Research Institute for Complex Issues of Cardiovascular Diseases

Proteomic profiling of native heart valves affected by infective endocarditis

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Motivation and aim:

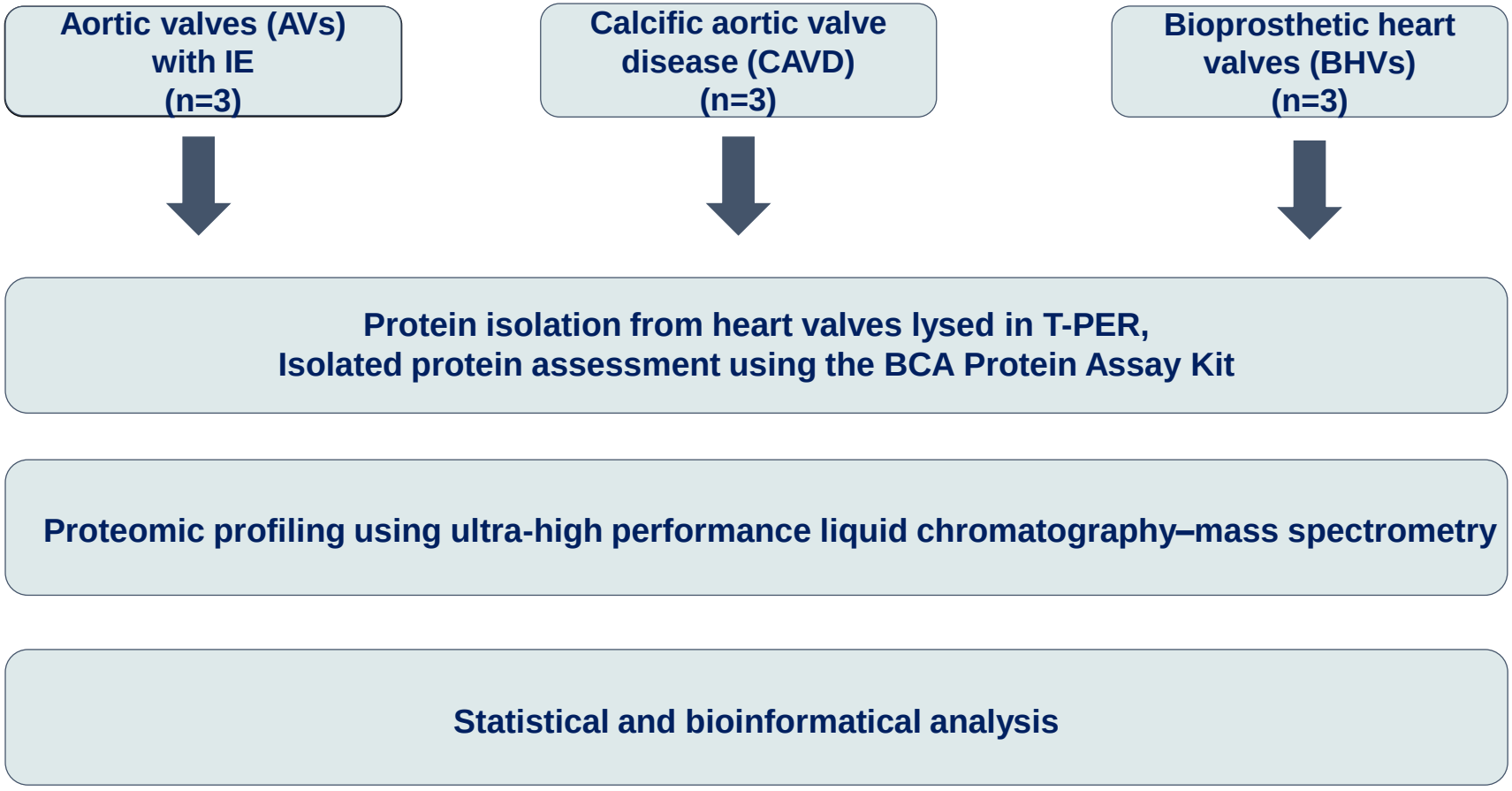
Infectious endocarditis (IE) is an infectious inflammatory disease of the endocardium of the heart valve structures characterized by a high risk of complications. The incidence of IE in 2019 was 13.8 cases per 100 thousand population

Despite all the achievements in IE diagnostics and treatment, a high level of hospital mortality from 17.1-31.3% is still remaining

Due to diagnostic difficulties, the IE incidence may be underestimated, which is especially important for biological prostheses (BP)

Aim: to the identification of key proteins and signaling pathways involved in IE pathogenesis.

Materials and methods



Results

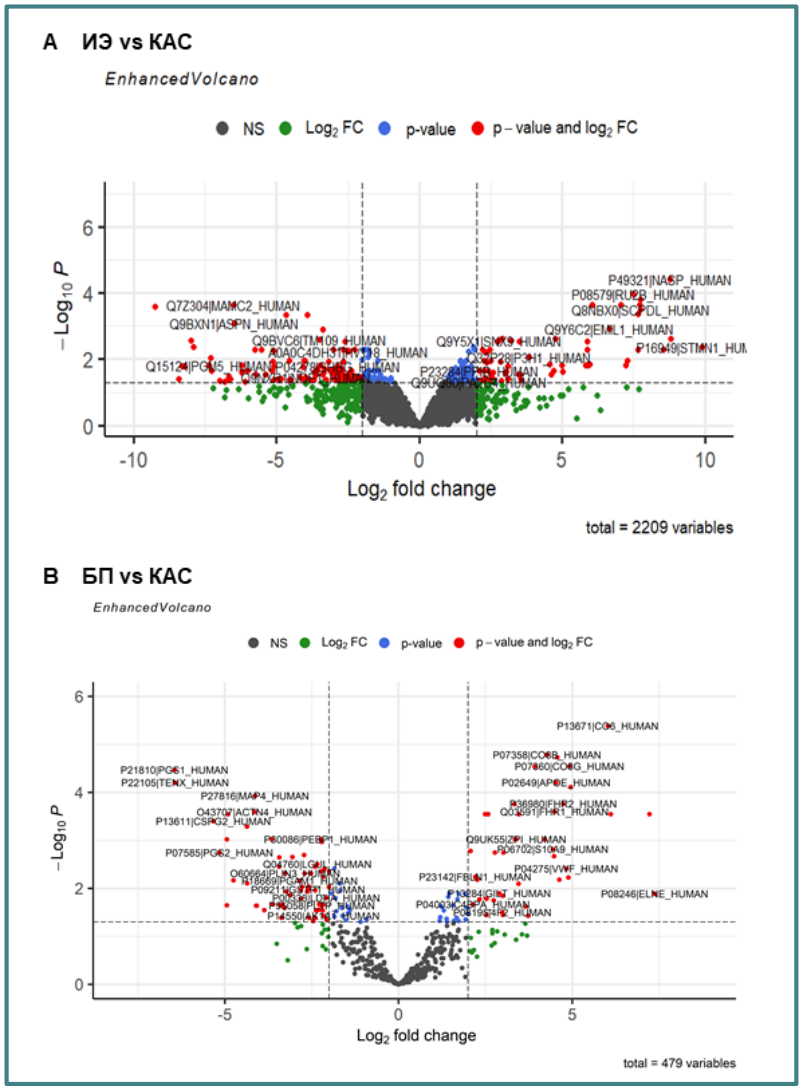


Figure. Results of proteomic profiling of native heart valves affected by IE (A), as well as BP (B) relative to native heart valves with CAVS

In the tissues of native heart valves affected by IE, when it was compared to heart valves affected by CAVD, 272 DEPs were identified according to the following criteria: log2-fold change in expression >1 and p value <0.05, corrected by correction FDR. 53.68% identified DEPs were downexpressed and 46.32% were overexpressed in the heart valves with IE. For 23 DEPs (PLOD, FNDC1, ADRM1, ACDSB, HARS1, NEB2, TPC6B, RBM4, EMIL1, DNJA2, SGTB, H32, RU2B, RS15A, RL15, ACTS, BT3L4, SCPDL, TRXR2, NASP, PKHO2, STMN1 and P4HA2) more then 5-fold increased expression was shown, and for 30 DEPs (FTO, HV321, LV39, CLC11, VP13C, HV333, PGM5, SUSD2, ACTA, CAH3, LV469, HV353, SPT6H, AL1A2, MAMC2, ASPN, HBS1L, IBP6, MINP1, CK068, NENF, PCOC2, FABP4, PLS3, SCRN2, TGFI1, CCD43, SPP24, BMPER and IF4E3) more then 5-fold decreased expression compared to the heart valve with CAVD was shown. Annotation of the identified DEPs using the Reactome database and enrichment analysis (Gene Ontology Enrichment Analysis) showed that the identified DEPs are involved in the following biological processes: regulation of the complement system, organization of the extracellular matrix, collagen formation, initiation of the innate immune response, activation of the complement system, vesicular transport, cellular response to parasitic infections, transmission of regulatory signals mediated by the B-cell receptor.

Results

Neutrophil markers

Protein	Description
PERM	Myeloperoxidase
ELNE	Neutrophil elastase
ITAX	Integrin alpha-X (CD11c)
PRTN3	Myeloblastin
PRG2	Bone marrow proteoglycan, eosinophil major basic protein
NCF1	Neutrophil cytosol factor 1
CATG	Cathepsin G
MNDA	Myeloid cell nuclear differentiation antigen
ECP	Eosinophil cationic protein
TRFL	Lactotransferrin

Complement components

Protein	Description
CO3	Complement C3
CO4A	Complement C4-A
CO4B	Complement C4-B
CO5	Complement C5
CO6	Complement component C6
CO7	Complement component C7
CO8A	Complement component C8 alpha chain
CO8B	Complement component C8 beta chain
CO8G	Complement component C8 gamma chain
CO9	Complement component C9
C1S	Complement C1s subcomponent
C4BPA	C4b-binding protein alpha chain
FHR5	Complement factor H-related protein 5
FHR3	Complement factor H-related protein 3
FHR2	Complement factor H-related protein 2
FHR1	Complement factor H-related protein 1

Platelet markers and coagulation factors

Protein	Description
ITA2B	Integrin alpha-IIb (CD41)
ITB3	Integrin beta-3
URP2	Fermitin family homolog 3 (kindlin-3)
CD36	Platelet glycoprotein 4
ITA6	Integrin alpha-6
CXCL7	Platelet basic protein (CXCL7)
GP1BB	Platelet glycoprotein Ib beta chain (CD42c)
MMRN1	Multimerin-1
PLEK	Pleckstrin
FA5	Coagulation factor V
TFPI1	Tissue factor pathway inhibitor
FA7	Coagulation factor VII
FA9	Coagulation factor IX
FA10	Coagulation factor X
CBPB2	Carboxypeptidase B2
HABP2	Hyaluronan-binding protein 2
ZPI	Protein Z-dependent protease inhibitor

Unique proteins detected in native valves with IE

Protein	Description
IL1ra	Interleukin-1 receptor antagonist protein
IL8	Interleukin-8
IL18	Interleukin-18
IL19	Interleukin-19
CXCL5	C-X-C motif chemokine 5
CCL5	C-C motif chemokine 5
NCF2	Neutrophil cytosol factor 2
uPAR	Urokinase plasminogen activator surface receptor
PAI	Plasminogen activator inhibitor 1

Conclusion: The key proteins and signaling pathways involved in the pathogenesis of cardiac valvular dysfunction caused by various etiological agents have been identified.

Native aortic heart valves affected by infection, and BP, regardless of cause of their dysfunction (structural degeneration or infective endocarditis), had common proteins related to neutrophil markers, platelet markers, coagulation factors, and complement components. In addition, the unique proteins were identified that are expressed only in native AVs affected by IE.