The quality of arterial hypertension treatment in cardiology service in Kosovo - a single center study

Kosova kardiyoloji servisinde arteryel hipertansiyon tedavi niteliği-Tek merkez çalışması

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ABSTRACT

Objective: The epidemiological data have shown that the goal blood pressure (BP) control is achieved in only a small percentage of the hypertensive patients. The aim of this study was to assess the quality of the management of arterial hypertension (AH) in patients hospitalized in Service of Cardiology, University Clinical Centre of Kosovo, in Prishtina, and to determine the predictors of uncontrolled AH.
Methods: This retrospective study included 938 consecutive hypertensive patients (63.1±11.3 years, 55.1% females), admitted to our institution between January 2003 and June 2006. Systolic and diastolic blood pressure, blood analyses, drug prescription and echocardiographic findings were analyzed in all study patients. Multiple regression analysis was used to identify the independent associates of poor BP control.
Results: Overall, 83%f of patients were discharged on angiotensin-converting enzyme inhibitors (A), 71% - on beta-blockers (B), 26% - on calcium channel blockers (C) and 60% - on diuretics (D). The most frequent drug combination used was ABD (30.5%), followed by AB (18%) and AD (8%). The goal systolic and diastolic BP was achieved in 50% of patients. Multivariate analysis identified diabetes, (OR=0.479, 95% confidence interval [CI] 0.339-0.677, p<0.001), creatinine level (OR=0.997, 95% CI 0.996-0.999, p=0.001], and ABCD combination therapy (OR=0.445, 95% CI 0.253-0.774, p=0.046)], as independent correlates of in-hospital poor BP control.
Conclusions: Half of hypertensive patients hospitalized in the Service of Cardiology had achieved the goal blood pressure. The diabetes, level of creatinine and a combination of 4 antihypertensive drugs were independent predictors of poor hypertension control.
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Key words: Antihypertensive drugs, arterial hypertension, blood pressure control, logistic regression analysis

ÖZET

Amaç: Epidemiyolojik veriler kan basıncı (KB) kontrolünde hipertansif hastaların yalnızca küçük bir oranında hedefin sağlanabildiğini göstermiştir. Bu çalışmanın amacı Priştina'daki Kosova Üniversitesi Klinik Merkezi, Kardiyoloji servisine yatarak tedavi edilen arteryel hipertansiyonlu (AH) hastaların takip niteliğini değerlendirmektir.
Yöntemler: Bu restrospektif çalışma, Ocak 2003-Haziran 2006 arasında kurumumuza kabul edilen 938 ardışık hipertansif hastayı (yaş 63.1±11.3 yıl, %55.1 kadın) kapsamaktadır. Tüm çalışma hastalarında sistolik ve diyastolik kan basıncı, kan analizleri, ilaç reçeteleri ve ekokardiyografik bulgular analiz edildi. Yetersiz KB kontrolünün bağımsız prediktörlerini belirlemekte çoklu lojistik regresyon analizi kullanıldı.
Bulgular: Hastaların %83'ü anjiyotensin-dönüştürücü enzim inhibitörü (A), %71'i beta bloker (B), %26'sı kalsiyum kanal blokeri (3) ve %60'ı diüretik ile taburcu edildi. En sık kullanılan ABD'li ilaç birleşimiydi ve AB (%18) ile AD (%8) izledi. Hastaların %50'sinde hedef sistolik ve diyastolik KB sağlandı. Multivaryans analizler hastanedeki yetersiz KB kontrolünde bağımsız değişkenler olarak diyabet (OR =0.479, %95 GA 0.339-0.677, p<0.001), kreatinin düzeyi (OR=0.997, %95% GA 0.996-0.999, p=0.001] ve ABCD kombinasyon tedavisini (OR=0.445, %95 GA 0.253-0.774, p=0.046)] ortaya çıkardı.
Sonuç: Kardiyoloji servisinde yatan hipertansif hastaların yarısında kan basıncı hedeflerine varıldı. Diyabet, kreatinin düzeyi ve 4 antihipertansif ilacın birleşimi yetersiz hipertansiyon kontrolü için bağımsız prediktörlerdir.
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Anahtar kelimeler: Antihipertansif ilaçlar, arteryel hipertansiyon, kan basıncı kontrolü, lojistik regresyon analizi

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Introduction

Arterial hypertension (AH) is a major risk factor for cardiovascular diseases and death (1). The heart, kidneys, brain and blood vessels are the main target organs damaged by AH (2). The Sixth Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) (3) and the World Health Organization-International Society of Hypertension (1999 WHO/ISH) guidelines (4) established or suggested that blood pressure (BP) control is adequate when achieved systolic and diastolic BP value are <140 mmHg and <90 mmHg, respectively. Furthermore, the JNC-VI and European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines (3, 5) have suggested systolic BP<130mmHg and diastolic BP <80 mmHg as goals for the special populations (diabetes, renal disease).

The epidemiological data have shown that the goal BP control is achieved in only a small percentage of the hypertensive patients (6-8). The small number of studies suggested that the adequate BP control was achieved significantly more often in in-hospital hypertension units than in primary health care units (9-11). The behavior of physicians attending hypertensive patients was shown to be a factor that may influence better BP control in in-hospital hypertension units (12, 13).

The aim of this study was to assess the quality of the management of AH in hospitalized patients and to determine the predictors of uncontrolled AH in these patients.

Methods

Of 6058 patients admitted to our Service, between January 2003 and June 2006, we included in the retrospective study only those with hypertension, defined as a systolic BP of ≥140 mm Hg or a diastolic BP of ≥90 mm Hg, or those who were receiving antihypertensive therapy at the time of admission. Our definition of hypertension coincides with the definitions used in NHANES III (9), and JNC-VI (3). The indications for the hospitalization of our study population were mainly the unsuccessful goal achieved treatment in outpatient clinic. Patients admitted to coronary care unit of our service for acute myocardial infarction, were not included in the study.

Data collection

Trained research medical students collected the information from the hospital medical records. The following data were obtained: age, gender, various cardiovascular risk factors such as previous history of coronary heart disease, diabetes, hypertension and smoking. Routine biochemical measurements including fasting blood glucose, cholesterol, triglycerides, urea, creatinine, blood count, hemoglobin, hematocrit and erythrocyte sedimentation rate were performed. Surface electrocardiogram was recorded and analyzed in all patients.

Blood pressure measurement

At each examination, BP was measured in the left arm by the examining physician using a mercury column sphygmomanometer after the subject had been at rest in the seated position for ≥ 5 minutes (14). The BP measurements that we registered for this study were the measurement in admission and the last measurement before discharge.

Echocardiographic examinations

Echocardiographic examination was performed in all patients with echocardiographic machines Agilent Image-Point and Philips E-33, equipped with probes from 2.5 to 5 MHz using standard views. The left ventricular (LV) end-diastolic dimension (EDD), LV end-systolic dimension (ESD), interventricular septal (IVS) thickness, LV posterior wall (LVPW) thickness, left atrium dimension, aortic root dimension, fractional shortening and ejection fraction were measured according to the guidelines (15).

Antihypertensive drug therapy

Goal BP was defined as systolic pressure <140mmHg systolic and diastolic pressure <90mmHg. For high-risk patients goals were: systolic pressure <130mmHg systolic and diastolic pressure <80mmHg. Poor BP control was considered in all patients that did not achieve these values. Antihypertensive drug therapy in our study population consisted of angiotensin-converting enzyme inhibitors (A) and angiotensin II receptor blockers, beta-blockers (B), calcium channel blockers (C) and diuretics (D) used as single drug therapy or in various combinations. Fifteen combinations of drugs were used.

Data analysis

All analyses were performed using Statview 4.5 (Abacus Concepts, Berkley, CA, USA). Data are presented as mean ± standard deviation or number of patients (%). Continuous data were compared using a two-tailed unpaired Student t test. Discrete variables were compared using χ^2-test or Fisher's exact probability test as appropriate. Multiple logistic regression analysis was used to identify the independent associates of poor BP control. Diabetes, interventricular and LV posterior wall thickness, LV end-systolic and end-diastolic diameter, LV fractional shortening and ejection fraction, fasting glycemia, level of creatinine, hemoglobin, erythrocytes, hematocrit, cholesterol, triglycerides, age, sex, smoking, atrial fibrillation, and antihypertensive drug combinations, were included in the regression analyses. P value less than 0.05 indicated statistical significance.

Results

Of 6058 patients admitted to our Service during the study period, 938 (15.5%) who were diagnosed with AH or were under antihypertensive treatment were included in the study. The mean age of patients was 63.1±11.3 years (range 20-92 years). Of them 517 (55.1%) were women (Table 1). Congestive heart failure was the most frequent co-morbidity (32% of patients), followed by ischemic heart disease (30%), diabetes mellitus (21.9%) and atrial fibrillation (12.9%). Hypercholesterolemia was encountered in 31% of these patients (Table 1).

Table 1. Clinical features of patients with arterial hypertension hospitalized in service of cardiology

Feature	Number/value
Age, years	63.1±11.3
Sex	
female n(%)	421 (44.9)
male n(%)	517 (55.1)
Associated conditions	
Ischemic heart disease, n(%)	281 (30)
Diabetes mellitus, n(%)	205 (21.9)
Atrial fibrillation, n(%)	121 (12.9)
Congestive heart failure, n(%)	300 (32)
Hypercholesterolemia, n(%)	291 (31)
Smoking, n(%)	195 (20.8)
COPD, n(%)	58 (6.2)
Arterial blood pressure at admission	
Systolic blood pressure, mmHg	156.8±31.8
Diastolic blood pressure, mmHg	93.9±17.5
Arterial blood pressure at discharge	
Systolic blood pressure, mmHg	132.5±19.6
Diastolic blood pressure, mmHg	83±10.6
Treatment at discharge	
ACE inhibitors, n(%)	779 (83)
Beta-blockers, n(%)	666 (71)
Calcium antagonists, n(%)	266 (26)
Diuretics, n(%)	563 (60)
Digoxin, n(%)	47 (5)
Aspirin, n(%)	657 (70)
Sedatives, n(%)	206 (22)

Data are represented as mean±SD and numbers/percentages
ACE-angiotensin converting enzyme, COPD-chronic obstructive pulmonary disease

On admission, only 173 (18.5%) of patients had controlled (goal) treatment of AH according to above mentioned criteria. Patients with uncontrolled AH in admission had higher level of fasting glycemia (6.82±3.9 mmol/L vs. 6.33±2.6 mmol/L, p=0.002), higher creatinine level (133.2±73.7 mmol/L vs. 121.3±107.7 mmol/L, p=0.032), and lower LVDd (3.5±0.9 cm vs. 3.7 ± 1.1 cm, p=0.021) compared with patients with controlled AH (Table 2). The other clinical and echocardiographic variables did not differ significantly between groups.

The mean systolic BP on admission was 156.8±31.8 mmHg, and the diastolic BP was 93.9±17.5 mmHg. At discharge the mean systolic and diastolic BP values were 132.5±19.6 mmHg and 83±10.6 mmHg, respectively.

Antihypertensive therapeutics

Angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin II receptor blockers were the pharmacological group most often prescribed on discharge (in 83% of patients, of whom 88% received ACE inhibitors and 12% received angiotensin II receptor blockers; 4% of patients received both ACE inhibitors and angiotensin II receptor blockers. Beta-blockers were used in 71% of patients, followed by diuretics (60%; of them 68% received hydrochlorothiazide, 30% received furosemide, 8% received spironolactone and 5% received both furosemide and spironolactone) and calcium channel blockers (26%; Figure 1). The most frequent drug combinations used in our patients were ABD combination (30.5% of patients), followed by AB combination (18%) and AD combination (8%) (Table 1, Fig. 2).

In 58% of hospitalized patients the goal systolic BP was achieved. The goal diastolic BP was achieved in 66% of patients. Goal systolic and diastolic BP was increased from 18.5% on admission to 50% of patients on discharge.

On univariate analysis the following characteristics were associated with poor BP control (Table 3): diabetes (p<0.001), high creatinine level (p<0.001), increased interventricular thickness (p=0.001), ABCD combination therapy (p=0.001), elevated fasting glucose level (p=0.002), female sex (p=0.007), elevated hemoglobin level (p=0.024) and high LV ejection fraction (p=0.046).

All variables that showed a significant association (p<0.05) with blood pressure control (Table 3) and known cardiovascular risk factors (age, smoking and hypercholesterolemia) are included into the multivariable model. Multivariate analysis showed that diabetes (OR=0.479, 95% CI 0.339-0.677, p<0.001), creatinine level (OR=0.997, 95% CI 0.996-0.999, p=0.001), and ABCD combination therapy (OR=0.445, 95% CI 0.253-0.774, p=0.046), were independently associated with poor BP control (Table 4).

Discussion

The present study aimed to assess the quality of the management of AH in patients hospitalized as well as to assess the predictors of uncontrolled AH in these patients. We have studied patients who were mainly referred from general practitioners, internists and cardiologists, for a better treatment

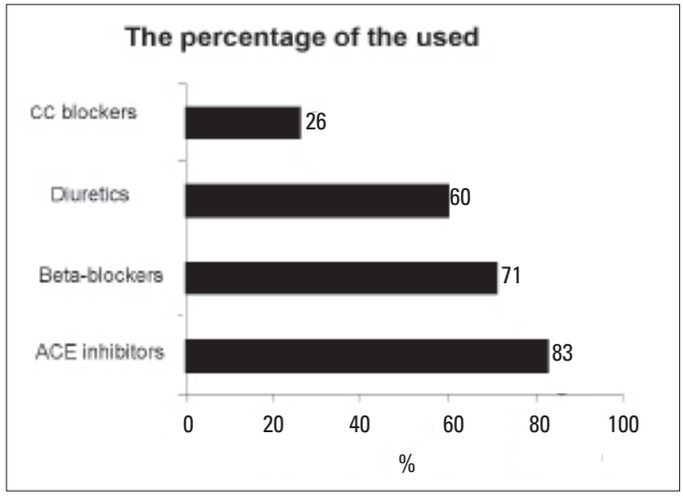

Figure 1. The percentage of used drug groups in hypertensive patients hospitalized in Service of Cardiology.
ACE - angiotensin-converting enzyme, CC- calcium channel

Table 2. Characteristics of admitted patients with arterial hypertension

Variables	Patients with goal blood pressure on admission (n = 173)	Patients with uncontrolled blood pressure on admission (n =765)	p*
Age, years	64.6±11.1	62.7±11.3	0.619
Sex, female, %	52.9	55.6	0.524
Smoking, %	20.9	20.9	0.99
Diabetes, %	17.4	23	0.126
Atrial fibrillation, %	13.3	12.7	0.462
Left ventricular hypertrophy, %	52.9	53.9	0.866
Glycemia, mmol/L	6.33±2.6	6.82±3.9	0.002
Cholesterol, mmol/L	4.4±1.3	4.67±1.3	0.601
Triglycerides, mmol/L	1.6±0.9	2.1±1.4	0.392
Creatinine, µmol/L	121.3±107.7	133.2±73.7	0.032
Hemoglobin, g/L	129.7±19.6	128.5±22.8	0.314
LV EDD, cm	5.1 ± 0.9	5.15 ± 0.8	0.158
LV ESD, cm	3.7 ± 1.1	3.5 ± 0.9	0.021
Fractional shortening, %	30.2 ± 13.4	30.3 ± 11.1	0.246
Ejection fraction, %	52.5 ± 14	55 ± 13	0.521
Interventricular septum, cm	1.21 ± 0.24	1.27 ± 0.26	0.576
LV posterior wall, cm	1.16 ± 0.64	1.17 ± 0.44	0.404

Data presented as mean ± standard deviation and percentages
*two-tailed unpaired Student t test, Chi-square and Fisher's exact tests
EDD - end-diastolic dimension; ESD - end-systolic dimension; LV- left ventricle

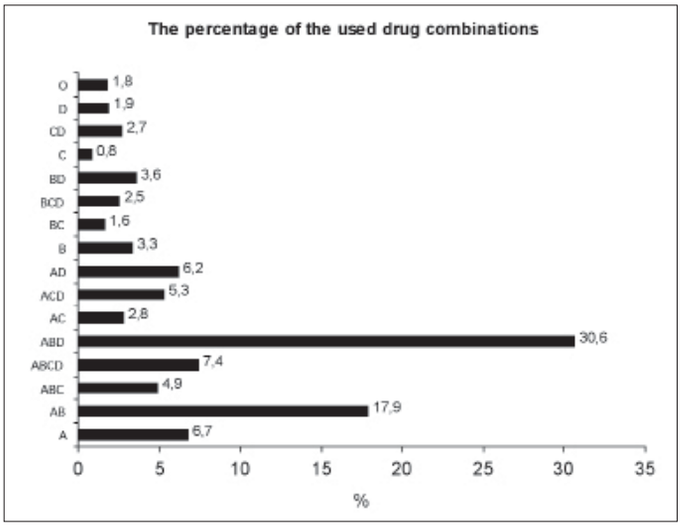

Figure 2. The percentages of used drugs combinations in hypertensive patients hospitalized in Service of Cardiology

A- angiotensin-converting enzyme inhibitors, B-beta-blockers, C-calcium antagonists, D-diuretics O- other

of AH or because AH was associated with other comorbidities needing hospitalization. The main findings of the study are: 1) In hospitalized patients with AH the adequate BP control was achieved in 50% of patients when both systolic and diastolic BP values were considered and 2) The presence of diabetes, impaired renal function and the need for a quadruple drug therapy were identified as independent correlates of poor BP control.

The ACE inhibitors and/or angiotensin II receptor blockers were the drugs more prescribed in our study patients (in 83% of hypertensive patients). Beta-blockers were the second group of the drugs that were prescribed in our study patients (71%), followed by diuretics (60%) and calcium channel blockers (26%). The higher rate of the ACE inhibitors is in line with some recent studies that included the hypertensive patients of the same period of time (16-18). On the other hand, the rate of the prescribing of calcium channel blockers was lower than in some of studies from the same period of time (19, 20). The high rate of the prescribed ACE inhibitors may also be explained with the high percentage of patients with congestive heart failure, ischemic heart disease and diabetes that associated AH and for which ACE inhibitors were also indicated. Conversely, calcium channel blockers are not the drugs of choice in these comorbidities. Other studies have reported that beta-blockers are still the most frequent drugs prescribed in hypertension (21). It has to be emphasized that a large number of randomized trials have confirmed that the main benefits of antihypertensive therapy are due to lowering of BP per se, independently of the drugs used to lower BP (22). However, the use of drugs in our study is in accordance with the recent guidelines (23).

Hypertension control was achieved in only half of hospitalized patients with AH included in our study, according to the actual guidelines (9, 10). The rate of optimal BP control in our study patients was higher than in previous studies (14, 24-29). Our better results may be attributed to the in-hospital treatment of

Table 3. Univariate predictors of blood pressure control in hypertensive patients hospitalized in Service of Cardiology

Variables	OR (95% CI)*	p
Diabetes	0.496 (0.361-0.683)	<0.001
Creatinine	0.998 (0.996-0.999)	0.001
Interventricular thickness	0.900 (0.844-0.959)	0.001
ABCD therapy	0.411 (0.242-698)	0.001
Fasting glycemia	0.942 (0.907-0.978)	0.002
Sex	0.834 (0.730-0.950)	0.007
Hemoglobin	1.007 (1.001-1.013)	0.024
LV ejection fraction	0.988 (0.977-1.000)	0.046
LV shortening fraction	0.983 (0.967-1.000)	0.051
Hematocrit	1.014 (0.999-1.029)	0.065
LV posterior wall thickness	0.965 (0.926-1.004)	0.079
Atrial fibrillation	1.390 (0.944-2.048)	0.095
Age	1.002 (0.991-1.01)	0.724
Smoking	1.250 (0.913-1.71)	0.172
Cholesterol	0.971 (0.862-1.113)	0.680
Triglycerides	1.035 (0.952-1.124)	0.414
Erythrocytes	0.977 (0.904-1.055)	0.550
Aortic root dimension	0.995 (0.959-1.032)	0.775
Left atrium dimension	0.991 (0.968-1.014)	0.449
LV end-diastolic diameter	1.002 (0.984-1.021)	0.802
LV end systolic diameter	1.006 (0.989-1.024)	0.487
ABD therapy	1.128 (0.854-1.490)	0.395
ABC therapy	1.000 (0.546-1.832)	0.99
A therapy	0.812 (0.484-1.363)	0.431
AD therapy	1.188 (0.742-1.901)	0.473
B therapy	1.855 (0.879-3.915)	0.105
AC therapy	0.636 (0.272-1.484)	0.295
D therapy	0.887 (0.339-2.319)	0.807
AB therapy	1.190 (0.852-1.663)	0.307
ACD therapy	0.806 (0.452-1.436)	0.464
BD therapy	1.000 (0.504-1.983)	0.99
CD therapy	1.517 (0.674-3.411)	0.314
BCD therapy	0.764 (0.332-1.761)	0.528
C therapy	0.665 (0.111-4.000)	0.656
BC therapy	1.000 (0.320-3.123)	0.99

*Logistic regression analysis
A- angiotensin-converting enzyme inhibitors, B - beta-blockers, C - calcium antagonists, D - diuretics, LV - left ventricle

Table 4. Multivariate model of poor blood pressure control in hypertensive patients hospitalized in Service of Cardiology

Variables	OR (95% CI)*	p
Diabetes	0.479 (0.339-0.677)	<0.001
Creatinine	0.997 (0.996-0.999)	0.001
ABCD therapy	0.445 (0.253-0.774)	0.046

*Logistic regression analysis
A- angiotensin-converting enzyme inhibitors, B - beta-blockers, C - calcium antagonists, D - diuretics,

the patients compared to the ambulatory treatment of the patients in the mentioned studies. Another factor that may explain the results of our study with regard to optimal BP control may be related to the fact that indication for hospital admission was not only failure to control BP in ambulatory patients, but also other indications (diabetes complications, heart failure, ischemic heart disease, etc). In fact it has been demonstrated that the optimal BP control is far better during in-hospital treatment of hypertensive patients than in those treated in primary health care units (9-11). Moreover, the behavior of physicians attending hypertensive patients was shown to be a factor that may influence better BP control in in-hospital hypertension units (12, 13).

Regarding the factors that were associated with a poor BP control such as diabetes and impaired renal function, our findings are in accordance with the most recent guidelines on hypertension management (3,5), reporting that only 10% of diabetic patients and 12% patients with renal disease achieve the goal objectives in AH treatment. Previous studies have found that diabetes is one of the strongest predictors of poor BP control (24, 30, 31).

In the present study, 15 drug combinations were tested and only a combination of all 4 groups of drugs (ACE inhibitors, beta-blockers, diuretics and calcium channel blockers) was found to be significant predictor of poor BP control. This finding is in line with findings of a previous study (26) that found that the using of ≥2 antihypertensive drugs is an independent predictor of the poor BP control. Results of our study could be explained by, at least, two factors: first, patients whose BP is more difficult to control are likely to be treated with multiple drugs, and second these patients could have secondary AH due to other causes (cardiovascular, chronic renal failure, uncontrolled diabetes) known to present resistance to antihypertensive drugs. With regard to the age of patients, known to affect the BP control in patients with AH (23, 24), we did not find an independent association between age and quality of BP control. This discrepancy with these studies may be explained by a younger age of patients included in our compared with prior studies (25, 26). With regard to beta- blockers use in patients with arterial hypertension, the high percentage of beta-blocker use in the current study may be related to the presence of patients with ischemic heart disease and congestive heart failure in which situations, beta-blockers are indicated. However, current evidence shows that they may be not indicated as a first line therapy in patients with AH in absence of these two morbid conditions (32).

Limitations of the study

Our study has several study limitations such as lack of data on body-mass index that could have been included into the multivariable model. Another limitation of our study was also the lack of data about the secondary hypertension in our study population. We also could not present data on the educational

level of patients, a factor known to underlie the successful treatment of AH. Furthermore, we have no information on the control of blood pressure after discharge of the patients from the hospital.

Conclusions

In conclusion, half of hypertensive patients hospitalized in the Service of Cardiology had achieved the goal BP. Diabetes, level of creatinine and the need for a combination of 4 antihypertensive drugs (ACE inhibitors, beta-blockers, calcium channel blockers and diuretics) are independent predictors of poor hypertension control.

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