The mean end-tidal breath carbon monoxide excretion was a quantitative indicator of erythrocyte turnover. We performed a single-center retrospective analysis of 211 patients who received a Heartmate II LVAD between Jan 1st 2007 and Dec 31st 2014. The inherent mechanical function of CF-LVAD induced significant sub-hemolysis, which was more pronounced in the presence of device thrombosis. Further studies are needed to elucidate the utility of erythrocyte lifespan for the detection of subclinical device thrombosis, as well as to assess its temporal relationship to the mechanism of thrombus formation.

**Background:** Continuous-flow left ventricular assist devices (CF-LVAD) have transformed treatment for end-stage heart failure. Device thrombosis is a feared complication with challenging diagnosis. We investigated the sub-hemolytic injurious effect of CF-LVAD on circulating erythrocytes, in-vivo, using erythrocyte lifespan. Erythrocyte lifespan is a well-validated marker that employs the endogenous breath carbon monoxide excretion as a quantitative indicator of erythrocyte turnover. Methods: Sixty non-smoking subjects were prospectively enrolled. Twenty-five subjects had a CF-LVAD with thrombosis (mean age 60.5 ± 15.3 years, 96% male), 10 subjects had a CF-LVAD without thrombosis (67.3 ± 5.1 years, 90% male), and 25 subjects were normal controls (57.2 ± 14.1 years, 92% male). Results: The mean end-tidal breath carbon monoxide level was significantly higher in CF-LVAD subjects with (5.69 ± 2.54 ppm) compared to those without (2.88 ± 0.70 ppm) device thrombosis (P < 0.0001). The levels in these 2 cohorts were significantly higher compared to normal controls (2.25 ± 0.59 ppm, P < 0.0001, and P = 0.001, respectively). The calculated mean erythrocyte lifespan was significantly shorter in CF-LVAD subjects with (29.7 ± 14.9 days) compared to those without (65.0 ± 17.3 days) device thrombosis (P < 0.0001). The lifespans in these 2 cohorts were significantly shorter compared to normal controls (96.0 ± 24.9 days, both P < 0.0001). Receiver operator curve analysis demonstrated high sensitivity and specificity for use of erythrocyte lifespan to detect device thrombosis (area under the curve = 0.94). Conclusion: The inherent mechanical function of CF-LVAD induced significant sub-hemolysis, which was more pronounced in the presence of device thrombosis. Further studies are needed to elucidate the utility of erythrocyte lifespan for the detection of subclinical device thrombosis, as well as to assess its temporal relationship to the mechanism of thrombus formation.