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Research Paper

The Outcomes and Cost of Therapeutic Interventions in Cardiovascular Patients: A Case Study for Application in Cost-Effectiveness Studies

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ABSTRACT

Background and Aim: Currently, cardiovascular diseases, including coronary heart disease, are one of the leading causes of death in humans worldwide. In the Eastern Mediterranean and the Middle East, including our country, cardiovascular diseases are major health and social problems, the size of which is rapidly increasing. Due to the growth of medical technologies, population growth, and lifestyle changes, studying the consequences and costs of healthcare is a critical issue in the health system. This study aimed to evaluate the outcomes and costs of revascularization interventions (angioplasty and surgery) and medical therapy in cardiovascular patients.

Materials and Methods: This is a descriptive applied study. Patients after angiography and diagnosis according to the available guidelines were treated by one of the three methods of angioplasty (644 patients), surgery (366 patients), and medical therapy (805 patients) in a public hospital in Iran. The data collection tool includes a questionnaire to collect demographic, clinical and cost information of patients. Quantitative variables, such as age and costs, in the form of Mean±SD, and qualitative variables, in the form of percentage and frequency, were presented and compared. The final result of the costs was in the form of average direct costs in coronary artery surgery, angioplasty, and drug therapy were extracted and reported using SPSS software. The considered complications are the occurrence of death, heart attack, and stroke as safety outcome (SO) and performing revascularization (angioplasty or coronary bypass operation) and disease progression confirmed by re-angiography as effectiveness outcome (EO).

Results: Out of 1815 patients studied, 790 patients (43.5%) experienced at least one of the following outcomes, 101 deaths (5.6%), 170 heart attacks (9.4%), 38 strokes (2.1%), 201 angioplasty (11%), 116 cases of coronary artery bypass grafting (6.4%), and 164 cases of new coronary artery involvement (9%). The frequencies of complications in the treatment subgroups were as follows: in the medical therapy group, 101 deaths (12.5%), 140 cases of SO (17.3%), and 223 cases of EO (27.7%); in the angioplasty group, 97 deaths (15%), 92 cases of SO (14.3%), and 167 cases of EO (25.9%), and in the surgical group, 38 cases of death (10.4%), 77 cases of SO (21%), and 91 cases of EO (24.9%). The probability of medical therapy for angioplasty and surgery during 8 years was 10.2% and 9.8%, respectively. Also, the probability of angioplasty for re-angioplasty and surgery was 12.3%

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and 4.3%, respectively, and the probability of surgery for re-angioplasty and surgery was 10.9% and 2.5%, respectively. The average cost of direct treatment (hospitalization) in the group of percutaneous coronary intervention was 148 million rials; in the group of the coronary artery bypass graft, it was 215 million rials, and in the group of medical therapy, it was 42 million rials.

Conclusion: Patients with coronary artery disease have a more than 43% chance of developing cardiovascular complications within 8 years after diagnosis. Patients treated with angioplasty had fewer complications. Also, surgical treatment costs are higher than the other two treatments. Cardiovascular diseases are a group of diseases with high costs and heavy economic burdens on society and the family. Health policymakers can limit the costs and outcomes of the disease by using resources efficiently and effectively by expanding screening and self-care programs.

1. Introduction

Cardiovascular diseases are the main cause of death and expensive healthcare costs [1, 2]. The prevalence and mortality rate of cardiovascular diseases varies from region to region, caused by several factors, such as lifestyle, eating habits, and access to medical care [3]. Furthermore, considering the high prevalence of this disease among adults aged 35 to 64 years who are in productive age, it is natural that in such a situation, the costs of this disease for countries will multiply [4].

Cardiovascular disease was the critical cause of death in Asia in 2019, with 10.8 million deaths, which accounted for almost 35% of all deaths in Asia. Nearly 40% of cardiac deaths occurred early (age less than 70 years). The early death in Asia was higher than in America (23%) and Europe (22%). From 1990 to 2019, the number of cardiovascular deaths in Asia increased from 5.6 million to 10.8 million, and the share of cardiac deaths in all deaths increased from 23% to 35%. The prevalence of cardiovascular diseases has almost doubled from 271 million in 1990 to 523 million in 2019, as well as deaths due to cardiovascular diseases have reached from 12.1 million in 1990 to 18.6 million in 2019 [5].

According to the global burden of disease report in 2010 and 2015, cardiovascular diseases were the 1st cause of death and DALYs (The disability-adjusted life year) in the world, which was the cause of 46% of all deaths and 20%-23% of disease burden in Iran [6, 7]. According to the global burden of disease report in 2015, Iran is one of the countries with the highest rate of this disease, with more than 9000 cases of cardiovascular disease per 100000 people [7].

Cardiovascular diseases cause huge costs for society, patients, and their families. To examine the costs of cardiovascular diseases, the time, and different geographical areas of the occurrence of the disease in terms of incidence and prevalence and the effectiveness of interventions should be considered. We should also note that the costs imposed on patients, families, and society are not limited to the bills paid (direct costs), and indirect costs, especially chronic and debilitating diseases, should be considered [8, 9]. In the United States, the costs of cardiovascular diseases were around 329.9 billion dollars, and it is estimated to reach 1.1 trillion dollars by 2035 [10]. Also, in Iran, cardiovascular diseases imposed a significant economic burden of about 17000 billion rials on the Iranian economic system in 2018 [11].

The population suffering from cardiovascular diseases continues to increase, and the improvement of treatment methods and related services leads to increased current treatment costs and follow-up of treatment complications and outcomes. Therefore, this study aims to investigate the outcomes and determine the direct costs of revascularization interventions (angioplasty and surgery) and drug therapy in cardiovascular patients.

2. Material and Methods

The current research is a descriptive applied type, and the information on the outcomes of this disease in a period of 8 years in 1815 hospitalized patients who received 3 coronary artery bypass surgery interventions, angioplasty intervention, and drug therapy, and the cost information related to 2019 was collected via invoices and were investigated. An information collection form was used to collect the cost and clinical information of the interventions in this research using the opinion of clinical experts. The cost, demographic, and clinical information of the disease were obtained via the study of patients' files and interviews with the patient and his companions. The form of information collection included two parts, the 1st part was related to the demographic and clinical information of the patient, and the 2nd part was related to the information concerning direct medical expenses, such as the cost of doctor's visits, the cost of cardiac

Table 1. Demographic and clinical characteristics of patients (1815 people)

Characteristics	No/Mean±SD/No. (%)		
	Angioplasty	Surgery	Drug Therapy
Number of patients	644	366	805
Age (y)	63±5.8	65±8.4	66±8.6
Male	457(71)	286(78)	507(63)
Smoking	181(28)	93(25.5)	213(26.5)
Normal weight	129(20)	92(25)	250(31)
Overweight	265(41.2)	183(50.5)	317(39.4)
Obese	250(38.8)	91(24.5)	238(29.6)
High blood pressure	271(42)	165(45)	387(48)
Fat	355(55)	209(57)	427(53)
Diabetes	200(31)	125(34)	258(32)

drugs, hospitalization and re-hospitalization costs, diagnostic measures and paraclinical.

Quantitative variables (age and costs) were presented and compared in Mean±SD, and qualitative variables were presented and compared in percentage and frequency. Also, the final result of the costs was extracted and reported in the form of average direct costs in coronary artery surgery, angioplasty, and drug therapy using SPSS software. The intended complications are the occurrence of death, heart attack, and stroke as safety outcome (SO) and performing revascularization (angioplasty or coronary bypass operation) and disease progression confirmed by re-angiography as effectiveness outcome (EO).

3. Results

Of 1815 patients studied, 644 were in the angioplasty intervention group, 366 in the coronary bypass surgery group, and 805 in the drug therapy group. The average age of patients in the percutaneous vascular intervention group was 63 years, in the coronary artery bypass graft-

Table 2. Average services used by patients in therapeutic interventions during one year

Service Type	Angioplasty	Surgery	Drug Therapy
Number of visits	5	5.9	4
Number of emergency clinics	1	1	0.7
Number of radiology	1	1	0
Number of dressings	0.2	1	0
Number of ECG	1	1	1
Number of arrhythmia clinics	0.04	0.5	0.05
Number of echoes	0.4	0.5	0.05
Number of tests	2.5	2.5	2
Number of rehabilitation	0.6	6	0

Abbreviation: ECG: electrocardiogram.

Table 3. Average consumption of drugs in three interventions (number)

Medication	Drug Therapy	Surgery	Angioplasty
Aspirin	88	89	99
Statin	97	89	96
Pantoprazole	78	82	88
Nitroglycerin	58	56	54
Beta-blockers	62	56	48
Furosemide	43	59	28
Clopidogrel	54	44	98
ACE inhibitors/ARB	58	64	92

Abbreviations: ACE: Angiotensin-converting enzyme; ARB: Angiotensin receptor blockers.

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ing was 65 years, and in the drug therapy was 66 years. Also, regarding the gender of the patients, in the percutaneous vascular intervention group, 78% were men; in the coronary artery bypass graft group, 78% were men, and in the drug therapy group, 63% were men (Table 1).`

According to Table 1, nearly 26.7% of all patients were smokers, and the highest percentage of smokers was observed in the angioplasty intervention. A higher percentage of patients in the drug intervention had a normal weight, while in the surgical intervention, a higher percentage were overweight. Also, the highest percentage of obese people was observed in the angioplasty intervention. Moreover, on average, 45% of all patients had high blood pressure. While on average, 55% and 32% of patients had obesity and diabetes.

Table 4. Average direct cost of treatment (hospitalization) of therapeutic interventions

Interventions	Mean±SD		
	Angioplasty	Surgery	Drug Therapy
Angioplasty-surgeon's right	24942400±3150121	38080000±1987100	---
Anesthesia	---	11237610±1490124	---
Operating room-cath lab	8101373±935876	7982612±682743	2139400±140212
Medicine ward-operating room–cath lab	7175000±947145	14332933±1992527	3551684±1212101
Ward supplies-operating room–cath lab	51201161±7607849	45342459±4838982	9142660±821773
Nursing services	1068281±813090	3 322578±467120	1060888±830338
Angiography	10362108±1663796	10222617±1530400	9833807±629256
Sonography	----	1991511±194125	---
Radiology	---	828142±92145	---
Laboratory	2278610±956122	9801732±950571	2178610±189249
Hoteling	17703335±2100124	51321522±4129872	11794000±1647489
Other costs	25101209±3201459	20135405±2874125	2235959±396492
Total amount	147933477±21375582	214599121±21229834	41937008±5866910

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Table 5. The average share of patient and insurance payments by different strategies (figures in rials)

Payments	Angioplasty		Surgery		Drug Therapy	
Supplementary insurance	No	Yes	No	Yes	No	Yes
The average share of basic insurance	125800000	125800000	154000000	154000000	37800000	37800000
Average supplemental insurance contribution	0	21 500000	0	80000 000	0	3800000
Average patient share	22200000	700000	36000000	4000000	4200000	400000
Average total amount	148000000	148000000	190000 000	238000000	42000000	42000000

Services used by patients according to the examination of patients' files and follow-up of patients were determined on average in one year, including the number of visits (including internal and surgical visits, risk factors, and intervention), number of emergency clinics, number of radiology, number of dressings, number of bandages heart, the number of arrhythmia clinics, the number of echoes, the number of tests, the number of rehabilitation. As it is clear from Table 2, the average number of visits for patients in the angioplasty intervention group is 5 times, coronary artery bypass grafting (surgery) is 5.9 times, and drug therapy intervention is 4 times, and the patients in all three groups have visited an average of 5 times in one year. Furthermore, the number of dressings and the number of rehabilitations in surgical intervention is more than the other two interventions. Moreover, each patient had 2 tests in all three therapeutic interventions.

As seen in Table 3, aspirin and statins were mostly used in all treatment interventions, and these drugs were mostly used in the angioplasty intervention. Clopidogrel (Plavix) and angiotensin-converting enzyme (ACE) inhibitors were the most used in the angioplasty group, which could be due to the better efficiency and effectiveness of these drugs. Furosemide drug was used in coronary artery bypass graft (CABG) intervention more than the other two interventions, which may be the reason for reducing the volume of fluids and the blood returned to

Table 6. The frequency of cardiovascular events in 1815 patients in the study by treatment methods

Events	No. (%)			
	Total Patients (n=1815)	Surgery (n=366)	Angioplasty (n=644)	Drug Therapy (n=805)
No event	1025(56.5)	198(54.1)	385(59.8)	442(55)
All-cause mortality	236(13)	38(10.4)	97(15)	101(12.5)
1st event	790(43.5)	168(45.9)	259(40.2)	363(45)
Cardiac death	101(56)	21(5.7)	22(3.4)	58(7.2)
Nonfatal MI	170(9.4)	48(13.1)	58(9)	64(7.9)
PCI	201(11)	40(10.9)	79(12.3)	82(10.2)
CABG	116(6.4)	9(2.5)	28(4.3)	79(9.8)
Stroke	38(2.1)	8(2.2)	12(1.9)	18(2.2)
New coronary involvement	164(9)	42(11.5)	60(9.3)	62(7.7)
Safety outcome	309(17.1)	77(21)	92(14.3)	140(17.3)
Effectiveness outcome	481(26.4)	91(24.9)	167(25.9)	223(27.7)

Abbreviations: PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; MT: myocardial infarction.

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the heart. Also, due to the high price and importation of the medicine, the highest drug cost was observed in angioplasty intervention.

According to the results, the average direct cost of treatment (hospitalization), which was extracted from the hospital bill, was about 148 million rials in angioplasty intervention. The highest cost was related to the cost of the ward and operating room supplies, which is due to the type of operation and the use of stents. Also, the average direct treatment cost of the surgical intervention was about 215 million rials; the highest cost was related to the hotel cost, one of the reasons for the longer length of stay of this intervention in the patients (the average length of stay was 13.5 days in the CABG group, 5 days in percutaneous coronary intervention [PCI] group, and 3.5 days in medical therapy [MT] group). The average direct treatment cost in the drug treatment intervention was about 42 million Rials, and the highest cost in this intervention was the cost of hoteling. One of the reasons is the condition of the patients who are only under observation in the hospital (Table 4).

As shown in Table 5, in angioplasty intervention, the average share of the basic insurance is the same for all people (with or without supplemental insurance), and the basic insurance pays about 85% of the costs. Furthermore, if the patient does not have supplemental insurance, he will pay about 15% of the expenses, and if the patient has supplementary insurance, about 0.5% of the expenses and the rest of the expenses will be paid by the supplemental insurance. In surgical intervention, the average share of basic insurance is about 154 million rials, about 81% of the total costs in patients without supplemental insurance. Moreover, the remaining 19% is paid by the patient. If the patient has supplemental insurance, the average share of the basic insurance is 65%, the supplemental insurance pays 33.5%, and the patient pays about 1.5%. In drug treatment intervention, the average share of basic insurance is about 37 million rials. In this intervention, if the patient does not have supplemental insurance, the basic insurance pays about 90%, and the patient pays about 10% of the costs. Moreover, if he has supplemental insurance, the basic insurance pay about 90%, the supplemental insurance about 9%, and the patient pays 1% of the costs.

Out of 1815 patients who were included in the study, 805 patients received drug treatment (44.4%), 644(35.5%) were treated by the angioplasty method, and 366(20.1%) were treated by coronary artery bypass surgery. By the end of the study, 790 patients had experienced at least one major cardiovascular complication. Table 6 lists the cumulative incidence of the 1st event of the outcome by separating the treatment groups. A total of 236 patients (13%) died, and death occurred as the 1st cardiac event in 101 patients (5.6%). The overall frequency of complications in patients who were treated with the angioplasty method was less compared to the other two groups. Although repeated angioplasty as the 1st event was seen more in the angioplasty group than surgery, this group had the least frequency of cardiac death and stroke. The groups treated with surgery and drug therapy at the time of diagnosis had the highest incidence of complications. Out of 1815 patients who received all three treatments, 201 patients (11%) underwent angioplasty, and 116(6.4%) received surgical treatment again during the 8 years. Out of 805 patients who received drug treatment, 82 patients (10.2%) underwent angioplasty during this period, and 79 patients (9.8%) underwent surgery. Out of 644 patients who were treated with angioplasty, 79 patients (12.3%) underwent re-angioplasty, and 28(4.3%) received surgical treatment. Out of 366 patients who underwent surgery, 40(10.9%) received angioplasty treatment, and 9(2.5%) received re-surgical treatment.

Three complications of death, heart attack, and stroke as SO were observed in 309 patients (17%), and three surgical incidents, angioplasty, and new coronary artery stenosis as EO were observed in 481 patients (26.4%). The lowest SO occurred in the angioplasty group (14.3%), and the EO was not significantly different between all three treatment groups

4. Discussion

The increase in the number of heart patients and, as a result, pressure on the health budget has led to a shift in focus from clinical evaluation alone to evaluating both aspects of clinical effectiveness and cost. Currently, this study is the 1st analysis of the costs and outcomes of cardiac patients (complications, revascularization, etc.) in three angioplasty interventions, surgery, and drug therapy in Iran. The study findings seem necessary for the understanding and awareness of the cost and clinical differences of interventions in cardiovascular patients. The main findings are as follows.

First, the rate of complications of angioplasty intervention was less than the other two interventions. Also, most complications during the follow-up period were related to surgical intervention. In terms of reducing complications, the effectiveness of the angioplasty intervention is more than the other two interventions. Also, death caused by any reason in the angioplasty intervention was more frequent than in the other two interventions.

In comparison, cardiac death in the angioplasty intervention was less than in the other two interventions, which means that the angioplasty intervention is more effective in reducing cardiac death than the other two interventions. Second, revascularization was significantly more in drug therapy intervention than surgical intervention and angioplasty during the follow-up period, and about 20% of people who received drug therapy intervention received angioplasty intervention (10.2%) and surgical intervention (9.8%). Third, SO in the angioplasty intervention showed the least amount and EO in all three interventions showed the same results. Fourth, the cost of hospitalization in the surgical intervention was higher than the other two interventions, and the patient paid the average surgical intervention.

The outcomes of treatment strategies in cardiovascular diseases have been widely discussed in various studies, including randomized controlled trials [12-14], registries [15], and pooled or meta-analyses [16-18]. In most studies, CABG was preferred over PCI in terms of revascularization in the long term, but no significant difference was observed between these interventions regarding death, stroke, or MI. Our study showed that in the long-term period, CABG has priority over PCI and drug therapy in terms of revascularization, and no difference was observed between all three interventions in terms of stroke. However, in terms of cardiac death, PCI has priority, and in terms of MI, drug therapy has less priority; considering that the samples of this research were from the group of occlusion of one vessel, two, and three vessels, it can be a factor for this difference. Also, death due to any cause was more in angioplasty intervention, which considering the high risk of surgery for patients who had several serious diseases at the same time, they may have to perform angioplasty despite the need for surgery; therefore, it is not far from expected that patients undergoing angioplasty are more likely to suffer from multiple chronic diseases.

Although revascularization is recommended for most cardiovascular patients to reduce cardiac death compared to drug therapy [19-21], about 44% of the patients in the present study received only drug therapy. In the 8-year follow-up period, less MI and more cardiac death, and revascularization were observed in the patients in the drug therapy intervention compared to the angioplasty and surgery interventions. In a study on 39131 patients with persistent cardiac ischemia over 2.5 years, Wijsandra et al. compared three interventions of drug therapy, surgery, and angioplasty and concluded that revascularization interventions (surgery and angioplasty) have less death and revascularization than drug therapy [22]. Brandau et al. conducted a study titled comparing the cost-effectiveness of surgery, angioplasty, and drug therapy in cardiovascular disease during a 5-year follow-up period and concluded that the rate of cardiac death in PCI is lower than in CABG, and this rate in PCI and CABG is lower than that in MT [23]. Ladwink et al. concluded that people treated with PCI intervention had a lower death rate than those treated with MT [24]. The results of these two studies in the field of comparing revascularization interventions with drug therapy are consistent with the findings of the present study. A meta-analysis of 28 clinical trials by Jeremias et al. showed that CABG and PCI interventions significantly reduce mortality in patients with coronary artery disease [25].

Several randomized controlled trial studies and meta-analyses in patients with stable coronary artery disease with multivessel occlusion showed that surgery was better than angioplasty and drug therapy in revascularization [26-28]. Katalin et al., during 5 years in advanced vascular disease, showed that revascularization was significantly higher in angioplasty than in surgery [29]. This research showed that revascularization in surgery was less than the other two interventions.

A meta-analysis study by Elm et al. showed that surgery compared to angioplasty, had a higher rate of stroke in patients over 70 years old [30]. However, in the present study, the number of strokes in three interventions did not significantly differ. These findings may be due to the characteristics of the patients, which include people of different ages with fewer problems, such as diabetes and coronary artery disease.

The medicine, angioplasty, or surgery study (MASS) II trial is a randomized study that showed the advantage of PCI and CABG over MT in 10 years [26]. Our study showed that cardiovascular patients who received only MT had more revascularization and cardiac death than surgery and angioplasty, and revascularization (surgery and angioplasty) is an optimal strategy compared to medication.

Several meta-analysis and cost-effectiveness studies conducted in one-year and multi-year periods showed that the cost of revascularization interventions (angioplasty and surgery) is higher than drug therapy. Also, the cost of surgery is more than angioplasty [21, 31, 33], which can be due to the length of hospitalization, and the number and type of items received in the surgery, which is consistent with the results of the present study. Therefore, it is suggested that cardiologists adopt the appropriate strategy by considering the clinical conditions and the outcomes and cost of these interventions.

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5. Conclusion

The increase in the number of cardiac patients and, as a result, pressure on the health budget has led to a shift in focus from clinical evaluation alone to evaluating both aspects of clinical effectiveness and cost analysis. Economic analysis provides a framework for the use of clinical evidence and documentation that, in an organized way, all options affecting health and healthcare costs are included in this framework. The present study is the 1st study in Iran regarding the analysis of clinical outcomes and costs of revascularization interventions compared to drug therapy in patients with coronary artery disease. The present study showed that in the index of death and revascularization, revascularization interventions are more effective than drug therapy interventions in patients with cardiovascular disease. Therefore, it is suggested that the managers and policymakers of the health system and cardiologists consider the clinical conditions and age of the patients, as well as the human capital approach and increasing the productivity of the health system, reducing costs and optimal allocation of resources, choose appropriate interventions to treat this group of patients.

Ethical Considerations

Compliance with ethical guidelines

This article is part of the project with the ethical code IR.IUMS.REC.1398.115.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors of the article declared no conflict in this study.

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