Speculation and Truth about the Sequence of Events in the Pathogenesis of Left Heart Failure

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During the last few years pathogenesis of left ventricular dysfunction has been extensively studied and it has been a subject of great attention among physiologists, pathomorphologists, pharmacologists and clinicians. Pathophysiology of left ventricular (LV) dysfunction is a complex phenomenon. A vast literature is available on this subject which describes in full detail the cardinal mechanisms involved in the development of LV failure and also defines the significance of compensatory mechanisms and reveals pathways for the correction of evolving functional disturbances. At present this subject still remains difficult for comprehensive understanding by clinicians. Physicians (like cardiologists, anaesthesiologists, rheumatologists and cardiac surgeons) often encounter great difficulties at circumstances requiring not only “clinical approach” but also profound knowledge of cardiac pathàphysiology. A typical example of this is an acute LV failure occurring during the first few hours of acute myocardial infarction. The pathogenesis of this formidable complication can be various including reduction in cardiac output; significant respiratory dysfunction causing disturbances in central haemodynamics; absolute or relative hypovolemia causing impairment of LV filing; myocardial ruptures, etc. It is very important to have a clear concept regarding individual features of pathogenesis of LV dysfunction because in a certain group of patients immediate application of apparently needed intervention for the correction of haemodynamic disturbances may become mischievous. Therefore, sometimes a physician has to make guess-work, wasting precious time and even causing harm to a patient for example, prescribing large dosage of saluretics in biventricular acute myocardial infarction complicated by right ventricular pump failure. In order to understand in detail, the pathogenesis of HF a universal logical scheme of the pathologic events in sequence must be kept in mind. Such logical scheme may be constructed relying on latest research data[1]. We will consider the primary myocardial weakness[2] as a typical example of acute HF - condition most suitable for logical analysis. For complete comprehension of this situation, it is necessary to know all about LV pressure-volume relationship during cardiac cycle. The dynamic relationship between LV pressure and LV volume are described by so called pressure-volume loop (PVL). The detailed description of LV pressure-volume relationship on each PVL segment is presented (Figure 1). Left vertical segment of PVL corresponds to end systole and early diastole. The overall duration does not exceed 100 ms. Three major events correspond to this segment. These are: a) end ejection phase (AB); b) isovolumic relaxation phase (BC) and c) early rapid filling phase (CD). Lower horizontal segment of PVL (DE) corresponds to diastole. Its duration varies (400-500 ms) depending on heart rate. This segment includes two phases of cardiocycle: a) rapid filling phase; b)slow filling phase (DE). Right vertical segment of pressure-volume loop corresponds to systole. Duration of this period not exceeds 100 ms. This segment includes: a) pre-ejection period (EF); b) early ejection period (FG). Upper horizontal segment of PVL totally corresponds to systole. It lasts 300-400 ms and includes only one phase of cardiac cycle, i.e., ejection period (GA). Having comprehensive knowledge of cardiac events presented on PVL, let us come to the discussion of two versions of LV failure.

1st Version

Condition which is under consideration is a purely abstract model. It is based on the assumption that catastrophic LV dysfunction occurs instantly within one cardiac cycle causing disturbances in central haemodynamics. Therefore, early compensatory mechanisms lag behind. Resorting to vulgarism the

whole sequence of events can be explained in the following manner: “In diastole LV becomes totally relaxed while in systole performs incomplete contraction”. Undoubtedly in real clinical situation such event cannot occur. The only pathological condition in which this can occur to some extent is an acute ischemic myocardial dysfunction. Nevertheless, profound analysis of this abstract model is necessary to proceed discussion on LV failure under real clinical condition The impairment LV myocardial contractility causing pump failure, results in the lowering of LV power indices (first of all stroke work and peak systolic power) and results in significant changes in phasic pattern of cardiac cycle[3-5]. The superposition of aortic and LV pressure curves (Figure 2)

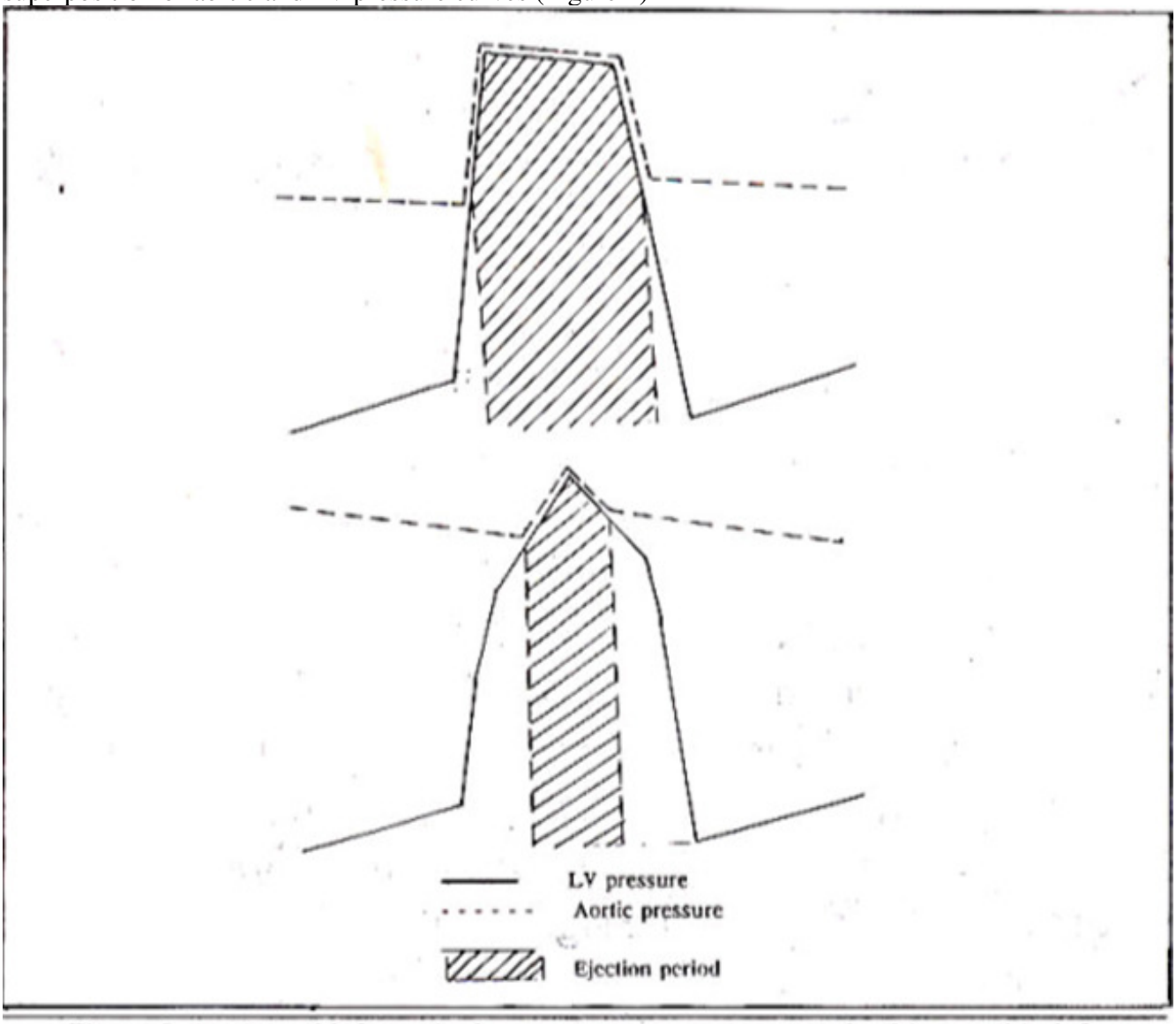

Figure 2. Aortic and left venticular pressure curves in normal subject and in left heart failure.

permits to define accurately the beginning and tennination of ejection period (time poin corresponding to opening and closure of aortic valve). Comparison of two pairs of curves representing the normal haemodynamics and model under consideration allows to demonstrate a number of haemodynamical features of an acute LV pump failure, such as: a) ascending limb of LV pressure curve becomes more sloping, therefore, aortic valve opening is delayed; b) descending limb of LV pressure curve becomes more steep and therefore, aortic valve closure occurs earlier (because of rapid rise of physiological pressure gradient between aorta and LV) First and second events together cause the reduction of

ejection period on account of simultaneous increase in pre-ejection and isovolumic relaxation periods. Let us moveover to the comparison of two PVL's representing normal haemodynamics and situation under discussion (Figure 1). Since aortic valve closure occurs earlier the ejection from LV ceases at relatively higher pressure and volume indices in comparison with a normal setting (Figure 1 .point B). This results in the premature beginning of isovolumic relaxation period. During this phase the LV pressure should fall to lower levels, because LA pressure remains within normal limits and mitral valve cannot open prematurely. After mitral valve opening rapid LV filling starts at a larger chamber volume but normal pressure. Rapid blood flow in LV results in a more significant rise in LV pressure in the presence of poor LV compliance. This can be seen in lower horizontal segment of PV loop in the form of evident change in curve course. Mathematical correlation between pressure and volume in this segment can be defined as:

$P=B \times e^{kv}$

(P = pressure, V= volume, B&K = coefficient constant). Mathematically changes in the course of PV loop may be determined by an increase in the value of coefficient B. The lower horizontal segment of PVL becomes more steep suggestive of an inevitable rise in LV end diastolic pressure. The significant rise in LV end diastolic pressure (EDP) results in premature mitral valve closure (Figure 1 point E). Thus in this situation a number of adverse mechanisms prevent complete LV filling. Such as: 1) increase in LV diastolic pressure which causes reduction. of pressure gradient between LA and LV; 2) early mitral valve closure restricting the filling period (pressure equilibrium between LA and LV occurs earlier, due to rapid increase in LV pressure while the LA pressure remains within a normal range; and 3) prolongation of isovolumic relaxation phase. Consequently, there is a LA volume overload (in situation under consideration) which causes a rise in LA pressure and engorgement of pulmonary veins. Further, various reflex mechanisms are activated that cause redistribution of circulating blood; the reduction of venous return and thus prevent acute pulmonary oedema. At the same time reduction of venous return restricts the rise in end diastolic LV volume and prevents the activation of Frank-Starling's mechanism. Significant increase in end systolic volume causes a reduction in cardiac output (stroke volume; ejection fraction, etc.).

2nd Version

Now let us proceed to the discussion of 2nd version of LV failure. This situation is very close to reality and occurs in various pathological conditions accompanying LV dysfunction. It is quite wise to mention here, once more, that all haemodynamic events discussed below are only hypothetical (logical) scheme of the pathogenesis of left heart failure. The main feature of 2nd haemodynamic version distinguishing it from more abstract 1st version is the participation of compensatory mechanisms. In real clinical setting the compensatory mechanisms start work. ing immediately after the appearance of any LVfunctional deterioration and significantly influence the central haemodynamics. Haemodynamic events occurring in 2nd version significantly differ from that of 1st version. LV power indices may be slightly reduced or remain within normal limits. The magnitude of changes in these indices depends on the extent of compensation. The relationship between aortic and LV pressure curves is the same as in 1st version. There is reduction of ejection time because of prolongation of pre-ejection period[3-5]. Nevertheless, comparative analysis of PVL\'s allows to reveal the significant difference between 1st and 2nd version. Aortic valve closure and the beginning of isovolumic relaxation occur early at a higher LV pressure and LV volume (Figure 1 point B).

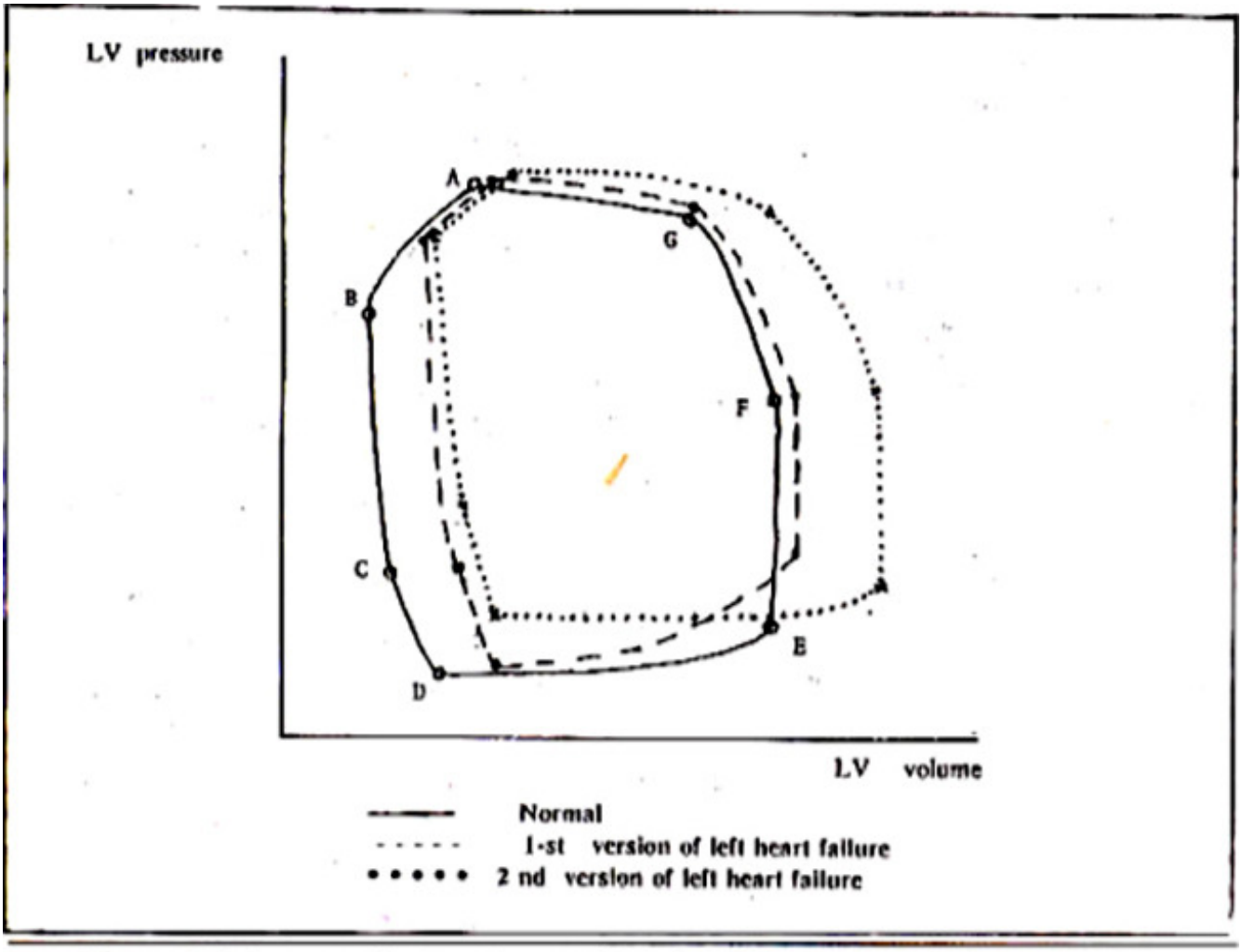

Figure 1. Left venticular "pressure-volume loops" in normal subject and in left heart failure.

However, in contrast with 1st version LV pressure does not fall to the normal level during isovolumic relaxation period. Since the LA pressure is significantly elevated as a result of increased venous return caused by peripheral vasoconstriction as. a compensatory mechanism. The premature mitral valve opening enhances the LV wall compliance during rapid filling phase; inspite of additional blood volume in LV chamber at the time of mitral valve opening. In this case the changes in the course oflower horizontal segment of PVL significantly differs from that in 1st version. The curve becomes more sloping that is mathematically determined by the decrease in coefficient B (in eq P = Bxekv). Reduction in the steepness of lower horizontal segment of PVL reflects the tendency towards reduction in EDP. By the time of mitral valve closure and the beginning of pre-ejection period (Figure 1 point E) pressure is relatively low in contrast to 1st version considered earlier. Therefore, in this situation EDP remains relatively low (within normal limits or slightly increased). Thus compensatory mechanisms are directed first of all towards the improvement of LV diastolic function. Contribution of these factors counteracts the pathological mechanisms restricting LV filling. First of all a significant rise in LA pressure increases the physiological pressure gradient between LA and LV during ventricular diastole. 2) Premature mitral valve opening results in prolongation of filling period and an increase in LV compliance. 3) The slow rise in LV pressure during diastole (in combination with elevation of LA pressure) also results in prolongation of filling period. The forced diastolic filling of LV in the presence of compensatory factors results in the activation of Frank-Starling's mechanism, Therefore, inspite of significant rise in LV end systolic volume, cardiac output remains on sufficient level because a systolo-

diastolic difference in myocardial fibre length and LV chamber volume remains well preserved. Thus we discussed in detail two schematic haemodynamic versions of LV failure. First version is an abstract logical model enabling us to speculate regarding LV pump failure in the absence of compensatory mechanisms. Second version is a situation very close to real clinical conditions, when compensatory mechanisms are inevitable and significantly influence the central haemodynamics and ensure satisfactory cardiac output.

References

1. Das Gupta, D. Principlea and practice of acute cardiac care. II year book. Medical Publiahera Inc., 1982; pp.102-104 111-118.
2. Northover, B.J. Estimation of the risk of death during the first year after acute myocardial infarction from systolic time intervals during the first week. Br.Heart. J., 1989;62:429-37.
3. Kinhal, V., Kulkani, A., Pozderac, Land Cubbon, J. Haemodynamic effects of dilevalol in patients with systemic hypertension and left ventricular dyafunction. AmJ.Cardicl., 1989;63:64-68
4. Skng, K. and Gibson, D.C. lmpairmentofdiastolic function byahortened filingperiod is severe leftventricular diseaae. Br.Heart.J., 1989;62:246-52.
5. Beme, R. and Levy, M. Cardiovaacular physiology. 5th ed. St. Louia. The CV Mosby Company, 1986.