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The Cervical Fat Tissue Volume is a Predictor for Moderate to Severe OSA

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Abstract

Objective Obstructive sleep apnea (OSA) is a disorder characterized by recurrent pharyngeal obstruction during sleep, in which upper airway anatomy plays a key role in its pathogenesis. The aim of this study was to describe whether the quantification of cervical fat tissue volume (CFTV) obtained by Computed Tomography (CT)cephalometry is related to the severity of OSA.

Methods Retrospective study between 2018 and 2020 in those patients > 18 years old, with diagnosis of OSA who performed a volumetric cephalometric imaging. Three-dimensional reconstruction of the images was performed and CFTV was measured.

Results 91 patients were included in this study of which: without OSA (n: 7), mild (n: 19), moderate (n: 39) and severe OSA (n: 26). We observed a progressive increase of CFTV related to OSA severity has been observed (without OSA: 58.9 ml (47.9-87.5), mild: 59.1ml (48.4-78.3), moderate: 71 ml (42.6-127.1) and severe OSA 103.6 ml (81-153); $p < 0.01$); nevertheless, no differences were found in the airway volume and neck area. It was showed a significant correlation between CFTV and OSA indicators: AHI, ODI and T90 (Sp r: 0.48; 0.38 and 0.36; $p < 0.01$ respectively). CFTV cut-off value to discriminate AHI >15 ev/h with best sensitivity-specificity relationship was 64.1 ml with an area under the curve of 0.6 ± 0.06. Multivariate analysis showed that CFTV is a predictor for moderate to severe OSA (OR:3.05, IC95%: 1.14-8.17).

Conclusion Cervical fat quantification by CT cephalometry correlates with OSA severity in adults. Fat volume > 64.1 ml increased more than three times the risk of OSA moderate to severe.

Keyword
- sleep apnea obstructive
- adiposity
- cephalometry

Introduction

International consensus of obstructive sleep apneas (OSA), has defined OSA as either, presence of an apnea-hypopnea index (AHI) ≥ 15/h, or presence of an AHI ≥ 5/h plus symptoms related to excessive tiredness.[1] OSA is a global public health problem which affects at least 936 million individuals aged 30 to 69 years,[2] whose prevalence is variable between 9% and 38%.[3–5]OSA is characterized by repeated collapse of the upper airway during sleep and it is associated with factors like as: obesity, gender, age and neck circumference.[6]

For diagnosis of OSA polysomnography (PSG) or respiratory polygraphy (RP) are validated as reference methods, however cannot reveal the locations of airway obstructions.

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Computer tomography, magnetic resonance imaging, nasolaryngoscopy with an optic fiber and lateral cephalogram can be used to detect airway obstructions. Lateral cephalogram and nasolaryngoscopy with optic fiber are diagnostic tools that aid in establishing the accurate location of the obstruction, which is a key element in treatment planning and prognosis in patients with OSA.[7,8] Morphological changes associated with apnea episodes have been described.[9,10]

It has been previously demonstrated that neck circumference is a specific indicator of OSA risk, especially in patients with excess neck fat deposition in the anterolateral neck.[11,12] Neck adipose tissue is directly associated with apnea hypopnea index (AHI) and represents an important characteristic associated with the presence accumulation and development of this collapse.[13,14] Moreover, Kritikou et al. has shown that in middle-aged adults, central and visceral adiposity are predominant risk factors for OSA, independent of obesity.[15] The accumulation of visceral fat may contribute to a reduction in longitudinal tracheal traction forces, which predisposes tracheal traction forces, predisposing to upper airway narrowing.[14]

Recently analyzed the association between adiposity phenotypes with respiratory disturbances in normal weight youth. For this purpose, dual-energy X-ray absorptiometry (DXA) studies were performed to determine the composition of subcutaneous (SAT) and visceral (VAT) adiposity.[16] It was shown that central adiposity predicts sleep disturbances even in individuals who have never been overweight.

With the aim to describe whether the quantification of cervical fat by CTcephalometry is associated with the OSA severity.

Material and Methods

Design of the Study

Retrospective study conducted between January 2018 and January 2020 from patientsover 18 years of age with a diagnosis of OSA in which the volume of fatty tissue was quantified using CT cephalometric images. This study has been approved by the Ethics Committee of the British Hospital (#2657).

Diagnosis of OSA was performed by recording of ambulatory respiratory polygraphy.Patients with insomnia, neurologic disorders, periodic limb movements or suspected non-respiratory sleep disorders were excluded. Patients with airways surgical procedures in last 2 years were excluded.

Computed Tomography Cephalometric

Images from the PACS system were reviewed, which were obtained in two multislicescanners, an 80-detector row and a 16- detector row. From the data obtained, the adipose tissue was extracted for 3D image reconstruction and fat volume measurement. Segmentation was carried out with semi-automatic analysis of the Hounsfield Units.

Two areas of interest were taken into account for this analysis. The first was an axial volume that covers from the lowest tip of the soft palate to the highest portion of the epiglottis. In this area, the volume of fat and the volume of the airway was measured semi-automatically in millilitres. The retrolingual area was selected because there are studies carried out by Welch et al[14] that showed that weight loss produced a greater change in the diameter of the airway in this selected area.

The second one was a single axial section where the airway has its smallest cross-sectional area. We measured the anteroposterior (AP) distance and the lateral width (LW). At the time of imaging, the patients were awake and in supine position, ►**Fig. 1**.

Cervical fat tissue volume (CFTV) was determined by Synapse 3d™ software (Fujifilm Healthcare™).

Respiratorypolygraphy (RP)

RP recordings were taken at night (1 night only) at patients' homes using a self-administered technique (i.e., the patient sets and starts the RP device before falling asleep). Patients received proper training on the use of the device at the

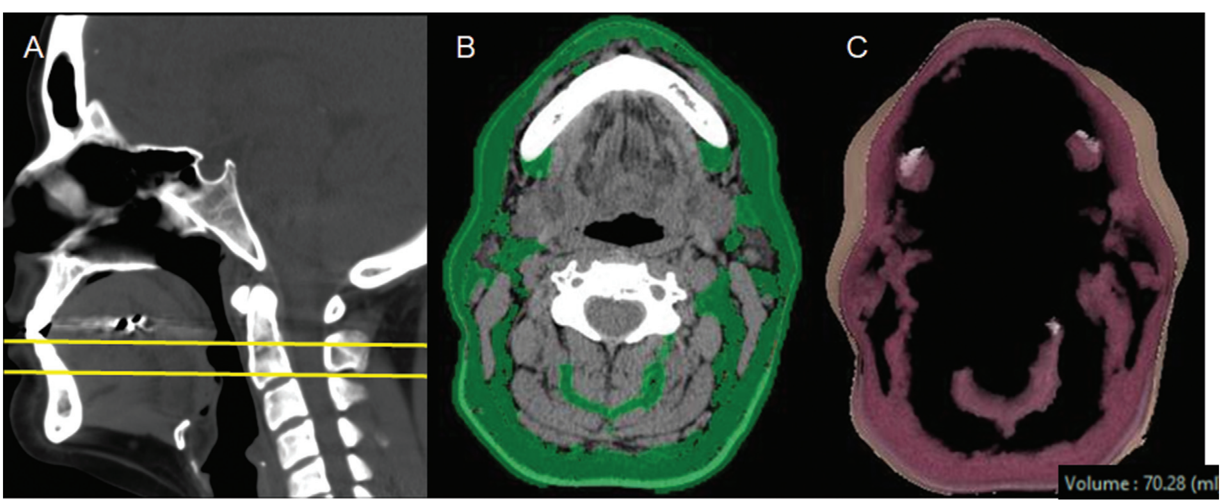

Fig. 1 Cervical fat volume quantified by CT. (**A**) Sagittal reconstruction showing the region of interest between lowest tip of the soft palate and the highest portion of the epiglottis. (**B**) Segmentation carried out with semiautomatic analysis of the Hounsfield units. (**C**) Fat tissue extracted for 3D image reconstruction and fat volume measurement.

hospital the morning before the test. The training session lasted 20 minutes and was delivered by nurses with experience in sleep medicine. Additionally, patients received an instruction manual withp res and information on how to set the device.RP devices used in this study were Apnea Link Plus-Air (ResMed; Australia) and Alice Night One (Philips-Respironics; USA). All polygraph data from at least three basic signals: pulse oximetry, thoracic effort band, and nasal Recordings were analysed in 3-5 minutes' epochs pressure canula. Ancillary signals included body position, actigraphy, and snoring. When necessary, respiratory events were corrected manually. Recording sections with low quality signals or transient disconnections were removed. Only recordings with a valid total recording time (TRT) of > 240 minutes (> 4 hours) were accepted.

Statistical Analysis

Categorical data are presented as absolute numbers and percentages, and continuous data as median and interquartile ranges (IQR). Comparison of categorical variables between groups was conducted using the chi2 test or the Fisher's exact test. To compare continuous variables among groups, Kruskal-Wallis test. We used Tukey's multiple comparisons test as post hoc range tests.Apnea and hypopnea were defined as a > 80% drop from baseline airflow for ≥ 10 seconds and a 50% drop for ≥10 seconds associated to ≥ 3% oxygen desaturation, respectively. The AHI was calculated as the number of apneas/hypopneas events per hour (ev/h) of valid TRT. Patients were classified either as normal (AHI < 5 ev/h), mild (AHI ≥ 5 and < 15ev/h), moderate (AHI ≥ 15 and < 30ev/h), or severe (AHI ≥ 30ev/h). Oxygen desaturations index (ODI) in ev/h was considered with de same cut-off.Time below saturation threshold 90% (T90) was measure automatically.

The cut-off value for neck fat volume was calculated to discriminate AHI ≥ 15 ev/h using ROC curves.To evaluate contribution of CFTV for presence of moderate to severe OSA (IAH ≥ 15 ev/h)a multivariate logistic regression model was analyzed.

Results

A total of 91 patients with a mean age of 49 years (39-57.2) were included in this study, 73.3% (n:67) of them were men. They were grouped according to AHI; without OSA (n: 7), mild (n: 19), moderate (n: 39) and severe OSA (n: 26). A progressive increase in BMI and obesity proportion related to OSA severity was observed, which was statistically significant between patients without OSA and severe OSA (►**Table 1**).

The findings have shown a progressive increase in neck diameter greater than 40 cm in women or greater than 42 cm in men (16% from patients without OSA, 33.3%mild, 52.6% moderate and 64% of severe OSA) ►**Fig. 2A**.

Similarly, a progressive increase ofCFTVrelated to OSA severity has been observed (without OSA: 58.9 ml (47.9-87.5), mild: 59.1ml (48.4-78.3), moderate: 71 ml (42.6-127.1) and severe OSA 103.6 ml (81-153); p < 0.001). ►**Fig. 2B**.

No differences were found in theairwayvolumeand neck area from patients with OSA grouped by severity. Airway

Table 1 Clinical and demographic characteristics from populations studied grouped by OSA severity

	Without OSA	Mild OSA	Moderate OSA	Severe OSA	Total	p
n	7	19	39	26	91	
Male (n, %)	4 (57.1%)	12 (63.1%)	29 (74.3%)	19 (52.7%)	67 (73.6%)	0.27
Age	37 (33-40)	49 (39-57)	50 (39-55)	45 (41-60)	49 (39-57.25)	0.27
BMI ≥ 30 (kg/m^2)	27 (25-29)	29 (26-32)	30 (27-33)	31 (29-35)	30 (27-32.25)	**0.04**
Overweight (n, %)	5 (71.4%)	9 (50%)	15 (39.6%)	9 (34.6%)	38 (41.7%)	0.47
Obese (n, %)	1 (4.5%)	7 (36.8%)	22 (56.4%)	17 (65.4%)	47 (51.6%)	**0.04**
Glycemia mg/dl	95 (84-144)	95.5 (90.25-101.8)	96 (92-99)	103 (97-120.5)	98 (92-103)	0.06
HDL mg/dl	–	47 (40.5-57)	44.5 (37.5-51.7)	45 (37-55)	45 (38-54)	0.94
Triglycerides mg/dl	–	136.5 (75.2-232.8)	127 (100-195)	138 (86-193)	132.5 (91.7-197.8)	0.88
Systolic blood pressure	110 (90-125)	115 (106.3-128.8)	124 (115.5-134.5)	120 (115-133)	120 (110-130)	0.46
Diastolic blood pressure	70 (60-80)	73.5 (70-80)	76.5 (70-86.7)	79 (70-88)	75.5 (70-82.2)	0.71
ESS	9.5 (5-12)	5 (4-8)	8 (4-11)	7 (3.25-12.5)	7 (4-11)	0.67
ESS≥ 10	4 (57.1%)	3 (15.8%)	12 (30.7%)	7 (26.9%)	26 (28.6%)	0.35
AHI (ev/h)	4 (2.8-4)	10.7 (7.2-13)	21 (17-23)	48.6 (42-71.1)	20 (13.2-32.5)	0.001
ODI (ev/h)	3 (2.5-5.7)	11 (8.9-12.7)	19 (17-23)	43 (38-67.5)	18.2 (12-33)	0.001
T < 90 (%)	0 (0-0)	2 (1-12)	10 (2-20)	36 (7-57)	6 (1-24)	0.001

(Obese was considered BMI ≥ 30 (kg/m^2) and overweight BMI between 25.1 and 29.9 kg/m^2, ESS: Epworth Sleepiness Scale).

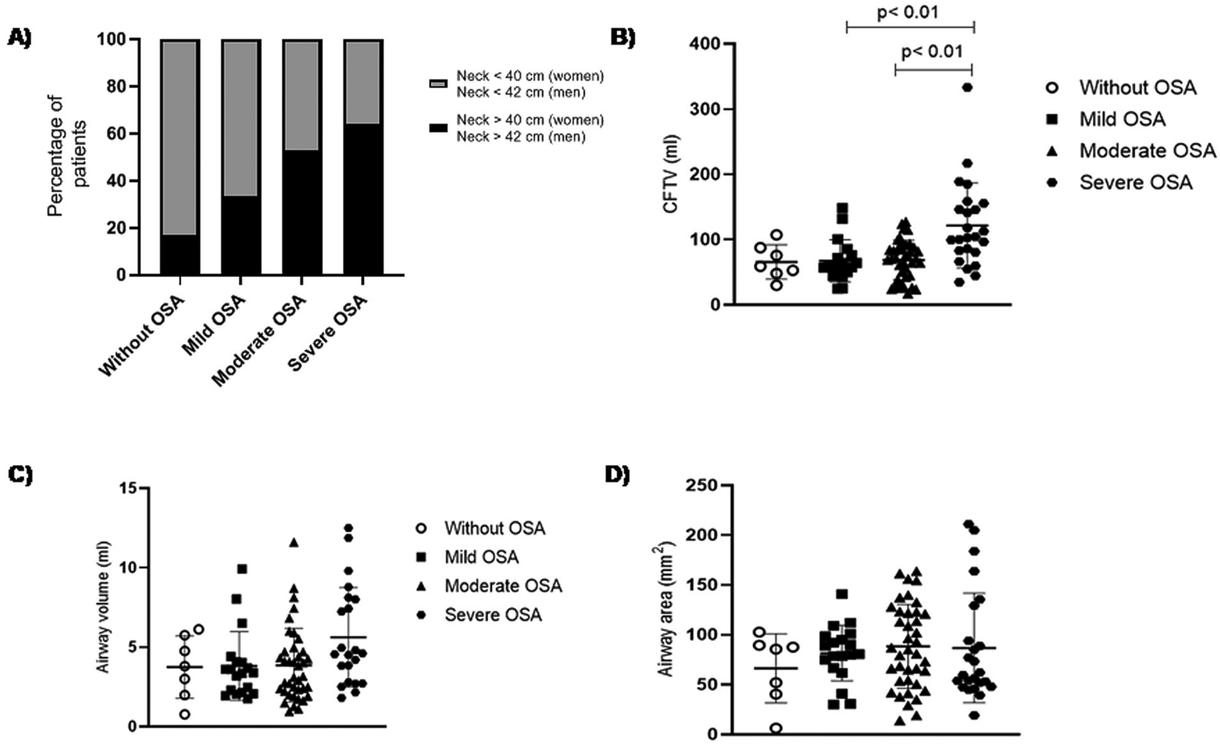

Fig. 2 Relationship between neck circumference and OSA severity (**A**) Percentage of patients with diameters of neck > 40 cm (female) or > 42 cm (men), (**B**) Total fat volume, (**C**) Airway volume and (**D**) Airway area.

volume: 3.8 ml (1.9-5.7), 3.4 ml (2.1-4.1), 3.1 ml (2.2-4.7) and 8.1 ml (4.6-18.8), and the neck area 85.6 mm^2 (40.5-89.6), 80.6 mm^2 (66.5-98.5), 85 mm^2 (53.5-123) and 60.9 mm^2(48.9-211); respectively, ►**Fig. 2 C** and **D**.

It was showed a statistically significant correlation between CFVT and OSA indicators: AHI, ODI and T90 (Sp r: 0.48; $p < 0.001$, 0.38; $p < 0.001$ and 0.36; $p < 0.01$ respectively), ►**Fig. 3 A-C**. Nevertheless, there was no correlation with airway volume (Sp r: 0.24; p: 0.07, 0.16; p: 0.13 and 0.08; p: 0.6) and airway area (Sp r: -0.08; p: 0.4, -0.17; p: 0.11 and -0.24; p: 0.17 respectively), ►**Fig. 3 D-I**.

CFVT cut-off value to discriminate AHI > 15 ev/h with best sensitivity-specificity relationship was 64.1ml (sensitivity of 71.4%; 95% CI: 58.5-82.1%, a specificity of 61.4%; 95% CI: 40.6-79.8%) with an area under the curve of 0.6 ± 0.06.

In a multivariate analysis adjusted for age and male gender and BMI, CFTV> 64.1 ml is a predictor for moderate to severe OSA (OR: 3.05, IC95%: 1.14-8.17).

Discussion

This study shows that CFVT quantification by CT cephalometrycorrelate with OSAseverity.The adipose distribution in the neck quantified by this method obtained better performance as OSA predictor and nocturnal hypoxemia than other classical measurements of airwaysvolume and area.

In our analysis, a CFTV> 64.1 ml increased more than three timestheprobabilitiesof showing a AHI > 15 ev/hour.

A recent study based on 119 obese adolescents studied by polysomnographyandMR (Magnetic Resonance) with cervical fatvolumetric analysis, found a relationship between neck adiposity and cervical circumference (especially in womenwith obesity), although it did not find a relationship with OSA severity.[17] Demographic characteristics of our population were different, the older adult population with OSA has different upper airway collapse factors than younger populations where the intraluminal soft content (adenoid or glandular tissue) is lower, with a higher representation of obesity-related disorders.

In accordance with our findings, have recently been shown that visceral adiposity is strongly associated with OSA severity in patients older than 65 years of age independently of obesity. However, in patients younger than 65 years, a BMI greater than 24.7 kg/m2 and a ratio of visceral to subcutaneous fat volume greater than 0.54 resulted in an area under the ROC curve greater than 0.66 for predicting moderate to severe OSA, concluding that in non-elderly subjects, overall adiposity is strongly related to the severity of OSAS. The authors defined the overall adiposity as the ratio of visceral fat to subcutaneous fat as determined by bioimpedance. In our study, was only measured cervical fat volume.[18]

Lui Y et al, have suggested that age modifies the associations between obesity indices and OSA severity. Their results showed that an increase in BMI was independently associated with an increase in AHI for men < 40 years old, nevertheless, in men > 40 years old this increase was lower. The authors observed a similar pattern with respect to the relationship of OSA severity to neck diameter.[19] No correlation between the severity of AOS and age was found in our analysis. This is probably because the patients we included are mostly young adults, which does not contribute to

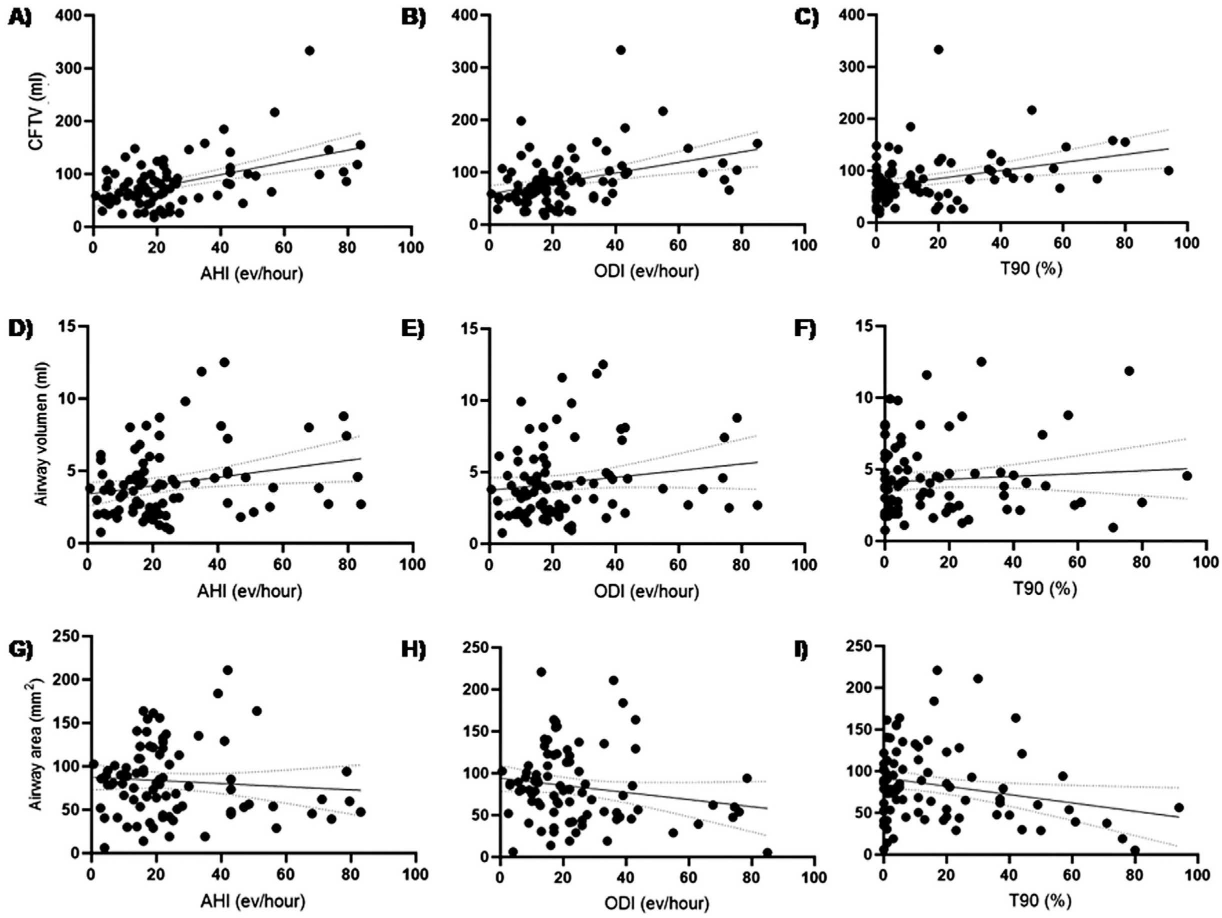

Fig. 3 A–C Relationship between neck fat volume and AHI, ODI and T90%. D–F. Relationship between volume of the airway volume and AHI, ODI and T90%. D–I. Relationship between airway area and AHI, ODI and T90%.

evaluate the role of age in severity. Our result shows that cervical fat volume is associated with moderate to severe AOS independent of age and BMI.

CFTVmay be a risk factor for OSA in adults, when tonsils and adenoids are smaller in relation to the airway volume.[20] Evidence suggests that fat deposition and increased of soft tissue volume in the airway contribute to OSAseverity.[21,22] Patients with confirmed OSA have larger soft tissue structures surrounding the upper airway, including lateral pharyngeal walls and greater tongue fat volume compared to patients without OSA.[23]

Our study has limitations. Retrospective design carried the typical associated restrictions.The smaller sample in normal-weight group difficult comparisons and limit our interpretation.

Our findings suggest that quantitative measurement (CFTV) was related with moderate to severity OSA and hypoxemia.

To conclude, cervical fat quantification by CT cephalometry correlates with OSA severity in adults. Fat volume >64.1 ml increased the risk of OSA moderate to severe. More studies with a higher number of patients are necessary to confirm our results.

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Conflict of Interest
All authors certify that they have non-conflict of interest.

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