27/28th International Conference
ENGINEERING MECHANICS 2022
Milovy, Czech Republic, May 9 –12, 2022
Paper **#53**, pp. 157–160, doi: 10.21495/51-2-157

PATIENT ANAMNESIS AND ITS IMPACT ON MECHANICAL PROPERTIES OF ATHEROSCLEROTIC CAROTID ARTERIES: AN EXPLORATIVE STUDY

Hrubanová A.*[1], Kubíček L.[2], Burša J.***[1]**

Abstract: *Atherosclerosis is a life-threatening disease characterized by progressive lipoprotein accumulation in the inner artery layer. The beginning and the first stages of the disease are linked with endothelial layer disruption. Since there is previous evidence that lifestyle (including diet, unhealthy habits such as smoking or alcohol dinking) can influence the atherosclerotic process, their impact on the mechanical properties should be investigated as well. In this study, 141 uniaxial tests on carotid endarterectomy samples were performed, and statistical analysis was made to investigate the possible influence of these factors from anamnesis on the stress-strain characteristics. The factors found as important were smoking and alcohol drinking, since the stress-strain curve proved to be significantly different from the group without the influence of addictive substances. However, only separate factors were investigated, and further analysis should be made to reveal possible corelations between these factors.*

Keywords: Atherosclerosis, Carotid artery, Mechanical properties, Uniaxial tensile test, Anamnesis.

1. Introduction

Atherosclerosis is one of the leading causes of death in developed countries. The disease is characterized by progressive accumulation of lipoproteins in the inner artery wall – intima. When left untreated, it can result in thrombosis with limitation or closure of blood flow and, in case of carotid arteries, often leads to stroke with high mortality of the patients (Fisher, 2005).

The inner surface of artery is covered with a monolayer of endothelial cells which acts as a semipermeable membrane and ensures the transfer of blood constituents into the artery wall (Ross, 2016). When unharmed, this layer disables a blood clot formation on its surface, but when it is damaged, it produces substances promoting blood thrombosis. The disruption of this layer promotes the accumulation of lipoproteins within the artery wall and thus is the first step in atherosclerosis development.

The process of atheroma formation begins with excessive amounts of LDL (Low Density Lipoproteins) in blood which cannot be disposed of by macrophages and are accumulated in intima. As the lesion grows, the lipid core (LC) is created and is covered by fibrous cap (FC) created during the progression of disease to keep the inside of the atheroma separated from blood and keeping it from rupture.

Endothelial layer can be damaged mechanically by turbulent blood flow (Cecchi, 2010). It is known that some life or diet regime changes can have positive effect in atherosclerosis treatment. In contrast, unhealthy habits such as smoking, excessive alcohol consumption, fat-based diet or sedentary lifestyle can play an important role in atherosclerosis creation and progression. It was previously shown that smoking causes impairment of endothelial layer (Heather et al., 2010). As cited earlier, the endothelial layer plays a key role in the disease incipience so external factors from anamnesis contributing to disruption of the endothelial layer could have significant impact on atherosclerosis development and thus on the mechanical properties of the artery.

[1] Inst. Solid Mechanics, Mechatronics and Biomechanics, Brno University of Technology, Technická 2896/2, 61669 Brno; CZ
[2] St. Anne's University Hospital Brno and Faculty of Medicine, Masaryk University, Brno, Czech Republic
* Ing. Anna Hrubanová; 191418@vutbr.cz „Brno Ph.D. Talent Scholarship Holder – Funded by the Brno City Municipality“
** MUDr. Luboš Kubíček, PhD; lubos.kubicek@fnusa.cz
*** Prof. Ing. Jiří Burša, PhD.; bursa@fme.vutbr.cz

Uniaxial tensile tests can help us reveal the non-linear behaviour of atherosclerotic tissue. Although biaxial tensile tests are more suitable for non-linear hyperelastic tissue, to the author's best knowledge, there is no study performing biaxial tensile test on atherosclerotic tissue. There are several studies performing uniaxial tensile tests on atherosclerotic carotid arteries focusing on different factors and their impact on mechanical properties such as the effect of calcifications (O'Reilly, 2020), the composition of the plaque (Teng, 2014; Kobielarz, 2020) or importance of different layers of carotid artery (Hoffman, 2017). However, there has been little focus on the external factors from anamnesis and their impact on mechanical properties. The factors from anamnesis, which are a priori known (and influenced in most cases by the patient) could have significant effect on the stress-strain response of the artery and enable thus to reduce the uncertainty of its constitutive model in computational modelling.

2. Methods

2.1. Specimen extraction and preparation, uniaxial tensile testing

All samples were acquired during standard endarterectomies in St. Anne's University Hospital in Brno from April 2019 to December 2020. In accordance with the ethical approval of the project, all the 44 patients had signed an informed consent. From these 44 samples 141 uniaxial testing specimens were prepared. The number of specimens per sample varied due to different size and quality of each sample. These samples were already evaluated in our previous research (Hrubanová et al., 2020) and (Lisický et al., 2021b) where the impact of some other factors (location and orientation of the sample, patient sex and age) on the mechanical response was assessed.

The sample consisted of diseased intima layer with atheroma lesion and a part of media layer which was dissected during the endarterectomy procedure. In most cases, the atheroma with lipid core (LC) was located at the bifurcation area. Typical sample is shown in figure 1. A tailored computer controlled tensile testing device (Camea s.r.o., CZ) was used to perform uniaxial tests. The detailed description of specimen storage and preparation (specimen location decision, size and shape of specimen, thickness measurements) together with the description of the testing protocol and evaluation can be found in previous work (Hrubanová et al., 2020).

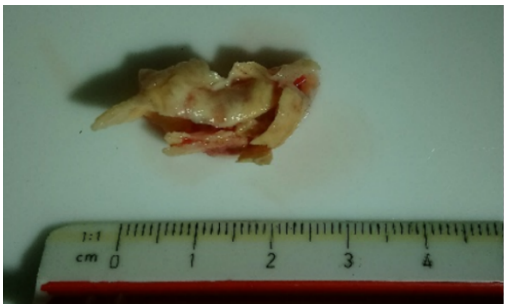

Fig. 1: Carotid sample with scale – the length does not exceed 30 mm.

3. Results

3.1. Statistical analysis

For each patient the following information about the anamnesis was gathered: the height and weight of the patient from which the BMI index was calculated; smoking and alcohol using history, hypertension, diabetes, HLP levels (dislipidemia – abnormal amount of lipoproteins in blood) and presence of symptoms of the atherosclerotic disease.

Since the objective was to separate the patients into two disjunct groups, for smoking and drinking alcohol, all the former or regular users were categorized as users; we considered as non-users only those who declared they never smoked or took alcohol. BMI value higher than 25 was considered as overweight. Note that the factor of hypertension was not considered for statistical analysis because only 4 of the 44 patients did not suffer from hypertension.

The stress-strain response for each specimen was averaged at different stress levels stepped by 10 kPa, as described and substantiated by Lisický et al. (2021a). Then, the specimens were sorted into couples of disjoint groups regarding the above factors. The normality distribution of the data was tested at each stress level using Anderson-Darling test, Shapiro-Wilk test and Cramer-Von Mises test with the significance level $\alpha = 0.05$. The null hypothesis about normal distribution was rejected at all stress levels, thus median was used below instead of the mean. The data was then tested using non-parametric Mann-Whitney test for null hypothesis that median of strain level of one group is equal to the median of the other group at each stress level at significance level of $\alpha = 0.05$. The resulting p-values are shown in Fig. 2.

The p-values for factors smoking, alcohol and HLP are below the significance level at almost all stress levels, which indicates that there is a significant difference between the groups in the couples. Note that only for 7 patients (corresponding to 24 specimens) the risk factor of HLP was not present, i.e., the amount of lipoproteins in their blood was not abnormally high. The factor of diabetes is close to statistical significance: it shows p-values close to 0.05 and even below at 160 – 190 kPa. The difference between groups for factors BMI and symptomatic/asymptomatic disease were not found statistically significant. The resulting median curves with interquartile range are shown in figure 2 for the statistically significant factors.

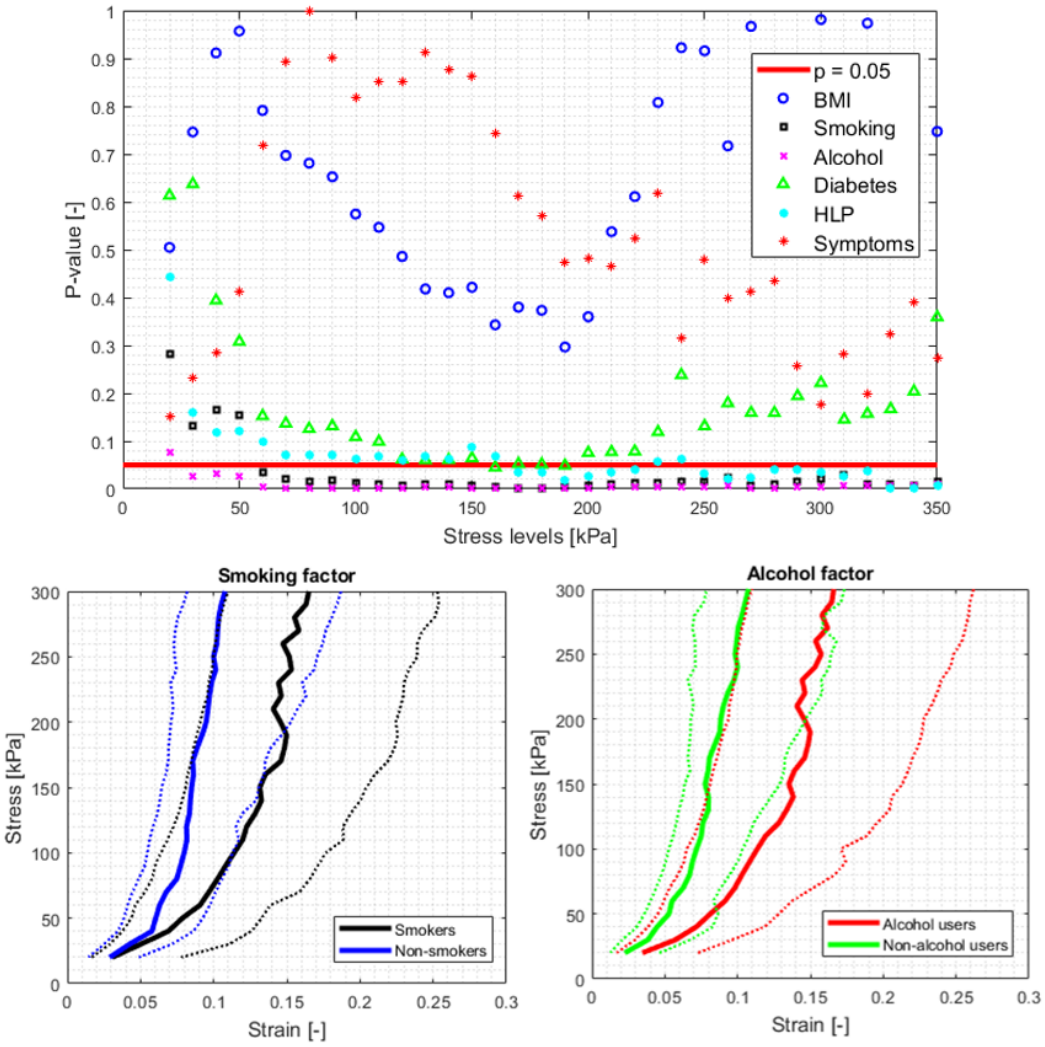

Fig. 2: Top: The p-values for each of the stress level for the selected anamnesis factors. The value below 0.05 suggests that there is a statistically significant difference between the medians. Bottom: Median (solid) and interquartile range (dotted) stress-strain curves for the groups with significant difference.

4. Discussion

Accuracy of the constitutive model of atherosclerotic arteries is fundamental for their credible computational modelling and prediction of plaque rupture. In this study, 7 factors from anamnesis were investigated whether they influence the tissue mechanical response in uniaxial tension.

Statistically significant impact was found for the factors of smoking, alcohol drinking and HLP. However, the group of specimens for which the HLP was below the critical value was significantly smaller compared to the group with high HLP (24/120 specimens) so the results are not confirmative as they can be affected by this disproportion. The factor may be significant, but it requires an additional investigation with a bigger statistical group.

The factor of diabetes was not proved statistically important, but the p-values are close to the significance level and even below between 160 – 190 kPa. This shows that also the effect of diabetes might be

significant, but it was not proven by the statistical test. This can be due to the small sample size or due to the small power of non-parametric tests.

The factors of smoking and alcohol taking proved their significant influence on the mechanical response. For both groups, the "unhealthy habit" causes the stress-strain curve to be more compliant and the dispersion of data was also greater for these groups. This surprising trend might be explained if bigger amounts of lipids in the atheroma were confirmed for these patients with the unhealthy lifestyle; the lipidous atheroma samples were already shown to be more compliant and less strong (Teng, 2014; Kobielarz, 2020). This indicates, that smoking and/or alcohol could contribute to atheroma creation and tissue remodelling and cause more compliant and more variable responses between patients.

However, among the 27 patient that admitted to smoking, 25 of them also stated alcohol consumption, thus these two factors cannot be distinguished from each other. Generally, investigation of impact of each factor separately represents a limitation of this study. A more thorough investigation of interactions between different factors should be made in future since it could bring clearer answers whether and how exactly these factors influence the mechanical response.

5. Conclusion

The realized uniaxial tensile testing together with statistical analysis of impact of different anamnesis factors showed a significant impact of smoking and alcohol drinking on the mechanical response of carotid atheromas; their compliance was bigger compared to the non-using group with much higher variance of the data. This enables use of more accurate constitutive models in computational simulations especially for the patients without these unhealthy habits. However, as the anamnesis factors may be mutually dependent, further statistical analysis should be made to determine possible correlations between the selected factors.

Acknowledgement

This work was supported by Czech Science Foundation Project No. 21-21935S.

References

Cecchi, E., Giglioli, C., Valente, S., Lazzeri, C., Gensini, G. F., Abbate, R., and Mannini, L. (2011). Role of hemodynamic shear stress in cardiovascular disease. *Atherosclerosis*, 214(2), pp. 249–256.

Fisher, M., Paganini-Hill, A., Martin, A., Cosgrove, M., Toole, J. F., Barnett, H. J. M., and Norris, J. (2005) Carotid plaque pathology: Thrombosis, ulceration, and stroke pathogenesis. *Stroke,* 36, pp. 253–257.

Hoffman, A. H., et al. (2017) Stiffness properties of adventitia, media, and full thickness human atherosclerotic carotid arteries in the axial and circumferential directions. *Journal of Biomechanical Engineering*, 139(12), 124501.

Hrubanová, A. (2020) Impact of formaldehyde on mechanical properties of atherosclerotic carotid arteries. In: Fuis, V. (ed) *Engineering Mechanics 2020*. VUT Brno, pp. 210-213.

Johnson, H. M., Gossett, L. K., Piper, M. E., Aeschlimann, S. E., Korcarz, C. E., Baker, T. B., Fiore, M. C., and Stein, J. H. (2010). Effects of smoking and smoking cessation on endothelial function: 1-year outcomes from a randomized clinical trial. *Journal of the American College of Cardiology*, 55(18), pp. 1988–1995.

Kobielarz, M., Kozuń, M., Gąsior-Głogowska, M., and Chwiłkowska, A. (2020). Mechanical and structural properties of different types of human aortic atherosclerotic plaques. *Journal of the Mechanical Behavior of Biomedical Materials*, 109, 103837.

Lisický, O., Hrubanová, A., and Burša, J. (2021a). Interpretation of Experimental Data is Substantial for Constitutive Characterization of Arterial Tissue. *Journal of Biomechanical Engineering*, 143(10), 104501.

Lisický, O., Hrubanová, A., Staffa, R., Vlachovský, R., and Burša, J. (2021b). Constitutive models and failure properties of fibrous tissues of carotid artery atheroma based on their uniaxial testing. *Journal of Biomechanics,* 129, 110861.

O'Reilly, B. L., Hynes, N., Sultan, S., McHugh, P. E., and McGarry, J. P. (2020). An Experimental and Computational Investigation of the Material Behaviour of Discrete Homogenous Iliofemoral and Carotid Atherosclerotic Plaque Constituents. *Journal of Biomechanics*, 106, 109801.

Ross, M.H., and Pawlina, W. (2016) *Histology: a text and atlas: with correlated cell and molecular biology*, Seventh edition. Wolters Kluwer Health, Philadelphia.

Teng, Z., Y., Zhang, Y., Huang, et al. (2014) Material properties of components in human carotid atherosclerotic plaques: A uniaxial extension study. *Acta Biomaterialia*., 10(12), pp. 5055-5063.