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SHORT COMMUNICATION

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Sirtuin 1 and Sirtuin 2 Plasma Concentrations in Patients with Ascending Aortic Dissection and Ascending Aortic Aneurysm

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Abstract

Background Previous studies explored multifactorial interactions and sirtuin expression in the aortic cells of laboratory rodents and humans. Human studies were limited due to the availability of biological material exclusively in the advanced stage of the disease. The role of sirtuins in aortic pathology has not been explained extensively therefore the aim of the study was to assess the plasma concentrations of human sirtuin 1 (SIRT1) and human sirtuin 2 (SIRT2) in patients with ascending aortic dissection and ascending aortic aneurysm.

Material and methods The study group included 43 adults (34 males and 9 females) aged 44–92 years with ascending aortic dissection ($n = 10$) or with ascending aortic aneurysm ($n = 33$). The SIRT1 and SIRT2 plasma concentrations in patients' blood samples were determined, and the differences between groups were observed ($p = 0.02$ for SIRT1, $p = 0.04$ for SIRT2).

Results Levels of both SIRT1 and SIRT2 were lower in patients with ascending aortic dissection (SIRT1: median = 6.5 ng/mL; SIRT2: median = 5.7 ng/mL) than in patients with ascending aortic aneurysm (SIRT1: median = 9.2 ng/mL; SIRT2: median = 7.8 ng/mL). The SIRT1 and SIRT2 cut-off levels differentiating both groups of patients were 6.7 ng/mL and 3.2 ng/mL, respectively.

Conclusions The patients with ascending aortic dissection had lower plasma concentrations of SIRT1 and SIRT2 than the patients with ascending aortic aneurysm. Calculated cut-off values for both enzymes may be helpful in laboratory differentiation of ascending aortic dissection from ascending aortic aneurysm.

Keywords Aortic aneurysm, Aortic dissection, Aortic pathology, Sirtuin 1, Sirtuin 2

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1 Background

Sirtuins are nicotinamide adenine dinucleotide-dependent histone deacetylases that modulate cellular processes of DNA repair, inflammatory response, cell cycle or apoptosis. Sirtuin 1 (SIRT1) protects cells from reactive oxygen species. Sirtuin 2 (SIRT2) regulates key oxidative stress genes and mechanisms [1, 2]. Therefore, changes in sirtuins levels may contribute to the development of numerous diseases: metabolic, neurodegenerative, inflammatory, neoplastic, and cardiovascular [3–5]. One of them may be aortic pathology. Since the previous studies on sirtuin impact on aortic cells were conducted mainly on animals [6–8], the role of sirtuins in human aortic pathology has not been explained extensively.

2 Aims

The aim of the study was to assess SIRT1 and SIRT2 plasma concentrations in patients with two manifestations of aortic pathology: ascending aortic dissection (AAD) and ascending aortic aneurysm (AAA).

3 Methods

3.1 Patients

The study was conducted on patients hospitalized in the University Teaching Hospital in Lodz, Poland and treated in its cardiology outpatient clinic between March 2019 and March 2020 for AAD or AAA diagnosed according to the 2014 European Society of Cardiology Guidelines on the Diagnosis and Treatment of Aortic Diseases.

The study was conducted after obtaining Ethics Committee approval (RNN/139/16KE from 10 May 2016). Written informed consent to participate in the study was obtained from each study participant prior in the study.

3.2 Analysis of Plasma SIRT1 and SIRT 2

Blood samples were collected in the morning in the fasting state from all the patients, and the analysis of the human SIRT1 and SIRT2 plasma concentrations was performed using human SIRT1 and SIRT2 enzyme-linked immunosorbent assay laboratory (ELISA) kits from Shanghai Sunredbio (SRB) Technology Co., Ltd. Optical density was determined at 450 nm using a microplate reader (SYNERGY HT, BioTek Instruments Inc., USA).

3.3 Statistical Analysis

The statistical analyses were performed with Statistica 13.1 software. The Mann–Whitney U test was used to compare the concentrations of SIRT1 and SIRT2 between the patients with AAD and those with AAA. A receiver operating characteristic curve (ROC) was used to determine the SIRT1 and SIRT2 concentration cut-off levels between the study groups. The Fisher test was used for the comparisons of the nominal parameters. The level of statistical significance was assumed to be $\alpha = 0.05$.

4 Results

4.1 Patients' Characteristics

The study involved 43 patients (79% women) aged 44–92 years—10 with AAD and 33 with AAA. Although the presence of cardiovascular comorbidities and in-hospital mortality differed slightly between groups, the differences did not reach statistical significance (Table 1).

Table 1 Clinical characteristics of the study groups

	Ascending aortic dissection ($n = 10$)	Ascending aortic aneurysm ($n = 33$)	p-value
Sex (*F*/*M*)	5/5	29/4	0.03
Age median (*Q*1–*Q*3), years	58.5 (53.0–67.0)	67.0 (60.0–76.0)	0.20
Arterial hypertension *n* (%)	10 (100%)	31 (91%)	0.87
Hyperlipidemia *n* (%)	7 (70%)	31 (91%)	0.20
Coronary artery disease *n* (%)	4 (40%)	13 (38%)	0.42
Atrial fibrillation *n* (%)	3 (30%)	15 (44%)	0.67
Chronic kidney disease *n* (%)	3 (30%)	12 (35%)	1.00
Heart failure with NYHA class III or class IV *n* (%)	4 (40%)	8 (24%)	0.49
In-hospital mortality *n* (%)	2 (20%)	1 (3%)	0.13

F female, *M* male, *NYHA* New York Heart Association, *Q* quartile

Table 2 The sirtuin 1 and sirtuin 2 plasma concentrations in study groups

	SIRT1 level (ng/mL) Median (*Q*1–*Q*3)	SIRT2 level (ng/mL) Median (*Q*1–*Q*3)
Ascending aortic dissection *n* = 10	6.5 (1.70–9.30)	5.7 (1.30–7.80)
Ascending aortic aneurysm *n* = 33	9.2 (7.20–20.50)	7.8 (6.6–15.9)

SIRT1 sirtuin 1, *SIRT2* sirtuin 2, *Q* quartile

4.2 Plasma Levels of SIRT1 and SIRT 2

Lower levels of both SIRT1 and SIRT2 were noted in the patients with AAD compared to subjects with AAA (Table 2). Differences in the plasma concentrations of both SIRT1 and SIRT2 between the study groups ($p = 0.02$ for SIRT1, $p = 0.04$ for SIRT2) were observed (Fig. 1).

The SIRT1 concentration cut-off level differentiating the patients with ascending aortic dissection from those

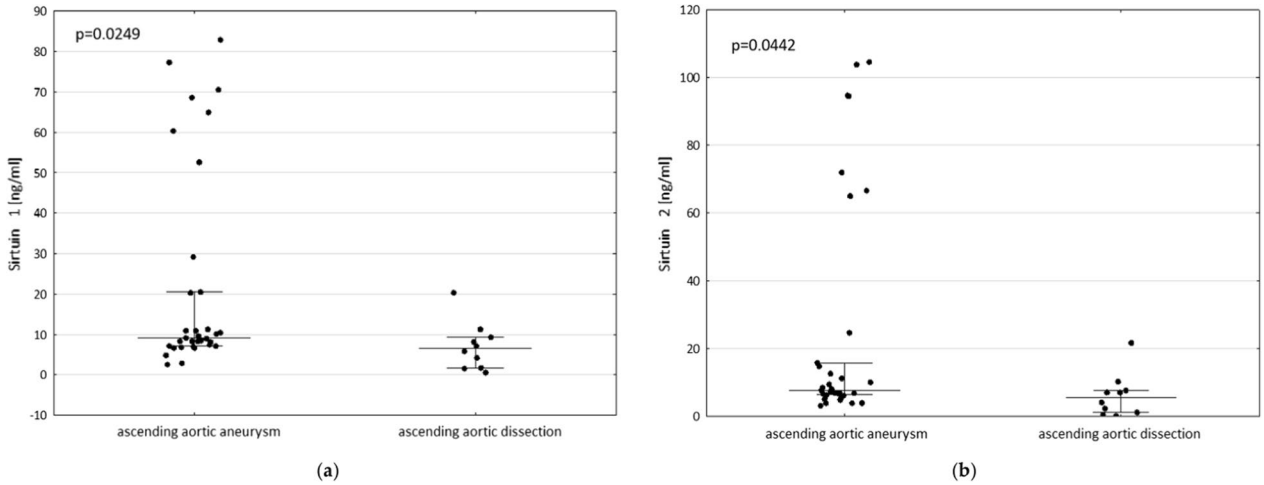

Fig. 1 Concentrations of sirtuin 1 (**a**) and sirtuin 2 (**b**) in study groups

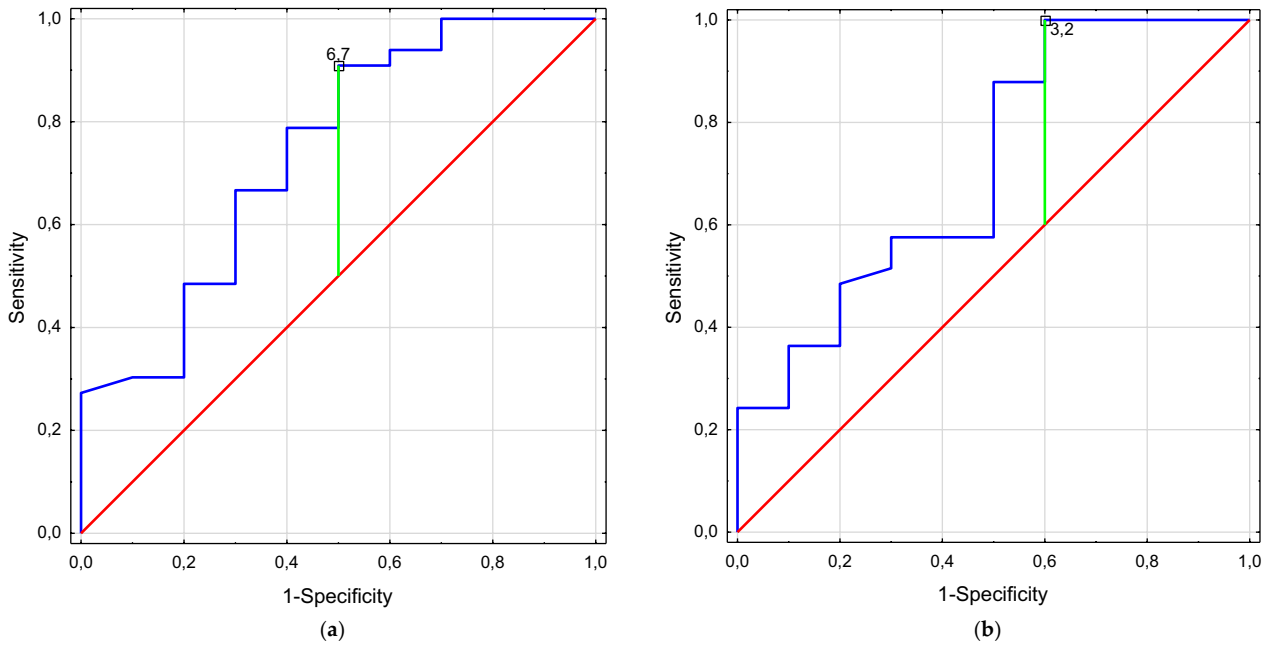

Fig. 2 Sirtuin 1 (**a**) and sirtuin 2 (**b**) cut-off levels between study groups

with ascending aortic aneurysm was 6.7 ng/mL (Fig. 2a). The SIRT2 concentration cut-off level differentiating the patients with AAD from those with AAA was 3.2 ng/mL (Fig. 2b).

According to the analysis, the distribution differences of males and females between the study groups did not affect the sirtuin plasma concentrations, and the concentrations of the analyzed proteins did not depend on sex ($p=0.11$ for SIRT1, $p=0.49$ for SIRT2).

5 Conclusion

Our study is probably the first to evaluate sirtuins plasma levels in living individuals undergoing diagnostic and therapeutic procedures during hospitalization. Previous publications concerned the examination of histopathological material acquired from laboratory animals, from in vitro cell cultures, or perioperatively from humans [6, 9, 10]. We demonstrated that plasma levels of SIRT1 and SIRT2 are significantly lower in patients with ascending aortic dissection as compared to patients with ascending aortic aneurysm. Although this study is just preliminary, our results suggest that determination of SIRT1 and SIRT2 plasma level may be an easy laboratory measurement to help in differentiation of individuals with a more pronounced manifestation of aortic pathology. Thus, SIRT1 and SIRT2 proteins may presumably be considered novel markers of elevated risk of developing a life-threatening condition. However, we are aware that inclusion of these markers in diagnostics and management of patients with aortic pathology should be preceded by more detailed research performed on larger groups of patients.

Abbreviations

AAA	Ascending aortic aneurysm
AAD	Ascending aortic dissection
Q1	25Th percentile value
Q3	75Th percentile value
ROC	Receiver operating characteristic curve
SIRT1	Sirtuin 1
SIRT2	Sirtuin 2

Author Contributions

JK was the project supervisor and validator, responsible for the methodology and for obtaining the Ethics Committee Approval. OMB was responsible for including the study individuals, for collecting the laboratory material, and for writing the manuscript. JS was responsible for the statistical methodology, data analysis, and visualization. WF was the validator of data analysis and the manuscript validator. JF was responsible for the methodology and for the laboratory analysis of sirtuin concentrations. PS was responsible for collecting the cardiac surgery data. MK was the validator of the cardiac surgery data. AS was the supervisor of the laboratory analysis of sirtuin concentrations. AR was responsible for the methodology and for obtaining the Ethics Committee approval. PM participated in writing—review and editing. DK participated in writing—review and editing. JD was the project supervisor and acquired the funding. All authors read and approved the final manuscript.

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Availability of Data and Materials

The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Conflict of Interest

The authors declare that they have no competing interests.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Medical University of Lodz (RNN/139/16KE from 10 May 2016).

Consent for Publication

Not applicable.

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