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Economic Evaluation

# Social and Economic Costs and Health-Related Quality of Life in Patients With Acute Coronary Syndrome

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## ABSTRACT

*Objectives:* Health-related quality of life (HRQOL) evaluation is an important measure of the impact of certain inerventions, epecially coronary artery diseases treatments. As more patients with acute coronary syndrome (ACS) live longer, doctors and researchers want to know how they manage in day-to-day life. The aim of this study was to compare costs and HRQOL of patients who underwent percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), and medical therapy (MT) and to assess its main determinants in the whole sample of patients with ACS for a period of 12 months.

*Methods:* The study was carried out to estimate costs and HRQOL evaluation of 310 patients who underwent coronary revascularization (PCI, n = 139; CABG, n = 128; and MT, n = 43). We estimated direct costs (medical costs and nonmedical costs) and indirect costs (productivity losses owing to morbidity and mortality) based on a societal perspective, and HRQOL was assessed using the EQ-5D-3L (5 dimensions and 3 levels) and visual analog scale (VAS). We applied costs and HRQOL 1 month before treatment and 12 months after treatment in 3 groups, and scores were compared. Data entry and analysis were performed with SPSS.

*Results:* Total EQ-5D index scores in PCI, CABG, and MT groups 1 month before treatment were 0.54 ± 0.26, 0.52 ± 0.25, and 0.56 ± 0.25, respectively. After 12 months, the HRQOL mean changed to 0.67 ± 0.20, 0.74 ± 0.15, and 0.65 ± 0.19, respectively, in PCI, CABG, and MT groups. The mean EQ-5D VAS score 1 month before treatment was 63 ± 15.4 for the PCI group, 62 ± 16.4 for the CABG group, and 64 ± 18.4 for the MT group; the mean EQ-5D VAS score 12 months after treatment was 74.8 ± 19.5 for the PCI group, 78.8 ± 18 for the CABG group, and 74 ± 19.7 for the MT group. All the 3 therapeutic strategies presented significant improvement in all dimensions of the follow-up. However, the CABG group was the one that had significantly greater improvement compared with PCI and MT. The mean (95% confidence interval) annual total cost for the overall sample was found to be $4940/patient. This cost was significantly higher among patients with CABG ($7327/patient) compared with PCI ($5225/patient) and MT ($2278/patient). Direct costs accounted for 87.7% and indirect costs for 12.3% of the total costs.

*Conclusion:* The quality of life was better in both CABG and PCI groups compared with MT after 1 year of follow-up. However, treatment with CABG is more difficult and expensive than PCI and MT, but it provides a better quality of life. The findings of the present study indicate the high economic burden of ACS in Iran.

*Keywords:* acute coronary syndromes, coronary artery bypass graft, cost, medical therapy, percutaneous coronary intervention, quality of life.

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## Introduction

Coronary artery disease (CAD) is a condition in which atherosclerotic plaque builds up in the wall of the coronary arteries, leading to narrowing and the clinical manifestations of acute coronary syndrome (ACS) including angina and myocardial infarction. It is a leading cause of mortality, morbidity, and disability around the world.[1] Therapeutic strategies for ACS are medical therapy (MT), percutaneous coronary intervention (PCI), and coronary artery bypass graft (CABG). All 3 treatment regimens have similar efficacy regarding prevention of myocardial infarction (MI) and death.[2-4]

Coronary heart disease is estimated to affect 15.5 million people in the United States, with a cost of $10.4 billion per year. In 2011, coronary artery disease (CAD) was the most frequent cause of death among Americans, causing more than 375 000 deaths.[5] In Iran, cardiovascular events are the most common cause of mortality; about 46% of deaths occur from CAD,[6] and the prevalence is increasing.[7] These diseases impose a lot of expenses om health systems, and still cardiovascular disease is one of the most preventable human noncommunicable diseases.[8] Cardiovascular diseases affect the physiological, physical, social, economic, mental, and emotional life of patients.[9]

The initial cost of medical treatment is usually lower than the initial cost for PCI and CABG, but it is less effective for symptom relief.[10] In addition, in the medium and long term, patients may require interventions that increase their costs. Therefore, further need for percutaneous coronary interventions in patients who initially underwent angioplasty may affect changes in cost-effectiveness in the long-term follow-up. Considerations regarding the occurrence of major adverse cardiovascular events associated with the costs and effectiveness of these strategies may contribute to better decision making.[11]

Recent data show a high prevalence of CAD and its risk factors, such as cigarette smoking, diabetes mellitus, hypertension, dyslipidemia, low level of physical activity, and obesity among Iranian population.[12,13]

Several studies have compared the outcomes of coronary revascularization with PCI, CABG, and MT, but beyond the survival benefit of CABG, PCI, and MT, functional recovery is the expectation of patients who receive these treatments for relief of symptoms. Therefore, the importance of HRQOL in clinical research has been extensively discussed over recent decades, and there is an increasing recognition among clinicians and researchers that the impact of chronic illnesses and their treatments must be assessed in terms of their HRQOL in addition to more traditional measures of clinical outcomes: morbidity and mortality.[14,15] The HRQOL has also been used increasingly as a factor in cost-effectiveness analyses and heath technology assessments that are used to determine the relative value for many of different forms of the treatment.[16] Hence, information on costs and HRQOL of patients in different interventions of coronary revascularization and its determinants is important to defining a comprehensive plan of care. Because there are few studies regarding costs and HRQOL of CAD in different therapeutic interventions in developing countries, the main aim of this study was to compare costs and HRQOL of patients who underwent CABG, PCI, and MT and to assess its main determinants in the whole sample of Iranian patients with ACS.

## Methods

### Study Type

A cross sectional descriptive study was performed among patients diagnosed with ACS presenting to the Tehran Heart Center Hospital in 2018.

### Sample Population and Inclusion and Exclusion Criteria

This study sample consists of a total of 310 patients who presented to the medical ward of the Tehran Heart Center Hospital with ACS during a period of 1 year. This includes patients who were between 40 and 90 years of age categorized into the 3 interventions of ACS: PCI, CABG, and MT.

After pretreatment assessments and screening, 310 patients with PCI (n = 139), CABG (n = 128), and MT (n = 43) were recruited in the study. All patients were followed for 12 months to collect robust and representative data. During the follow-up period, 3 visits (1 when admitted, 6 months, and the other at the end of the 12-month period) were conducted. If patients were unable to attend the follow-up visits, they were reached by the investigator over the phone in to complete the questionnaire.

### Data Collection

Data were collected by an interviewer-administered structured questionnaire by qualified physicians who were specially trained for this research. Changes in electrocardiogram and troponin I results were collected from bed head tickets. Data included:costs, demographic and clinical data, such as triglycerid and cholesterol.. The HRQOL data were obtained using a EuroQol-5D-3L (EQ-5D) questionnaire that is disease specific.

In total, 310 patients completed the questionnaire, which was designed in accordance with the objectives of the study. The questionnaire consisted of several parts including demographic characteristics, direct costs (direct medical costs, direct nonmedical costs), and indirect costs. In addition to the questionnaire, hospital bills for outpatient and inpatient costs of the interviewed patients were reviewed. The information was collected from the governmental hospital in Tehran because most of the patients in the surrounding cities are referred there for treatment.

Note a disease can not only generate costs for patients and their families, but also it can produce costs for government, employers, insurance companies, and other members of the society. Therefore, to achieve a comprehensive analysis, this study was performed from the societal perspective, including all direct medical and indirect costs and QALY interventions.

### Direct Cost

Direct cost was divided in to medical and nonmedical costs. Medical use has been divided into 3 categories: outpatient care, hospital inpatient care, and drugs.[17] Direct medical costs include hospital inpatient costs and outpatient costs (physician outpatient, rehabilitation care, specialists and other health professionals, diagnostic tests, prescription drugs, and medical supplies). To obtain more accurate estimates, we measured the payments made by insurance and direct payments by the patients obtained from the hospitalization and outpatient bills. Direct nonmedical costs include the portion of direct payments made by the patient and his or her family to receive the services. Direct nonmedical costs include nonmedical cost (transportation costs to receive healthcare from the service providers, relocation expenses, complementary or alternative therapies, domestic help, house, car, special equipment, communication, mobile, telephone, housekeeping, food cost, and childcare or related items) and informal care.

### Indirect Costs

In this part of the study, we focused on estimating productivity losses (temporary and permanent disability). For the estimation of indirect costs and the subsequent conversion into monetary units, in most of the studies of this type, the human capital approach has been used.[18] The human capital method transforms years of life into monetary units by using the average gross earning per worker. Although the human capital approach has often been criticized, it has been widely used because it is an easy assessment and the lack of existing alternative approaches.[19,20] The information regarding days of temporary disability, reduction in working time, permanent disability, and early retirement caused by ACS was obtained from the questionnaires filled out by the patients or the patient's caregivers. Information about employment and wages was obtained from the Iran National Statistics Institute.

### EQ-5D Health Survey

The EQ-5D covers 5 domains including mobility, self-care, usual activities, pain, and anxiety and depression.[21] An index score is produced ranging from −0.594 to 1, where a score below zero indicates a state "worse than death" and a score of 1 indicates the optimal health state. The EQ-5D also administers a visual analogue scale (VAS), which asks patients to rate their pre- and posthealth state on a scale from 0 to 100, where 0 indicates the worst imaginable health state and 100 indicates the best imaginable health state.

### Statistical Analysis

The data were coded and entered into an excel data sheet and were analyzed using SPSS, version 20.0 (IBM, Armonk, NY). Analysis of variance was conducted initially, and for selected variables a bivariate analysis was conducted subsequently. The $\chi^2$ test for nominal scale data was used to identify statistical significance. One-way analysis of variance was used to compare differences in age and body mass index among 3 ACS interventions. Because the *P* value was nonsignificant, no post hoc tests (Bonferroni test) were used. *P* value of less than .05 was used to ascertain statistical significance.

## Results

A total of 310 patients with ACS were identified and divided into 3 groups according to treatment strategy during their 1-year follow-up: PCI (n = 139), CABG (n = 128), and MT (n = 43) with a mean age of 60.4 ± 10.27. This included 219 (71%) men (mean age 59.7 ± 10.66) and 91 (29%) women with a mean age of 62.17 ± 9.20. The man-to-woman ratio was approximately 2:1. Of the total patients who underwent CABG, a majority of 99 (78%) were men, and a more significant majority of the patients who underwent PCI were men (93 [67%]). In addition, 27 patients who underwent MT were men (63%). Thus, the male patients showed a higher association with all 3 interventions of ACS with a *P* = .040 (Table 1).

The highest percentage of patients who underwent MT and CABG belonged to the 60-to-69–year age group, which accounted for 51% and 35%, respectively, whereas the highest percentage of patients who underwent PCI (33%) were between 50 and 59 years of age (Fig. 1). Our study showed a higher mean age of 61.9 ± 9.4 years in patients who underwent CABG and 60.7 ± 9.6 years in patients who underwent MT compared with 59.1 ± 10.9 years for patients who underwent PCI, without a significant statistical difference between age with interventions (*P* = .08; Table 1).

The prevalence of ACS risk factors, including hypertension (HT), dyslipidemia, diabetes mellitus (DM), obesity, and current smoking, were 57%, 56%, 37%, 30%, and 23.5% among the Iranian population aged >40 years, respectively (Table 1).

### Direct Costs

The mean annual direct cost per patient was $4387. This cost was found to be statistically significantly lower in the MT group ($1906/patient) compared with the other 2 groups of participants ($P < .001$ for all comparisons). Moreover, this cost was found to be statistically significantly lower per patient with PCI $4710 compared with that calculated per patient with CABG $6543 (Table 2).

The mean of direct costs, 81.2% were direct medical costs and 18.8% direct nonmedical costs. Hospital costs were the main cost categories of ACS direct costs (64.5%); outpatient cost was 16.7%, nonmedical cost was 8.9%, and informal care was 9.9% of ACS direct cost (Fig. 2).

### Indirect Costs

The mean annual indirect cost for the total sample was $550/patient. This cost was higher among patients who underwent CABG $782/patient, whereas it was $515 and $372 per patient in the PCI and MT groups, respectively. However, a significant difference was detected in the indirect cost among these 3 groups of interventions ($P < .004$, Table 3).

### Mean Total Cost

The mean annual total cost for the overall sample was $4940/patient. This cost was significantly higher among patients who underwent CABG ($7327 per patient) compared with PCI ($5225 per patient) and MT ($2278 per patient; Table 4). The total cost in all groups of patients was mainly attributed to direct costs (90.1%, 89.3%, and 83.7% for patients with PCI, CABG, and MT, respectively). Direct costs accounted for 87.7% and indirect costs for 12.3% of the total costs (Fig. 3).

### HRQOL in Patients With ACS

Of the total 318 questionnaires, only 8 were excluded from the HRQOL analysis because the information was insufficient or inadequate. Lower scores on the EQ-5D index reflected poorer health status. The mean EQ-5D index score 1 month before treatment was 0.54 ± 0.26 for the PCI group, 0.52 ± 0.25 for the CABG group, and 0.56 ± 0.25 for the MT patients; the mean EQ-5D index score 12 months after treatment was 0.67 ± 0.20 for the PCI

**Table 1.** Baseline demographics and clinical characteristics per patient according to the type of interventions acute coronary syndrome.

| | PCI | CABG | MT | *P* value |
|---|---|---|---|---|
| No. of patients | 139 | 128 | 43 | |
| Male (%) | 93 (67) | 99 (78) | 27 (63) | .040 |
| Age (y) | 59.1 ± 10.9 | 61.9 ± 9.4 | 60.7 ± 9.6 | .083 |
| Current smoker (%) | 37 (26.6) | 26 (20.3) | 10 (23.3) | .458 |
| BMI (kg/m$^2$) | | | | |
| Normal weight (%) | 29 (21) | 25 (19) | 11 (25 ) | .340 |
| Overweight (%) | 62 (45) | 69 (54) | 20 (47) | .867 |
| Obese (%) | 48 (34) | 34 (27) | 12 (28) | .456 |
| Comorbidity history | | | | |
| Hypertension (%) | 77 (55) | 73 (57) | 25 (58) | .444 |
| Dyslipidemia (%) | 80 (57) | 64 (50) | 26 (60) | .327 |
| Diabetes mellitus (%) | 46 (33) | 51 (40) | 16 (37) | .527 |

BMI indicates body mass index; CABG, coronary artery bypass graft; MT, medical therapy; PCI, percutaneous coronary intervention.

**Figure 1.** Age distribution of the sample according to the type of interventions acute coronary syndrome.

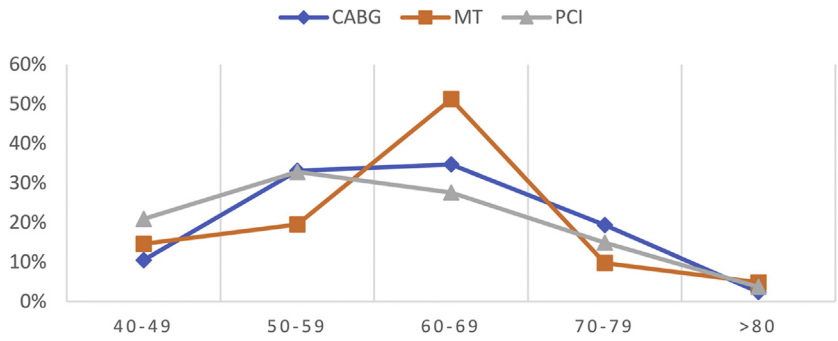
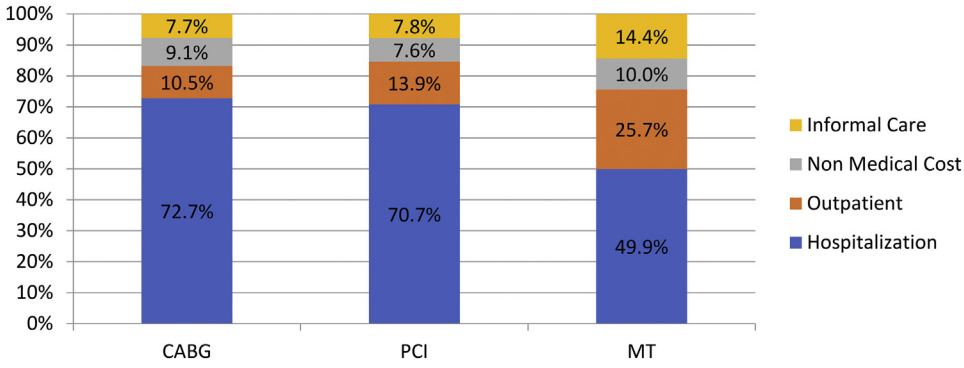



**Table 2.** Mean direct costs (in dollars) per patient according to the type of interventions acute coronary syndrome.

| | PCI | CABG | MT | P value |
|---|---|---|---|---|
| Direct medical costs Hospitalization | 3333 (2619-3809) | 4762 (4286-5476) | 952 (714-1190) | <.001 |
| Outpatient | 654 (357-857) | 684 (381-872) | 490 (357-619) | <.001 |
| Direct nonmedical costs | | | | |
| Nonmedical costs | 357 (178-476) | 595 (380-714) | 190 (90-238) | |
| Informal care | 366 (90-540) | 504 (119-814) | 274 (57-393) | |
| Total direct cost | 4710 | 6545 | 1906 | <.001 |

CABG indicates coronary artery bypass graft; MT, medical therapy; PCI, percutaneous coronary intervention.

**Figure 2.** Percentage of total annual direct cost per patient according to the type of interventions acute coronary syndrome.




group, 0.74 ± 0.15 for the CABG group, and 0.65 ± 0.19 for the MT patients.

The mean EQ-5D VAS score 1 month before treatment was 63 ± 15.4 for the PCI group, 62 ± 16.4 for the CABG group, and 64 ± 18.4 for the MT group; the mean EQ-5D VAS score 12 months after treatment was 74.8 ± 19.5 for the PCI group, 78.8 ± 18 for the CABG group, and 74 ± 19.7 for the MT group.

It was observed that the values for HRQOL differed significantly according to disease severity and showed that the HRQOL scores 12 months after treatment, measured by the EQ-5D, were related to disease severity. The greatest changes in scores were observed in the CABG group and the least changes in scores were observed in the MT group (Table 5).

## Discussion

To the best of our knowledge, this is the first study performed to estimate and compare costs and QALY measurements among symptomatic patients with ACS undergoing CABG, PCI, or MT. Moreover the in-hospital course and therapeutic approach, were studied and the annual cost and QALY in patients hospitalized with ACS in Tehran Heart Center Hospital, Iran, was calculated.

This is the first study on ACS disease performed in Iran and is broadly unique in its kind. The findings of the present economic analysis indicate a significant economic burden for the management of ACS in various patient populations, with the highest

**Table 3.** Mean indirect costs (in dollars) per patient in study.

| | PCI | CABG | MT | P value |
|---|---|---|---|---|
| Productivity loss | 515 (198-790) | 782 (356-1195) | 372 (132-554) | <.004 |

CABG indicates coronary artery bypass graft; MT, medical therapy; PCI, percutaneous coronary intervention.

**Table 4.** Mean total costs (in dollars) per patient according to the type of interventions acute coronary syndrome.

| | PCI | CABG | MT |
|---|---|---|---|
| Direct costs | 4710 | 6545 | 1906 |
| Indirect cost | 515 | 782 | 372 |
| Total cost | 5225 | 7327 | 2278 |

CABG indicates coronary artery bypass graft; MT, medical therapy; PCI, percutaneous coronary intervention.

amount of expenditures attributed to direct healthcare for patients. These findings are consistent with those reported from previous studies, indicating that participants with CAD disease incur substantial direct costs.[22-25]

Regarding the significant differences between an invasive (PCI and CABG) and noninvasive (MT) approach, researchers have conducted large clinical trials to assess and compare medical therapy with revascularization and CABG with PCI.[26] The finding also showed that 44.8% of patient with PCI, 41.3% of patient with CABG and 14.3% of patient with MT had mean age of 60.4 ± 10.27. In addition, it also showed a slightly higher mean age for CABG (61.9 ± 9.4 years) and MT (60.7 ± 9.6 years) compared with PCI (59.1 ± 10.9 years) without a statistical significance ($P$ = .083). Brandão et al showed a mean age of 60 ± 9 years among in 3 interventions patients with no significant statistical difference ($P$ = .959).[27]

South Asians showed a higher rate of MI at a younger age (mean age 53 years) compared with those in other countries (mean age 58.8 years). This is very likely due to South Asians having more risk factors at ages <60 years when stratified by age, including high apolipoprotein B100/apolipoprotein A-I ratio and higher waist-to-hip ratio.[28] However, our study showed a mean age of presentation of ACS in Iran to be around 60.4, whereas it was 60 years according to Brandão et al.[27] Therefore, the Iranian population develops ACS later in their life compared with other Asian countries. Larger scale studies within the region are needed to explain this difference.

In our study nearly a 2:1 ratio (71%) of patients with ACS were men, and male sex was strongly associated with all 3 interventions of ACS compared with female sex. A study done in Brazil also showed a strong association of ACS with male sex (69.5%).[27] While the male population in Inter Heart study and South Asian cohort were about 76% and 85%, respectively.[29] In our study a higher percentage of women (52%) had PCI compared with CABG (30.2%) and MT (17.5%), indicating a higher risk for PCI than CABG and MT in women.

Our study showed that the mean age for women (62.2 years) was significantly higher compared with men (59.7 years). Studies have shown that the onset of cardiovascular disease in women occurs 7 to 10 years after that for men.[30] Exposure to endogenous estrogens during the premenopausal period are assumed to delay the manifestation of atherosclerotic disease in women, likely due to estrogens having a regulatory effect on lipids, inflammatory

**Figure 3.** Percentage of total cost attributed to each type of cost.

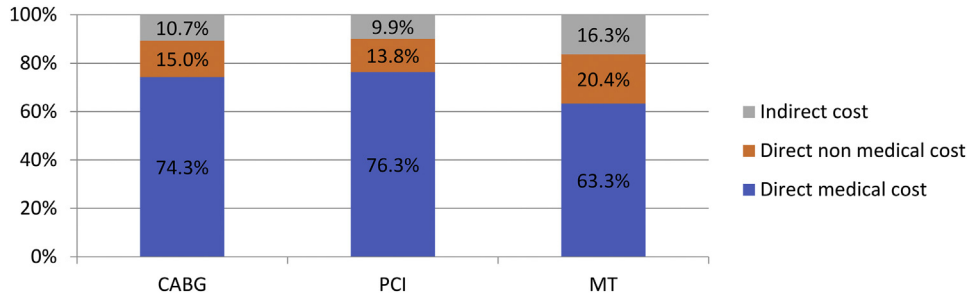



**Table 5.** Mean QALY and EQ-5D VAS scores

| | Interventions | | | | | |
|---|---|---|---|---|---|---|
| | PCI | | CABG | | MT | |
| QALY | 1 month before treatment 0.54 ± 0.26 | 12 months after treatment 0.67 ± 0.20 | 1 month before treatment 0.52 ± 0.25 | 12 months after treatment 0.74 ± 0.15 | 1 month before treatment 0.56 ± 0.25 | 12 months after treatment 0.65 ± 0.19 |
| VAS | 1 month before treatment 63 ± 15.4 | 12 months after treatment 74.8 ± 19.5 | 1 month before treatment 62 ± 16.4 | 12 months after treatment 78.8 ± 18 | 1 month before treatment 64 ± 18.4 | 12 months after treatment 74 ± 19.7 |

CABG indicates coronary artery bypass graft; EQ-5D, EuroQol- 5 Dimension; MT, medical therapy; PCI, percutaneous coronary intervention; QALY, quality-adjusted life-year; VAS, Visual Analog Scale.

markers, coagulant system, and promoting a direct vasodilatory effect through α and β receptors in vessel walls.[31,32]

The present study showed that the highest proportion of patients who underwent MT (51%) and those who underwent CABG (35%) were between 60 and 69 years of age, and the highest percentage of patients who underwent PCI (33%) were aged between 50 and 59 years, with the majority being between 50 and 69 years of age. Medagama et al showed no significant difference in age distribution of patients with all groups, with the majority being between 51 and 70 years of age.[33]

The estimated cost of ACS disease varies widely among countries. These differences can be explained by variations in local treatment patterns, the stage at which ACS disease is diagnosed, severity of disease of patients enrolled in the studies, and unit costs for the several resources expensed for ACS management.[4,25,34]

In our study, direct costs accounted for 87.7% and indirect costs for 12.3% of the total costs. Similarly, a study conducted in Greece showed that the direct costs were nearly 92% and indirect costs were 8% of the total costs.[35] Also, in another study conducted in the enlarged European Union, of the total cost of CVD, 62% were due to healthcare, 17% due to informal care, and 21% due to productivity losses.[25]

In this study, direct costs comprised the largest component of overall expenditure related to ACS, with inpatient hospitalization as the main cost driver of direct costs (64.5%). This finding is consistent with other studies,[25,36] but differs from a Korean study[37] in which the cost of outpatient care accounted for the largest proportion of the total costs.

In this study, after proving similarity of patients in 3 groups in the aspect of sociodemographic and clinical characteristics, data analysis revealed that patients who underwent CABG experienced significantly higher HRQOL compared with PCI and MT, and patients who underwent PCI experienced significantly higher HRQOL compared with MT 12 months after treatment. The analyses of QOL in patients showed improvement with all 3 therapeutic interventions. This finding agrees with results of a study by Favarato et al to assess HRQOL after CABG, PCI, and MT in patients with CAD. They found that the quality of life was better in both the CABG and PCI groups compared with MT after 1 year of follow-up. However, the patients in the CABG group had greater and more progressive improvement of QOL.[38]

Our findings are similar to the Study of Economics and Quality of Life results in which CABG with or without extracorporeal circulation and PCI were compared for 10 years. In this study, utility was more favorable among patients who underwent CABG for the first year, although the values became similar thereafter,[39] which was similar to our results. Another study performed in Iran also showed that treatment with CABG is more expensive than PCI , but it provides a better quality of life.[40] Our study will have implications for the implementation of future cost-utility analyses of ACS therapies, and our results provide information to regulatory agencies for decision-making processes.

### *Limitations of the Study*

A limitation of our study is that participants represented only a fraction of patients attending public health settings and the patients were followed only for one year. Nonetheless, we have noted the paucity of information regarding HRQOL in ACS patients, particularly about 3 interventions of coronary revascularization in developing countries.

## Conclusion

Results achieved in this study show that there was an improvement in quality of life in acute coronary syndrome patients, regardless of the treatment options. HRQOL is another source of information that contributed to define the global impact on society of a specific health problem and is also useful to set priorities and allocate resources, together with some others information sources (incidence, prevalence, mortality, costs). During the past few decades, ACS appears to be an important health-related problem with important social consequences, not only in Iran, but also in the rest of the industrialized countries. The effect that ACS has on society in terms of mortality, morbidity, and economic and social costs implies a necessary increase in attention by health authorities and society in general.

ACS represents a significant cost that society should be made aware of and that should be considered in the design, implementation, and evaluation of support programs for people who have this disease and their families, as well as in the economic evaluation of new treatments.

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