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### **Original Research Article**

## In-silico evaluation of left ventricular unloading under varying speed continuous flow left ventricular assist device support

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#### ABSTRACT

Continuous flow left ventricular assist device (cf-LVAD) operating speed modulation techniques are proposed to achieve different purposes such as improving arterial pulsatility, aortic valve function or ventricular unloading etc. Although it is possible to improve the left ventricular unloading by modulating the operating speed of a cf-LVAD, it is still unclear what type of pump operating mode should be applied to generate a better left ventricular unloading. This study presents a comparison of different heart pump support modes including constant speed support, copulsative and counterpulsative direct cf-LVAD speed modulation and pump flow rate control to regulate the cf-LVAD operating speed. The simulations were performed using a cardiovascular system model, which consists of active left atrium and ventricle, mitral and aortic valve leaflets, circulatory loop and a cf-LVAD. The cf-LVAD was operated between 7500 rpm and 12,500 rpm with 1000 rpm intervals to simulate constant speed support. The same mean pump operating speeds over a cardiac cycle were applied in the direct operating speed modulation for the copulsative and counterpulsative direct speed modulation cf-LVAD support as in the constant speed support while the same pump-output over a cardiac cycle was applied to drive the pump in flow rate controlled copulsative and counterpulsative cf-LVAD support modes as in the constant speed support. Simulation results show that flow rate controlled counterpulsative pump support mode generates lower end-diastolic left ventricular volume and pressure-volume area while generating more physiological left ventricular volume signals over a cardiac cycle with respect to the other pump operating modes.

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#### 1. Introduction

18 Heart failure is the end result of several different disease processes that may be subject to a variety of therapies. It is 19 conventionally treated with inotropic support, diuretics, and 20 moderate exercise. In a failing heart, myocardial remodelling 21 22 occurs and progresses due to an increased ventricular volume 23 and the altered load of the left ventricle [1]. When the 24 conventional methods fail, especially towards the final stage 25 of the disease, a heart transplantation is called for. For the 26 patients who would not be able to be treated due to a lack of a 27 fitting donor organ, to bridge the time between the decision to 28 transplant and the actual transplantation, continuous flow left 29 ventricular assist device (cf-LVAD) therapy is used [2]. A continuous unloading of the left ventricle by a cf-LVAD 30 reduces the stress and volume, and causes reverse remodel-31 ling in the myocardium [3]. Even in some cases myocardial 32 33 recovery which allows for the removal of the cf-LVAD may 34 occur due to this reverse remodelling [4], although the exact 35 mechanism of ventricular recovery under mechanical circula-36 tory support remains unclear [5]. Nevertheless, in any case it is 37 expected from the mechanical circulatory support to reduce the left ventricular pressure-volume area while generating 38 39 sufficient blood flow in the arteries to provide perfusion [6]. 40 Reportedly the exercise capacity of patients increases after cf-LVAD implantation [7]. However, this effect becomes less than 41 42 expected [8] and the operating speed of the cf-LVAD should be 43 regulated in an upward direction to increase cerebral perfusion 44 and to reduce left ventricular filling pressure [9,10]. Neverthe-45 less, studies reporting that a cf-LVAD operating speed increase does not provide any benefit to the patient also exists [11]. It 46 47 should be noted that factors influencing the flow through continuous-flow left ventricular assist devices at rest and with 48 exercise may vary significantly and [12] quality of life needs to 49 50 be increased under the support of these devices [13]. 51 Therefore, a better left ventricular unloading under cf-LVAD 52 support may provide benefits to the patients by way of 53 increased activities.

54 It is shown that synchronised pulsatile LVAD support 55 improves the unloading of the left ventricle better with respect to continuous cf-LVAD support [14]. Nevertheless, modulating 56 the cf-LVAD operating speed offers possibilities to improve left 57 ventricular unloading [15,16]. Asynchronous regulation of the 58 cf-LVAD operating speed alters the haemodynamic signals in 59 60 the arteries significantly although such an operating mode improves ventricular unloading [17]. Asymmetric cf-LVAD 61 62 operating speed modulation reduces the cardiac workload 63 significantly while a relatively high unloading can be obtained with the highest speed during diastole with respect to constant 64 speed cf-LVAD support [18]. Similarly, optimal left ventricular 65 unloading can be achieved when a minimum cf-LVAD 66 operating speed is applied at the end-diastole [19]. It is 67 68 possible to maximise the arterial pulsatility and improve the left ventricular unloading by shifting the phase of an impeller 69 70 pump operating speed in a pulsatile operating mode [20]. 71 Specialised cf-LVAD operating speed modulation algorithms 72 targeting to control the left ventricular end diastolic volume can reduce or increase it depending on the speed variation that 73 74 is applied to counter or copulsatively [21]. It might be feasible

to apply a flow tracking algorithm and to reduce the left ventricular stroke work [22]. However, this requires a detailed investigation and comparison of the mean pump flow and operating speed over a cardiac cycle. It is also possible to improve left ventricular unloading by changing the constant cf-LVAD operating speed level. For instance, a physiological control algorithm which is inspired by the preload recruitable stroke work was used to avoid ventricular suction and backflow from the aorta to the left ventricle [23]. A similar study aiming to control the left ventricle afterload impedance was proposed as a potential recovery tool for the cf-LVAD supported failing left ventricle [24]. It should be noted that the proposed cf-LVAD speed variation algorithms directly modulate the pump operating speed and the generated pump flow depends on the pressure-flow rate characteristics of the pump and the contraction strength of the left ventricle. Although it is possible to improve left ventricular unloading by modulating the operating speed of a cf-LVAD, it is still unclear what type of pump operating mode should be applied to render better left ventricular continuous unloading. Moreover, cf-LVAD operating speed regulation by controlling the pump flow rate has been successfully applied to improve physiologic outcome of these devices in terms of arterial pulsatility and aortic valve function etc. It has shown superiority in generating more physiological haemodynamic signals in the arteries with respect to constant speed and direct speed modulation support modes [25,26].

In this study, it is aimed to investigate left ventricular unloading under cf-LVAD support modes including constant speed support, copulsative and counterpulsative direct cf-LVAD speed modulation and pump flow rate control to regulate cf-LVAD operating speed using numerical simulations.

#### 2. Materials and methods

Simulations were performed using a cardiovascular system model which includes the left atrium and left ventricle, mitral and aortic valves, a circulatory loop and a cf-LVAD model.

The applied left ventricle model simulates the ventricular wall mechanics using myocardial constitutive properties and intramyocardial pressure. The wall mechanics model relates the macroscopic ventricular pressure and volume with microscopic tissue properties which are fibre stress, fibre strain, radial wall stress and radial wall strain. Active and passive fibre stresses include the myocardial constitutive laws for fibre stress and radial stress [27]. The left ventricular pressure ( $p_{lv}$ ), volume change ( $dV_{lv}/dt$ ) and active fibre stress ( $\sigma_a$ ) are given below.

$$p_{lv} = (\sigma_{f} - 2\sigma_{m,r}) \ln(1 + V_{w}/V_{lv})/3$$
(1)

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$$\frac{dV_{lv}}{dt} = Q_{mv} - Q_{av} \tag{2}$$

$$\sigma_a = c\sigma_{ar} f(l_s) g(t) h(\upsilon_s)$$
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