Understanding and Recognition of the Right Ventricular Function and Dysfunction: A Numerical Study

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Understanding and recognition of the right ventricular function and dysfunction: A numerical study

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24 **ABSTRACT**

25 The role played by the right ventricular (RV) dysfunction has long been underestimated in clinical practice.
26 Recent findings are progressively confirming that when the RV efficiency deteriorates both the right and the
27 left circulation is (significantly) affected, but studies dedicated to a detailed description of RV hemodynamic
28 role still lack. In response to such a gap in knowledge, this work proposes a numerical model that for the first
29 time evaluates the effect of isolated RV dysfunction on the whole circulation.

30 Lumped parameter modelling was applied to represent the physio-pathological hemodynamics. Different
31 grades of impairment were simulated for three dysfunctions i.e., systolic, diastolic, and combined systolic and
32 diastolic.

33 Hemodynamic alterations (i.e., of blood pressure, flow, global hemodynamic parameters), arising from the
34 dysfunctions, are calculated and analysed. Results well accord with clinical observations, showing that RV
35 dysfunction significantly affects both the pulmonary and systemic hemodynamics. Successful validation
36 against *in vivo* data proved the clinical potentiality of the model i.e., the capability of identifying the degree of
37 RV impairment for given hemodynamic conditions.

38 This study aims at contributing to the improvement of RV dysfunction recognition and treatment, and to the
39 development of tools for the clinical management of pathologies involving the right heart.

40

41

42 **A. Index Terms**

43 Biventricular circulation, Numerical analysis, Right ventricle, Ventricular dysfunction, 0D model

44

45 INTRODUCTION

46 Left ventricular systolic and diastolic dysfunctions have been studied extensively and are described as main
47 causes of heart failure (HF)¹⁻³, whereas less attention has been paid to systolic and diastolic dysfunctions of
48 the right ventricle (RV). In the literature, the role played by RV has been largely underestimated compared to
49 the left ventricle (LV) and, in the past, it was wrongly believed that RV could not affect cardiac output (CO)
50 and systemic pressures⁴⁻⁶. Nowadays the importance of RV has been recognized, and its role in the cardiac
51 hemodynamics has been highlighted^{7,8}. Actually, the circulatory system is a closed-loop where the function of
52 both ventricles is crucial. Therefore, not infrequently, impairment of one of the two ventricles precipitates
53 impairment of the other⁹. Although LV dysfunction is most common, a recent study reported that RV
54 myocardial infarction is not an infrequent problem, with an estimated occurrence of about 20-50% among
55 patients with inferior myocardial infarction¹⁰. Unfortunately, the limited information about RV dysfunction
56 effects does not allow to easily distinguish RV from LV dysfunctions, whereas it is evident that early diagnosis
57 of RV myocardial infarction reduces the risk of death, cardiogenic shock, ventricular tachycardia and
58 fibrillation, and atrioventricular block¹⁰.

59 In the present study, we implemented a lumped parameter model of the complete circulation in order to analyse
60 for the first time the consequences of *isolated* RV dysfunction on global cardiovascular conditions. We are
61 aimed at highlighting to what extent RV (dys)functional properties impact blood pressures and flows, so that
62 the understanding of the “forgotten ventricle”⁷ physiopathology improves, and an easier clinical management
63 of ventricular dysfunction will be gained in the future. The paper is structured as follows. In Section 2 we
64 introduce the numerical model and describe the simulations performed to analyse the different forms of right
65 ventricular dysfunction. In Section 3 we report the results of the numerical analysis. First, we focus on flow
66 and pressure waveforms in specific districts of the cardiovascular system, as well as on some global indexes
67 related to the performance of the ventricles. Second, we setup the model in order to compare the outputs with
68 clinical results of patients affected by right ventricular dysfunctions. In Section 4 some comments to the results
69 are drawn and the limitations of the model are considered. Finally, conclusions on the present problem are
70 reported in Section 5.

71 METHODS

72 In order to carry out an extensive analysis of different degrees of right ventricular dysfunction, we developed
 73 a lumped parameter (0D) model able to reproduce the entire cardiovascular system. This choice represents the
 74 best cost/benefit option since 0D models provide reliable results in terms of pressure and flow waves with low
 75 computational cost^{11–14}.

76 Hemodynamic model

77 The circulation was simulated considering the scheme of Fig. 1. It comprises the systemic and pulmonary
 78 circulations, the four heart chambers, and valves. To simulate the conduit vascular networks, we reproduced
 79 the small resistance to flow due to blood viscosity (R) and the compliance due to vessel elasticity (C); whereas
 80 the vascular beds were represented considering only the dissipation effects (represented by R). The heart was
 81 represented by the elastance model¹⁵, employing a time-varying elastance ($E(t)$) to reproduce the myocardial
 82 activity¹⁶. $E(t)$ was simulated via a ‘two-Hill’ function which accounts for contractile (g_1) and relaxation (g_2)
 83 phases of the cardiac cycle as

$$84 \quad E(t) = k \left(\frac{g_1}{1+g_1} \right) \left(\frac{1}{1+g_2} \right) + E_{min} \quad (1)$$

85 where k is a factor to guarantee that $\max(E(t)) = E_{max}$, E_{max} being the maximum contraction force and
 86 E_{min} the ventricular stiffness.

87 The two functions g_1 and g_2 are defined through the following expressions

$$88 \quad g_1 = \left(\frac{t-t_{onset}}{\tau_1} \right)^{m_1} \quad (2)$$

89 and

$$90 \quad g_2 = \left(\frac{t-t_{onset}}{\tau_2} \right)^{m_2}, \quad (3)$$

91 where τ is the relative appearance in time within the heartbeat, t_{onset} is the time-shift for the atrial contraction,
 92 and m a suitably coefficient that controls the elastance steepness.

93 From Eq. (1), the pressure within each chamber ($p(t)$) reads

$$94 \quad p(t) = E(t)(V(t) - V_{p=0}), \quad (4)$$

95 $V(t)$ and $V_{p=0}$ being the chamber volume and the unstressed volume at zero pressure, respectively.

96 Last, the presence of the valves was considered with linear resistance effects when they are open. Detailed
97 equations of all the elements that compose the lumped model are reported in the Supplementary Information.
98 The resulting system of ODE equations was run exploiting the built-in MATLAB® function *ode15s*, solving
99 a closed-loop system for 30 cycles, allowing the system to converge. Results were extracted after reaching the
100 periodic steady state.

101 *Healthy case*

102 First, the model was set up to reproduce the physiological hemodynamics of a representative healthy person.

103 *1) Numerical simulation*

104 The model of Fig. 1 was calibrated to meet the hemodynamics of an average adult of 75 Kg and body surface
105 area (BSA) of 1.9 m², having an heart rate (HR) of 75 bpm, a cardiac output (CO) of 6.5 L/min, and a perfusion
106 pressure of 97 mmHg¹⁶. Moreover, a sensitivity analysis to verify the influence of parameters on the model
107 was carried out (as reported in the Supplementary Information).

108 *2) Parameters' values*

109 To properly calibrate the model, the methodology proposed in Comunale et al.¹⁷ was used to represent the
110 physiological hemodynamics. For the systemic circulation, systemic vascular resistance (*SVR*) was computed
111 as $SVR = P_{perf}/CO$, where P_{perf} is perfusion pressure, i.e., the mean pressure that perfuses the systemic
112 organs. The systemic vascular resistance has three components: the arterial, venous, and vascular bed
113 resistances. The arterial (R_{art}) and venous (R_{ven}) resistances represent the flow resistance in the large vessels,
114 and they are 5%*SVR* and 3%*SVR*, respectively. The larger dissipation effect was considered in the small
115 vessels simulated by the vascular bed resistance (R_{vb}) which is 92%*SVR*. The arterial compliance was then
116 computed as $C_{art} = \tau/R_{vb}$, with τ the time constant of the circulation ($\tau = 0.81 \text{ s}^{18}$), and the venous
117 compliance as $C_{ven} = 30 \cdot C_{art}^{19}$. For the pulmonary circulation, the value of the pulmonary vascular
118 resistance (*PVR*) was taken from the literature²⁰ ($PVR = 0.06 \text{ mmHg} \cdot \text{s/mL}$), and we assumed the same
119 distribution of the systemic circulation among pulmonary arterial, venous and vascular bed resistances, i.e.,
120 $R_{art} = 5\%PVR$, $R_{ven} = 3\%PVR$, and $R_{vb} = 92\%PVR$. Finally, the arterial and venous pulmonary
121 compliances were taken from Tanaka et al.²¹ ($C_{pua} = 6.7 \text{ mL/mmHg}$, $C_{puve} = 15.8 \text{ mL/mmHg}$). For the
122 heart, values from Mynard et al.^{16,22} were used. Notice that for the healthy simulation adjustment of the

123 unstressed volume ($V_{p=0}$) of Eq. (4) was required to meet the desired hemodynamics. These values were then
124 kept constant when simulating right ventricular dysfunction. Finally, valve parameters were set to simulate the
125 resistance observed in the healthy condition. All the heart parameters are reported in Supplementary Table S1.

126 *Dysfunctional cases*

127 Starting from the healthy configuration, we defined the alterations required to simulate the RV dysfunction.

128 *1) Numerical simulation*

129 The dysfunction of the ventricle is due to pathologies that can affect both/either the contractility of the
130 myocardial fibers and then their capability to eject blood i.e., systolic dysfunction, and/or the ventricular
131 passive mechanism of filling i.e., diastolic dysfunction. Accordingly, we analysed the global hemodynamics
132 considering the following scenarios: *i)* isolated right ventricular systolic dysfunction, *ii)* isolated right
133 ventricular diastolic dysfunction, and *iii)* combined systolic and diastolic dysfunction.

134 As mentioned in the Introduction, few data are available to date for modelling the impairment of the right
135 ventricle. In this work, the following assumptions were hence made:

- 136 - RV dysfunction is caused by the same types of impairments that affect LV i.e., systolic dysfunction is mainly
137 determined by a reduction in RV contractile force whereas diastolic dysfunction is mostly due to increased
138 ventricular stiffness. Thus, the parameters of the dysfunctional right heart were determined in analogy with
139 those usually adopted for the LV impairment;
- 140 - secondary mechanisms due to the primary RV dysfunction e.g., adaptation mechanisms such as the variations
141 of the systemic vascular resistance, were excluded to avoid additional mechanisms in the evaluation of the
142 pathological hemodynamics given by a primary RV dysfunction.

143 Specific descriptions of the mechanisms of ventricular impairment are briefly described in the following.

144 *Isolated systolic dysfunction*

145 Systolic dysfunction (SD) refers to the ventricle's inability to pump the adequate amount of blood due to
146 impaired myocardial function, increased afterload, structural abnormalities, or the combination of the previous
147 diseases²³. SD is here reproduced through a reduction of the maximal contraction force, $E_{\max_{RV}}$, together with
148 an increase in systolic times (controlled by $\tau_{1_{RV}}$ and $\tau_{2_{RV}}$ of Eq. (2)-(3)). Indeed, it has been shown that the

149 myocardial performance index (MPI), i.e., the ratio between the atrioventricular closure opening time (TCO)
150 and the ejection time (ET), increases with systolic impairment^{24,25}.

151 *Isolated diastolic dysfunction*

152 Diastolic dysfunction (DD) refers to the ventricular inability to fill its cavity due to decreased distensibility,
153 delayed relaxation, and abnormal filling. For DD, there are three patterns of impaired filling, which represent
154 progressively worse diastolic dysfunction^{23,26}. In the present work, we focused on the most life-threatening
155 condition (grade III of diastolic dysfunction) i.e., the restrictive filling. In this stage of DD, the ventricular wall
156 stiffness ($E_{min_{RV}}$) largely increases whereas the tricuspid filling deceleration time ($m_{2_{RV}}$) decreases²⁷.

157 *Combined diastolic and systolic dysfunction*

158 Combined diastolic and systolic dysfunction (CD) results from the combination of SD and DD, and it was
159 reproduced by superimposing the two previous dysfunctions. The same grade of impairment p was adopted
160 for both SD and DD for sake of simplicity in order to analyse the relative weight of each of them on the
161 resulting hemodynamics.

162 *2) Parameters' Values*

163 Once the parameters reproducing the hemodynamics of a representative healthy person were determined, we
164 introduced the percentage of impairment (p) in the range 0% (healthy condition) - 100% (complete
165 dysfunctional condition) to simulate the RV dysfunction. Particularly, we defined the value of the parameters
166 in the presence of a complete (systolic/diastolic) dysfunctional ventricle ($p=100\%$) and we varied linearly all
167 the parameters involved. To simulate the systolic dysfunction, $E_{max_{RV}}$ was reduced to zero when the
168 ventricular contractility is fully compromised, whereas $\tau_{1_{RV}}$ and $\tau_{2_{RV}}$ were increased from 0.215 s and 0.362
169 s ($p=0\%$) to 0.430 s and 0.723 s ($p=100\%$), respectively. In the DD case, we increased $E_{min_{RV}}$ from 0.035
170 mmHg/mL to 0.140 mmHg/mL and $m_{2_{RV}}$ from 21.9 to 87.6, similarly to other works focused on the LV
171 dysfunction²⁸. Analogously, to simulate CD, $E_{max_{RV}}$ was reduced, $\tau_{1_{RV}}$ and $\tau_{2_{RV}}$ were increased, and $E_{min_{RV}}$
172 and $m_{2_{RV}}$ were increased as defined above. It is worth noting that with the percentage of 100% the ventricle
173 loses any contractility and/or compliance property, making the right ventricle a totally passive chamber with
174 no pumping or suction function. This condition is rarely met in clinical practice because of its extreme severity,
175 and it was here considered to obtain a full description of the pathophysiology.

176 See the Supplementary Information (section Time-varying elastance) and the Supplementary Fig. S3 for the
177 description and the graphical representation of the time-varying elastances for the different dysfunctions.

178 *Clinical case*

179 To compare model predictions and a real scenario, the *in vivo* investigation of Browning et al.²⁹ was considered.
180 In this study, patients are affected by pulmonary arterial hypertension (PAH) and DD i.e., they suffer from a
181 condition that matches our definition of combined RV dysfunction since PAH is known to be associated with
182 severe systolic dysfunction³⁰. To setup the model, we identified the degree of impairment as follows. First,
183 knowing that the systolic functionality alters ventricular performances i.e., EF^{31} , we determined the systolic
184 dysfunction required to obtain the EF_{RV} reduction reported by the authors²⁹. Second, we tuned the degree of
185 diastolic dysfunction to minimize the difference between the predicted results and measured data²⁹.

186 **RESULTS**

187 Table 1 reports the comparison between the outputs of the healthy simulation and *in vivo* reference data. The
188 model well represents the global hemodynamic variables, with both volumes and pressures within the
189 physiological ranges. As shown in Fig. 2, the computed pressures, flows, and volumes waveforms are
190 representative of familiar waveforms seen in these territories. The left heart is characterized by higher flow
191 peaks than the right side, and LV exhibits a pressure almost 6 times greater than that in the RV, both having a
192 stroke volume of about 80 mL.

193 Fig. 3 shows the pressures and flows estimated in various districts of the vascular circuit for the three RV types
194 of dysfunction. In the first column, SD outputs are presented. As p increases, the right atrial (RA) pressure
195 increases. The exacerbation of the impairment also flattens the late-systolic peak (v-wave) and emphasizes the
196 end-diastolic peak (a-wave), despite the unaltered right atrial functionality. On the other hand, RV pressure
197 exhibits a marked reduction of the systolic peak and an increase of the diastolic pressures. On the contrary, the
198 pulmonary arterial pressure (P_{PuA}) substantially reduces on the whole heartbeat. Both the two pressures curves
199 have flattened profiles as the pathology worsens and the systolic phase increases according to $E(t)$ displayed
200 in Supplementary Fig. S3a. The increase in P_{ra} is offset by the increase in the diastolic P_{rv} , resulting in a
201 reduction of the E wave. Such a reduction is partly compensated by an increase of the A wave on the tricuspid
202 valve flow (Q_{tv}) (Fig. 3a4). From an impairment of 70% E wave completely disappears, and the A wave reaches

203 a peak of about 600 mL/s, double compared to the healthy case (300 mL/s), whose maximum is observed for
 204 $p=80\%$. The loss of contractility affects also the flow across the pulmonary valve (Q_{pv}) (Fig. 3a₅). Q_{pv} abruptly
 205 lessens at systolic peak and, for a complete SD, Q_{pv} shows an almost constant waveform.
 206 The outputs due to DD are reported in the second column of Fig. 3. According to $E(t)$ function, the shape of
 207 all the variables during the cardiac cycle remains unaltered for the different grades of p . The simulated
 208 pressures in the right atrium and in the pulmonary artery exhibit a positive and negative shift with p increasing,
 209 respectively. Consistently, P_{rv} decreases during systole and increases during diastole as DD increases. The
 210 flow between RA and RV (Q_{tv}), due to their pressure variations, shows higher peaks for both the E and A
 211 waves. The former results to be characterized by an increasing flow deceleration and the latter by an increasing
 212 flow acceleration (Fig. 3b₄). At the same time, the peak of Q_{pv} reduces, but the ejection time of the ventricle
 213 slightly increases. Interestingly, for severe DD ($p>60\%$), the pulmonary valve opening is anticipated at the
 214 end of diastole i.e., atrial contraction is causing pressure to rise above pulmonary arterial pressure, such that
 215 the pulmonary valve opens before the onset of ventricular systole (Fig. 3b₅).
 216 Finally, the results provided by the CD case are reported in the third column of Fig. 3. The diastolic dysfunction
 217 mostly affects the output variables during the diastole, whereas the systolic dysfunction influences the results
 218 during the whole cardiac cycle since the increment of the ejection time has an effect also in the early-diastole.
 219 Fig. 4 reports the pressure-volume (PV) loops for RV (subscript 1) and LV (subscript 2) for the three
 220 dysfunctions considered. When SD is imposed on the right ventricle, RV end-systolic volume (ESV) increases
 221 and so does the RV end-diastolic volume (EDV). However, ESV increases more than EDV, resulting in a
 222 reduction of the stroke volume ($SV = EDV - ESV$). The impaired pumping activity causes a reduction in RV
 223 systolic pressures that, considering the volume increase, shifts the RV PV loops in downward/rightward
 224 direction. For the worst pathological condition, RV completely loses the ability to eject blood and the PV loop
 225 collapses in a line, as expected when the ventricle becomes a passive chamber (Fig. 4a₁). The impairment of
 226 RV affects also LV, that shows a reduction of both the volumes and pressures (Fig. 4a₂). The diastolic
 227 dysfunction has an effect on RV PV loops opposite to that due to SD (Fig. 4b₁). Both RV ESV and RV EDV
 228 reduce of about 30% and 20%, respectively. The inability to fill the cavity significantly increments the end-
 229 diastolic pressures (EDPs) and at the same time reduces the systolic pressures, causing the shrinking of the
 230 loops with leftward/downward shifts. The effects on the LV are similar to the SD case, although the

231 leftward/downward shift of the loops for $p > 60\%$ is lower (Fig. 4b₂). In the presence of the combined
 232 dysfunction, the pressure-volumes of RV move downward such that the systolic dysfunction shift is
 233 counterbalanced by the diastolic one (Fig. 4c₁). Also LV PV loops are affected by both systolic and diastolic
 234 dysfunction with PV loops in intermediate positions with respect to the SD and DD cases (Fig. 4c₂).
 235 Fig. 5 presents the mean central venous pressure (CVP), the cardiac index (defined as $CI = CO/BSA$), and the
 236 ejection fraction (EF) of both the ventricles. The quantities are compared to *in vivo* reference values, whose
 237 normal physiological ranges are indicated by grey areas. All the types of dysfunction determine an increase in
 238 CVP (Fig. 5a). SD is outside the physiological ranges for severe impairments ($p > 80\%$), DD oversteps for
 239 moderate dysfunction ($p > 40\%$), and CD goes beyond the ranges for $p > 30\%$. All the dysfunctions depress the
 240 ventricular functionality resulting in hypoperfusion (Fig. 5b). In the early stage of impairment, SD determines
 241 a lower CI reduction than DD. For $p > 70\%$ CI is outside the physiological ranges for both SD and DD, however,
 242 for SD, CI plummets. On the other hand, the combination of dysfunctions speeds the overstepping of the ranges
 243 ($p > 40\%$). The response in terms of EF highlights the role of RV contractility (Fig. 5c). EF_{RV} is estimated about
 244 55% in the whole range of DD impairment. Conversely, SD causes a significant EF reduction (from 55% to
 245 15% for $p = 0\%$ and $p = 100\%$, respectively), and in the CD case, the loss of contractility determines an EF
 246 decrement up to $p = 70\%$. For more severe CD impairment EF is almost constant. As already pointed out for
 247 the PV loops, RV dysfunction causes a diminution of LV performance for all types of dysfunction (Fig. 5d).
 248 Generally, LV results to be less compromised by the RV impairment than what RV itself is, and EF is lower
 249 than the *in vivo* threshold only for severe impairments in the SD and CD cases, reaching values of about 50%.
 250 On the other hand, in the DD case, EF_{LV} worsens of about 8%, remaining within physiological ranges.
 251 Finally, in Table 2 we report the comparison between the numerical results and the *in vivo* data of Browning
 252 et al.²⁹ for RV EDV, RV ESV, EF_{RV} , and CI. The best match between clinical measurements and model
 253 prediction is found for a systolic and diastolic impairment of 67% and 20%, respectively i.e., CD with different
 254 degree of systolic and diastolic dysfunctions. In that case, the model outputs consistently estimate the indexes
 255 reported in Browning et al.²⁹, with differences within the measurement error.

256 **DISCUSSION**

257 The importance of the right ventricle has often been underestimated in the clinical practice and research^{4,6,7,32,33}.
258 A recent review even highlights that “the perception of the right ventricle has fluctuated between an essential
259 and a nonessential ventricle”⁷. Actually, observing for example that patients with a Fontan circulation (i.e. who
260 do not have a sub-pulmonary ventricle) survive into adulthood with quite a good life quality one might presume
261 that RV is nonessential indeed. However, *in vivo* evidences are pointing out that the RV plays a key role in the
262 onset and progression of a number of diseased conditions as well as in exercise capacity³⁴. So, in order to
263 contribute to improve the knowledge of right ventricular (dys)function effects on the complete circulation
264 hemodynamics, we studied the *isolated* RV dysfunction by physically based numerical simulations.
265 We built up a lumped parameter model of both the right and left circulation that proved its capability to
266 reproduce the physiological condition with pressures, flows, and global hemodynamic variables in a very
267 satisfying agreement with literature data of healthy subjects^{20,35–39}. In particular, hemodynamics of the right
268 side is found to be well represented in all its characteristics, right heart flow waveforms included⁴⁰.
269 A large number of information worth of discussion emerges from model simulations when RV dysfunction is
270 taken into account. We first recall that our model includes for the first time prolonged cardiac time intervals
271 among the mechanisms that drive the isolated systolic dysfunction (SD) condition. Indeed, the variation of
272 systolic time with the rate of impairment, which is peculiar to the ventricular systolic dysfunction^{24,25}, emerged
273 as crucial in order to obtain results in accordance with clinical evidences. In particular, the increase in
274 ventricular end-diastolic pressure and the reduction in the systolic one, well known for the left ventricular
275 failure^{31,41}, has been recently reported also in the case of RV systolic impairment⁴². This result is clearly
276 represented by the model in presence of *right* systolic dysfunction. Such pressure behaviour can be seen as a
277 consequence of the impairment of contractility, which causes blood accumulation in RV as well as congestion
278 in RA and in systemic veins, with an obvious reduction in the amount of ventricular blood ejected. In this
279 condition, RA is forced to increase its pressure to overcome the pressure into the ventricle and open the
280 tricuspid valve, while P_{pua} decreases^{4,43}. At the same time, the computed Q_{tv} E wave disappears due to the
281 reduction of the tricuspid pressure gradient, in part compensated by the increase of the A wave. Notice that a
282 similar atrioventricular valve flow is known in *left* ventricular disfunction⁴⁴. Hence, we can speculate that it is
283 the impairment of the right/left systolic function the pathologic condition that leads to such a right/left

284 atrioventricular flow behaviour. We also observed that, importantly, when the contractile activity is absent
 285 ($p=100\%$), the model captures the nearly constant P_{rv} and Q_{pv} . Such a result is somehow expected since in
 286 absence of any contractile ventricular activity the model reproduces the passive conduit behaviour in which
 287 the blood flows from RA into PuA. Thus, the nonfunctional RV leads to condition similar to the spontaneous
 288 evolution of the Fontan circulation, as highlighted in Saran et al.⁴⁵. However, in the simulated case, RA
 289 function is maintained and therefore RA effectively ‘takes over’ as the main right-sided pump.

290 For what the isolated diastolic dysfunction (DD) is concerned, model results suggest that when the right
 291 ventricle suffers from *restrictive filling* the ejection fraction EF_{RV} is almost preserved. In other words, the
 292 ventricle exhibits the well-known features of heart failure with preserved ejection fraction (HFpEF) i.e., of the
 293 pathology that is usually attributed to LV³³. Such an evidence seems quite interesting since it might help in
 294 answering some of the questions left open in Gorter et al.³³ about “the determinants of RV dysfunction in
 295 HFpEF”. While it is true that EF_{RV} is substantially maintained, on the other hand DD results to alter pressures
 296 and flows. In this sense, it is worth noting that model predictions for severe impairment show the appearance
 297 of a secondary peak in Q_{pv} at late diastole which, according to Gatzoulis et al.⁴⁶ for Tetralogy of Fallot patients,
 298 could be ascribed to atrial contraction. Notice that the debate about the aetiology of such a secondary peak in
 299 Q_{pv} is still open⁴⁷. Among possible explanations⁴⁷, we here recall the one that ascribes the peak appearance to
 300 the atrial, ventricular, and pulmonic pressure state in *restrictive filling*, which forces the ventricle to behave
 301 like a ‘passive conduit’⁴⁶. Indeed, since the model assumes *isolated* dysfunction and does not account for
 302 adaptive processes, the ventricular stiffness does seem to be the actual leading cause of the diastolic flow peak
 303 occurrence.

304 Finally, in the combined systolic and diastolic dysfunction (CD) the effects of the two previous dysfunctions
 305 sum, and both their footprint can be easily recognised in CD simulations’ results. However, the superposition
 306 of SD and DD follows a non-linear behaviour, so that CD hemodynamics exhibits an overall worst
 307 performance.

308 The hemodynamic alterations visible in calculated PV loops (Fig. 4) can also be commented and compared to
 309 clinical evidences. In the SD scenario the reduction of the end-systolic pressure and the increment of the
 310 volume correspond to the ventricular response reported in Monnet et al.⁴⁸, and the computed EDPVR increase
 311 well compares to that typically occurring in diastolic dysfunction⁴⁹. In the CD case, the right ventricle attempts

312 to dilate for the lower contractility due to SD, but the increased passive stiffness due to DD opposes this volume
 313 dilation. For $p \geq 80\%$, the increased stiffness prevails so that the RV EDV reduces, resulting also in a slight
 314 increment of ventricular performance (Fig. 5b-d). Focusing on the LV PV loops, the computed shift is always
 315 downward/leftward in all the investigated cases i.e., LV work reduces. Obviously, since the left ventricle
 316 mechanical functionality is fully maintained, such a ventricular work reduction results from the entanglement
 317 between the LV and the suffering RV, which progressively drops the SV⁵⁰. Notice also that the effect of RV
 318 systolic dysfunction on LV is more severe in the CD than in the SD case. This result is not surprising since the
 319 loss of the passive action of the right myocardium, expressed by its relaxation, worsens the ventricular working.
 320 For what CVP and CI are concerned (Fig. 5a-b), clinical limits usually associated to potential ventricular
 321 disease^{51,52} are found to be overpassed for all the three different types of reproduced dysfunction, although for
 322 different degrees. Such an occurrence strengthens the idea that the correct functioning of the right ventricle
 323 during the whole cardiac cycle is of crucial importance in assuring overall physiological hemodynamic
 324 conditions. Passing now to EF, we observe that, as expected from PV loops' evidences, our results confirm the
 325 strong interaction between the two ventricles. In particular, the computed EF behaviour suggests that both
 326 EF_{RV} and EF_{LV} have to be evaluated in right diseases (e.g., Tetralogy of Fallot). Indeed, van der Ven et al.⁵⁰
 327 recently pointed out that the role of LV in Tetralogy of Fallot can not be neglected, despite LV parameters are
 328 not considered in current guidelines for the assessment of the most appropriate timing of intervention⁵⁰.
 329 Finally, the comparison between the numerical simulation with the *in vivo* clinical data of Browning et al.²⁹
 330 (Table 2) is illustrative for the potential of the model as predictive tool to be applied to real scenarios. The
 331 model's ability to reproduce the hemodynamic indexes seems to be particularly promising. Indeed, the
 332 differences between simulated and observed outputs are more than acceptable, for example the computed CI
 333 is 2.4 L/min/m² versus the measured 2.5 L/min/m². Notice that such a result is even more remarkable when
 334 considering that we did not account for the alterations connected to the ventricular pathologies that may
 335 enhance the model predictions. In other words, the dysfunction model here proposed seems to be effectively
 336 representative of the real pathological mechanisms governing the depressed/stiffened ventricle.
 337 The diagnosis and treatment of diseased conditions might hence benefit from the application of the model
 338 thanks to its ability in determining flow and pressure changes as a result of RV dysfunction. For example:

339 1) *Isolated right ventricular dysfunction: Uhl disease, right ventricular dysplasia, post-surgical right*
340 *ventricular dysfunction.* This condition is rare, and the knowledge of heart chambers physiopathology as well
341 as the clinical evolution assessment are hardly feasible. The present model may help to grade the correct
342 ventricular dysfunction.

343 2) *Pulmonary arterial hypertension.* In this case, the pulmonary arterial pressure is augmented. The
344 associated right heart hemodynamics can be due to the increased afterload or associated with a percentage of
345 RV dysfunction. Distinguishing between these two cases is still a clinical challenge and a suitably
346 implementation of the model assigning augmented pulmonary artery pressure conditions may help to identify
347 the patients at higher risk to develop right HF.

348 3) *Cor pulmonare.* Left HF usually affects RV function due to the increase of left atrial pressure and the
349 pulmonary arterial pressure. Similarly to setting 2), the RV dysfunction model, implemented with the LV
350 impairment, may be appropriate to recognize the hemodynamics due to the left HF or associated to primitive
351 right HF (bi-ventricular failure). This distinction is particularly important when a left ventricular assist device
352 (VAD) is required. In the case of induced right HF, the right ventricular function recovers, partially or
353 completely, after the left VAD implantation. Conversely, when the right ventricular dysfunction occurs,
354 usually a bi-VAD is the best clinical option.

355 Finally, study limitations and possible future improvements can be summarized. Cardiac valve flow was
356 modelled according to a simple linear flow/pressure gradient relationship, which is likely the reason why Q_{ao}
357 and Q_{mv} (E/A ratio) are found to have peaks somehow higher than physiological ones³⁹. The inclusion of valve
358 dynamics is expected to overcome this issue (Mynard et al.²²). Moreover, neither physiological compensatory
359 mechanisms e.g., ventricular remodelling and venous constriction, nor secondary diseases e.g., tricuspid valve
360 insufficiency⁵³, were accounted for in the model since we aimed at highlighting primary RV dysfunction effects
361 alone. However, the inclusion of the above mechanisms/conditions in the model is quite easily feasible. Last
362 but not least, further development can arise from taking into account sex differences in model parameter values
363 and/or cardiovascular functional response i.e., differences that has been recognised as pivotal in both healthy
364 and pathological hemodynamics^{17,54–56}.

365 **CONCLUSIONS**

366 Our study highlights the effect of RV (dys)function on the overall hemodynamics. The 0D circulation model
367 seems to correctly simulate the pressures and flows in both the pulmonary and systemic circulations. Changes
368 in RV functions lead to significant modifications of the overall hemodynamics, affecting also LV output due
369 to a decreased preload. To the best of our knowledge, there is not such a previous engineering work aimed at
370 understanding the hemodynamic implications of the development of RV impairment. In addition, the model
371 matches clinical data of patients presenting RV diseases, providing a first step towards the set up and the
372 assessment of a numerical tool able to support clinicians to improve the knowledge and the understating of the
373 role played by RV on the blood circulation with potential future benefits in the diagnosis and treatment of RV
374 pathologies.

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379 **Competing interests**

380 The authors declare no competing interests.

381 **Data availability**

382 The datasets generated and analysed during the current study are available from the corresponding author on
383 reasonable request.

384 **Ethical approval**

385 This article does not contain any studies with human participants or animals performed by any of the authors.

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388

389 REFERENCES

- 390 1. Sun, J. C. & Joffe, H. *The Most Common Inpatient Problems in Internal Medicine E-Book: Ward*
391 *Survival*. (Elsevier Health Sciences, 2007).
- 392 2. Bonnema, D. D., Baicu, C. F. & Zile, M. R. Pathophysiology of Diastolic Heart Failure : Relaxation
393 and Stiff ness. in *Diastology Clinical Approach to Diastolic Heart Failure* 11–25 (Elsevier Inc., 2008).
394 doi:10.1016/B978-1-4160-3754-5.50008-1
- 395 3. Treece, J. *et al.* A Review of Prognostic Tools in Heart Failure. *Am. J. Hosp. Palliat. Med.* **35**, 514–
396 522 (2018).
- 397 4. Haddad, F., Doyle, R., Murphy, D. J. & Hunt, S. A. Right ventricular function in cardiovascular disease,
398 part II: Pathophysiology, clinical importance, and management of right ventricular failure. *Circulation*
399 **117**, 1717–1731 (2008).
- 400 5. Kagan, A. Dynamic responses of the right ventricle following extensive damage by cauterization.
401 *Circulation* **5**, 816–823 (1952).
- 402 6. Silverton, N. & Djaiani, G. Right Ventricular Function and Perioperative Risk Assessment: The Time
403 Has Come to Stop Being Sinister. *J. Cardiothorac. Vasc. Anesth.* **33**, 1287–1289 (2019).
- 404 7. Amsallem, M., Mercier, O., Kobayashi, Y., Moneghetti, K. & Haddad, F. Forgotten No More: A
405 Focused Update on the Right Ventricle in Cardiovascular Disease. *JACC Hear. Fail.* **6**, 891–903
406 (2018).
- 407 8. Mehta, S. R. *et al.* Impact of right ventricular involvement on mortality and morbidity in patients with
408 inferior myocardial infarction. *J. Am. Coll. Cardiol.* **37**, 37–43 (2001).
- 409 9. Padang, R. *et al.* Aetiology and outcomes of severe right ventricular dysfunction. *Eur. Heart J.* **41**,
410 1273–1282 (2020).
- 411 10. Selton-Suty, C. & Juillière, Y. Non-invasive investigations of the right heart: How and why? *Arch.*
412 *Cardiovasc. Dis.* **102**, 219–232 (2009).

- 413 11. Kokalari, I., Karaja, T. & Guerrisi, M. Review on lumped parameter method for modeling the blood
414 flow in systemic arteries. *J. Biomed. Sci. Eng.* **6**, 92 (2013).
- 415 12. Korakianitis, T. & Shi, Y. A concentrated parameter model for the human cardiovascular system
416 including heart valve dynamics and atrioventricular interaction. *Med. Eng. Phys.* **28**, 613–628 (2006).
- 417 13. Shi, Y., Lawford, P. & Hose, R. Review of Zero-D and 1-D Models of Blood Flow in the Cardiovascular
418 System. *Biomed. Eng. Online* **10**, (2011).
- 419 14. Formaggia, L. & Veneziani, A. Reduced and multiscale models for the human cardiovascular system.
420 *Lect. notes VKI Lect. Ser.* 120 (2003). doi:10.13140/RG.2.1.3668.8088
- 421 15. Suga, H., Sagawa, K. & Shoukas, A. A. Load independence of the instantaneous pressure-volume ratio
422 of the canine left ventricle and effects of epinephrine and heart rate on the ratio. *Circ. Res.* **32**, 314–322
423 (1973).
- 424 16. Mynard, J. P. & Smolich, J. J. One-Dimensional Haemodynamic Modeling and Wave Dynamics in the
425 Entire Adult Circulation. *Ann. Biomed. Eng.* **43**, 1443–1460 (2015).
- 426 17. Comunale, G., Susin, F. M. & Mynard, J. P. A female-specific cardiovascular lumped-parameter model.
427 in *2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society*
428 *(EMBC)* 2654–2657 (IEEE, 2020). doi:10.1109/EMBC44109.2020.9175427
- 429 18. Mynard, J. P. Computer modeling and wave intensity analysis of perinatal cardiovascular function and
430 dysfunction. 76–125 (2011).
- 431 19. Kam, P. & Power, I. *Principles of Physiology for the Anaesthetist*. (CRC Press, 2012).
432 doi:10.1097/00003643-200202000-00021
- 433 20. Milnor, W. R. Hemodynamics. *Card. Dyn.* (1989).
- 434 21. Tanaka, T. *et al.* Compliance of human pulmonary ‘venous’ system estimated from pulmonary artery
435 wedge pressure tracings - Comparison with pulmonary arterial compliance. *Jpn. Circ. J.* **50**, 127–139
436 (1986).

- 437 22. Mynard, J. P., Davidson, M. R., Penny, D. J. & Smolich, J. J. A simple, versatile valve model for use
438 in lumped parameter and one-dimensional cardiovascular models. *Int. j. numer. method. biomed. eng.*
439 **28**, 626–641 (2012).
- 440 23. Fukuta, H. & Little, W. C. General Principles, Clinical Definition, and Epidemiology. in *Diastology*
441 *Clinical Approach to Diastolic Heart Failure* 63–72 (Elsevier Inc., 2008). doi:10.1016/B978-1-4160-
442 3754-5.50012-3
- 443 24. Tei, C. *et al.* New index of combined systolic and diastolic myocardial performance: a simple and
444 reproducible measure of cardiac function - a study in normals and dilated cardiomyopathy. *J cardiol*
445 **26**, 7–366 (1995).
- 446 25. Oketona, O. A. *et al.* Right ventricular systolic function in hypertensive heart failure. *Vasc. Health Risk*
447 *Manag.* **13**, 353–360 (2017).
- 448 26. Mottram, P. M. & Marwick, T. H. Assessment of diastolic function: what the general cardiologist needs
449 to know. *Heart* **91**, 681–695 (2005).
- 450 27. Nagueh, S. F. & Zoghbi, W. A. Evaluation of Right Ventricular Diastolic Function. in *Diastology*
451 *Clinical Approach to Diastolic Heart Failure* 171–180 (Elsevier Inc., 2008). doi:10.1016/B978-1-
452 4160-3754-5.50020-2
- 453 28. Luo, C., Ramachandran, D., Ware, D. L., Ma, T. S. & Clark, J. W. Modeling left ventricular diastolic
454 dysfunction: Classification and key indicators. *Theor. Biol. Med. Model.* **8**, 14 (2011).
- 455 29. Browning, J. R., Hertzberg, J. R., Schroeder, J. D. & Fenster, B. E. 4D flow assessment of vorticity in
456 right ventricular diastolic dysfunction. *Bioengineering* **4**, (2017).
- 457 30. Rain, S. *et al.* Right ventricular diastolic impairment in patients with pulmonary arterial hypertension.
458 *Circulation* **128**, 2016–2025 (2013).
- 459 31. Chatterjee, K. & Massie, B. Systolic and Diastolic Heart Failure: Differences and Similarities. *J. Card.*
460 *Fail.* **13**, 569–576 (2007).

32. Haddad, F., Hunt, S. A., Rosenthal, D. N. & Murphy, D. J. Right ventricular function in cardiovascular disease, part I: Anatomy, physiology, aging, and functional assessment of the right ventricle. *Circulation* **117**, 1436–1448 (2008).
33. Gorter, T. M., Rienstra, M. & van Veldhuisen, D. J. Right ventricular dysfunction in heart failure with reduced vs. preserved ejection fraction: non-identical twins? *Eur. J. Heart Fail.* **19**, 880–882 (2017).
34. Vonk-Noordegraaf, A. & Westerhof, N. Describing right ventricular function. *Eur. Respir. J.* **41**, 1419–1423 (2013).
35. Hudsmith, L. E., Petersen, S. E., Francis, J. M., Robson, M. D. & Neubauer, S. Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging. *J. Cardiovasc. Magn. Reson.* **7**, 775–782 (2005).
36. Sievers, B., Addo, M., Breuckmann, F., Barkhausen, J. & Erbel, R. Reference right atrial function determined by steady-state free precession cardiovascular magnetic resonance. *J. Cardiovasc. Magn. Reson.* **9**, 807–814 (2007).
37. Maceira, A. M., Prasad, S. K., Khan, M. & Pennell, D. J. Reference right ventricular systolic and diastolic function normalized to age, gender and body surface area from steady-state free precession cardiovascular magnetic resonance. *Eur. Heart J.* **27**, 2879–2888 (2006).
38. Argiento, P. *et al.* Exercise Stress Echocardiography of the Pulmonary Circulation Limits of Normal and Sex Differences. *Chest* **142**, 1158–1165 (2012).
39. Demir, M., Acarturk, E. & Turkey, A. Clinical characteristics influence left and right ventricular diastolic function in healthy individuals. *Angiology* **52**, 25–30 (2001).
40. Kachenoura, N. *et al.* Right Ventricular Diastolic Function Evaluation in Magnetic Resonance Imaging Department of Cardiovascular Radiology , Hôpital Européen Georges Pompidou , Paris , France. 89–92 (2015).
41. Klabunde, R. E. *Cardiovascular physiology concepts*. (2011).

- 485 42. Monitillo, F. *et al.* Right Ventricular Function in Chronic Heart Failure: From the Diagnosis to the
486 Therapeutic Approach. *J. Cardiovasc. Dev. Dis.* **7**, 12 (2020).
- 487 43. Fitchett, D. H., Sugrue, D. D., MacArthur, C. G. & Oakley, C. M. Right ventricular dilated
488 cardiomyopathy. *Br. Heart J.* **51**, 25–29 (1984).
- 489 44. Nagueh, S. F. *et al.* Recommendations for the Evaluation of Left Ventricular Diastolic Function by
490 Echocardiography: An Update from the American Society of Echocardiography and the European
491 Association of Cardiovascular Imaging. *J. Am. Soc. Echocardiogr.* **29**, 277–314 (2016).
- 492 45. Saran, M., Sivasubramonian, S., Abhilash, S. P. & Tharakan, J. A. Acquired fontan paradox in isolated
493 right ventricular cardiomyopathy. *Ann. Pediatr. Cardiol.* **9**, 251–253 (2016).
- 494 46. Gatzoulis, M. A., Clark, A. L., Cullen, S., Newman, C. G. H. & Redington, A. N. Right ventricular
495 diastolic function 15 to 35 years after repair of tetralogy of Fallot: Restrictive physiology predicts
496 superior exercise performance. *Circulation* (1995). doi:10.1161/01.CIR.91.6.1775
- 497 47. Kutty, S. *et al.* Usefulness of Pulmonary Arterial End-Diastolic Forward Flow Late After Tetralogy of
498 Fallot Repair to Predict a “Restrictive” Right Ventricle. *Am. J. Cardiol.* **121**, 1380–1386 (2018).
- 499 48. Monnet, X., Marik, P. E. & Teboul, J. L. Prediction of fluid responsiveness: an update. *Ann. Intensive*
500 *Care* **6**, 1–11 (2016).
- 501 49. Rommel, K. P. *et al.* Load-independent systolic and diastolic right ventricular function in heart failure
502 with preserved ejection fraction as assessed by resting and handgrip exercise pressure–volume loops.
503 *Circ. Hear. Fail.* **11**, 1–11 (2018).
- 504 50. van der Ven, J. P. G., van den Bosch, E., Bogers, A. J. C. C. & Helbing, W. A. Current outcomes and
505 treatment of tetralogy of fallot [version 1; peer review: 2 approved]. *F1000Research* **8**, 1–15 (2019).
- 506 51. Miller, R. D., Eriksson, L., Fleisher, L. A., Wiener-Kronish, J. P. & Young, W. L. *Miller’s anesthesia*.
507 (2010).
- 508 52. Edwards. Normal Hemodynamic Parameters and Laboratory Values. *Edwards Corp.* **2**, 0–3 (2014).

- 509 53. Schwartz, M. C., Glatz, A. C. & Gillespie, M. J. *Valvular Insufficiency and Heart Failure. Heart*
510 *Failure in the Child and Young Adult: From Bench to Bedside* (Elsevier Inc., 2018). doi:10.1016/B978-
511 0-12-802393-8.00022-3
- 512 54. Appelman, Y., van Rijn, B. B., ten Haaf, M. E., Boersma, E. & Peters, S. A. E. Sex differences in
513 cardiovascular risk factors and disease prevention. *Atherosclerosis* **241**, 211–218 (2014).
- 514 55. Purkiss, S. & Huckell, V. F. Cardiovascular Physiology: Similarities and Differences between Healthy
515 Women and Men. *J. SOGC* **19**, 853–859 (1997).
- 516 56. Schiebinger, L. & Klinge, I. Gendered innovation in health and medicine. *Adv. Exp. Med. Biol.* **1065**,
517 643–654 (2018).
- 518 57. Rudski, L. G. *et al.* Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A
519 Report from the American Society of Echocardiography. Endorsed by the European Association of
520 Echocardiography, a registered branch of the European Society of Cardiology, and . *J. Am. Soc.*
521 *Echocardiogr.* **23**, 685–713 (2010).
- 522 58. Luis, S. A., Chan, J. & Pellikka, P. A. Echocardiographic Assessment of Left Ventricular Systolic
523 Function: An Overview of Contemporary Techniques, Including Speckle-Tracking Echocardiography.
524 *Mayo Clin. Proc.* **94**, 125–138 (2019).
- 525 59. Maksuti, E. *et al.* Cardiac remodeling in aortic and mitral valve disease: A simulation study with clinical
526 validation. *J. Appl. Physiol.* **126**, 1377–1389 (2019).
- 527 60. Bozkurt, S. Mathematical modeling of cardiac function to evaluate clinical cases in adults and children.
528 *PLoS One* **14**, 1–20 (2019).
- 529 61. Seemann, F. *et al.* Noninvasive Quantification of Pressure-Volume Loops From Brachial Pressure and
530 Cardiovascular Magnetic Resonance. *Circ. Cardiovasc. Imaging* **12**, e008493 (2019).
- 531

532 **Authors contributions**

533 Conceived and designed the research: GC, BC and FMS. Developed of numerical model: GC and BC. Data
534 analysis: BC, PP, RR, GDS and MP. Drafted the manuscript: GC and PP. Review and editing: RR, MP, GDS
535 and FMS. Supervision of the activities: FMS.

536

538

539 **Fig. 1.** Circulation model composed of: left ventricle (LV), systemic arteries, vascular bed, and veins, right
540 ventricle (RV), right atrium (RA), pulmonary arteries, bed, and veins, left atrium (LA) and heart valves (►).

541

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543

544 **Fig. 2.** Hemodynamic waveforms of the healthy condition. *a)* Pressures, *b)* flows, and *c)* pressure-volume (PV)
545 loops. Subscripts: lv, left ventricle; Ao, aortic and arterial vessels; sr, systemic vascular bed; rv, right ventricle;
546 PuA, pulmonary arteries; pr, pulmonary vascular bed; Aov, aortic valve; Mv, mitral valve; Pv, pulmonary
547 valve, and Tv, tricuspid valve. The LV presents with flow peaks which are higher than the RV, exhibiting an
548 LV pressure almost 6 times greater than the RV estimated one, both having a stroke volume of about 80 mL.

549

550

Fig. 3. Pressures and flows for a heartbeat in the dysfunctions. *a)* systolic dysfunction, *b)* diastolic dysfunction and *c)* combined dysfunction. P_{ra} , RA pressure (subscript 1); P_{rv} , RV pressure (subscript 2); P_{pua} , PuA pressure (subscript 3); Q_{tv} , tricuspid valve flow (subscript 4); Q_{pv} , pulmonary valve flow (subscript 5). Black solid line,

555 healthy configuration ($p=0\%$); coloured lines; the corresponded degree of RV impairment, p , from 10% to
 556 100%.

557
 558 **Fig. 4.** Pressure-volume loops for RV (subscript 1) and LV (subscript 2). *a)* systolic dysfunction; *b)* diastolic
 559 dysfunction, and *c)* combined systolic and diastolic dysfunction. Black solid line, healthy configuration
 560 ($p=0\%$); coloured lines; the corresponded degree of RV impairment, p , from 10% to 100%.

561

Fig. 5. Comparison at various rates of impairment between the different types of dysfunction (symbols) and *in vivo* reference data (grey area). $\square$, systolic dysfunction, Δ , diastolic dysfunction, and $\circ$, combined systolic and diastolic dysfunction. a) CVP, mean pressure in the central veins and *in vivo* data⁵², b) CI, cardiac index and *in vivo* data⁵², and EF, ejection fraction for c) RV (EF_{RV}) and *in vivo* data⁵⁷, and d) LV (EF_{LV}) and *in vivo* data⁵⁸.

569 **TABLES**

570 **Table 1.** Comparison of the healthy condition outputs with *in vivo* reference data given as a mean, with range
571 or standard deviation in parentheses.

Parameters	Units	Model	Reference
CO	[L/min]	6.2	6.5 (3.6-9.4) ²⁰
Total vascular resistance			
SVR	[mmHg · s/mL]	0.89	0.8 (0.5-1.1) ²⁰
PVR	[mmHg · s/mL]	0.06	0.06 (0.02-0.09) ²⁰
Volume			
LV_{max}	[mL]	144	150 ± 31 ³⁵
RV_{max}	[mL]	153	173 ± 39 ³⁵
LA_{max}	[mL]	111	97 ± 27 ³⁵
RA_{max}	[mL]	107	101 (37-177) ³⁶
LV_{min}	[mL]	62	47 ± 15 ³⁵
RV_{min}	[mL]	71	69 ± 22 ³⁵
LA_{min}	[mL]	72	44 ± 13 ³⁵
RA_{min}	[mL]	66	50 (15-92) ³⁶
Pressure			
SBP	[mmHg]	120	125 ± 7 ³⁷
DBP	[mmHg]	66	73 ± 5 ³⁷
PuA (systolic)	[mmHg]	18.3	22.5 ± 1.0 ³⁸
PuA (mean)	[mmHg]	13.5	15.5 ± 2.6 ³⁸
E/A ratio			
Mitral	[-]	4.6	0.6-2.6 ³⁹
Tricuspid	[-]	1.1	0.8-2.3 ³⁹

572

573

574 **Table 2.** Comparison of the CD condition outputs with *in vivo* reference data from Browning et al. ²⁹.

Parameters	Units	Reference	CD
			$p_{systolic}=67\% - p_{diastolic}=20\%$
RV_{max}	[mL]	181±17	172
RV_{min}	[mL]	123±17	112
EF_{RV}	[%]	35±3	35
CI	L/min/m ²	2.5±0.2	2.4

575

Figures

Figure 1

Circulation model composed of: left ventricle (LV), systemic arteries, vascular bed, and veins, right ventricle (RV), right atrium (RA), pulmonary arteries, bed, and veins, left atrium (LA) and heart valves (⌘).

Figure 2

Hemodynamic waveforms of the healthy condition. a) Pressures, b) flows, and c) pressure-volume (PV) loops. Subscripts: lv, left ventricle; Ao, aortic and arterial vessels; sr, systemic vascular bed; rv, right ventricle; PuA, pulmonary arteries; pr, pulmonary vascular bed; Aov, aortic valve; Mv, mitral valve; Pv, pulmonary valve, and Tv, tricuspid valve. The LV presents with flow peaks which are higher than the RV, exhibiting an LV pressure almost 6 times greater than the RV estimated one, both having a stroke volume of about 80 mL.

Figure 3

Pressures and flows for a heartbeat in the dysfunctions. a) systolic dysfunction, b) diastolic dysfunction and c) combined dysfunction. P_{ra} , RA pressure (subscript 1); P_{rv} , RV pressure (subscript 2); P_{puA} , PuA pressure (subscript 3); Q_{tv} , tricuspid valve flow (subscript 4); Q_{pv} , pulmonary valve flow (subscript 5). Black solid line, healthy configuration ($p=0\%$); coloured lines; the corresponded degree of RV impairment, p , from 10% to 100%.

Figure 4

Pressure-volume loops for RV (subscript 1) and LV (subscript 2). a) systolic dysfunction; b) diastolic dysfunction, and c) combined systolic and diastolic dysfunction. Black solid line, healthy configuration ($p=0\%$); coloured lines; the corresponded degree of RV impairment, p , from 10% to 100%.

Figure 5

Comparison at various rates of impairment between the different types of dysfunction (symbols) and in vivo reference data (grey area). □, systolic dysfunction, Δ, diastolic dysfunction, and ●, combined systolic and diastolic dysfunction. a) CVP, mean pressure in the central veins and in vivo data52, b) CI, cardiac index and in vivo data52, and EF, ejection fraction for c) RV (EFRV) and in vivo data57, and d) LV (EFLV) and in vivo data58.

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