Clinical diagnoses and characteristics of women entering the Reykjavik Emergency Departments during the economic collapse in 2008

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Final project for a Bachelors degree in Medicine

University of Iceland
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Abstract

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Background: The Prime Minister's speech to the Icelandic nation on October 6th 2008 dramatically signalled the start of a swift economic collapse in Iceland. An earlier study reported a 40% increase in women attending to the Cardiac Emergency Department (ED) of Landspitali University Hospital in the following week. This spike is now being investigated further to determine underlying clinical characteristics and diagnoses of these women.

Methods: Using electronic medical records at Landspitali, we conducted a retrospective study of all women attending the EDs with an admittance diagnosis of non-cerebrovascular cardiovascular disease and excluding diseases of veins, lymphatic vessels and lymph nodes (ICD 10: I00-I99; I60-69 and I80-89 excluded). The index week started after 4:00pm on October 6th 2008 (week 41) and a comparison period consisted of two weeks before October 6th (weeks 39 and 40). Extensive data was collected including ICD 10 discharge diagnosis, results from blood analysis, ECG results and cardiac catheterization. Information regarding admittance characteristics including risk factors for CVD and length of stay was recorded.

Results: In the week of the economic crisis 25 women were admitted with cardiovascular diagnosis compared to 34 in the preceding two weeks, representing an increase of approximately 47%. Overall, we did not observe differences in admittance characteristics although women attending in the week of the collapse appeared more likely to have arrived with ambulance (p=0.01) and less likely to have reported lipid abnormalities (p=0.05) or a family history of heart disease (p=0.09). Attendees in the collapse week were more likely to be discharged with a diagnosis of ischemic heart disease (ICD 10; I20-I25) (p=0.07). This is, primarily, explained by an increase in cases of angina pectoris (ICD 10 I20) (p=0.03). Blood analysis and ECG results revealed no significant differences when ICD 10 I20-I25 diagnoses were compared. The rate of cardiac catheterization was lower among women in the collapse week (50%) compared to preceding weeks (100%).

Conclusions: Our data confirm increased attendance of women to Reykjavik emergency departments for cardiovascular disease in the week of the economic collapse, particularly due to angina pectoris. These women appeared to some extent to have a more subtle risk profile while small numbers and incompleteness of the data hamper definite conclusion.

Abbreviations

ApoA1	Apolipoprotein A1
ApoB	Apolipoprotein B
BMI	Body Mass Index
CVD	Cardiovascular Disease
ECG	Electrocardiogram
ED	Emergency Departments
GDP	Gross Domestic Product
HDL	High Density Lipoprotein
ICD-10	International Classification of Diseases 10th Revision
IMF	International Monetary Fund
LDL	Low Density Lipoprotein
OECD	Organisation for Economic Co-operation and Development
SD	Standard Deviation
TIMI	Thrombolysis In Myocardial Infarction
VLDL	Very-Low-Density Lipoprotein
WHO	World Health Organisation

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1 Background

Ischemic heart disease is the leading cause of death in the world today.[1] In 2010, the mortality rate for ischemic heart disease among Icelandic women was 55 per 100,000 after age standardisation for women, and 118 per 100,000 for Icelandic men. Ischemic heart disease is thus a substantial portion of the 507 deaths per 100,000 in Iceland during the same year.[2] This is despite the fact that Iceland is a low risk country, as defined by the European Guidelines on cardiovascular disease, having cardiovascular disease mortality of less than 220/100,000.[3]

Ischemic heart disease is characterized by an imbalance of blood supply and myocardial oxygen demand, typically due to an obstruction that hampers blood flow. The clinical syndromes of ischemic heart disease are angina pectoris (which can be either stable or unstable), acute myocardial infarction, chronic ischemic heart disease and sudden cardiac death. Acute coronary syndrome is often used for unstable angina, acute myocardial infarction and sudden cardiac death.[4]

Atherosclerosis is the result of the process atherogenesis, where atherosclerotic plaques form in the arteries. Many of the risk factors for cardiovascular diseases accelerate this process. Plaque forms in the intima layer by accumulation of lipoproteins and cholesterol esters, lipid droplets and macrophages.[5] Cholesterol is transported via lipoproteins, predominantly low density liproteins (LDL), through the bloodstream and can be taken into the intimal cells, forming an integral part of plaque. [6] Apolipoprotein B (ApoB) is the primary protein moiety associated with very-low-density lipoprotein (VLDL) and low density lipoprotein[7], making it highly atherogenic. Apoliprotein A1 (ApoA1) is a component of high density lipoproteins (HDL).[8] In advanced plaques a lipid core has formed.[9] Plaque is staged into 6 different types. The earliest stages occur early in life and later develop into advanced lesions (IV-VI).[5] These advanced lesions can rupture and cause most acute coronary syndromes.[10] Phase III lesions can also rupture, causing angina pectoris, but are more frequently asymptomatic.[11] When plaque ruptures there may be hemorrhage, luminal thrombosis or vasospasm, that contribute to sudden flow obstruction and give rise to the symptoms of ischemic heart disease.[10]

1.1 Risk factors

It is well established that cardiovascular disease is sensitive to certain risk factors. These can be used to determine which individuals are likely to succumb to the disease and to target for preventative measures. There have been various attempts to create a risk profile that can categorize individuals and determine their risk levels.

The Framingham heart study is a cohort study with 5127 individuals from the town of Framingham, Massachusetts. Its purpose is to study the epidemiology of coronary heart disease. [12] The research plan and aims were outlined in 1951 and include biennial examination. [13] Researchers of the Framingham heart study created a risk profile using a 12 year follow up.[14] It has now been expanded to a 30 year prediction of cardiovascular disease.[15] A European scoring system has also been created using twelve cohorts. It is called the SCORE project and is a scoring system for fatal cardiovascular disease.[16] The Framingham heart study and the SCORE project both use gender, age, smoking, cholesterol levels (total and HDL level) and systolic blood pressure. The Framingham study also requires knowledge of antihypertensive treatment and whether the individual has diabetes mellitus. A third risk profile has been created with the PROCAM study that may have greater predictive value. It includes family history, triglycerides level and LDL cholesterol.[17] There is also an Icelandic risk score called the Icelandic Heart Association's risk calculator, and is based on data collected over forty years in Icelandic cohorts. An online version is available where the public can calculate their ten year risk of heart disease. The Icelandic Heart Association has also used their data to modify the SCORE project chart to better reflect the risk for the Icelandic population.[18]

These risk factors are considered traditional risk factors but novel risk factors are emerging. The INTERHEART study investigated nine risk factors for an acute myocardial infarction. They found that all together, they explained 90% of the population attributable risk in men, and 94% in women. These nine risk factors are smoking, raised ApoB/ApoA1 ratio, history of hypertension, diabetes, abdominal obesity, psychosocial factors, daily consumption of fruits and vegetables, regular alcohol consumption, and regular physical activity.[19] There were four psychosocial factors used in this study; financial stress, stress at home and at work, and major life events in the last year. A predetermined list of major life events was provided and the respondent was asked which had occurred in the past year.[20]

Established risk factors are generally divided into two categories, modifiable and non-modifiable. The modifiable risk factors discussed here are high cholesterol levels, elevated

blood pressure, diabetes, smoking, diet, and lifestyle. On the other hand, the non-modifiable risk factors discussed here are family history, age and gender.

1.1.1 Modifiable risk factors

High levels of cholesterol have long been thought to promote the formation of atherosclerotic plaques. This was first demonstrated in animal models such as dogs[21] at the turn of the century. High serum cholesterol was quickly identified as a risk factor for human cardiovascular disease in the Framingham study.[22] The field quickly diversified to account for the different lipoproteins that affect cardiovascular disease. That levels of high density lipoproteins are lowered in ischemic heart disease[23] demonstrates that this is a complicated system that needs to be properly balanced. The INTERHEART study, published in 2008, investigated total cholesterol, HDL cholesterol, ApoA1 and ApoB and found that abnormal values were all risk factors for myocardial infarction with the ApoB/ApoA1 ratio having the strongest association.[24]

Elevated blood pressure has been established as a risk factor for cardiovascular disease.[25] Hypertension was, early on, shown to accelerate the onset of atherosclerotic plaque in dogs.[26] Hypertension was later identified as significantly associated with arteriosclerotic heart disease in the Framingham study.[27] Hypertension and lipid abnormality interact and together create an excess risk that is not present when only one factor is at play.[28]

In the Framingham study diabetics were shown to have a mortality rate almost three times higher than that of the general population. This could not be entirely explained by their higher rates of other risk factors.[29] Studies have found that diabetics have lower HDL cholesterol levels and higher levels of VLDL triglycerides[30] , which is often referred to as diabetic dyslipidemia. Abnormal glucose levels have also been shown to impact cardiovascular risk.[31] This abnormal metabolic state cause arterial dysfunction and atherosclerosis as reviewed by Dr. Beckman et al. in the Journal of the American Medical Association.[32]

The mortality rate of cigarette smokers from coronary artery disease was shown to be twice the rate of non smokers. [33] Smoking reduced flow-dependent dilation of the epicardial arteries regardless of atherosclerotic plaques.[34] Smoking also increases serum cholesterol levels.[35] The INTERHEART study shows a dose dependent response to smoking, as well as to tobacco, with an increased risk of myocardial infarction.[36]

Diet and lifestyle can affect the risk for a cardiovascular event. Women in the Nurses' Health Study were followed and variables regarding body mass index, alcohol consumption, exercise, and diet were recorded. The researchers found that the population attributable risk was 74% and only 3% of the study population was regarded as low risk with regards to these factors.[37] Another study found that women who exercised at least 2.5 hours a week reduced their risk by 30%. The positive results of exercise remained after adjusting for possible variables in the causal pathway.[38] Exercise increases insulin sensitivity, lowering the risk of diabetes mellitus.[39] A prospective study on men indicated that alcohol intake was inversely related to the incidence of coronary disease. [40] This is also reflected in a study on moderate drinking with only women where higher alcohol intake was related to lower cardiovascular risk.[41] A joint association analysis for drinking and physical activity was done to determine the risk of cardiovascular mortality. The study indicates that within each given alcohol group, low activity was linked to increased mortality but was negated by high physical activity.[42]

The Mediterranean diet has received much interest as the populations following this diet have had low rates of cardiovascular disease. This diet is characterized by olive oil as the primary fat source, a high intake of vegetables and cereals, and a higher intake of fish. Food from animal sources is used in moderation as is alcohol intake. [43] A small trial suggests that adhering to this diet increases insulin sensitivity and endothelial function. [44]A randomized secondary prevention trial indicated that a Mediterranean type diet had a protective effect against recurrence of a cardiovascular event.[45] A new study, published in 2013, divided the study population into three dietary intervention groups. Two groups went on the Mediterranean diet with either extra-virgin olive oil or nuts supplemented and one group was used as a control. Both versions of the diet had a protective effect for high risk individuals, with a relative risk reduction of approximately 30% of a primary cardiovascular event.[46]

1.1.2 Non-modifiable risk factors

Family history is an independent risk factor for coronary artery disease.[47] The risk is impacted by the age of the parent's first event, that is the younger the parent, the more likely the subject is to experience a cardiovascular event, such as myocardial infarction.[48] Genetics play a role in coronary artery disease and 46 susceptible loci have been discovered that explain 10.6% of the heritability.[49]

It is well known that age has negative effects on the cardiovascular system. The changes are both on a cellular and structural level as reviewed by Dr. Lakatta in Heart Failure

Reviews.[50] The changes in vascular stiffness, vascular intimal thickness and altered regulation of vascular tone all contribute to atherosclerosis. This is caused in part by growing arterial stiffness, though endurance training may mitigate some of the effects.[51] Flow mediated dilation declines with age despite good health but is stable in men until ~41 and early fifties for women. Interestingly, women retain optimum flow-mediated dilation for almost a decade longer. However, the rates of decline are much higher for women, at 0.49% per year and only 0.21% for men.[52] Using non-invasive techniques researchers have seen that thickening of the intima-media occurs with advancing age. Women seem to develop the thickening about five to ten years later than men.[53] Why this happens is still unknown, but it might be chronic increase in local distending pressure, that leads to the thickening of the arterial wall.[54] These differences help explain why women develop cardiovascular disease later in life than men, or about ten years later.[25]

The first prevention guideline for women by the American Heart Association was published in 1999.[55] Though the risk factors are the same for both genders they have differing strengths depending on the gender. Patients with diabetes mellitus have a higher incidence of mortality from cardiovascular diseases. Diabetic women have a 3-fold increased risk of mortality and the men 2-fold in the Framingham study.[56] The European Society of Cardiology and the European Atherosclerosis Society guidelines for the management of dyslipidemias places the relative risk even higher at ~5 for women and ~3 for men.[57] This may be explained by the difference in lipoprotein levels. Diabetic women have significantly higher markers of the lipoproteins apoB, LDL cholesterol, non-HDL cholesterol and LDL particle count which are all associated with atherogenesis. This difference is not significant when diabetic and non-diabetic men are compared.[58] Smoking seems to have a larger effect on women than men. Using data from three studies in Denmark, researchers showed a higher relative risk in current female smokers, of 2.24, than male smokers, of 1.43, when compared to non-smokers.[59] This finding has also been confirmed in a large meta analysis that uses data from prospective cohort studies around the world with almost 4 million participants.[60] Other studies suggest that gender differences are rather based on environmental factors and are therefore modifiable.[61]

1.2 Stressors

In 1990 an article was published from the MILIS study examining possible triggers for myocardial infarction. These included physical activity and emotional upset, and were

reported in almost half the subjects.[62] Certain trends such as variance in circadian rhythm have also been documented.[63] The mechanisms behind these triggers are still debated though the empirical evidence is steadily increasing.

1.2.1 Possible mechanisms

Mental stress has been shown to have an effect on cardiovascular disease in various ways. Mental stress has, in experimental studies, been induced using a combination of stressors such as public speaking and mental arithmetic. [64] These methods have been used to clinically mimic those of emotional stressors. In such experimental settings mental stress tests have an effect on those with diagnosed coronary artery disease[65], as well as healthy individuals[66], causing transient endothelial dysfunction. Under this kind of strain researchers have observed that the endothelium dependent flow mediated dilatation is greatly reduced for up to four hours[66] . This is possibly induced via activation of ET_A receptors that mediate the effects of endothelin on arterial contraction.[67] In subjects with coronary artery disease there was vasoconstriction in diseased segments.[68] Another study using healthy individuals tried to block the reduction of the endothelial vasodilatation function by infusing different blockades during a mental stress test. Their results showed that beta adrenergic blockade reduced the negative effects of the mental stress test but alpha adrenergic blockades had no effect.[69]

Japanese researchers first discovered that many stress related incidents closely resemble myocardial infarction except there was an absence of obstructive coronary disease.[70] This was first described in an English language journal in 1991[71] and was called Takotsubo cardiomyopathy by the Japanese researchers. There are now several names describing this phenomenon including apical ballooning syndrome and stress cardiomyopathy.[72] The pathogenesis of Takotsubo cardiomyopathy is still unknown but a few mechanisms have been suggested. High levels of plasma catecholamines and stress related peptides have been measured in patients,[73] giving rise to a catecholamine mediated mechanism. Intravenous injections of adrenaline induced takotsubo-like cardiomyopathy in cynomolgus monkeys[74] further solidifying the role of the sympathetic nervous system.

The exact mechanism is still debated but one theory is that microvascular dysfunction occurs. This has been supported by the abnormal Thrombolysis In Myocardial Infarction (TIMI) frame count found in studies.[75] Direct myocyte effects with a unique contraction band necrosis[76] have been reported but the body of evidence is still scarce. Another issue is the discrepancy in age and gender of the patients as they are primarily postmenopausal women.[77] This raises the question of the role of sex hormones in the pathogenesis since there are gender

differences in the regulation of the sympathetic nervous system.[78] It is interesting to note that the akinesia is transient[71] and four year survival is comparable to the general population.[79]

In addition to Takotsubo cardiomyopathy, rising incidence of classic myocardial infarctions and thrombotic disease have been reported under stressful circumstances.[80] Plaque rupture and arrhythmias can be triggered by emotional stressors. [81] Plaque may rupture due to increased shear stress at the site of a weak atherosclerotic plaque. Evidence from earthquake survivors suggests that blood viscosity and blood pressure increases during an emotional trigger.[82]

1.2.2 Grief

The effects of grief of have been of interest to poets, philosophers and scholars through the ages. In the 1950's there were systematic studies to explore mortality rates of widowers[83] and close relatives of the deceased.[84] When the causes of death were examined there was a striking increase in cardiovascular diseases, especially coronary thrombosis and other arteriosclerotic and degenerative heart diseases. One study revealed 77 deaths when 46 were expected in the first six months.[83] A more recent study using a case crossover method demonstrated that the risk of an acute myocardial infarction peaks during the first 24 hours with a 21.1 fold risk, and remains significant for the first month.[80]

1.2.3 Anxiety

A study of postmenopausal women who recently experienced panic attacks found that they had a higher risk of coronary heart disease. The risk remained in the fully adjusted model indicating that panic attacks are an independent risk factor[85] for coronary heart disease. A population based study assessing anxiety disorders found that any anxiety disorder increased the likelihood of cardiovascular disease, with an odds ratio of 1.43. This was also true for generalized anxiety disorder and specific phobias.[86] However there is still a question whether this risk is entirely independent from the increased risk associated with depression.[87]

1.2.4 Emotional stress

The majority of studies reporting evidence for the association between emotional stress and heart disease have focused on stressors on a personal basis, such as the loss of a loved one by death[70] or receiving a cancer diagnosis.[88] A study has also shown worse prognosis for women with coronary heart disease who experience marital stress.[89] Growing evidence indicates that these effects can be more far reaching and that the risk for cardiovascular events may be

affected in entire populations following a mass-trauma, such as the aftermath of earthquakes.[90] Los Angeles County was rocked by an earthquake and atherosclerotic cardiovascular deaths soared in the next 24 hours. This was followed with a, potentially compensatory, dip in recorded deaths.[91] An extreme case is a study in Israel tracking mortality during missile attacks in the Persian Gulf War. A 58% increase in mortality during the 24 hours after the first strike was noted and women were especially affected. Mortality rates did not rise in consequent attacks.[92] Even seemly innocuous events such as watching a football game can trigger a cardiac emergency. This was evident during the World Cup in Germany where men had an incidence rate 2.66 times higher than the control period and the incidence rate for women was 1.82.[93]

A study investigated the mortality rates in the first year of a banking crisis, from 1960 to 2002, for males. The study used the World Health Organization (WHO) Global Mortality Database and information on bank crises from the World Bank. When looking only at nineteen high income countries, including Iceland, the short-term increase in cardiovascular disease mortality was 6.4%. For low income countries the increase was a staggering 26%.[94] The INTERHEART study also showed that severe financial stress had an odds ratio of 1.33 for experiencing an acute myocardial infarction. Business failure especially had a high risk and job loss was also a significant risk.[20]

1.3 The economic crisis in Iceland

The economy of Iceland had been experiencing a banking boom with rapid economic growth during the early 2000‘s. This culminated in 2007 when unemployment was only 2.3%[95] and the annual gross domestic product (GDP) rose by 4.9% in Iceland compared to 2.7% in the OECD countries.[96] The three main Icelandic banks had grown substantially and their assets were 923% of Iceland’s GDP at the end of 2007.[97]

In October of 2008 the three main banks were nationalized, representing 85% of total banking assets.[98] This happened very suddenly with the Financial Supervisory Authority temporarily suspending trading of the banks on the morning of October 6.[99] Emergency laws regarding banking[100] took effect the next day to take over the failing banks. This date is often marked by the unusual address made by Prime Minister Geir H. Haarde where he asks the Icelandic people to, “show fortitude in the face of adversity“, and “to guard that which is most important in the life of everyone of us”.[101] The banks were nationalized the same week.[102]

The nationalization of Landsbanki sparked an international dispute with the British government. The United Kingdom parliament invoked the Anti-terrorism, Crime and Security Act 2001 to seize the bank's assets through Landsbanki Freezing Order 2008 on October 8.[103] This further destabilized the economy and there was talk of national bankruptcy. Finally on October 24 the International Monetary Fund (IMF) announced an outline for a two year loan to Iceland for $2.1 billion.[104]

The main concern during the immediate aftermath was the free-fall of the krona.[105] The Central Bank stepped in with a directive to control currency flow on October 10th. This included prioritizing payments for foodstuffs and pharmaceuticals. [106] This was followed by a sharp increase in unemployment, with levels around 9% in 2009.[107] Stress levels also increased in the Icelandic population. A prospective cohort study examined stress levels during 2007 and 2009. The researchers found significantly higher stress levels in women in 2009 and higher stress levels in families in the middle income bracket.[108]

1.4 Aim

A previous observational study investigated the changes in attendance at the Emergency Departments (EDs) in Reykjavik following the economic crisis. It revealed a surge in visits with discharge diagnoses of I00-I99 and R00-R09. This was particularly among women or a 44% increase when compared with the weeks leading up to the banking crisis.[109] This raises the question whether and how the women entering the EDs during the week of the economic crisis are different from those attending when no societal disaster is ongoing. The aim of this new study is to further determine underlying clinical characteristics and diagnoses of women attending EDs for cardiovascular disease during the week of the national economic collapse in 2008.

1.4.1 Specific aims:

A) To contrast attending and discharge diagnoses of female attendees in the week of the collapse compared to two preceding weeks.

B) To contrast presenting symptoms, cardiovascular risk factors and vital signs at arrival of attendees in the collapse week versus non-collapse weeks.

C) To contrast length of stay, rates of hospitalization and test results of women attending in the week of the economic collapse compared to women attending during two previous weeks.

2 Methods

2.1 Study design, setting and population

The subjects of this paper are Icelandic women admitted to the Emergency Departments of Landspitali University Hospital (EDs) with an ICD 10: I00-I99 diagnosis during the collapse week of the 2008 economic crisis in Iceland. Women entering the EDs with an ICD 10: I00-I99 diagnosis during the two weeks prior served as controls. This is a retrospective study of electronic records and charts of female attendees to the emergency departments with symptoms in the cardiovascular system during a three week period, from September 22nd to October 13th 2008. The study base constitutes all women in the larger Reykjavik area (population size: 98,021 females including children).[110] The study population is all women attending the emergency departments with admittance diagnoses of I00-I099 (excluding ICD 10: I60-I69 and I80-I89) during this period.

Landspitali is a tertiary care facility and mainly serves the inhabitants of the greater area of Reykjavik. However in times of crisis and for specialized cases Landspitali can be used by the entire nation. There are two Emergency Departments that can admit patients to Landspitali. The first is a general emergency department located on the Fossvogur campus and the second is a cardiac emergency department on the Hringbraut campus.

Person identification numbers are given to all Icelanders at birth or on obtaining Icelandic citizenship and are maintained through the National Register of Persons.[111] These personal identification numbers are used to track patients through the hospitalization and can be linked with other registries such as the Mortality Files with the Directorate of Health. The same personal identification number is used throughout a person's life.

Information on the number of visits and their personal identification number was attained through Landspitali University Hospital Health Information Technology Department. Each medical record was then examined electronically through the SAGA system and paper charts were retrieved as necessary from Medical Charts Storage System of Landspitali.

After collecting data on all women admitted to the EDs during the three week period the decision was made to exclude two groups due to lack of relevant data. The two diagnostic subgroups excluded were cerebrovascular cardiovascular disease (ICD 10: I60-69) and diseases of veins, lymphatic vessels and lymph nodes (ICD 10: I80-89). One woman was excluded from the study on the basis that she arrived with an emergency flight from Greenland and had no connection with Iceland. In addition, one woman admitted during the

collapse week was a patient of the Landspitali Department of Mental Health and her length of stay may have been underestimated.

2.2 Exposure definition

Exposure was defined by the calendar week (week 41) after the Prime Minister's address to the Icelandic nation on the pending economic collapse, at 4:00pm on October 6th 2008 and during one week after that, or to 4.00pm on October 13th 2008. Women admitted during this period were considered exposed to the economic crisis. Women admitted during the two weeks prior to 4.00pm on October 6, 2008 - weeks 39 and 40 - were considered as unexposed to the economic crisis.

2.3 Ascertainment of outcomes

Information was collected from electronic records of the SAGA system and paper charts were retrieved as necessary from Medical Charts Storage System of Landspitali.

The following variables were collected electronically: all diagnoses, age, timing of attendance, admittance to Landspitali, date of discharge, and date of death. The diagnoses collected were admittance and discharge diagnoses as well as prior diagnosis of mental disorders and heart disease. Diagnosis of heart disease is defined as ICD 10 I00-I99 and mental disorders as ICD 10 F00-F99. Diagnoses are made using the International Classification of Diseases and Related Health Problems, 10th Revision (ICD 10). This is a coding system created by the World Health Organization (WHO) and ensures clarity with diagnoses. All discharge diagnoses of heart disease are made in conjunction with attending cardiologists.

The majority of variables were obtained manually from the electronic medical charts. Data recorded from the EDs and admittance charts if hospitalized includes presenting symptoms (yes/no), vital signs, risk factors for cardiovascular disease (CVD) (yes/no), occupation, residency, method of arrival (yes/no) and medication. Method of arrival and risk factors for CVD were also examined in the paper charts. The data from the EDs relied on self reporting. Presenting symptoms recorded were with chest pains with exertion, chest pain without exertion, tachycardia, irregular heartbeat, dyspnea, dizziness, nausea and radiating pain. Radiating pain was differentiated into arm, neck, jaw and between the shoulder blades. Vital signs recorded were heart rate (beats per minute), blood pressure (mmHg), temperature (°C), respiratory rate (breaths per minute) and oxygen saturation levels (%). The CVD risk

factors recorded were history of smoking, family history of CVD, hypertension, diabetes mellitus and lipid abnormalities.

Diagnostic tests were recorded manually from electronic charts. The diagnostic tests recorded were results from blood analysis, electrocardiography (ECG), echocardiograms, stress tests, ambulatory ECG, pulmonary x-rays and cardiac catheterization. Diagnostic tests, excepting ECG and pulmonary x-rays, were considered part of the stay if they were completed within three months of admittance. ECGs and pulmonary x-rays were only recorded if ordered during the stay. Two ECG results were collected when available, the first and last of the stay. The data recorded was heart rate, cardiac rhythm, T wave inversion, ST depression and elevation, axis deviation, R wave progression and ectopic beats. Blood analysis was also collected twice when possible, the first and last of the visit. Blood analysis results collected were levels of troponin T, C reactive protein, myoglobin, N terminal fragment of B type natriuretic protein, creatine kinase, creatine kinase MB, white blood cell count, catecholamines, cortisol, haemoglobin, glucose, creatinine, cholesterol and HDL cholesterol.

The following variables were obtained manually from the medical paper charts: height (meters) and weight (kilos), method of arrival, risk factors for CVD, and ECG results. If an ambulance was used the log was filed with the individual's medical record. Height and weight measurements were collected from the medical charts if the statistics had been reported within three months before or after the visit to the EDs. The original paper chart from the EDs was used to ascertain negative risk factors. Paper records of ECG's were used to determine PR interval, QRS complex duration and QT interval. Normal ranges for PR interval were 120-200ms, QRS complex duration 80-120ms and QT intervals up to 420ms with a heartbeat of 60 beats per minute.

2.4 Data analysis

Using descriptive statistics, we contrasted frequencies in characteristics, attending symptoms and proportions in each diagnostic category of female attendees during the week of the economic crisis vs. preceding comparison weeks. Data was presented as counts, percentages and means ± standard deviation (SD) of the groups. We used chi2 or simple t-test to compare proportions with characteristics or symptoms or means in clinical parameters. We considered p-values of <0.05 as statistically significant. Data was collected using Filemaker Pro 12 and all results were calculated using SAS 9.2.

2.5 Ethics approval

Approval for this study was obtained from the Science Ethics Committee of Landspítali University Hospital and the Data Protection Authority.

3 Results

In the weeks 39, 40 and 41 of 2008, 78 women were admitted with ICD 10: I00-I99 diagnoses to the Emergency Departments in Reykjavik. 29 women were admitted during week 41, and 49 women in weeks 39 and 40. After excluding those admitted to the EDs with ICD 10: I60-I69 and I80-I89 diagnoses there were 59 female attendees during the weeks of the study; leaving 25 women in the index week and 34 in the preceding two weeks that were included in this study.

The increase reflects a 47% increase in attendance during the collapse week. The difference in admittance rates is not statistically significant (p=0.07). Time of arrival indicates that there is an increase in visits on Monday 6th of October 2008 when compared against arrivals the previous Mondays. After 4 pm on the 6th there were seven visits compared with four visits on the 29th of September.

3.1 Baseline characteristics

Table 1. describes the baseline characteristics of women admitted to the Emergency Departments in Reykjavik during weeks 39-41 in 2008. It was possible to calculate the body mass index (BMI) of 8 (32%) women in the index group and 16 (47%) in the control group. The eight women had a mean BMI of 26.3±4.3. The 16 women had a mean BMI of 31.1±6.0. The differences in BMIs between the groups yielded a p value of 0.06. Over 90% of the women entering the EDs had a prior history of heart disease. In the index week 9 (36%) women had a prior diagnosis of chronic ischemic disease (ICD 10: I25) and 12 (35%) women in the preceding two weeks. Overall, no statistically significant differences were observed between women attending in the week of the collapse compared to women attending in preceding weeks with respect to age distribution, residency, or smoking history. Differences were not either observed with regards to admittance rates or duration of stay. Women attending in the week of the collapse were marginally less likely to report lipid abnormalities (p=0.05) and family history of cardiovascular disease (p=0.09). Women in the collapse week were also more likely to have arrived with an ambulance (Table 1).

Table 1. Baseline characteristics of women admitted to the Emergency Departments in Reykjavik during weeks 39-41 in 2008.

Characteristic	Exposed N = 25	Unexposed N = 34	P Value
No. of women ≤ 50 years old (%)	4 (16)	4 (12)	0.64
No. of women > 50 years old (%)	21 (84)	30 (88)	0.64
Mean age (years) (SD)	70.1 (18.1)	69.1 (15.2)	0.83
Resident of the greater Reykjavik area (%)	21 (84)	30 (88)	0.71
Hypertension (%)	16 (64)	20 (59)	0.69
Diabetes mellitus (%)	5 (20)	4 (12)	0.39
Lipid abnormalities (%)	3 (12)	12 (35)	0.05
Family history of CVD (%)	5 (20)	14 (56)	0.09
Current smoker (%)	8 (32)	6 (18)	0.35
Non-smoker (%)	14 (56)	18 (53)	0.40
Previous I00-I99 diagnosis	24 (96)	32 (94)	0.75
Arrival by ambulance (%)	9 (36)	4 (12)	0.01
Overnight observation (%)	3 (12)	5 (15)	0.95
Admitted to the hospital (%)	10 (40)	12 (35)	0.62
Length of stay if admitted (days) (SD)	12.4 (11.9)	7.2 (7.5)	0.22
Length of stay if not admitted (hours) (SD)	8.5 (6.5)	12.7 (9.9)	0.16
Death within 30 days (%)	2 (8)	1 (3)	0.38

3.2 Discharge diagnosis

Discharge diagnoses of attendees in the week of the economic collapse and preceding comparison weeks are presented in Table 2. In the two comparison weeks the two largest discharge groups were hypertensive diseases (I10-I15) and other forms of heart disease (I30-I52) with 30% of patients in each group. This is different in the index week where the largest diagnosis group is ischemic heart disease (I20-I25). In the index week 8 (32%) patients had a diagnosis of ischemic heart disease and 4 (12%) in the preceding two weeks. This increase from 12% to 32% represents an odds ratio of 3.53 (0.92-13.4). Seven (88%) of the patients with an ischemic heart disease diagnosis in the collapse week had the diagnosis of angina pectoris (I20). This is different from preceding weeks where one (25%) had that diagnosis yielding a p value of 0.03.

Table 2. Discharge diagnoses for women admitted to the Emergency Departments in Reykjavik during weeks 39-41 in 2008.

Discharge diagnosis	Exposed N = 25	Unexposed N = 34	P Value
I10-I15 Hypertensive diseases (%)	3 (12)	10 (30)	0.12
I20-I25 Ischemic heart diseases (%)	8 (32)	4 (12)	0.07
I26-I28 Pulmonary heart disease and diseases of pulmonary circulation (%)	0 (0)	1 (3)	0.96
I30-I52 Other forms of heart disease (%)	3 (12)	10 (30)	0.66
I70-I79 Diseases of arteries, arterioles and capillaries (%)	0 (0)	1 (3)	No value obtained
I95-I99 Other and unspecified disorders of the circulatory system (%)	1 (4)	1 (3)	No value obtained

3.3 Presenting symptoms

Similar proportion of individuals presented with chest pains with exertion, four, chest pain without exertion, ten, tachycardia, nine, and irregular heartbeat, five, during the index and preceding weeks demonstrating an odds ratio respectively of 1.4(0.32- 6.36), 1.6 (0.54 – 4.75), 1.5 (0.5- 4.77) and 1.5 (0.37-5.67). Nausea seemed more prevalent in the index week with five cases vs. only one in the weeks prior and an odds ratio of 8.3 (0.90-75.80). Dyspnea was recorded in seven cases in the index week and thirteen cases in the comparison weeks with an odds ratio of 0.6 (0.21-1.91). Dizziness was observed twice in the index group and four times in the control group with an odds ratio of 0.7 (0.11-3.88). Radiating pain was recorded in nine cases during the entire three week period. Oxygen saturation was recorded on arrival in 15 (60%) patients during the index week and 23 (68%) in the previous two weeks. Three (12%) patients needed oxygen on arrival in the index week and two (6%) patients in the comparison weeks.

The vital signs upon arrival at the ED's are recorded in Table 3. Overall, no statistically significant differences were observed between women attending in the week of the collapse compared with women attending in preceding weeks with respect to blood pressure readings, heart rate, temperature and respiratory rate. When women with an I20-I25 diagnosis are examined specifically there are still no significant differences between the groups on presentation.

Table 3. Vital signs of women admitted to the Emergency Departments in Reykjavik during weeks 39-41 in 2008. Comparison of all cases with cases presenting with I20-I25 diagnoses.

Vital sign	Exposed All diagnoses N = 25	Unexposed All diagnoses N = 34	P value All diagnoses	Exposed I20-I25 dignoses N = 8	Unexposed I20-I25 diagnoses N = 4	P value I20-I25 diagnoses
Heart rate (SD)	84.8 (24.5)	92.4 (33.7)	0.36	69.1 (16.7)	74.5 (10.5)	0.57
Missing	2	3		0	0	
Systolic pressure (SD)	142.9 (29.1)	152.0 (31.0)	0.28	141.3 (34.2)	141.3(22.6)	1.00
Missing	2	3		0	0	
Diastolic pressure (SD)	73.8 (15.6)	80.4 (18.1)	0.17	70.1 (14.4)	77.3 (18.0)	0.47
Missing	2	3		0	0	
Temperature (°C)(SD)	37.0 (0.8)	36.6 (0.7)	0.17	36.6 (1.0)	36.0 (0.8)	No value obtained
Missing	14	15		3	1	

3.4 Clinical tests

Echocardiograms were performed on seven (28%) patients in the collapse week and eight (24%) in the preceding weeks. Three (43%) echocardiograms in the index week were normal and two (25%) in the preceding weeks. Of the women with an I20-I25 diagnosis 3 (38%) from the collapse week underwent an echocardiogram and two (25%) women from the preceding weeks. Pulmonary x-rays were taken 17 (68%) times in the index week and 14 (41%) times in the preceding weeks. Six of the index week's pulmonary x-rays were normal and five in the preceding two weeks. When examining I20-25 diagnoses seven (88%) women from the collapse week had a pulmonary x ray and one (13%) woman from the previous two weeks. 11 cardiac catheterization were performed during the three week period. Patients with an I20-I25 diagnosis underwent the procedure eight times. Four (50%) of the women from the index week underwent cardiac catheterization. Four (100%) women from the previous two weeks underwent cardiac catheterization. All but one had percutaneous coronary intervention and the final woman had a coronary artery bypass graft.

3.5 ECG results

The ECG results are presented in Table 4. They include heart rate, cardiac rhythm, and number of patients with ST depression and T wave inversion. 21 paper ECG were studied, 11 (44%) from the exposed group and 10 (29%) from the control group. They revealed a mean PR interval, QT interval and QRS duration in the normal range. The axis was normal in all cases studied. There was not a significant difference between the two groups in regards to the

ECG results. In addition, those diagnosed with an I20-I25 diagnosis were examined separately. All patients had an ECG recording but seven paper records were recovered. There were five (63%) from the exposed group and two (50%) from the control group. They revealed a mean PR interval, QT interval and QRS duration in the normal range. There was not a significant difference between the two groups in regards to the ECG results. However three (38%) women from the collapse week had T wave inversions and ST depressions compared with one (25%) woman from the preceding two weeks.

Table 4. ECG results from women admitted to the Emergency Departments in Reykjavik during weeks 39-41 in 2008. Comparison of all cases with cases presenting with I20-I25 diagnoses.

Characteristic	Exposed All diagnoses N = 25	Unexposed All diagnoses N = 34	P value All diagnoses	Exposed I20-I25 dignoses N = 8	Unexposed I20-I25 diagnoses N = 4	P value I20-I25 diagnoses
No. of patients undergoing procedure (%)	23 (92)	30 (88)	0.64	8 (100)	4 (100)	No value obtained
Heart Rate (SD)	90.4 (27.3)	90.8 (36.4)	0.97	71.0 (16.7)	67.66	0.75
Missing	6	16		1	1	
Sinus rhythm	20	24	0.38	7	4	1
Atrial fibrillation	3	4	0.94	0	0	No value obtained
T–wave inversion	5	2	0.14	3	1	No value obtained
ST depression	3	1	0.23	3	1	No value obtained

3.6 First blood analysis

The results of the first blood analysis are presented in Table 5. Hemoglobin levels were marginally lower in patients admitted during the index week with a mean of 120.4 g/L compared to 130.9 g/L in the prior two weeks (p=0.06). Cholesterol and HDL cholesterol levels were measured in 22 individuals. The mean of the results lie in the normal range and there was no significant difference between the groups. Creatinine kinase MB was measured in 6 (24%) exposed individuals and 9 (26%) individuals in the previous weeks. The mean of both groups were lower than the cutoff value of < 7 µg/L.[112] All individuals with an I20-I25 diagnosis had blood work done but no significant differences were detected.

Table 5. The first blood analysis from the women admitted to the Emergency Departments in Reykjavik during weeks 39-41 in 2008. Comparison of all cases with cases presenting with I20-I25 diagnoses.

Blood test	Exposed All diagnoses N = 25	Unexposed All diagnoses N = 34	P value All diagnoses	Exposed I20-I25 dignoses N = 8	Unexposed I20-I25 diagnoses N = 4	P value I20-I25 diagnoses
No. of patients undergoing procedure (%)	25 (100)	33 (97)	0.96	8 (100)	4 (100)	No value obtained
Troponin T (ng/L) (SD)	0.37 (1.52)	0.02 (0.03)	0.32	0.87 (2.31)	0.04 (0.07)	0.35
Missing	6	13		0	0	
C reactive protein (mg/L) (SD)	36.5 (57.9)	16.7 (32.8)	0.32	30.7 (47.9)		No value obtained
Missing	14	17		5	4	
Creatinine (µmól/L) (SD)	82.6 (27.2)	89.7 (42.2)	0.47	85.3 (30.3)	78.5 (14.8)	0.78
Missing	2	4		2	2	
White blood cell count (x 109/L) (SD)	8.62 (3.7)	7.37 (1.5)	0.13	9.87 (4.2)	6.63 (0.9)	0.12
Missing	2	1		2	0	
Hemoglobin (g/L) (SD)	120.4 (22.3)	130.9 (19.2)	0.06	118.0 (17.0)	129.8 (26.4)	0.41
Missing	2	0		2	0	
Glucose (mmol/L) (SD)	5.8 (2.3)	5.6 (0.8)	0.61	6.9 (4.2)	5.5 (0.9)	0.62
Missing	7	9		3	1	

3.7 Second blood analysis

The second blood analysis was taken from 13 (52%) patients in the index week and 16 (47%) in the preceding weeks. The hemoglobin levels are now similar, 122 g/L for the index week, from 11(44%) patients, and 123.6 g/L for the preceding weeks, from 12 (35%) patients. Troponin T was measure again in 5 (20%) patients from the index week with a mean of 0.09±0.15ng/L. Nine (27%) patients in the preceding weeks had a second troponin T measurement with an average level of 0.06±0.10 ng/L. C reactive protein was measured for a second time in 6 (24%) patients from the index week and 3 (9%) in the preceding weeks. 4 of the 6 measurements were above the cut off value of <10 mg/L[112] and 1 from the comparison group. A second white blood cell count was taken from 11(44%) patients in the index week with a mean of 8.3±3.1 x 10^9/L. 12 (35%) patients from the previous weeks had lower counts with a mean of 5.9±1.4 x 10^9/L. This difference is statistically significant with a p value of 0.04. Creatinine levels were measured a second time for 10 (40%) women in the index week with a mean of 101.6±47.4. This is higher than for the 11 (32%) women who had a second test and had a mean of 83.5±37.8. This difference is not significant with a p value of 0.34. Nine women with an I20-I25 diagnosis had a second blood test, but no one test was performed in more than half of the women.

4 Discussion

Our population-based study of attendance to the Emergency Departments in Reykjavik indicates approximately 47% increase in female attendance for cardiovascular problems during the week of the economic collapse week in Iceland Female attendees in the collapse week were more likely than women attending during the two preceding weeks to be discharged with a diagnosis of ischemic heart disease which primarily was explained by a drastic increase in cases of angina pectoris. Female attendees in the collapse week were less likely to report lipid abnormalities or family history of cardiovascular disease, although small numbers and missing data hinder definite conclusions.

4.1 Comparison with earlier studies

The economic crisis in Iceland constitutes a unique opportunity to observe a prosperous country swiftly sink into a recession. Earlier studies examine mostly mortality rates over longer periods of time. A few studies have examined the collapse of the Soviet Union. They found that the life expectancy declined steeply from 1990 to 1994. This was largely explained an increase in accidents, alcohol related causes, and cardiovascular disease. However, this situation is not completely comparable as the social upheaval was immense for the newly formed Russia.[113] A better comparison is the recession in South Korea in 1997. One study found that cardiovascular mortality rose immediately with all cause mortality rising after the first year.[114] During Argentinean financial crisis in 1999 the incidence of in-hospital myocardial infarction and congestive heart failure rose significantly. [115] In fact a study examined the mortality rates in the first year of a banking crisis in 19 high income countries during a 42 year period. They discovered a 6.4% increase in short term cardiovascular disease mortality.[94] However another study examining deaths from coronary heart disease in the United States from 1979-1998 drew the opposite conclusions. The researchers found a one-percentage-point reduction in unemployment raised mortality by 0.75%.[116]These studies do not look at the immediate impact of the financial crisis and do not examine subgroups or perform further analysis of these individuals.

An earlier study of visits to the EDs in Reykjavik in the weeks surrounding the economic collapse in Iceland revealed an increase in attendees of the cardiac ED during the collapse week. This increase was marginal in males but significant for women, especially with

regards to ischemic heart diagnoses (ICD 10: I20-I25). This increase is confirmed in our study which in addition narrows down these diagnoses to an increase in cases of angina pectoris (I20).

The increase in ischemic heart disease diagnoses during this time falls in line with other studies on mass-trauma, such as after earthquakes[90] and even football matches.[93] It is well established that emotional triggers can set off acute coronary syndrome[81] which includes unstable angina. Stable angina has also been linked to greater psychosocial stress, including a higher incidence of stressful life events.[117] A highly stressful event, such as receiving a cancer diagnosis, raises the short-term relative risk of death from cardiovascular causes substantially.[88] Another common event is the loss of a loved one which has a 21.1 fold risk of an acute myocardial infarction during the first 24 hours. [80]

Overall we did not observe any differences in characteristics of female attendees during the week of the economic collapse compared to attendees of the two preceding weeks, except with respect to self-reported lipid abnormalities. A study examining Takotsubo syndrome, reported that 73.7% of women over 50 had hypertension and 43.9% hyperlipidemia. In our study the rates of hypertension was lower with 64% of exposed women and 59% of the control group. The rates of blood lipid abnormalities are much lower in this study, with 12% of the collapse group and 35% of the control group reporting abnormalities. [118]

4.2 Possible mechanisms

A possible mechanism is an increase in Takotsubo syndrome which is catecholamine mediated stunning of the heart.[73] The exact mechanism is unknown. It affects mostly postmenopausal women and is characterized by its distinctive areas of akinesia and the lack of obstructive coronary arteries.[119] One possibility is that this is through microvascular dysfunction. This is supported by the abnormal TIMI frame count found in studies.[75] Another possibility is that the catecholamines have a direct myocyte effect. A unique contraction band necrosis has been found during autopsy of confirmed cases.[76]

Half of the women with an ischemic heart diagnosis in the collapse week underwent cardiac catheterization but all had obstructive coronary arteries. Another possibility is that weak atherosclerotic plaque may have ruptured. [81] Over 90% of women in both groups had a prior diagnosis of heart disease. The groups did not either differ in regard to prior diagnosis of chronic ischemic heart disease with a third in each group. Yet, small numbers and missing data hinder definite conclusions in comparisons.

4.3 Strengths and limitations

An important strength of this study is the setting. The personal identification numbers and complete electronic registries entails that we have an opportunity to look at the capital population as a whole. This crisis was very contained and had a very definitive trigger point that is often missing when financial crises occur and enables us to create a collapse week with confidence. The short study period was chosen to limit seasonal variation, and to hone in on the immediate aftermath, but a longer control period may have strenghtened our findings. Also, the study base of Reykjavik did not change much during the three weeks of observation, thus it is unlikely that confounding or selection forces affect our results.

Using electronic medical charts we are dependent on others (clinicians) to correctly regiser the data and we may therefore miss individuals who are incorrectly filed. Many variables used in this study were indeed lacking in completeness as clinicans may not complete items that they felt did not apply to their patient. Unfortunately there was more missing data than first thought which hampered our ability to draw definite conclusions. There also seems to be more missing data in the non-exposed group (before the collapse) compared to the week of the collapse. Fewer blood tests were ordered and fewer paper ECGs were recorded before the collapse which may have generated some bias. Lastly, an important weakness in this study is the small population and how few visits there are to Landspitali during the study period. This limits our statistical power.

4.4 Conclusions and implications

We can conclude that the economic recession in Iceland had a short term affect on attendance of women to the Emergency department for cardiovascular symptoms, particularly for angina pectoris. Thus these findings may even be considered as a confirmation of the stressful circumstance that Icelanders found themselves in. The dramatic downturn of this prosperous economy created a unique opportunity to study the emotional effects. This study is part of a growing literature demonstrating the variety of emotional stressors that can trigger cardiovascular incidents. To strengthen the findings it might be valuable broaden the scope and examine the entire country and include a longer observation period.

Due to the sudden nature of these events it is difficult to prevent them but it is possible to plan for them when a mass crisis occurs. This relates to both natural disasters and manmade occurrences. Subjective crises and societal changes can have a real physical effect and must be taken into account when planning hospital services.

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