Title: HbA1c in pulmonary arterial hypertension – A marker of prognostic relevance?

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Body: Background: Patients with pulmonary arterial hypertension (PAH) exhibit impaired glucose metabolism and increased insulin resistance. The clinical consequences of these metabolic changes are not known. Patients and methods: We assessed HbA1c levels (indicative of perturbed glucose metabolism) in 115 patients newly diagnosed with PAH (79 female, 36 male; median age 48.8 years; idiopathic n=66, collagen vascular disease n=17, congenital heart defect n=19, pulmonary veno-occlusive disease n=8, porto-pulmonary n=5). No patients had been diagnosed with diabetes, or received antidiabetic medication or systemic steroids. After initiation of pulmonary vasoactive treatment, patients remained in long-term follow-up. Results: At initial presentation patients were in an advanced stage of disease (mean pulmonary arterial pressure 53±18 mmHg, median pulmonary vascular resistance 767 dyn.s.cm-5, cardiac index 2.3±0.8 l.min-1.m-2) with a six-minute walking distance of 334±126 m, and were categorised as NYHA functional class 3.0±0.7. The HbA1c was 5.73±0.75%. The 5-year survival rate for the entire group was 68%. Univariate Kaplan-Meier analysis and multivariate Cox proportional hazard models based on initial HbA1c levels revealed that patients in the lowest HbA1c quartile had a significantly better 5-year survival rate compared with the highest (83.6% versus 50.6%; log-rank p=0.038). Correcting for demographic and clinical covariates HbA1c was a predictor of all-cause mortality with a hazard ratio of 2.29 (95% CI, 1.20 to 4.38; p=0.012) per 1 Unit increase. Conclusion: In patients with pulmonary arterial hypertension, the HbA1c level at time of diagnosis is an independent predictor of long-term prognosis.