INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

PREVALENCE, ASSESSMENT AND CLINICAL OUTCOME DISPARITIES IN CARDIOVASCULAR DISEASE: AN IMPACT OF GENDER

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ABSTRACT

The purpose of this study was to identify relationship of quality of care, access and utilization of available treatments with gender perspectives; to determine gender difference in incidence and natural history of cardiovascular disease (CVD); to determine the difference in proportion of access to medical therapy and cardiac procedures between the two genders, and to determine the impact of gender differences on clinical outcome and complications.

Keywords: Coronary artery bypass grafting, percutaneous coronary intervention.

INTRODUCTION

Cardiovascular disease (CVD) is the number one cause of death worldwide. CVDs are responsible for 30% of all deaths globally, and are the leading cause of death amongst non-communicable diseases. They are also responsible for 10% of the global burden of disease. It is envisaged that the 21st century will witness a global pandemic of heart disease and around 50% of cardiac patients of the world would be from India[1,2].

Differences in CVD incidence, complications and burden exist between men and women. Approximately 90% of individuals with coronary heart disease (CHD) have at least 1 antecedent, traditional risk factor such as smoking, diabetes, hypertension, and/or hypercholesterolemia. The origin of CVDs is multifactorial, but cardiovascular risk factors (CVRF) represent some of the most important causes. Of importance among CVRF are age and sex, which are not modifiable CVRF; and smoking, high blood pressure, hypercholesterolemia, and diabetes mellitus (DM) as modifiable CVRF. Throughout the lifespan, exposure to high levels of these risk factors increases atherosclerotic burden resulting in an increased risk for the future clinical CVD events[2-4].

The impact of the different CVRF on the onset of CVD differs among countries with similar levels of development. Results from a National Health Survey suggest that Asian race was generally associated with lower risk for CVD, but certain risk factors were particularly high among some Asian subgroups[4,5].

CVD is the primary cause of death among women[6]. Correlations among CVRFs are marginally stronger in women than in men. It suggests that the existence of one additional risk factor may increase the risk of CVD more steeply in women than in men. [7] Additionally, the risk of several major cardiac outcomes in adult patients with congenital heart disease appeared to vary by gender[8]. Potentially modifiable factors are associated

with increased prevalence of CVD risk factors[9]. It is clear that the presence of certain factors contributes to increased morbidity and mortality in affected individuals[10]. In the Euro Heart Study, women with chronic stable angina and proven coronary artery disease (CAD) had a two-fold greater risk of death or myocardial infarction compared to men[11].

Gender disparities in the management and outcomes of CVD exist among patients in commercial managed care plans despite similar access to care. Poor performance in low-density lipoprotein (LDL) control was seen in both men and women, with a lower rate of control in women suggesting the possibility of less intensive cholesterol treatment in women. The differences in patterns of care demonstrated the need for interventions tailored to address gender disparities. [12] Eliminating gender disparities in selected CVD preventive quality of care measures has the potential to reduce major cardiac events. Health plans should be encouraged to collect and monitor quality of care data for CVD for men and women separately as a focus for quality improvement [13].

Despite women being an integral and important component of the family and society, gender disparity in various socioeconomic, cultural and health care spheres is a common phenomenon in India[14].The high burden of multiple CVD risk factors in women compared to men highlighted the need for targeting this vulnerable segment of population in CVD prevention programs[9].Numerous studies that examined gender difference in presentation, diagnosis, treatment and outcome among patients with acute coronary syndrome have been reported in last few years[15,16] however not many studies testing the hypothesis of gender heterogeneity in CVDs among Indian population have been reported so far.

The present study aims to contribute to gender congruent preventive and health modification strategies. The results of this study will increase the knowledge on the risk factors contributing to the differences in the incidence of CVD amongst two genders, reinforce preventive and promotional programmes and measures for early detection of genders at risk and; help them gain more insight into their disease and enable implementation of precautionary measures to prevent progression of the disease.

OBJECTIVES

- ✓ Identify the relationship of quality of care, access and utilization of available treatments with gender perspectives.
- ✓ Determine the gender difference in incidence and natural history of CVD.
- ✓ Determine the extent and difference in proportion of access to medical therapy and cardiac procedures between the two genders.
- ✓ Determine the impact of gender differences on the clinical outcome and complications.

PARTICIPANTS AND METHODS

Study design

This was a single-centric, randomized study including 6870 patients of CVD from CIMS Hospital, Ahmedabad from January 2008 to December 2010. There were 5681 males (82.7 %) and 1189 females (13.3 %). Gender-based difference in clinical presentation and patient-related pre-operative risk factors were analyzed and their impact on surgical management and clinical outcome were studied. Patients were included in the study according to their inclusion and exclusion criteria. Study evaluation criteria were demographic data, risk factors, vital signs, angiography and angioplasty. Study patients were grouped according to gender. Accordingly, the collected data was separated and analyzed. The measured primary outcomes were revascularization and death; and secondary outcome was assessment of complications.

Statistical analysis

The analysis of the data was carried out by using chi – square test and student's *t* – test. Categorical data were presented as percent frequencies and compared by chi-square statistics. Continuous variables were presented as mean ± Standard deviation (SD) and compared with unpaired *t* test. A p value ≤ 0.05 was considered statistically significant. All analysis was performed using Graphpad Prism version 5.04.

RESULTS

Six thousand eight hundred seventy patients of CVD who underwent cardiac procedures (e.g., Coronary artery bypass grafting (CABG) surgery or percutaneous coronary intervention (PCI)) or medical therapy were included in the

present study from January, 2008 to December, 2010. There were 5681 males and 1189 females whose mean age was 57.02 years and 56.24 years (p = 0.01), respectively. According to study design, patients were divided into three different groups as per treatments: CABG, PCI and Medical therapy.

The patient characteristics between male and female, i.e., age, body mass index (BMI), vital details, risk factors, angiographic details and angioplasty details, are shown in Table 1. Various patient characteristics are also shown according to different treatments in Table 2.

Demographic data

There was no significant difference in mean age, BMI, vital signs (i.e., pulse, systolic BP, diastolic BP, pulse pressure, mean pressure) among male and female [Table 1]. Mean age was significantly high among female undergone PCI (66.39 years vs. 57.18 years, p < 0.0001) and among male treated with medical therapy (51.97 years vs. 45.60 years, p < 0.0001) [Table 2]. According to BMI, patients were separated as overweight (25-29.9 kg / m^2) and obese (≥ 30 kg / m^2). Obesity was significant in female population as compared to male (p < 0.001).

Male and female populations with CABG, PCI and medical therapy were further separated according to different age groups [Table 3]. Maximum numbers of patients underwent cardiac procedures like CABG and PCI were older than 50 years of age. Significantly, highest number of patients who have undergone CABG and PCI were among the age group 61 – 70 years and 51 – 60 years, respectively.

Number of male patients who had undergone PCI was significantly high in age group 41 – 60 years than female. And female patients who have undergone PCI were significantly high in age group 61 – 80 years than male. It shows that as age increases, number of female patients increases compared to male.

Risk factors

The study results showed that the prevalence of hypertension and diabetes were 35.85 % and 26.26 %, respectively. The female population had an increased prevalence of hypertension (41.38 % vs. 34.69 %, p < 0.05); and prevalence of smoking was high in male (17.34 % vs. 0.96 %, p < 0.0001), but there was no significant difference in other risk factors such as diabetes, obesity and family history of early onset CVD between the gender [Table 1].

Prevalence of hypertension was significant in female undergoing CABG (50.98 % vs. 34.35 %, p < 0.001) and PCI (53.40 % vs. 36.30 %, p < 0.0001). Further, prevalence of diabetes was significant in female undergoing PCI (35.90 % vs. 26.60%, p < 0.05) [Table 2].

Further, males and females were separated according to individual risk factors and multiple risk factors and are shown in Table 4. Individual risk factors like diabetes, obesity and family history of CVD were significant among male population. But women with three or more risk factors were significant to be suffered from CVD compared to men [Table 4].

Angiography

The analysis of angiographic procedures showed that significant number of female (28.51%) underwent angiography through femoral site (p < 0.05) whereas significant number of male (39.15%) underwent angiography procedure through radial site (p < 0.0001). Prevalence of single vessel disease was high in male compared to female, although the difference was not significant [Table 1].

Patients who visited the hospital were suggested for angiography by physicians according to their individual characteristic. Angiography was carried out significantly in male population compared to female (61.11 % vs. 47.18 %, p < 0.0001) [Table 5].

Angioplasty

Single vessel angioplasty was significant in male as compared to female (32.21 % vs. 23.89 %, p < 0.05). But there was no significant difference in angioplasty between sub-groups [Table 1].

Gender difference in proportion of access to medical therapy and cardiac procedures

During study period, male population was vast in number to visit the hospital (82.69% vs. 13.31%, p < 0.0001). Number of patients who had undergone cardiac procedures and medical therapy are shown in Table 5. It shows that percentage of male population was extremely significant for cardiac procedures (CABG: p = 0.014; PCI: p = 0.0017) and female population was significant for medical therapy compared to male (p < 0.0001).

Gender differences on clinical outcome

During the study, revascularization and death were measured as clinical outcomes [Table 5], revascularization was significant in male (58.83% vs. 40.95%, $p < 0.0001$) and death was significant in female (0.42 % vs. 0.33 % vs., $p < 0.0001$ for death).

Patient characteristics in women ≥ 51 years

In our study, we considered 51 years of age for the onset of menopause in women and accordingly, we presented study results in Table 6.

This table shows analysis of results of female characteristics according to menopausal age range (< 51 years and ≥ 51 years of age). All characteristics like number of patients, risk factors, angiography and angioplasty were extremely significant in menopausal female patients.

DISCUSSION

CVD is the number one cause of death worldwide. CVDs are responsible for 30% of all deaths globally, and are the leading cause of death amongst non-communicable diseases. CVD is the primary cause of death among women[6]. Correlations among CVRFs are marginally stronger in women than in men. It suggests that the existence of one additional risk factor may increase the risk of CVD more steeply in women than in men. [7]

Despite women being an integral and important component of the family and society, gender disparity in various socioeconomic, cultural and health care spheres is a common phenomenon in India[14]. Numerous studies that examined gender difference in presentation, diagnosis, treatment and outcome among patients with acute coronary syndrome have been reported in last few years[15,16] however not many studies testing the hypothesis of gender heterogeneity in CVDs among Indian population have been reported so far. This study was aimed to study an impact of gender on prevalence, assessment and clinical outcome in CVD.

This study showed that obesity was significant in female population as compared to male ($p < 0.001$) [Table 1]. Obesity and the metabolic syndrome have been shown to frequently coexist[17]. Not surprisingly, current analysis of the present study showed that BMI was also independently associated with the coexistence of these risk factors in Indian population. It is quite possible that the high prevalence of coexistence of CVD risk factors is a reflection of sedentary life style of the urban population of India[9].

Presented data revealed that the female population had an increased prevalence of hypertension (41.38 % vs. 34.69 %, $p < 0.05$). Prevalence of hypertension was significant in female undergone CABG (50.98 % vs. 34.35 %, $p < 0.001$) and PCI (53.40 % vs. 36.30 %, $p < 0.0001$). Hypertension was significantly high in female than in male. Higher BMI has been independently associated with hypertension, diabetes, and central obesity in the Pakistani population[18]. It has been shown in various studies that female CAD patients had an adverse risk factor profile for the prevalence of diabetes mellitus, hypertension and hypercholesterolemia with the exception of smoking which was more prevalent in males[19]. Similarly, prevalence of diabetes was significantly high among female undergone PCI (35.90 % vs. 26.60%, $p < 0.05$). This study supports the findings of Framingham Heart Study / National Heart, Lung, and Blood Institute that the hazard ratio (HR) of developing CVD for women with DM (HR = 2.5 for women, 2.4 for men) and ultimately dying from CVD (HR = 2.2 for women, 1.7 for men) is slightly higher in women than in men[20].

The onset of menopause usually begins between ages 45 and 55, with a worldwide average of 51[21]. The mean age at menopause in Indian women was 45.03 years in this study[22]. The average age at menopause amongst the north- Indian women was 48.7 ± 2.3 years (46.4 – 51.0 years)[23]. So, in this study, it was decided to consider 51 years or greater than that as an average menopausal age. Results of this study suggest that all the parameters (Number of patients, risk factors, angiography and angioplasty [Table 6]) were extremely significant in menopausal female patients. Reasons for increased cardiovascular risk are multifactorial, stemming from changes in sex hormones. After physiological and surgical menopause, serum estradiol and inhibin A and B were found to be significantly decreased, whereas follicle-stimulating hormone was significantly increased[24].

Findings of this study indicate that women are at greater risk for CVD than men, and this difference increases in magnitude with

advancing age. The loss of hormonal protection in the postmenopausal age probably leads to this age related increase[9].

The analysis of the data showed that angiography was extremely significant in male population compared to female (61.11 % vs. 47.18 %, $p < 0.0001$) [Table 5]. It is known that when female patients present with chest pain, they are more likely to have other problems than CAD compared to males with chest pain. This notion may probably been the cause of gender disparities noted in the management of female CAD population not only at primary healthcare level but also at the level of diagnostic work up and choice of revascularization procedure. Under-referral of female patients for exercise test and coronary angiography has not only been shown when they present with chest pain but also when they have proven CAD presenting in the form of acute myocardial infarction. This pattern is, however, not universal and there are other reports denying the presence of such a bias. The variability in the results of these studies could be explained by differences in the practice patterns of different centres and could also be influenced by regional, cultural and socio-economic factors affecting the healthcare dynamics of female patients. Since the interplay of above factors is unique in each society, the results from any given study cannot be universally applied. There is thus need to study the local factors affecting any population before healthcare practices and policies may be modified[19].

Data presented in this study suggests that single vessel angioplasty was significantly high in male as compared to female (32.21 % vs. 23.89 %, $p < 0.05$). But there was no significant difference in angioplasty between sub-groups [Table 1]. The data analysis also showed that male population was significantly high for cardiac procedures (CABG: $p = 0.014$; PCI: $p = 0.0017$) and female population was significantly high for medical therapy as compared to male ($p < 0.0001$). These results are in concordance with the report that high-risk women with ACS undergo less coronary angiography, angioplasty, and CABG surgery compared to men[25].

Analysis for revascularization and death suggested that revascularization was extremely significant in male (58.83% vs. 40.95%, $p < 0.0001$) and death was significant in female (0.42 % vs. 0.33 %, $p < 0.0001$). The retrospective analysis of Ayanian and Epstein[26] of hospitalizations for coronary heart disease reported a 3-fold increase in revascularization procedures in men with stable angina compared with women, similar to that reported by Tobin et al[27] in a much smaller population.

CONCLUSION

This study showed that,

- → Prevalence of obesity, hypertension and diabetes was highly significant in female population as compared to male.
- → Women were at greater risk for CVD than men, and this difference increased in magnitude with advancing age.
- → Angiography was extremely significant in male population compared to female.
- → Male population was significantly high for cardiac procedures and female population was significantly high for medical therapy as compared to male.
- → Revascularization and death were significant in male and female, respectively.

The cause of these gender disparities might be explained by influence of regional, cultural and socioeconomic factors affecting the healthcare dynamics of female patients in India.

The results of this study will increase the knowledge on the risk factors contributing to the differences in the incidence of CVD amongst two genders; reinforce preventive and promotional programmes and measures for early detection of genders at risk.

Table 1: Patient characteristics and risk factors of male and female suffering from CVD

	Male (n= 5681)	Female (n= 1189)	Total (n= 6870)
Age (years)	57.02 ± 11.79	56.24 ± 11.76	56.63 ± 11.77
BMI			
Overweight (25-29.9kg/m^2)	26.98 ± 1.39 (1143)	27.15 ± 1.24 (180)	27.07 ± 1.31 (1323)
Obese (≥ 30kg/m^2)	32.86 ± 2.72 (348)	33.93 ± 2.97 (103) §	33.40 ± 2.84 (451)
Pulse/min	73.32 ± 10.72	75.79 ± 10.69	74.56 ± 10.7
Systolic BP (mm Hg)	122.24 ± 18.08	124.82 ± 18.38	123.53 ± 18.23
Diastolic BP (mm Hg)	75.71 ± 9.64	75.06 ± 10.3	75.39 ± 9.97
Pulse-Pressure (mm Hg)	46.84 ± 13.36	48.22 ± 14.29	47.53 ± 13.82
Mean-Pressure (mm Hg)	90.85 ± 12.11	91.81 ± 13.17	91.33 ± 12.64
Risk factors			
Hypertension	1971 (34.69%)	492 (41.38%) ‡	2463 (35.85%)
Diabetes	1473 (25.93%)	331 (27.84%)	1804 (26.26%)
Obesity	1236 (21.76%)	208 (17.49%)	1444 (21.02%)
Family-History-of-Early-onset-CVD	708 (12.46%)	120 (10.09%)	828 (12.05%)
Smoking	985 (17.34%) ¶	5 (0.96%)	990 (14.40%)
Angiography			
Procedure-Approach			
Femoral	1210 (21.30%)	339 (28.51%) ‡	1549 (22.55%)
Radial	2224 (39.15%) ¶	220 (18.50%)	2444 (35.57%)
Final-Impression			
Single Vessel Disease	1388 (24.43%)	236 (19.85%)	1624 (23.64%)
Double Vessel Disease	946 (16.65%)	128 (10.77%)	1074 (15.63%)
Triple Vessel Disease	742 (13.06%)	88 (7.40%)	830 (12.08%)
Multi Vessel Disease	78 (1.37%)	7 (0.60%)	85 (1.24%)
Normal Coronaries	134 (2.36%)	71 (5.97%)	205 (2.98%)
Insignificant CAD	73 (1.28%)	23 (1.93%)	96 (1.40%)
Coronary-Artery			
Proximal RCA	1705 (30.01%) ‡	255 (21.45%)	1960 (28.53%)
Proximal LAD	1325 (23.32%) ‡	187 (15.73%)	1512 (22.01%)
Mid LAD	279 (4.91%)	56 (4.71%)	335 (4.88%)
Left Main Coronary Artery	128 (2.25%)	25 (2.10%)	153 (2.23%)
Proximal Lcx	120 (2.11%)	12 (1.01%)	132 (1.92%)
Angioplasty			
Single Vessel Angioplasty	1830 (32.21%) ‡	284 (23.89%)	2114 (30.77%)
Double Vessel Angioplasty	352 (6.20%)	56 (4.71%)	408 (5.94%)
Triple Vessel Angioplasty	9 (0.16%) ¶	2 (0.17%)	11 (0.16%)
CABG	1234 (21.72%) ¶	153 (12.87%)	1387 (20.19%)

Mean ± SD (n), n (%), where n= Number of patients; ¶ $p \leq 0.0001$; § $p \leq 0.001$; ‡ $p \leq 0.05$

Table 2: Patient characteristics of male and female according to different cardiac procedures

	CABG		PCI		Medical therapy	
	Male	Female	Male	Female	Male	Female
	(n= 1234)	(n= 153)	(n= 3287)	(n= 543)	(n= 1160)	(n= 493)
Age (years)	61.91 ± 9.5	62.94 ± 8.3	57.18 ± 10.5	66.39 ± 10.7 ¶	51.97 ± 15.4 ¶	45.6 ± 16.3
BMI						
Overweight (25-29.9 kg/m²)	27 ± 1.4 (200)	27.17 ± 1.2 (22)	27.09 ± 1.4 (763)	27.22 ± 1.4 (130)	26.84 ± 1.4 (180)	27.06 ± 1.1 (28)
Obese (≥ 30 kg/m²)	33.02 ± 2.7 (63)	32.73 ± 1.7 (18)	32.68 ± 3.1 (244)	33.41 ± 2.9 (68)	32.87 ± 2.4 (41)	35.64 ± 4.3 (17) ‡
Risk Factors						
Hypertension	424 (34.35%)	78 (50.98%) ‡	1258 (36.30%)	290 (53.40%) ¶	289 (24.90%)	124 (25.15%)
Diabetes	399 (32.33%)	61 (39.87%)	873(26.60%)	195 (35.90%) ‡	201 (17.30%)	75 (15.21%)
Obesity	63 (5.10%)	18 (11.78%)	247 (7.51%)	68 (12.5%)	41 (3.53%)	17 (3.44%)
Family-History –early-onset-CVD	131 (10.61%)	19 (12.42%)	465(14.10%)	73 (13.40%)	112 (9.65%)	28 (5.67%)
Smoking	133 (10.78%)	-	653 (19.87%)	3 (0.55%)	199 (17.14%)	2 (0.41%)
Angiography						
Single Vessel Disease	51 (8.33%)	7 (9.46%)	1113 (53.60%)	190 (54.90%)	224 (32.60%)	39 (28.46%)
Double Vessel Disease	157 (25.65%)	10 (13.51%)	627 (30.20%)	99 (28.60%)	162 (23.60%)	19 (13.86%)
Triple Vessel Disease	347 (56.69%)	44 (59.46%)	255 (12.30%)	34 (9.83%)	140 (20.40%)	10 (7.29%)
Multi Vessel Disease	42 (6.86%)	6 (8.11%)	21 (1.01%)	-	15 (2.18%)	1 (0.72%)
Normal Coronaries	5 (0.81%)	4 (5.40%)	27 (1.30%)	8 (2.31%)	102 (14.90%)	59 (43.06%) §
Insignificant CAD	7 (1.14%)	3 (4.05%)	24 (1.15%)	11 (3.18%)	42 (6.11%)	9 (6.56%)

Mean ± SD (n), n (%), where n= Number of patients; ¶ $p \leq 0.0001$; § $p \leq 0.001$; ‡ $p \leq 0.05$

Table 3: Age and gender in CVD patients

Age groups (years)	CABG		PCI		MT	
	Male n (%)	Female n (%)	Male n (%)	Female n (%)	Male n (%)	Female n (%)
< 41	13 (1.05)	2 (1.31)	179 (5.45)	20 (3.68)	236 (20.34)	201 (40.77)¶
41 - 50	136 (11.02)	9 (5.88)	665 (20.23)¶	68 (12.52)	252 (21.72)	114 (23.12)
51 - 60	398 (32.25)	47 (32.03)	1224 (37.24)‡	182 (33.52)	319 (27.50)¶	76 (15.42)
61 - 70	459 (37.20)	69 (45.10)	869 (26.44)	174 (32.04)‡	245 (21.12)‡	74 (15.01)
> 70	228 (18.47)	26 (15.69)	350 (10.65)	99 (18.23)	108 (9.31)	28 (6.69)

n= Number of patients; ¶ $p \leq 0.0001$; ‡ $p \leq 0.05$

Table 4: Risk factors in male and female

Risk factors	Male	Female
Hypertension(H)	738 (13.00%)	157 (13.20%)
Diabetes(D)	429 (7.55%) ‡	60 (5.05%)
Obesity(O)	323 (5.69%) ¶	17 (1.43%)
Family history(F)	642 (11.30%) §	93 (7.82%)
H+D	528 (9.29%)	119 (10.00%)
H+O	396 (6.97%)	93 (7.82%)
D+O	207 (3.64%) ‡	29 (2.44%)
H+D+O	242 (4.26%)	95 (7.99%) ¶
H+D+O+F	67 (1.18%)	28 (2.35%) ‡

¶ $p \leq 0.0001$; § $p \leq 0.001$; ‡ $p \leq 0.05$

Table 5: Invasive cardiac procedures and clinical outcome in male and female

	Male (5681)	Female (1189)	*p* value
Number of patients	5681 (82.69%)	1189 (13.31%)	< 0.0001
Angiography			
Yes	3472 (61.11%)	562 (47.18%)	< 0.0001
No	2209 (38.89%)	627 (52.73%)	
Treatments			
CABG	1234 (21.72%)	153 (12.87%)	0.014
PCI	2108 (37.11%)	334 (28.09%)	0.0017
MT	2339 (41.17%)	702 (59.04%)	<0.0001
Clinical outcome			
Revascularization	3342 (58.83%)	487 (40.95%)	< 0.0001
Death	19 (0.33%)	5 (0.42%)	< 0.0001

Table 6: Patient characteristics in women

	< 51 years	≥ 51 years
Number of patients	414 (34.82%)	775 (65.18%) ¶
Hypertension (H)	79 (6.64%)	413 (34.74%) ¶
Diabetes (D)	63 (5.30%)	268 (22.54%) ¶
Obesity (O)	53 (4.46%)	209 (17.58%) ¶
Family History (F)	33 (2.78%)	87 (7.32%) ¶
Angiography	104 (8.75%)	463 (38.94%) ¶
Angioplasty	47 (3.95%)	440 (37.01%) ¶

¶ $p \leq 0.0001$

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