction, there is histologic evidence of inflammation in the chamber and infiltration of mononuclear cells.[39,40] A lot of researchers agree on this: calcium controls contraction in heart muscle cells by attaching to troponin C, a thin filament regulatory protein.This, in turn, induces a conformational change in the other troponin subunits, namely troponin I and T, which in turn allows myosin velocity to actin. In a broad sense, the sensitivity and intensity of a contraction are governed in one of two ways: either by the available velocity of myosin or by the unit sensitivity of the contractile apparatus. It is conceivable that there are changes in the myofilaments' calcium sensitivity as a result of the changes in myofilament function in skinned preparations. The way calcium is handled in failing myocytes is undoubtedly different.[13]

CONCLUSION

Ultimately, two main points become apparent: firstly, the RV exhibits distinct behavior compared to the LV in both normal and pathological conditions, due to its embryology, geometry, and cell biology. Secondly, the decline in clinical function of the RV is a strong indicator of LVO in various scenarios. Given the circumstances, continuing to disregard the RV would be unwise. It is evident that possessing a thorough understanding of its physiology and developing targeted therapeutic approaches will have significant clinical value. In recent years, there has been a growing understanding of the RV in both health and illness. This has been achieved through rigorous invasive determinations for fundamental research issues and the validation of NIM to determine clinical relevance. Through extensive research, a more comprehensive comprehension of the RV's function in both health and disease has been achieved. Further clinical research is needed to determine the optimal conditions for an RV stress test. However, the necessary tools have already been properly approved so that a full study of the pathobiology of RVF and testing of possible treatments can begin.

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CONFLICT OF INTEREST

There are no conflicts of interest

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