An increase in N-terminus-pro-B-type natriuretic peptide (NT-proBNP) during exercise is related to myocardial ischemia, myocardial dysfunction, and inflammatory stress. Its value for patients with a univentricular heart after total cavopulmonary connection (TCPC) is unknown. For 66 patients with TCPC, a cardiopulmonary exercise test was performed. Venous NT-proBNP samples were drawn with the patient at rest and then 2-3 min after peak exercise. The median NT-proBNP during rest was 82 ng/l (range, 11-2,554 ng/l), with 22 patients above the upper reference limit. A higher NT-proBNP during rest was related to a worse peak oxygen uptake (peak [Formula: see text]), a higher ventilatory equivalent (VE/VCO₂ slope), and a need for diuretics administration. A small but significant increase in NT-proBNP during exercise at 6 ng/l (range, 0-314 ng/l) was related mainly to its resting value. The relative increase was solely related to a higher body mass and not to any of the investigated functional parameters. Usually, NT-proBNP during rest is not elevated in TCPC patients. If so, it is a valuable predictor of cardiac function. During exercise, only a minor increase in NT-proBNP occurs. Its extent is not related to any of the investigated functional parameters. Maybe the filling restriction from the lungs prevents atrial and ventricular overload as well as BNP secretion in TCPC patients.