

Role of SORT1 gene in Patients with Coronary Artery Disease.

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ABSTRACT

Background: Genome wide association studies shows SORT1 expression to affect lipid metabolism and thus identifies it as risk gene for coronary artery disease (CAD). Higher circulating levels of Sortilin in patients with atherosclerosis is reported. However very little is known about its expression in patients with CAD. In hepatocytes, Sortilin interacts with PCSK9 in Tans Golgi network and helps its secretion from liver. In macrophages, Sortilin promotes LDL uptake, form cell formation and atherosclerosis.

Objectives: To analyze the expression of SORT1 gene at mRNA and protein level in patients with CAD.

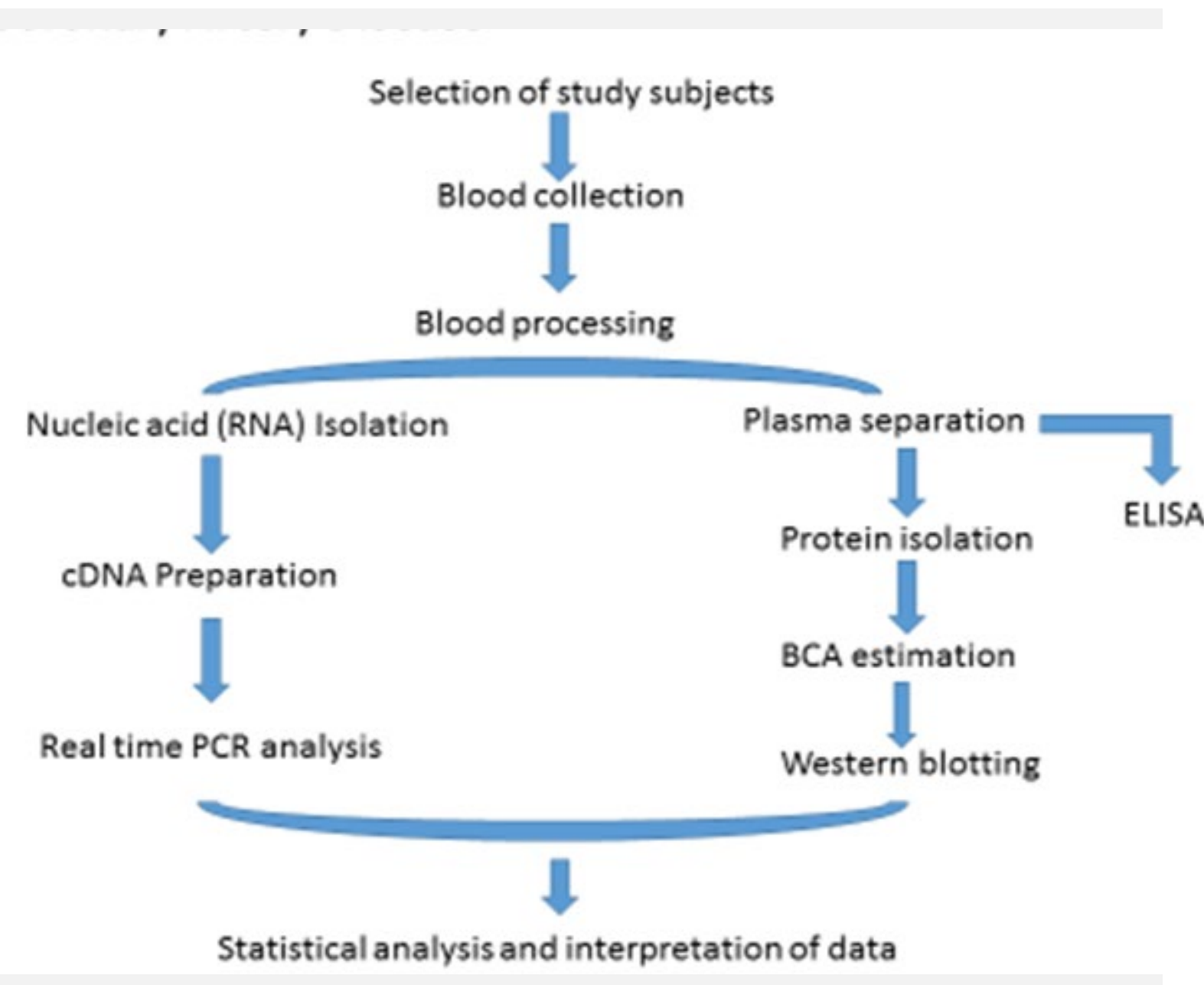
Method: Quantitative Real Time PCR and western blotting determined the expression of SORT1 at mRNA and protein levels, respectively in 150 patients with different clinical and subclinical stages of CAD and 150 healthy controls.

Results: Significant difference in average delta-CT value (approximately 5-fold change) in SORT1 gene and higher circulating levels of Sortilin proteins was observed in CAD patients with and without diabetes when compared to healthy controls. In addition, there is difference in expression of SORT1 gene in patients with Angina, Myocardial infarction, acute coronary syndrome, CAD with diabetes. While, highest expression is observed in patients with acute coronary syndrome.

Conclusion: Differential expression of Sortilin in different stages of CAD could be a useful biomarker for the disease. There is no such study available to the best of our knowledge globally.

METHODS

Target sample size was **150 Patients and 150 controls**. The peripheral venous blood was drawn from the study subjects and the total RNA extraction was carried out. Extracted RNA was used for the cDNA synthesis and Real time quantitative PCR analysis for SORT1 gene was done. 18S rRNA served as a housekeeping gene. Total protein was extracted from the plasma samples and SDS PAGE and western blotting experiments measured expression for Sortilin protein. Plasma levels of Sortilin was determined by enzyme-linked immunosorbent assay. All computations was carried out with STATA program, version 8.

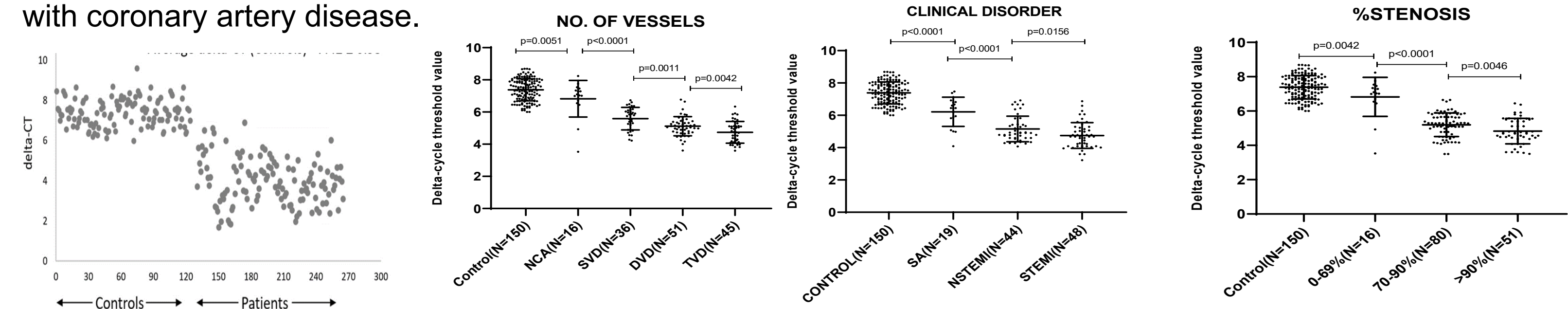


OBJECTIVE

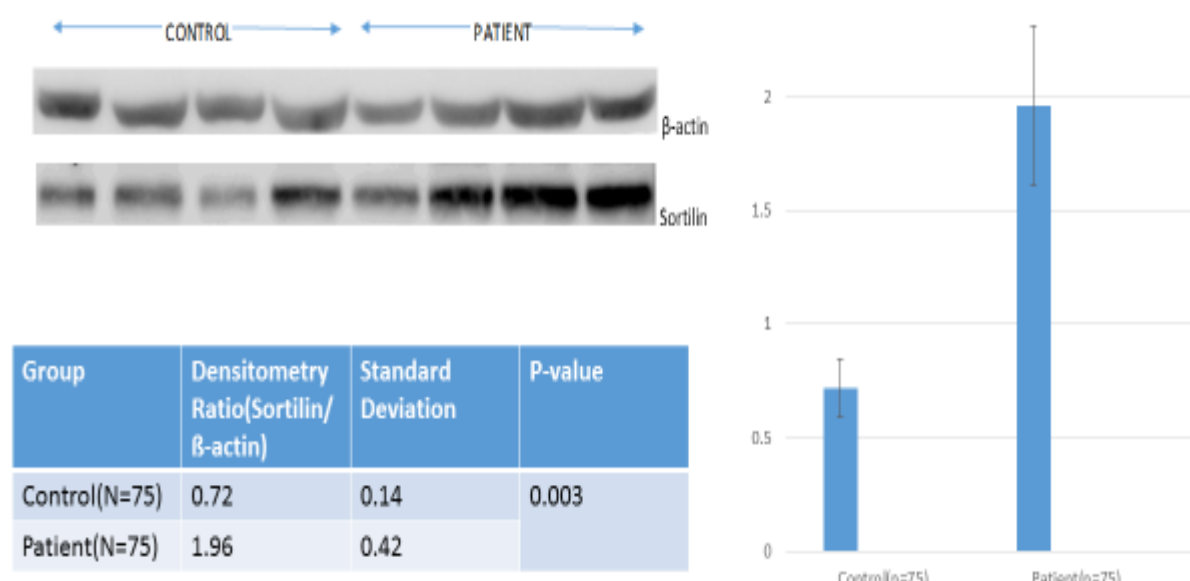
To analyze the expression of SORT1 gene at mRNA and protein level in patients with CAD.

RESULTS

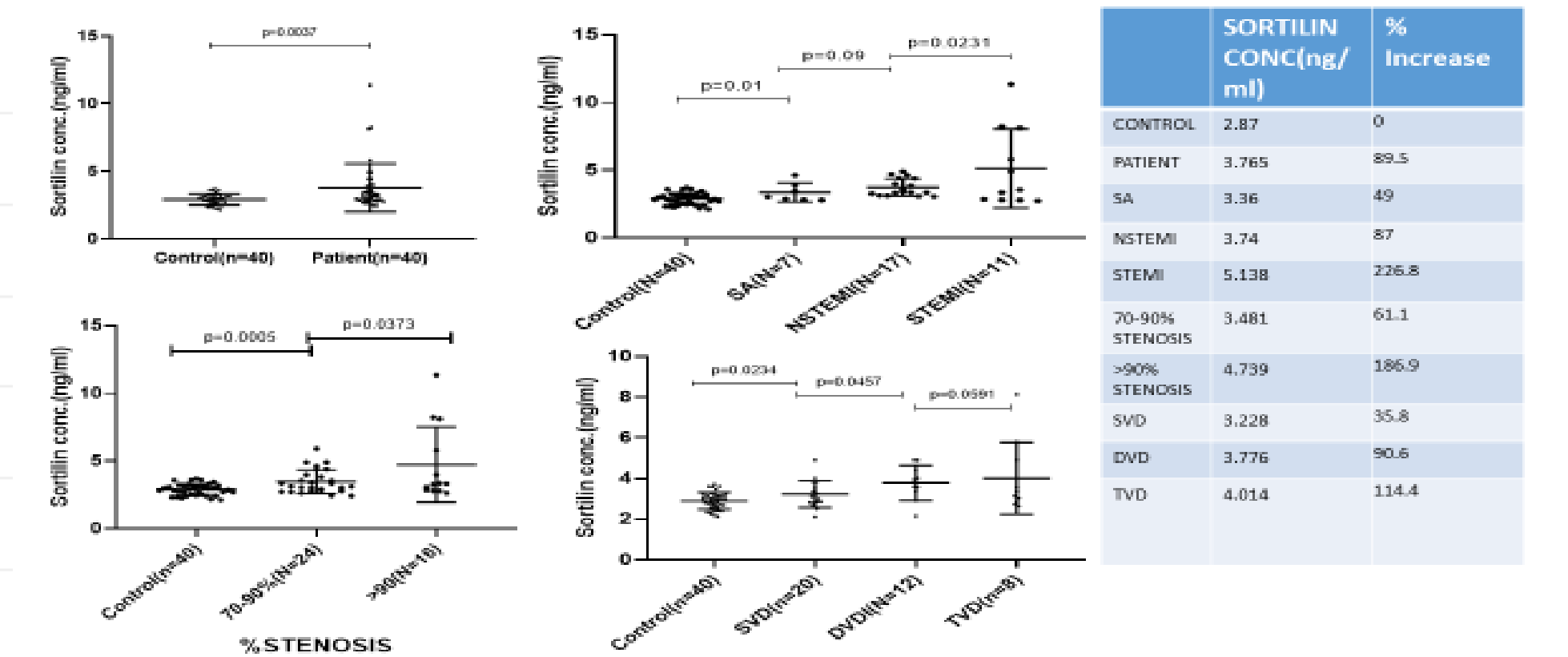
- The relative expression of SORT1 gene was upregulated by 4.438 fold in patients with CAD as compared those of the control samples.
- SORT1 gene expression level was significantly upregulated by 3.4 fold in single vessel disease patients, 4.7 fold in double vessel disease patients and 6.09 fold in triple vessel disease patients as compared to healthy subjects.
- The expression level of SORT1 gene was significantly higher in patients with STEMI as compared to NSTEMI and patients with stable angina.
- Expression level of SORT1 gene showed positive association with percentage stenosis detected in the patients with coronary artery disease.



Differential expression at protein level of Sortilin in patients with coronary artery disease.



The circulating level of the Sortilin protein in patients with coronary artery disease



CONCLUSIONS

- Quantitative real time analysis of SORT1 gene clearly indicates the upregulation its expression in patient samples with coronary artery diseases compared to that of controls.
- Also, An altered expression pattern was observed in patients with different clinical sub-categories of CAD.
- The densitometry analysis of western blots for Sortilin protein and β-actin indicates increased expression of Sortilin protein in patient with CAD w.r.t healthy controls.
- The circulating Sortilin levels in patients with coronary artery disease is higher as compared to healthy individuals.
- Therefore, there is positive association of SORT1 gene with Coronary artery disease.

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