

The External-Work Pressure-Time Integral Relationships and the Frank Starling Law of the heart.*Sela, G; [Landesberg, A](#)**Technion - IIT, Haifa, Israel*

The mechanisms underlying the Frank-Starling Law of the heart are elusive. Despite the prevalent notion that it is afterload independent, isolated fiber studies reveal that the afterload affects this mechanism. The study explores the roles of the afterload, in situ. Methods: The LV was exposed by left-thoracotomy in adult sheep (72.6 ± 8.2 Kg, $n=8$). Flowmeter was placed around the aortic root. LV volume was assessed by sonocrystals. Occluders around the aorta and the inferior vena-cava enabled to control the afterload and preload. Different afterloads were imposed by partial aortic occlusions. Transient inferior vena-cava occlusions (IVCOs) were performed at each steady afterload. Results: A highly linear relationship was found between the external work (EW) and pressure-time integral (PTI) ($R^2=0.98 \pm 0.01$) during each transient IVCO ($n=48$). These EW-PTI relationships (WPTiRs) were preload independent since the preload had a proportional effect on the EW and PTI at constant afterload. Interestingly, the slope of the WPTiR was afterload dependant. The slope was 33.3 ± 4.1 mJ/(mmHg·s) at baselines and decreased by 1.0 ± 0.50 mJ/(mmHg·s) per 1 mmHg·min/L increase in the peripheral resistance. A unique WPTiR was obtained during both the occlusion and release phases of each IVCO, while two distinct EW-preload or PTI-preload relationships were observed. The same WPTiRs were also obtained for steady state conditions where the afterload was constant and the preload changes were only due to changes in lung ventilation and not an invasive IVCO. Conclusions: The novel WPTiR ties the Frank (pressure development) and Starling (EW production) phenomena together. The dependence of the WPTiR on the afterload highlights the adaptive control of the Frank-Starling mechanisms to changes in the afterload. Since the WPTiR can be obtained in a minimally invasive manner, it also has the potential to be of clinical use.