Original Article

Age-Connected Variations of Clinical and Angiographic Profiles and Outcomes in an Urban Population With Acute Coronary Syndrome

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ABSTRACT

Background: Acute coronary syndrome (ACS) is a rapidly growing concern, especially among younger urban communities. We aimed to study age-based differences in clinical and angiographic profiles and outcomes in an urban population.

Methods: This study recruited 2 independent, equal-sized cohorts of consecutive patients with ACS undergoing coronary angiography: younger and older cohorts (based on an age cutoff point of 35 years). Clinical and angiographic profiles were compared as primary endpoints, and in-hospital and 3-month major adverse cardiovascular events (MACE) were compared between the 2 cohorts as secondary endpoints.

Results: Each cohort was composed of 103 patients. The younger cohort, compared with the older cohort, revealed higher overweight (69.9% vs 51.5%), positive family history (12.6% vs 4.9%; *P*=0.048), use of gutka (smokeless tobacco) (56.3% vs 14.3%; *P*=0.017), smoking (41.7% vs 33%; *P*=0.195), total cholesterol (155.05±46.6 mg/dL vs 140.40±35.6 mg/dL; *P*=0.012), low-density lipoprotein cholesterol (96.74±41.23 mg/dL vs 84.14±27.25 mg/dL; *P*=0.010), normal/nonobstructive coronaries (15.5% vs 1.9%; *P*<0.001), single-vessel disease (60.2% vs 35.0%), type A lesions (36.8% vs 17.8%), left ventricular ejection fraction exceeding 40% (57.3% vs 42.7%; *P*=0.037), medical treatment only as the management strategy (16.5% vs 2.9%), in-hospital MACE (8.7% vs 12.6%; *P*=0.0367), and 3-month MACE (4.9% vs 12.6%; *P*=0.048), respectively.

Conclusions: Our younger subjects tended to have higher weight, gutka use, and positive family history than traditional risk factors with a greater frequency of single-vessel disease with type A lesions and normal or nonobstructive disease amenable to medical treatment only.
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KEYWORDS: ACS, CAD, Urban population, Young, Age-related differences

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Acute coronary syndrome (ACS) is a group of disorders that covers all patients with suspected or confirmed myocardial ischemia or infarction as a result of the partial or complete occlusion of blood supply of heart muscles and comprises unstable angina (UA), non–ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).[1] ACS is a rapidly increasing concern of public health, especially at younger age. In earlier studies, the incidence of ACS was reported to be 0.05% to 0.4% up to the age of 30 years.[2,3] Nonetheless, recently, its incidence has risen to 2.1% up to 30 years and 6.2% up to the age of 35 years.[4] The prevalence of ACS in a young individual leads to the premature occurrence of morbidity or mortality in the most productive years of life.[5] Though earlier studies have shown smoking, hyperlipidemia, or family history as major risk factors[6-10] for predisposition to coronary artery disease (CAD) in the younger population rather than traditional risk factors, data are very limited in our population. Moreover, information is also scarce on local urban populations with head-to-head comparisons on the basis of age, addressing both clinical and angiographic factors and outcomes in the ACS setting. This is why we decided to study this subject and aimed to determine the peculiar risks and angiographic characteristics that make younger people different from older subsets in our population. Hence, the objectives of the present study were to compare clinical and angiographic profiles and clinical outcomes between younger and older patients presenting with ACS to an urban tertiary care cardiac hospital.

METHODS

The present study was a prospective cohort study carried out in the National Institute of Cardiovascular Diseases (NICVD), a tertiary care cardiac hospital located in the urban area of the province of Sindh, in the southern region of Pakistan. NICVD is the largest public sector of cardiac care, with an average annual percutaneous coronary intervention (PCI) volume of around 10 000, mainly covering the urban population and providing 24/7 free-of-cost services supported by the provincial government. Two independent, equal-sized cohorts of consecutive patients presenting to the cardiac catheterization laboratory for coronary angiography with the diagnosis of ACS between August 2020 and February 2021 were recruited. Two cohorts were designed as younger and older cohorts based on the stated age at presentation. While earlier studies used an age cutoff point of 40 or 45 years for categorizing the young population, recent local data showed a significant rise in the incidence of ACS at the very younger age of up to 35 years.[4] Hence, in this study, the age cutoff value was equal to or less than 35 years for the younger cohort and greater than 35 years for the older cohort. Each cohort was independently recruited. The required number of consecutive patients aged 35 years or younger fulfilling the study inclusion criteria were recruited as the younger cohort, and the required number of consecutive patients aged above 35 years fulfilling the study inclusion criteria were recruited as the older cohort.

The ACS diagnosis was made as UA, STEMI, or NSTEMI. Patients with chest discomfort with ST-segment elevations or left bundle branch blocks of presumably new onset in electrocardiographic (ECG) leads were classified as STEMI. Patients with anginal pain at rest with no elevation in the ST segment were tagged as NSTEMI if their levels of the cardiac marker (troponin I) exceeded 0.05 ng/mL and as UA if their cardiac marker levels were found to be lower.[11]

The study protocol was approved by the ethics review board of the institution, and informed consent was taken at the time of recruitment. The inclusion criteria for the study were adult patients (≥18 y) diagnosed with ACS based on history, presentation, ECG, and cardiac biomarkers at presentation and having undergone coronary angiography for the routine management of ACS. Patients who refused to participate in the study or had pre-existing congenital or valvular heart disease or pericarditis or patients who died before reaching the catheterization laboratory were excluded from the study. The sample size for the study was calculated with the expected proportion of single-vessel disease as 62% among young patients and 32% among old patients[12] at a 5% level of significance and 80% power to detect differences in proportions. The minimum required sample size for each cohort was computed to be 43 patients. However, in addition to the number of vessel involvement, other angiographic findings and outcomes 3 months after the index hospitalization were the focus of this study. Keeping in mind the time constraints, expected loss to follow-up, and patient selection bias due to the disproportionate flow of young and old patients, the sample size was decided to inflate by a factor of 2.4. Hence, a final sample size of 103 in each cohort was decided.

Demographics characteristics and the clinical profile including biological sex ratio, hemodynamics, body mass index, hypertension, diabetes mellitus, lipid profile, smoking, family history of premature CAD, chronic kidney disease, history of prior MI, use of smokeless tobacco (eg, gutka [a form of tobacco mixed with minced areca nuts, catechu, and paraffin wax with flavor], naswar [a moist powdered form of tobacco], and paan [a combination of tobacco, areca nuts, and betel leaf]) or plain tobacco, and alcohol consumption were recorded. The type of ACS (NSTEMI, STEMI, or UA); the angiographic profile, including the number of diseased vessels, the culprit vessel, the lesion type, and the location of the lesion; and the management strategy were also documented and compared between the 2 age groups as primary endpoints. The left ventricular ejection fraction (LVEF) was assessed by an experienced echocardiographer blinded to the patient at the time of discharge and 1 month after discharge.

In-hospital mortality and other major adverse cardiovascular events (MACE), composed of re-infarction (nonfatal MI or stent thrombosis), repeat revascularization (repeat PCI or bypass graft placement for restenosis at the lesion treated during the index PCI, or occurring within 5 mm of the PCI site),[13] cerebrovascular accidents (nonfatal ischemic stroke or transient ischemic attack), heart failure,[14] and arrhythmias (requiring pharmacological or electrical interventions) were noted and compared. Patients in each cohort were followed up for 3 months. At follow-up, all-cause mortality, re-infarction, repeat revascularization, cerebrovascular accident, hospitalization due to heart failure, medication compliance, and resumption of routine activity were assessed and compared between the 2 cohorts as secondary endpoints. Medication compliance and resumption of routine activity were both self-reported by the patients at the time of follow-up. However, medication compliance was further verified by the achievement of the targeted heart rate and blood pressure recorded at the same time.

IBM SPSS, version 21, was used for data analysis. Descriptive statistics such as the mean ± the standard deviation (SD) or frequencies and percentages were calculated for quantitative and qualitative variables, respectively. Outcomes were compared between the 2 age groups with the aid of an

appropriate χ^2 test or the Fisher exact test or the independent sample *t* test. A 2-sided *P* value of 0.05 or less was taken as the criterion for significance.

RESULTS

Each cohort was comprised of 103 patients. The mean age was 32.36±3.38 years in the younger cohort and 57.49±10.9 years in the older cohort.

Table 1 and Figure 1 present the demographic characteristics and the clinical profile in the 2 cohorts. The findings in the younger cohort and the older cohort, respectively, were as follows: overweight (69.9% vs 51.5%; *P*=0.005); hypertension (31.1% vs 62.1%; *P*<0.001), diabetes mellitus (11.7% vs 33%; *P*<0.001), total cholesterol (155.05±46.6 mg/dL vs 140.40±35.6; *P*=0.012), low-density lipoprotein cholesterol (96.74±41.23 mg/dL vs 84.14±27.25 mg/dL; *P*=0.010), history of prior CAD (7.8% vs 17.5%; *P*=0.036), use of smokeless tobacco (paan: 25% vs 71.4%; *P*=0.011 and gutka: 56.3% vs 14.3%; *P*=0.017), positive family history (12.6% vs 4.9%; *P*=0.048), chronic kidney disease (1% vs 2.9%; *P*=0.621), and alcohol consumption (1% vs 1.9%; *P*≥0.99).

Concerning angiographic data, in the younger cohort and the older cohort, respectively, the frequency of STEMI was 94.2% vs 88.3%, the frequency of single-vessel disease was 60.2% vs 35.0%, the frequency of multivessel disease (triple-vessel disease [3VD]) was 6.8% vs 30.1% (*P*<0.001), the frequency of double-vessel disease (3VD) was 17.5% vs 33% (*P*=0.01), the frequency of normal coronaries was 6.8% vs 1%, the frequency of nonobstructive coronaries was 8.7% vs 1%, the frequency of type A lesions was 36.8% vs 17.8%, the frequency of type C lesions was 24.1% vs 45.5%, the frequency of primary PCI was 79.6% vs 87.4%, and the frequency of medical treatment only as the management strategy was 16.5% vs 2.9% (Table 2). Among the 17 (16.5%) medically managed young patients, 1 patient had diffused disease not amenable to revascularization, 9 patients had nonobstructive disease due to recanalization, and all presented with STEMI; in addition, the remaining 7 patients had normal coronaries with ECG changes mimicking STEMI (early repolarization or pericarditis), for whom medications were prescribed for risk modification if indicated.

Echocardiographic data in the 2 groups revealed LVEF exceeding 40% in 57.3% of the younger cohort and 42.7% of the older cohort (*P*=0.037) at the time of discharge (Fig. 1).

In-hospital MACE occurred in 8.7% of the younger cohort and 12.6% of the older cohort (*P*=0.0367). The mortality rate was 1% in the younger cohort and 1.9% in the older cohort (*P*≥0.99), and the heart failure rate was 6.8% and 11.7% in the younger and older groups, respectively (*P*=0.229). The MACE rate after 3 months was 4.9% in the younger cohort and 12.6% in the older cohort (*P*=0.048). The mortality rate was 2% in the younger group and 5.9% in the older group (*P*=0.170). Hospitalization due to heart failure occurred in 2% of the younger cohort and 5% of the older cohort (*P*=0.279). The rate of medication compliance was 94.1% in the younger group and 91.1% in the older group (*P*=0.410). The rate of the resumption of routine activity was 91.2% in the young group and 72.3% in the old group (*P*=0.001) (Table 3).

Table 1: Comparison of the demographic and clinical characteristics of the study population by age group

Characteristics	Age Group		*P* value
	≤ 35 y	> 35 y	
Total (N)	103	103	-
Age (y)	32.36 ± 3.38	57.49 ± 10.9	<0.001*
Biological Sex			
Male	89 (86.4%)	80 (77.7%)	0.102
Female	14 (13.6%)	23 (22.3%)	
Body mass index (kg/m^2)	27.14 ± 2.99	26.87 ± 3.76	0.571
Under weight	1 (1%)	0 (0%)	0.005*
Normal weight	14 (13.6%)	35 (34%)	
Overweight	72 (69.9%)	53 (51.5%)	
Obese	16 (15.5%)	15 (14.6%)	
Heart rate (bpm)	85.48 ± 14.35	83.68 ± 13.73	0.36
Hypertension	32 (31.1%)	64 (62.1%)	<0.001*
Diabetes mellitus	12 (11.7%)	34 (33%)	<0.001*
NIDDM	10 (83.3%)	33 (97.1%)	0.162
IDDM	2 (16.7%)	1 (2.9%)	
Smoking	43 (41.7%)	34 (33%)	0.195
Current smokers	38 (88.4%)	26 (76.5%)	0.224
Ex-smokers	5 (11.6%)	8 (23.5%)	
Family history of premature CAD	13 (12.6%)	5 (4.9%)	0.048*
Chronic kidney diseases	1 (1%)	3 (2.9%)	0.621
Prior myocardial infarction	8 (7.8%)	18 (17.5%)	0.036*
History of stroke	0 (0%)	2 (1.9%)	0.498
Smokeless tobacco use	16 (15.5%)	14 (13.6%)	0.693
Paan	4 (25%)	10 (71.4%)	0.011*
Gutka	9 (56.3%)	2 (14.3%)	0.017*
Naswar	3 (18.8%)	1 (7.1%)	0.602
Chewable tobacco	2 (12.5%)	2 (14.3%)	>0.999
Alcohol consumption	1 (1%)	2 (1.9%)	>0.999
Drug abuse	3 (2.9%)	1 (1%)	0.621

NIDDM, Non–insulin-dependent diabetes mellitus; IDDM, Insulin-dependent diabetes mellitus; CAD, Coronary artery disease
*significant at 5%

Table 2: Comparison of the type of ACS, angiographic findings, and management strategies by age group

Characteristics	Age Group		*P* value
	≤ 35 y	> 35 y	
Type of Acute Coronary Syndrome			
Unstable angina	0 (0%)	1 (1%)	0.264
Non-ST-elevation myocardial infarction	6 (5.8%)	11 (10.7%)	
ST-elevation myocardial infarction	97 (94.2%)	91 (88.3%)	
Anterior wall	65 (67%)	55 (60.4%)	0.349
Inferior wall	32 (33%)	36 (39.6%)	
^Culprit Vessel			
Left anterior descending artery	65 (67.7%)	61 (59.8%)	0.156
Right coronary artery	16 (16.7%)	28 (27.5%)	
Left circumflex	13 (13.5%)	13 (12.7%)	
Left main	2 (2.1%)	0 (0%)	
****Lesion Location**			
Proximal	52 (59.8%)	59 (58.4%)	0.891

Mid	26 (29.9%)	33 (32.7%)	
Distal	9 (10.3%)	9 (8.9%)	
Management Strategy			
Primary PCI	82 (79.6%)	90 (87.4%)	0.004*
Early invasive PCI	4 (3.9%)	9 (8.7%)	
Medical treatment Only	17 (16.5%)	3 (2.9%)	
CABG	0 (0%)	1 (1%)	

ACS, Acute coronary syndrome; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting
^patients with normal coronaries excluded
**patients with normal coronaries and nonobstructive coronaries excluded
*significant at 5%

Table 3: Comparison of in-hospital and 3-month follow-up outcomes by age group

Characteristics	Age Group		*P* value
	≤ 35 y	> 35 y	
In-Hospital Outcomes			
Major adverse cardiovascular events	9 (8.7%)	13 (12.6%)	0.367
Re-infarction	1 (1%)	2 (1.9%)	>0.999
Repeat revascularization	1 (1%)	2 (1.9%)	>0.999
Cerebrovascular accident	0 (0%)	1 (1%)	>0.999
Heart failure	7 (6.8%)	12 (11.7%)	0.229
Arrhythmias	4 (3.9%)	5 (4.9%)	>0.999
Expired	1 (1%)	2 (1.9%)	>0.999
Successful 3-month Follow-up	103 (100%)	103 (100%)	-
Follow-up Outcomes			
MACE	5 (4.9%)	13 (12.6%)	0.048*
Expired	2 (2%)	6 (5.9%)	0.17
Re-infarction	1 (1%)	1 (1%)	>0.999
Repeat revascularization	1 (1%)	0 (0%)	>0.999
Cerebrovascular accident	2 (2%)	2 (2%)	>0.999
Hospitalization due to heart failure	2 (2%)	5 (5%)	0.279
Medication compliance	96 (94.1%)	92 (91.1%)	0.410
Back to routine/work	93 (91.2%)	73 (72.3%)	0.001*

*significant at 5%

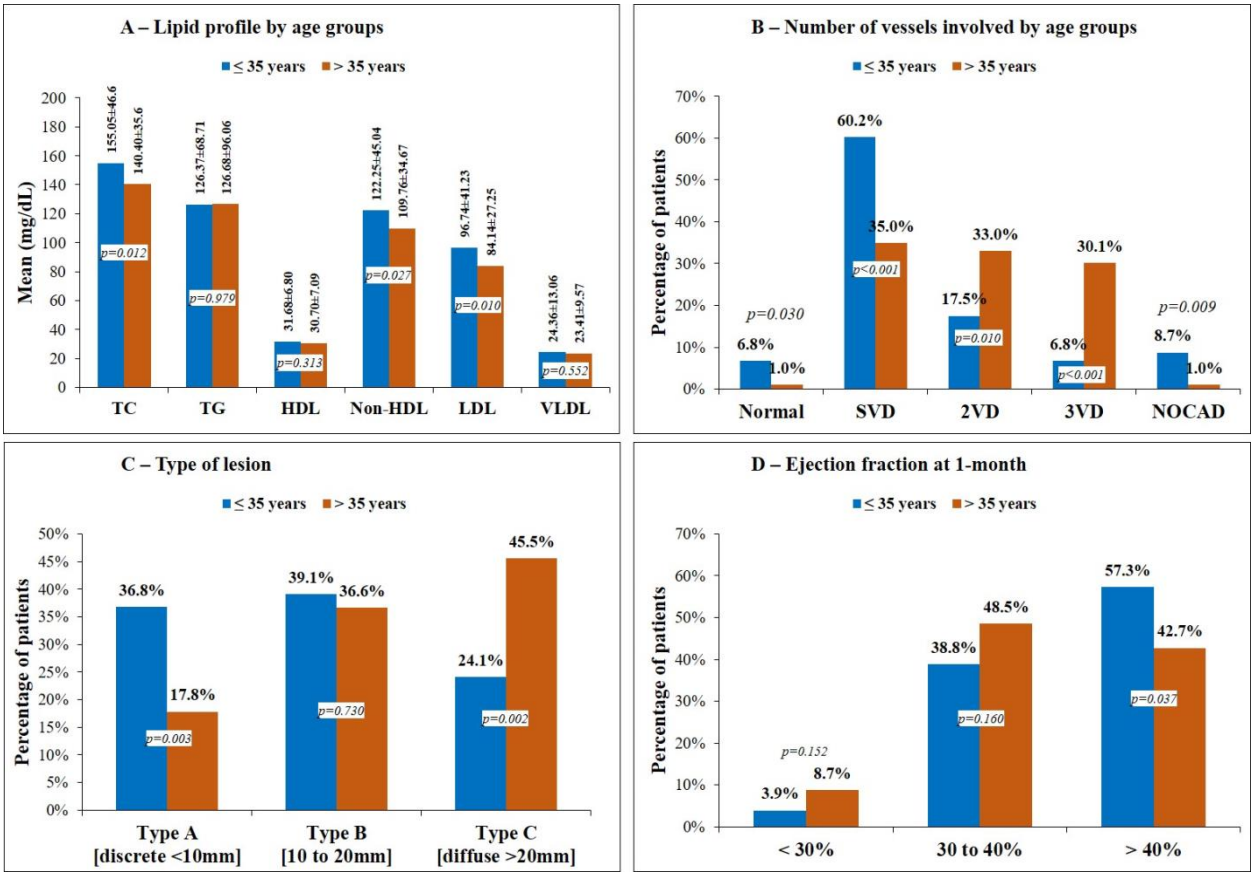

Figure 1: The figures illustrate comparisons of the lipid profile (A), the number of vessels involved (B), the type of lesion (C), and the ejection fraction at 1 month (D).

DISCUSSION

ACS in the younger population has rapidly progressed in the last decade, with its incidence now ranging from 0.7% as reported by Schoenebenrger et al[15] in 2011 to 6.2% as recently reported by Khan et al.[4] Although the burden of cardiovascular diseases has been declining in the older population, the same is not true in younger adults.[16] The majority of patients in these studies were from urban communities. Gestro et al[17] reported an association between air pollutants in urban areas and the increased risk of ACS. This might be one of the reasons for the increase in the frequency of younger ACS as this population group is more exposed to the open environment due to work-related movements.

Apropos of the comparative analysis of the 2 cohorts, the majority of the subjects were male. We found no difference in the male-to-female proportion between the younger and older patients, which is in line with earlier studies.[18-21] Still, the younger cohort had a high frequency of overweight, positive family history of premature CAD, hyperlipidemia (as shown by higher total cholesterol, low-density lipoprotein, and high-density lipoprotein cholesterol [Fig. 1A]), smoking, and consumption of smokeless tobacco in the form of gutka in comparison with the older substrate in this study. The majority of our findings chime in with the studies in other regions. For instance, a study from Egypt by Obaya et al[22] showed similar risk profiles in younger individuals, except for dyslipidemia, which was more common in older subjects. In

contrast, a study by Lv et al[23] from China reported a higher proportion of dyslipidemia in combination with hyperuricemia in the younger population. By and large, smoking was the consistent predisposing factor in younger people in earlier studies.[22,24] Of note, gutka (a form of smokeless tobacco) was a frequent risk factor in younger people in our region, and its use was more common in low socioeconomic people, especially in small social and business community gatherings. The traditional risk factors such as hypertension, diabetes mellitus, prior history of CAD, and chronic kidney disease were more frequent in the older population. These findings are corroborated by various previous studies. For instance, a study by Adam et al[25] in 2017 from the same region showed diabetes mellitus in 61.5% vs 37% and prior CAD in 64.2% vs 36.3% in older and younger people, respectively. Likewise, another study by Alberty et al[26] in 2017 from Slovakia reported a higher prevalence of conventional risk factors in older people (≥65 y) than the younger substrate.

Our study did not reveal any significant differences in the presentation of ACS type, the involvement of the culprit vessel, and the location of the lesion between the 2 cohorts (Table 2). Be that as it may, in the angiographic profile, there was a higher proportion of single-vessel disease, type A lesion, and nonobstructive or normal coronaries in the younger cohort (Fig. 1B & and 1C). In contrast, we found that the older cohort had a higher frequency of multivessel disease and type C lesions. Prajapati et al[27] and Haque et al[28] also reported similar findings with the predominant occurrence of single-vessel disease in younger people (52.3% vs 53.12%). Furthermore, Anjum et al[29] showed a higher proportion of normal coronaries up to 23.1%, which is a much higher percentage than that in the current study (6.8% normal and 8.7% nonobstructive). They also reported American Heart Association (AHA) type A lesions in 47.8% of younger people, in line with our findings. Interestingly, these observations support the view that younger people are more amenable to management with aggressive medical therapy only and have less atherosclerotic burden than older individuals as witnessed by a significantly higher frequency of medical management alone in the current study. A recent study from the same region also reported a more frequent thrombogenic environment in the younger ACS substrate, explaining their better response to medical treatment alone.[21]

Another finding of note in this study was a higher frequency of LVEF of 40% or higher at 1 month in the younger cohort than in the older group, suggesting their better response to either medical management or revascularization (Fig. 1D).

The composite in-hospital MACE showed a lower trend in our younger group. Nonetheless, at 3 months, the rate was significantly lower in the younger cohort than in the older cohort, mainly due to the lower frequency of heart failure and mortality (Table 3). Moreover, our younger cohort was also distinct from our younger cohort given its significantly higher resumption of routine activity.

Even though this study was conducted at a tertiary care cardiac hospital, which is the largest public sector of cardiac health with the flow of patients from all across the country, the single-center coverage of the study remains the main limitation. Furthermore, due to the observational study design, with around 90% of the patients suffering from acute STEMI, several non-traditional CVD factors such as rheumatologic disorders and inflammatory markers could not be assessed. Additionally, because of the lower number of young patients, the sample size for the 2 cohorts was not statistically powered enough to draw any meaningful conclusion in the

analysis of multiple variables and their interactions.

CONCLUSIONS

In the current study, the younger cohort tended to have higher weight, gutka use, and positive family history than traditional risk factors with a greater frequency of single-vessel disease with AHA type A lesions and normal or nonobstructive disease amenable to medical treatment only compared with the older cohort with ACS. Moreover, the younger group was distinct from the older cohort because of its lower rates of heart failure and mortality and the higher rate of the restoration of routine daily life.

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