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Prevalence and clinical characteristics of Egyptian patients with myocardial infarction with non-obstructive coronary arteries

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Abstract
Objective: Myocardial infarction (MI) with non-obstructive coronary arteries (MINOCA) is the presence of the universal acute myocardial infarction (AMI) criteria, stenosis less than 50%, and no overt cause for the clinical presentation at the time of angiography. Diagnosis of MINOCA may require multiple diagnostic tools, including cardiac imaging or provocative tests, in addition to standard coronary angiography, according to clinical suspicion. The aim of this study is to assess the prevalence and predictors of myocardial infarction with non-obstructive coronary arteries in Egyptian patients.
Methods: This prospective and observational study was conducted in Tanta university hospital and El Zeitoun specialized hospital from April 2022 till April 2023. All patients who were ≥18 years old, diagnosed with MI according to the Fourth Universal Definition of Myocardial Infarction, and undergone Coronary Angiography included in the study while patients with history of revascularization (PCI or CABG) or diagnosed as MI type 4 or 5 excluded from our study.
Results: 844 patients diagnosed with MI and had undergone CA were screened between April 2022 and april 2023. The prevalence of MINOCA was 8.06% (n=68) in our study. MINOCA patients were found to be younger, had a higher incidence of the female gender. MINOCA patients has lower incidence of risk factors such DM, HTN, smoking and dyslipidaemia (p<0.05, for all). ST elevation ECG is significantly higher in OCA-MI than in MINOCA. WBCs, neutrophils and CKMB level was higher in OCA-MI patients than MINOCA patients (p<0.001), While MINOCA patients have higher systolic and diastolic BP at presentation with Killip class less than 2 (p<0.001). Also, the mean left ventricular ejection fraction by the echocardiography was significantly higher in MINOCA patients (p<0.001), While OCA-MI patients have more dilated LVEDD, LVESD and higher incidence of both WMA and LV thrombus (p<0.001). Patients with MINOCA has lower range of hospital stay (p<0.001), less liable to worse in hospital outcome such as complete heart block, LV thrombus, temporary pacing and heart failure development (p<0.05).
The culprit of MI in was found to be LAD in 369 patients, LCx in 116, RCA in 237 patients, OM in 36 patients and LM in 18 patients. While coronary angiography in MINOCA group normal in 36 patients, ectasia in 9 patients, dissection in 8 patients, myocardial bridge in 3 patients and slow flow in 12 patients
Conclusion: The prevalence of MINOCA in our study is 8.06% in patients who were admitted with MI. Also, as compared to OCA-MI patients, the MINOCA patients are younger, more female incidence, have fewer traditional factors and more benign inhospitable course.

Keywords: Myocardial infarction with non-obstructive coronary arteries, myocardial infarction, and coronary angiography

Introduction
Myocardial infarction with nonobstructive coronary arteries (MINOCA) is clinically defined by the presence of the universal acute myocardial infarction (AMI) criteria, stenosis less than 50%, and no overt cause for the clinical presentation at the time of angiography [1].
The estimated prevalence of MINOCA is approximately (6 - 8) % among patients presenting with AMI and is more common in women than in men. MINOCA is considered a working diagnosis until a specific cause has been secured so that clinicians looking after these patients may institute appropriate treatment and assess prognosis based on cause [3].

Diagnosis may require variable investigations beside the standard coronary angiography, according to clinical suspicion [2].

The noncardiac causes of increased level of cTn, such as pulmonary embolism and kidney damage, should be first excluded. Cardiac causes, including diseases relevant to structural myocardial dysfunction and ischemic myocardial injury, should then be considered. Clinical history, myocardial enzymes, ECG, echocardiography and CA are the techniques used to provide an initial diagnosis which forms the basis for determining the cause of MINOCA [4].

The predictors for MINOCA patients remain unclear although the prognosis is slightly better for MINOCA patients than for MI-CAD patients, however MINOCA isn't always benign [5].

Patients and Methods

After approval of the Local Institutional Ethical Committee of Tanta University Hospital, after taking a written consent from the participants and giving them code numbers (ID) not names, this cross-sectional study was conducted on 844 patients admitted at Cardiology Department at Faculty of Medicine Tanta University and El Zeitoun specialized Hospital in the period from April 2022 to April 2023.

Inclusion criteria

Patients older than 18 years of age who were diagnosed with MI according to the Fourth Universal Definition of Myocardial Infarction and undergone Coronary Angiography and has stenosis less than 50% [1].

Exclusion criteria included

1. Patients younger than 18 years.
2. Patients with stable CAD.
3. Patients with unstable angina pectoris.
4. Patients with history of revascularization (PCI or CABG).
5. Patients with MI types 3 ⁄4 ⁄5 MI [6].
6. Those who had not provided informed consent were excluded from the study.

For all patients the following was done

I-History taking

- **Personal history:** (Age, sex, weight, height, BMI, marital status, address and special habits of medical importance).
- **Complain:** (Chest pain, palpitation, shortness of breath or syncope),
- **Present history** e.g., full analysis of pain
- **Past medical history of other comorbidities:** (DM, HTN, CKD, dyslipidemia, PVD, prior CAD or revascularization).
- **Family history of**: coronary artery disease, heart failure or sudden cardiac death.

Clinical examination

General examination

(Pulse, heart rate, Blood pressure, Respiratory signs of heart failure and classification of patients according to Killip's class).

Local examination: Heart sounds and murmurs.

Investigations

ECG: For diagnosis of ACS with special stress on the ST Segment elevation and Q waves.

Routine Labs: CBC, CK-MB, creatinine, Na, Ka, HbAIC and virology.

Coronary angiography: All patients transferred directly to cath. Lab. in accordance with guidelines [7, 8].

Echocardiography

All patients will be subjected to transthoracic echocardiographic examination within 36 h of admission for assessment of LV global and regional systolic function

Then patients were grouped into two groups

- **Group 1:** Acute myocardial infarction Patients with obstructive coronary artery (OCA Group), who were 776 patients.
- **Group 2:** Acute myocardial infarction patient with non-obstructive coronary artery (MINOCA Group), who were 68 patients, MINOCA patients were defined to have normal coronaries or luminal stenosis less than 50%.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and comparison between the two groups utilizing unpaired Student's t- test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered statistically significant.

Results

Demographics and risk factors

A total 844 patients were enrolled in our study including 776 patients with OCA-MI and 68 patients with MINOCA. The mean age of patients in the MINOCA group is significantly lower at 47.57 years compared to 53.05 years in the obstructive coronary artery disease group (p-value < 0.001). In terms of sex distribution, a higher percentage of males is observed in both groups, but the difference is statistically significant (58.82% in the MINOCA group vs. 71.26% in the Obstructive Coronary Artery Disease group, p-value = 0.031). (Table 1)

Regarding the risk factors, DM, hypertension, special habits of medical importance and dyslipidemia were significantly higher in obstructive coronary artery disease group than MINOCA group (P value was 0.001, 0.012, 0.001 and 0.001 respectively). Family history and PVD were insignificantly different between both groups. (Table 1)

Table 1: Demographics and clinical risk factors of groups

		MINOCA group (n=68)	Obstructive coronary artery disease group (n=776)	P value
Age (years)	Mean ± SD	47.57±5.59	53.05±7.6	<0.001*
Sex	Male	40 (58.82%)	553 (71.26%)	0.031*
	Female	28 (41.18%)	223 (28.74%)	

BMI (kg/m^2)	Mean ±SD	26.57±2.27	28.44±3.79	<0.001*
DM		16 (23.53%)	366 (47.16%)	<0.001*
Hypertension		20 (29.41%)	350 (45.1%)	0.012*
Special habits of medical importance		21 (30.88%)	477 (61.47%)	<0.001*
+ve Family history		11 (16.18%)	185 (23.84%)	0.151
Dyslipidaemia		14 (20.59%)	352 (45.36%)	<0.001*
PVD		6 (8.82%)	86 (11.08%)	0.567

BMI: Body mass index, DM: Diabetes mellitus, PVD: Peripheral vascular disease, *: Significant as P value< 0.05.

Clinical presentation

Duration of chest pain, HR and palpitations were insignificantly different between both groups. SBP and DBP were significantly lower in obstructive coronary artery disease group than MINOCA group (P value =0.029 and 0.026 respectively). Killip's classes were significantly different between both groups as Killip's class > class I in less frequent in MINOCA group (P value = 0.036) (table 2).

Table 2: Clinical presentation and vital signs

		MINOCA group (n=68)	Obstructive group (n=776)	P value
Onset of chest pain (h)	Mean ±SD	7.15±2.05	7.54±2.86	0.273
SBP (mmHg)	Mean ±SD	125.88±19.79	119.01±25.22	0.029*
DBP (mmHg)	Mean ±SD	76.99±12.64	72.01±17.96	0.026*
HR (beats/min)	Mean ±SD	80.4±14.29	81.43±19.34	0.668
Killip. Class	I	56 (82.35%)	499 (64.3%)	0.007*
	II	10 (14.71%)	197 (25.38%)	
	III	0 (0%)	69 (8.9%)	
	IV	2 (2.94%)	53 (6.82%)	
Palpitations		4 (5.88%)	92 (11.85%)	0.164

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate.

Investigations

Regarding noninvasive investigations

ECG: ST segment elevation was significantly higher in obstructive coronary artery disease group than MINOCA group (P value = 0.005). Q waves and other ECG changes was significantly higher in MINOCA group than obstructive coronary artery disease group (P value was 0.04 and 0.005 respectively) while new onset LBBB was insignificantly different (Table 3).

Table 3: ECG diagnostic changes

	MINOCA Group (n=68)	Obstructive group (n=776)	P value
ST elevation	12 (17.64%)	428 (55.15%)	0.005*
New onset LBBB	0 (00%)	17 (2.19%)	0.22
Q waves	7 (10.29%)	36 (4.63%)	0.04*
Other changes	49 (72.05%)	295 (38.00%)	0.005*

LBBB: Left bundle branch block

Labs: HB, platelets and creatinine were insignificantly different between both groups. WBCs, neutrophils and CKMB were significantly higher in Obstructive coronary artery disease group than MINOCA group (P value<0.001). (Table 4).

Table 4: Labs of the groups

		MINOCA Group (n=68)	Obstructive group (n=776)	P value
HB	Mean± SD	12.63±1.3	13±1.85	0.106
WBCs	Mean± SD	9.75±3.3	11.64±3.58	< 0.001*
Neutrophils	Mean± SD	5.93±1.85	7.77±3.006	< 0.001*
Platelets	Mean± SD	266.3±113.3	242±112	0.086
Creatinine (mg/dL)	Mean± SD	1.1±0.23	1.11±0.43	0.871
CKMB (U/L)	Mean± SD	67.6±15.8	77.56±23.72	<0.001*

CKMB: Creatine kinase-MB. WBCs: White blood cells

Echo: EF was significantly lower in obstructive coronary artery disease group than MINOCA group (P value<0.05). EF was significantly lower in OCA-group than MINOCA group (P value<0.001)

Table 5: Echo data of the groups

	MINOCA group (n=68)	Obstructive group (n=776)	Value
EF (%)	60.46±5.54	46.22±10.09	<0.001*
LVEDD	54.2±5	60.3±9.32	< 0.001*
LVESD	38±4.8	41.489±7.62	<0.001*
WMA	2 (2.9%)	612(78.8%)	< 0.001*
Mechanical complications	0	1(0.1%)	1

LV thrombus	0 (0%)	51 (6.57%)	0.029*

EF: Ejection fraction, LVEDD: Left ventricular end diastolic dimension,
LVESD: Left ventricular end systolic dimension, WMA: Wall motion abnormality, LV thrombus: Left ventricle thrombus, *: Significant as P value < 0.05

Regarding Coronary angiography

In MINOCA group, Coronary artery was normal in 36 (52.94%) patients, ectasia in 9 (13.24%) patients, dissection in 8 (11.59%) patients, bridge in 3 (4.41%) patients and slow flow in 12 (17.65%) patients. (Table 6).

Table 6: CA of the MINOCA group

Coronary Angiography	Normal	36 (52.94%)
	Ectasia	9 (13.24%)
	Dissection	8 (11.59%)
	Myocardial bridge	3 (4.41%)
	Slow flow	12 (17.65%)

In obstructive coronary artery disease group, Coronary artery obstruction occurred in LAD in 369 (47.55%) patients, LCx in 116 (14.95%), RCA in 237 (30.54%) patients, OM in 36 (4.64%) patients and LM in 18 (2.32%) patients (Table 7).

Table 7: Culprit vessel of OCA-group.

Coronary Angiography	LAD	369 (47.55%)
	LCx	116 (14.95%)
	RCA	237 (30.54%)
	OM	36 (4.64%)
	LM	18 (2.32%)

CA: Coronary angiography, LAD: left anterior descending artery, LCx: Left Circumflex, RCA: Right coronary artery, OM: Obtuse marginal, LM: Left Main Coronary Artery

Inhospitable course and related complications

Arrhythmic complications and related management

CHB and TPM were significantly higher in obstructive coronary artery disease group than MINOCA group (P value=0.011 and 0.023 respectively) (Table 8). Life threatening ventricular arrythmia, DC and AFib were insignificantly different between both groups (Table 8).

Table 8: Arrhythmic complications and related mangement for both groups

MINOCA group (n=68)		Obstructive group (n=776)	P value
Life threatening ventricular arrythmia	1 (1.47%)	58 (7.47%)	0.063
DC	1 (1.47%)	58 (7.47%)	0.063
A Fib	3 (4.41%)	34 (4.38%)	0.991
CHB	0 (0%)	68 (8.76%)	0.011*
TPM	0 (0%)	55 (7.09%)	0.023*
TPM	0 (0%)	55 (7.09%)	

DC: Direct cardio version, A Fib: Atrial fibrillation, CHB: Complete heart block, TPM: Temporary pacemaker, *: Significant as P value < 0.05.

In hospital course, compications and mortality

Hospital admission and heart failure were significantly higher in obstructive coronary artery disease group than MINOCA group (P value<0.001) (table 9). Mechanical ventilation, CIN, inotropes, HD, shock, pain recurrence, arrest and mortality were insignificantly different between both groups.

Table 9: In-hospital course and related complications

	MINOCA group (n=68)	Obstructive group (n=776)	P value
Days of hospital admission (Range)	1 - 8	1 - 16	<0.001*
Mechanical ventilation	1 (1.47%)	52 (6.7%)	0.088
CIN	2 (2.94%)	34 (4.38%)	0.573
Inotropes	2 (2.94%)	69 (8.89%)	0.090
HD	0 (0%)	11 (1.42%)	0.323
Shock	2 (2.94%)	53 (6.8%)	0.305
Pain recurrence	2 (2.94%)	19(2.45%)	0.683
Heart failure	2 (2.9%)	293 (37.7%)	< 0.001*
Arrest	2(2.9%)	47 (6.05%)	0.419
Mortality	1 (1.47%)	29 (3.74%)	0.333

MV: Mechanical ventilation, CIN: Contrast induced nephropathy, HD: Hemodialysis, *: Significant as P value < 0.05

Predictors and regression

In univariate regression, age, female, BMI, DM, HTN, smoking, systolic, diastolic blood pressure, Killip class, CKMB, hospital admission, WBCs neutrophil and EF were independent predictors of MINOCA group (P value <0.05).

In Multivariate regression, Age, BMI, DM, smoking, Killip class, CKMB hospital admission, WBCs neutrophil and EF were independent predictors of MINOCA group (P value<0.05) while female, HTN, systolic and diastolic blood pressure were not.

Table 10: Univariate and multivariate regression

	Univariate			Multivariate		
	Odds ratio	95% CI	P	Odds ratio	95% CI	P
Age	1.1015	1.06- 1.13	<0.001*	1.1836	1.09 -1.27	<0.001*
Female	0.5761	0.346-0.95	0.03*	1.4514	0.405 - 5.19	0.566

BMI	1.1504	1.06 -1.23	<0.001	1.2987	1.122 - 1.50	<0.001*
DM	2.9012	1.62- 5.17	<0.001*	2.9851	1.11 - 7.97	0.029*
HTN	1.9718	1.14- 3.38	<0.001*	2.1860	0.798 - 5.98	0.128
Smoking	0.2801	0.16 -0.47	<0.001*	0.2018	0.059 -0.687	0.01*
Systolic blood pressure	0.9884	0.97 -0.99	0.029*	1.0305	0.99- 1.065	0.078
Diastolic blood pressure	0.9827	0.96- 0.99	0.026*	0.9673	0.921 to 1.015	0.181
Killip. Class	1.8605	1.18 -2.92	0.007*	0.1138	0.034 - 0.37	<0.001*
CKMB	1.0214	1.008-1.03	<0.001*	1.0368	1.012 - 1.06	0.002*
CHB	971	---	0.9978			
LV thrombus	948	---	0.9981			
Hospital admission	13.7466	7.94-23.77	<0.001*	2.6316	1.45 - 4.74	0.001*
TPM	953	---	0.998			
HB	1.1204	0.97- 1.28	0.102			
WBCs	1.1668	1.08 - 1.25	<0.001*	1.1894	1.039 -1.36	0.01*
Neutrophil	1.3414	1.21 -1.47	<0.001*	0.1138	0.034- 0.379	<0.001*
EF	0.7421	0.68 - 0.79	<0.001*	0.6868	0.608- 0.775	<0.001*

*Significant as P value≤0.05, BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, CKMB: Creatine kinase-MB. CHB: Complete heart block, TPM: The temporary pacemaker, HB: Hemoglobin, WBCs: White blood cells, EF: Ejection fraction.

Discussion

Acute myocardial infarction (MI) is a life-threatening condition that is associated with obstructive coronary artery disease (CAD) (defined as >50% stenosis) in patients undergoing coronary angiography (CA). However, a significant proportion of patients with MI who are indicated for CA do not have obstructive CAD (defined as <50% stenosis). This condition is called myocardial infarction with non-obstructive coronary arteries (MINOCA) [9].

This prospective and observational study was conducted at Tanta university hospital and El Zeitoun specialized hospital on 844 patients, divided into MINOCA group (n=68) and obstructive coronary artery disease group (n=776) thus the prevalence of MINOCA among our sample was 8.06%.

Previous registries had reported a varying prevalence of MINOCA with values ranging from 2.6% to 15% [10, 11]

In our study, the mean age of patients in the MINOCA group is significantly lower at 47.57 years compared to 53.05 years in the obstructive coronary artery disease group (p-value < 0.001). In terms of sex distribution, a higher percentage of males is observed in both groups, but the difference is statistically significant for relatively lower male incidence in MINOCA than obstructive coronary artery disease group (58.82% in the MINOCA group vs. 71.26% in the Obstructive Coronary Artery Disease group, p-value = 0.031). Regarding the risk factors, DM, hypertension, smoking and dyslipidemia were significantly higher in obstructive coronary artery disease group than MINOCA group (P value <0.05). Family history and PVD were insignificantly different between both groups.

This is similar to Kilic *et al*., (2020) [12] who aimed to document the prevalence and demographics of MINOCA in a Turkish population. They determined that MINOCA patients were younger, more likely to be female, and accompanied by fewer traditional cardiovascular risk factors.

In study by Pasupathy *et al.* (2018) [13] reported that 36 (8.2%), from a total of 440 AMI cases in the Queen Elizabeth Hospital, were diagnosed as MINOCA cases. Of which, cases that had HTN were 60% followed by DM, as 24%, and 24% were smokers.

In our study, duration of chest pain and HR were insignificantly different between both groups. SBP and DBP were significantly lower in obstructive coronary artery disease group than MINOCA group (P value =0.029 and 0.026 respectively). Killip's classes were significantly different between both groups as Killip's class > class I in less frequent in MINOCA group (P value = 0.036). creatinine was insignificantly different between both groups. CKMB was significantly higher in obstructive coronary artery disease group than MINOCA group (P value<0.001).

This is in agreement with Williams *et al.* (2019) [14] who reported that MINOCA cases had higher systolic blood pressure (143.3±27.2 vs. 141±27.2 mmHg, *P* = 0.021).

This is partially similar to Abdelmonem *et al*. (2017) [15] reported that, patients with insignificant CAD (Lesions < 50% stenosis) were less likely to present with Killip Class ≥ II ($p < 0.001$) and as regards qualitative laboratory data, less likely also to have elevation in serum CK-MB ($p < 0.001$) but in contrast to our study no significant difference between two groups regarding both blood pressure and heart rate.

In our study, regarding ECG changes, ST segment elevation was significantly higher in obstructive coronary artery disease group than MINOCA group (P value = 0.005). Q waves and other ECG changes was significantly higher in MINOCA group than obstructive coronary artery disease group (P value was 0.04 and 0.005 respectively) while new onset LBBB was insignificantly different. EF was significantly lower in obstructive coronary artery disease group than MINOCA group (P value<0.001).

Similar to our study, Kilic *et al*., (2020) [12] found that the left ventricular systolic function (LVSF) of MINOCA patients was significantly higher than that of non-MINOCA patients.

This was in agreement with Barr PR *et al*., (2018) [16] found that MINOCA can present with or without ST-segment elevation on the ECG, patients with MINOCA are less likely to have electrocardiographic ST-segment deviations than their AMI counterparts with obstructive CAD.

In our study, in MINOCA group, Coronary artery was normal in 36 (52.94%) patients, ectasia in 9 (13.24%) patients, dissection in 8 (11.59%) patients, bridge in 3 (4.41%) patients and slow flow in 12 (17.65%) patients. In obstructive coronary artery disease group, Coronary artery obstruction occurred in LAD in 369 (47.55%) patients, LCx in 116 (14.95%), RCA in 237 (30.54%) patients, OM in 36 (4.64%) patients and LM in 18 (2.32%) patients.

Abdelmonem *et al*. (2017) [15] reported that, a normal coronary angiogram without any suspected atherosclerosis was present in 44%, whereas the rest (56%) of patients showed signs of atherosclerosis (<50%). among patients

with coronary stenosis (>0% and <50%), LAD occlusion presents in (33.0%), RCA (15.0%), LCX (4.0%), LM (2.0%), LAD & LCX (2.0%).

In our study, as regards in-hospital course, Shock, Life threatening ventricular arrythmia, A Fib, contrast induced nephropathy, inotropes, direct cardio version, Hemodialysis and mortality were insignificantly different between both groups. Complete heart block, temporary pacing and LV thrombus were significantly higher in obstructive coronary artery disease group than MINOCA group (P value=0.011, 0.23 and 0.029 respectively).

This was in agreement with Pasupathy *et al*., (2015) [17] found that patients with non-obstructive coronary artery disease (NOCAD) have a significantly reduced all-cause mortality compared with those with obstructive coronary artery disease (OCAD), including a 63% lower in-hospital mortality (p = 0.001).

Similar to our study Abdelmonem *et al*. (2017) [15] reported that, Patients with insignificant CAD significantly had lower rates of recurrent angina (p = 0.029), and cardiogenic shock (p = 0.029). However, there was no significant difference between both groups regarding heart failure, mechanical complications, sustained VT, stroke and in-hospital mortality.

The prognosis of MINOCA patients depends on the underlying etiology. Although most studies have reported a better prognosis for MINOCA patients, this result is not consistent across all reports (Agewall *et al*., 2017) [18].

In contrast,Ciliberti *et al*. (2018) [19] observed that patients presenting with MINOCA and mild coronary artery disease (stenoses ≥30% but <50%) of three vessels or left main coronary artery characterized with worse long-term clinical outcomes in comparison to a mild coronary artery of one or two vessels.

Conclusion

In conclusion, this study sheds light on the clinical characteristics of Egyptian patients with MINOCA compared to those with obstructive coronary artery disease, the former was found to be 8.06% among all patients diagnosed with MI in our sample. The MINOCA group had a younger age and a higher female incidence. The coronary artery findings emphasized the diversity of abnormalities in the MINOCA group (, e.g., coronary dissection, myocardial bridge, slow flow phenomena or coronary stenosis less than 50%).

In our study, age, female, BMI, DM, HTN, smoking, systolic, diastolic blood pressure, Killip class, CKMB, hospital admission, WBCs neutrophil and EF were independent predictors of MINOCA group (P value <0.05).

Conflict of Interest

Not available

Financial Support

Not available

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