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RESEARCH ARTICLE

Secondary Prevention of Cardiovascular Disease in Patients after Myocardial Infarction: Pharmacoepidemiological Study

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Abstract

Diseases of the cardiovascular system are among the main factors of premature death in the 21st century. However, the effectiveness of secondary prevention of coronary heart disease in developed Western countries and CIS countries can vary greatly. The purpose of this study is to evaluate the effectiveness of the application of international recommendations for secondary prevention in Russia in patients after myocardial infarction. The time of the study covers a 9-year period (2010-2019) in Cardiological Dispensary No. 3 of Moscow (Russia). A total of 9000 medical records were processed, of which 900 met the selection criteria. The average age of the patients was 61.5±9.7 years in an age range of 30-89 years. A survey of 606 doctors from private (1 group, 303 doctors) and state (2 groups, 303 doctors) dental clinics was conducted. Results the sample recorded a large scatter of data - from the moment the patient suffered a first heart attack - from a period of less than one year at a minimum to 43 years at a maximum. The average value of the interval was 4.6±5.3 years. Doctors on medical records most often paid attention to measuring blood pressure. 2-10 times less often (p≤0.001) met anthropometric indicators and analyzes for the lipid profile, and an order of magnitude less - control of the level of physical activity (p≤0.001). Differences were found between the therapy of patients depending on the type of medical institution - patients in cardiological dispensaries, on average, are 2-4 times more likely to receive prescription drugs (p≤0.001) compared with patients in polyclinics. It is noted that doctors, as a rule, do not note at the first visit to the patient in the cardiologic dispensary what kind of therapy he underwent in the clinic. It is necessary to promote a healthy lifestyle, with a complete cessation of smoking and the use of alcoholic beverages. This will minimize the cost of expensive drugs for the population. On the patient's medical records: the minimum occurrence rates of the following risk factors were recorded: smoking (3%), as well as physical activity (less than 1%) and overweight (25%). Medications are rarely prescribed: anticoagulants in 1% of medical records, as well as statins (10%). The use of an articain-containing anesthetic with a vasoconstrictor concentration of 1:200000 or without a vasoconstrictor during dental surgery helps to prevent the risk of complications of the cardiovascular system, especially with prolonged dental surgery, and especially in patients at risk.

Keywords: Myocardial infarction, Risk factors, Secondary prevention, Invasive therapy, Cardiovascular disease.

Introduction

In the 21st century, cardiovascular disease remains one of the leading causes of death [1]. According to statistics, at least 17 million people worldwide die from these diseases each year [2]. Half of the deaths occurring in the European Union are attributable to

cardiovascular diseases [3]. Previously, cardiovascular diseases manifested mainly in old age, but now an increasing percentage of them occur in the interval of 30-40 years, with serious consequences - disability and premature death [4].

Nevertheless, in developed countries (European Union, USA, Canada, Australia, Japan), there is a decrease in mortality rates due to cardiovascular diseases [5]. The opposite trend is recorded in the countries of the former Soviet Union - Russia, Ukraine and others. Among cardiovascular diseases, half of the cases are coronary heart disease [6]. The clinical variant of coronary heart disease is acute myocardial infarction, leading to disability and premature death.

The incidence of myocardial infarction in Russia and developing countries is increasing - up to one third of patients are under the age of 40 years [7]. It should be borne in mind cardiovascular that among diseases. myocardial infarction is one of the most difficult for the prevention and management diseases. Persons who have myocardial infarction are very likely to have it again.

Within 6 years after the first heart attack, up to one fifth of men and one third of women suffer a repeated heart attack [8]. In 70% of cases, the consequences of a second heart attack are death [9]. The most difficult for patients who have had a heart attack is the first year, which accounts for up to 10% of all cases of repeated heart attack [10]. The use of advanced methods of surgery, as an element of primary prevention, such as angioplasty, has not fully paid off. The goal of angioplasty is the partial or complete restoration of coronary circulation [11]. One of the disadvantages of angioplasty is its low availability for the population.

Thus, methods of secondary prevention of cardiovascular diseases are becoming more important. In advanced countries, a decrease in the number of cases of cardiovascular diseases has become possible mainly due to their prevention, taking into account risk factors of cardio logical origin [12]. In practice, this is realized by changing the lifestyle of patients, as well as using pharmacotherapy methods. The purpose of pharmacotherapy is to achieve and normalize the parameters of risk factors, which include blood pressure, blood lipid composition and some others. With strict implementation of secondary prevention methods according to

international recommendations, it is possible to significantly reduce the level of mortality or disability from cardiovascular diseases. It is known that with strict adherence to the recommendations of secondary prevention, the number of cases of sudden death caused by complications of myocardial infarction is reduced by a third [13].

In the prevention of this disease, the key role is played by local doctors (in Russia and other CIS countries), in whom patients are registered for medical examination. It remains relevant to conduct studies related to the monitoring of secondary prophylaxis of patients after their myocardial infarction in practical use [14]. At the same time, the application of practical recommendations in medicine in many countries remains an unresolved problem. These countries include Russia.

One of the possible ways out seems to us to be an increase in the number of studies devoted to this problem, both on a national scale and on the example of its individual regions. The results of such studies can be a convenient model on which you can trace all the stages of the implementation of practical recommendations for secondary prevention. This determined the relevance of our study. The purpose of the study was to study the effectiveness of secondary prevention in the pharmacological aspect in a group of patients with a diagnosis of myocardial infarction on the basis of specialized medical institutions.

Material and Methods

Material

The study was conducted in 2010-2019 on the basis of cardiological dispensary No. 3 of Moscow. Randomly, 9,000 medical records were selected for patients who visited a cardiologic dispensary during the indicated period. The age of the patients in the sample exceeded the value of 30 years, which amounted to 40% of the total visits to the cardiologic dispensary for 9 years of the study. This study included 900 medical records of patients who were included in the list of inclusion criteria in the sample. The main data on anthropometry are presented in Table. 1.

Table 1: Anthropometry and physiological parameters of 900 patients included in the study

Indicator and measurement unit	Average number±standard deviation	Median
Age (years)	61.5±9.7	62
Height (cm)	170.1±10.9	168

Body weight (kg)	81.6±15.8	80
Obesity index (in kg/m²)	28.5±6.1	26.9
Systolic blood pressure (mmHg)	142.1±20.9	141
Diastolic blood pressure (same units)	83.0±10.6	79
Heart rate (beats per 1 min)	74.1±10.9	73
Total cholesterol (mmol/l)	5.91±1.35	5.8

The age interval was 30 years (minimum)-89 years (maximum). All 900 patients had myocardial infarction at least once. The average number of years for patients from the sample corresponded to old age (Table 1). Moreover, more than half of the patients were over 62 years old (Table 1). Men made up the majority of the sample - 61.4%. 13.1% of patients had a history of more than one myocardial infarction. The following diseases were included in the history of patients to reduce the percentage of occurrence: arterial hypertension (87%), stable angina pectoris (85%), heart failure (55%), diabetes mellitus (13%), as well as stroke (8%).

In a number of cases, cardiac arrhythmias were recorded (20% of patients), half of the patients had a trial fibrillation (49%). In parallel with the processing of medical records in the same period of time, a survey of 606 doctors was conducted by questioning from private and state dental clinics. The first group (303 people) included doctors from private clinics; the second was 303 doctors from state medical institutions. This choice of clinics is due to the fact that a heart attack is a combined pathology with dental diseases, so patients with a heart attack are almost always observed at the dentist.

Inclusion and Exclusion Criteria

The criteria for inclusion in the sample were: a) belonging to the age group of 30 years; b) a visit to the dispensary during the specified period of the study; c) the mandatory presence of a diagnosis of myocardial infarction in the patient's history; d) the signing of an agreement on the observance of ethical rules by doctors and an anonymity agreement on the information provided by the patient in his medical record.

For this, they contacted patients through the contact information indicated on the medical card. In the absence of communication and consent of the patient, his information was not processed and was not included in this study. Patients with the following characteristics were not included in the study due to: a) lack of an agreement on compliance with the rules of ethics and anonymity of

information (see above); b) age up to 30 years; c) the absence of a diagnosis of myocardial infarction in the medical history or the presence of other diseases of the cardiovascular system instead.

Study Protocol

The data obtained from medical records were divided into 4 groups. The first group included data related to the social status of the patient, namely: the presence of disability, employment at work and social status in society. The second group included data on anthropometry (age and gender groups, height, weight, etc.) and information on risk factors - the presence of bad habits (smoking, drinking alcohol), lipid profile and the presence of other diseases.

The third group included data obtained from the patient's history, as well as data on laboratory and instrumental methods of research. The last, fourth group included information on the medical methods of therapy applied to the patient, and in the division - the therapy prescribed in the clinics before entering the cardiologic dispensary and the therapy used in the cardiologic dispensary itself. If available, the use of invasive methods for diagnosing the disease (for example, the method of coronaroangiography), or invasive methods of therapy - coronary angioplasty and coronary bypass surgery, used in the diagnosis of coronary heart disease, was recorded.

Anesthetics of the articaine series with a vasoconstrictor concentration of 1:100000, 1:200000 and without a vasoconstrictor were used. When choosing the methods for examining the patient's cardiovascular system, it was taken into account that they should be a traumatic. The obtained data were entered into the Microsoft Excel 2010 database, if necessary; these were imported into the statistical program.

Statistical Data Processing

Statistical analysis was performed using the program Statistica v. 6.0 (Stat soft Inc.). Signs were divided into two groups qualitative and quantitative.

The former were characterized by two indicators - the frequency and proportion (in percent, %) of the total cases. For quantitative features, the arithmetic mean, standard error of the mean, standard deviation, and the minimum and maximum values were calculated. The significance of differences between the characters was determined using a two-sample t-test for independent samples. The differences are significant at a significance level of p \leq 0.05. Different levels of significance are negotiated separately.

Results

The number of years in which the first heart attack occurred almost corresponds to the age interval in the studied sample, with a minimum of 30 years and a maximum of 85 years. At the same time, the average age of the patient in whom the first heart attack

was transferred is slightly less than the average age in the sample: 56.9 ± 10.1 years versus 61.5 ± 9.7 years of middle age (Table 1). In a third of patients, the first heart attack occurred before the age of 55 (33%), in 32% - under the age of 60, and in 35% - under the age of 65. Since the first heart attack was transferred, a large scatter of data was recorded in the study sample - from a period of less than one year to 43 years at the maximum, on average, this is an interval of 4.6 ± 5.3 years.

Interesting, but disappointing results were obtained in the analysis of risk factors, the secondary prevention of which was recommended by international and Russian experts. These factors should have been taken by doctors under control during examination and treatment of patients (Table 2).

Table 2: The frequency of occurrence of risk factors in patients after myocardial infarction (information from medical records)

Risk factor present in the patient's outpatient record	The proportion of patients with this risk factor (100% - the whole sample),%
Hereditary manifestations of ischemia	13.1
Smoking	3.1
Physical activity	0.3
Body weight and height	6.9
Arterial pressure	96.1
Total blood cholesterol	45.9
Blood triglycerides	33.2
Low Density Lipoproteins in the Blood	14.9
High Density Lipoproteins in the Blood	14.9
Abnormal blood glucose concentration (before meals)	22.3

If we arrange the factors in decreasing incidence of indicators in medical records, then it is clear that the main attention was paid to measuring blood pressure (Table 2), then with a gap of 2-10 times (p=0.001), anthropometric indicators and lipid profile analyzes follow and control of physical activity is found an order of magnitude less (p=0.001). It should be noted that physical activity (its presence) is one of the basic requirements of the secondary prevention of

cardiovascular diseases. From this we can conclude that the information provided in the medical records is incomplete, and for a number of parameters analysis is not possible - namely, hereditary, in relation to smoking, physical activity and others. Therefore, the data provided by official statistics may be incomplete or unreliable. A similar situation was observed when trying to normalize the parameters of risk factors and lipid metabolism in patients (Table 3).

Table 3: Normalization of parameters of lipid metabolism and risk factors in patients

Indicator	Share (%) of the total number of patients with myocardial infarction
	myocartilar infarction
Overweight (up to 25 kg per m^2)	25.1
Systolic blood pressure (up to 140 mmHg)	42.4
Diastolic blood pressure (up to 90)	60.1
Combination of the previous two parameters	39.4
Total cholesterol (up to 5 mmol per liter)	25.8
Low Density Cholesterol (up to 3 mmol per liter)	33.3

The entire sample of patients is characterized by a low percentage of achieving normal values of risk factors and lipid metabolism parameters, despite the fact that they play a key role in predicting the outcome of the disease. So, in 45% of cases, we recorded the fact of the presence in the medical record of marks on excess body weight (more than 30 kg per m²). Also, 33.3% of patients had an excess level of cholesterol in the blood, in the case of at least a one-time measurement of this parameter. It is worth noting that dyslipidemia was observed in all patients who studied lipid metabolism.

In most cases, according to international recommendations, after treatment, the doctor is obliged to give a patient who has had myocardial infarction a full consultation. The essence of the consultation should be displayed on the patient's medical record. The consultation should be aimed at changing the lifestyle, in particular the rejection of bad habits (smoking, drinking alcohol), the transition to regular physical activity, a rational diet and diet. In 6 cases, smoking cessation was noted, out of 21

recorded cases of smoking. According to our data, only a quarter of cases (25.9%) contained records of physical activity on the medical record. A slightly larger number of patients (45%) were advised on the need to switch to a special diet regimen. Despite the fact that there is a possibility of an oral consultation with a doctor, in accordance with international requirements, the consultation should be displayed in writing on the patient's medical record.

The best results (two-thirds of patients, Table 3) were achieved with normalization of diastolic blood pressure, systolic pressure, and their combination. The remaining parameters in the norm were achieved only in a third or a quarter of cases. Such results may be due to improper treatment or choice of treatment strategy. The results of the analysis of prescribing drugs to patients with a diagnosis of myocardial infarction are presented in Table. 4.

Table 4: Prescribing drugs to patients with a diagnosis of myocardial infarction in clinics and

cardiological dispensaries, comparative indicators

(PG) pharmacological group	Clinic, frequency of appointment	Cardiologic dispensary, frequency of appointment
Inhibitory angiotensin-converting enzyme	48.1	75.1
Beta blockers	45.1	75.4
Antiplatelet agents	34.1	72.7
Statins	9.6	36.6
Anticoagulants	0.6	1.5
Sustained nitrates	32.9	49.1
Diuretics	16.2	40.2
Calcium ion channel blockers	13.0	30.1
Antihypoxants and antioxidants (trimetazidine)	12.4	28.2
Angiotensin 2 Receptor Antagonists	2.9	0
Cardiac glycosides	2.1	5.3

Table 4 shows the groups of drugs recommended by international medical organizations for the secondary prevention of myocardial infarction and other diseases of the cardiovascular system.

Application anesthesia of the injection point was carried out in 54.29% of cases by doctors of the first group, the second group of 62.5%. 88.57% of the concentration of vasoconstrictor, which they often use in dental interventions, is 1:100000, the second group is 70%. The respondents of the first group anesthesia without use а vasoconstrictor for pathology of the cardiovascular system of 17.14%, during pregnancy 22.86%, 42.86% of doctors did not note in which cases they use local anesthesia without a vasoconstrictor.

At the same time, 97.5% of respondents of the second group use anesthesia without a vasoconstrictor pathology for of the cardiovascular system, and 2.5% pregnancy. Of the 606 doctors interviewed in the first and second groups, 17.14% (n=53) and 17.5% (n=55) indicated that they had severe general disorders in their practice due to the introduction of anesthetic before dental surgery in their patients.

Moreover, according to the respondents of the first group, the most common errors are associated with the choice of anesthetic 26.73%. At the same time, 82.86% of the respondents of the first group believe that many working doctors make mistakes.

According to our data, patients in cardiac dispensaries, on average, are 2-4 times more likely to receive prescription drugs (p≤0.001), that is, more intensive therapy is performed here. Negative is the fact that doctors, as a rule, do not notice at the first visit to the patient in the cardiologic dispensary what kind of therapy he received in the clinic. We note a small share of the prescription of vital drugs - indirect anticoagulants.

And this despite the fact that a significant part of the patients are patients with arrhythmias, heart failure and myocardial infarction (from 10 to 30%). Prescribing drugs such as antiplatelet agents and statins is also inadequate. This indicates insufficient or improper treatment and secondary

prophylaxis for patients who have had myocardial infarction in clinics, as well as in the cardiac dispensary. Polyclinics showed an extremely low level of work with patients, which results in the low efficiency of secondary prevention of cardiovascular diseases in these institutions.

The remaining drugs (starting with nitrates, table 4) were prescribed in case of concomitant diseases of the cardiovascular system. The use of methods of invasive diagnostics and invasive therapy is at an extremely low level, primarily due to the high cost of these technologies, which most patients are not able to pay. This is another reason for the high mortality from repeated heart attacks in Russia compared to other countries, such as the EU or the USA.

Table 5: Frequency of use of invasive therapies for patients with myocardial infarction

Method name	Frequency of use, %
Coronary angiography	7.6
Coronary artery bypass grafting	4.1
Coronary angioplasty	2.2
Surgery or angioplasty	6.4
Pacemaker	0.7

Among the invasive methods used, coronary angiography predominated (Table 5). Shunting was used 2 times more often during therapy compared with angioplasty (p=0.001). Least of all, in less than 1% of cases, the installation of a pacemaker was used

Discussion

We took into account exclusively medical records of patients who suffered the first or one of the following times myocardial infarction. We also took into account the opinion of the doctors who are carrying out therapy or data processing. Thus, the opinions of doctors, as well as the condition of patients from different types of medical institutions, are taken into account.

In a number of countries, including Russia, there has recently been an increase in the quantitative indicators of prescribing to patients with coronary heart disease, including myocardial infarction, drugs such as statins [15, 17]. This is a belated time repetition of the tactics of developed countries, in which secondary prophylaxis with the use of statins has led to the normalization of indicators ofcholesterol. In Russia, this trend is not observed for the following reasons. Patients can move away from the prescribed course of treatment with quite expensive drugs, for financial reasons. The work of doctors in this direction is not effective enough. Another reason is the short-term treatment with statins, and the results of therapy are not

checked by doctors through analyzes. The low level of taking statins, as well as other expensive drugs, is reflected in the results of our work. Another characteristic feature of statin administration is their minimum dosage, which, accordingly, minimizes their effect. The above tendency is characteristic not only in the case of statins, but also, for example, in the case of antihypertensive drugs.

In the case of their minimal use or its absence, one of the necessary parameters of secondary prevention, namely, normalization of blood pressure is not achieved at all [18]. All this leads to an increase in risk factors and the likelihood of myocardial infarction or second attack [19,23]. The representation diagnostic ofinvasive methods and invasive therapy in Russia also indicates an increased risk of mortality.

The main reason for all the aforementioned drawbacks of the use of methods of secondary prevention of cardiovascular diseases is the high cost for the population of medicines and methods of surgery and diagnosis. The way out of this situation is a comprehensive approach.

Given international recommendations on the prevention of cardiovascular secondary disease, it is necessary to conduct training courses among patients. Given the specifics of the financial situation of most patients and the high cost of drugs, one of the possible solutions is to promote a healthy lifestyle, with a complete cessation of smoking and the use of alcoholic beverages. The latter are one the most serious factors at times increasing the likelihood of heart attacks, diseases strokes and other of the cardiovascular system [24, 30].

Some studies indicate a steady increase in another risk factor among young people obesity [31, 32]. Together with the lack of full-fledged physical activity, this only exacerbates existing statistics. There is also evidence of differences in drug treatment among populations of different ages - young patients received a statistically greater number of adrenergic blockers compared with older ones [33].

But this study was conducted in the Union, where initially European conditions for medical care are better than in Russia, as well as the solvency of the population and the availability of health insurance. According to our results, patients with myocardial infarction Russia, not only is there a lack of prescription of the necessary drugs, but there is also an incomplete assessment of the level of manifestation of risk factors, which is displayed on medical cards.

References

- 1. Stone NJ, Robinson JG, Lichtenstein AH, Merz CNB, Blum CB, Eckel RH, McBride P (2014) 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular riskadults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology, 63(25 Part B): 2889-2934.
- 2. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Hindricks G (2018) 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-

Conclusions

As shown by the data of a wide examination of medical records of patients in Russian polyclinics and cardiac dispensaries, doctors do not fully follow the recommendations on secondary prevention ofcardiovascular from World diseases the Health Minimum Organization. indicators occurrence were noted for such risk factors as smoking (3%) and the presence of physical activity (less than 1%), as well as overweight (25%). Medicines are also not prescribed in the proper amount, which determines the minimum results for the normalization of risk factors, in particular anticoagulants (1%), as well as statins (10%). Moreover, the difference between the quality of medical care in polyclinics and a cardiological dispensary can reach 2-5 times in favor of the latter. Thus, the outcome of a patient's health after a myocardial infarction may even depend on the type of institution where he (she) will go.

Our study also showed minimal results from invasive examination and invasive therapy, which do not exceed 10%. The use of an articain-containing anesthetic with vasoconstrictor concentration of 1:200000 or without a vasoconstrictor during dental surgery helps to prevent the risk of complications of the cardiovascular system, especially with prolonged dental surgery, and especially in patients at risk. It is necessary to adhere to the recommendations of the WHO. both for doctors during examination and prescription of therapy, and for patients in lifestyle.

- segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European heart journal, 39(2): 119-177.
- 3. Drozda JP, Ferguson TB, Jneid H, Krumholz HM, Nallamothu BK, Olin JW, Ting HH (2016) 2015 ACC/AHA focused update of secondary prevention lipid performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. Journal of the

- American College of Cardiology, 67(5): 558-587.
- 4. Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, Bengtsson O (2015) Long-term use of ticagrelor in patients with prior myocardial infarction. New England Journal of Medicine, 372(19): 1791-1800.
- 5. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, De Ferrari GM (2015) Ezetimibe added to statin therapy after acute coronary syndromes. New England Journal of Medicine, 372(25): 2387-2397.
- 6. Lloyd-Jones DM, Morris PB, Ballantyne CM, Birtcher KK, Daly DD, DePalma SM, Smith SC (2017) 2017 focused update of the 2016 ACC expert consensus decision pathway on the roleof non-statin therapies for LDL-cholesterol lowering in management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. Journal of the American College of Cardiology, 70(14): 1785-1822.
- 7. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, Sever PS (2017) Evolocumab and clinical outcomes in patients with cardiovascular disease. New England Journal of Medicine, 376(18): 1713-1722.
- 8. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, Woo V (2016) Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N. Engl. J. Med., 375: 1834-1844.
- 9. Fonarow GC, Keech AC, Pedersen TR, Giugliano RP, Sever PS, Lindgren P, Sabatine MS (2017) Cost-effectiveness of evolocumab therapy for reducing cardiovascular events in patients with atherosclerotic cardiovascular disease. JAMA cardiology, 2(10): 1069-1078.
- 10. Villa G, Lothgren M, Kutikova L, Lindgren P, Gandra SR, Fonarow GC, Van Hout B (2017) Cost-effectiveness of evolocumab in patients with high cardiovascular risk in Spain. Clinical therapeutics, 39(4): 771-786.
- 11. Gandra SR, Villa G, Fonarow GC, Lothgren M, Lindgren P, Somaratne R, Van Hout B (2016) Cost- effectiveness of LDL- C lowering with evolocumab in

- patients with high cardiovascular risk in the United States. Clinical cardiology, 39(6): 313-320.
- 12. Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, May M, Brindle P (2007) Derivation and validation of QRISK, a new cardiovascular disease risk scores for the United Kingdom: prospective open cohort study. BMJ, 335(7611): 136.
- 13. Morrow DA, Braunwald E, Bonaca MP, Ameriso SF, Dalby AJ, Fish MP, Ophuis AO (2012) Vorapaxar in the secondary prevention of atherothrombotic events. New England Journal of Medicine, 366(15): 1404-1413.
- 14. Bohula EA, Bonaca MP, Braunwald E, Aylward PE, Corbalan R, De Ferrari GM, Sabatine M S (2016) Atherothrombotic risk stratification and the efficacy and safety of vorapaxar in patients with stable ischemic heart disease and previous myocardial infarction. Circulation, 134(4): 304-313.
- 15. Wong KL, Wong YTA, Yung SYA, Tam CCF, Lam CCS, Hai SHJ, Chan HWR (2015) A single centre retrospective cohort study to evaluate the association between implementation of an acute myocardial infarction clinical pathway and clinical outcomes. International journal of cardiology, 182: 82-84.
- 16. Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, Reiner Ž (2016) 2016 ESC/EAS guidelines for the management of dyslipidaemias. European heart journal, 37(39): 2999-3058.
- 17. Bohula EA, Morrow DA, Giugliano RP, Blazing MA, He P, Park JG, Brady AJ (2017) Atherothrombotic risk stratification and ezetimibe for secondary prevention. Journal of the American College of Cardiology, 69(8): 911-921.
- 18. Chiang CE, Okumura K, Zhang S, Chao TF, Siu CW, Lim TW, Teo WS (2017) 2017 consensus of the Asia Pacific Heart Rhythm Society on stroke prevention in atrial fibrillation. Journal of arrhythmia, 33(4): 345-367.
- 19. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Hindricks G (2016) 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. European

- journal of cardio-thoracic surgery, 50(5): 2893-2962.
- 20. Chan PH, Huang D, Lau CP, Chan EW, Wong IC, Lip GY, Siu CW (2016) Net clinical benefit of dabigatran over warfarin in patients with atrial fibrillation stratified by CHA2DS2-VASc and time in therapeutic range. Canadian Journal of Cardiology, 32(10): 1247-e15.
- 21. Chan PH, Lau CP, Tse HF, Chiang CE, Siu CW (2016a) CHA2DS2-VASc recalibration with an additional age category (50-64 Years) enhances stroke risk stratification in Chinese patients with atrial fibrillation. Canadian Journal of Cardiology, 32(12): 1381-1387.
- 22. Siu CW, Lip GY, Lam KF, Tse HF (2014) Risk of stroke and intracranial hemorrhage in 9727 Chinese with atrial fibrillation in Hong Kong. Heart rhythm, 11(8): 1401-1408.
- 23. Siu CW, Tse HF (2014) Net clinical benefit of warfarin therapy in elderly Chinese patients with atrial fibrillation. Circulation: Arrhythmia and Electrophysiology, 7(2): 300-306.
- 24. Mehta SR, Granger CB, Boden WE, Steg PG, Bassand JP, Faxon DP, Avezum A (2009) Early versus delayed invasive intervention in acute coronary syndromes. New England Journal of Medicine, 360(21), 2165-2175.
- 25. Wanner C, Inzucchi SE, Lachin JM, Fitchett D, Von Eynatten M, Mattheus M, Zinman B (2016) Empagliflozin and progression of kidney disease in type 2 diabetes. New England Journal of Medicine, 375(4): 323-334.
- 26. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Broedl UC (2015) Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine, 373(22): 2117-2128.
- 27. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Graham I (2016) 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task

- of Force of the European Society Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association Cardiovascular Prevention Rehabilitation (EACPR). European heart journal, 37(29): 2315-2381.
- 28. Neal B, Perkovic V, Matthews DR, Mahaffey KW, Fulcher G, Meininger G, Yee J (2017) Rationale, design and baseline characteristics of the CANagliflozin cardio Vascular Assessment Study-Renal (CANVAS- R): A randomized, placebo-controlled trial. Diabetes, Obesity and Metabolism, 19(3): 387-393.
- 29. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Bhatt DL (2019) Dapagliflozin and cardiovascular outcomes in type 2 diabetes. New England Journal of Medicine, 380(4): 347-357.
- 30. Perkovic V, de Zeeuw D, Mahaffey KW, Fulcher G, Erondu N, Shaw W, Neal B (2018) Canagliflozin and renal outcomes in type 2diabetes: results from the CANVAS Program randomised clinical trials. The lancet Diabetes & endocrinology, 6(9): 691-704.
- 31. Radholm K, Figtree G, Perkovic V, Solomon SD, Mahaffey KW, de Zeeuw D, Matthews DR (2018) Canagliflozin and heart failure in type 2 diabetes mellitus: results from the CANVAS Program. Circulation, 138(5): 458-468.
- 32. Neal BC, Neuen BL, Ohkuma T, Matthews DR, De Zeeuw D, Mahaffey KW, Rosenthal N (2018) Cardiovascular and renal outcomes with canagliflozin according to baseline kidney function: data from the CANVAS Program. Circulation, 138(15): 1537-1550.
- 33. Wanner C, Lachin JM, Inzucchi SE, Fitchett D, Mattheus M, George J, Zinman B (2018) Empagliflozin and clinical outcomes in patients with type 2 diabetes mellitus, established cardiovascular disease, and chronic kidney disease. Circulation, 137(2): 119-129.