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LONGITUDINAL PRESTRAIN IN MALE ABDOMINAL AORTA FROM PULSE WAVE VELOCITY VIEWPOINT

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Summary. *Arteries in situ are subjected to the pretension developed upon the growth period. The magnitude of the pretension was shown to be age-dependent. Detailed statistics are, however, rare. This study was designed to expand our knowledge of the prestrain sustained by arteries during the lifespan. Age-related distribution of the longitudinal prestrain in the male abdominal aorta obtained within 93 regular autopsies is shown (age = 41.6±15.8 years; prestretch =1.174±0.099). Data indicate that the prestrain decreases nonlinearly during the aging. Bilinear regression function revealed the breakpoint in the prestrain–age dependency at age about 40. The comparison of this result with studies which document the nonlinearity in the pulse wave velocity–age dependency indicates that steep increase of the velocity is preceded by the loss of the pretension. It suggests that the pretension could play a compensation role within artery stiffening.*

1 INTRODUCTION

Computational methods of biomechanics become increasingly directed to the so-called patient-specific analyses[1-2]. They can help in customized therapy. Such an approach, however, necessitates patient-specific (and pathology-specific) constitutive models, loading conditions and geometries to be known during computer modeling.

Geometrical patient-specific models of tissues and organs can be obtained by modern computer imaging methods. It is well-known, however, that arteries in situ (under geometry observed with CT, MRI or IVUS in vivo) are not in the zero stress and strain state. Beside the blood pressure-induced loading there is significant residual stress acting in the circumferential direction[3-5]. In the longitudinal direction arteries exhibit significant pretension. This can be proved upon the excision of a sample. The sample will retract[6-9]. Hence direct incorporation of in situ geometry into the computational model can lead to nonrealistic results.

The existence of the longitudinal prestrain (pretension) is known more than a century[14]. Bergel[6] reported mean shrinkage of the excised samples of the canine arteries ranging between 32% - 42% (percentage of original length) depending on the position in the arterial tree. Han and Fung[7] confirmed this result. They reported monotonically increasing longitudinal prestretch (from 1.2 to 1.5) with the increasing distance from the heart. Learoyd and Taylor[8] measured 59 samples of arteries obtained from 12 human donors. Their results proved the position dependency of the prestrain. They also found negative correlation between the age and the prestrain[10].

The species and position dependency of the longitudinal prestrain seems to be explainable by means of the intramural collagen-to-elastin ratio[11]; the higher the ratio, the lower the prestrain. The key role of the elastin was proved by enzyme digestion and also in animal models with the elastin insufficiency[12,13,16].

Recent papers have shown that the longitudinal prestrain is involved in the artery remodeling and adaptation. Jackson at al. [16] shown that elevated axial prestrain in rabbit carotid arteries was normalized within 7 days after the surgery. It was accompanied by increased endothelial and smooth muscle cell replication rate[16,17]. Also increased extracellular matrix content was observed. In contrast to the elevated longitudinal load the culturing under infraphysiological axial strain resulted in a mass loss and decreased cell proliferation[18].

It is well known that arteries stiffen with increasing age. This process is called arteriosclerosis. Increased stiffness of conduit arteries results in the increase of the pressure pulse wave velocity (PWV)[19,22,23]. Elevated PWV, however, lead to early pressure wave reflections which contribute to the heart load. The artery wall exhibits nonlinear and anisotropic mechanical behavior. In such a material actual stiffness depends on actual strain/stress state[20,21]. Concerning these facts rather surprising hypothesis can be derived. Although the loss of the longitudinal strain is likely negative consequence of the aging, it reduces overall strain state of an artery. Reduced axial strain results in the reduction of actual stiffness. This mechanism could compensate for increased stiffness developed within arteriosclerosis.

To test the hypothesis of the compensation ability we compared the age-related distribution of the longitudinal prestrain with the distribution of the pulse wave velocity in human aorta. It will be shown that progressive decrease of the prestrain magnitude in male abdominal aorta is followed by only small change at age above 40 years. Our data indicate that rapid increase of PWV is preceded by the period of the progressive loss of the prestrain.

2 METHODS

The statistics of 93 abdominal aortic longitudinal prestrains was collected within regular autopsies of male Caucasian cadavers of known age in the University Hospital Na Kralovskych Vinohradech in Prague. The longitudinal prestrain was quantified by the stretch ratio λ defined in (1). l and L denote the length of the tubular sample (below renal arteries branching and above aortoiliac bifurcation) before and after the excision.

$$\lambda = \frac{l}{L} \tag{1}$$

It was hypothesized that the age-dependency of λ can be expressed by means of stepwise linear function with the breakpoint, t_k, corresponding to the loss of the compensation ability (2).

$$\lambda(t) = \begin{cases} at + b & \text{if } t \le t_k \\ ct + d & \text{if } t_k < t \end{cases} \tag{2}$$

Where a, b, c, d are real parameters and t denotes the age [years]. The condition of continuity has to be added, $at_k + b = ct_k + d$, to obtain meaningful results.

Constrained optimization problem was solved in Maple 13. It should be mentioned that besides parameters a, b, c and d, the position of the breakpoint, t_k, was also the subject of the optimization. The final model was evaluated with generalized F-test. The null hypothesis, $H_0 : [a,b] = [c,d]$, was tested against the alternative $H_A : [a,b] \neq [c,d]$.

The regression was accompanied with the correlation analysis exploring the link between the prestrain and additional cardiovascular indices. The correlations include carotid-femoral pulse wave velocity (cfPWV), distensibility of descending aorta (DDA), maximum strain of descending aorta (mS), central aortic systolic (SP), diastolic (DP) and pulse pressure (PP), and augmentation index (AI). Since there is no possibility to find out these quantities post mortem we had to incorporate data from the literature[23]. The data were obtained within MRI investigation and tonometry. Here we will not repeat details of the procedure. We only mention that mS was obtained as the relative change of the lumen area; DDA denotes the change in the lumen area with respect to minimal area and PP, and AI is the ratio between systolic pressure augmentation and PP. The simple correlation coefficients, R, were computed based on data averaged through decades of the life.

3 RESULTS

Data sample involved in our study consisted of 93 male subjects with age ~ 17—81 (41.6±15.8) and prestretch ~ 1.023—1.417 (1.174±0.099); minimum—maximum (mean±SD). The study proved significantly decreasing prestrain upon increasing age. It was found that the stepwise linear model (2) fits prestrain–age relationship with lower sum of squares than simple linear. The parameters estimating resulted in $a = -9.556 \cdot 10^{-3}$; $b = 1.520$; $c = -2.588 \cdot 10^{-3}$; $d = 1.241$; and $t_k = 40$ years. F-test proved that there are strong statistical evidences against the null hypothesis (the risk of true hypothesis rejection $p < 0.0001$). Results are depicted in Fig. 1. Fig. 2 shows the ratio between residual standard deviation (RSD) computed for optimal model and RSD obtained in models with t_k in different positions (and different valaues of the parameters).

Table 1 documents age-related mean values of the prestrain and data adopted from the literature[23]. Results suggest that especially non-dimensional indices are highly correlated. The correlation found for entire sample of the prestrain and age reached $R = -0.856$. It proves strong age-dependency of the prestrain. High correlation between the carotid-femoral pulse wave velocity and prestrain was also confirmed, $R = -0.884$.

4 DISCUSSION

We postulated the hypothesis that decreasing longitudinal prestrain could compensate artheriosclerosis-induced stiffening of an artery. This compensation ability would be, however, limited with the initiative value of the prestrain developed within the growth period. The analysis suggests that the process of the prestrain decrease is not linear. The stepwise linear model revealed the breakpoint at age about 40 years.

Table 1: Prestrain correlations. X denotes the number of our observations. Y denotes the number of observations involved in [23]. Used acronyms: cfPWV – carotid-femoral pulse wave velocity; DDA – distensibility of descending aorta; mS – maximum strain; AI – augmentation index; DP, SP and PP denote central diastolic, systolic and pulse pressure, respectively. *The correlation between age and prestrain was based on non-averaged data.

Number of samples X/Y	Age [years]	Prestretch [1]	cfPWV [ms^{-1}]	DDA [$10^{-3}\cdot kPa^{-1}$]	mS [%]	DP [mm Hg]	SP [mm Hg]	PP [mm Hg]	AI [%]
22/21	20-29	1.296	6.2	72	33	59	109	48	-10
19/15	30-39	1.199	6.7	70	27	66	113	46	-4
20/31	40-49	1.135	8.8	38	15	75	122	46	16
18/16	50-59	1.091	9.5	29	11	77	134	55	31
7/14	60-69	1.068	12.8	18	9	75	143	66	26
5/14	70-	1.061	13.8	17	8	69	135	66	32
Correlation	-0.856*	1	-0.884	0.949	0.985	-0.828	-0.932	-0.748	-0.958

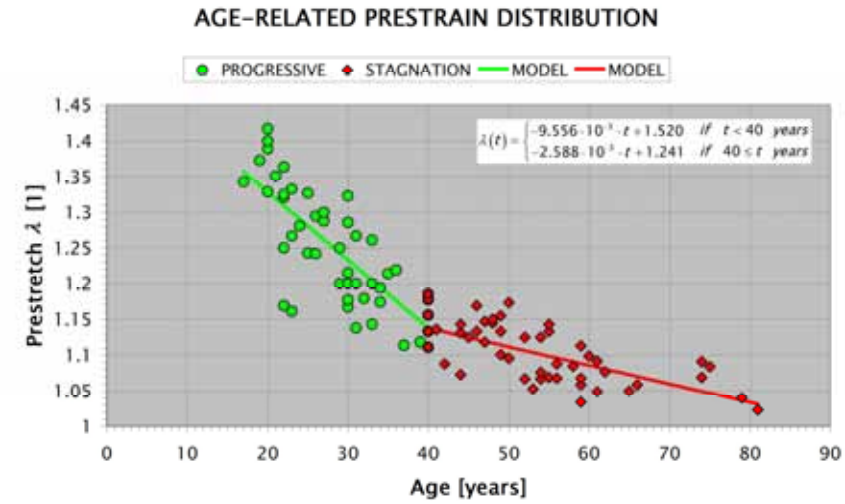

Figure 1: Optimal stepwise linear regression. We suggested the hypothesis that progressively decreasing prestrain could compensate for overall stiffening of an artery. It would mean that only small increase in pulse wave velocity should be expected before the breakpoint.

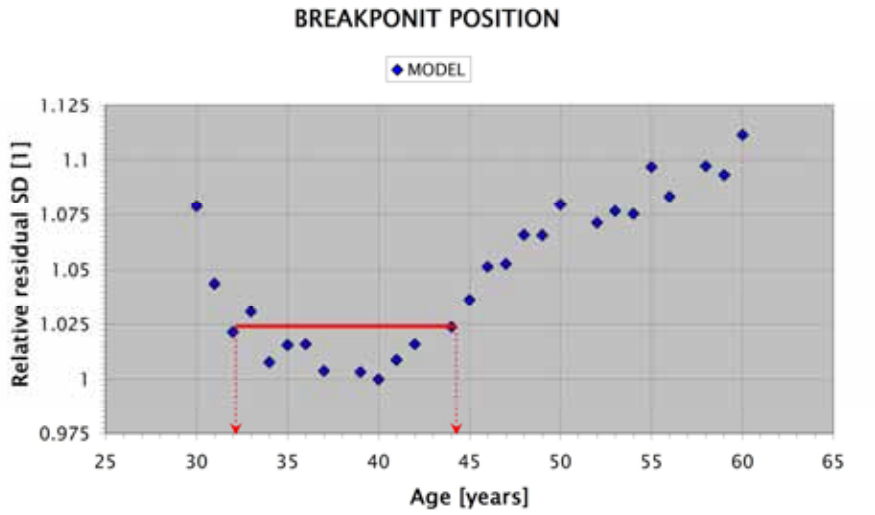

Figure 2: Uncertainty of the breakpoint position. Breakpoint position can be affected with the data sample character. The graph shows rather flat character of the extreme. Hypothetical variability of the breakpoint position is outlined with the interval of 2.5% difference from the optimum.

It has to be mentioned, however, that post mortem collected data may not correspond exactly to in vivo pretensions. There are some sources of differences: 1. influence of post mortem interval (PMI); 2. necessity of the removing tethering tissue during preparation; 3. absence of the blood pressure. Previous analysis proved that PMI does not correlate with the prestrain in our statistical sample[24]. Nevertheless, the removing of the tethering tissue and the absence of the blood pressure can cause that the in vivo prestrains are higher than herein reported. Bearing this in mind our data should only be considered as the estimations of the in vivo longitudinal prestrain.

Thus the position of the breakpoint, identified here at 40 years, can also move depending on the specific statistics. To emphasize this fact we included Fig. 2. It shows the character of the change in RSD with relation to the breakpoint position. The minimum is rather flat which indicates an uncertainty of the estimation.

Herein presented statistical analysis can not give evidences how much longitudinal prestrain affects PWV. It only proves that PWV and prestrain are correlated. The true link between the age, PWV and prestrain must be clarified by methods of the computational mechanics. They can incorporate constituent-based models to explain this link.

Strong correlations between the prestrain, PWV and other indices were found. They, however, can be overestimated due to averaging of the data which has a smoothing effect. Nevertheless, Redheuil et al.[23] shown the breakpoint in the PWV-age and ascending aortic distensibility-age dependency (see Fig. 2 in their study; http://hyper.ahajournals.org/cgi/reprint/55/2/319) at age 50 years. Our study shown the breakpoint in the prestrain at age about 40 years. The preceding loss of the prestrain before the increase of PWV is consistent with the hypothesis of the compensation ability.

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