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Increased miR-7641 Levels in Peritoneal Hyalinizing Vasculopathy in Long-Term Peritoneal Dialysis Patients

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Abstract: Peritoneal hyalinizing vasculopathy (PHV) represents the cornerstone of long-term peritoneal dialysis (PD), and especially characterizes patients associated with encapsulating peritoneal sclerosis. However, the mechanisms of PHV development remain unknown. A cross sectional study was performed in 100 non-selected peritoneal biopsies of PD patients. Clinical data were collected and lesions were evaluated by immunohistochemistry. In selected biopsies a microRNA (miRNA)-sequencing analysis was performed. Only fifteen patients (15%) showed PHV at different degrees. PHV prevalence was significantly lower among patients using PD fluids containing low glucose degradation products (GDP) (5.9% vs. 24.5%), angiotensin converting enzyme inhibitors (ACEIs) (7.5% vs. 23.4%), statins (6.5% vs. 22.6%) or presenting residual renal function, suggesting the existence of several PHV protective factors. Peritoneal biopsies from PHV samples showed loss of endothelial markers and induction of mesenchymal proteins, associated with collagen IV accumulation and wide reduplication of the basement membrane. Moreover, co-expression of endothelial and mesenchymal markers, as well as TGF-β1/Smad3 signaling activation were found in PHV biopsies. These findings suggest that an endothelial-to-mesenchymal transition (EndMT) process was taking place. Additionally, significantly higher levels of miR-7641 were observed in severe PHV compared to non-PHV peritoneal biopsies. Peritoneal damage by GDPs induce miRNA