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Obesity, fat distribution and large artery wall properties

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SUMMARY

Large artery wall properties - compliance (CC) and distensibility (DC)- may play a role in cardiovascular disease. The purpose of this study was to investigate the relation between obesity - an independent cardiovascular risk factor - and large artery wall properties. In a population sample of 250 men and 243 women, 20-79 years, diameter, DC and CC of the elastic aorta and common carotid artery (CCA) and muscular brachial (BA) and femoral arteries (FA) were measured with an echo-tracking device. The effects of body mass index (BMI), waist-to-hip ratio (W-H ratio) and skinfold thickness were assessed and adjusted for confounding factors. BMI was positively ($p<0.01$) related to arterial diameter. Obesity was not significantly related to aortic stiffness. Except for carotid artery DC in women, BMI was negatively ($p<0.05$) related to DC of CCA, BA and FA in men and women. BMI was also negatively related to CC of the BA ($p<0.05$) and FA ($p<0.05$) only in men. An increased waist-to-hip ratio was negatively related to FA DC and CC ($p<0.01$) in men. Skinfold thickness was negatively related to BA DC in women ($p<0.001$). Associations between obesity and arterial wall properties depend on the index of obesity, gender and the vascular territory. BMI-based effects on arterial wall properties are more important than those of W-H ratio or skinfold thickness. BMI-based obese subjects have a larger arterial diameter and stiffer arteries, which may be compatible with flow-dependent vasodilation. The effects of W-H ratio on arterial wall properties are restricted to men, those of skinfold thickness to women.

INTRODUCTION

Overweight and obesity, defined as a body mass index greater than 25 and 30 kg/m^2, respectively, are common in Westernized societies with an overall prevalence of 50% and 30%[1]. Obesity is a well-known independent risk factor for the development of cardiovascular disease[2,3]. One of the possible targets of obesity-related risk is a change in vascular function.

Compliance and distensibility are vessel wall properties of large arteries, which might be important in the development of cardiovascular disease[4]. Compliance, defined as the absolute change in volume per unit of pressure ($\Delta V/\Delta P$), reflects the buffering capacity of the arterial system. Distensibility, defined as the relative change in volume per unit of pressure ($(\Delta V/V)/\Delta P$), reflects the elastic properties of the wall.

Little is known about the relation between obesity and vessel wall properties of large arteries. The few studies investigating the relation between obesity and large artery properties show different results[5-10]. This could be due to different techniques, small number of subjects, the involvement of different arteries and different definitions of obesity. Obesity can be expressed in different ways: body mass index (BMI), waist-to-hip ratio and thickness of skinfold. These indices do not describe the same entity. For example waist-to-hip ratio can differ substantially between two subjects with the same BMI, indicating a difference in fat distribution. The pattern of fat distribution itself also seems to add in the cardiovascular risk[11,12]. Skinfold thickness is a measure of subcutaneous fat.

The aim of the present study was to investigate the relation between indices of obesity and fat distribution (BMI, waist-to-hip ratio and thickness of skinfold) and large artery wall properties of the elastic aorta and common carotid artery and the more muscular brachial and femoral arteries in a population sample. Since body height contributes to body mass, the relation between height and large artery wall properties was also studied.

METHODS

Six hundred and fourteen subjects from a random population sample[13,14] took part in vascular measurements. Of these participants 121 subjects were not included in the final analysis, because the necessary data were not complete. The number of subjects finally considered in the analysis totalled 493 subjects (250 men and 243 women).

The cardiovascular examinations took place at a locally organised clinic. All participants were asked to refrain from eating, smoking, caffeine containing beverages and heavy exercise for at least 3 hours before being examined. Data of systolic (SBP) and diastolic blood pressure (DBP) are mean of five measurements, measured conventionally with a sphygmomanometer. Mean blood pressure (MBP) was calculated as (2*x*DBP+SBP)/3. A standardized questionnaire gave insight into their current health status, smoking and drinking habits and intake of drugs. Height and weight were measured. Body mass index (BMI) was calculated as weight/height^2. Waist circumference was measured with a tape measurer midway between the lower rib and the iliac crest. Hip circumference was measured at the point yielding maximum circumference over the buttocks. Waist-to-hip ratio (W-H ratio) was used as an indicator of centrally localized body fat distribution. Skinfold thickness, a measure of subcutaneous fat, was measured on the left arm, halfway between the upper arm, with a skinfold caliper (British Indicators LTD).

After 15 minutes of supine rest in a quiet room diameter and change in diameter of the right elastic common carotid artery (CCA) and right muscular femoral (FA) and brachial arteries (BA) during the heart cycle were measured with a vessel wall movement detector system[14,15].

The same observer, at an arterial segment, which showed no echocardiographical signs of atherosclerosis in B-mode, made all measurements.

Simultaneously with the assessment of the vessel wall properties blood pressure and pulse rate were recorded every 3 minutes at the left arm with a semiautomated device (Dinamap; Critikon, Tampa, Florida). The mean of these recordings (at least 15) was taken as the subject's reading. Brachial artery pulse pressure was defined as systolic minus diastolic blood pressure. Pulse pressure at CCA and FA were calculated by calibration of the distension curves[16]. From D, ΔD and ΔP, local distensibility and compliance were calculated using the following equations:

$$DC = (\Delta A/A)/\Delta P = (2\Delta D.D+\Delta D^2)/(\Delta P.D^2) \quad (1)$$

$$CC = (\Delta V/L)/\Delta P = \Delta A/\Delta P = \pi(2D.\Delta D+\Delta D^2)/4\Delta P \quad (2)$$

A is cross-sectional area, V is arterial volume, L is length. Depending on the vascular territory intraobserver intersession coefficient of variation varied between 2.1 and 3.3 % for arterial diameter and between 9.2 and 12.8% for the change in diameter[17].

With the vessel wall movement detector system also carotido-femoral transit time of the pulse wave (T) was recorded[18]. The length of the carotido-femoral segment (L_{ao}) was measured with a tape measurer[19]. From length and transit time, the average pulse wave velocity (PWV) in this segment was calculated[20]. Pulse wave velocity is related to arterial distensibility (DC) by the formula:

$PWV = \sqrt{1/\varrho DC}$ (Moens Korteweg[21,22]), (ϱ=blood density).

Database management and statistical analyses were performed with the SAS software (The SAS Institute Inc., Cary, North Carolina). The methods of analysis included Mann-Whitney-U tests for continuous variables and Chi-square tests for the dichotomous parameters. To test the influence of height, an analysis of covariance was used with factors for age, gender, mean arterial pressure, pulse rate, smoking, use of alcohol, total cholesterol and antihypertensive treatment. Factors with a p-value >0.10 were dropped from the model. In addition, the same analysis with height as an additional confounding factor was repeated to investigate the effect of BMI, waist-to-hip ratio and skinfold thickness. To investigate which index of obesity was best related to large artery wall properties, an analysis of covariance with all indices of obesity was done. F values were used to show the importance of the factors to explain variance. Data are presented as mean ±SD for demographic values and mean ±SE for regression coefficients. A p-value <0.05 was considered as statistically significant. The Ethics Committee of Leuven University approved the study and all subjects gave their written informed consent.

RESULTS

The 250 men and 243 women were between 26 and 79 years old (Table 1). Men had a larger body mass index, W-H ratio and blood pressure, while women had a larger skinfold thickness and heart rate. One hundred and fiftynine participants smoked a median of 15 cigarettes per day (range 1-70). One hundred and thirteen subjects drank a median of 20 g alcohol per day (range 1-196). A total of 76 subjects were taking antihypertensive treatment either in monotherapy or in combination. Vessel wall properties in this population are described in Table 2.

Table 1. Demographic characteristics of the study population

	male	**female**	**p**
n	**250**	**243**	
Age (years)	50.4±13.0	49.8±12.3	.61
Body mass index (kg/m^2)	26.0±3.3	25.2±4.0	.005
Waist/Hip ratio	0.89±0.09	0.83±0.12	<.001
Skinfold	1.24±0.47	2.01±0.62	<.001
Blood Pressure (mmHg)†			
Systolic	132±15	128±19	.003
Diastolic	84±10	81±10	<.001
Heart rate (bpm)	61±10	64±10	.001
Smokers	84 (33.6 %)	75 (30.9%)	.52
Drinking alcohol	85 (34%)	28 (11.5%)	<.001
Antihypertensive treatment	38 (15.2%)	38 (15.6%)	.89

Results are mean±SD or number of subjects with percentage in brackets. † Measured with a sphygmomanometer in sitting position. bpm. beats/minute

Table 2. Vessel wall properties in the study population

	male	**female**	**p**
PWV Aorta ↑ (m/s)	7.0±1.9	6.5±1.7	.002
Diameter (mm)			
CCA	7.71±0.79	6.92±0.78	<.001
BA	4.64±0.63	3.61±0.62	<.001
FA	10.06±1.11	8.49±1.09	<.001
Distensibility Coefficient (10^{-3}/kPa)			
CCA	21.4±8.4	21.9±8.6	.62
BA	20.8±10.0	24.4±11.8	<.001
FA	7.9±4.1	9.0±4.7	.012
Compliance Coefficient (mm^2/kPa)			
CCA	1.04±0.32	0.78±0.31	<.001
BA	0.33±0.16	0.21±0.16	<.001
FA	0.63±0.32	0.53±0.16	<.001

Results are mean±SD. ↑Measurements available in 464 subjects. PWV pulse wave velocity, CCA common carotid artery, FA common femoral artery, BA brachial artery

Table 3. Relation between arterial wall properties and height, after adjustment †

Slope++ (height (cm)$^{-1}$).10^2	**male**	**female**
PWV Aorta§ (m/s)	n.s.	n.s
Diameter (mm)		
CCA	1.6±0.7*	1.6±0.7*
BA	n.s.	1.2±0.5*
FA	4.1±1.0***	4.3±0.9***
Distensibility Coefficient (10^{-3}/kPa)		
CCA	n.s.	n.s.
BA	n.s.	n.s.
FA	n.s.	n.s.
Compliance Coefficient (mm^2/kPa)		
CCA	0.9±0.3***	0.5±0.2*
BA	n.s.	n.s.
FA	0.8±0.3**	n.s.

† adjustment for age, mean arterial pressure, heart rate, smoking, use of alcohol, total cholesterol and antihypertensive treatment. ++Regression coefficients ± SE. § Measurements available in 464 subjects. PWV pulse wave velocity, CCA common carotid artery, FA common femoral artery, BA brachial artery, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, n.s. not significant.

In both sexes, after adjustment for age, mean arterial pressure, pulse rate, smoking, use of alcohol, total cholesterol and antihypertensive treatment, height was positively related to carotid and femoral artery diameter and only in women to brachial artery diameter (Table 3).

Height was not related to arterial distensibility. In both sexes height was positively related to carotid artery CC, while only in men there was also a positive relation with femoral artery CC.

In both sexes, after adjustment for the factors mentioned above, BMI was positively related to arterial diameter (Table 4). Except for carotid artery DC in women, BMI was negatively related to DC of all arteries. There was no relation with PWV of the aorta. Only in men, BMI was negatively related to CC of the FA and BA. W-H ratio was not related to vessel wall properties in women. In men W-H ratio was positively related to diameter of the CCA and BA, negatively related to DC of the BA and FA and to CC of the FA. Thickness of skinfold was in both sexes positively related to carotid artery diameter. In women skinfold thickness was negatively related to brachial artery DC. Skinfold thickness did not relate to arterial compliance in both sexes.

Table 5 shows the importance of the different indices of obesity as determinants of the large artery wall properties. W-H ratio was the more important determinant of FA compliance in men, whereas skinfold thickness was the most important determinant of BA distensibility in women. BMI was the most important determinant of all other arterial wall properties, which were related to obesity.

DISCUSSION

This is the first study investigating the association between three indices of obesity and wall properties of different arterial territories. Since body height contributes to body mass, we also analysed the effects of height separately.

The present study showed that taller subjects have a higher compliance of the carotid and femoral arteries. This larger arterial compliance may contribute to a smaller cardiac afterload in taller men. This could contribute to the observation that short men are more prone to ischemic heart disease[23]. This larger compliance was the result of a larger diameter in taller subjects, which was also described by others[24,25]. This result could also partly explain the difference in arterial diameter between men and women, since most women are shorter than men.

Obesity can be defined in different ways. One of the most frequently used indices is BMI. In the present study, the majority of associations between obesity and vessel wall properties were found for BMI.

In accordance with others[8,9,26,27], in the present study, arterial diameter of all arteries studied was

Table 4. Relation between large artery wall properties and BMI, waist-hip ratio and skinfold thickness, after adjustment for confounding factors†

Slope.10[§]	Men BMI kg/m²	Men W-H ratio	Men Skinfold	Women BMI kg/m²	Women W-H ratio	Women Skinfold
Pulse Wave Velocity (m/s)[++]						
Aorta	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Diameter (mm)						
CCA	4.4±0.7**	235.7±77**	23.2±8.9**	21.6±11.2*	n.s.	13.8±6.8*
BA	7.1±1.0***	296.5±59.6***	n.s.	3.3±0.8***	n.s.	n.s.
FA	6.8±2.1***	n.s.	n.s.	5.6±1.4***	n.s.	n.s.
Distensibility (10^{-3}/kPa)						
CCA	-21.1±10.3*	n.s.	n.s.	n.s.	n.s.	n.s.
BA	-82.4±17.6***	-2992±1000**	n.s.	-46.3±18.3*	n.s.	-327.7±11.9**
FA	-25.6±7.3***	-1162±4007**	n.s.	-14.6±6.9*	n.s.	n.s.
Compliance (mm^2/kPa)						
CCA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
BA	-0.5±0.2*	n.s.	n.s.	n.s.	n.s.	n.s.
FA	-1.2±0.6*	-102.1±29.4***	n.s.	n.s.	n.s.	n.s.

† age, mean arterial pressure, heart rate, height, smoking, use of alcohol, total cholesterol and antihypertensive treatment. [++]Measurements available in 464 subjects. [§]Regression coefficients ± SE. PWV pulse wave velocity, CCA common carotid artery, BA brachial artery, FA femoral artery, BMI body mass index, W-H ratio waist to hip ratio, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, n.s. not significant.

Table 5. Covariance analysis with BMI, waist-hip ratio and skinfold thickness together, after adjustment for confounding factors †

	Common Carotid Artery			Brachial Artery			Femoral Artery			Aorta
	D (mm)	**DC 10^{-3}/kPa**	**CC mm^2/kPa**	**D (mm)**	**DC 10^{-3}/kPa**	**CC mm^2/kPa**	**D (mm)**	**DC 10^{-3}/kPa**	**CC mm^2/kPa**	**PWV m/s**
Men										
R2	0.26	0.63	0.45	0.22	0.18	0.08	0.16	0.19	0.19	0.43
F values										
BMI	4.17	4.20	n.s.	30.02	22.02	3.93	18.11	12.25	n.s.	n.s.
W-H ratio	n.s.	n.s.	n.s.	5.53	n.s.	n.s.	6.93	n.s.	12.03	n.s.
Skinfold	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Women										
R2	0.31	0.61	0.38	0.26	0.18	0.08	0.33	0.23	0.11	0.42
F values										
BMI	4.13	n.s.	n.s.	17.27	5.14	n.s.	15.56	4.49	n.s.	n.s.
W-H ratio	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Skinfold	n.s.	n.s.	n.s.	n.s.	8.58	n.s.	n.s.	n.s.	n.s.	n.s.

† age, mean arterial pressure, heart rate, height, smoking, use of alcohol, total cholesterol and antihypertensive treatment. F value is shown if factor was significant in covariance analysis. PWV pulse wave velocity, D diameter, DC distensibility coefficient, CC cross-sectional compliance.

increased in subjects with a higher BMI. This can be the result of the hyperdynamic circulation in obese subjects: obese subjects have a higher cardiac output, stroke volume and circulating blood volume and lower peripheral resistance[28-31]. This hyperdynamic circulation may cause flow-dependent vasodilatation, leading to a larger arterial diameter.

BMI was negatively related to brachial and femoral artery DC in both men and women and carotid artery DC in men. However, like previous studies[5,7], the present study did not find a relation between BMI and aortic distensibility. The exact cause of this higher arterial stiffness is not known. Several explanations could be hypothesized: (1) it could be due to flow-dependent vasodilatation, thereby shifting the wall stress from elastic to more rigid collagen fibres· (2) the increased stiffness is caused by an increased size of adipocytes (surrounding the vessel wall), which may affect the transmural pressure[6]· (3) the increased stiffness could also be due to early atherosclerotic disease. It's however not clear whether a direct relation between obesity and atherogenesis exists. A recent report described an association between adipose tissue and C reactive protein, an inflammatory mediator, which may be directly involved in atherogenesis[32]· (4) it could also be an indirect relation; other factors, which often coincide with obesity, like hyperinsulinemia might be involved[7,33-35]. A decrease in DC may increase wall stress, which may lead to atherogenesis and cardiovascular events[36].

Arterial compliance is determined by arterial diameter and distensibility. The increase in diameter in BMI-based obese subjects was often accompanied by a decrease in arterial distensibility. The net result was no change in arterial compliance of all three arteries in women. In men it resulted in a smaller arterial compliance of the muscular brachial and femoral arteries.

The associations between arterial wall properties and obesity, discussed so far, were based on obesity defined as a higher BMI. BMI is, however, not only an estimate of fat, it also comprises musculoskeletal mass. This means subjects with a high BMI can also be very well trained, non-obese subjects. Other estimates of obesity are waist-to-hip ratio and thickness of skinfold. The waist-to-hip ratio discriminates between fat deposited in the upper (android) and lower trunk (gynaecoid). Lately several reports showed that subjects with an android fat distribution have an increased cardiovascular risk, independent of BMI[11,12]. In the present study, waist-to-hip ratio was not significantly related to large artery wall properties in women. In men waist-to-hip ratio was negatively related to femoral artery distensibility and compliance. This is in line with an earlier study describing a negative relation between distensibility of the abdominal aorta and visceral fat accumulation[37]. Of all three indices of obesity, waist-to-hip ratio was also the most important determinant of femoral artery DC and CC in men, independent of BMI. The reason for this lower distensibility and compliance of the abdominal aorta and femoral artery is not clear. It has been suggested that it could be caused by the pressure of fat, surrounding the artery[37].

Another method to assess fat distribution is by measuring skinfold thickness. In women thickness of skinfold was negatively related to brachial artery DC. Of the three obesity-indices studied, skinfold thickness was also the most important determinant of brachial artery DC in women. The cause of this is not clear, like for waist-to-hip ratio local pressure of fat might be hypothesized. This parameter does not seem to be of importance in determining large artery distensibility and compliance in men.

In conclusion, the present study shows that height is a determinant of the buffering capacity of large arteries, but not of arterial stiffness. The main findings of the study are that associations between obesity and arterial wall properties depend on the index of obesity, gender and the vascular territory. The majority of associations are found with BMI. BMI-based obese subjects have a larger arterial diameter and stiffer arteries in both sexes. Fat distribution assessed by waist-to-hip ratio (an android body habitus) does not appear to be of importance in women, but in men it is associated with a lower femoral artery distensibility and compliance. Skinfold thickness is negatively associated with brachial artery distensibility in women, whereas it does not appear to be of importance in men. Whether the described effects are caused by obesity induced flow-dependent vasodilatation, local pressure of fat or by obesity-induced factors like hyperinsulinemia remains to be further investigated. Also whether these effects are reversible is not fully known. A preliminary study showed an increase in arterial elasticity after weight loss, but this effect could be fully explained by the simultaneous decrease in blood pressure[38]. Two very recent studies showed that physical activity alone[39] or in combination with a program of dietary modification[40], reduced the genetic predisposition to increased central systolic pressure augmentation index and the vascular dysfunction associated with obesity.

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ΠΕΡΙΛΗΨΗ

Zebekakis PE, Nawrot T, van der Heijden-Spek JJ, Staessen JA, Fagard RH, Struijker Boudier HA, Van Bortel LM, Lasaridis AN. **Παχυσαρκία, κατανομή του σωματικού λίπους και ελαστικές ιδιότητες των μεγάλων αρτηριών.** *Arterial Hypertension 2004; 13: 00.*

Οι ελαστικές ιδιότητες του τοιχώματος των μεγάλων αρτηριών – η ευενδοτότητα (compliance) και η διατασιμότητα (distensibility) – είναι πολύ πιθανό να παίζουν σημαντικό ρόλο στην εξέλιξη της καρδιαγγειακής νόσου. Σκοπός αυτής της μελέτης ήταν να διερευνήσει τις σχέσεις μεταξύ των δεικτών της παχυσαρκίας – ενός ανεξάρτητου δείκτη καρδιαγγειακού κινδύνου- και των ελαστικών ιδιοτήτων (της ευενδοτότητας και της διατασιμότητας) των μεγάλων αρτηριών. Σε δείγμα πληθυσμού αποτελούμενο από 250 άνδρες και 243 γυναίκες, ηλικίας 20-79 ετών, μετρήθηκαν με ειδική συσκευή υπερήχων η διάμετρος και οι συντελεστές διατασιμότητας (ΣΔ) και ευενδοτότητας (ΣΕ) των ελαστικού τύπου αρτηριών [αορτή και κοινή καρωτίδα (ΚΚ) και των μυϊκού τύπου αρτηριών, βραχιόνια (ΒΑ) και μηριαία αρτηρία (ΜΑ)]. Στη συνέχεια εκτιμήθηκαν, με ή χωρίς διόρθωση, ως προς συνυπάρχοντες παράγοντες, οι σχέσεις του δείκτη μάζας σώματος (ΔΜΣ), του λόγου περιμέτρου μέσης / ισχίων (W/H ratio) και του πάχους της δερματικής πτυχής (ΠΔΠ) με τις παραπάνω αγγειακές παραμέτρους-δείκτες των ελαστικών ιδιοτήτων των αρτηριών. Ο ΔΜΣ σχετιζόταν θετικά και στατιστικά σημαντικά ($p<0.01$) με την αρτηριακή διάμετρο σε όλα τα αγγεία. Η παχυσαρκία δεν σχετιζόταν σημαντικά με την αρτηριακή σκλήρυνση. Με εξαίρεση τον ΣΔ της κοινής καρωτίδας στις γυναίκες, ο ΔΜΣ σχετιζόταν αρνητικά ($p<0.05$) με τον ΣΔ της ΚΚ, της ΒΑ και της ΜΑ τόσο στους άνδρες, όσο και στις γυναίκες. Ο ΔΜΣ σχετιζόταν επίσης αρνητικά με τον ΣΕ της ΒΑ ($p<0.05$) και της ΜΑ ($p<0.05$) μόνο στους άνδρες. Η αύξηση του δείκτη W/H σχετιζόταν αρνητικά με τον ΣΔ και τον ΣΕ της ΜΑ ($p<0.01$) στους άνδρες. Το πάχος της δερματικής πτυχής συσχετιζόταν αρνητικά με τον ΣΔ της ΒΑ στις γυναίκες ($p<0.01$). Συμπερασματικά, οι συσχετίσεις μεταξύ των δεικτών της παχυσαρκίας και των ελαστικών ιδιοτήτων των αρτηριών εξαρτώνται από το είδος του εξεταζόμενου δείκτη, το φύλο και την αγγειακή περιοχή που μελετάται. Γενικά, οι συσχετίσεις που βασίζονται στον ΔΜΣ είναι πιο ισχυρές απ' ότι αυτές που βασίζονται στο λόγο W/H ή το πάχος της δερματικής πτυχής. Έτσι, οι παχύσαρκοι, σύμφωνα με τον ΔΜΣ έχουν αρτηρίες με μεγαλύτερη διάμετρο και σκλήρυνση του τοιχώματός τους, η οποία θα μπορούσε να αποδοθεί σε εξαρτώμενη από τη ροή αγγειοδιαστολή. Οι επιδράσεις του λόγου W/H στις ελαστικές ιδιότητες των αρτηριών είναι πιο έκδηλες στους άνδρες, ενώ του πάχους της δερματικής πτυχής είναι πιο έκδηλες στις γυναίκες.

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