

Actual and Perceived Risk of Cardiovascular Disease among Sample of Iraqi Patients with Rheumatoid Arthritis

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Abstract Background: Independent of conventional risk factors, patients with rheumatoid arthritis (RA) have a significantly increased risk of cardiovascular disease (CVD). **Aims of the Study:** To evaluate the actual and perceived 10-year CVD risk among Iraqi patients with RA as well as their level of knowledge about CVD risk. **Patients and methods:** This cross-sectional study included 100 RA patients (85 females and 15 males) who visited Baghdad Teaching Hospital/Rheumatology Unit from January 2021 to July 2021. The Framingham Risk Score (FRS) was used to calculate the actual 10-year risk of CVD. The Heart Disease Fact-Rheumatoid Arthritis Questionnaire (HDFQ-RA) was used to assess the subjects' knowledge of cardiovascular disease. **Results:** Among hundred Iraqi patients with RA, the median age was 51.23 ± 8.4 years. The study's findings revealed that 23% had a high risk for CVD and 27% & 50% had moderate and low risk, respectively, based on the FRS calculator. The risk of CVD was significantly affected by the age of disease onset and seropositivity and steroid use (p-value 0.001). When the perceived risk was compared to the actual risk of cardiovascular disease, there was a weak agreement between them; only 31% had corresponding answers. **Conclusions:** The study showed an elevated risk of CVD in rheumatoid arthritis patients and a gap between actual and perceived CVD risk.

Key Words Rheumatoid arthritis, Iraq, Cardiovascular disease risk, Framingham risk score (FRS)

1. Introduction

It is generally known that individuals with RA have an increased risk of cardiovascular disease (CVD)-related morbidity and mortality [1]. It is a significant contributor to the growing mortality disparity between RA patients and the general population [2]. The increased CVD risk associated with RA is now obviously comparable to that of people with diabetes mellitus [3]. Studies have provided evidence indicating a significantly elevated risk of atherosclerosis and coronary calcification in patients with RA [4]–[6].

Moreover, individuals with RA are often less susceptible to experiencing angina symptoms, resulting in a considerable portion of their CVD going undetected or untreated. This lack of recognition or management of CVD among RA patients increases the potential for occurrences of sudden cardiac death [7]–[9].

A. Traditional and Rheumatoid Arthritis-Related Cardiovascular Risk Factors in Collaboration

The relationship between traditional risk factors and RA-related mechanisms is complicated and frequently bidirec-

tional. For instance, oxidative stress characterizes systemic inflammation in RA and encourages insulin resistance, which in turn exacerbates the imbalance between ROS and antioxidants [10]–[14].

B. Treatments of RA and Cardiovascular Disease Risk

1) Glucocorticoids

Given the adverse impacts on the cardiovascular system, such as hypertension, dyslipidemia, insulin resistance, and diabetes, the overall benefit of glucocorticoids in RA is controversial. On the other hand, glucocorticoids increase mobility and appear to have favorable effects on the lipid profile [15].

2) Non-Steroidal Anti-Inflammatory Drugs

Except for etoricoxib, which indicated a greater risk, users of NSAIDs generally had similar CVD risk [16]. COXIBs should not be administered to patients with known CV disease, according to European guidance from the registration authorities (EMA) [17].

3) Conventional Disease Modifying Anti Rheumatic Drugs (cDMARDs)

More evidence is pointing to the possibility that efficient anti-inflammatory therapy reduces the CVD risk in RA, and it appears that methotrexate reduces mortality and morbidity [18]–[20].

4) Biological and Small Molecule Disease Modifying Anti Rheumatic Drugs

When compared to cDMARDs, anti-TNF medicines had a decreased risk of CVD [21]. Tofacitinib has been attributed to a higher CVD risk and death, according to U S Food and Drug Administration (FDA) study of a large randomized safety clinical trial [22]. To compare the cardiovascular safety of various treatments for RA patients, further prospective trials are required [23].

C. Cardiovascular Disease Prevention and Management among those with Rheumatoid Arthritis

1) Assessment of Cardiovascular Disease Risk

Patients with rheumatoid arthritis cannot be appropriately categorized based on risk using conventional CVD risk models [24], [25]. There are no RA-specific recommendations for CVD risk prediction from the ACR. Nonetheless, the European League Against Rheumatism (EULAR) recommends that in situations where national guidelines are unavailable, individuals with RA should undergo assessments for their 10-year CVD risk at least once every five years. Additionally, these assessments should be conducted following any alterations in medications. This recommendation emphasizes the importance of regularly monitoring and evaluating CVD risk in RA patients to ensure appropriate management and preventive measures that must be implemented [26].

2) Management of Traditional Cardiovascular Risk Factors

The advantages of adopting a healthy lifestyle, exercising regularly, and quitting smoking should be emphasized [24]. The recommendations for managing CVD risk in RA patients are similar to those for the general population [26].

3) Management of Rheumatoid Arthritis

According to current guidelines from the European League Against Rheumatism (EULAR), rheumatologists play a vital role in assessing and coordinating the management of CVD risk in patients with RA [27]. These guidelines prioritize achieving disease control rather than focusing solely on the specific class of medication chosen for treatment [28], [29].

2. Patients and Method

A. Study Design

A cross-sectional study was carried out in The Rheumatology Unit of Baghdad Teaching Hospital from January 2021 to July 2021.

B. Patient Eligibility

In this study, 100 patients of either gender who were older than 40 years were enrolled. Patients who matched the 2010 American ACR/EULAR classification criteria for rheumatoid arthritis were eligible for enrollment. All trial participants were determined to be free of any prior CVD events, including myocardial infarction, stroke, transient ischemic attack, coronary artery disease/reperfusion therapy, and peripheral arterial disease.

C. Clinical Evaluation and Measurements

A. Sociodemographic Data

- Age, gender, educational level, occupation, and smoking status.
- Questions about lifestyle habits include those related to eating a balanced diet, described by the American Heart Association (AHA) as eating a variety of fruits and vegetables as well as grains and grains. In addition to fish, poultry, lean meats, low-fat or fat-free dairy products (Mediterranean diet). Being physically active is defined as engaging in at least 150 minutes per week of moderate-intensity aerobic activity, 75 minutes per week of vigorous aerobic activity, or a combination of both [28].

B. Medical history

- Including comorbidities (hypertension, DM, dyslipidemia and renal disease), current medications, and family history in first-degree relatives for CVD.

C. Body Mass Index /BMI

- The BMI of all patients was calculated using the formula: $BMI = \text{weight (kg)} / \text{height (m)}^2$ [29].

D. Disease duration

- It was calculated with respect to the date of the study.

E. Disease features

- Using the Clinical Disease Activity Index (CDAI) score to assess the patient's disease activity [30].
- Physical examination including (general, eye, cardiovascular, respiratory, and neurological examination, searching for extra-articular manifestations).
- Rheumatoid Factor (RF) and Anti Citrullinated Peptide antibodies (ACPA) were collected from RA registry data of the Rheumatology Consultant Clinic in our hospital.

D. Perceived Cardiovascular Risk

How likely will you develop a CVD in the next ten years? Is the likelihood low, moderate, or high, or do you not know? This inquiry was used to evaluate people's perceptions of the risk of developing CVD.

E. Actual cardiovascular disease risk

- The risk was calculated using Framingham risk score (FRS) [31].
- Serum total cholesterol (TC) and serum high-density lipoprotein cholesterol (HDL) were measured using the spectrophotometric method.
- The risk is determined using (FRS) and multiplied by 1.5 per EULAR recommendations for managing CVD risk in RA patients [25].

F. Cardiovascular Disease Knowledge

The subject's knowledge about CVD was measured with the Heart Disease Facts Questionnaire-Rheumatoid Arthritis (HDFQ-RA) (appendix). Those who had < 25 percent correct answers were considered as poor knowledge, 25-74% and > 75% were considered as fair and good, respectively. The questionnaires were translated into Arabic and validated.

G. Statistical Analysis

The data was analyzed using Statistical Package for Social Sciences (SPSS) version 26. The data is presented as mean, standard deviation, and ranges. Frequencies and percentages present categorical data. Analysis of Variance (ANOVA) (two-tailed) was used to compare the continuous variables accordingly. The Chi-square test was used to assess the association between FRS and knowledge levels with certain information, while the Fisher exact test was used instead when the expected frequency was less than 5. A level of P-value less than 0.05 was deemed significant.

H. Patient Consent and Ethical Approval

The Iraqi Board for Medical Specializations obtained a letter of ethical approval with reference number (363) dated 25 January 2021. This paper was carried out by the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

3. Results

A. General Characteristics

1) Socio-demographic

The age of patients ranged from 40-71 years with a mean of 51.23 ± 8.4 years. The proportion of females was much higher than males (85% versus 15%). The male to female ratio was 1:5.66 (Figure 1,2)

B. Clinical Characteristics

In this study, the most common age of diagnosis was < 40 years (48%); duration of disease was <10 years in 53%; Extra-articular disease was presented in 36%; and RF was positive in 69%. Regarding CDAI, 48% of cases showed low disease activity. The management included csDMARD in 91% of cases; steroids in 48%; NSAIDs in 32%; and biological in 72% (Table 1).

Variable	No. (n= 100)	Percentage (%)
Age of diagnosis (Year)		
<40	48	48.0
40 – 49	36	36.0
≥ 50	16	16.0
Duration of disease (Year)		
<10	53	53.0
10 – 19	33	33.0
≥ 20	14	14.0
Extra-articular disease		
Yes	36	36.0
No	64	64.0
Positive RF or ACPA antibody		
Yes	69	69.0
No	31	31.0
(CDAI)		
Remission	4	4.0
Low disease activity	48	48.0
Moderate disease activity	44	44.0
High disease activity	4	4.0
csDMARD		
Yes	91	91.0
No	9	9.0
Steroid		
Yes	48	48.0
No	52	52.0
Biological		
Yes	72	72.0
No	28	28.0
NSAIDs		
Yes	32	32.0
No	68	68.0
Hypertension		
Yes	30	30.0
No	70	70.0
Diabetes mellitus		
Yes	20	20.0
No	80	80.0
Dyslipidemia		
Yes	7	7.0
No	93	93.0
Statin		
Yes	3	3.0
No	97	97.0
Parental history of CVD		
Positive	36	36.0
Negative	64	64.0
Total cholesterol level		
High	10	10.0
Normal	90	90.0
HDL level		
Low	23	23.0
Normal	77	77.0
LDL level		
High	17	17.0
Normal	83	83.0

Table 1: Distribution of study patients by clinical characteristics

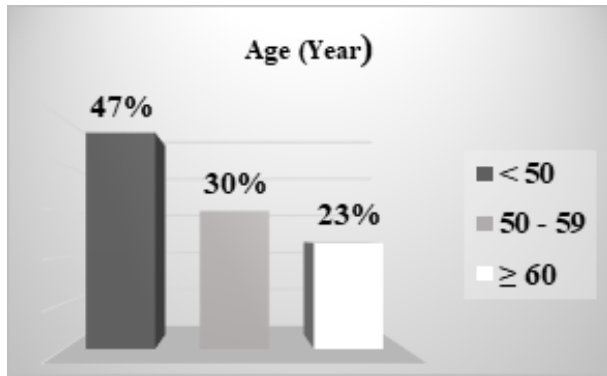


Figure 1: Distribution of study patients by age

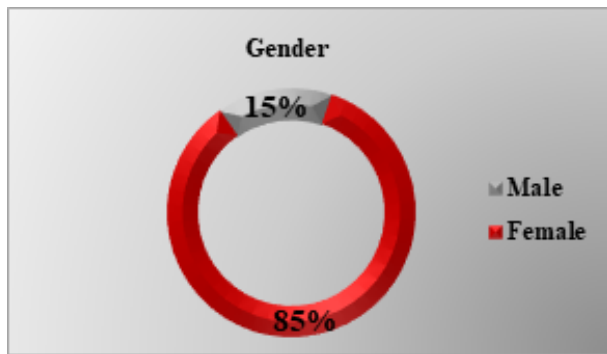


Figure 2: Distribution of study patients by gender

C. Cardiovascular Disease Risk Factors

In this study, 12% of patients were current smokers; 79% had high Body mass index; 41% were eating unhealthy diet; and 85% were physically inactive. We noticed that 30% of study patients were hypertensive; 20% were diabetics; 7% had dyslipidemia; and 36% had positive family history of CVD. Total cholesterol level was high in 10% of cases; LDL in 17%; and HDL was low in 23% (Table 2).

D. Framingham Risk Score (FRS) and Perceived Risk

Actual risk assessed by Framingham risk score (FRS) calculator, showed that half of study patients (50%) had low risk for CVD development, 27% moderate, and 23% had

Variable	No. (n= 100)	Percentage (%)
Smoking status		
Current smoker	12	12.0
Non-smoker	88	88.0
BMI Level		
Normal	21	21.0
Overweight	44	44.0
Obese	35	35.0
Healthy diet		
Yes	59	59.0
No	41	41.0
Physical activity		
Inactive	85	85
Active	15	15

Table 2: Distribution of study patients by CVD risk factor

Variable	No. (n= 100)	Percentage (%)
FRS (actual risk)		
Low	50	50.0
Moderate	27	27.0
High	23	23.0
Perceived risk		
Low	44	44.0
Moderate	10	10.0
High	3	3.0
Don't know	43	43.0

Table 3: Distribution of study patients by actual and perceived risk

Perceived risk	Actual risk (FRS level)			Total	Kappa value	P-value
	Low	Moderate	High			
Low	26	11	7	44	0.169	0.049
Moderate	1	4	5	10		
High	2	0	1	3		
Total	29	15	13	57		

Table 4: Comparison between actual and perceived risks

high risk. Regarding the perceived risk, only 3% of studied patients thought that they were in high risk level for CVD development, 10% moderate, 44% low risk, and 43% their risk level was not known (Table 3).

E. Comparison between Actual and Perceived Risks

High risk was determined by FRS in 23 cases; only one of them was confirmed by patients' perception and 10 of them did not have any idea about the CVD risk. Low risk was determined by FRS in 50 cases; 26 of them were confirmed by patients' perception, and 21% had no idea about the risk. In conclusion, there was a weak agreement between actual and perceived risk, and this agreement was statistically significant (kappa= 0.169, P=0.049) (Table 4).

The prevalence of high CVD risk was increasing significantly with advancing in age to reach the highest at age > 60 years (47.8%, P= 0.001). Regarding gender, males had significantly higher prevalence of high CVD risk than females (33.3% versus 21.2%, P= 0.038) (Table 5).

F. Knowledge about CVD Risk

The highest percentage of correct responses (97%) was to the question if keeping BP under control will reduce a person's chance of developing cardiovascular disease, while the highest proportion of incorrect responses (96%) were recorded when the patients asked if RA affects the balance of 'good' and 'bad' cholesterol in the blood in an undesirable way (Table 6).

G. Total Knowledge Score

Regarding the total score of patients about knowledge toward CVD risk, 25% of patients scored within good score level, while remaining 72% and 3% of them scored within fair and poor scores respectively as shown in the Figure 3.

Variable	Actual CVD risk level (FRS level)			Total (%) n= 100	P- Value
	Low (%) n= 50	Moderate (%) n= 27	High (%) n= 23		
Age of diagnosis (Year)					
<40	30 (62.5)	9 (18.8)	9 (18.8)	48 (48.0)	0.001
40 – 49	18 (50.0)	13 (36.1)	5 (13.9)	36 (36.0)	
≥ 50	2 (12.5)	5 (31.3)	9 (56.3)	16 (16.0)	
Duration of disease (Year)					
<10	29 (54.7)	13 (24.5)	11 (20.8)	53 (53.0)	0.84
10 - 19	15 (45.5)	9 (27.3)	9 (27.3)	33 (33.0)	
≥ 20	6 (42.9)	5 (35.7)	3 (21.4)	14 (14.0)	
Extra-articular disease					
Yes	15 (41.7)	10 (27.8)	11 (30.6)	36 (36.0)	0.334
No	35 (54.7)	17 (26.6)	12 (18.8)	64 (64.0)	
Positive RF or ACPA					
Yes	25 (36.2)	21 (30.4)	23 (33.3)	69 (69.0)	0.001
No	25 (80.6)	6 (19.4)	0 (0)	31 (31.0)	
Clinical disease activity index (CDAI)					
Remission	3 (75.0)	0 (0)	1 (25.0)	4 (4.0)	0.062
Low	27 (56.3)	10 (20.8)	11 (22.9)	48 (48.0)	
Moderate	19 (43.2)	17 (38.6)	8 (18.2)	44 (44.0)	
High	1 (25.0)	0 (0)	3 (75.0)	4 (4.0)	
csDMARD					
Yes	45 (49.5)	26 (28.6)	20 (22.0)	91 (91.0)	0.485
No	5 (55.6)	1 (11.1)	3 (33.3)	9 (9.0)	
Steroid					
Yes	14 (29.2)	17 (35.4)	17 (35.4)	48 (48.0)	0.001
No	36 (69.2)	10 (19.2)	6 (11.5)	52 (52.0)	
Biological					
Yes	36 (50.0)	19 (26.4)	17 (23.6)	72 (72.0)	0.962
No	14 (50.0)	8 (28.6)	6 (21.4)	28 (28.0)	
NSAID					
Yes	17 (53.1)	11 (34.4)	4 (12.5)	32 (32.0)	0.192
No	33 (48.5)	16 (23.5)	19 (27.9)	68 (68.0)	

Table 5: Association between actual risk and clinical characteristics

Knowledge Questions	Correct response no. (%)	Incorrect response no. (%)
General questions		
When someone has heart disease, they always know.	24 (24.0)	76 (76.0)
A person who smokes is more likely to develop stroke and heart disease.	91 (91.0)	9 (9.0)
Keeping BP under control will reduce a person's chance of developing cardiovascular disease.	97 (97.0)	3 (3.0)
A person with high cholesterol is more likely to develop heart disease.	79 (79.0)	21 (21.0)
If your good cholesterol (HDL) is high, you are more likely to develop heart disease.	48 (48.0)	52 (52.0)
A person's risk of acquiring heart disease can only be reduced by working out in a gym or taking fitness classes.	51 (51.0)	49 (49.0)
Eating fatty foods does not affect blood cholesterol levels.	50 (50.0)	50 (50.0)
Diabetes increases a person's risk of cardiovascular disease.	56 (56.0)	44 (44.0)
You are more prone to get heart disease if you have a family history of it.	71 (71.0)	29 (29.0)
A person's risk of developing heart disease increases with age.	93 (93.0)	7 (7.0)
RA related questions		
A person with RA can reduce their chance of heart disease by keeping their weight under control.	96 (96.0)	4 (4.0)
By giving up smoking, a person with rheumatoid arthritis can lower their risk of developing heart disease.	87 (87.0)	13 (13.0)
Exercise should not be done by those who have rheumatoid arthritis because it may harm their joints.	54 (54.0)	46 (46.0)
Patients with RA who take anti-inflammatory drugs such diclofenac or ibuprofen may be at an increased risk for heart disease.	47 (47.0)	53 (53.0)
Frequent rheumatoid arthritis flare-ups (or "flares") increase the risk of heart disease.	15 (15.0)	85 (85.0)
Rheumatoid arthritis affects the balance of 'good' and 'bad' cholesterol in the blood in an undesirable way.	4 (4.0)	96 (96.0)
A person with rheumatoid arthritis who uses steroids long-term or at high doses runs the risk of developing diabetes.	28 (28.0)	72 (72.0)

Table 6: The results of patients' response about knowledge questions

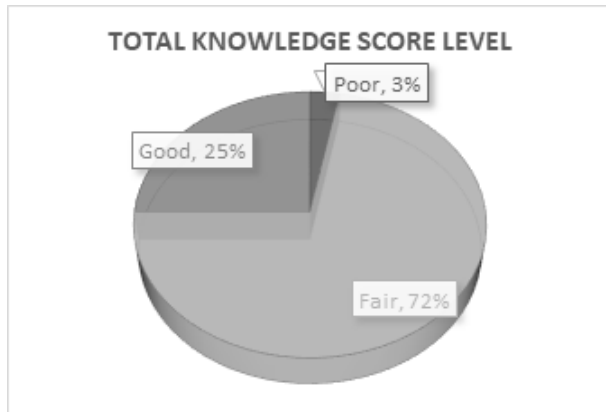


Figure 3: Total knowledge score level

It was obvious that there was a statistically significant association ($P=0.001$) between knowledge toward CVD risk and each of educational level and occupation as 78.3% of participants with good score were highly educated. No significant associations ($P \geq 0.05$) were found between knowledge toward CVD risk and all other variables.

4. Discussion

It is a common belief that atherosclerosis is the primary cause of mortality in RA patients. However, there needs to be more published studies to date that comprehensively assess the knowledge about CVD risk or the actual risk among RA patients in Iraq. In the first part of this study, we assessed the actual CVD risk. Our findings revealed that 23% of the patients had a high risk for CVD based on the FRS calculator, and 27% & 50% have moderate and low, respectively. A similar study was done in Korea by Boo et al. [32]. Out of the subjects with RA, only 12% were classified as having a high risk for CVD, although they had a close median age of 52.61 ± 7.97 . This may be due to the difference in ethnicity, lifestyle, and the prevalence of traditional risk factors among these populations.

In this study, the risk for CVD was higher in men (33.3% versus 21.2% in women, $P=0.038$). Regarding the prevalence of traditional CVD risk factors, about 12% of studied patients were current smokers, 79% had high BMI, 41% were eating unhealthy diets, and 85% were physically inactive. So, we need a strong effort to educate our patients about the importance of lifestyle modification to reduce future CVD risk. About the other modifiable risk factors, we noticed that 30% of studied patients were hypertensive, and 20% were diabetics. The total cholesterol level was high in only 10% of cases, and HDL was low in 23%. We also found that LDL and TC/HDL ratios were significantly lower in patients with low CVD risk levels than in patients with moderate and high CVD risk levels ($P < 0.05$). These results, as compared to the result of the Korean study by Boo et al. [32], are approximately the same.

The study showed that 56.3% of late disease onset had high risk (p -value 0.001). All of the high-risk groups had

positive serology (p -value 0.001), and this result reflects the importance of rheumatoid arthritis itself as a risk factor. Drugs may play a role in CVD risk. In this study, 48% of the studied patients were on steroids, and there was an obvious association between steroid use and the actual risk of CVD (p -value 0.001). Seventeen of 23 patients (73%) who were categorized as high-risk were on steroids. Several studies discussed the association between steroid use and CVD risk [16], [17]. Initiating glucocorticoids in steroid-naïve RA patients is associated with increased risk of CVD at daily doses ≥ 5 mg as Ocon et al. said [33].

According to the 2019 ACC/AHA guidelines, individuals with chronic inflammatory disorders, including RA with LDL-C 70 to 189 mg/dL and a 10-year atherosclerotic cardiovascular disease risk of over 5%, (low, borderline), moderate or high-intensity statin therapy should be discussed (class IIA recommendation) [27]. If we applied these guidelines to our studied sample, about 38% of them would be better off starting statin, while unfortunately, only 3% are currently on it. In a study by Chhibber et al., [34], they found that starting statins were linked to a 21% decreased mortality risk in RA patients.

The last part of the current thesis assessed the level of CVD knowledge among the studied patients. This study showed that the response to questions related to smoking, high blood pressure, and dyslipidemia and its association with CVD was good. These results are similar to the result in Boo et al. [32] and Michos et al. [35]. While the right responses to the questions about exercise and healthy lifestyle were low compared to the other two studies, It was evident, as we had expected, that there was a statistically significant association ($P=0.001$) between good knowledge of CVD risk and a higher educational level. Only 15% of our patients think that their disease activity influenced the development of CVD. A possible reason is the lack of educational programs by healthcare providers.

5. Conclusions

- 1) Patients with rheumatoid arthritis (RA) face a heightened risk for cardiovascular disease (CVD), and implementing measures to reduce this risk is particularly challenging.
- 2) The study highlighted a lack of knowledge regarding the associations between rheumatoid arthritis (RA) and cardiovascular disease (CVD). Furthermore, there seems to be a discrepancy between RA patients' actual and perceived CVD risk, which may be partially attributed to the absence of adequate education programs on this matter.

Limitations

The current study had some limitations including:

- 1) It is a small-sample study conducted in a single center. Additional research with a larger sample size.
- 2) The Framingham Risk Score calculator (FRS) was utilized in this study to estimate the 10-years CVD

risk due to the lack of a specific tool. It's crucial to remember, though, that evidence exists that suggests the FRS may significantly underestimate the real risk.

Conflict of interest

The authors declare no conflict of interests. All authors read and approved final version of the paper.

Authors Contribution

Both authors contributed equally in this paper.

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