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Research Article

Lifestyle Modifications Reduce Blood Pressure in Obese Hypertensive Patients Independently of the Obesity Phenotype and Weight Changes

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Abstract

Despite the overwhelming evidence that weight reduction lowers blood pressure (BP), the magnitude of the effects and whether obese hypertensive with higher or lower BP andbody weight mightbenefit in a different way from weight lossis still unclear. Four hundred and ninety obese hypertensive patients (32.6%, class I, 41.2 % class II and 26.1% class III obesity) entered a 3-month lifestyle intervention. The intervention induced a significant reduction in weight (-4.9 %,-4.8 kg), SBP (-6.3%, - 9.3 mmHg) and DBP (-4.3%, -3.9 mmHg). In patients who lost >10% of weight, DBP decrease was significantly greaterthan in those who lost less weight. The SBP and DBP reduction was similar in the 3 classes of obesity and was stronger in patients with uncontrolled hypertension:-23.6 mmHg (95% CI, -26.3 to -20.8) of SBP and -9. 2 mmHg (95% CI,-11.2 to -7.2) of DBP. SBP and DBP changes were strongly correlated with pre-intervention BP levels (r – 0.623 for SBP and r – 0.613, for DBP, p< 0.0001 for both). SBP was very slightly associated with weight changes (r 0.116, p<0.01).BP changes were unaffected by age, sex, presence of metabolic alterations, family history of obesity, cardiovascular diseases and diabetes and by changes in waist circumference, fat mass and metabolic variables. Baseline BP values explained 38.8% of variance of SBP changes and 37.4% of DBP changes, whereas weight changes explained only 1.7% of SBP changes. In conclusion, in obese hypertensive patients short-term lifestyle changes lead to a clinically significant BP reductionthat is independent of degree of obesity, age, sex and concomitance of metabolic alterations. The efficacy of intervention is greater in patients with higher BP levels and has a nonlinear relation with weight changes.

ABBREVIATIONS

SBP: systolic blood pressure; DBP: diastolic blood pressure; IFG: impaired fasting glucose; IGT: impaired glucose tolerance; GFR: glomerular filtration rate; FH: family history; CVD: cardiovascular disease; BMI: body mass index; HDL: high density lipoprotein; LDL: low density lipoprotein

INTRODUCTION

Raised BMI is a major risk factor for cardiovascular diseases, which are the leading cause of death. Hypertension is very common in obese patients and is interrelated with other major risk factors of death like hyperglycemia and physical inactivity [1]. The obesity-related hypertension is associated with a more common treatment-resistant hypertension and is a major challenge in the management of hypertension [2]. This form of hypertension is a distinct phenotype in view ofits complexpathophysiology that involves adipose tissue dysfunction, adipokine alterations, insulin resistance, and dysfunctional immunity, inappropriate activity of the sympathetic nervous system and renin-angiotensin-aldosterone system and abnormal renal and vascular function [2]. Anyhow, the rootof these alterations is theexcessivefat accumulation that is mostlydue to unhealthy behaviors such as food overconsumption and physical inactivity.Weight reduction is therefore recommended for the treatment of the obesity-related hypertension [3].

Despite the overwhelming evidence that weight reduction lowers blood pressure (BP) in hypertensive and non-hypertensive obese patients [3,4], some issues remain unclear.

A Cochrane review published in 2011 in overweight patients with essential hypertension, showed that a body weight reduction of approximately 4 kg is necessary to reduceSBP by approximately 4.5 mm Hg and DBP by 2 mm Hg. However, the magnitude of the effects as well as whether patients with higher or lower BP or higher or lower body weight mightbenefit in a different way from body weight reduction remains unclear [5].

A recent randomized study in 101 patients with severe obesity, reported that each kg of weight loss induced by lifestyle intervention is associated with a 1 mm Hg reduction in SBP of and 0.92 mm Hg in DBP and the intervention efficacy in reducing BP is greater in class II and III than in class I obesity [6]. Studies in hypertensive patients with severe obesity are scarse and whether the BP reduction observed after lifestyle modifications is proportional to weight loss is undefined.

This study investigated what factor spredict the magnitude of BP reduction in a large cohort of hypertensive obese patients who underwenta3-month weight loss lifestyle intervention.

MATERIALS AND METHODS

The study sample consisted in 490white obese patients who had been treated with one or more antihypertensive drugs for at least 6 months. Patients were recruited between 2008 and 2014 from obese individuals referred to the Istituto Auxologico Italiano for a weight-loss lifestyle intervention.In all subjects, information on smoking habits, use of medications and family history of obesity, diabetes and cardiovascular disease was collected.

Participants entered a 3-month lifestyle intervention which consisted in weekly individual sessions for nutritional education, advice reinforcement on exercise activity and peer group psychological support. A self-monitor diary including food consumption, daily physical activity and emotional reactions was used as a tool for education and reinforcement.Daily caloric requirement was calculated using the Harris-Benedict equation and an individual activity factor.A diet based on a 500-kcal/d deficit from the individual estimated caloric requirement was prescribed. Diet included 25% of total energy intake as protein, 20% as fat and 55% as carbohydrate, was high in vegetables, low in salt and simple sugars. Fresh foods, at least three fish meals per week and avoiding alcohol was recommended. A physical activity program was prescribed consisting in 210 minutes per week (70% of moderate-intensity aerobic physical activity and 30% of muscle-strengthening activities).

Before and after the 3-month lifestyle intervention, anthropometric measures, BP and heart rate were measured and body compositionassessed by bioelectric impedance assay (BIA 101-RJL Systems Akern srl, Firenze, Italy). Waist circumference was measured at the level of the umbilicus. Blood pressure was measured in a sitting position, three times every 5 min with a standard mercury sphygmomanometer and a cuff size optimized for arm circumference. Phase I and V (disappearance) Korotkoff sounds were used to identify SBP and DBP. Patients were defined as having uncontrolled hypertension if having mean BP levels≥140/90 mmHg.

A blood sample was taken for the measurement of glucose, HDL and LDL cholesterol, triglycerides, uric acid,creatinine.Three morning urine samples were collected for the measurement of albumin/creatinine ratio. Microalbuminuria was definedby meanalbumin/creatinine ratio ≥2.5 (men) and 3.5mg (women) $mmol^{-1}$.

In non-diabetic subjects, the oral glucose tolerance test was performed for the measurement of glucose and insulin. Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) were defined using the American Diabetes Association criteria [7]. Dyslipidaemia was defined by the presence of high triglycerides (≥150 mg/dl) and/or low HDL cholesterol (<40 mg/dl in men and <50 mg/dl in women) or the use of lipid-lowering therapy. Glomerular filtration rate (GFR) was estimated using the recalibrated version of the four-variable Modification of Diet in Renal Disease study equation [8].Metabolic syndrome was defined using the National Cholesterol Education Program, Adult Treatment Panel III criteria [9].

The Ethics Committee of our Institute approved the study, and informed consent was obtained from all subjects after a full explanation of the study.

Biochemical measurements

Glucose, lipids, uric acidand creatinine were measured using an automated analyzer (Roche Diagnostics, Mannheim, Germany). Insulin was measured by a chemiluminescent assay (Roche Diagnostic, Mannheim, Germany) with a sensitivity of 0.2 μU/ml and intra- and inter-assay CV of 3.3 and 4.1%, respectively. Urine albumin excretion was determined by an immunoturbidimetric assay (Roche Diagnostics, Mannheim, Germany).

Statistical analyses

Variables that were not normally distributed were log transformed for the analysis.Changes induced by lifestyle intervention were calculated as the ratio between the value at the end of intervention less baseline value, and baseline value.Analysis of variance was used to compare differences among groups. Frequencies were compared using a χ^2 test. Pearson correlation analyses were used to evaluate bivariate relationships. Test *t* for one sample was used to analyse changes from baseline. Linear regression analysis was performed to assess the proportion of the variance of BP changes explained by baseline BP levels and weight changes. A probability value < 0.05 was considered significant. Data are given as the means ± SD or median (interquartile range) for variables that were not normally distributed. Changes induced by the intervention are expressed as mean (95% CI). All analyses were performed using SPSS version 21.0 (SPSS, Chicago, IL, US).

RESULTS

Characteristics of obese hypertensive patients

Before the intervention, 29.6% of patients were on β-blockers, 30.6% on angiotensin-converting enzyme inhibitors, 34.9% on angiotensin receptor blockers, 32% on diuretics, 14.7% on calcium antagonistsand4.2percentage on α-blockers. One hundred and one patients (20.7%) had uncontrolledhypertension (47.5% hadisolated systolic uncontrolled hypertension).

The proportion of participants belonging class I, II and III obesity was 32.6%, 41.2 % and 26.1% respectively. (Table 1) shows the baseline characteristics of the 490 obese hypertensive patients according to the obesity class. Levels of BP, heart rate, fasting glucose and insulin were higherand those of HDL cholesterol lower in patients with a more severe obesity. Despite the youngest age, class III patients included the highest proportion of uncontrolled hypertension and metabolic alterations.

Table 1: Baseline characteristics of 490 obese hypertensive patients according to the obesity class.

	BMI 30-34.9 kg/m² n=160	BMI 35-39.9 kg/m² n=202	BMI≥ 40 kg/m² n=128
Age, years	61.1±9.8	59.9±9.9	56.1±10.1***
Men, %	27.5	23.8	28.9
FH for obesity, %	59.4	61.2	67.7
FH for diabetes, %	44.9	55.2	55.1
FH for CVD, %	50.0	46.8	46.0
BMI, kg/m²	32.7±1.5	37.3±1.4	43.9±3.6***
Weight, kg	86.2±8.9	96.5±12.1	114.2±16.6***
Waist circumference, cm	109.8±6.6	116.8±7.6	129.4±9.9***
Fat mass, %	43.5±6.4	46.9±6.2	48.7±6.4***
Fat free mass, %	56.3±7.1	53.1±6.5	51.3±6.4***
Systolic BP, mmHg	130.1±14.3	133.5±13.4	134.7±14.1*
Diastolic BP, mmHg	78.7±6.9	82.0±7.2	81.3±7.6***
Heart rate, beats/min	72.2±12.5	74.9±12.4	76.7±12.8*
Uncontrolled hypertension, %	15.0	19.3	29.7**
Fasting glucose, mg/dl	101.3±23.3	102.4±23.5	114.4±48.4**
Fasting insulin, µU/ml	10.0(7.2-14.8)	12.7(8.3-19.7)	14.5(8.9-22.4)***
HDL cholesterol, mg/dl	55.4±17.5	54.7±13.8	49.1±10.1**
LDL cholesterol, mg/dl	126.0±35.4	122.8±31.4	124.6±34.7
Triglycerides, mg/dl	115.0(86.0-144.0)	114.0(91.0-149.0)	119.0(93.5-147.7)
Uric acid, mg/dl	5.7±1.4	5.8±1.2	5.8±1.2
Smoking status, %	10.0	7.0	10.0
Diabetes, %	18.8	19.3	29.4*
IFG/IGT, %	25.0/11.3	24.0/14.2	29.2/19.6
Dislypidemia, %	52.0	48.5	62.1*
Metabolic Syndrome, %	67.7	67.7	76.6
Microalbuminuria, %	13.6	13.4	23.7
GFR < 60 mL/min	16.6	14.7	12.2

*p<0.05, **p<0.005, ***p<0.0001for trend

FH: family history; CVD: cardiovascular disease; BMI: body mass index; BP: blood pressure; HDL: high density lipoprotein; LDL: low density lipoprotein; GFR: glomerular filtrate rate; IFG: impaired fasting glucose; IGT impaired glucose tolerance. Insulin levels and percentage of IGT refer to data obtained in non diabetic patients. Data are expressed as mean ± SD except for triglycerides and insulin that are expressed as median (interquartile range).

Compared to patients with controlled hypertension, patients with uncontrolled hypertension were more obese (BMI 39.3±5.5 vs 37.14.5 kg/m2; waist circumference 116.9±10.6 vs 121.0±11.8 cm, p<0.01 for both) but had similar age, sex, body composition, uric acid, albumin/creatinine ratio, family history of obesity, cardiovascular diseases and diabetes and prevalence of glucose abnormalities, microalbuminuria, renal insufficiency (GFR <60mL/min)and tobacco use. Mean SBP and DBP levels of patients with uncontrolled hypertension were 153.3±9.7 and 87.6±7.5 mmHg respectively.

Effects of 3-monthlifestyle intervention

In the whole cohort of obese hypertensive patients, the intervention induced a significant reduction in weight [average-4.9 % (95% CI -5.2 to -4.7), -4.8 kg (95% CI-5.1 to-4.6), p<0.0001 vs baseline], and BP [average SBP -6.3% (95% CI-7.3 to -5.4),- 9.3 mmHg (95% CI -10.6 to -8.0) ; average DBP-4.3% (95% CI -5.2 to -3.4),-3.9 mmHg (95% CI -4.7 to -3.2), p < 0.0001 vs baseline].Fiftysix percent of patients lost less than 5% of baseline weight, 39% between 5 and 10% and 5 % more than 10%.In patients who lost >10% of weight,SBP and DBP decreased significantly more than in those with lower weight loss (Figure 1).

Figure 2 shows the mean relative changes in obesity indexes and BP obtained with the intervention in the classes of obesity. Obesity indexes and BP decreased to the same extent inthe three classes of obesity. SBP decreased by an average 8.5 mmHg (95% CI -10.7 to -6.3) in class I, 9.8 mmHg, (95% CI,-11.9 to-7.8)in class II and 9.5 mmHg (95% CI, -12.1 to -6.8)in class III (p<0.0001 vs baseline for all). DBP decreased by an average 3.1 mmHg, (95% CI, -4.3 to -1.8) in class I, 4.7 mmHg (95% CI, -5.8 to -3.5)in class II and 3.8 mmHg (95% CI, -5.4 to-2.2)in class III (p<0.0001 vs baseline for all).

In patients with uncontrolled hypertension, despite weight changes similar to patients with controlled hypertension,the intervention induced a stronger BP decrease:-23.6 mmHg (95% CI, -26.3 to -20.8) of SBP and -9. 2 mmHg (95% CI,-11.2 to -7.2) of DBP (p<0.0001 vs patients with controlled hypertension).BP levels were normalized by the intervention in 88.1% of these patients.

Predictors of BP changes

In the univariate correlation in the whole cohort of obese patients, SBP and DBP changes were strongly correlated with pre-intervention BP values (r – 0.623 for SBP and r – 0.613, for DBP, p< 0.0001 for both). SBPbut not DBP changes were slightly correlated with weightchanges (r 0.116, p<0.01) and this correlation wasdue to patients with controlled hypertension. SBP and DBP changeswere unaffected by age, sex, presence of metabolic alterations, family history of obesity, cardiovascular diseases and diabetes and by changes in waist circumference, fat mass and metabolic variables.In the regression analysis, baseline BP values explained 38.8% of variance of SBP changes and 37.4% of DBP changes, whereas weight changes explained only 1.7% of SBP changes.

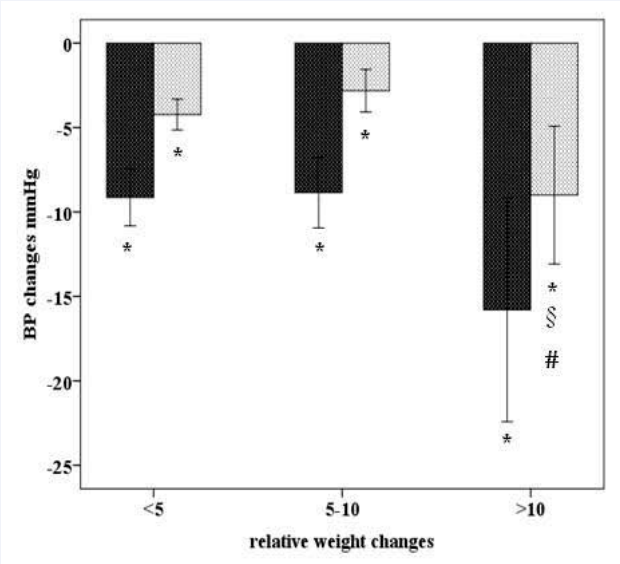

Figure 1 Changes of SBP (black bars) and DBP (grey bars) in obese patients who lost <5%, between 5 and 10% and >10% of baseline weight. Data are expressed as mean (95% CI). *p<0.0001 vs baseline values; § p<0.05 vs patients who lost <5% of weight; # p<0.01 vs patients who lost 5-10% of weight.

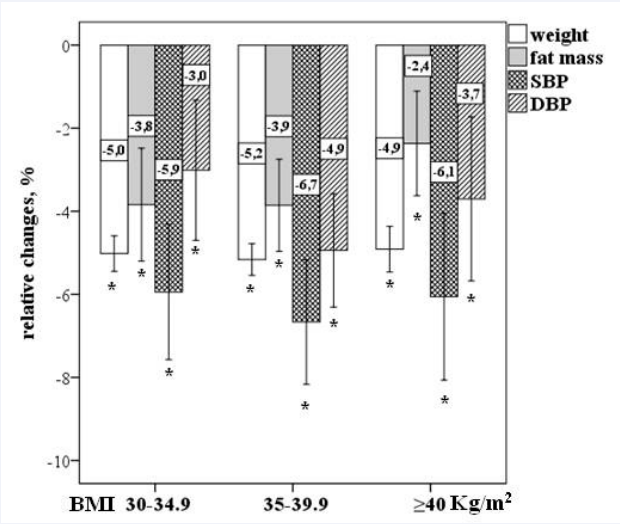

Figure 2 Relative changes observed after lifestyle intervention in weight, fat mass and blood pressure (SBP and DBP) in class I, II and III obesity. Data are expressed as mean (95% CI). *p<0.0001 vs baseline values.

DISCUSSION

Results from this study show that in obese hypertensive patients 1) a moderate weight loss obtained with 3-month lifestyle intervention is highly effective in reducing SBP and DBP levels independently of the presence of metabolic complications, 2) the benefits of intervention in lowering BP is similar in patients with different degrees of obesity and is stronger in patients with uncontrolled hypertension, 3) BP reduction is mostly predicted by pre-intervention BP levels and is poorly correlated with the amount of weight lost.

In our cohort, cardio-metabolic conditions worse with the degree of obesity, despite the youngest age of patients with more severe obesity. This confirmsthe observationthat being obeseat a young ageincreasesthe risk of developingearly and severecardio-metabolic complications [10].

The proportion of uncontrolled hypertension (21%) in our cohort was super imposable to that (21.7%) reported in in hypertensive Israeli population [11].

The 3-month llifestyle intervention reduced body weight by about 5%regardless of the degree of obesity. Weight loss was accompanied by an average reduction of 9.3 mmHg of SBP and 3.9-mmHg ofDBP, that was similar in the three class of obesity. These results differ from those of a study in non-hypertensive patients, which reported that the weight and BP lowering effect of 1-year lifestyle intervention is more dramatic in class II and III than in class I obesity [6]. However our data are in accord with a meta-analysis of 12intervention studies in obese hypertensive patients, that described BP lowering effects independent upon baseline obesity [12].

The intervention-induced BP reduction was particularly evident in patients with uncontrolled hypertension in whom a 5% weight loss resulted in a decrease of SBP and DBP of 23.6 and 9.2 mmHg respectively. Accordingly, about one fourth of BP changes was explained by pre-intervention BP values. This finding agrees with the observation that the effects of lifestyle intervention are more pronounced in hypertensive than in pre-hypertensive and normotensive subjects [13].

In the present study, changes in BP and weight were weakly linked, however DBP reduction was definitely greater in patients who had a >10% weight loss than in those with lower weight loss. This finding demonstrates that the association between reductions in weight and BP is not linear at least in the first three months of lifestyle modification.

The poor relation between BP and weight changes is also supported by the demonstration that in obese diabetic patients undergoing gastric bypass, the weight reduction was 3 times greater than in those in lifestyle-medical management, but was not associated with a greater BP reduction [14].

It should be assumed that obese individuals are particularly sensitive to qualitative changes in the diet such asincreased vegetable proteins andlow sodium and fructose intake. From this perspective,in the early period of lifestyle modifications, BPdecrease wouldbe mostly affected by the improvement in dietary habitsrather thanthe amount of weight lost(2).Supporting this viewin obese hypertensive women,weight loss obtained with three monthsof aerobic activitydid not significantly modify BPvalues [15].

Regarding the long-term effects of lifestyle modifications on BP, a one-year weight loss intervention that ensured the quality of the diet by providing pre-packaged meal replacements, demonstrated a progressive increasing effect in lowering BP [6]. Furthermore,ten years after bariatric surgery,theBPloweringeffectof weight loss was considerably decreasedin patients notfollowingalow-sodium diet [4]. These data suggest that even long-term lifestyle changes are useful in controlling BPlevels only if a proper diet is maintained.

CONCLUSIONS

In obese hypertensive patients, short-term lifestyle changes induce a clinically significant BP reduction that is independent of the degree of obesity, age, sex and presence of metabolic alterations. The intervention efficacy is greater in patients with higher BP levels and has a nonlinear relationship with weight changes.

REFERENCES

1. World Health Organization. Obesity and overweight. Fact sheet N°311. Updated March 2011
2. DeMarco VG, Aroor AR, Sowers JR. The pathophysiology of hypertension in patients with obesity. Nat Rev Endocrinol. 2014; 10: 364-376.
3. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013ESH/ESC Practice Guidelines for the Management of Arterial Hypertension.Task Force for the Management of Arterial Hypertension of the European Society of Hypertension and the European Society of Cardiology. Blood Press. 2014; 23: 3-16.
4. Hallersund P, Sjöström L, Olbers T, Lönroth H, Jacobson P, Wallenius V. Gastric bypass surgery is followed by lowered blood pressure and increased diuresis - long term results from the Swedish Obese Subjects (SOS) study. PLoS One. 2012; 7: e49696.
5. Siebenhofer A, Jeitler K, Berghold A, Waltering A, Hemkens LG, Semlitsch T. Long-term effects of weight-reducing diets in hypertensive patients. Cochrane Database Syst Rev. 2011; : CD008274.
6. Goodpaster BH, Delany JP, Otto AD, Kuller L, Vockley J, South-Paul JE. Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial. JAMA. 2010; 304: 1795-1802.
7. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2013; 36: S67-74.
8. Chronic Kidney Disease Epidemiology Collaboration. Expressing the Modification of Diet in Renal Disease Study equation forestimating glomerular filtration rate with standardized serum creatinine values. Clin Chem. 2007; 53: 766–772.
9. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). J Am Med Association. 2001; 285: 2486–2497.
10. Juonala M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA. Childhood adiposity, adult adiposity, and cardiovascular risk factors. N Engl J Med. 2011; 365: 1876-1885.
11. Weitzman D, Chodick G, Shalev V, Grossman C, Grossman E2. Prevalence and factors associated with resistant hypertension in a large health maintenance organization in Israel. Hypertension. 2014; 64: 501-507.
12. Staessen J, Fagard R, Amery A. The relationship between body weight and blood pressure. J Hum Hypertens. 1988; 2: 207-217.
13. Svetkey LP, Erlinger TP, Vollmer WM, Feldstein A, Cooper LS, Appel LJ. Effect of lifestyle modifications on blood pressure by race, sex, hypertension status, and age. J Hum Hypertens. 2005; 19: 21-31.
14. Ikramuddin S, Korner J, Lee W, Connett JE, Inabnet WD, Billington CJ, et al. The Diabetes Surgery Study Randomized Clinical Trial Roux-en-Y Gastric Bypass vs Intensive Medical Management for the Control of Type 2Diabetes, Hypertension, and Hyperlipidemia. JAMA. 2013; 309: 2240-2249.
15. Trachta P, Drápalová J, Kaválková P, Toušková V, Cinkajzlová A, Lacinová Z, et al. Three months of regular aerobic exercise in patients with obesity improve systemic subclinical inflammation without major influence on blood pressure and endocrine production of subcutaneous fat. Physiol Res. 2014; 63 Suppl 2:S299-308.

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