Original Article

Cost-Utility Analysis of Rosuvastatin (20 mg) to Prevent Cardiovascular Diseases in Iran

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Abstract

Background: Cardiovascular diseases are a main cause of disease burden in developing and developed countries. This study aimed to evaluate the cost-utility of rosuvastatin 20 mg in contrast with no intervention for the prevention of cardiovascular disease in Iran.

Materials and Methods: The costs and utility of rosuvastatin 20 mg were compared to nonintervention in patients with cardiovascular disease for the whole lifetime horizon in this study using the Markov model. Cost and utility data were taken from literature. After estimating the incremental cost-effectiveness ratio, a sensitivity analysis was performed using TreeAge Pro 2011 software to cope with uncertainty.

Results: Based on finding, the expected cost and quality-adjusted life years (QALYs) of using rosuvastatin 20 mg were $300 and 12, and the values for no intervention were $56 and $10, respectively. Given the threshold of $20800, using rosuvastatin 20 mg was cost-effective compared to no intervention and the incremental cost was $122 per QALY. The results showed that the highest costs were related to admission to the coronary care unit (CCU) ward. Moreover, among the costs of paraclinical services, the highest were those of echocardiography. Furthermore, Troponin accounted for most of the cost of laboratory tests.

Conclusion: It is recommended that policymakers consider using rosuvastatin 20 mg by cardiologists while designing clinical guidelines for the diagnosis of patients with cardiovascular diseases. Because of the high cost of cardiovascular diseases in Iran, it is suggested that policymakers should consider cost control strategies to impose lower costs on patients.

Keywords: Cardiovascular diseases, cost-utility, quality-adjusted life years (Qalys), rosuvastatin

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Introduction

Today, cardiovascular diseases are one of the main causes of disability and death in the world. Estimates of the leading causes of death worldwide show that 61% of deaths are due to chronic diseases and 30% are due to cardiovascular diseases. Also, 48% of the burden of diseases is caused by chronic diseases, 10% of which are due to cardiovascular diseases.[1] The cardiovascular disease burden ratio is about 10% of the total burden of diseases and is the third leading cause of the burden of illnesses after accidents and mental illnesses in Iran. About 80% of the burden of cardiovascular disease is because of ischemic heart and cardiovascular diseases.[2]

Preventing cardiovascular diseases is practiced at different levels. Preventive interventions and activities lead to a 20–30% reduction in the incidence of cardiovascular disease, stroke,

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mortality, and an increase in life quality. Besides preventive interventions, drug interventions can be used to reduce cardiovascular disease complications as well. Statins are one of the most important medical interventions for the prevention of cardiovascular diseases. Statins are a group of drugs that are most prescribed today to lower blood cholesterol. Statins block the liver's production of cholesterol, so the liver cells are emptied of cholesterol, ultimately causing the liver to remove and collect cholesterol from the blood. Statins also help to reabsorb cholesterol from the deposits in the artery wall, thereby eliminating coronary artery disease. Therefore, statins are a group of blood cholesterol-lowering drugs that are usually used to prevent cardiovascular diseases caused by blood lipids. These drugs block the cholesterol production pathway by inhibiting the enzyme (HMG-CoA reductase). There are many drugs from the statin family in the world pharmaceutical market, the most common of which are atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin.[3-5]

One of the newest drugs in the family of statins, which is undoubtedly the most widely used, is rosuvastatin. It was first introduced in England in 2003 and entered the world market in a few years and has gained the status of the best-selling antihypertensive drug for several years, which has maintained its status to date. Rosuvastatin is the only drug authorized by the US Food and Drug Administration for early prevention of cardiovascular events.[6-10]

Due to the fact that this medicine is produced domestically, economic evaluation studies about this medicine have not been done yet. The purpose of this study was to investigate the cost-consumption of rosuvastatin 20 mg for the prevention of cardiovascular diseases using the Markov model in Iran.

It should be noted that despite the production of this drug domestically, no economic studies have been conducted on the cost-utility and cost-effectiveness of this drug domestically. The purpose of this study was to evaluate the cost-utility of rosuvastatin 20 mg for the prevention of cardiovascular disease using the Markov model in Iran.

Materials and Methods

This study was part of a full economic evaluation and utility-cost analysis study. The purpose of this research was to investigate the cost-effectiveness of rosuvastatin 20 mg for the prevention of cardiovascular diseases in Iran using the cohort Markov model. In our study, rosuvastatin 20 mg was used; based on an internal study (reference below), high-dose rosuvastatin significantly increased HDL levels, was effective in improving lipid profile, and was also able to reduce inflammatory responses.[11]

The population was 10,000 hypothetical cohorts of individuals over 45 years of age distributed among Markov states over a one-year cycle according to the probability of transmission (patients passing through different Markov states). These states were complete health status, first-year myocardial infarction, and myocardial infarction after the first year, death because of myocardial infarction, and death because of other factors. This model is plotted in Figure 1. According to this model, people with full health status may remain in good health, have a heart attack, and die of a heart attack or because of other factors. Furthermore, the patients with a heart attack may experience new heart attacks as well, die from a heart attack, or die from other causes. It should be noted that the competing option in the present study is nonintervention and the effectiveness index in this study is quality-adjusted life year (QALY), estimated from the utility value of each Markov state taken from other literatures. The time horizon of the study was the life time. According to domestic studies, 7.2% and 3% discount rates were applied for costs and QALY, respectively.[12] The data needed for the study were cost, utility, relative risk, probability of transmission, mortality because of heart disease, and mortality rates because of other causes. Direct medical costs such as drug costs, laboratory tests, doctors' visit costs, hospitalization costs, and the cost of paraclinical services, which were extracted using an internal study,[13] were entered into the Markov model. Because of the lack of domestic studies regarding the likelihood of transmission, utility, and relative risk, data on these variables were extracted from external studies and data on specific heart disease mortality rates because of other causes of studies were extracted from internal epidemiology. After drawing the Markov model in TreeAge Pro 2011 software, the incremental cost-effectiveness ratio is obtained by dividing the cost difference by the effectiveness difference. The sensitivity analysis was a one-way deterministic sensitivity analysis, and probabilistic sensitivity analysis was performed to increase the accuracy of the results.

Results

The following table shows the results of the relative risk of using rosuvastatin. According to the results of this study, the relative risk of nonfatal stroke is 0.65 and 0.74, respectively. Table 1 (supplementary file) shows the transition probabilities

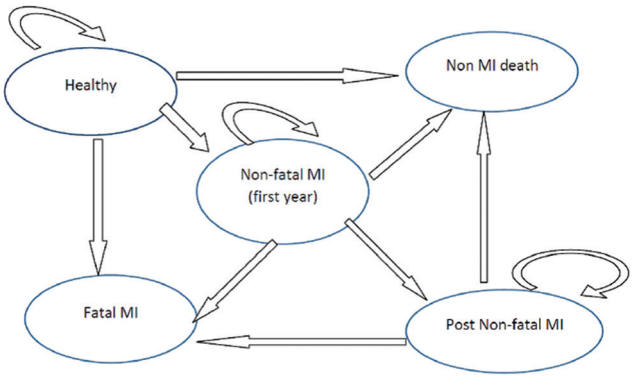

Figure 1(Markov model): Schematic diagram of Markov model. In this diagram, ovals represent health states; arrows represent all possible transitions between health states. During each month, patients stay in the current health state without hospitalization or are readmitted and move to the next state

in the Markov model [Table 1]. These are complete health status, first-year myocardial infarction, and myocardial infarction after the first year, death because of myocardial infarction, and death because of other factors. According to the above table, people with complete health status may remain in good health, have a heart attack, die of a heart attack, or die because of other factors. Patients with a heart attack may experience new heart attacks as well, die from a heart attack, or die from other causes. The probabilities of transitioning from post- myocardial infarction (MI) to other health conditions are similar to nonfatal MI. The results from the above table show that most of the cost items are the cost of admission to the CCU ward. Moreover, most of the cost items in paraclinical services are echocardiographic costs. Troponin also costs the most for laboratory tests. Furthermore, the drug Streptokinase is the most expensive drug. The cost-utility results of rosuvastatin 20 mg versus nonintervention are shown in the table below. In the above figure, the cost-effectiveness graph of rosuvastatin 20 mg versus nonintervention shows the horizontal axis of effectiveness (QALY index) and the vertical axis of cost. According to this figure, 20 mg rosuvastatin increased cost and efficacy compared to nonintervention [Table 1].

Table 2 as well as Figure 2 results shows that using rosuvastatin increased cost by $ 244 and increased QALYs by two QALY. In order to make the decision, one must first calculate the incremental cost-effectiveness ratio (ICER) and then compare it with the threshold. The results of this section are presented below.

$$ICER = \frac{\Delta C}{\Delta E}$$

$$ICER = \frac{300 - 56}{12 - 10} = 122$$

WHO method was used to calculate the threshold, so that if ICER is less than three times the GDP per capita (USD20800),[14] the program is cost-effective. As the ICER value is less than the threshold level, rosuvastatin 20 mg is more cost-effective than nonintervention.

Sensitivity analysis

To cope with uncertainty, deterministic and probabilistic sensitivity analysis has been used.[15] Sensitivity analysis assists in identifying which parameters are the main determinants of the results of an economic evaluation and, in fact, determines the strength of the results of the economic evaluation.[16,17] In one-way sensitivity analysis, the value of each variable was increased by 20% and the Tornado diagram was drawn. Based on the Tornado diagram [Figure 2], the results are most sensitive to the increase in QALY in no intervention arm. Figure 2 shows the results of the probabilistic sensitivity analysis. The horizontal axis is incremental QALY, and the vertical axis is incremental cost. The chart is plotted using Monte Carlo simulation for a sample of 1000 with the Gamma distribution for cost and Beta distribution for utility. The results showed that rosuvastatin was more cost-effective than no intervention with a maximum willingness to pay threshold of USD20800 estimated based on the WHO approach (three times of per capita GDP, USD20800).

Figure 3 indicates the cost-effectiveness acceptability curve. The curve showed that rosuvastatin versus no action was more cost-effective at the majority of willingness-to-pay thresholds. Rosuvastatin has a 62% probability of being cost-effective compared with no intervention with thresholds higher than USD20800 [Figure 3].

Table 1: The cost components of rosuvastatin (13)

Cost items	Cost (dollars)	Cost items	Cost (dollars)	Cost items	Cost (dollars)	Cost items	Cost (dollars)
Cost of admission to CCU	78	Fitness test	19	BS	0.45	CPK	2.49
Cost of admission to General Care Unit	61	The cost of laboratory tests		TG	0.71	SGOT	0.63
Cost of a consultation visit	3	CBC Dif.	0.74	Cholesterol	0.52	SGPT	0.63
The cost of a GP visit	3	BUN	0.41	PTINR	0.93	ESR	0.26
Cost of paraclinical services		Cr	0.52	PTT	0.93		
Electrocardiogram	3	Na	0.59	Troponin	2.45		
Eco cardiography	36	K		LDH	1.86		

Cost (dollars)	Pharmaceutical items	Cost (dollars)	Pharmaceutical items	Cost (dollars)	Pharmaceutical items
0.01	Captopril	3.72	Enoxaparin	0.148	Rosuvastatin 20 mg
9.29	Streptokinase	0.03	Atorvastatin10	0.01	ASA
0.2	Cost of prescription medication	0.02	Ranitidine	0.29	Clopidogrel
		0.01	Oxazepam	0.01	Metoprolol

Table 2: Cost-utility analysis of rosuvastatin 20 mg versus nonintervention

Items compared	Cost	QALY	Cost difference	QALY difference	Incremental cost per QALY Gained
Rosuvastatin 20 mg	$300	12	$244	2	$122
No intervention	$56	10			

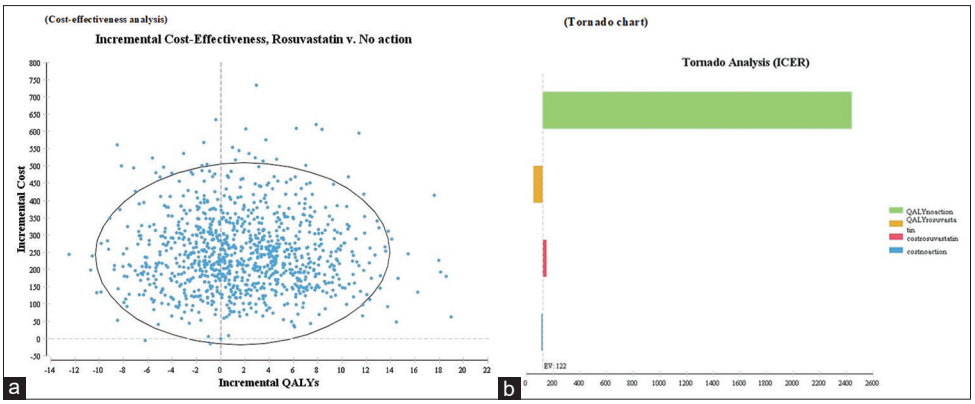

Figure 2: Sensitivity analysis probabilistic sensitivity (a). Tornado chart (b) of 20 mg rosuvastatin compared to no intervention. (a) The results of the probabilistic sensitivity analysis. Each point indicates the differences in the costs and effectiveness of rosuvastatin vs. noninterventional methods assessment. The results showed that rosuvastatin was more cost-effective than noninterventional methods assessment with a maximum willingness to pay threshold of USD20800. (b) Tornado diagram for one-way sensitivity analysis. The diagram indicated the results of one-way sensitivity analysis. The value of each variable was increased and decreased by 20% and the results are shown by the Tornado diagram. The ICER had the highest sensitivities to the increase in the QALY of noninterventional

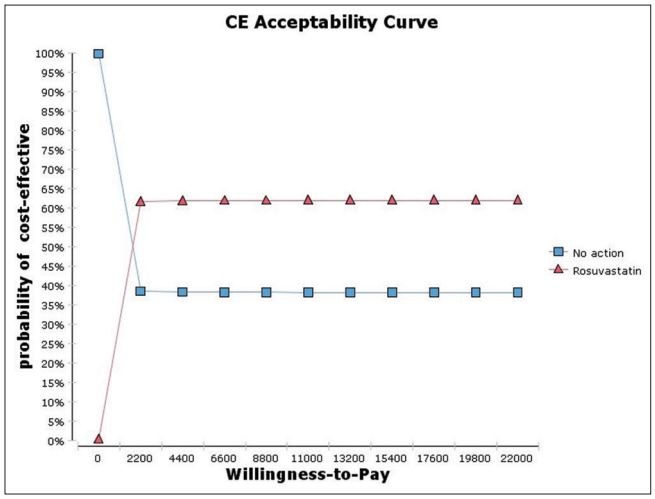

Figure 3: Cost-effectiveness acceptability curve. The curve shows that rosuvastatin compared with noninterventional methods assessment was more cost-effective at the majority of willingness to pay thresholds

Discussion

Understanding the relative benefits and costs of alternative therapies for preventing cardiovascular events in patients is essential to ensure they receive an acceptable level of care while effectively managing healthcare resources.

Economic evaluation studies have a significant role in the optimal allocation of resources and decision-making by policymakers in the health system. The purpose of this study was to evaluate the cost-utility of rosuvastatin 20 mg in preventing cardiovascular diseases in Iran using the Markov model. This study was conducted for the first time in, and its results showed that the use of rosuvastatin 20 mg is cost-effective compared to no intervention. The results of one-way sensitivity analysis and probabilities also confirmed the research results. Also, the results showed that most of the cost items are the cost of hospitalization in the CCU department. In addition, the most expensive items in paraclinical services are related to echocardiography costs, and troponin is the most expensive for laboratory tests. In addition, streptokinase is the most expensive drug.

The results of Palmer *et al*.'s[17] study on the cost-effectiveness of rosuvastatin in England showed that rosuvastatin is cheaper and more effective than fluvastatin. Our results are consistent with those of Palmer *et al*. In a study conducted by Hirsch *et al*.[18] in England, the results showed that rosuvastatin is more cost-effective than similar doses of atorvastatin, pravastatin, and simvastatin. The results of this study were consistent with the results of Hirich *et al*. The results of Costa-Scharplatz *et al*.'s[19] study showed that rosuvastatin is more cost-effective than atorvastatin. In addition, the results of the sensitivity analysis showed that this drug is more likely to be cost-effective than any other statin in a wide range of monetary targets for each unit of clinical effectiveness. The results of this study are in line with the research results of Costa-Scharplatz *et al*. In the current research, sensitivity analysis was performed to evaluate the accuracy of the economic In a study conducted by Barrios *et al*.,[8] the results showed that rosuvastatin is more cost-effective compared to generic atorvastatin (costs are reduced by 30,000 euros per QALY). This drug is useful for the primary prevention of cardiovascular diseases for most subgroups and it was cost-effective in all-male subgroups of this study. Researchers conducted a systematic cost-effectiveness review in the United Kingdom. High-dose statins (atorvastatin 80 mg per day, simvastatin 80 mg per day, and rosuvastatin 40 mg per day) were used to prevent Cardiovascular disease (CV) events in patients with acute coronary syndrome.[20] The efficacy threshold of ≤20,000 per QALY was considered in the UK, and the results showed that rosuvastatin was the optimal treatment based on low-density lipoprotein cholesterol (LDL-C) reduction, and it was hypothesized that incremental LDL-C reduction with

rosuvastatin would lead to a corresponding reduction in CV events.

In another study, British researchers analyzed data from three clinical trials and assessed the cost-effectiveness of rosuvastatin (10 mg/day) versus atorvastatin (10 mg/day) in terms of percent reduction and achievement of LDL-C. C was assessed at 12 weeks. The results of this research showed that rosuvastatin is more effective than atorvastatin and lowers LDL-C more.[21] In terms of cost, the average costs of both drugs were almost the same.

The findings of this research are consistent with the findings reported in other studies.[22-27] In all studies, rosuvastatin was a dominant or cost-effective choice under various assumptions about drug dose, analysis perspective, and study population characteristics. From an economic perspective, since rosuvastatin has a higher capacity to lower LDL-C than other statins; it minimizes the frequency of costly events such as stroke.[28]

Therefore, it can be stated that the results of one-way sensitivity analysis show the generalizability of the current study and the cost-effectiveness of rosuvastatin compared to noninterventional methods for the treatment of this disease. Furthermore, the results of the probabilistic sensitivity analysis showed that with a 95% confidence interval, rosuvastatin (20 mg) is the optimal strategy for treatment. The results of the definite and possible sensitivity analysis show the strength of the research results, and its findings can be generalized to the entire country. Considering the generalizability of the results of this study, it can be concluded that the use of rosuvastatin can be prescribed in other Iranian hospitals in the treatment of cardiovascular patients. However, due to the wide coverage of insurers, the ability to pay patients' fees, and the incidence and prevalence of heart diseases in different countries, the results of this study cannot be definitively generalized to other countries.

Conclusion

The results of our study indicated the cost-effectiveness of 20 mg rosuvastatin in contrast with no intervention; it is suggested that policymakers consider using rosuvastatin 20 mg while designing clinical guidelines to diagnose cardiovascular diseases. Additionally, because of the unclear symptoms of cardiovascular diseases in the early stages of the disease, it is suggested that health department managers of medical universities in Iran develop guidelines for identifying and screening risky populations across the country.

Limitation

Few studies have been done on the economic evaluation of drugs used to prevent cardiovascular diseases in developing countries, whereas people with these diseases mostly live in middle- and low-income countries. The present study examined the economic evaluation of 20 mg rosuvastatin compared with nonintervention in Iran for the first time. Most studies in this regard have been designed and implemented in developed and high-income countries, and their use in developing countries is limited.

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Authors' contribution

AR and AJ contributed to conceiving and designing the study. The data were analyzed and interpreted jointly by HT, AJ, and AR. All authors contributed equally in writing the manuscript. All authors reviewed and approved the final manuscript.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Transition probability in Markov model

TP/age	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-100	Referer
MI To MI	0.1280	0.1280	0.1152	0.1152	0.1019	0.1019	0.0874	0.0874	0.0711	[16]
MI To FMI	0.0224	0.0348	0.0348	0.0700	0.0700	0.1054	0.1054	0.1270	0.1270	[34–37]
Post-MI To MI	0.0162	0.0162	0.0179	0.0179	0.0185	0.0185	0.0178	0.0178	0.0160	[16]
Post-MI To FMI	0.0052	0.0052	0.0092	0.0092	0.0152	0.0152	0.0235	0.0235	0.0340	[16, 38]
Non MI death	0.0028	0.0043	0.0056	0.0084	0.0131	0.0213	0.0426	0.0705	0.1143	[39, 40]
Healthy To MI (ICS)	0.0031	0.0031	0.0044	0.0044	0.0094	0.0094	0.0061	0.0061	0.0061	[19]
Healthy To FMI (ICS)	0.0015	0.0015	0.0050	0.0050	0.0082	0.0082	0.0080	0.0080	0.0080	[19]

TP = transition probability, *MI* = non-fatal myocardial infarction in first year, *FMI* = fatal myocardial infarction, *Post-MI* = subsequent years of non-fatal myocardial infarction, *ICS* = Isfahan Cohort Study