

Urinary collagen degradation products as early markers of progressive renal fibrosis

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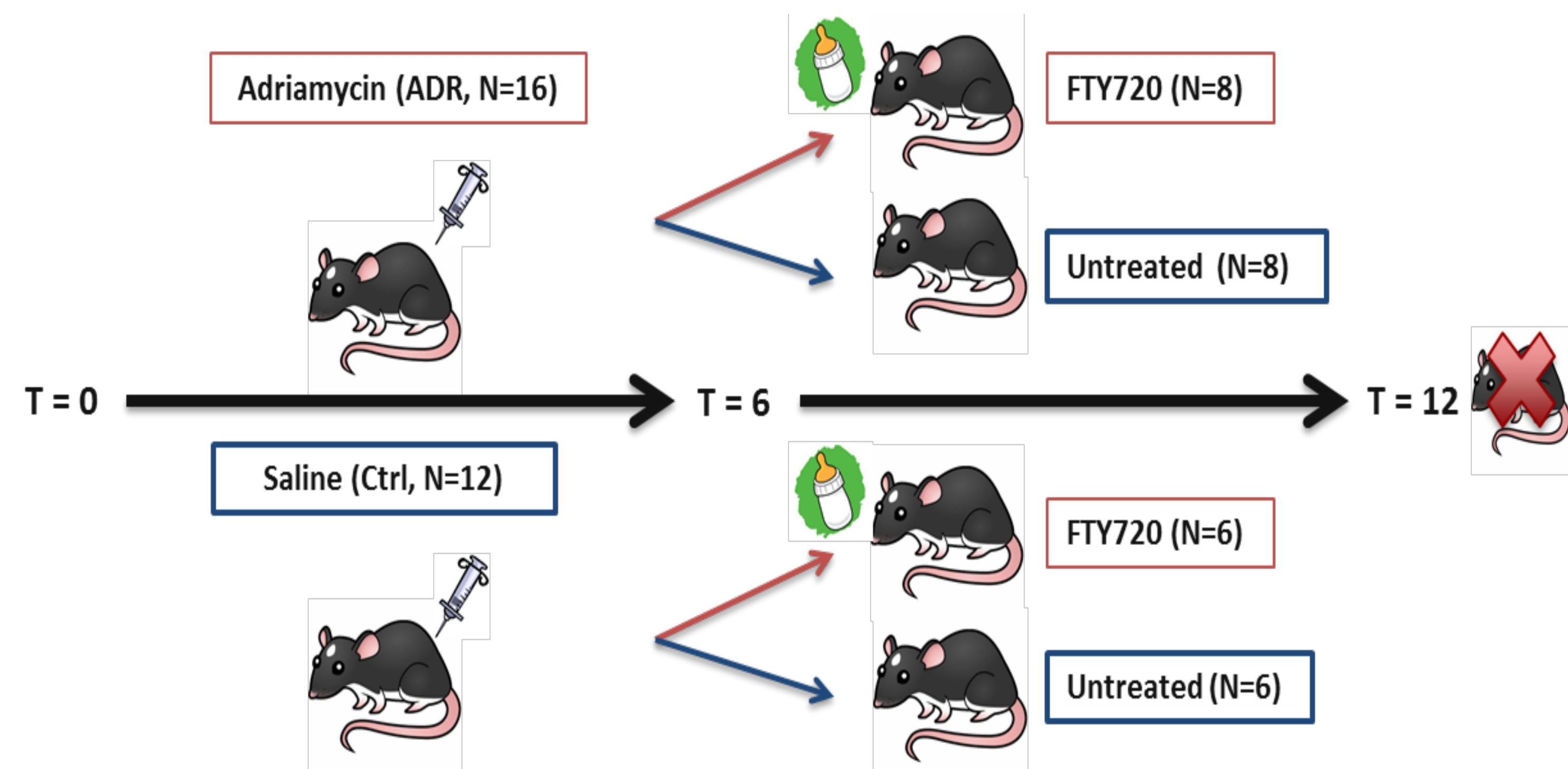
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Background

In renal disease, fibrosis leads to loss of renal function. A renal biopsy is the golden standard to assess the extent of fibrosis, since there are no reliable biomarkers yet. During the process of fibrosis, the extracellular matrix undergoes remodeling via matrix metalloproteinase-mediated degradation. This results in the release of collagen fragments, which can be detected in the urine and/or circulation.

The aim of our study is to investigate the diagnostic and monitoring value of collagen degradation products in the urine and plasma.

Methods



We measured plasma and urine collagen type I and III degradation fragments (C1M, C3M) using ELISA. We stained for tissue collagen type 3 (Coll3), fibronectin, myofibroblasts (α -SMA), PDGF receptor, hyaluronan and fibrosis (PAS).

Results

Figure 1. Effects of Adriamycin on collagen III metabolism.

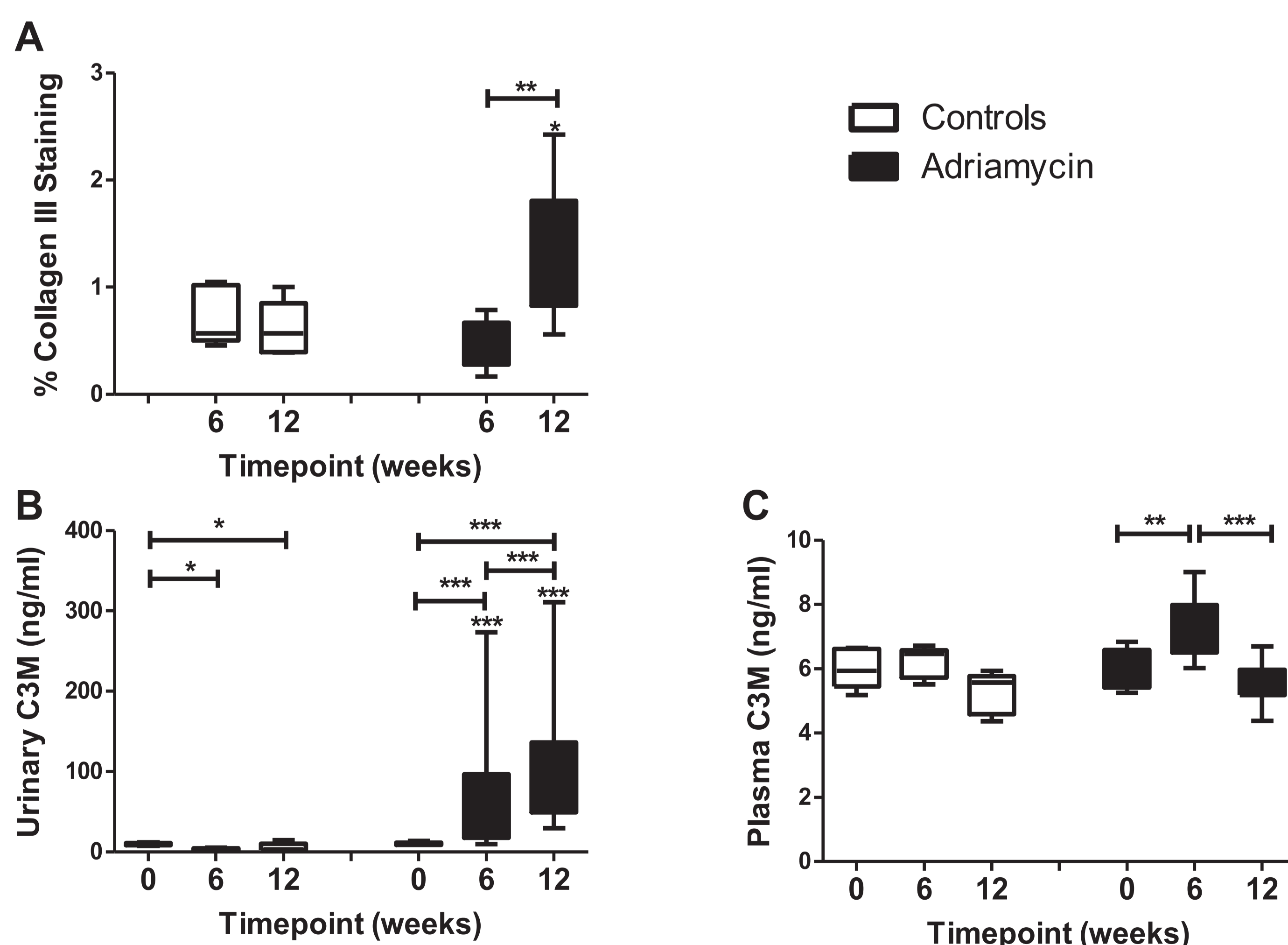


Figure 2. Effects of Adriamycin and FTY720 on histologic fibrotic markers at 12 weeks.

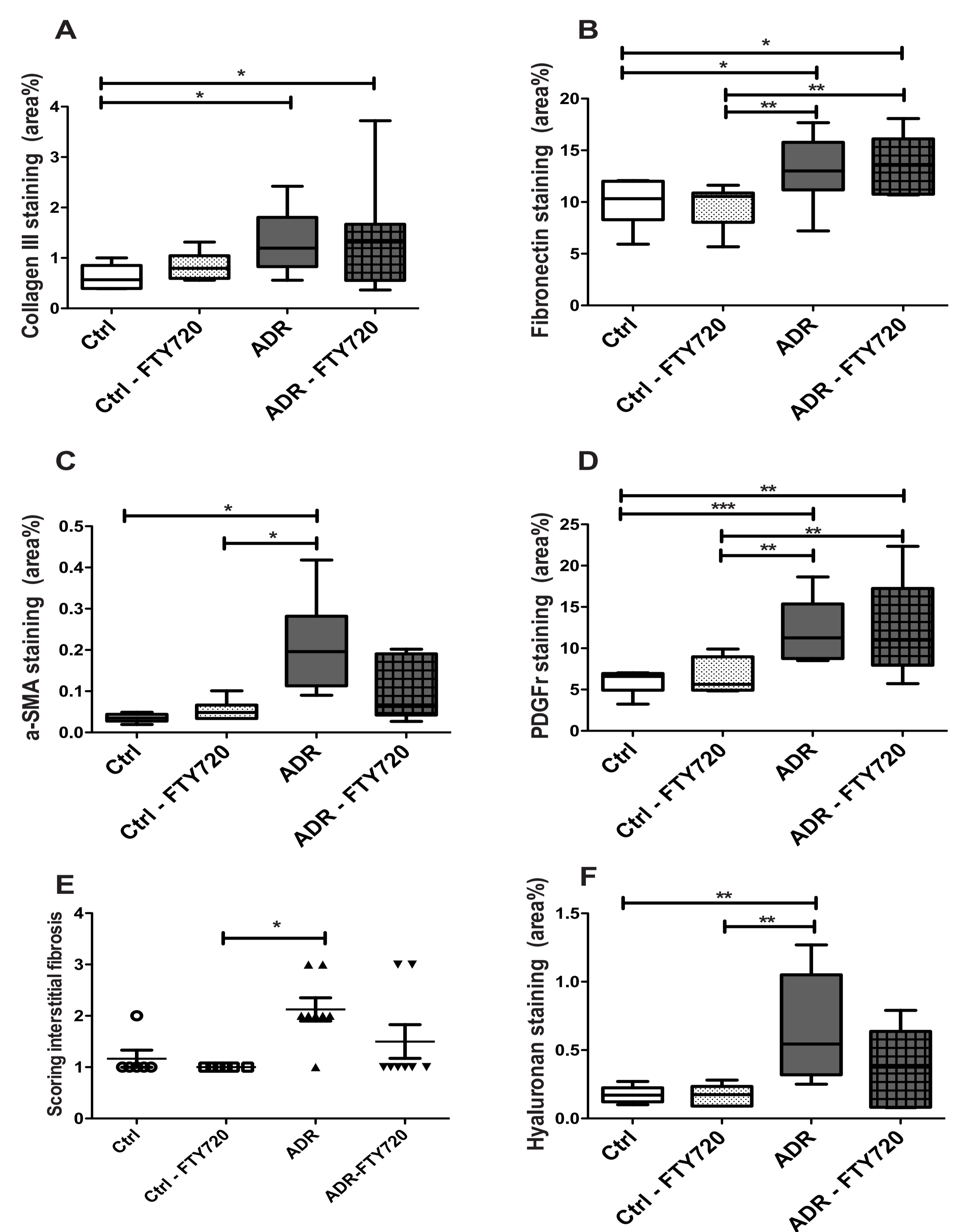


Table 1. Predictive value of C3M and C1M at week 6 for histological fibrotic markers at week 12.

	Urinary C3M/Cr 6 weeks		Urinary C1M/Cr 6 weeks	
	r_s	P-value	r_s	P-value
Histological markers – 12 weeks				
Collagen type III	0,565	0,023	0,624	0,010
Fibronectin	0,147	0,587	0,197	0,464
Myofibroblasts(α -SMA)	0,359	0,172	0,447	0,083
PDGF receptor	0,715	0,002	0,682	0,004
Tubulo-interstitial fibrosis (PAS)	0,562	0,024	0,538	0,032
Hyaluronan	0,689	0,003	0,632	0,009

Conclusion

Urinary C3M is a sensitive early marker of interstitial fibrosis, preceding histological signs of fibrosis. On FTY720 intervention the reduction of myofibroblasts and interstitial fibrosis dissociates from Coll3 metabolism (and urinary C3M), which warrants further research.