Cost-Effectiveness Of Atrial Fibrillation Screening Strategies: A Systematic Review

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Abstract

Objective: This study aims to analyze the cost-effectiveness of atrial fibrillation screening strategies.

Design: Systematic review

Setting: Literature

Patient(s): Patients with atrial fibrillation.

Intervention(s): To find related research and articles in this field, articles published in Iranian and international databases and based on inclusion and exclusion criteria were searched and reviewed. The quality-adjusted life-years (QALYs) were the main outcome used for measuring the effectiveness.

Main Outcome Measure(s): Incremental cost-effectiveness ratios (ICER) per gained or additional QALY, additional case detected, and avoided stroke.

Result(s): Out of 3,360 studies found in the field of the present study, finally, fifteen studies were included in the research. The lowest ICER numerical value was 78.39 for AF screening using ECG for 65-85-year-old Japanese women. The highest value of this index is equal to 70864.31 for performing ECG monitoring for more than 60 days for Canadians over 80 years without AF history who have been referred to outpatient clinics. In two studies, the results were expressed with the Years of life gained (YLG) measure. Of course, in one study, the results were not reported with this measure and in one study, the results were reported with ICER.

Conclusion(s): According to the results of all the studies analyzed, most of the studies acknowledged the cost-effectiveness of different AF screening strategies. However, studies that confirmed the cost-effectiveness of population-based screening were more than studies that confirmed the cost-effectiveness of other screening strategies.

Introduction

AF is the most common cardiac arrhythmia that occurs in more than 10% of patients 75 years and older [1–3]. The incidence and prevalence of AF are increasing worldwide, growing threefold over the past 50 years and becoming the epidemic of cardiovascular disease in the 21st century [1, 4–6]. The prevalence of this complication increases with being more grown, from about 1–5% of the total population of people over 65 years of age [7]. Also, the risk of stroke due to AF decreases from 9.9% in the age range of 70-79 years to 5.23% in the age range of 80-89 years [8]. In Iran, the prevalence of this disease is around 2.8% in people above 50 years, which is somewhat similar to this rate in developed countries [9]. In recent years, AF has become a health and economic issue, with 33 million people worldwide being infected in 2010, and that number is expected to double by 2050 [10].

The cost of treatment of asymptomatic AF and its complications impose a significant economic burden on health care systems [11–14]; so that the cost of treatment of people with AF and its complications is about 2% of total health care costs in high-income countries [15].

The risk of death from this disease has also increased significantly [16]; so that during the last decade, it has reached 1 person for every 3 to 5 people [17]. AF is associated with an increased risk of stroke. However, the disease is often asymptomatic and may not be known before a stroke [18–20]. People with asymptomatic AF may be up to three times more likely to have a stroke before being diagnosed with AF [2]. Early detection and management of AF [1–48] prophylactic treatments such as oral anticoagulants can decrease the risk of stroke; As a result, patient health outcomes (e.g., quality of life and life expectancy) improve [25, 27] and the economic burden on health care providers reduce [30].

Despite all the research efforts in the field of AF, the prevention of this disease and its associated complications remains a challenge [23]; Due to its cost and lack of evidence and more effective than conventional care for AF, international groups continue to oppose the use of systematic population-based screening in asymptomatic patients [26, 34]. Currently, the importance of screening to detect asymptomatic AF has been realized in collaboration with the Medical Association. Opportunistic screening for AF is also recommended by international guidelines. Screening may reduce the risk of death and complications from a stroke, but its widespread implementation is costly. Judging whether spending money for clinical gain is still a matter of debate [22]. In Canada, the results of a study showed AF screening strategies with pulse screening were less expensive and more quality-adjusted life years (QALYs) compared to no screening. Also, screening usage of a blood pressure monitor by AF detection algorithm was superior to the no screening strategy. The incremental cost of QALYs single-lead electrocardiogram (SL-ECG) was C\$ 4788 compared to no screening [45].

In general, two potential population screening strategies include opportunistic case detection and systematic screening. In finding patients' opportunistic cases, a health professional takes the patient's pulse during the consultation. If the pulse is irregular, an ECG is taken from the patient as a confirmatory test; But in systematic screening, the entire target population is called in for ECG testing [19]. Considering the upward trend in the incidence and prevalence of AF in different parts of the world and its significant economic burden at the individual, social and national levels, this study by searching international scientific and specialized databases and also by reviewing articles extracted from these databases, The cost-effectiveness of the AF screening program systematically reviewed and analyzed.

Method

This study aimed to systematically review the cost-effectiveness of screening strategies for patients with AF. To find related research and articles in this field, articles published in Iranian databases including SID, Magiran, Irandoc, ISC, Iranmedix, and also international databases including Web of Science, Medline, Pubmed, Embase, Scopus, National Health Services Evaluation Database, Cochrane of Reviewed Systematic Database: DAHTA-Database Searched and reviewed by using a combination of key and

MeSH Terms: Cost-Effectiveness Analysis (CEA), AF Screening, systematic population screening strategy, targeted screening strategy, and opportunistic screening strategy.

Criteria for study inclusion were as follows:

In this study, studies that examined the cost-effectiveness of screening strategies for patients with AF based on RCTs and decision analysis models on relevant patients were included.

The population in this study includes all patients with AF who have used screening strategies to diagnose the disease early. Intervention includes recurrent ECG recording, continuous Holter ECG, use of manual ECG devices, etc. Comparators are All screening strategies that can be substituted. Furthermore, outcomes are reported based on ICER and costs per natural unit of health measurement. Finally, the setting in this study Includes economic evaluation in a purely cost-effective manner. It is necessary to mention that all selected studies were in English and Persian.

Exclusion criteria:

In this study, articles were excluded that had the following criteria:

- 1- Items such as review articles, abstracts, protocols, letters to the editor, etc.
- 2- Articles whose full text has been published other than in English and Persian.
- 3- Studies for which full text was not available. Google Scholar sites were also used to complete the search.

Also, by referring to the list of included study sources, we tried to include qualified articles that were related to the study. In this study, no sampling and a clinical trial were performed and all published articles related to cost-effectiveness analysis of screening strategies for patients with AF were selected according to the entry and exit of articles. Potential studies and researches eligible for inclusion in this study were retrieved and duplicates were removed using Endnote software. Then screening studies based on title and abstract and based on inclusion and exclusion criteria were evaluated and reviewed by two people, at this stage the principles of PRISMA were followed. The CHEERS checklist was followed to assess the quality of the studies. Moreover, all costs were converted to US \$ based on the purchasing power parity index for 2021 to make cost comparisons easy.

Specifications of data collection tools and how to collect

Relevant data were collected through searches in related databases, and based on the PRISMA statement, including article search and how to report systematically review studies. The quality of the methodology of the studies was evaluated using the CHEERS checklist to assess the methodological quality of the selected studies. [32] The CHEERS checklist consists of 5 questions with 24 criteria that

examine the design of each economic evaluation study. Any disagreement between the two authors was resolved through the involvement of a third author, who acted as the final referee.

The data extraction form includes the title of the article, year of publication, screening strategies used, the population used, effectiveness index, determination of the type of study perspective, type of model used, results related to cost-effectiveness of the methods used, and type of sensitivity analysis method.

Method of data analysis and reporting: After evaluating the quality of articles, the required data will be presented in two parts: The first part includes: characteristics of studies, such as author name, date of publication, country, type of study, currency, sample size, the study is the study population, disease stage, effectiveness index, type of model used and type of sensitivity analysis method and results related to cost-effectiveness.

The second part contains data related to the average cost of the disease since different studies have been done at different times and based on different exchange rates, to increase the comparability of the studies, the following measures were taken: Step 1: Because some studies may not calculate the patient's annual cost per year, the average annual cost per patient was calculated. Step 2: Because different studies have been done at different times, the appropriate time adjustment to adjust the value of money time was done by referring to the World Bank website and using the Consumer Price Index (CPI). In the next step, since the costs of different studies were reported with different currencies, to unify the currencies and compare costs in different countries by referring to the World Bank website and with the help of the purchasing power parity index, we reported expenses.

Findings

Based on the PRISMA diagram in Appendix 1, which shows the process of reviewing and selecting articles, out of 3360 studies found in the field of the present study, 1236 studies were omitted due to duplication between databases and other information sources. Due to the inclusion and exclusion criteria of the research, 2124 studies in the title review, 81 studies in the abstract review, and 56 studies in the full-text review were excluded, and finally, 15 studies were included in the research. The specifications and results of the studies are presented in Annexes 2 and 3. Also, as mentioned, in Appendix 4, the final articles are evaluated based on the CHEERS checklist.

According to the findings in Appendix 2, published studies on the cost-effectiveness of various AF screening methods in Sweden include 3 articles, Germany, the United Kingdom, and Australia each with 2 articles, and finally the Netherlands, USA, Denmark, Japan, Ireland, and Canada, each one included an article. Therefore, most studies in this field have been done in European countries. (Figure 1)

The two articles combine cost-Utility and cost-effectiveness analysis. Other studies have only evaluated the cost-effectiveness of various AF screening strategies. Also, under the principles of AF screening, except for one study in which participants were 50 years of age or older, in other studies, participants were older than 65 years. Based on different AF screening strategies, out of fifteen finalized studies, eight

studies have analyzed the cost-effectiveness of systematic population screening strategy, three articles on targeted screening strategy, and two articles on opportunistic screening strategy. Finally, two studies analyzed all three screening strategies. (Figure 2)

Also, out of the total number of studies found, three studies were from the patient perspective, six studies were from the social perspective, three studies were from the health system perspective, and finally, two studies did not mention the study perspective. (Figure 3)

Eight studies used different types of electrocardiograms (ECGs) including handheld ECG and Holter single-lead ECGs (single-lead ECGs) and 12-lead ECG, ECG between 1 and 12 leads as a screening test for AF. [21, 22, 28, 31, 33, 36, 39, 43] Furthermore, three studies used two pulse palpation methods and one type of ECG as a screening test method [37, 38, 41]. One article also used ECG screening versus no screening [42]. In addition, an article used a method to prevent heart palpitations [30]. In one article, referring to the myocardial infarction risk prediction algorithm, the screening test method was not explicitly mentioned, [30] and in one article, the screening test method for diagnosing AF was not reported [44]. (Figure 4)

The main measure of results of final studies was based on the incremental cost-effectiveness ratios (ICER) per gained or additional QALY, additional case detected, and avoided stroke. The lowest ICER numerical value was 78.39 for AF screening using ECG for 65-85-year-old Japanese women [38]. The highest value of this index is equal to 70864.31 for performing ECG monitoring for more than 60 days for Canadians over 80 years without AF history who have been referred to outpatient clinics [39]. Also, ICER levels have been reported in some studies separately for men and women [31, 38] In two studies, the results were expressed with the Years of life gained (YLG) measure. Of course, in one study, the results were not reported with this measure [28] and in one study, the results were reported with ICER [22].

In 2004, The oldest study in this field was conducted in Japan. The intervention and comparison in this study include annual screening with ECG and pulse touch for arrhythmias detected by ECG and no screening. The final QALYs after discounting 3% in the ECG mode in men and women were 78.39 and 80.37, respectively. In the case of pulse touch, in men and women, it was equal to 102.32 and 71.593, respectively. As a result of this study, annual screening programs by ECG or pulse palpation were described as a simple and cost-effective way to manage AF in the community [38].

Another study was conducted in 2005 in the United Kingdom. In this study, 10,000 people were randomly divided into two categories: systematic screening (5,000 persons) and opportunistic (5,000 persons). ICERs for men and women were \$ 11738.31 and \$ 14672.89 per QALYs, respectively. As a result of this study, opportunistic screening was cost-effective compared to systematic screening [31].

In 2014, a study conducted in Australia examined 1,000 people over 65 age who went to a pharmacy. The cost-effectiveness ratio was reported to be \$ 4677.94 per QALYs and \$ 23812.34 per stroke avoided. The study concluded that ECG screening in pharmacies with an automated algorithm was both feasible and cost-effective [37].

In a study conducted this year in Australian hospitals, 1,000 patients were diagnosed with AF during hospitalization. In this study, the cost was reported to be \$ 338.4 per QALYs. The study concluded that silent AF screening with intermittent ECG recording in patients with recent ischemic stroke was a cost-effective use of health care resources that saves costs and improves the quality of life [36].

In 2014, in a study conducted in Sweden, 1,000 people were screened to identify a patient with unknown AF. In this study, the final cost was \$ 6377.66 and the cost was \$ 46677.94 per QALYs and \$ 23812.34 per prevented stroke [29]. Two years later, in a study conducted in Ireland, the cost-effectiveness ratio was reported to increase by \$ 30,30124.31. The study found that annual screening of people over the age of 65 using opportunistic heart rate during GP consultations is more cost-effective than conventional care [41].

In 2017, in a study conducted in Sweden, the final cost per QALYs was reported at \$ 588.88. As a result of this study, it was stated that repeated screening for AF shows additional health benefits at a reasonable cost compared to one-off screening. [21] In 2018, in a study conducted in the Netherlands, a population of 2919,000 people aged 65 and over in 2014 were surveyed. In this study, the total cost of \$ 1016.64 and the ratio of cost and effectiveness of AF screening in these studies were reported since 448.44 in each additional case identified to 5739.22 per QALYs obtained [33].

In 2019, in a study in the United States, American patients over 75 years of age were screened. In this study, the final cost and ICER with 12-lead ECG were equal to \$ 188484860 and 6129.59, respectively. Furthermore, the final cost and ICER with Z14 were equal to \$ 65.4848194 and 77.49967, respectively [42].

This year, in a study conducted in Denmark, the general population of 65-75-year-olds who were members of the Belgian national campaign were surveyed. In this study, ICER was reported as equal to 3465.71. As a result, it was stated that in a large screening group, the use of a manual ECG device was cost-effective to identify people with newly diagnosed AF and as well, in people aged 65 to 75 years [29].

The following are four studies published in 2020. In a German study, 10,000 people of 75-year-old insured were screened. In this study, the final cost and ICER were \$ 144.39 and 56663.57 per additional QALY, respectively. Modeling in this study showed that by performing systematic AF screening through Preventicus heart rate, health benefits and economic effects were increased [24]. In another study conducted in Germany, 30,000 Female patients for each CHA2DS2-VASc (with congestive heart failure, hypertension, and age 75, as well as with diabetes, stroke, vascular disease aged 65-74 Years) from a score of one to nine, were simulated. As a result of this study, it was stated that the use of mHealth devices for AF screening leads to increased costs and reduced incidence of stroke. The risk of stroke and death from a stroke can be significantly reduced in all individuals, especially patients with high CHA2DS2-VASc scores [28]. In a UK study, targeted screening using risk prediction algorithms resulted in fewer AF patients (61 per 1,000 patients compared with 534 and 687 patients in systematic and opportunistic strategies) and more Patients needed AF (11 per 1,000 patients compared with 6 and 8 cases of AF in systematic and opportunistic screening strategies). In this study, systematic screening and

opportunistic screening ICERs were reported equal to 7098.75 and 8115.55 per QALYS, respectively [30]. In a study in Australia, AF screening was performed in a rural setting for people 65 and older. The AF screening program screened 34% of eligible patients through eHealth and was cost-effective. The rate of oral anticoagulant therapy was relatively high at first and was increasing during the study. Increasing the screening ratio prevented many more strokes with minimal changes in the cost-effectiveness ratio [43]. Finally, in a Canadian study, AF screening was performed in people 80 years of age or younger in outpatient clinics without a history of screening. This study stated that the final cost and ICER in the case of seven days of monitoring were equal to \$ 23,231,981 and 42.666, respectively, in the case of more than 30 days of monitoring were equal to \$ 41,065,06 and 59095.92, and in the case of more than 60 days of monitoring were equal to \$ 645,991,25 and \$ 70,864, respectively [39].

Discussion

This study is the first systematic review study in the last five years that comprehensively evaluates the cost-effectiveness of various AF screening strategies. Out of 15 studies reviewed, eight studies were conducted after 2017, the year in which a similar study was published [48]. Most studies have been conducted in high-income countries (United States, Canada, Japan, the United Kingdom, and Germany). However, studies from middle-income countries (Ireland, Australia, Sweden, Denmark, the Netherlands) were also considered to expand the study and analysis. As noted in the findings, of all the studies found, most studies considered the systematic population screening strategy. Although most studies have considered screening strategies based on designated people to diagnose AF, the NICE guidelines^[1] recommend opportunistic case finding and not screening strategies. Also in this guideline has been emphasized the use of clinical judgments of health care professionals when examining irregular heart rhythms and possible diagnosis of AF and providing standard care. Furthermore, The wearable device is recommended as an effective factor to follow up with a health care professional; However, this issue has been addressed in a study reviewed in this study [29].

Screening test methods for diagnosing AF in this study included a handheld ECG and a 12-lead Holter (single-lead ECG) and an ECG between 1 and 12 leads, a pulse palpitation pulse, and Zenicor EKG and heart rate prevention was Preventicus Heartbeats. Except for one study that combined the two methods of economic evaluation (cost-effectiveness analysis and cost-utility analysis), other studies examined screening strategies of AF only through cost-effectiveness analysis. According to the studies reviewed, various screening methods have been performed mainly on people in the age range of 65 to 75 years. Of course, a number of these studies have been conducted outside this age range, and presenting the results and analyzing them in this age range is more documented and evidence-based. Also, a review of the extracted studies showed that economic evaluation of each of the three AF screening strategies with the comparator of no screening, each of the strategies was cost-effective, which indicates the importance of screening to identify and diagnose people at risk of AF. For example, Mattias Aronsson and et al. examined asymptomatic intermittent screening AF with asymptomatic screening conditions using the analytical decision-making simulation model. In this study, a cost of € 4313 per QALYs and € 6583 per

stroke was prevented and the final cost was reported to be € 5,512. This study has acknowledged that screening for asymptomatic AF in the elderly is cost-effective and that the effectiveness of AF screening, despite its cost, is higher than no screening. [22]

In Mustafa Oguz's study, non-valvular AF (NVAF) screening through single 12-lead ECG and single 12-lead ECG compared with 14-day extensive screening through the hand-held ECG device (Zenikor single-lead ECG, Z14) and also, no screening. ICER in this study reported \$ 58,728 in the 12-lead ECG mode and \$ 47,949 in the Z14. The study also reported that screening the general population at age 75 for NVAF was cost-effective on the threshold of willingness to pay of \$ 100,000 [42].

Also, in two studies, one of the screening strategies as an intervention was compared with the other two strategies as a comparator. In a study by Nathan R. Hill et al., Targeted screening was compared with opportunistic AF screening and population screening strategies. The final QALYs for every 1000 patients diagnosed through targeted screening is 34.71 compared to population screening and 20.95 compared to opportunistic screening, which refers to the cost-effectiveness of the targeted screening strategy. This can be reduced as well as the higher effectiveness of this type of screening strategy due to the diagnosis and diagnosis of AF with a focus on people at higher risk such as patients with heart failure, hypertension, with a history of myocardial infarction MI, diabetes, Hyperthyroidism, etc [30].

In Hobbs et al. 's study, opportunistic screening was compared with systematic screening (targeted and total population screening). In this study, while pointing to the higher prevalence of AF in men and the more predictable prevalence among patients aged 75 years and older, it is stated that the incidence and prevalence of the disease in the control population compared to both populations are a systematic intervention. And the systematic or opportunistic intervention population is higher, which is also logical because the control population includes a group of people with a higher risk of AF and the prevalence rate is higher among such people. In this study, model-based analyzes showed small differences in cost and quality of life with different methods and severity of screening, but opportunistic annual screening resulted in the lowest number of ischemic strokes and the highest incidence of AF [31]. Sensitivity results showed that screening for AF in men and women 65 years of age was about 60% more cost-effective. In the implementation of the opportunistic screening strategy, 243 patients had irregular pulse without an initial diagnosis of AF, and in the ECG examination of 177 patients, 31 new cases were identified, which showed a prevalence of 0.69%. 44 new cases were identified without a screening program. In addition, in the implementation of the systematic screening strategy, by performing ECG on 2357 patients, 52 new cases were identified with an incidence of 1.1% per year. Of these, 31 were diagnosed by targeted screening and another 21 by total population screening. Another 22 cases were diagnosed outside the screening program. Typically, systematic high risk cost 21 21,119 and Systematic population 40 40,882, which is higher than opportunistic screening due to the size of the target community, the way it is run, and the variety of screening programs. Therefore, considering the number of people diagnosed and identified without a screening program, it seems that for economic justification, planning should be done in such a way that all people with AF are identified under a screening program [31].

Limitations:

Despite some measures such as converting different currencies in the articles into a single currency and unifying them to facilitate calculations and validate comparisons between studies, but because of the heterogeneity and differences between the final studies in terms of model structure, different study time intervals, comparative interventions and cases, different screening strategies and tests, and different outcome indicators, etc., cannot provide a comprehensive and conclusive conclusion. In addition, in this systematic review study and based on the designed search approach, only studies published in English and Persian were considered.

[1] [National Institute for Health and Clinical Excellence](#)

Conclusion

According to the results of all the studies analyzed in this study, which are related to high-income and middle-income countries, most of the studies acknowledged the cost-effectiveness of different AF screening strategies. However, studies confirming the cost-effectiveness of population-based screening were more than studies that confirmed the cost-effectiveness of strategies other than population-based screening. In general, this can be attributed to lower costs and higher effectiveness of this type of screening strategy due to earlier detection of AF disease, which in total can reduce direct costs from out-of-pocket and third-party payers and from On the other hand, it leads to an increase in the number of timely diagnoses of patients with AF. In addition, the implementation of AF screening strategies can be a good alternative to clinical delayed assessments and diagnoses and the subsequent expensive diagnostic and treatment methods.

Declarations

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Ethics declarations

The authors declare that due to no containment of clinical studies and patient data in this manuscript, there is no contrast with ethical standards.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Figures

Figure 1

Contribution of each country in the implementation of the study " Cost-Effectiveness Analysis Of Atrial Fibrillation Screening Strategies"

Figure 2

Number of studies evaluating the cost-effectiveness of atrial fibrillation screening according to them different strategies

Figure 3

Number of studies in terms of different perspectives

Figure 4

Number of studies in terms of different screening tools

Supplementary Files

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