# Simulation of left ventricular function during dyskinetic or akinetic aneurysm

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## Abstract

The purpose of our study was to simulate the hemodynamics of left ventricular function after left ventricular aneurysm (LVA) of various sizes and to validate the results of this computer based simulation with patient data. We developed an equivalent electronic circuit (EEC) that reflects the hemodynamic conditions of LVA (after acute myocardial infraction) while taking into consideration the resetting of the sympathetic nervous tone in the heart and systemic circuit, the fluctuating intrathoracic pressure during respiration and passive relaxation of the ventricle during diastole. The key feature of the EEC was a subcircuit representing the LVA, with a subcircuit to measure ventricular blood volume (*i.e.* intraventricular "shunting" of blood flow during systole and diastole) between the unaffected section of the left ventricle and its aneurysm. This EEC model can simulate akinetic or dyskinetic LVAs of different sizes and provides realistic beat-to-beat ventricular blood flow and pressure tracings that were validated by pressure-volume loop diagrams and by published patient data. In agreement with published data, simulated dyskinetic LVAs have a considerably greater impact on ventricular function than akinetic LVAs. The hemodynamic effects of ventricular systolic dysfunction following LVA were also evaluated. We conclude that the EEC model qualitatively and to a significant degree quantitatively represents conditions in patients with a dyskinetic or an akinetic LVA and provides realistic beat-to-beat ventricular blood flow and pressure tracings.



KEY WORDS: computer simulation, myocardial infarction, heart ventricle, aneurysm

## INTRODUCTION

Left ventricular aneurysm (LVA) is a mechanical complication of an acute transmural myocardial infarction (AMI). It can follow AMI immediately or can develop weeks to months later and has a reported frequency of 10 - 31% [1]. LVA can be defined as any localised area of left ventricular akinesia or dyskinesia that reduces left ventricular ejection fraction [2]. Ventricular akinesia denotes a segment of the ventricular wall that has essentially no contractile function (does not contract during systole). Ventricular dyskinesia denotes a segment of the ventricle wall that exhibits a paradoxical, outward movement during systole causing intraventricular "shunting" of blood flow between systole and diastole. After AMI, a portion of the affected ventricular wall loses the ability to contract during systole, but retains its elastic properties during diastole, and, provided the affected area is of sufficient size, manifests a ventricular dyskinesia. For the same cardiac output, a heart with a dyskinetic LVA needs to increase "stroke" volume (to inflate the dyskinetic aneurysm during systole and still maintain a normal cardiac output) and has consequently an increased oxygen demand and a lower work reserve. Patient data suggests, that the acute compensatory mechanisms, the Frank-Starling mechanism and the baroreceptor reflex mediated increase in chronotropic and inotropic activity of the heart, can maintain stroke volume if the noncontractile region involves less than 20% of the left ventricular circumference [3]. Over time, the section of the ventricle that experienced AMI undergoes tissue remodelling from muscle tissue to granulation tissue and finally to fibrous tissue [3]; the noninfarcted ventricular region can develop systolic or diastolic dysfunction [3,4]. The wall of a chronic LVA has essentially a low compliance and no contractile properties, qualities of an akinetic aneurysm. Compared to a dyskinetic LVA, that affects an equal portion of the ventricular wall, an akynetic LVA represents a lesser work load for the healthy segment of the ventricle and a relative improvement of heart function. Cardiovascular physiology can be simulated using either an analog or a digital approach [5] but only a few studies have modelled left ventricular function or hemodynamic changes after LVA [6-8]. In this paper we present an equivalent electronic circuit (EEC) computer model that

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simulates the hemodynamic changes of akinetic or dyskinetic LVA while taking into consideration the resetting of the sympathetic nervous tone in the heart and systemic circuit, the fluctuating intrathoracic pressure during respiration and passive relaxation of the ventricle during diastole.

## MATERIALS AND METHODS

*Procedures*

Simulations of cardiovascular variables during left ventricular aneurysm (LVA) were performed by developing an equivalent electronic circuit (EEC) with Electronics Workbench (EWB) Personal version 5.12 [9]. Left ventricular acute myocardial infarction (LVAMI) and the resulting LVA are simulated by modifying a previously developed model of the cardiovascular system for a healthy, young adult under resting conditons (*i.e.* heart frequency rate 60 beats/min) in a recumbent position [10-12]. In this model venous tone, heart rate and contractility of both ventricles is modulated by a negative feedback mechanism and the influence of respiration on cardiac filling and output is also taken into account. The EEC of left ventricle was modified to simulate LVAMI and subsequent LVA (Figure 1). It consists of two, electronically almost identical, sections S1 (simulating an initially normal ventricular section) and S2 (simulating the ventricle section that developed LVAMI and LVA), with two capacitors, C1 and C2. The main components of sections S1 and S2 are (a) the "gain stage" (simulating contractility) of the ventricle and (b) the capacitor, simulating part of the left ventricle. Total left ventricular mass, and its total capacitance should be constant, *i.e.* 300 mL/mm Hg. Therefore the sum of both capacitors, C1 in S1 and C2 in S2, should be always 3 μF (Figure 1). Gain (contractility) in sections S1 and S2 is modulated by homeostatic negative feedback. In resting conditions the modulation factor is 1. If *e.g.* arterial pressure is decreased, the modulation factor can be - via the myocardial contractility circuit - increased to 2 [10-12]. To simulate a "mild" LVAMI and a subsequent small LVA (involving 20% of left ventricular mass), the capacitance of C2 (section S2) is set to 0.6 μF and the capacitance of C1 (section S1) is set to 2.4 μF. A "severe" LVAMI and a large LVA (involving 50% of left ventricular mass), is simulated by adjusting the capacitance of C2 (section S2) to 1.5 μF and the capacitance of C1 (section S1) to 1.5 μF. The voltage (pressure) output from capacitors C1 and C2 (in sections S1 and S2), representing the complete ventricle, is fed directly between both diodes D1 (representing the mitral and the aortic valve; Figure 1). To record the charge (volume) at capacitors C1 and C2, a convenient voltage/charge (pressure/volume) conversion is set up and the recorded values are multiplied by factors equal to the value of capacitors C1 and C2 (*i.e.* in "mild" infarction by factors 0.6 and 2.4, respectively; in "severe" infarction by factors 1.5 and 1.5, respectively; Figure 1). In this way the total volume of left ventricle, or volumes of sections S1 and S2 can be recorded separately. The EEC model uses time-delay switches (SW1-

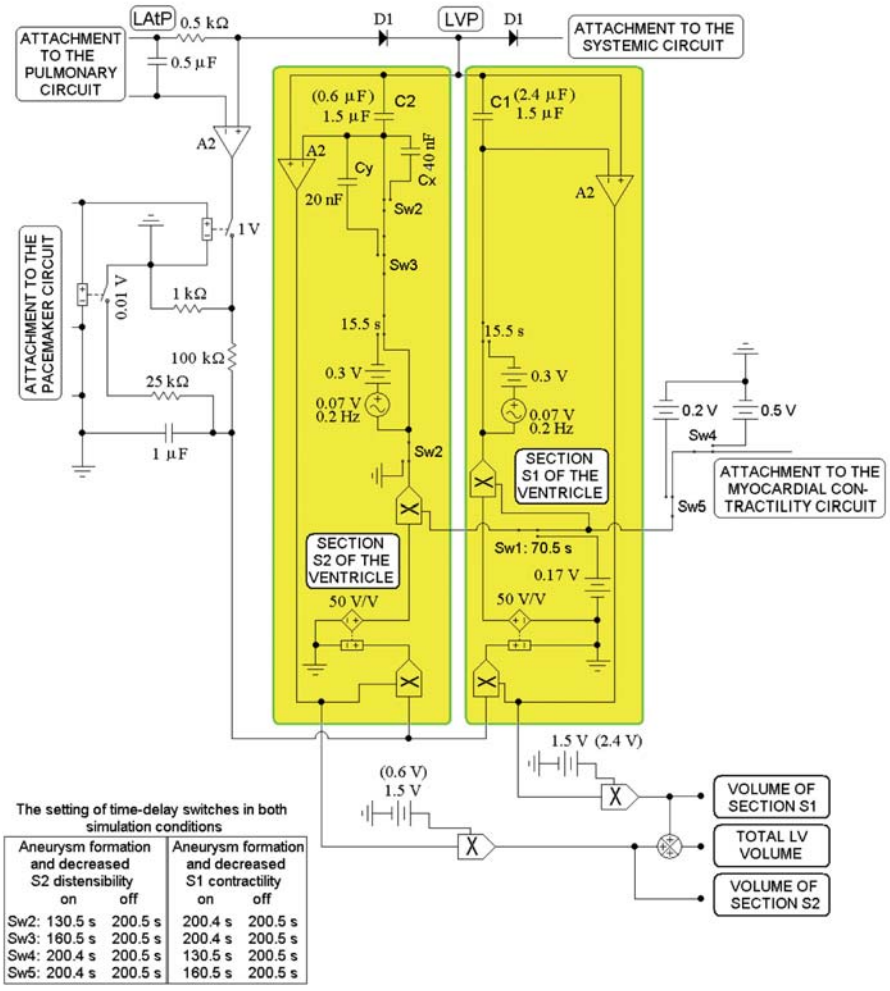



FIGURE 1. Electronic circuit of the left ventricle subdivided in section S1 (with initial normal function) and S2 (developing infarction and aneurysm). The time setting of switches in S2 determine whether S1 and S2 operate as a single unit, or as two distinctly separate units.

SW5) to simulate the time course of LVA formation and its consequences on ventricular hemodinamics. 1. LVA formation (defined in our model as an acute, regional ventricular failure with strongly decreased contractility, but conserved diastolic distensibility) is induced by operating Sw1 at 70.5 s. The section S2 is switched off from the myocardial contractility circuit, thereby decreasing the modulation factor from 1 to 0.17. Contrary to that, gain is normal in section S1 and modulation factor is controlled by homeostatic negative feedback. 2. The setting of additional switches (Sw 2 to 5), shown in the table in Figure 1, simulates two possible outcomes that follow an acute LVA: a decreased diastolic distensibility and scarring of the ventricular mass forming the LVA (in ventricle section S2) and a systolic dysfunction (a reduced contractiliy) of the prevoiusly unaffected portion of the left ventricle (in ventricle section S1). 2.1 *Simulation of a decreased diastolic distensibility and scarring of the LVA* (while the rest of the myocardium, S1, is functioning normally) is achieved by operating Sw2 at 130.5 s and Sw3 at 160.5 s to simulate a progressive, two-step decrease in distensibility (step I and step II in Figure 2). In this way either capacitor Cx (40 nF) or capacitor Cy (20 nF) is connected to capacitor C2. In this condition switches Sw4 and Sw5 are not activated. Therefore in this condition the contractility of section S1, functioning normally, is modulated by negative feedback (Figure 2). 2.2 *Simulation of reduced contractility of S1* (the initially normal ventricular section, unaffected by LVA) is achieved by operating Sw4 at 130.5 s and Sw5 at 160.5 s to simulate a progressive, two-step (mild and severe) decrease in contractility of section S1 (step I and step II in Figure 3). In this way the modulation circuit is switched-off completely and either battery 0.5 V or battery 0.2 V is connected to the contractility circuit of S1. Thus the contractility of S1 is decreased, inducing a mild or severe S1 systolic dysfunction (Figure 3). We studied how the size of LVA affects not only the end-diastolic pressure and the end-diastolic volume of the whole left ventricle, but also the end-diastolic volume of section S2 (that developed the LVA). To meet this end the ratio between the section of the LV unaffected by LVAMI (section S1) and the affected portion of the LV that developed a LVA (section S2), the S1/S2 ratio, is varied in 10% increments to affect 10%, to 50% of total left ventricular mass. In Figures. 4 and 5 this is indicated by acronyms 10-90, 20-80, 30-70, 40-60 and 50-50, respectively. Results of the simulations are shown graphically as the time course of equivalent variables. Thus electrical variables (voltage, current, resistance, capacitance and charge) correspond to physiological variables (pressure, blood flow, resistance, capacitance and volume). The interdependence of pressure and volume of the left ventricle is shown by pressure-volume analysis (P-V loop diagrams) describing the left ventricle work-load during one cardiac cycle (Figure 4). Acronyms of variables studied are listed in Table 1.

**TABLE 1.** Recorded variables (with corresponding units) and acronyms used in text and illustrations.

| Variable | Acronym |
|---|---|
| aortic pressure (mm Hg) | AoP |
| mean arterial pressure (mm Hg) | MAoP |
| cardiac output (mL/min) | CO |
| "contractible" volume of veins (mL) | CVV |
| sympathetic (inotropic) homeostatic contractility modulation | Sy |
| ejection fraction of the left ventricle | EF |
| end-diastolic volume of left ventricle (mL) | EDVLV |
| end-diastolic volume of section S2 of left ventricle | EDVS2 |
| end-diastolic pressure in left ventricle (mm Hg) | EDPLV |
| end-systolic volume of left ventricle (mL) | ESVLV |
| stroke volume of the left ventricle (mL) | SVLV |
| left atrial pressure (mm Hg) | LAtP |
| left ventricular pressure (mm Hg) | LVP |
| left ventricular volume (mL) | LVV |
| intrathoracic pressure (mm Hg) | ITP |

## RESULTS

*Simulation of a large LVA and its subsequent decreased distensibility*

The simulation of a large LVA and its subsequent, two-step decreased distensibility is presented in Figure 2. Changes in cardiovascular variables in "severe" myocardial infarction and a large myocardial aneurysm (involving 50% of left ventricle mass) are presented in the upper, middle and bottom graphs of Figure 2. Each graph is subdivided into four time intervals: normal conditions - before development of an LVAMI and LVA (50 s - 70.5 s); consequences of LVAMI and subsequent LVA - decreased contractility and conserved distensibility in S2 (70.5 s - 130.5 s); loss of contractility in S2 with its distensibility decreased first mildly (step I; 130.5 s - 160.5 s) and then strongly (step II; 160.5 s - 200 s). In normal conditions AoP, MAoP, CO, CVV, Sy, LAtP, ITP are in steady state; heart rate is 60/min. Decreased contractility in S2 results in a Sy, LAtP and heart rate increase (90/min), and an AoP, MAoP, CVV and CO decrease for about 10 s. Steady state is established at about 90 s of simulation time. Therefore heart rate is 60/min again. AoP, MAoP, CO are almost normal, CVV decreased while LAtP is strongly and Sy is slightly increased. A decrease in distensibility of S2 (step I, step II) results in a temporary increase in AoP, slight increase in MAoP and a decrease in Sy (Figure 2, Top graph). Before myocardial infarction, EDVLV and ESVLV are in a steady state. SVLV is 83 mL, EF is 44.4%. Decreased contractility in S2 results in a large increase of EDVLV and ESVLV. Steady state is established within about 90 s. SVLV is 83 mL

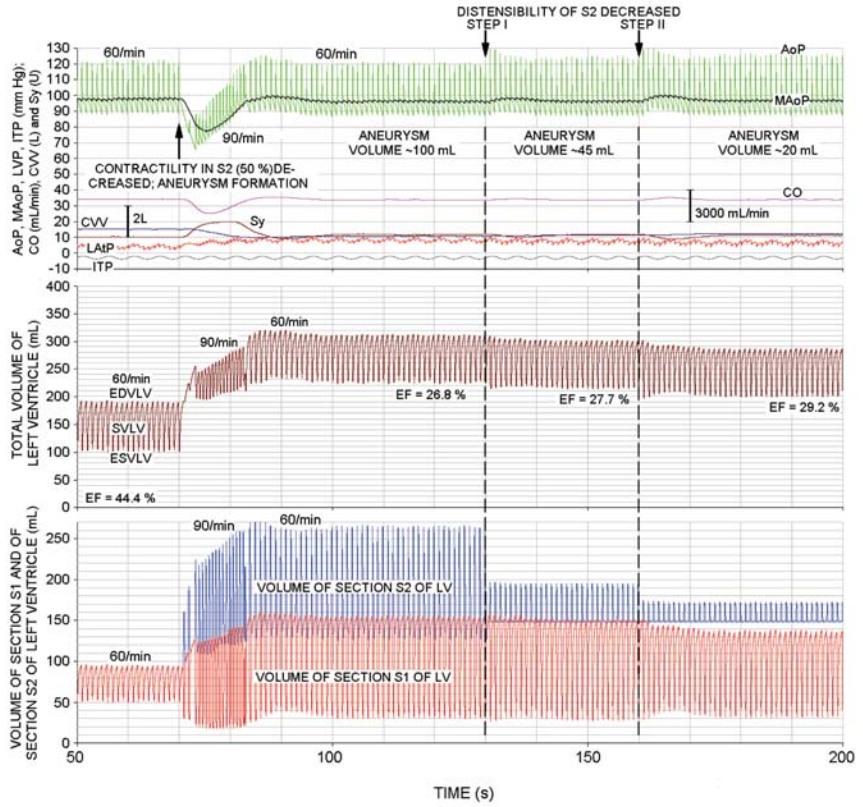
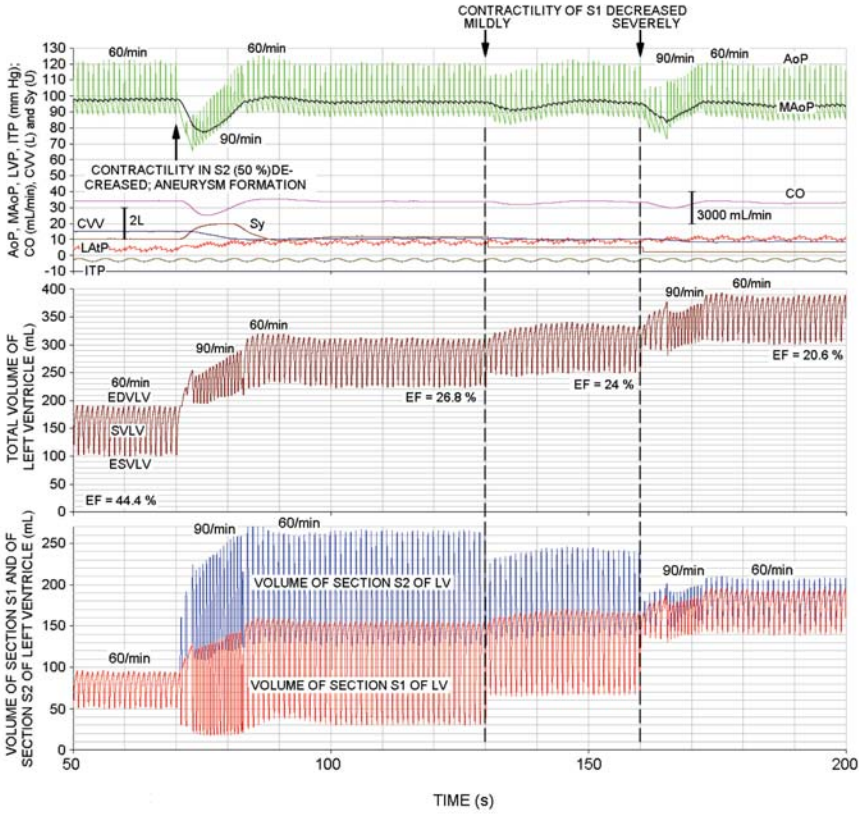



FIGURE 2. The time course of cardiovascular variables showing initially normal conditions when ejection fraction (EF) is 44. 4%, the effects of reduced contractility in 50% of left ventricle mass (in section S2) due to development of myocardial infarction and aneurysm (EF is 26.8%) and finally if in section S2 the distensibility is decreased in two steps (step I and step II) thus improving EF first to 27.7% and later to 29.2%. Acronyms are explained in Table 1.




and EF is 26.8%. A decrease in distensibility in S2 (step I, step II) results in a decrease of EDVLV and ESVLV, not greatly affecting the SVLV, but improving EF first to 27.7% and then to 29.2% (Figure 2, Middle graph). Initially, sections S1 and S2 operate as a single unit. Their volumes overlap, their volume relation being 50/50, their sum is equal to SVLV. When contractility in S2 is decreased, then during systole the volume of S1 is decreased (due to contraction of normal ventricular muscle) while the volume of S2 is paradoxically increased. During mid- and late-diastole, volumes of S1 and S2 are equal. As soon as the distensibility of S2 (step I, step II) is decreased, its systolic paradoxical volume increase is attenuated (Figure 2, Bottom graph).

*Simulation of a large LVA with a subsequent LV systolic dysfunction*

The simulation of a large aneurysm with a subsequent LV systolic dysfunction is presented in Figure 3. If the simulation shown in Figure 2 is repeated and modified by inducing first a mild (130.5 s - 160.5 s) and later a severe (160.5 s - 200 s) attenuation of S1 contractility, it results in a increase of EDVLV and ESVLV, maintaining the SVLV, but further decreasing EF (first to 24% and later to 20.6%). The paradoxical increase of S2 blood volume is maintained.

FIGURE 3. The time course of cardiovascular variables showing initially normal conditions when ejection fraction (EF) is 44.4%, the effects of a strongly decreased contractility in 50% of left ventricle mass (in section S2) due to development of LVAMI with LVA (EF is 26.8%) and finally after contractility in section S1 is decreased, first mildly and later severely (*i.e.* development of systolic dysfunction in the ventricle section S1 initially unaffected by AMI and the subsequent LVA) decreasing EF first to 24% and then to 20.6%. Acronyms are explained in Table 1.

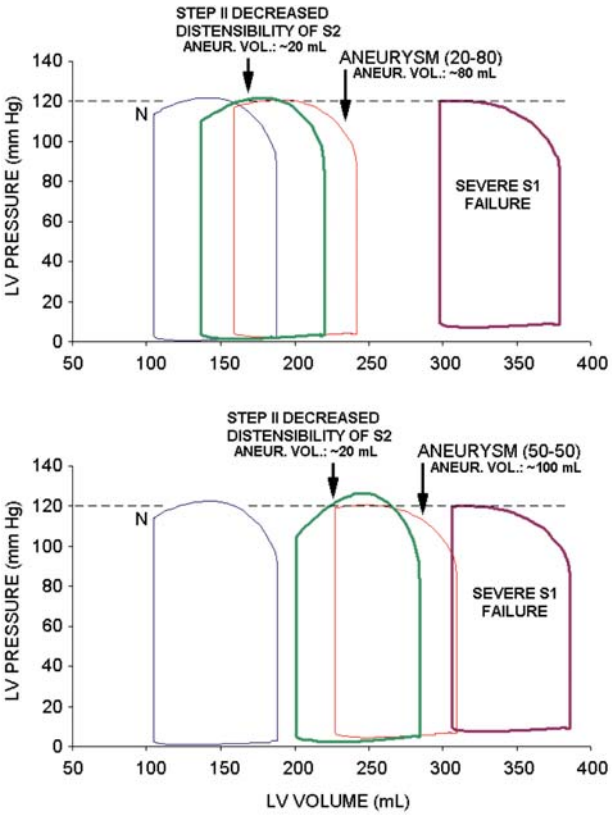



FIGURE 4. Pressure-Volume loop diagrams of left ventricle (LV) in normal conditions (N) aneurysm formation (Aneurysm), after distensibility of aneurysm is maximally decreased (STEP II) and after severe systolic dysfunction of section S1 (*i.e.* in the LV section that did not develop an aneurysm). Top graph: aneurysm in 20% of left ventricle mass. Bottom graph: aneurysm in 50% of left ventricle mass.

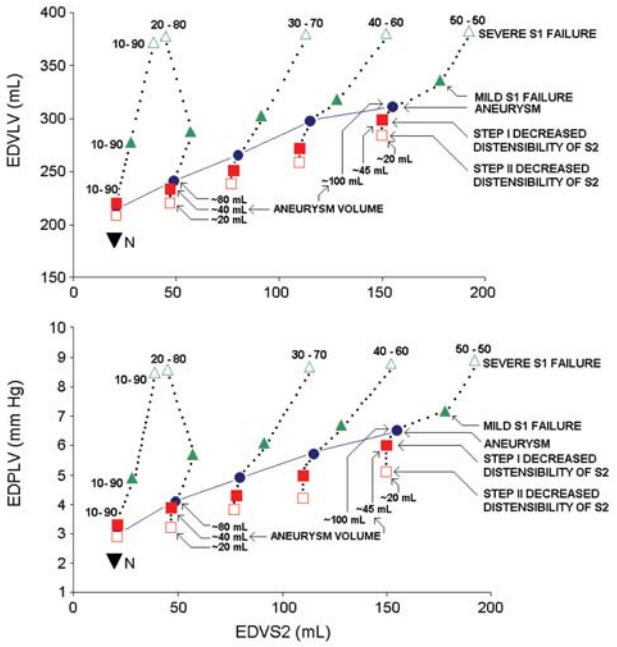



FIGURE 5. The effect of aneurysm size - measured as its end-diastolic volume (EDVS2) - on left ventricle end-diastolic volume (EDVLV) and left ventricle end-diastolic pressure (EDPLV). Symbols: S1 (section of left ventricle initially unaffected by aneurysm), S2 (section of left ventricle developing an aneurysm), solid circles (initial aneurysm size expressed as a ratio of the S2 and S1 sections from 10-90 to 50-50); solid squares (mildly decreased distensibilty of section S2), white squares (severely decreased distensibilty of section S2), solid triangles (mild systolic insufficiency of section S1), white triangles (severe systolic insufficiency of section S1).

*Analysis of left ventricle P-V loop diagrams after LVA and its subsequent decreased distensibility or after left ventricle systolic dysfunction*

In a relatively small aneurysm (20-80; S2 is 20% of ventricular mass) the P-V loop diagram is shifted to the right and to slightly higher left ventricle (LV) pressures. If in this condition the diastolic distensibility of section S2 is decreased (step II), the P-V loop diagram is shifted to the left and to slightly lower LV pressures. Contrary to that, in severe S1 systolic dysfunction the P-V loop diagram is shifted extremely to the right side of the diagram, showing also relatively high LV pressures (Figure 4., Top graph). In a relatively large aneurysm (50-50; S2 is 50% of ventricle mass) the P-V loop diagram is qualitatively similar as in the Top graph of Figure 4, but quantitatively all changes are more pronounced (Figure 4., Bottom graph).

*Effect of aneurysm size on left ventricle EDP and EDV*

By increasing the size of the LVA, from 10% to 50% of the left ventricle, the end-diastolic volume of the aneurysm (EDVS2) is increased. At the same time also the EDVLV is increased. However, the EDVS2/EDVLV relation is shifted to lower EDVLV levels, if S2 distensibility is decreased. And, contrary to that, this relation is shifted to even higher EDVLV levels, if S1 is affected by systolic dysfunction (Figure 5, Top graph). EDPLV changes follow the changes in EDVLV (Figure 5, Bottom graph).

## DISCUSSION

The presented EEC model, adapted to simulate LVA, is very similar to that already described [10-12]. Qualitatively, its cardiovascular variables resemble quite well to those *in vivo*. Quantitatively, however, there are some minor differences which have already been discussed [10-12]. Thus, also in the presented EEC the ejection fraction of the left ventricle is slightly lower (about 44%) than *in vivo* (above 55%). However, the simulated acute compensatory mechanisms can increase the EF to about 80% [10-12]. The simulated hemodynamics during LVA cannot be perfectly matched to individual patient data due to the lack of relevant, patient information and also due to the inherent limitations of the model. Relevant patient information, that is usually not available, is (a) the degree of right and left heart failure, (b) the degree of left ventricular tissue remodelling in the area of LVA and in the surrounding ventricular muscle region and (c) the efficiency of short, medium and

long term compensatory mechanisms that can be modified by the individuals life-style, age, previous or ongoing diseases or medication. Limitations specific to the presented model are the assumption of a normal short-term compensatory mechanism and the exclusion of medium (hormonal) and long-term (water and sodium retention) compensatory mechanisms at the time of a LVA. Also the model does not simulate the effect of ventricular arrhythmias that can occur after LVA [13] and can only partially model the ventricular functional changes due to heart tissue remodelling and alterations of ventricular geometry after a LVA [4]. Well documented hemodynamic changes in patients with LVA are, for example, a reduced ejection fraction and an increased left ventricular end diastolic pressure (LVEDP) and volume (LVEDV) [14-19]. The relationship between the size of aneurysm and LVEDV or LVEDP was first studied by Klein et al. [14]. Small aneurysms, with a LVA-to-chamber surface ratio below 15%, did not cause a significant change in LVEDV or LVEDP. However, when the size of LVA exceeded 20%, both the LVEDV and LVEDP increase proportionally with the volume of the aneurysm. The results of the EEC computer simulation are qualitatively and to a significant degree quantitatively consistent with the observed hemodynamic changes after LVA in clinical studies [14-19]. Also, the model highlighted the influence of LVA on the overall ventricular contractile properties. Systolic ventricular function can be evaluated by EF. In normal conditions, in the EEC model, EF is 44.4%. In a 50% LVA, the EF is decreased to 26.6%. However, after LVA distensibility is strongly decreased (step II), EF is improved to 29.2%. Contrary to that, when in the same simulation conditions, severe ventricular systolic dysfunction occurs, EF is decreased to 20.6%. In our model we recorded a minimal increase of LVEDV and LVEDP when the size of LVA was below 20% of ventricular mass and a proportional increase in LVEDV and LVEDP when the size of LVA was 20% or more. After LVA, the changes in LVEDV and LVEDP are reduced by decreased distensibility of the aneurysm and increased by systolic dysfunction (Figure 5). The pressure-volume loop diagrams, constructed with the EEC model, correctly reflected the hemodynamic changes after LVA, reduced aneurysmal distensibility or ventricular systolic dysfunction (Figure 4). This is consistent with the improvement in left ventricular function after LVA surgery [15-18, 20]. As reported, the acute compensatory mechanisms can maintain stroke volume if the noncontractile region involves less than 20% of the left ventricular circumference [3]. Our computer model assumed a normal acute compensatory mechanisms, thus LVAs involving more that 20% of left ventricular mass could theoretically be compensated. Excluding the possibility of a model generated artefact, we suggest that patients with LVA could have a less efficient acute compensatory mechanism than healthy persons. For example, the acute compensatory response could be suboptimal due to right heart failure or due to a reduced right ventricular filling pressure. Cardiovascular drugs, such as nitro-glycerine, reduce both systemic arterial pressure and venous return, thus reducing the right ventricular filling pressure and indirectly the left ventricular filling pressure [21]. Evaluation of LVA is important for understanding the hemodynamic impact of an aneurysm and for planning optimal surgical treatment [8, 15, 19, 20]. The hemodynamic properties of LVA were simulated with a computer-driven biomechanical model of the left ventricle using a pressure wave chamber system to simulate ventricular and aortic pressures and volumes [7]. However, this mechanical model cannot simulate passive relaxation of the ventricle during diastole, nor the resetting of the sympathetic nervous tone or the changes in intrathoratic pressure during respiration; it can quantify the different effects of dyskinetic and akinetic aneurysms of different sizes on ventricular function. Therefore, an additional advantage of the present EEC model of LVA over previous models is a realistic beat-to-beat ventricular blood flow and pressure tracing during LVA. Realistic beat-to-beat tracings (Figures 2, 3) enable the construction of pressure-volume loop diagrams (Figure 4) that facilitate our understanding of the effects of dyskinetic or akinetic aneurysms on ventricular function. A LVA shifts the ventricles pressure-volume loop to the right, this shift is partially reversed by a decrease in aneurysmal distensibility or alternatively, further aggravated by systolic dysfunction of the initially intact ventricular section (*i.e.* section S1; Figure 4). In addition, the EEC model adjusts the shape of the ventricles pressure-volume loop to reflect the corresponding changes in ventricular contractility (Figure 4).

## CONCLUSION

The model enables realistic beat-to-beat ventricular blood flow and pressure tracings that facilitate the understanding of the effects of akinetic or dyskinetic aneurysms of various sizes on ventricular function and correctly predicts the effect of systolic dysfunction or decreased aneurysmal distensibility on ventricular hemodinamics.

## DECLARATION OF INTEREST

The authors report no conflict of interest.

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