CLINICAL STUDY

Hypertension and the Risk of Acute Myocardial Infarction in Argentina

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The relationship between a history of hypertension and the quality of its control in routine clinical practice and the risk of acute myocardial infarction was examined in a multicenter, case-control study conducted in Argentina between November 1991 and August 1994, within the framework of the FRICAS study. The cases were 939 patients with acute myocardial infarction and without a history of ischemic heart disease. The controls were 949 subjects identified in the same centers as the cases and admitted with a wide spectrum of acute disorders unrelated to known or suspected risk factors for acute myocardial infarction. The odds ratios and the 95% confidence intervals were derived from multiple logistic regression equations, including terms for age, gender, education, social status, exercise, smoking status, cholesterolemia, history of diabetes, body mass index, and family history of myocardial infarction. The quality of hypertension control was assessed with the most recent blood pressure reading reported by the subjects. Seventy-two percent of hypertensive cases and 62.6% of hypertensive controls had a history of antihypertensive therapy by self-report, when admitted to the medical center.

The adjusted odds ratio for acute myocardial infarction due to hypertension was 2.58 (95% confidence interval, 2.08–3.19). The odds ratio was 2.42 (95% confidence interval, 1.88–3.11) when hypertensives reported that their greatest systolic value was below 200 mm Hg (moderate status) and 4.12 (95% confidence interval, 2.87–5.89) when it was above 200 mm Hg (severe status). When the highest diastolic blood pressure value was below 120 mm Hg (moderate status), the risk increased to 2.48 (95% confidence intervals, 1.90–3.24) and to 4.12 (95% confidence interval, 2.83–5.99) when it was above 120 mm Hg (severe status). If the most recent systolic blood pressure was ≤140 mm Hg, the odds ratio was 2.59 (95% confidence interval, 1.96–3.41), and it was 3.42 (95% confidence interval, 2.40–4.87) when the value was >140 mm Hg. If the most recent diastolic blood pressure was ≤ 90 mm Hg, the risk increased more than two fold (odds ratio=2.48; 95% confidence interval, 1.91–3.22), and if it was >90 mm Hg, it increased nearly four-fold (odds ratio=3.72; 95% confidence interval, 2.33–5.96). In smokers, the odds ratio was 2.28 in the absence of hypertension and increased to 7.51 when hypertension was present.

In this Argentine population, hypertension is a strong and independent risk factor for acute myocardial infarction. In routine clinical practice, the control of blood pressure to levels below 140/90 seems to be required in order to reduce part (but not all) of the risk of acute myocardial infarction in hypertensive patients. (Prev Cardiol. 2001;4:57–64) © 2001 by CHF, Inc.

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Epidemiologic studies conducted in developed countries have established a positive association between blood pressure levels and cardiovascular disease.[1–4] MacMahon et al.[5] showed a direct relationship between diastolic and systolic blood pressure and the risk of suffering cardiovascular disease. Hypertension does indeed predispose to all the major atherosclerotic cardiovascular clinical events, including stroke, cardiac failure, peripheral arterial disease, and coronary artery disease.[6,7]

Since the 1970s, considerable progress has been made in the treatment of hypertension. In large-scale and properly controlled trials, antihypertensive drugs have been shown to reduce clinical end points related to stroke, coronary artery disease, left ventricular failure, and mortality.[8–11]

Meta-analyses, including the major outcome trials, have demonstrated that the effects of antihypertensive treatment for reduction of the incidence of stroke are entirely consistent with the benefits predicted from epidemiologic data.[5] They have shown a uniform and persistent reduction in morbidity and mortality from stroke, averaging 40%, a reduction similar to that predicted from observational studies.

The impact on coronary heart disease reported in 1990 on the basis of data from several trials showed a reduction of 14%, still below the 20%–25% predicted if the attributed risk had been completely reversed.[5] This lower than expected efficacy of antihypertensive therapy in preventing coronary artery disease has caused some unjustified uncertainty about the influence of hypertension on the evolution of atherosclerosis. Furthermore, the benefit of reducing coronary heart disease in hypertensives was obtained from selected populations included in observational and interventional studies, whereas the benefit obtained in routine clinical practice is unclear. Epidemiologic studies conducted in developed countries have shown that most patients with hypertension are inadequately controlled.[12–15] Thus, nearly three fourths of hypertensive individuals are not controlled by treatment. These findings are believed to be due to poor compliance with long-term antihypertensive therapy.[15]

Information about the relative role of hypertension in myocardial infarction and the effects of antihypertensive therapy in general practice would be valuable in terms of public health, especially in populations and areas of the world from which available data are scarce. The aim of the present work was to analyze, in a South American population, the relationship between the risk of acute myocardial infarction (AMI) and the history of hypertension, its severity, and the quality of its control in a primary care setting.

METHODS

Subjects and Design

This report is derived from the FRICAS (Factores de Riesgo Coronario en América del Sur) study, an ongoing case-control study conducted in several countries of South America in which the main objective is to determine the coronary risk factors for AMI. Our analysis is based on information collected in Argentine medical centers from November 1991 to August 1994.[16] We included 35 coronary care units from various clinical centers.

All cases and controls were interviewed by trained interviewers using a structured questionnaire to obtain information on socio-demographic factors, including education, personal characteristics, and such habits as smoking, alcohol intake, coffee consumption, frequency of consumption of a few selected dietary items, some indicators of physical activity, self-reported weight and height, history of diabetes, and history of AMI in first-degree relatives. Income level was classified in three strata according to the ownership of a house and/or car: it was high if subjects owned both a house and a car, medium if they owned either a house or car, and low if they owned neither. Additionally, serum cholesterol levels were measured at admission in both cases and controls.

We defined as hypertensives those subjects who had been prescribed antihypertensive treatment (diet and/or drugs) at any time. Of the hypertensive cases and controls, 75% self-reported hypertension treatment with drugs at admission to the medical center.

Severity of blood pressure was graded according to the highest value of systolic or diastolic blood pressure reported by the subjects at any time. We defined the following strata: less (moderate) or more (severe) than 200 mm Hg for systolic blood pressure and less (moderate) or more (severe) than 120 mm Hg for diastolic blood pressure. Subjects who were unaware of their highest blood pressure value (missing values) were included in other strata.

Quality of hypertension control was assessed from the most recent blood pressure measurement (before entry to the study), systolic or diastolic, reported by the subjects within the previous year. They were stratified according to the categories in Table I.

Subjects who were not aware of their most recent blood pressure value (missing values) and those who reported no treatment (not treated) were assigned to other strata.

The reliability of this information was confirmed in most cases and controls by examination of the clinical records. In addition, further details were sought about hospital or physician diagnosis in order to confirm, whenever possible, the subjects' replies to the questions.

The cases were 939 patients (734 males, 205 females) admitted to the hospital for a first episode of AMI, 75 years of age or younger at the date of diagnosis of AMI, and with no history of cardiovascular conditions predisposing to AMI. AMI was diagnosed according to World Health Organization criteria.[17] The median age of the cases was 58 years.

Controls comprised a sample of 949 subjects (727 males, 222 females) younger than 75 years of age and free of coronary heart disease. They were matched to

TABLE I. BLOOD PRESSURE MEASUREMENTS

	Well Controlled	Not Controlled
Systolic blood pressure	≤140 mm Hg	>140 mm Hg
Diastolic blood pressure	≤90 mm Hg	>90 mm Hg

the cases for age, gender, and medical center. Patients with conditions judged to be related to risk factors for myocardial infarction or with other ischemic heart diseases, including angina pectoris or cardiac surgery, were excluded from the comparison group. Also excluded were subjects admitted for neoplastic and cerebrovascular disorders, or with any chronic condition. Forty-five percent of controls were admitted for traumatic conditions, 30% for acute surgical diseases, and 25% for miscellaneous illnesses, such as skin, nose, ear and throat, or dental disorders. The median age of the controls was 58 years. On average, fewer than 4% of cases and controls refused to be interviewed.

Analysis of Data

Categorical variables were compared with Pearson's chi-square test. The odds ratio (OR), used as a close approximation to relative risk, and the corresponding 95% confidence interval (CI) were computed from data stratified by gender and age decade (<45, 45–54, 55–64, and 65–75 years) with the Mantel-Haenszel procedure.[18] Multivariate analysis by means of multiple logistic regression was used, including terms for gender, age, years of education, social status, smoking, physical exercise, Quetelet's index (body mass index [BMI]), history of diabetes, cholesterolemia, and family history of myocardial infarction.[19]

Proportions were computed by means of the method described by Bruzzi et al.[20] which allows their estimation by use of data from case-control studies. The method requires knowledge of the prevalence of the risk factor among cases, provided that they are representative of the whole diseased population and of the OR associated with the exposure.

RESULTS

Table II shows the distribution of the variables analyzed in the 939 cases and 949 controls. There were

TABLE II. DISTRIBUTION OF SELECTED VARIABLES IN 939 CASES OF ACUTE MYOCARDIAL INFARCTION AND 949 CONTROLS

	Cases		Controls	
	N	%	N	%
Age (years)				
<45	121	12.89	136	14.33
45–54	250	26.62	242	25.50
55–64	293	31.20	266	28.03
65–75	275	29.29	305	32.14
Sex				
Males	734	78.17	727	76.61
Females	205	21.83	222	23.39
Social status				
1	168	17.89	172	18.12
2	378	40.26	394	41.52
3	393	41.85	383	40.36
Exercise				
None	817	87.01	771	81.24
1–3 times/week	79	8.41	113	11.91
>3 times/week	43	4.58	65	6.85
Years of education				
<7	201	21.41	224	23.60
7–12	564	60.06	517	54.48
>12	165	17.57	208	21.92
Body mass index (kg/m^2)				
<25	258	27.48	354	37.30
25–30	480	51.12	434	45.73
>30	201	21.41	161	16.97
Diabetes				
No	799	85.09	866	91.25
Yes	140	14.91	83	8.75
Hypercholesterolemia (≥240 mg/dL)				
No	604	64.32	788	83.03
Yes	335	35.68	161	16.97
Smoking				
No	484	51.54	665	70.07
Yes	455	48.46	284	29.93
Family history of myocardial infarction				
No	631	67.20	806	84.93
Yes	308	32.80	143	15.07

no significant differences with regard to income level indicators and education. Cases reported less frequent physical activity, whereas they more frequently reported diabetes, hypertension, and a family history of myocardial infarction; additionally, cases were more often smokers, had higher serum cholesterol levels, and a higher BMI than controls.

The prevalence of a history of hypertension in cases and controls is shown in Table III. Fifty-one percent of cases vs. 29% of controls reported a history of hypertension. Compared to controls, cases reported elevated systolic and diastolic blood pressure values more often.

The gender and age-adjusted OR of AMI was 2.71 for subjects with a history of hypertension (Table III). After adjusting for age, years of education, social status, BMI, history of diabetes, cholesterolemia, exercise, smoking, and family history of myocardial infarction, the OR was 2.58 (95% CI, 2.08–3.19).

The risk was more than two-fold when hypertensives reported that their highest systolic blood pressure value was below 200 mm Hg (moderate status) and more than four-fold when it was above 200 mm Hg (severe status). A maximal diastolic value below 120 mm Hg (moderate status) increased the risk to 2.48 and to 4.12 when it exceeded 120 mm Hg (severe status).

Table IV shows the OR of AMI according to the history of hypertension in separate strata of selected covariates. Increased risks were observed across all strata of the variables considered. The OR were particularly high when subjects were female, younger, well educated, smokers, and had a low or high BMI (kg/m^2).

Association of Hypertension with Other Coronary Risk Factors

To investigate the interaction between hypertension and other coronary risk factors, the OR for each of these was evaluated, both alone and in combination with the presence of a history of hypertension (Table V). The effect of hypertension and smoking on the OR was multiplicative. In smokers, the OR increased from 2.28 in those without a history of hypertension to more than seven-fold (OR=7.51) in those with hypertension. An additive model was found when the relation of hypertension and hypercholesterolemia was analyzed. In subjects with hypercholesterolemia (≥240 mg/DL), the OR was 2.39 in the absence of hypertension and increased to 5.83 when hypertension was present.

Quality of Blood Pressure Control in Hypertensive Subjects

Table VI shows the OR for AMI in hypertensive

TABLE III. PREVALENCE OF HYPERTENSION IN 939 CASES OF ACUTE MYOCARDIAL INFARCTION AND 949 CONTROLS, AND ODDS RATIOS FOR INFARCTION ACCORDING TO HYPERTENSION SEVERITY

	Cases n=939		Controls n=949		Odds Ratio (95% CI)	
	n	%	n	%	MH**	MLR†
Nonhypertensive	456	48.56	676	71.23	1*	1*
Hypertensive	483	51.44	273	28.77	2.71 (2.23–3.33)	2.58 (2.08–3.19)
Highest systolic value (systolic hypertension severity)						
≤200 mm Hg (moderate)	259	27.58	158	16.65	2.47 (1.95–3.16)	2.42 (1.88–3.11)
>200 mm Hg (severe)	167	17.78	55	5.80	5.02 (3.56–7.27)	4.12 (2.87–5.89)
Missing data	57	6.07	60	6.32	1.44 (0.97–2.18)	1.52 (1.00–3.29)
Highest diastolic value (diastolic hypertension severity)						
≤120 mm Hg (moderate)	230	24.49	131	13.80	2.68 (2.08–3.50)	2.48 (1.90–3.24)
>120 mm Hg (severe)	143	15.23	49	5.16	4.46 (3.16–6.59)	4.12 (2.83–5.99)
Missing data	110	11.71	93	9.80	1.82 (1.33–2.52)	1.81 (1.30–2.51)

CI=confidence interval
*Reference
**Mantel-Haenszel estimates adjusted for age in decades and sex
†Estimates are for multiple logistic regression equations including terms for age in years, sex, cholesterolemia (mg/dL), diabetes, smoking, body mass index, years of education, social status, exercise, and family history of myocardial infarction.

TABLE IV. ODDS RATIOS OF ACUTE MYOCARDIAL INFARCTION IN RELATION TO THE HISTORY OF HYPERTENSION IN STRATA OF SELECTED COVARIATES

	Odds Ratio (95% CI)** Hypertension	
	No	Yes
Sex		
Male	1*	2.32 (1.82–2.95)
Female	1*	3.30 (2.08–5.25)
Age (years)		
≥55	1*	2.16 (1.67–2.79)
<55	1*	3.70 (2.52–5.44)
Exercise		
None	1*	2.51 (1.99–3.15)
1–3 times per week	1*	2.50 (1.12–5.59)
≥–3 times per week	1*	2.89 (1.05–7.96)
Years of education		
<7	1*	2.43 (1.56–3.78)
7–12	1*	2.18 (1.64–2.88)
>12	1*	3.49 (2.06–5.90)
Social status		
1	1*	2.67 (2.03–3.52)
2	1*	2.59 (1.96–3.43)
3	1*	2.07 (1.24–3.46)
Body mass lndex (kg/m^2)		
<25	1*	3.51 (2.37–5.21)
25–30	1*	1.82 (1.36–2.44)
>30	1*	4.02 (2.35–6.89)
Diabetes		
No	1*	2.59 (2.07–3.24)
Yes	1*	1.95 (0.99–3.82)
Smoking		
No	1*	2.22 (1.71–2.89)
Yes	1*	3.24 (2.22–4.73)
Hypercholesterolemia (≥240 mg/dL)		
No	1*	2.49 (1.96–3.17)
Yes	1*	2.40 (1.55–3.73)
Family history of myocardial infarction		
No	1*	2.81 (2.21–3.58)
Yes	1*	1.90 (1.22–2.97)

CI=confidence interval
*Reference
**Estimates are from multiple logistic regression equations including terms for age, sex, choleterolemia, diabetes, smoking, body mass index, years of education, social status, exercise and family history of myocardial infarction.

treated subjects, according to their most recent blood pressure value. Those with a systolic pressure below 140 mm Hg increased their risk to 2.59 and to 3.42 when it was above 140 mm Hg. If the most recent diastolic pressure was below 90 mm Hg, the OR was 2.48, and it increased to 3.72 when the diastolic pressure exceeded 90 mm Hg.

DISCUSSION

This study confirms that hypertension is associated with an increased risk of AMI. Compared with normotensives, hypertensive males, risk was increased by more than two-fold and that of females more than three-fold, and the OR remained consistently elevated in various strata of selected covariates.

Our findings regarding the relationship between hypertension and AMI are in agreement with other prospective studies. For example, the Framingham study,[21] in which a cohort of subjects from the general population was followed biennially for the development of cardiovascular events related to their blood pressure levels, showed that in hypertensives, the age-adjusted relative risk was 2 for men and 2.2 for females after 36 years of follow-up. In the Multiple Risk Factor Intervention Trial,[22] the relative risk of coronary heart disease was 3.23 in subjects with an isolated increase in diastolic pressure and 4.19 in those with an isolated increase in systolic blood pressure.

Our study shows that the risk of AMI was significantly related to the severity of hypertension. We observed a trend toward an increase in risk as the history of hypertension increased from moderate to severe. The OR increased markedly if the systolic or diastolic blood pressure reported by the subjects at any time exceeded 200 or 120 mm Hg, respectively. This direct relationship between hypertension and coronary heart disease was reported by MacMahon et al.[5] who provided information about 418,343 adults, aged 25–70 years included in nine prospective observational studies. The difference between highest and lowest strata of blood pressure was 30 mm Hg, and within this narrow range the risk increased almost five times.

Several randomized trials have indicated that treatment with antihypertensive drugs reduces the risk of cardiovascular disease.[11] But efficacy of antihypertensive therapy in preventing coronary artery disease has been lower than expected and thus caused some unjustified uncertainty about the influence of hypertension on the evolution of atherosclerosis. The detrimental effect of antihypertensive drugs on other coronary risk factors, late initiation of antihypertensive treatment, and inadequate treatment of other risk factors are some of the explanations for this discrepancy.

In our study, in subjects without a history of cardiovascular disease, the risk of AMI was related to the quality of hypertension control. Compared with normotensives, treated hypertensives with uncontrolled blood pressure (most recent blood pressure >140/90) had a significantly increased risk of AMI: more than three-fold in uncontrolled systolic blood pressure and nearly four-fold in uncontrolled diastolic blood pressure. Those with controlled blood pressure (most recent blood pressure >140/90) had lower risk, but their OR did not reach 1. This suggests that the link between hypertension and coro-

TABLE V. ODDS RATIOS (AND 95% CONFIDENCE INTERVALS) FOR INTERACTION BETWEEN HYPERTENSION AND OTHER SELECTED RISK FACTORS FOR ACUTE MYOCARDIAL INFARCTION

	Odds Ratio (95% CI)**	
	Non-Hypertensives	Hypertensives
Diabetes		
No	1*	2.61 (2.08–3.26)
Yes	1.99 (1.25–3.18)	3.64 (2.37–5.58)
Smoking		
No	1*	2.16 (1.67–2.80)
Yes	2.28 (1.74–2.99)	7.51 (5.25–10.74)
Hypercholesterolemia (≥240 mg/DL)		
No	1*	2.58 (2.04–3.28)
Yes	2.39 (1.78–3.21)	5.83 (4.05–8.38)
Family history of myocardial infarction		
No	1*	2.76 (2.18–3.50)
Yes	2.85 (2.07–3.91)	5.04 (3.52–7.21)

*Reference
**Estimates are from multiple logistic regression equations including terms for age, sex, cholesterolemia (mg/DL), diabetes, smoking, body mass index, years of education, social status, exercise, and family history of myocardial infarction.

nary artery disease is a complex process that includes other factors besides the increase in blood pressure values. Several mechanisms can account for the increased coronary risk in hypertensive patients. Hypertension accelerates the effects on atheroma, increases shear stress on plaques, exerts adverse functional effects on the coronary circulation, and impairs endothelial function and control of sympathetic tone.[23] Furthermore, dyslipidemia, glucose intolerance, excess body weight, and hyperinsulinemia represent independent predictors of both coronary artery disease and hypertension.

The possibility of a selection bias in the present study must be considered, but the rates of participation among cases and controls were high. In addition, myocardial infarction is a condition for which admission to the hospital is usually mandatory; hence, the possibility of selective admission of the cases is small.

Another limitation of the present study design is that patients who died out of hospital or in hospital before the investigation were not included. However, it seems unlikely that the exclusion of these patients affected our findings. Except for diabetics, who die more frequently, the prevalence of coronary risks factors in fatal AMI is quite similar to that of nonfatal AMI.

Another possible source of bias is the recall bias. The assessment of information regarding the highest and most recent blood pressure value was based on self-reports, and considerable underestimation may occur here. It is unknown whether the experience of myocardial infarction as such may influence participants' answers to the questions. It is possible that during an AMI a patient may misinterpret his or her memories of blood pressure control before the infarction. Hence, cases with hypertension may have been more prone to misreport lower values and adequate management of their blood pressure than controls. This would have resulted in an underestimation of the risk of AMI in treated hypertensive patients. Nevertheless, this recall bias between cases and controls, if present, is difficult to assess.

In our study, hypertensives without treatment had a lower odds ratio (2.44) than expected. But this lower risk could be explained because this stratum included not only hypertensive subjects who had discontinued their drug treatment, but also those with mild hypertension who were managed with diet only.

A major strength of this study lies in the accuracy of the diagnosis of AMI and in the exclusion of subjects with a history of cardiovascular disease from the analysis, which could have led to modifications in lifestyle habits. Furthermore, using a case-control study, we were able to collect information on risk factors for AMI from a larger sample size in a short period of time. With regard to confounding factors, the main findings of this study were not materially influenced by known or suspected risk factors for myocardial infarction.

Our results suggest that there could be an increased risk of AMI for hypertensive subjects, particularly if they smoke or have cholesterol values above 240 mg/dL. We found an additive model when hypertension was associated with hypercholesterolemia and a multiplicative model when it was associated with smoking. These examples of synergy are of public health interest and suggest an important direction for further investigations.

In this population from Argentina, hypertension accounted for about 27% of all cases of AMI in males and 49% in females. These findings underline the importance of preventive intervention in this country, where hypertension is a prevalent risk factor. A recent study conducted in Argentina showed that 28% of active workers in Buenos Aires were hypertensive.[24] About one third of this population were aware of their condition and 75% of these were receiving treatment. Of those treated, 16% were controlled.

Hypertensive status is easy and inexpensive to investigate and could be used to identify people who are potentially at risk of developing coronary heart

TABLE VI. DISTRIBUTION OF 939 CASES OF ACUTE MYOCARDIAL INFARCTION AND 949 CONTROLS, AND ODDS RATIOS FOR INFARCTION ACCORDING TO THEIR MOST RECENT BLOOD PRESSURE VALUE

	Cases n=939		Controls n=949		Odds Ratio (95% CI)	
	n	%	n	%	MH**	MLR†
Nonhypertensives	456	48.56	676	71.23	1*	1*
Hypertensives	483	51.44	273	28.77	2.71 (2.23–3.33)	2.58 (2.08–3.19)
Treated hypertensives						
Most recent systolic blood pressure						
≤140 mm Hg (controlled with treatment)	205	42.44	120	43.96	2.57 (1.96–3.41)	2.59 (1.98–3.40)
>140 mm Hg (not controlled with treatment)	147	30.43	58	21.25	3.93 (2.83–5.70)	3.42 (2.40–4.87)
Missing data	10	2.07	27	9.89	0.60 (0.27–1.34)	0.63 (0.29–1.35)
Most recent diastolic blood pressure						
≤90 mm Hg (controlled with treatment)	240	49.69	144	52.75	2.51 (1.97–3.26)	2.48 (1.91–3.22)
>90 mm Hg (not controlled with treatment)	83	17.18	29	10.62	4.32 (2.76–7.03)	3.72 (2.33–5.96)
Missing data	39	8.07	32	11.72	1.97 (1.17–3.36)	1.89 (1.12–3.19)
Untreated hypertensives	121	25.05	68	24.91	2.70 (1.96–3.84)	2.44 (1.73–3.46)

CI=confidence interval
*Reference
**Mantel-Haenszel estimates adjusted for sex and age in decades.
†Estimates are for multiple logistic regression equations including terms for age in years, sex, cholesterolemia (mg/DL), diabetes, smoking, body mass index, years of education, social status, exercise, and family history of myocardial infarction.

disease. The knowledge of their blood pressure as well as data regarding other modifiable risk factors, such as hypercholesterolemia or smoking, may help individuals to modify their lifestyles and thus reduce their risk of developing coronary heart disease.

Thus our data suggest that hypertension increases the risk of AMI, and its inadequate management in routine clinical practice was associated with very high risk. Hypertensives whose most recent blood pressure measurement is below 140/90 mm Hg reduce part (but not all) of their risk of AMI.

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