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MORPHOLOGICAL CHANGES IN ARTHEROSCLEROTIC PLAQUE IN DIABETIC PATIENTS

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Resume. This study investigates coronary plaque changes in diabetics, highlighting increased MMP-1, MMP-9, a-SMA, and CD68 levels, which correlate with plaque instability and rupture risk, emphasizing the role of metalloproteinases in plaque degradation and cardiovascular risk

Keywords: *atherosclerosis, MMP-1, MMP-9, a-SMA, CD68.*

Actuality. The increased levels of smooth muscle actin-alpha, macrophage marker CD68, and matrix metalloproteinases (especially MMP-9 and MMP-1) in diabetic individuals' atherosclerotic plaques indicate a complex interplay of cellular proliferation, inflammation, and enzymatic tissue degradation. These processes collectively contribute to the destabilization of plaques, making them more susceptible to rupture, which is a primary event leading to acute coronary syndromes. Understanding these molecular and cellular mechanisms provides crucial insights into the heightened cardiovascular risk associated with diabetes and underscores the importance of targeted therapies aimed at modulating inflammation and ECM remodelling in diabetic patients

Aim: The main aim of the thesis is to analyse the distribution and variation of morphological and immunohistochemical changes in coronary vessels with atherosclerotic plaques in diabetic patients, focusing on structural alterations and biomarker expression related to plaque stability and instability.

Objectives:

1. Digital scanning of the received slides with Aperio Image scope for Immunohistopathological analysis.
2. Stained slides were analysed with the Positivity of the presence of the respective markers by digital annotations with the positive pixel count
3. The results were obtained for all the chosen markers and the positivity degree were compared with the statistical correlations.

Material and Methods. Coronary artery atherosclerotic plaques from diabetic and non-diabetic patients were analysed using immunohistochemical staining, revealing the presence of CD68, MMP-1, MMP-9, and a-SMA. Patient data was collected from the cardiology departments of several hospitals in Minsk. The corresponding stained pathological slides, used for immunohistochemical analysis, were obtained from the Pathological Anatomical Bureau of Minsk. This allowed for the correlation of clinical information with pathological findings. Quantitative analysis of expression was performed using the programme Aperio Image Scope 12.4.6 and calculation of the ratio of positive markers to the total number of markers present, thereby determining the overall positivity for each marker.

Results and Discussion. The statistical analysis conducted in this study identified a noteworthy correlation between the presence of diabetes mellitus, whether type 1 or type 2, and the expression levels of MMP-1 within atherosclerotic plaques. This suggests that diabetic patients tend to exhibit higher levels of MMP-1, which is an enzyme involved in the breakdown of extracellular matrix components, possibly reflecting a heightened enzymatic activity associated with diabetes-related vascular changes. However, when the researchers compared the average expression levels of all the studied biomarkers — including MMP-1, MMP-9, alpha-SMA, and CD68 — between groups of patients with and without diabetes, they did not observe statistically significant differences. Similarly, the degree of diabetes control or compensation, which indicates how well blood glucose levels are managed, did not significantly influence the expression levels of these markers. This indicates that while diabetes may be associated with increased MMP-1 activity, overall biomarker expression does not differ markedly across diabetic and non-diabetic groups, nor does it vary significantly with the level of glycaemic control.

Further analysis revealed that the expression levels of both MMP-1 and MMP-9 were strongly dependent on the stability of the atherosclerotic plaques. Specifically, in large, unstable plaques characterized by a lipid-rich core and a thin fibrous cap, the expression of these metalloproteinases was markedly higher. This heightened enzymatic activity is likely to contribute to the degradation of critical structural components of the plaque, such as collagen and elastin, weakening the fibrous cap and increasing the risk of rupture. The significance of this finding is underscored by the observation that MMP-1 levels were particularly elevated in plaques from patients who had succumbed to acute myocardial infarction, suggesting that increased MMP-1 activity may be directly involved in the processes leading to plaque rupture and subsequent cardiac events.

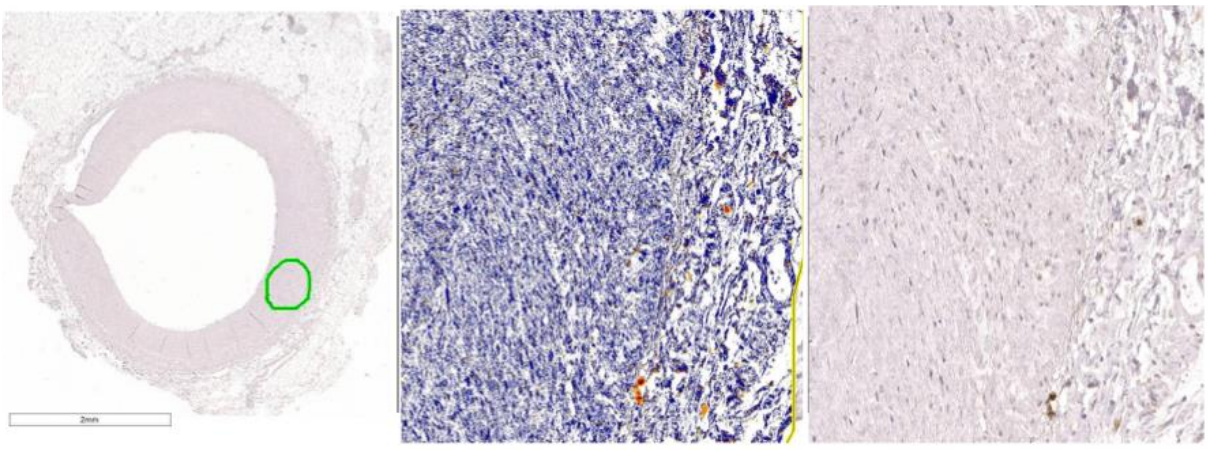
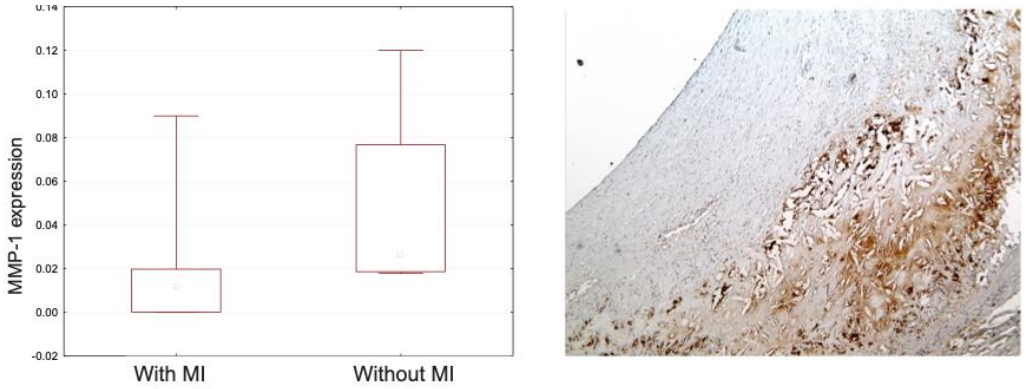


Fig 1. Representing the marked area of a coronary leumen with the scanned prevelance of MMP-1 Markers and the normal picture on the right corner before analyzed annotations

Overall, these findings highlight the complex and multifaceted nature of atherosclerosis in diabetic individuals. While certain enzymes like MMP-1 and MMP-9 are clearly associated with plaque instability and rupture, cellular markers such as alpha-

SMA and CD68 do not show consistent relationships with plaque severity. This emphasizes the importance of focusing on enzymatic activity and extracellular matrix degradation pathways when assessing plaque vulnerability and developing targeted therapies aimed at preventing rupture and adverse cardiovascular events in diabetic patients.



The level of MMP-1 expression was also higher in atherosclerotic plaques in patients who died of acute myocardial infarction

Conclusion: Significant expression of metalloproteinases (MMP-1 and MMP-9) results in more active degradation of extracellular matrix components, increases a risk of rupture of atherosclerotic plaques fibrous cover and makes them less stable.

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