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**Title:** Role of C-terminal pro-endothelin in pulmonary hypertension

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**Body:** Introduction: The endothelin pathway is upregulated in various forms of pulmonary hypertension. Its disease promoting activity has lead to the development of endothelin receptor blockers as specific therapeutics. The highly unstable active form requires greatest care in sample preparation to acquire reproducible results. In this study we examined the role of the more stable CT-proET in pulmonary hypertension using a high precision and standardized system. Methods: We examined 36 patients retrospectively. Therapy was applied following contemporary guidelines. Samples of platelet free EDTA plasma were stored at -80°C since collection between 2000 and 2003. Biomarker levels were determined by a Kryptor compact (BRAHMS, Germany) according to vendor instructions. Results: Patients were categorized according to DanaPoint classification as class 1 (n=16), class 2 (n=1), class 3 (n=9), class 4 (n=8) and class 5 (n=2). The mean follow-up time was 4.67 years. Survivors had significantly lower levels of CT-proET (53.7 [31.2-171.8] vs 91.1 [30.6-151.6] pmol/L, p=0.006). ROC analysis for survival yielded an AUC of 80.8%. The optimized cut-off for survival was determined as 65pmol/L. The log-rank test of Kaplan-Meier-analysis for survival was highly significant (p=0.01) with a hazard ratio of 3.06. Conclusions: CT-proET was significantly elevated in non-survivors of the follow-up period. Optimized cut-offs at 65pmol/L resulted in a significant Kaplan-Meier-analysis for survival. CT-proET-levels above 65 pmol/L are associated with decreased survival in pulmonary hypertension. CT-proET might be a useful biomarker to determine high-risk patients, while offering the advantage of a stable product of the endothelin cascade.