Inflammation III

PO329-WED

Association between a pro-inflammatory axis comprised by TSP1-TGFB-CTGF with three micro-RNAS, MIR-19A, 122, and 133A in the pathophysiology of diabetic retinopathy: a therapeutic novel modality

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Background: Diabetic retinopathy (DR) is a severe complication of type-2-diabetes (T2DM). Our laboratory has been studying the role of a pro-inflammatory axis comprised by TSP1-TGFβ and CTGF in T2DM. The axis is differentially expressed in patients with T2DM and non-proliferative DR (NPDR) when compared with patients with T2DM and proliferative DR (PDR).
Aims: The purpose of this study was to evaluate selected plasma circulating microRNAs potentially associated with plasma biomarkers including the abovementioned axis and cytokines.
Methods: Institutional IRB and informed consent allowed this prospective study to recruit a total of 23 individuals afflicted by T2DM (n = 10 NPDR and n = 13 PDR) from the Ophthalmology Department Diabetes Clinic at Temple Hospital, normal controls (n = 10) were recruited from the Sol Sherry Thrombosis Research Center at Temple. Multiplexed protein profiling on microarrays by rolling-circle amplification was employed to determine cytokines. Commercially available ELISA was utilized to determine the plasma concentration of TSP1, TGFβ and CTGF. Total RNA was extracted from human plasma using the miRCURY ™ RNA isolation kit by Exiqon at their facility in Denmark.
Results: TSP1, TGFβ, CTGF, IL4, MIP-1β were significantly elevated in NPDR patients when compared to PDR patients. Only three microRNAs were differentially expressed in the normal group when compared with NPDR (decreased), namely miR-133a ($P < 0.005$), miR-19a ($P < 0.008$), and miR-122 ($P < 0.02$) or PDR (decreased), miR-19a $P < 0.000096$) and miR-122 ($P < 0.005$).
Conclusion: miR-19a has been implicated with expression of TSP1 and CTGF, glucose levels, and insulin resistance. miR-133a has been associated with cardiac hyperthrophy, fibrosis and heart failure in diabetes. miR-122 has been identified as a potential biomarker for non-alcoholic fatty liver. In summary our results link for the first time in the literature three circulating microRNAs with the above pro-inflammatory axis as well as the cytokine profile in the pathophysiology of NPDR and PDR.
Disclosure of Interest: None Declared.

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Fibrinogen in sepsis: crosstalk between coagulation and inflammation

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Background: The latest findings have revealed fibrinogen and its cleavage products as the new actors in the innate immune system. Fibrinogen (F1) plays a pivotal role in preventing pathogen invasion and dissemination, as well as, a protective role for the endothelium via coagulation and fibrinolysis. However, F1 enhances the pro-inflammatory state and if coagulation is exaggerated, it can contribute to disease. Therefore, what is the role of fibrinogen during sepsis?
Aims: The purpose of the study was to evaluate if high F1 levels are associated with survival or non-survival in sepsis.
Methods: We retrospectively analysed 915 adult septic patients, hospitalized within 2000 to 2014 at the University Hospital Innsbruck (Austria). Peak of C-reactive protein (CRP) level was defined as the most intense period of sepsis. CRP and F1 values were collected 3 days before (day -3, day -2, day -1) until 3 days after (day 1, day 2, day 3) peak of CRP level (day 0).
Results: Fibrinogen levels follow the C-reactive protein (CRP) course, though there is no significant difference of CRP-levels between survivor and nonsurvivor. F1 levels in survivors were significantly higher than in non-survivors on each day (day -3 and day -2: $P < 0.05$; day -1: $P < 0.01$; day 0, day 1 and day 2: $P < 0.001$;day 3: $P < 0.01$). In patients with hyperfibrinogenemia survival rate was significantly higher ($P < 0.001$) than in patients with levels within normal range or below. Septic patients with an underlying disease of the central nervous system had higher F1 levels than patients without (day -1 and day 0: $P < 0.01$; day 1, day 2 and day 3: $P > 0.001$) whereas there was no significant difference in F1 levels between survivors and nonsurvivors.
Conclusion: Hyperfibrinogenemia in septic patients is associated with higher survival rate except for patients with a neurological underlying disease where the beneficial role of F1 could not be detected.
Disclosure of Interest: None Declared.

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Increased biomarkers of metabolic syndrome in total joint arthoplasty patients

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Background: Patients undergoing total hip and total knee arthroplasty (THA/TKA) represent a diverse group of individuals with a variety of pre-existing co-morbidities including metabolic syndrome (Mes). Recently several biomarkers of Mes have been identified and may be helpful in the risk stratification and management of arthroplasty patients.
Aims: This study is designed to profile biomarkers of Mes in total joint arthroplasty patients.
Methods: Citrated plasma samples were collected from 42 patients undergoing THA/TKA pre-operatively and day 1 post-operatively (POD1). Control group consisted of 48 healthy, non-smoking and non-medicated donors. Both groups of samples were profiled for Mes biomarkers utilizing a Randox biochip array technology which included C-peptide, ferritin, IL-6, insulin, resistin, TNFa, IL-1a, leptin, and PAI-1.
Results: Compared to normal controls, pre-operative levels of C-peptide and ferritin did not differ significantly ($P > 0.05$). IL-6, resistin, insulin, TNFa, IL-1a, leptin, and PAI-1 levels were significantly higher in the arthroplasty group in comparison to normal controls ($P < 0.05$ to 0.001). Post operative plasma samples exhibited marked augmentation of the biomarkers of Mes with wider variations in comparison to pre-operative levels.
Conclusion: The pre-existing Mes has been reported to contribute to surgical complications in THA/TKA. The increased levels of leptin, insulin, C-peptide, along with inflammatory biomarkers underscore the interplay of Mes mediators and inflammatory process. Profiling of Mes biomarkers provides an added tool to risk stratify arthroplasty patients and optimize their clinical management.
Disclosure of Interest: None Declared.