

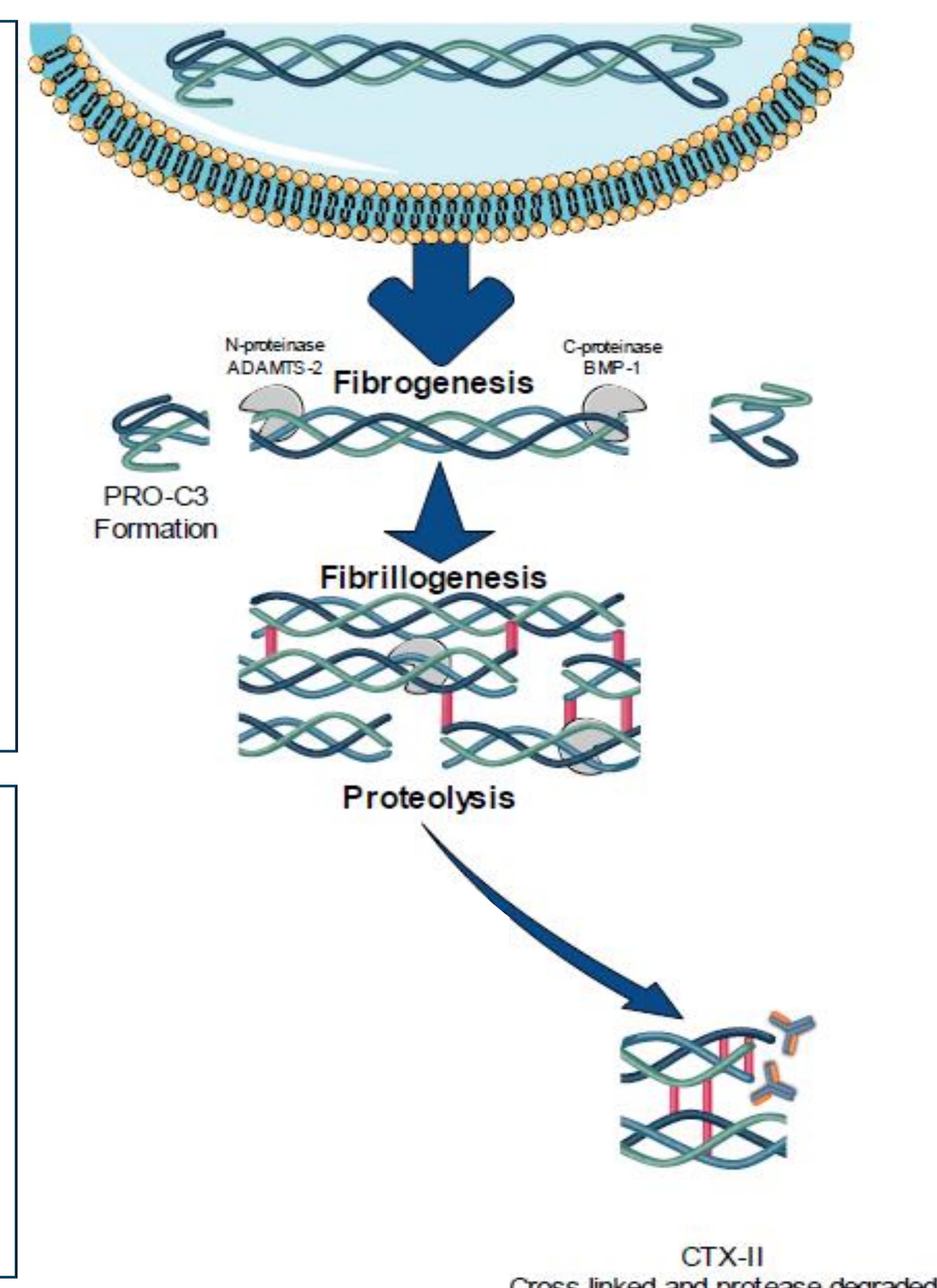
# A BIOMARKER OF FIBROSIS RESOLUTION, CTX-III, INCREASES AFTER BARIATRIC SURGERY IN EARLY NAFLD PATIENTS WITH HISTOLOGICAL LIVER IMPROVEMENTS

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## Background and aim

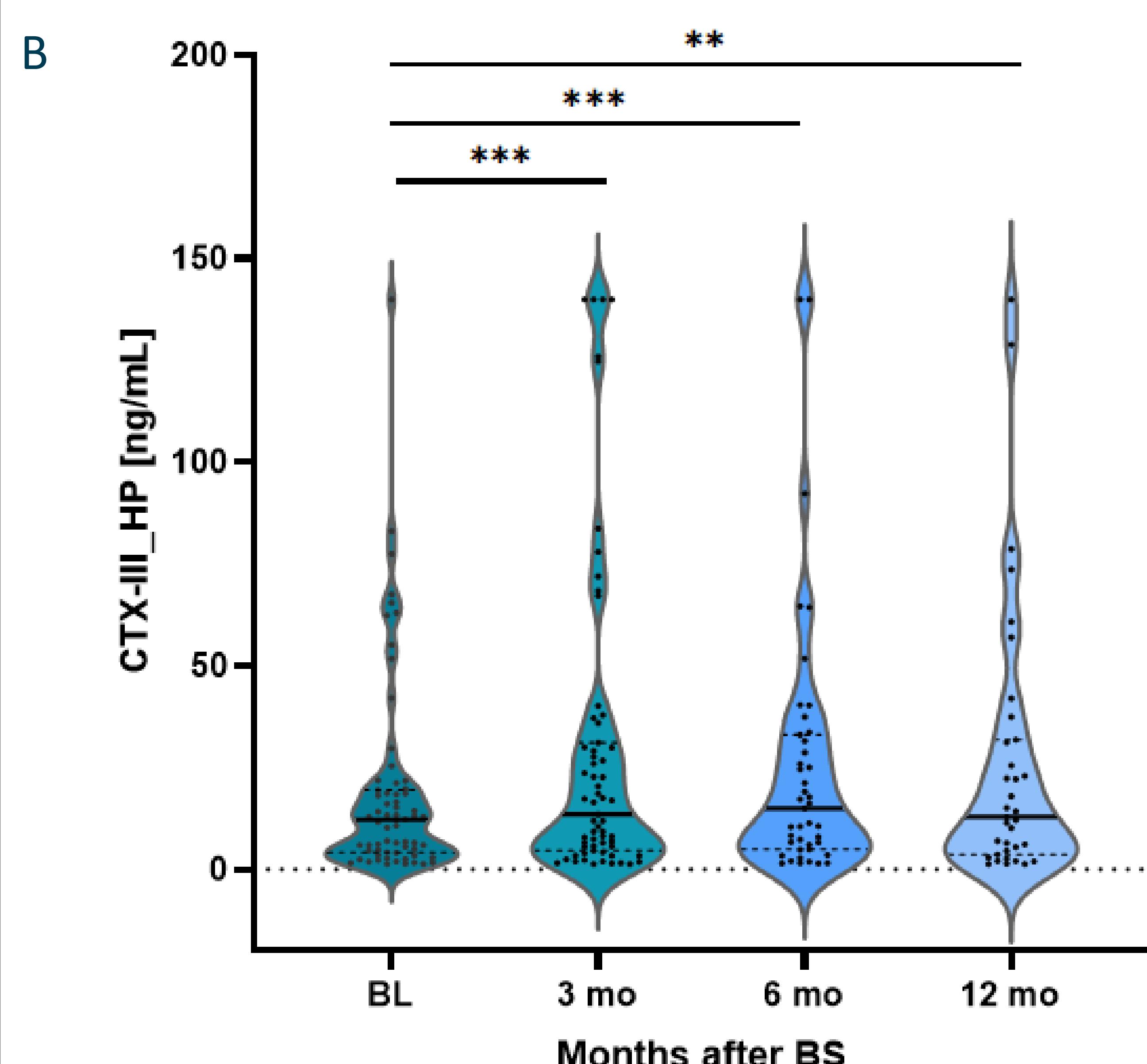
The formation of fibrotic bands is characterized by an increase in extracellular matrix components such as collagens. Over time, collagens become inter- and intramolecularly cross-linked. Thus, serological detection of cross-linked collagens resulting from collagen degradation may non-invasively detect fibrosis resolution. Here, we investigated a neo-epitope marker of cross-linked type III collagen resolution mediated by matrix metalloproteinases (CTX-III). We aimed to investigate whether changes could be observed in CTX-III levels in patients with early-stage non-alcoholic fatty liver disease (NAFLD) with observed improvements in liver histology induced by weight loss after bariatric surgery.



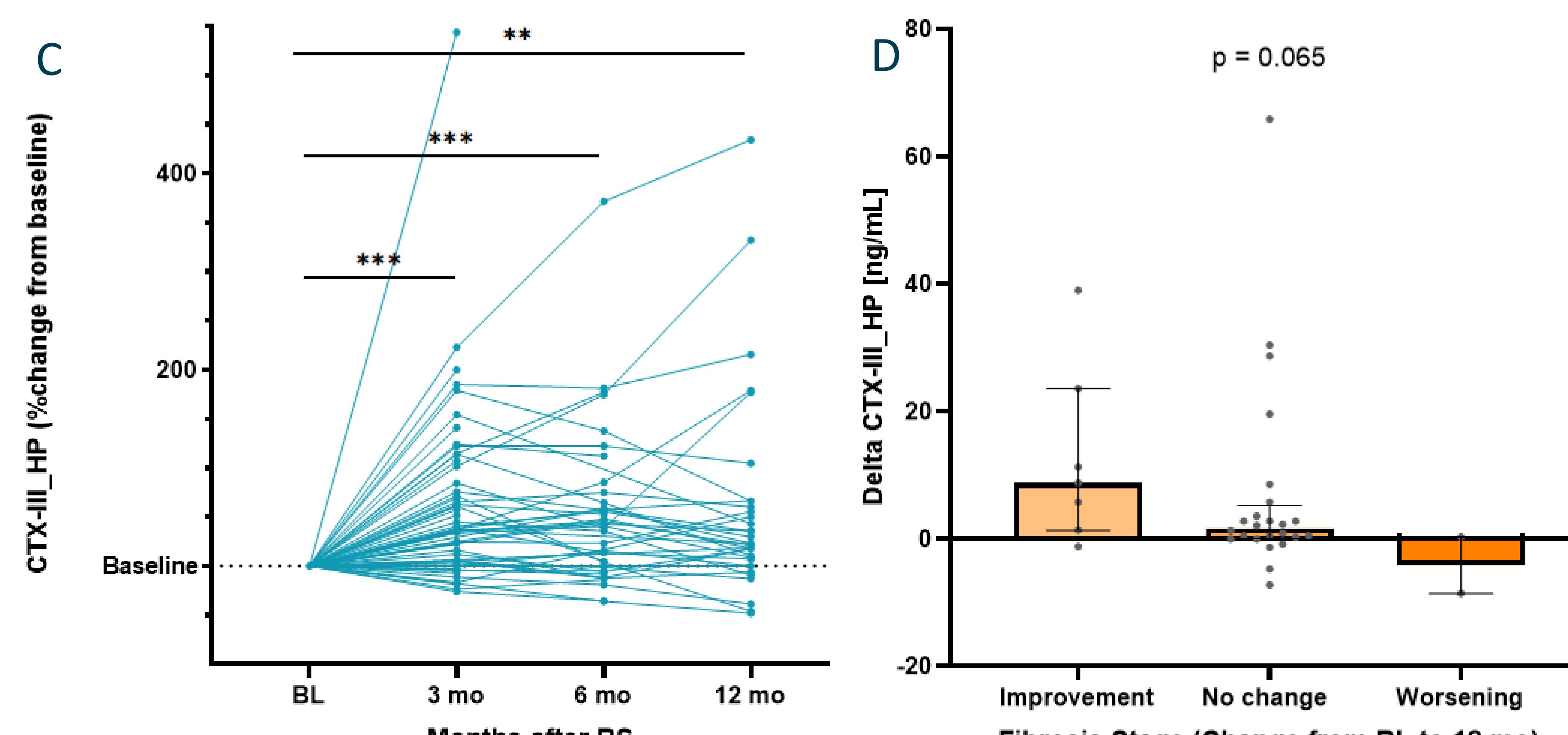
## Methods

Blood samples and liver biopsies were collected from 70 patients on the day of bariatric surgery. Additional blood samples were taken at three, six, and twelve months post surgery and forty patients had an additional liver biopsy at twelve months follow-up. CTX-III was measured using a fully validated sandwich chemiluminescence immunoassay and levels were analyzed using a linear mixed-effect analysis on log-transformed data.

## Patient characteristics and Results



A	Baseline (n=40)	Follow-up (n=40)	P-value
BMI, kg/m <sup>2</sup>	41.7 (37.5-44.7)	31.7 (28.5-34.7)	<0.001
AST, U/L	22.5 (18.3-30)	24 (21-27.5)	0.893
ALT, U/L	30.5 (23-37.5)	22 (17-29.5)	0.006
Bilirubin, µmol/L	7.5 (6-9.3)	10 (8-16)	<0.001
GGT, U/L	30 (18.3-40.5)	17 (11.5-24)	<0.001
Platelets, 10 <sup>9</sup> /L	292 ± 160	229 ± 57	<0.001
ALP IU/L	68 (57.0-83.5)	65 (54.0-81.5)	0.955
Fibrosis 0-4, n	1/34/5/0/0	6/33/1/0/0	0.023
Steatosis 0-3, n	19/15/6/0	35/5/0/0	<0.001
Ballooning 0-2, n	0/26/14	32/7/1	<0.001
Inflamm. 0-3	3/28/9/0	20/20/0/0	<0.001



**A) Patient characteristics.** There were no significant differences between the 40 patients who had follow-up at 12 months and the total study population of 70 patients. **B) CTX-III measurements in the cohort.** P-values were calculated using a linear mixed-effect model on log-transformed data. **C) Percent change in CTX-III from baseline.** Values shown are percent increase from CTX-III baseline measurements. **D) Delta CTX-III stratified by fibrosis improvement.**

## Conclusions

This study indicates that CTX-III may be a biomarker of fibrosis resolution in patients with NAFLD undergoing bariatric surgery.