

## The Relationship Between the Age of First Acute Coronary Syndrome Episode and Internal Migration

### İlk Akut Koroner Sendrom Atağını Geçirme Yaşı İle İç Göç Arasındaki İlişki



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#### ORIGINAL ARTICLE KLİNİK ÇALIŞMA

#### ABSTRACT

**Objective:** It has been shown that migration has an increasing effect on the risk of cardiovascular events. However, these studies are mostly related to international migration. There are very few studies on the relationship between internal migration and cardiovascular disease. The aim of the current study was to evaluate the effect of internal migration on the age of the first acute coronary syndrome episode.

**Methods:** The study was designed as a cross-sectional, observational study that enrolled 1261 consecutive patients diagnosed with the first episode of acute coronary syndrome between 2014 and 2020. Patients born and living in Antalya were included in the nonimmigrated group, and those born in another city in Türkiye and settled to live in Antalya were included in the immigrated group. The effect of internal migration and other risk factors on the age of the first acute coronary syndrome was calculated by regression analysis.

**Results:** Immigrants were younger than nonimmigrants at the time of acute coronary syndrome ( $55.4 \pm 10.7$  years vs.  $60.0 \pm 13.36$  years,  $P < 0.001$ ). Linear regression analysis showed that migration is an independent risk factor for acute coronary syndrome at an earlier age ( $-2.07$ ,  $P < 0.001$ ). The socioeconomic status of the migrant group was not lower than the nonimmigrant group.

**Conclusions:** Internal migration may be a risk factor associated with acute coronary syndrome at an earlier age when compared to nonimmigrants. This finding needs to be tested in multicenter epidemiological studies.

**Keywords:** Acute coronary syndrome, age, cardiovascular risk, immigration

#### ÖZET

**Amaç:** Göçün kardiyovasküler olay riskini arttırıcı etkisi olduğu gösterilmiştir. Ancak mevcut çalışmalar daha çok uluslararası göçle ilişkilidir. İç göç ve kardiyovasküler hastalık riski arasındaki ilişkiyi inceleyen az sayıda çalışma vardır. Bu çalışmanın amacı, iç göçün ilk akut koroner sendrom (AKS) atak yaşı üzerindeki etkisini değerlendirmektir.

**Yöntem:** Bu çalışma, 2014–2020 yılları arasında ilk AKS atağı tanısı alan ardışık 1261 hastayı içeren kesitsel, gözlemsel bir çalışma olarak tasarlandı. Antalya’da doğup yaşayan kişiler göç etmemiş gruba, Türkiye içinde başka bir şehirde doğup Antalya’ya yerleşen kişiler göç eden gruba dahil edildi. İç göç ve diğer risk faktörlerinin ilk AKS yaşı üzerindeki etkisi doğrusal regresyon analizi ile hesaplandı.

**Bulgular:** Göç edenlerin ilk AKS yaşı, göçmen olmayanlara göre daha düşük idi ( $55,4 \pm 10,7$  yıl;  $60,0 \pm 13,36$  yıl,  $P < 0,001$ ). Doğrusal regresyon analizi, göçün erken yaşta AKS için bağımsız bir risk faktörü olduğunu gösterdi ( $-2,07$ ;  $P < 0,001$ ). Göçmen grubun sosyoekonomik durumu göçmen olmayan grup ile benzer olarak saptandı.

**Sonuç:** İç göç, göçmen olmayanlarla kıyaslandığında daha erken yaşta AKS ile ilişkili bir risk faktörü olabilir. Bu bulgunun çok merkezli epidemiyolojik çalışmalarda test edilmesi gerekmektedir.

**Anahtar Kelimeler:** Akut koroner sendrom, göç, kardiyovasküler risk, yaş

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Migrants' health has become an important issue worldwide due to increasing global migration. Nearly one-seventh of the world's population now lives in a location different from the one in which they were born.<sup>1</sup> A migrant is someone who has moved across an international border (international migration) or within their own country

away from their habitual place of residence (internal migration). Individuals or communities are immigrating from one country to another, from one settlement to another due to economic, social, and political reasons.<sup>2</sup> Migration is a social determinant of health. One of its major influences is cardiovascular health.

The relationship between health status and migration is complex. It was documented by several studies that immigrants have a higher risk of coronary heart disease (CHD) than the native population.<sup>3-5</sup> However, the immense heterogeneity of this population and the insufficient data on country of origin and/or migration status among many of the sources used to ascertain population health status complicate the understanding of the health consequences of migration.<sup>6</sup> The vast majority of studies on the cardiovascular health status of immigrants have focused on international migration. However, little is known about whether or not internal immigrants, who have moved within the same country, have a higher risk for CHD than local-born people.

Internal migration is widely occurring in countries across the world. Internal migration rates are also quite high in Türkiye. With increasing urbanization, internal migration in Türkiye is more common when compared to international migration. It was determined that 2 256 083 people moved between regions in 2018, out of Türkiye's total population of 80 810 525.<sup>7</sup> With the present-day large internal migration, increasing populations live in a different region from the city they were born in. In recent years, Antalya has experienced a high immigration flow from other areas of Türkiye and became one of the cities people mostly migrated to from other regions of Türkiye. Despite increasing internal migration, little is known about the health situation among internal immigrants. Furthermore, it is crucial to understand how cardiovascular disease (CVD) risk factors differ between internal immigrants and native people, as CVD risk factors are influenced by behavioral, social, cultural, and economic factors.<sup>8</sup>

Most of the studies have focused on the impact of international migration on CVD risk. According to our knowledge, the current study is the first study that examined the CVD risk factors and the age of the first acute coronary syndrome (ACS) in internal immigrants compared to native residents of Antalya city in Türkiye. The present study aimed to determine the impact of internal migration on the age of first ACS in patients admitted with first ACS, taking into account educational and occupational characteristics and cardiovascular risk factors of patients.

## Materials and Methods

This cross-sectional observational study enrolled consecutive adult patients (> 18 years) who were admitted to the intensive coronary care unit with the diagnosis of ACS for the first time in Antalya Training and Research Hospital in Turkey, between 2014 and 2019. The exclusion criteria were as follows: CVD (patients

with documented CVD and stable angina pectoris receiving treatment); chronic renal disease; chronic obstructive pulmonary disease; malignancy; regular use of statins, antiplatelets, or anticoagulants; situations where oral communication with the patient is impossible; situations where coronary angiography could not be performed. Patients with findings that might be related to previous myocardial infarction (MI) on electrocardiography or echocardiography, the presence of total occlusion other than "culprit" lesion, and no critical stenosis on coronary angiography were also excluded (Supplementary Figure 1).

Our study conformed to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Antalya Training and Research Hospital (2014-097) (clinical trial number: NCT04578964). Written informed consent was obtained from all participants. Data were collected in face-to-face interviews by study administrators with the help of a structured questionnaire that assessed demographic, socioeconomic, and psychosocial characteristics and coronary risk factors of the patients.

## Statistical Analysis

We present normally distributed continuous variables by arithmetic mean  $\pm$  standard deviation, nonnormal distributed or ordered variables by median (interquartile range), and categorical variables by frequency and percentage. Normal distribution was analyzed by the Lilliefors-corrected Kolmogorov-Smirnov test. The homogeneity of the variances was determined by Levene's test. The dependent groups of categorical variables were compared by McNemar's test. Normally distributed continuous variables with 3 or more independent groups were evaluated by one-way analysis of variance, while the nonnormally distributed variables were examined by the Kruskal-Wallis test. When the *P* values from the Kruskal-Wallis test statistics were statistically significant, the group that differed from the other groups was determined by Dunn's post-hoc test. Furthermore, the *P* values were corrected for multiple comparisons, and the dependent groups were compared using the Wilcoxon test. The age during the first ACS episode was estimated by multiple linear regression analysis. Multiple linear regression analysis was performed with variables determined as *P* < 0.25 as a result of univariate statistical analysis. Starting from the most significant value, individual values were added to the model, and the final regression model was established. All statistical data were analyzed by R version 3.4.4, and *P* < 0.05 was considered to be statistically significant.

## Results

From 2014 to 2020, we included a total of 1261 (n: 244, 19.4% female) patients presenting with first ACS. The mean age was  $57.4 \pm 12.3$  years, and 623 (49.4%) patients were internal immigrants. Immigrants were younger than natives at the time of ACS ( $55.4 \pm 10.7$  years vs.  $60.0 \pm 13.36$  years, *P* < 0.001).

Concerning classical risk factors, the analysis showed no statistically significant difference in the prevalence of hypertension (42.9% vs. 45.9%, *P*=0.273), diabetes mellitus (29.1% vs. 27.9, *P*=0.650), hyperlipidemia (22.0% vs. 25.9%, *P*=0.107), and positive family history (46.7% vs. 44.8%, *P*=0.502) between immigrants and nonimmigrants. However, immigrants had nicotine abuse and psychosocial stress more often than nonimmigrants (61.3% vs. 46.4%, *P* < 0.001; 76.7% vs. 67.7%,

## ABBREVIATIONS

ACS	Acute coronary syndrome
BMI	Body mass index
CHD	Coronary heart disease
CVD	Cardiovascular disease
MI	Myocardial infarction

$P < 0.001$ , respectively). There was no statistically significant difference between body mass index (BMI) values, frequency of physical activity, and antihypertensive/antidiabetic medication of patients between the 2 groups. Sociodemographic data showed differences in education and occupation status between the 2 groups. Unlike previous studies with international immigrants, in the current study, internal immigrants had jobs with high skill levels more often than nonimmigrants (26.3 % vs. 14.1 %,  $P < 0.001$ ). Furthermore, the prevalence of having a high education degree (international standard classification of education  $\geq 3$ ) was significantly higher in immigrants compared to nonimmigrants. Considering the reasons for migration, the frequencies of migration due to work, family, and lifestyle preferences were 69.8% (n = 435), 22.3% (n = 139), and 7.9% (n = 49) in 623 immigrant patients, respectively. Table 1 lists the demographic characteristics of patients according to their migration status.

When we examined from which regions people migrated to Antalya, it was shown that the most migration was from the other provinces in the Mediterranean region. The age at first ACS was 3.8 years lower for people who had migrated from the other provinces in the Mediterranean region compared to natives. While the decrease in the first ACS age was found most in those who migrated from the western Marmara region (-6.8 years), the lowest decline was in those who migrated from the west Black Sea region (-2.4 years) (Table 2).

In the correlation analysis, there was a negative correlation between male gender, immigration, stress, current smoking, BMI, and age at first ACS. Among cholesterol parameters, HDL showed a positive correlation with age, while there was a negative correlation between other cholesterol parameters. There was no correlation between the reason for migration and the age of the first ACS (Table 3).

In the linear regression analysis, migration status was detected as an independent risk factor associated with ACS at an earlier age. In addition, family history, male sex, diabetes, smoking, LDL-C value, psychosocial stress, and BMI were also found to be independent variables associated with ACS at an earlier age (Table 4).

**Discussion**

The main finding of the current study is that internal immigrants had the first ACS episode at an earlier age compared with native residents of Antalya city, after adjustment for smoking, diabetes, BMI, psychosocial stress, and cholesterol levels. This finding of our study is consistent with the previous studies that have documented the increased CVD risk in international immigrants. In addition, there was no difference in the incidence of classical risk factors of CHD between the two groups except smoking. Furthermore, the impact of internal migration was found to be independent of socioeconomic status.

The majority of the studies have focused on the effect of international migration on CVD. A Danish study that compared the incidence of CVD and AMI between native-born people and the immigrant population between 1997 and 2000 (n=1 837 707) found that immigrants had an increased incidence of CVD compared with natives.<sup>5</sup> An Austrian prospective study,<sup>13</sup> which

**Table 1. General Characteristics of the Studied Population**

	Nonimmigrant n=638	Immigrant n=623	P
Gender Male n (%)	495 (77.6)	522 (83.8)	<0.001
Age (mean ± SD)	60.0 ± 13.36	55.4 ± 10.7	<0.001
Currently smoker n (%)	296 (46.4)	382 (61.3)	<0.001
Diabetes mellitus n (%)	178 (27.9)	181 (29.1)	0.650
Hypertension n (%)	293 (45.9)	267 (42.9)	0.273
Hyperlipidemia n (%)	165(25.9)	137 (22.0)	0.107
Positive family history n (%)	286 (44.8)	291 (46.7)	0.502
Perceived psychosocial stress n (%)	432 (67.7)	478 (76.7)	<0.001
Employment status			<0.001
Former/never worked n (%)	312 (48.9)	230 (36.9)	0.030
Currently working-Group1 n (%)	236 (37.0)	229 (36.8)	0.932
Currently working-Group 2 n (%)	90 (14.1)	164 (26.3)	<0.001
Retired n (%)	45 (7.1)	55 (8.8)	0.244
Education status			<0.001
ISCED 1-2 n (%)	588 (92.2)	522 (83.8)	<0.001
ISCED 3 n (%)	38 (6.0)	67 (10.8)	0.002
ISCED 4-6 n (%)	12 (1.9)	34 (5.5)	<0.001
Regular physical activity			0.674
≥ 3 days per week n (%)	10 (1.6)	14 (2.2)	
1-2 days per week n (%)	93 (14.6)	89 (14.3)	
None n (%)	545 (83.8)	520 (83.5)	
Body mass index (mean ± SD)	27.98 ± 4.56	28.09 ± 4.13	0.661
Systolic blood pressure (mean ± SD)	135.8 ± 20.4	136.5 ± 22.0	0.599
Diastolic blood pressure (mean ± SD)	81.49 ± 12.03	82.58 ± 14.21	0.141
Total cholesterol (mean ± SD)	205.5 ± 48.8	209.3 ± 49.4	0.181
HDL cholesterol (mean ± SD)	43.14 ± 10.2	41.34 ± 9.8	0.002
LDL cholesterol (mean ± SD)	134.19 ± 38.8	136.78 ± 39.4	0.239
Non-HDL cholesterol (mean ± SD)	160.8 ± 44.7	166.6 ± 47.4	0.024
Drugs			
Oral antidiabetic n (%)	107 (16.8)	108 (17.39)	0.790
Insulin n (%)	38 (6.0)	32 (5.1)	0.525

(Continued)

**Table 1. General Characteristics of the Studied Population (Continued)**

	Nonimmigrant	Immigrant	P
	n = 638	n = 623	
Antihypertensive n (%)	241 (37.8)	208 (33.4)	0.104
ACEI/ARB n (%)	82 (12.3)	73 (11.7)	0.539
CCB n (%)	74 (11.6)	65 (10.4)	0.509
BB n (%)	48 (7.5)	46 (7.4)	0.905
Diuretic n (%)	61 (9.6)	71 (11.4)	0.287

ACEI, angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; BB, beta-blocker; CCB, calcium channel blocker; HDL, high-density lipoprotein; ISCED, international standard classification of education; LDL, low-density lipoprotein, SD, standard deviation.

investigated the patients admitted with the first ACS similar to the current study, demonstrated that immigrants were younger than nonimmigrants at the time of the first ACS. They also concluded that low socioeconomic status could cause increased psychosocial stress, which might be an additional risk factor for CVD, especially in immigrants. An Italian observational study similarly found that immigrant citizens with ACS were younger than Italians, although they did not differ regarding classical risk factors.<sup>14</sup>

**Table 2. Average Age of First Acute Coronary Syndrome Episode by Geographic Regions**

Region	Age of First ACS, Years (Mean ± SD)	Difference with the Average Age of Nonimmigrants (Years)
Istanbul Region (TR1) (n = 18)	56.3 ± 12.5	-3.7
West Marmara Region (TR2) (n = 24)	53.2 ± 9.9	-6.8
East Marmara Region (TR4) (n = 9)	56.2 ± 11.4	-3.8
Aegean Region (TR3) (n = 79)	55.5 ± 10.8	-4.5
West Anatolia Region (TR5) (n = 65)	54.4 ± 9.4	-5.6
Mediterranean Region (TR6) (n = 144)	56.1 ± 10.6	-3.9
Central Anatolia Region (TR7) (n = 60)	55.8 ± 9.4	-4.2
West Black Sea Region (TR8) (n = 51)	57.6 ± 11.9	-2.4
East Black Sea Region (TR9) (n = 29)	54.4 ± 8.4	-5.6
Northeast Anatolia Region (TRA) (n = 34)	54.5 ± 10.2	-5.5
Central East Anatolia Region (TRB) (n = 44)	56.1 ± 12.4	-3.9
Southeast Anatolia Region (TRC) (n = 66)	54.2 ± 12.3	-5.8

ACS, acute coronary syndrome; SD, standard deviation

**Table 3. Correlation Analysis Between First Acute Coronary Syndrome Age and Risk Factors**

	Correlation Coefficient	P
Migration status	-0.184**	<0.001
Male sex	-0.212**	<0.001
Systolic blood pressure	0.035	0.220
Diastolic blood pressure	-0.087**	0.002
Hyperlipidemia	-0.001	0.986
Perceived psychosocial stress	-0.297**	<0.001
Total cholesterol	-0.167**	<0.001
HDL cholesterol	0.170**	<0.001
LDL cholesterol	-0.123**	<0.001
Non-HDL cholesterol	-0.190**	<0.001
Triglyceride	-0.209**	<0.001
Hypertension	0.219**	<0.001
Diabetes mellitus	-0.04185	0.138
Smoking status	-0.462**	<0.001
Body mass index	-0.133**	<0.001
Education status	-0.267**	<0.001
Family History	0.197**	<0.001
Employment status	-0.356	<0.001
Migration reason	0.033	0.413

HDL, high-density lipoprotein; LDL, low-density lipoprotein

Low socioeconomic status is a well-established risk factor for CHD. It is of great importance to evaluate socioeconomic factors in studies on CHD and immigrants because, in most studies conducted in most countries, the socioeconomic status of immigrants was worse compared with the nonimmigrant population. However, studies have had conflicting results regarding the influence of socioeconomic status on CVD risk. Hedlund et al<sup>3</sup> showed that immigrants have a higher incidence of first

**Table 4. Effect of Risk Factors on The Age of First acute Coronary Syndrome**

	b	P
Male sex	-4.68	<0.001
Smoking status	-13.86	<0.001
Diabetes mellitus	-3.06	<0.035
Perceived psychosocial stress	-4.99	<0.001
Immigration status	-2.07	<0.001
LDL cholesterol	-0.02	0.006
BMI	-0.402	<0.001
Family history	-3.41	<0.001
Diabetes mellitus x Smoking	3.618	0.004
Gender x Smoking	3.624	0.022

BMI: Body mass index, LDL: Low density lipoprotein Multiple linear regression model: dependent variable is age; R<sup>2</sup>=0.261 P < 0.001



MI than Sweden-born people after adjustment of age and socioeconomic status. However, they concluded that it is not explained by socioeconomic differences.<sup>3</sup> However, other studies demonstrated some or little effect of socioeconomic status on the incidence of stroke, CHD, or CVD.<sup>15,16</sup> Previous studies have observed that international immigrants have lower socioeconomic and education levels and lower job qualities.<sup>6,13</sup> However, in our study, the factors associated with socioeconomic statuses, such as education and occupation of the immigrant group, were better than the majority. This indicates that we cannot explain the increased risk with socioeconomic factors alone. For example, immigrants lose the health advantages of protective cultural and social factors related to increased stress.

Internal migrants are individuals who migrate between regions in 1 country. Antalya provides an excellent site to investigate the impact of internal migration as being one of the cities with the largest migrant concentration in Türkiye. Internal migration, which can positively affect the welfare of the society and the development potential of the country, can also create many social, economic, cultural, and psychological disadvantages for immigrants.<sup>7</sup> Immigrants naturally lose their social networks. The effect of social networks on reducing cardiovascular events and mortality is known.<sup>17</sup>

There are several studies that evaluated the differences in metabolic profile and CVD risk factors among internal migrants and native residents. A population-based study conducted on internal migrants and native residents of Sao Paulo demonstrated differences in diet quality and cardiovascular risk factors among the groups.<sup>18</sup> The analysis of Peruvian demographic and health surveys found that internal migration is associated with higher odds of obesity.<sup>19</sup> The Peru migrant study demonstrated the relationship between urban exposure and the risk of developing diabetes over the life.<sup>20</sup> In our study, no difference was found in the prevalence of classical risk factors such as hypertension, diabetes, hyperlipidemia, and family history. The rate of male gender and smoking was found to be higher in the immigrant group. However, migration was found to be an independent factor associated with the first episode of ACS at an earlier age. Besides CV risk factors, environmental factors such as stress caused by loss of network and lack of acculturation.<sup>21,22</sup>

Stress also plays a role in the development of CVD in immigrants. The stress level was found to be higher in immigrants in general, and it was commented that this might be related to low socioeconomic levels. However, in the present study, the perceived stress level was found to be higher in the immigrant group despite the higher socioeconomic level. These results suggest that factors other than low socioeconomic conditions, as stated in previous studies, may be effective in the high level of stress in immigrants. Factors related to not being able to create an adequate social environment or not receiving social support after migration may expose people to higher psychosocial stress.

Türkiye comprises 12 geographic regions. Antalya is in the Mediterranean region (TR6). Similar to those who migrated from the other regions, the age at first ACS was found to be lower in people who lived in the Mediterranean region and migrated to Antalya. This shows that the result obtained in the study is

not related to being born in the Mediterranean region. Despite being born in the Mediterranean region, the age of the first ACS is also earlier in people who have migrated. When the differences between the regions are examined, the age difference of the people who migrated from the western Black Sea region was the lowest, while the age difference was found to be the highest in those who migrated from the western Marmara region. In other words, those who migrated from western Marmara constituted the group of people who had ACS at the earliest age. However, the small number of people who migrated from this region in the study requires considering the randomness. Table 2 shows that migration from less urban areas had a greater impact on the age at first ACS. Migration and its effects are quite complicated. However, this table suggests that the power of adaptation to the new region after migration may affect the first ACS age. The breaking of strong social and environmental ties of people in migration people from rural areas and the inability to establish these ties in the new living area may be associated with ACS at an early age. People migrating from the urbanized region could easily adapt to new living areas. On the other hand, regional differences also suggest that the risk of the region in which people lived before may have an additive effect on the risk of migration. However, in order to have a clear idea of this subject, the results should be examined with epidemiological studies.

The majority of the patients migrated for work reasons, followed by familial reasons, which is mostly the fact that a member of the family migrated due to work. The reason for migration was not identified as a risk factor associated with ACS age. However, since the main reason for migration is work, we think that the contribution of the institutions to the adaptation of the people to the place where they migrate can contribute to reducing the risk of cardiovascular events. The results of our study need to be supported by epidemiological studies, but the hypothesis it creates should be taken into account. It imposes a duty on both the immigrants and the establishments that are effective in their migration. Migration, a concept almost as old as human history, will continue as long as humanity exists. For this reason, it is beneficial to gain a precautionary perspective against the potential health problems caused by migration in the modern era.

Our results are promising and indicate the need for further research to clarify the impact of internal migration on CVD risk. However, some limitations should be pointed out. The main limitation is that the study was conducted in a single center from a single city. It can not be representative of the whole immigrant population in Türkiye. Another limitation of the study is that no internationally confirmed test was used to evaluate the level of psychosocial stress. The findings of the present study will inspire multicenter studies. It is valuable in that it is the first study on the impact of internal migration on the age of the first ACS.

## Conclusions

The study showed that among patients with the first ACS episode, those with a history of internal migration had ACS at an earlier age. No difference was found in the incidence of classical risk factors of CHD between immigrant and nonimmigrant groups, except smoking. We also demonstrated that the impact of internal migration was independent of socioeconomic status.

These findings suggest that internal migration might be an independent risk factor associated with ACS at an earlier age. This hypothesis needs to be tested with larger multicenter studies and epidemiological studies.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee of Antalya Training and Research Hospital (Date: 08.05.2014, Approval No: 2014-097, NCT04578964).

**Informed Consent:** Written informed consent was obtained from all participants.

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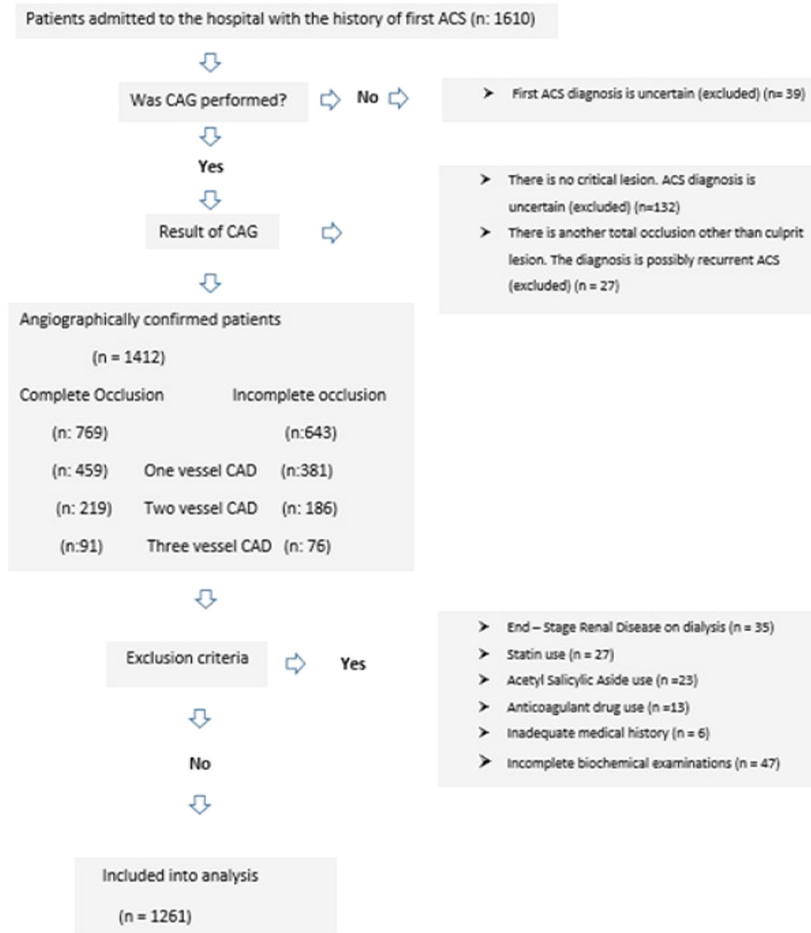
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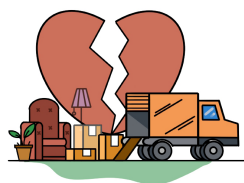
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Supplementary Figure 1. Flow chart of the study.

## The Relationship Between the Age of First Acute Coronary Syndrome Episode and Internal Migration

1261 pts presenting w/ first ACS



Immigrants

vs.



Non-Immigrants

Age  
(mean ± SD)

55.4 ± 10.7 years

vs.

60.0 ± 13.36 years

P < .001



Internal migration may be a risk factor associated with acute coronary syndrome at an earlier age when compared to nonimmigrants.