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Current interventional approach to coronary artery disease

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SUMMARY

Coronary artery disease is the main cause of death in both genders worldwide. Many preclinical and clinical studies present the concept of modifiable and non modifiable cardiovascular risk factors. The basic management of the coronary artery disease is medical, but the prognosis in many patients can be improved by potentially invasive procedures, such as the percutaneous coronary intervention (PCI) and the coronary artery bypass grafting (CABG). The cardiovascular risk scores may help cardiologists and cardiac surgeons alike to individualize the risk profile of patients in order to better define the revascularization strategy and to appropriately counsel the patient, in same time reducing the morbidity and mortality.

The first part of the thesis evaluates the validity of both forms of the most used cardiovascular tool in the present day, the European System for Cardiac Operative Risk Evaluation (EuroSCORE). This prospective study tests the validity of a preoperative risk stratification model EuroSCORE in predicting short-term mortality after coronary artery bypass surgery in Czech adult cardiac population. The other benefit is that it is first study in the literature that showed that EuroSCORE, can be routinely used to estimate not only the perioperative risk of patients undergoing CABG, but also to predict short-term prognosis of patients undergoing percutaneous coronary intervention in elective settings and/or medical treatment.

The second part of the thesis concentrates on the prevalence of stress-induced myocardial stunning (Tako-Tsubo syndrome) among patients undergoing urgent coronary angiography for suspected acute myocardial infarction. Only 4 of the 5876 patients undergoing urgent coronary angiography for suspected acute myocardial infarction at three tertiary cardiology centers in the Czech Republic, during a four-year period, fulfilled the criteria for stress-induced myocardial stunning. This proves that it is extremely rare distinct syndrome among European patients undergoing emergency coronary angiography for suspected acute myocardial infarction.

The third part of the thesis obtains a realistic contemporary picture of how patients with ST-elevation myocardial infarction (STEMI) are treated in different European countries.

Most North, West and Central European countries used primary-percutaneous coronary intervention (PCI) for the majority of their STEMI patients. Primary PCI was the dominant reperfusion strategy in 16 countries and thrombolysis in 8 countries. The lack of organised primary percutaneous coronary intervention networks was associated with fewer patients overall receiving some form of reperfusion therapy. The best results are achieved in countries with PCI centers that offer 24/7 primary percutaneous coronary intervention services.

1. Introduction-risk prediction in cardiology

1.1. Cardiovascular statistics

Heart diseases and circulatory system are the main cause of death in both genders in almost all countries of Europe. Almost half of all deaths in Europe (48%) are from cardiovascular disease (CVD) (54% of deaths in women and 43% of deaths in men).

The main forms of cardiovascular diseases are coronary heart disease (CHD) and stroke. Less than half of all deaths from CVD are caused by coronary heart disease and nearly third are provoked by stroke (1).

Coronary heart disease by itself is the single most common cause of death in Europe accounting for 1.92 million deaths in Europe each year. Over one in five women (22%) and over one in five men (21%) die from this disease (Figure 1 and Figure 2).

Stroke by itself is the second most common cause of death in Europe, accounting for 1.24 million deaths in Europe each year. Over one in six women (17%) and one in ten men (11%) die from the disease.

Death rates from CVD in the United States in 2005 have declined by 26.4%, during the period from 1995-2005, but the burden of the disease still remains high.

In 2006, coronary heart disease was estimated to occur in 80,000,000 individuals in the United States, resulting in approximately 864,480 deaths, and 7 095 000 hospital discharges. The cost to society was 475 billion dollars in 2009. (2)

Nearly 2400 Americans die of CVD each day, an average of 1 death every 37 seconds. CVD claims approximately as many lives as cancer, colo-rectal diseases, accidents and diabetes mellitus combined. (2)

There are different measures of morbidity such as prevalence, incidence, years of healthy life cost etc. Therefore, it is difficult to obtain comparable data on morbidity from CVD. Presently, there are no readily available sources of CVD morbidity data in Europe. (3)

The most recent Europe-wide comparable study on CVD morbidity is the project WHO MONICA (monitoring trends and determinants in cardiovascular disease) (4). It examined the incidence of major coronary events in 37 different groups in 21 countries. The project has shown that the incidence of coronary events is higher in MONICA project populations in Northern, Central and Eastern Europe than in Southern and Western Europe. The incidence of coronary events is falling in most of the MONICA project populations in Western and Northern Europe, while the tendency of falling is not so fast in Southern, Central and Eastern Europe. In some cases the incidence of coronary events within these population groups is rising. The geographical pattern in coronary event rates is similar to the pattern in death rates (Table 1).

In the United States, the average annual rates of first cardiovascular events rise from 3 per 1000 men in the age range 35 to 44 years, to 74 per 1000 men at 85 to 94 years of age. For women, comparable rates occur 10 years later in life. The gap narrows with advancing age (Figure 3).

In adults younger than 75 years, cardiovascular events due to coronary heart disease occur in men more often than in women. Women have a higher proportional share in the total number of stroke related events than men.

Despite the great improvements in the risk factors control and the fast evolution of the revascularization methods, the cardiovascular diseases remain the biggest health burden of the modern civilization.

Figure 1. Yearly mortality in men by all causes in Europe

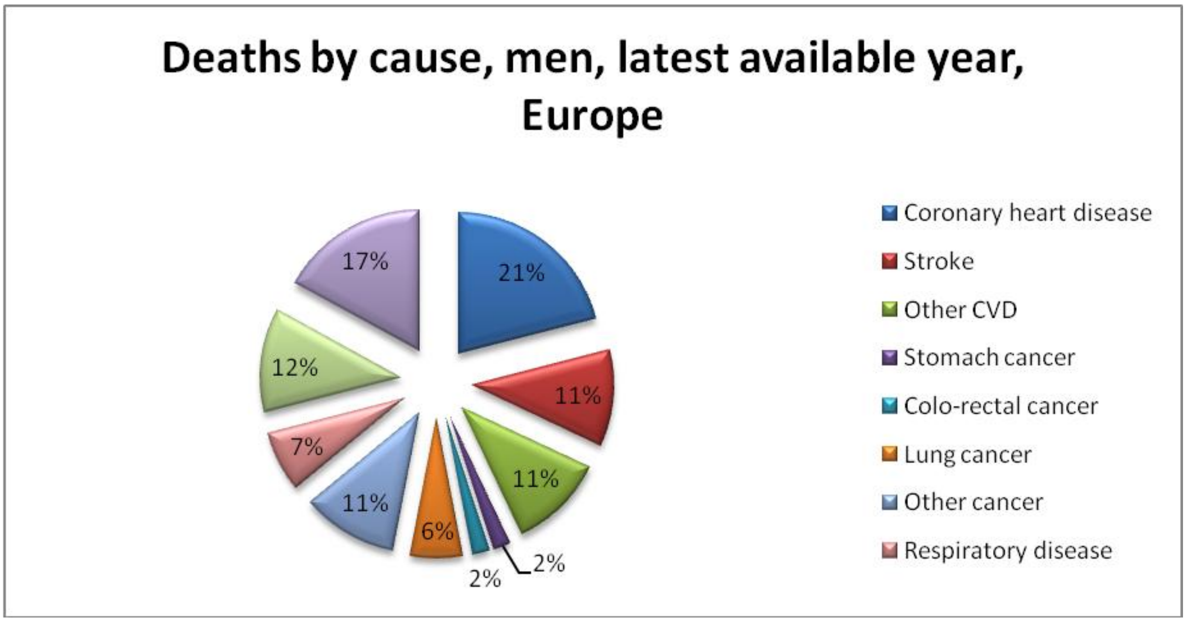


Figure 2. Yearly mortality in women by all causes in Europe

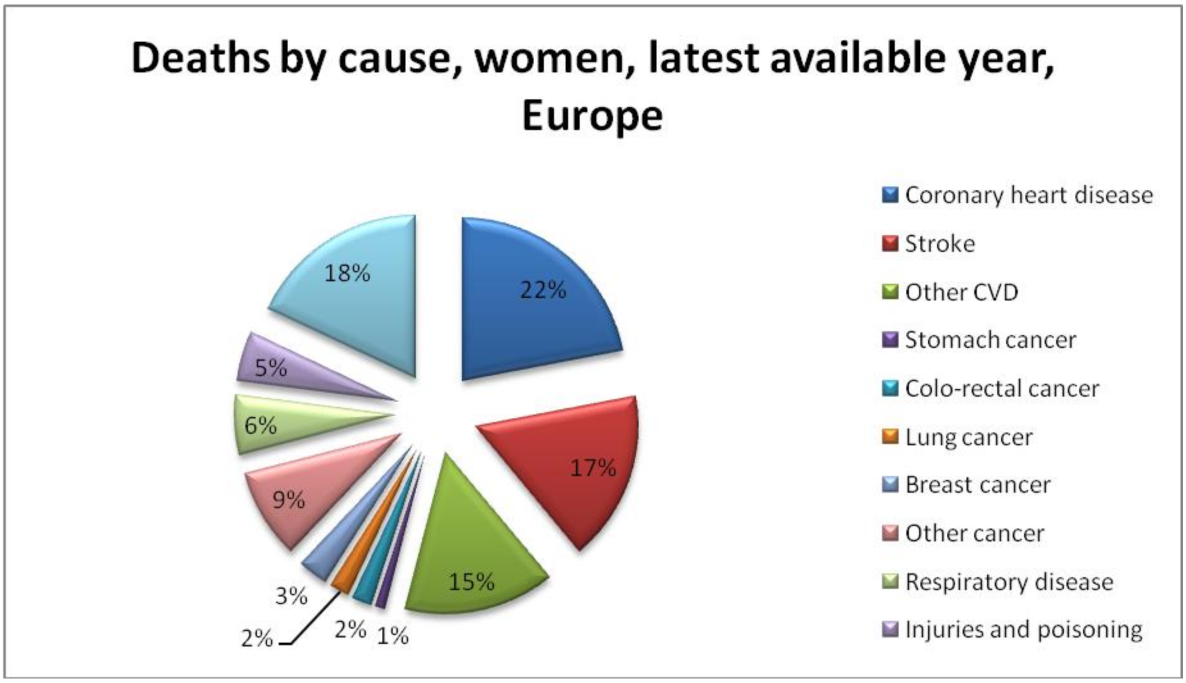


Figure 3. Prevalence of CVD in adults≥20 years of age by age and sex (NHANES: 2005-2006). Source: NCHS and NHLBI. These data include coronary artery disease, heart failure, stroke and hypertension.

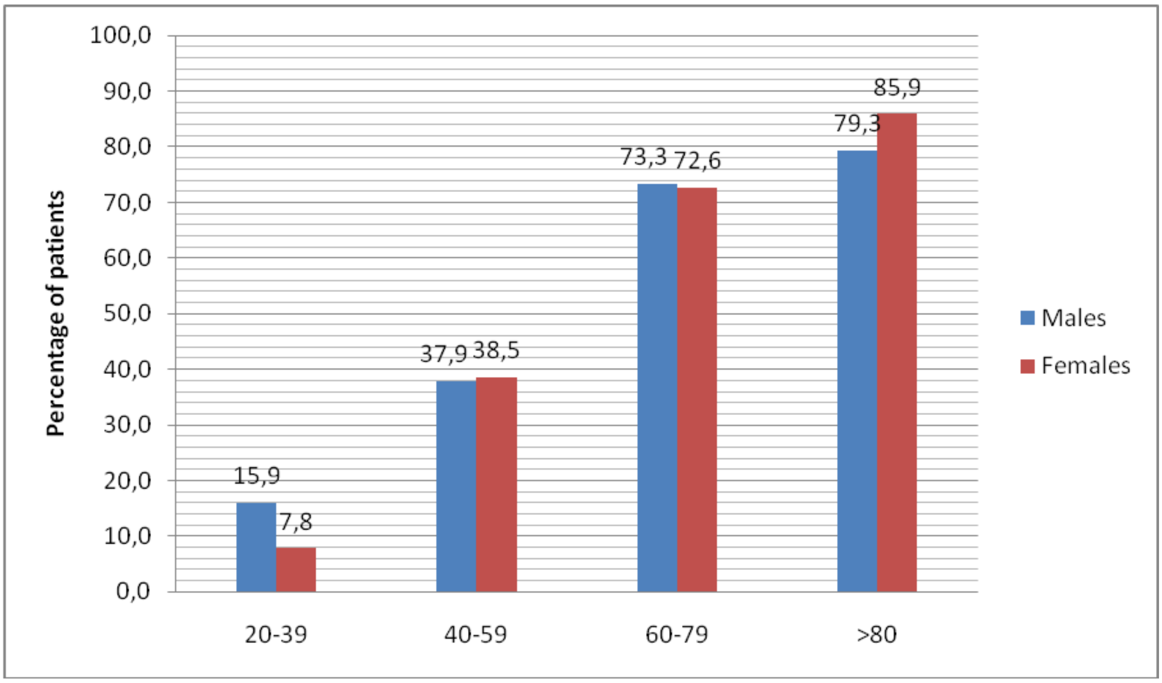


Table 1. Coronary event rates, coronary case fatality, annual change in coronary event rates and annual change in coronary case fatality by sex, adults aged 35-64, latest available year, MONICA European Project populations

MONICA population	MONICA population code	Survey years	Coronary event rate	Coronary case fatality within 28 days	Annual change in coronary event rate	Annual change in coronary case fatality
			Events per 100,000	%	%	%
MEN						
Belgium-Charleroi	BEL-CHA	1983/92	487	50	0.3	-1.8
Belgium-Ghent	BEL-GHE	1983/92	346	47	-3.2	-1.6
Czech Republic	CZE-CZE	1984/93	515	53	-0.4	0.7
Denmark-Glostrup	DEN-GLO	1982/91	517	53	-4.2	1.5
Finland-Kuopio Province	FIN-KUO	1983/92	718	46	-6.0	1.0
Finland-North Karelia	FIN-NKA	1983/92	835	48	-6.5	-0.5
Finland-Turku/Loimaa	FIN-TUL	1983/92	549	49	-4.2	-0.2
France-Lille	FRA-LIL	1985/94	298	59	-1.1	-0.3
France-Strasbourg	FRA-STR	1985/93	292	49	-3.9	-1.7
France-Toulouse	FRA-TOU	1985/93	233	40	-2.1	-3.8
Germany-Augsburg	GER-AUG	1985/94	286	55	-3.2	1.3
Germany-Bremen	GER-BRE	1985/92	361	50	-3.4	-0.9
Germany-East Germany	GER-EGE	1985/93	370	50	-0.5	1.7
Iceland	ICE-ICE	1981/94	486	37	-4.7	-2.1
Italy-Area Brianza	ITA-BRI	1985/94	279	41	-2.3	-0.8
Italy-Friuli	ITA-FRI	1984/93	253	45	-0.9	-2.0
Lithuania-Kaunas	LTU-KAU	1983/92	498	55	1.2	1.0
Poland-Tarnobrzeg Vovoidship	POL-TAR	1984/93	461	83	1.1	1.2
Poland-Warsaw	POL-WAR	1984/94	586	60	0.8	-0.4
Russia-Moscow (control)	RUS-MOC	1985/93	477	61	-1.0	3.0
Russia-Novosibirsk (control)	RUS-NOC	1984/92	464	60	0.9	-0.1
Spain-Catalonia	SPA-CAT	1985/94	210	37	1.8	-1.7
Sweden-Gothenburg	SWE-GOT	1984/94	363	44	-4.2	0.3
Sweden-Northern Sweden	SWE-NSW	1985/95	509	36	-5.1	-2.9
Switzerland-Ticino	SWI-TIC	1985/93	290	34	-2.6	-4.2
Switzerland-Vaud/Fribourg	SWI-VAF	1985/93	231	38	-3.6	-3.0
United Kingdom-Belfast	UNK-BEL	1983/93	695	41	-4.6	-1.5
United Kingdom-Glasgow	UNK-GLA	1985/94	777	48	-1.4	-1.3
Yugoslavia-Novi Sad	YUG-NOS	1984/95	422	52	0.4	-0.4
Women						
Belgium-Charleroi	BEL-CHA	1983/92	118	59	1.1	-1.8
Belgium-Ghent	BEL-GHE	1983/92	77	58	-3.0	-1.8
Czech Republic	CZE-CZE	1984/93	101	54	2.1	-1.2
Denmark-Glostrup	DEN-GLO	1982/91	140	58	-2.5	2.5
Finland-Kuopio Province	FIN-KUO	1983/92	124	39	-4.5	1.0
Finland-North Karelia	FIN-NKA	1983/92	145	41	-5.1	-0.2
Finland-Turku/Loimaa	FIN-TUL	1983/92	94	49	-4.5	-1.9
France-Lille	FRA-LIL	1985/94	64	70	-1.6	0.8
France-Strasbourg	FRA-STR	1985/93	64	57	-6.6	-2.3
France-Toulouse	FRA-TOU	1985/93	36	60	-1.7	-3.6
Germany-Augsburg	GER-AUG	1985/94	63	65	0.9	-0.4
Germany-Bremen	GER-BRE	1985/92	81	52	0.7	-2.9
Germany-East Germany	GER-EGE	1985/93	78	63	2.5	-2.2
Iceland	ICE-ICE	1981/94	99	34	-3.7	-1.0
Italy-Area Brianza	ITA-BRI	1985/94	42	53	-3.5	-4.8
Italy-Friuli	ITA-FRI	1984/93	47	50	-0.8	-2.0
Lithuania-Kaunas	LTU-KAU	1983/92	80	54	2.7	-1.2
Poland-Tarnobrzeg Vovoidship	POL-TAR	1984/93	110	88	-0.1	-0.7
Poland-Warsaw	POL-WAR	1984/94	153	59	1.0	-2.1
Russia-Moscow (control)	RUS-MOC	1985/93	92	60	-6.7	1.5
Russia-Novosibirsk (control)	RUS-NOC	1984/92	111	67	2.3	0.3
Spain-Catalonia	SPA-CAT	1985/94	35	46	2.0	1.5
Sweden-Gothenburg	SWE-GOT	1984/94	84	45	-3.7	1.2
Sweden-Northern Sweden	SWE-NSW	1985/95	119	34	-2.4	0.4
United Kingdom-Belfast	UNK-BEL	1983/93	188	42	-2.4	-1.7
United Kingdom-Glasgow	UNK-GLA	1985/94	265	46	0.2	-2.1
Yugoslavia-Novi Sad	YUG-NOS	1984/95	101	50	2.8	0.5

1.2. Cardiovascular Risk Factors

The prospective community based Framingham Heart Study provided rigorous support for the concept that hypertension, hypercholesterolemia, and other factors are correlated with cardiovascular risk. Similar observational studies performed bolstered the concept of “risk factors” for cardiovascular disease.

The cardiovascular risk factors that have emerged from such studies fall into two categories: those modifiable by lifestyle and/or pharmacotherapy and those such as gender and age that are immutable. Hypertension and hypercholesterolemia predict coronary risk, but other nontraditional risk factors, such as level of homocysteine, lipoprotein (a) or infection remain controversial. The causality of some biomarkers that predict cardiovascular risk, such as C-reactive protein, still remains uncertain.

The table 2 lists the currently accepted cardiovascular risk factors. (5)

The analysis of the major cardiovascular risk factors and mortality shows a high correlation between the expected and observed mortality rates with respect to the main three risk factors: smoking, serum cholesterol and hypertension (6).

Table 2: Cardiovascular risk factors

Risk factors that cannot be changed
Age
Gender
Heredity
Risk factors that can be changed
Hypertension
Hypercholesterolemia
Lipoprotein(a)
Cigarette smoking
Obesity
Glucose intolerance
Diabetes Mellitus
Fibrinogen
Cocaine
Behavioral factors (stress, type A)
Protective factors
HDL cholesterol
Exercise
Estrogen
Moderate alcohol intake

1.2.1. Smoking

Cigarette smoking currently causes an estimated 5 million deaths annually (9% of all deaths). If current smoking patterns continue, by 2030 the global burden of disease attributable to smoking cigarettes will reach 10 million deaths annually. (6)

Cigarette smoke is a complex mixture of over 4,000 chemical components, distributed in particulate and gaseous phases. (7)

Two components of the cigarette smoke cause cardiovascular diseases: nicotine and carbon monoxide. Nicotine causes acute and chronic cardiovascular effects, mainly through sympathetic activation. (8)

Carbon monoxide (CO) is suspected to play a major role in cigarette smoke-induced cardiovascular diseases. There is epidemiologic evidence that workers exposed to high CO concentrations have more cardiovascular morbidity and mortality than the expected rate in population. (9)

Cigarette smoke is supposed to have a direct influence in the vessel endothelium. The production of the superoxide radical has been increased, thus inactivating the production of NO. Higher oxidative stress in vessel endothelium in smokers increases the LDL oxidation.

In smokers, there is no adequate vasodilatation during the physical activation (same changes have been noticed also in passive smokers).

1.2.2. Hypertension

Worldwide nearly 1 billion individuals are hypertensive. (10) Based on a Framingham Heart study, normotensive patients age 55 can expect 90% lifetime risk for subsequent development of hypertension. (11)

Despite the asymptomatic nature of hypertensive disease with symptom onset delayed 20-30 years after development of systemic hypertension, there is direct association between systemic hypertension and increased morbidity and mortality. World Health Organization (WHO) estimates that hypertension underlies one in eight deaths worldwide, making elevated blood pressure the third leading cause of mortality. (10) In fact, hypertension accounts for the single most treatable risk factor for myocardial infarction, peripheral vascular disease, chronic heart failure, renal failure and aortic dissection. (12)

In prospective randomized trials, successful treatment of hypertension has been associated with 35-40% reductions in the incidence of stroke, 50% reduction in chronic heart failure, and 25% reduction in myocardial infarctions. (10) (12)

Pathophysiologic mechanisms underlying predisposition to hypertension remain, for the most part, unclear. Both genetic and environmental factors play contributory roles. (13) By some estimations, genetic predominance account for only 30-40% of the hypertensive disease. (13) With respect to environmental factors, the reports suggest that there is an association between the body mass index and hypertension, and dietary sodium intake is associated with long term risk for development of hypertension. (14), (15)

Hypertension causes mechanical endothelial injury. Endothelium dependant relaxation is damaged; the response to acetylcholine has been reduced. The answer of the direct muscle relaxants, such as nitroprusid is normal. Hypertension provokes an oxidative stress in the vessel's wall with production of superoxide radical, which inactivates NO. This leads to dominance of the vasoconstriction effects of the endothelin. (16) In addition, increased blood pressure suppresses the platelet NO production and responsiveness. This may contribute to the increase in platelet P-selectin and hence in circulating monocyte-platelet aggregates. (17)

The system renin – angiotensin - aldosteron also plays an important role (18). The production of NO has been decreased, with increased activity of the renin-angiotensin-aldosteron system. The endothelium has been damaged also with angiotensin II, which produces vasoconstriction, increases the permeability of the endothelium, stimulates the proliferation of the fibrous tissue and increases the oxidative stress (endothelial cells contain angiotensin converting enzyme). (19)

1.2.3. Hypertension as an operative risk factor

In a perioperative setting, there is little evidence to suggest that mild-to-moderate degrees of hypertension adversely affect morbidity and mortality. In fact, ACC/AHA guidelines state that mild-to-moderate hypertension does not represent and independent risk factor for perioperative cardiovascular complications. (20)

In cases of mild-to-moderate hypertension, few controlled trials assessing the association between preoperative hypertension and perioperative morbidity and mortality are available. Howell and colleagues published a meta-analysis summarizing 30 studies including more than 12,995 patients for whom and association between hypertension and perioperative complications could be assessed. The odds ratio of 1.31 suggested a slightly increased risk for perioperative cardiovascular complications in patients with preexisting hypertension. In conclusion, the authors mention that such a small odds ratio in the setting of a "low perioperative event rate" likely represents a clinically insignificant association between preexisting hypertension and cardiac risk. (21)

As opposed to the apparently low perioperative risk posed by mild-to-moderate hypertension, cases of severe hypertension (diastolic blood pressure ≥ 110mm Hg) frequently lead to questions as to whether elective surgery should be postponed to allow for titration of antihypertensive therapy to acceptable systemic blood pressures. Guidelines published by the ACC/AHA suggest that systemic blood pressures exceeding 180 mm Hg systolic pressure and/or 110 mm Hg diastolic pressure should be controlled before surgery. (20) According to the meta-analysis performed by Howell and colleagues, a surgery should not be canceled in the setting of severe hypertension, however a careful preoperative assessment for target organ damage (e.g. cardiovascular, renal, cerebrovascular disease) should be performed preoperatively, and intraoperative arterial pressure should be maintained within 20% of preoperative blood pressures. (21)

In addition, uncorrected hypertension predisposes to myocardial ischemia and/or heart failure during angiography. (22)

1.2.4. Serum cholesterol

Worldwide, high cholesterol levels are estimated to cause 56% of ischemic heart disease and 18% of strokes, amounting for 4.4 million deaths annually.

As countries move through the epidemiologic transition, the plasma cholesterol levels tend to rise. Social and individual changes that accompany urbanization clearly play a role because plasma cholesterol levels tend to be higher among urban residents than among rural residents. In high income countries, mean population cholesterol levels are generally falling, but in low and middle income countries, there is wide variation in these levels. (23)

Early clinical trials of cholesterol (mainly LDL-C) found a small but significant reduction in cardiac events, but no decrease in total mortality, which lead to aggressive population-based treatment of hypercholesterolemia. The Scandinavian Simvastatin Survival Study in men with hypercholesterolemia and coronary heart disease showed reduced major coronary events by 44% and total mortality by 30% with simvastatin. (24) The Cholesterol and Recurrent Events (CARE) study and the Long-Term Intervention with Pravastatin in Ischemic Heart Disease (LIPID) demonstrated reduced cardiac events and cardiovascular deaths in women and men with coronary heart disease and normal to only mildly elevated LDL-C levels. (25), (26)

Some of the early statin trials performed in patients without preexisting coronary heart disease and increased cholesterol levels, such as the West of Scotland Coronary Prevention Study (WOSCOPS) with pravastatin and the Air Force/Texas Coronary Atherosclerosis Study (AFCAPS/TexCAPS) with lovastatin demonstrated significant reductions in cardiovascular events even in the patients without preexisting symptomatic coronary heart disease.

More recent studies have enrolled patients with dyslipidemia and other risk factors (diabetes mellitus, hypertension), with established cardiovascular disease or high risks for coronary heart disease. The Heart Protection Study (HPS), the Anglo-Scandinavian Cardiac Outcomes Trial Lipid-Lowering Arm (ASCOT-LLA), the Collaborative Atorvastatin Diabetes Study

(CARDS) terminated earlier than initially planned demonstrating significant reduction in major cardiovascular events reducing the lipids levels.

The most compelling data supporting the concept that “lower is better” come from studies in which different statin regimens were directly compared. Such a study is the Treat to New Targets (TNT) trial and the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT). The results from these studies have been widely embraced, and clinical practice is clearly evolving to treating coronary heart disease and high-risk patients more aggressively for LDL reduction.

One percent reduction of LDL concentration leads to 2% reduction of cardiovascular events. Low levels of HDL cholesterol present independent cardiovascular risk factor. The increased levels of HDL eliminate the risks of elevated LDL. Increasing the levels of HDL for 1% reduces the cardiovascular events for 2-3%. (27)

Increased triglyceride concentration presents also an independent cardiovascular risk factor especially for females. Increased level of triglycerides by 1% increases the level of cardiovascular events by 15% in males and 37% in females. (27)

1.2.5. Diabetes Mellitus

Worldwide rates of diabetes mellitus, predominantly diabetes mellitus type 2 are in rise, as a consequence of, or in addition to increased body mass index and decreasing levels of physical activity. The prevalence of diabetes mellitus is estimated to increase to 4.4% of the population by the year 2030 (366 million individuals) from 2.8% in 2000 (171 million individuals). (28)

The frequency and severity of cardiovascular disease is increased in individuals with type 1 or type 2 diabetes mellitus. The American Heart Association has designated diabetes mellitus as a major risk factor for cardiovascular disease (same category as smoking, hypertension and hyperlipidemia). The Framingham Heart Study revealed a marked increase in peripheral artery disease, chronic heart failure, coronary artery disease, myocardial infarction and sudden death (risk increase in one to fivefold) in diabetes mellitus. (29)

Type 2 diabetes patients without prior myocardial infarction have a greater risk for coronary artery events than nondiabetic individuals who have had a prior myocardial infarction. (30) This was demonstrated by Haffner, who compared the prognosis of 1,373 nondiabetic patients with that of 1,059 diabetic patients. With a follow up of 7 years, the incidence of myocardial infarction in nondiabetic patients with or without a history of myocardial infarction was 18.8% or 3.5% respectively. For diabetic patients, these percentages were 45% and 20.2% respectively ($p<0.001$).

Pathophysiologically, the production of superoxide radicals, which inactivates nitric oxide have increased in patients with diabetes mellitus. On the other hand, the production of vasoconstrictive prostaglandins has been increased, while the endothelium dependent and independent vasodilatation has been disturbed.

The prognosis for individuals with diabetes mellitus who have coronary artery disease is worse than that for patients without diabetes mellitus. Coronary artery disease in diabetic patients is marked by the extent and dissemination of anatomical lesions, by its latency, as it often remains asymptomatic or minimally symptomatic, and by its more severe clinical course. Coronary heart disease is more likely to involve multiple vessels in individuals with diabetes mellitus. (31)

Type 2 diabetes mellitus significantly increases the recurrence rate and the incidence of heart failure or death. In the study of Miettinen based on data from the final MONICA register (FIN-MONICA) concerning 4.065 patients including 620 diabetic patients aged 25 to 64 years hospitalized for a first myocardial infarction, the presence of diabetes significantly increased mortality at the 28^{th} day by 58% in men and by 160% in women. At 1 year, the mortality of diabetic vs. nondiabetic patients was 44.2% vs. 32.6% in men and 36.9% vs. 20.2% in women, respectively. At 5 years, the mortality was as high as 50% in diabetic patients, i.e. more than twice that observed in nondiabetic patients. (32)

In diabetic patients, global management of other risk factors significantly improves the cardiovascular prognosis, especially in patients with microalbuminuria. In the Danish Steno 2 randomized, open label study conducted in 160 patients with type 2 diabetes with a mean age of 55 years and a mean follow up of 7.8 years, intense multifactorial management vs. conventional treatment significantly decreased all physiological risk factors and reduced the primary endpoint of the study combining mortality, nonfatal myocardial infarction, nonfatal stroke, revascularization or reduced the risk of amputation by 53%, the risk of nephropathy by 61%, the risk of retinopathy by 58% and the risk of autonomic neuropathy by 63%. (33)

In addition to coronary artery disease, cerebrovascular disease is increased in patients with diabetes mellitus (1.8 to nearly 6 fold increase in stroke). (34), (35)

1.3. Cardiovascular treatment choices

The coronary artery diasease is a lifelong condition and the basic management is medical, but the prognosis in many patients can be improved by potentially invasive procedures, such as the percutaneous coronary intervention (PCI) and the coronary artery bypass grafting (CABG). The choice of therapy for multivessel coronary artery disease must be made by comparing percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). (36)

In the mid 1980s, when PCI comprised only percutaneous transluminal coronary angioplasty (PTCA), the first comparisons of catheter intervention to CABG were begun. By the early to mid 1990s, nine randomized clinical trials had been published comparing PTCA with CABG in patients with significant coronary artery disease. Only the BARI trial was statistically appropriate for assessing mortality. (37) The conclusions of these studies included similarities between the two approaches with respect to relief of angina and 5-year mortality. Costs were initially lower in PCI group, but by 5 years had converged because of repeat PCI procedures precipitated by restenosis, occurring in 20% to 40% of the PCI group. (38)

The only clear difference between PCI and CABG for patients with multivessel disease was identified in the diabetic patient subset of the Bypass Angioplasty Revascularization Investigation (BARI) trial. (39), (40), (41)

A difference in mortality was seen in a subgroup analysis of the BARI trial where both insulin dependent and non-insulin-dependent diabetic patients with multivessel disease had lower 5-year mortality with CABG (19.4%) than with PCI (34.5%). (41)

These studies were outdated by the time of their publication. For the patient undergoing PCI, stents had become the standard with a significant decrease in emergent CABG, due to reduced acute closure, as well as a decrease in repeat procedures, due to less restenosis. (42), (43)

For the patient undergoing CABG, off-pump bypass (OPCAB) became more common during this time period with its potential to decrease complications. (44), (45) Additionally, the importance of arterial grafting with its favorable impact on long-term patency was recognized. (46), (47)

To address the changes in PCI and CABG therapy, four more randomized trials were undertaken. The results of these newer studies were similar to the results of the earlier ones. In the ARTS trial, diabetic patients had poorer outcomes with PCI. Repeat procedures, though higher in the PCI group at 20%, were significantly lower than with the earlier trials. (48) CABG patients also had improved outcomes, for instance, cognitive impairment occurred in fewer patients in the recent studies. (38)

A meta-analysis of 13 randomized trials identified a 1.9% absolute survival advantage at 5 years in the CABG patients, but no significant difference at 1,3, or 8 years. For patients with multivessel disease, CABG provided survival advantage at five to eight years (Figure 4) and for four years for diabetics. Trials that included stents reduced the need for repeat revascularization by half. (49)

As with the first generation of PCI versus CABG trials, the second generation trials were outdated before publication due to the introduction of the drug eluting stents. These stents introduced new standards in the interventional cardiology, demonstrating superior effectiveness in reducing the incidence of in-stent restenosis.

The ARTS II and BARI II trials address this issue. The ARTS II trial suggests the possibilities that drug eluting stents (DESs) make higher influence on myocardial infarction and mortality than coronary artery bypass grafting. (50)

Most of the observational studies that have been reported show that patients with multivessel coronary artery disease who are treated with DESs or CABG have similar rates of death, myocardial infarction and stroke, but repeat revascularization is more frequent after DES (Table 3). (50)-(58) Two of the studies showed lower mortality rates after CABG. The New York registry study demonstrated lower mortality after CABG but only after risk adjustments,

(51) while another study showed survival benefit for CABG patients with diabetes mellitus. (52)

Most of these studies showed that diabetic patients have worse outcomes regardless of treatment approach, and some, but not all of these studies suggest that diabetic patients receive more benefit from CABG than from PCI with DESs. (50), (52)-(58)

According to the present knowledge, CABG offers a survival advantage over medical therapy in patients where the stenosis in the left main coronary artery is greater than 50%. (59)

Despite the lack of clear evidence for the long term safety and efficacy DESs have been used in 21% in North America and 26% in Europe. (60)

In two registry studies that compared the outcomes of CABG versus PCI with DESs in patients with left main disease, both treatments produced similar 1-year mortality rates, but repeat revascularization was more frequent after PCI. (61), (62)

Outcomes appear to be much better when the disease is proximal and does not involve the distal bifurcation or trifurcation. (63), (64)

Given the current data, CABG remains the standard of care for patients with left main stenosis. This treatment will likely continue to be the best option for most of these patients, because most left main disease is accompanied by other features that make PCI challenging (such as bifurcating or multivessel disease and heavy calcification). However, it seems that PCI with DESs can achieve reasonable results and is still an option for patients, who are hemodynamically unstable or ineligible for CABG, especially those without distal bifurcating disease.

Figure 4: Randomized trials of coronary artery bypass graft surgery (CABG) versus coronary angioplasty (PTCA) in patients with multivessel coronary disease showing risk difference for all cause mortality in 1, 3, 5, and 8 years post initial revascularization. A. All trials. B. Multivessel trials. CABG=coronary artery bypass graft surgery; PTCA=coronary angioplasty.

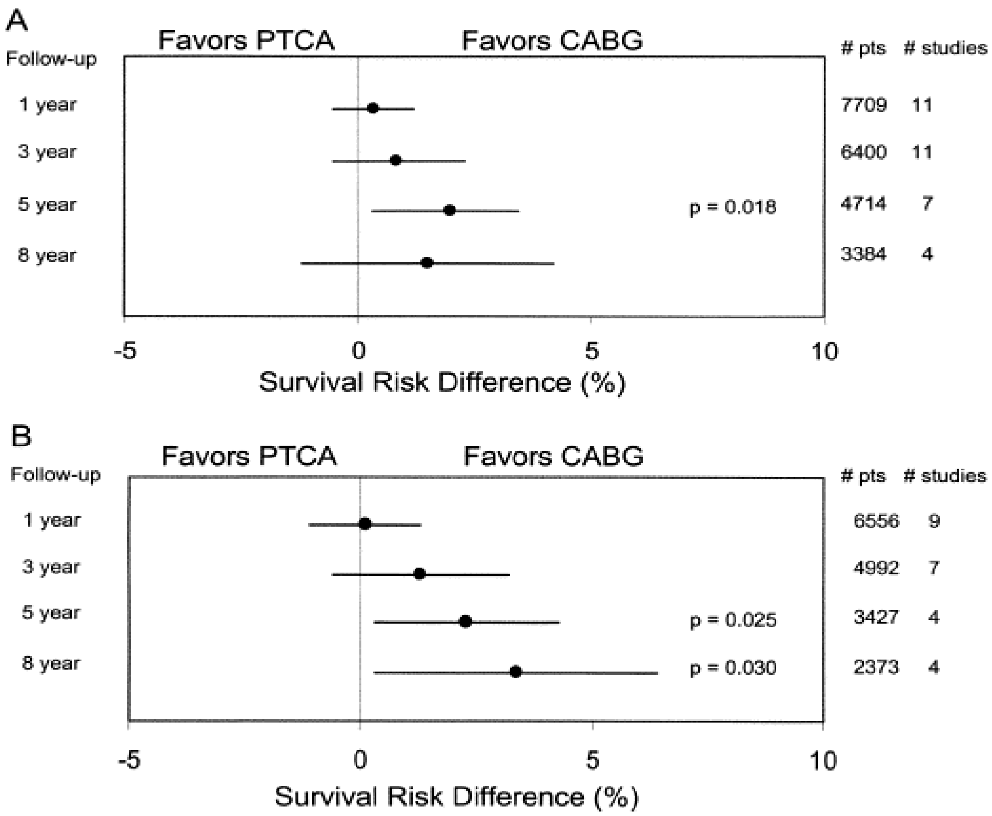


Table 3. Observational studies of percutaneous coronary intervention with drug eluting stents versus coronary artery bypass grafting in multivessel coronary artery disease

Authors	Type	Follow -Up (yr)	Treatment	No.	Death (%)	MI (%)	Stroke (%)	Repeat Revasc. (%)	Adjusted Mortality Rate (HR DES:CABG)
Hannan EL,et al.[51]	State registry (New York)	1.5	DES-2v	7,482	5.3	2.1	NR	*	1.41, P=0.003
			CAB-2v	2,235	5.3	1.7	NR	*	
			DES-3v	2,481	6.9	3.1	NR	*	1.25, P=0.03
			CAB-3v	5,202	6.7	1.9	NR	*	
Javaid A, et al.[52]	Single-center (Washington, DC)	1	DES-2v	884	8.1	2.7	2	13.3	3.3, P=0.01
			CAB-2v	196	2.6	0.5	0.1	5.5	
			DES-3v	95	10.9	3.6	1.1	18.8	3.9, P=0.002
			CAB-3v	505	3.1	2	1	5.7	
Park DW, et al.[54]	Single-center (Seoul, Korea, Asan Medical Center)	3	DES	1,547	4.4	1.2	0.5	11.8	0.85, P=0.45
			CAB	1,495	7	0.9	1.1	4.6	
Rodriguez AE, et al.[55]	Multicenter registry (Argentina)	3	DES	225	13	14	7	32	NR
			CAB	225	22	14	3	13	
Serruys PW, et al.[56]	Multicenter registry (International)	3	DES	607	3	2.8	2.5	11	NR
			CAB	602	4.3	4	2.5	5.3	
Varani E, et al. [57]	Single-center (Italy)	1	DES	111	3.6	1.8	0	12.6	NR
			CAB	95	5.3	4.2	3.2	2.1	
Yang JH, et al. [58]	Single-center (Seoul, Korea, Samsung Medical Center)	1	DES	441	2.1	1.4	0.7	9.2	NR
			CAB	390	3.2	0.3	0.8	0.5	

Abbreviations: CAB = coronary artery bypass; DES = drug eluting stent; HR = hazard ratio**;** MI = myocardial infarction; NR = not reported; Revasc = revascularization; TVR = target vessel revascularization; v = vessel

*2-vessel and 3-vessel data reported collectively, 28.4% after DES (but only 7% TVR) vs 5.2% after CAB.

1.3.1. Predicting periprocedural risk

According to the results from a number of studies, revascularization can be achieved equally well with PCI or CABG in many patients. Therefore, a reliable method of estimating a given patient's risk with each procedure would be helpful. Several risk prediction scores have been validated for CABG and PCI individually, but these have not been applied to both approaches concurrently. (65),(66) These scores frequently do not help to accurately determine the risk-to-benefit ratio of a given procedure, because many of the same features that suggest high periprocedural risk also predict the most potential benefit (for example, LV dysfunction).

Many of the risk factors are shared among the risk scores (such as age, LV dysfunction, and urgency). Thus, risk factors rarely can help to determine the advantage of one revascularization method over another.

With these limitations in mind, the preponderance of evidence appears to provide weak support for the following statements: First, patients with severe pulmonary disease have particularly high perioperative mortality rates after CABG. (67), (68) Second, patients with diabetes mellitus have particularly high rates of repeat revascularization after PCI and may survive longer after surgery—particularly if the surgery involves a LIMA-to-LAD bypass. (41), (49) Third, patients with reduced LV systolic function may live longer after CABG than after PCI. (69), (70) Fourth, patients with dementia have a decreased rate of further cognitive decline after PCI than after CABG. (71), (72)

The literature is mixed and indeterminate for patients with chronic kidney disease. (73), (74), (75), (76)

1.4. Cardiac risk assessment and cardiac risk stratification models

Risk prediction and stratification models play an important role in current cardiac surgical practice, as health authorities, hospitals and individuals (such as medical practitioners and patients) are paying more attention to objective risk-adjusted predictions of mortality after cardiac surgery. These models allow more meaningful comparisons of outcomes among institutions and surgeons by adjusting for different case-mix. In addition, they are also useful in decision-making, preoperative patient education and consent, and quality assurance measures. They can detect and quantify differences and changes in risk profiles of patients undergoing cardiac surgery. Furthermore, risk prediction allows more objective balancing of potential risks and benefits for individual patients. (77)

In defining important risk factors and developing risk indices, each of the studies has used different primary outcomes. Postoperative mortality remains the most definitive outcome that is reflective of patient injury in the perioperative period. This parameter is reported as either in-hospital or 30 day mortality. The rate of postoperative mortality has also been used as a comparative measure of quality of cardiac surgical care. (78)

Clinical and angiographic predictors of operative mortality were initially defined from the Coronary Artery Surgery Study (CASS). (79), (80)

A total of 6630 patients underwent isolated CABG between 1975 and 1978. Women had significantly higher mortality than men, mortality increased with advancing age in men, but this was not a significant factor in women. Increasing severity of angina, manifestations of heart failure, and number and extend of coronary artery stenoses all correlated with higher mortality, while EF was not a predictor. Urgency of surgery was a very strong predictor of outcome; with those patients requiring emergency surgery in the presence of a 90% left main coronary artery stenosis sustaining 40% mortality.

A risk-scoring scheme for cardiac surgery (CABG and valve) was introduced by Paiement et al at the Montreal Heart Institute in 1983. (81)

Eight risk factors were identified: (1) poor left ventricular function, (2) chronic heart failure, (3) unstable angina or recent (within 6 weeks) myocardial infarction, (4) age greater than 65 years, (5) severe obesity (body mass index greater than 30kg/m^2), (6) reoperation, (7) emergency surgery, and (8) other significant or uncontrolled systemic disturbances. Three classifications were identified: patients with none of these factors (normal), those presenting with one risk factor (increased risk), and those with more than one factor (high risk). In a study of 500 consecutive cardiac surgical patients, it was found that operative mortality increased with increasing risk (confirming their scoring system).

One of the most commonly used scoring systems for CABG was developed by Parsonnet and colleagues (82) (Table 4). Fourteen risk factors were identified for in-hospital or 30-day mortality following univariate regression analysis of 3500 consecutive operations. An additive model was constructed and prospectively evaluated in 1332 cardiac procedures. Five categories of risk were identified with increasing mortality rates, complication rates, and length of stay. The Parsonnet Index is frequently used as a benchmark for comparison between the institutions. However, the Parsonnet model was created earlier than the other models and may not be representative of the current practice of CABG. During the period following publication of the Parsonnet model, numerous technical advances, which are now routine have diminished CABG mortality rates.

Bernstein and Parsonnet simplified the risk-adjusted scoring system in 2000 to provide a handy tool in preoperative discussions with patients and their families and for preoperative risk stratification calculation. The authors developed a logistic regression model in which 47 potential risk factors were considered, and a method requiring only sample addition and graphic interpretation was designed for relatively easily approximating the estimated risk. The final estimates provided by the simplified model correlated well with the observed mortality (Table 5). (83)

O'Connor et al. used data collected from 3055 patients undergoing isolated CABG at five clinical centers between 1987 and 1989 to develop a multivariate numerical score. (84)

A regression model was developed in a training set and subset subsequently validated in a test set. Independent predictors of in-hospital mortality included patient age, body surface area, comorbidity score, prior coronary artery bypass grafting, ejection fraction, left ventricular end–diastolic pressure, and priority of surgery. The validated multivariate prediction rule was very robust in predicting the in-hospital mortality for an individual patient, and the authors proposed that it could be used to contrast observed and expected mortality rates for an institution or a particular clinician.

Higgins et al developed a Clinical Severity Score for coronary artery bypass grafting at The Cleveland Clinic. (85) A multivariate logistic regression model to predict perioperative risk was developed in 5051 patients undergoing CABG between 1986 and 1988 and subsequently validated in a cohort of 4069 patients. Independent predictors of in-hospital and 30-day mortality were emergency procedure, preoperative serum creatinine level of greater than 168μmol/L, severe left ventricular dysfunction, preoperative hematocrit of less than 34%, increasing age, chronic pulmonary disease, prior vascular surgery, reoperation, and mitral valve insufficiency. Predictors of morbidity (AMI and use of intra-aortic balloon pump [IABP], mechanical ventilation for 3 or more days, neurologic deficit, oliguric or anuric renal failure, or serious infection) included diabetes mellitus, body weight of 65kg or less, aortic stenosis, and cerebrovascular disease. Each independent predictor was assigned a weight or score, with increasing mortality and morbidity associated with an increasing total score.

The New York State model of Hannan et al. collected data over the years of 1989 through 1992 with 57.187 patients in a study with 14 variables. (86) It was validated in 30 institutions. The mortality definition was "in hospital". The crude mortality rate was 3.1%; the receiver operating characteristic (ROC) curve was 0.7, with the Hosmer-Lemeshow (H-L) statistic 0.005. Observed mortality was 3.7%, and the expected mortality rate was 2.8%. They included only isolated CABG operations.

The Society of Thoracic Surgeons national database represents the most robust source of data for calculating risk adjusted scoring systems. Established in 1989, the database has grown to include 638 participating hospitals in 2004. This provider-supported database allows participants to bench-mark their risk-adjusted results against regional and national standards. New patient data are brought into the Society of Thoracic Surgeons database in an annual and, semiannual basis. These data have been analyzed, modeled and tested using a variety of statistical algorithms. Since 1990, when more complete data collection was achieved, risk stratification models were developed for both CABG and valve replacement surgery. Models developed in 1995 and 1996 were shown to have good predictive value. (87)

In 1999, the Society of Thoracic Surgeons analyzed the database for valve replacement with and without CABG to determine trends in risk stratification. Between 1986 and 1995, 86.580 patients were analyzed. The model evaluated the influence of 51 preoperative variables on operative mortality by univariate and multivariate analysis for the overall population and for each subset. After determining the significant risk factors using univariate analysis, a standard logistic regression analysis was performed using the training-set population to develop a formal model. The test set population was then used to determine the validity of the model. The preoperative risk factors associated with highest operative mortality rates were salvage status, renal failure (dialysis dependent and non-dialysis dependent), emergent status, multiple reoperations, and New York Heart Association class IV. The multivariate logistic regression analysis identified 30 independent preoperative risk factors among the six valvular models, isolated or in combination with CABG. The addition of CABG increased the mortality rate significantly for all age groups and for all subset models. (88)

Using the knowledge of these models, the STS created new, more comprehensive models in 2008 year. (89), (90), (91) These models include coronary artery bypass grafting surgery, valve surgery, valve plus coronary artery bypass grafting surgery, making difference between mitral valve replacement and repair. In addition, they include expanded set of outcomes such as mortality, stroke, reoperation, renal failure, deep sternal wound infection, prolonged ventilation, composite major morbidity, prolonged length of stay, and short length of stay. The risk score can be measured by online risk calculator available at the Society of Thoracic Surgeons website (http://209.220.160.181/STSWebRiskCalc261/de.aspx).

Tu and collegues collected data from 13.098 patients undergoing cardiac surgery between 1991 and 1993 at all nine adult cardiac surgery institutions in Ontario, Canada. (92) Six variables (age, sex, left ventricular function, type of surgery, urgency of surgery, and repeat operation) predicted in-hospital mortality, ICU stay, and postoperative stay in days after cardiac surgery. Subsequently, the Working Group Panel on the Collaborative CABG Database Project categorized 44 clinical variables into 7 core, 13 level 1, and 24 level 2 variables, to reflect their relative importance in determining short-term mortality after CABG. Using data from 5517 patients undergoing isolated CABG at nine institutions in Ontario in 1993, a series of models were developed. The incorporation of additional variables beyond the original six added little to the prediction of in-hospital mortality.

Spivack et al collected data during the years of 1991 and 1992 and included 513 patients with 15 variables, validated only in their institution. (93) They used only isolated CABG population, and the outcomes measured were mortality and morbidity. The morbidity definition was ventilator time and ICU days. Both prolonged mechanical ventilation and death were rare events (8.3% and 2.0%, respectively). The combination of reduced left ventricular ejection fraction and the presence of selected preexisting comorbid conditions (clinical chronic heart failure, angina, current smoking, and diabetes mellitus) served as modest risk factors for prolonged mechanical ventilation; their absence strongly predicted and uncomplicated postoperative respiratory course.

Dupius and colleagues attempted to simplify the approach to risk of cardiac surgical procedures in a manner similar to the original ASA physical status classification. (94) They developed a score that uses a simple continuous categorization, using five classes plus an emergency status. The Cardiac Anesthesia Evaluation Score (CARE) model collected data from 1996 to 1999 and included 3548 patients to predict both in-hospital mortality and a diverse group of major morbidities. It combined clinical judgment and the recognition of three risk factors previously identified by multifactorial risk indices: comorbid conditions categorized as controlled or uncontrolled, the surgical complexity and the urgency of the procedure. The CARE score demonstrated similar or superior predictive characteristics compared to more complex indices.

Nowicki and colleagues used data on 8943 cardiac valve surgery patients aged 30 years and older from eight northern New England medical centers from 1999 through 2001 to develop a model to predict in-hospital mortality. (95)

In the multivariable analysis, 11 variables in the aortic model (older age, lower body surface area, prior cardiac operation, elevated creatinine, prior stroke, NYHA class IV, congestive heart failure, atrial fibrillation, acuity, year of surgery and concomitant CABG) and 10 variables in the mitral model (female sex, older age, diabetes, coronary artery disease, prior cerebrovascular accident, elevated creatinine, NYHA class IV, congestive heart failure, acuity and valve replacement) remained independent predictors of outcome. They developed a look up table for mortality rate based on a simple scoring system.

Hannan and colleagues also evaluated predictors of mortality after valve surgery but used data from 14,190 patients from New York State. (96) A total of 18 independent risk factors were identified in the six models of differing combinations of valve and CABG. Shock and dialysis-dependent renal failure were among the most significant risk factors in all models. Eleven risk factors were found to be independently associated with higher readmission rates: older age, female sex, African American race, greater body surface area, previous AMI within 1 week, and six comorbidities. Except these patient related risk factors, two provider characteristics (annual surgeon CABG volume <100 and hospital risk-adjusted mortality rate in the highest deciles) and two postoperative factors (discharge to nursing home or rehabilitation and length of stay during index CABG admission of ≥5 days) were related to higher readmission rates.

Table 4. Components of Parsonnet's Additive Model (82)

Risk factor	**Assigned weight**
Female gender	1
Morbid obesity (≥1.5 x ideal weight)	3
Diabetes (unspecified type)	3
Hypertension (systolic BP>140mmHg)	3
Ejection Fraction (%) (actual value when available) Good(≥50) Fair (30-49) Poor(<30)	 0 2 4
Age (yr): 70-74 75-79 ≥80	 7 12 20
Reoperation First Second	 5 10
Preoperative IABP	2
Left ventricular aneurysm	5
Emergency surgery following PTCA or catheterization complications	10
Dialysis dependency (PD or Hemo)	10
Catastrophic states (e.g. acute structural defect, cardiogenic shock, acute renal failure)	10-50
Other rare circumstances (e.g.paraplegia, pacemaker dependency, congenital HD in adult, severe asthma)	2-10
Valve surgery Mitral PA pressure ≥ 60 mmHg	 5 8
Aortic Pressure gradient > 120mmHg	5 7
CABG at the time of valve surgery	2

Abbreviations: BP=blood pressure**;** IABP=intra-aortic balloon pump; PTCA=percutaneous transluminal coronary angioplasty; PD=peritoneal dialysis; Hemo=hemodialysis; HD=heart disease; PA=pulmonary artery; CABG=coronary artery bypass graft.

Table 5. Preoperative Risk Estimation Worksheet (83)

RISK FACTOR	SCORING (APPROXIMATE SYSTEM 97)		VALUE
Female gender		6	6
Age	70-75 76-79 80+	2.5 7 11	7
Congestive failure		2.5	
COPD, severe		6	
Diabetes		3	
Ejection fraction	30-42% <30%	6.5 8	
Hypertension	Over 140/90, or history of hypertension, or currently taking anti-hypertension medication	3	3
Left-main disease	Left-main stenosis is 50%	2.5	
Morbid obesity	Over 1.5 times ideal weight	1	1
Preoperative IABP	IABP present at the time of surgery	4	
Reoperation	First reoperation Second or subsequent reoperation	10 20	
One valve, aortic	Procedure proposed	0	
One valve, mitral	Procedure proposed	4.5	
Valve+ACB	Combination valve procedure and ACB proposed	6	
Special conditions	See reverse side		

Abbreviations: COPD=chronic obstructive pulmonary disease; IABP=intra-aortic balloon pump; ACB=aorto-coronary bypass

RISK VALUES FOR SPECIAL CONDITIONS

Cardiac

Cardiogenic shock (urinary output <10 cc/hr)	12
Endocarditis, active	6.5
Endocarditis, treated	0
LV aneurysm resected	1.5
One valve, tricuspid: procedure proposed	5
Pacemaker dependency	0
Transmural acute MI within 48 hr	4
Ventricular septal defect, acute	12
Ventricular tachycardia, ventricular fibrillation, aborted sudden death	1

Pulmonary

Asthma	1
Endotracheal tube, preoperative	4
Idiopathic thrombocytopenic purpura	12
Pulmonary hypertension (mean pressure >30)	11

Hepato-renal

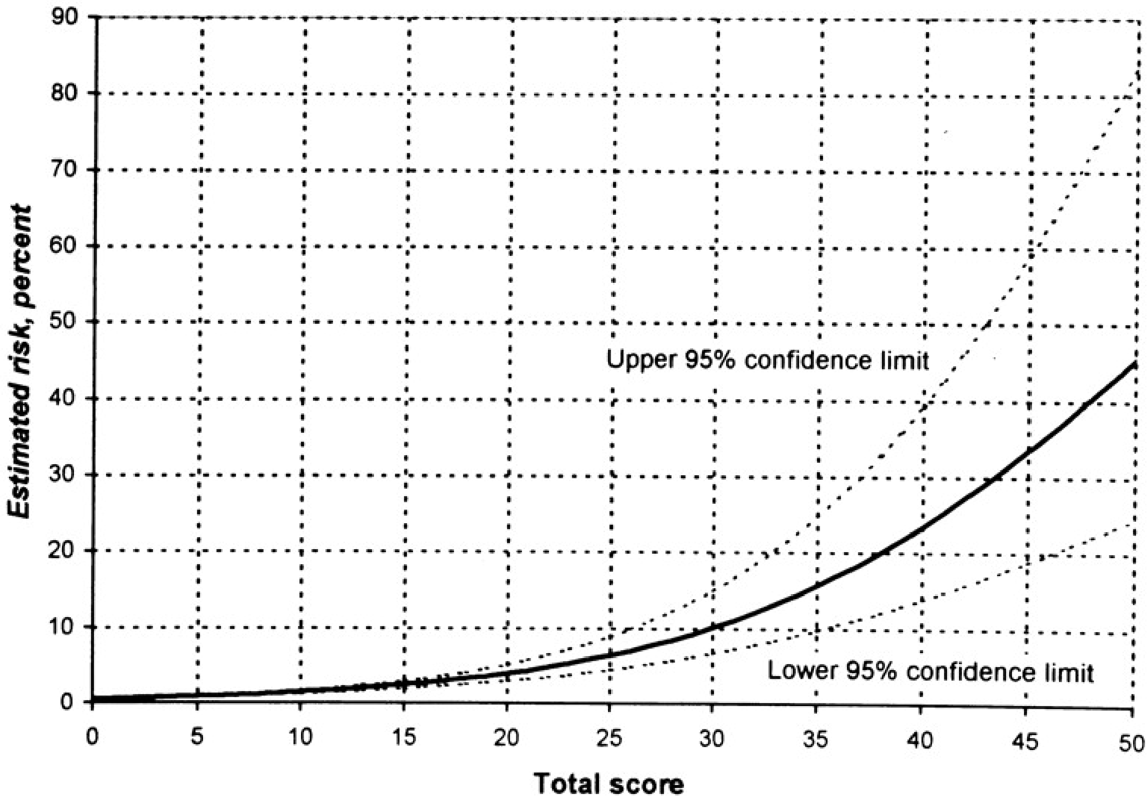
Cirrhosis	12.5
Dialysis dependency	13.5
Renal failure, acute or chronic	3.5

Vascular

Abdominal aortic aneurysm, asymptomatic	0.5
Carotid disease (bilateral or 100% unilateral occlusion)	2
Peripheral vascular disease, severe	3.5

Miscellaneous

Blood products refused	11
Severe neurologic disorder (healed CVA, paraplegia, muscular dystrophy, hemiparesis)	5
PTCA or catheterization failure	5.5
Substance abuse	4.5



Use the total score to read the estimated preoperative-risk range from this plot, which shows the estimated risk of mortality together with 95% confidence limits.

1.4.1. Risk model development

To understand how best to apply a given risk index to a specific patient or population, it is essential to understand how these indices were created. These risk models must be applied with caution after careful study for any specific population. One critical factor in the choice of model to use for a given practice is to understand the clinical goals used in the original development process. Despite extensive research and widespread use of risk models in cardiac surgery, there are methodological problems. Different conclusions can be reached depending on the risk model used. Processes critical to the development of the risk models are shown in Figure 5.

The underlying assumption in the development of any risk index is that specific factors (disease history, physical finding, laboratory data, and nature of surgery) cannot be modified with respect to their influence on outcome i.e. the perioperative period is essentially a black box. If a specific factor is left untreated, it could lead to major morbidity or mortality.

However, the models themselves depend on the appropriate selection of baseline variables or risk factors to study, and their prevalence in the population of interest is critical in order for them to affect outcome. For example, referral patterns to a given institution may result in an absence of certain patient populations and therefore the risk factor would not appear in the model. Also, the use of multivariate logistic regression may eliminate biologically important risk factors, which are not sufficiently present to achieve statistical significance.

In developing a risk index, it is important to validate the model and to benchmark it against other known means of assessing risks (Figure 6). It is important to determine whether a given index predicts morbidity, mortality, or both. Typically, a model's performance is first evaluated on the developmental data, evaluating its goodness of fit. Alternatively, the original data can be split and the model can be built on half of the data and validated on the other half. This reduces the total number of patients and outcomes available to create the model. This model is best suited to situations where data on tens of thousands of patients are available. The internal validation does not provide the practitioner with information on the generalizability of the model. External validation on a large completely independent test dataset is the best approach to satisfying this requirement.

Calibration refers to a model's ability to predict mortality accurately. There are numerous tests that can be applied, the most common being the H-L test. If the p value from an H-L test is greater than 0.05, the current practice of the developers is to claim that the model predicts mortality accurately.

Discrimination is the ability of a model to distinguish patients who die from those who survive. The area under the ROC curve is the common method of assessing this facet of the model. The test is determined by evaluating all possible pairs of patients, determining if the predicted probability of death should ideally be higher for the patients who died than for the ones who survived. The ROC area is the percentage of pairs for which this is true.

The current practice in cardiac surgery is to conclude that a model discriminates well if the ROC area is higher than 0.7. If predictions are used to identify surgical centers or surgeons with unexpectedly high or low rates, achieving a high ROC area alone is not adequate, but good calibration is also critical.

A poorly calibrated model may cause large numbers of institutions or surgeons to reveal excessively high or low rates of mortality, when in fact the fault lies with the model, not the clinical performance. If predictions are used to stratify patients by disease severity in order to compare treatments or to decide on patient management, both calibration and discrimination aspects are important. (97)

Figure 5. Risk model development

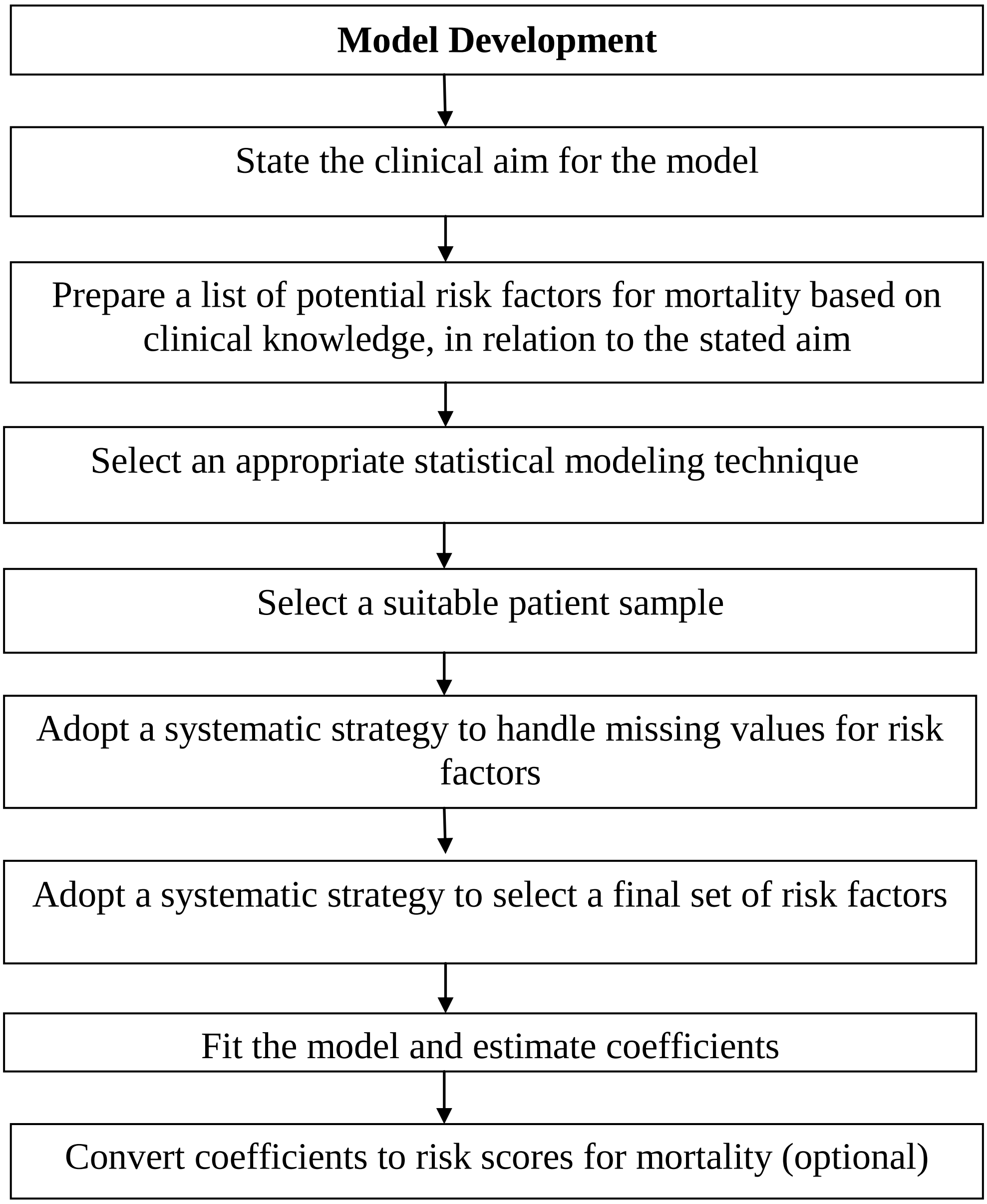
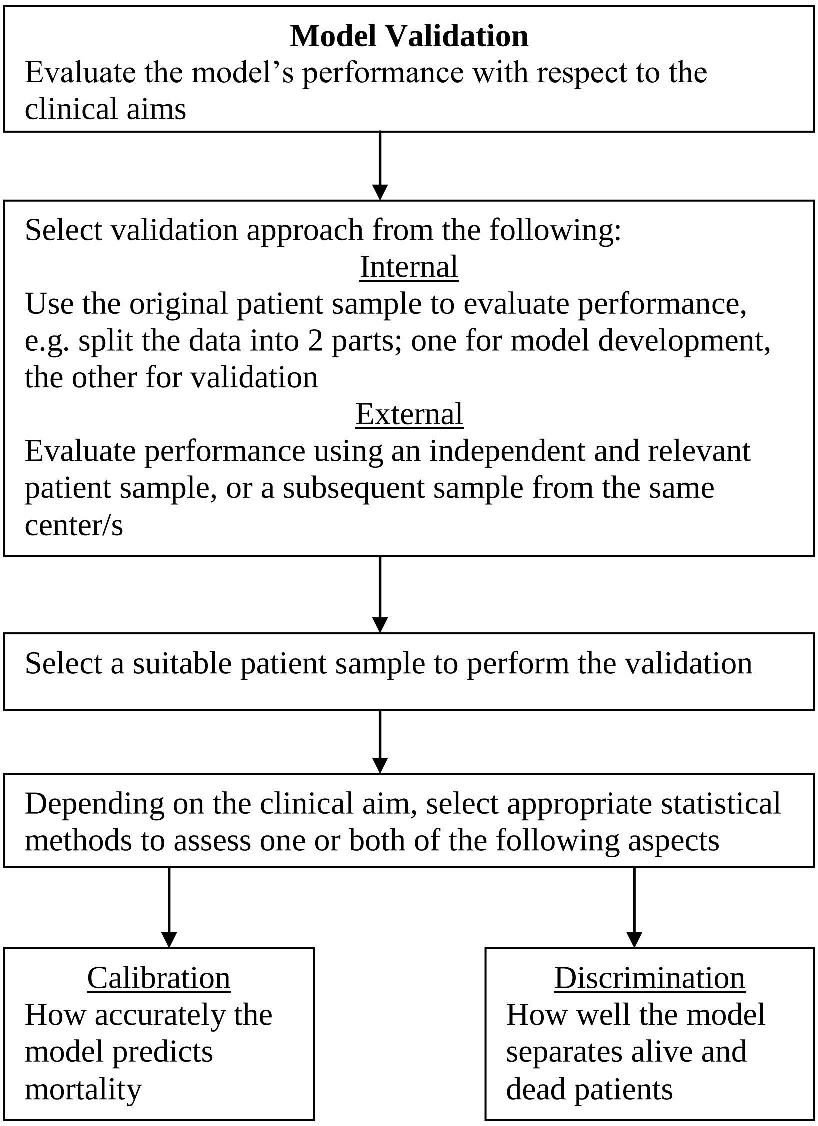


Figure 6. Steps involved in model validation



2. EuroSCORE before cardiac surgery

In-hospital mortality is frequently used as an indicator of the quality of care in cardiac surgery, and the European System for Cardiac Operative Risk Evaluation (EuroSCORE) has gained wide popularity among risk stratifying tools. The EuroSCORE yielded the highest predictive value in in-hospital mortality comparing with other risk scores. (98), (99)

Nashef et al. introduced the EuroSCORE in 1999, as a tool in order to score the early mortality after cardiac surgery in cardiac patients with numerous risk factors. (100) The EuroSCORE was based on a large and tightly controlled database, comprising 19,030 adult patients undergoing a diverse group of cardiac surgical procedures under cardiopulmonary bypass from 128 surgical centers in eight European countries (Germany, France, United Kingdom, Italy, Spain, Finland, Sweden and Switzerland) during three months (September-December 1995) (Table 6 and Table 7). (101)

Data were collected preoperatively from all patients, considering 68 preoperative and 29 operative risk factors shown or believed to influence in-hospital mortality. Using logistic regression calculations, risk factors showing a close correlation with in-hospital mortality have been identified. The following risk factors were associated with increased mortality: age, female gender, serum creatinine, extracardiac arteriopathy, chronic airway disease, severe neurologic dysfunction, previous cardiac surgery, recent myocardial infarction, left ventricular ejection fraction, chronic congestive heart failure, pulmonary hypertension, active endocarditis, unstable angina, procedure urgency, critical preoperative condition, ventricular septal rupture, noncoronary surgery, and thoracic aortic surgery.

Table 6. Risk factors, Definitions and Weights (Score)

Patient-Related Factors	**Definition**	**Score**
Age	Age 60+ (per half decade) (60-64 = 1, 65-69 = 2, etc.)	1
Sex	Female	1
Chronic pulmonary disease	Long-term use of bronchodilators or steroids for lung disease	1
Extracardiac arteriopathy	Any one or more of the following: claudication, carotid occlusion or >50% stenosis, previous or planned intervention on the abdominal aorta, limb arteries or carotids	2
Neurological dysfunction	Disease severely affecting ambulation or day-to-day functioning	2
Previous cardiac surgery	Requiring opening of the pericardium	3
Serum creatinine	>200 μmol/L preoperatively	2
Active endocarditis	Patient still under antibiotic treatment for endocarditis at the time of surgery	3
Critical preoperative state	Any one or more of the following: ventricular tachycardia or fibrillation or aborted sudden death, preoperative ventilation before arrival in the anesthetic room, preoperative intra-aortic balloon counterpulsation or preoperative acute renal failure (anuria or oliguria <10mL/hr)	3
Cardiac-Related Factors		
Unstable angina	Rest angina requiring IV nitrates until arrival in the anesthetic room	2
Left ventricular dysfunction	LV dysfunction moderate or LVEF 30-50% Poor or LVEF<30%	1 3
Recent myocardial infarction	(<90 days)	2
Pulmonary hypertension	Systolic pulmonary artery pressure >60mmHg	2
Surgery-Related Factors		
Emergency	Carried out on referral before the beginning of the next working day	2
Other than isolated CABG	Major cardiac procedure other than or in addition to CABG	2
Thoracic aorta surgery	For disorder of ascending aorta, arch or descending aorta	3
Postinfarction septal rupture		4

Abbreviations: CABG=coronary artery bypass graft surgery; LVEF=left ventricular ejection fraction, IV=intravenous.

Table 7. Application of EuroSCORE Scoring System

EuroSCORE	**Patients (n)**	**Died (n)**	**Observed Mortality***	**Expected Mortality***
0-2 (low risk)	4529	36 (0.8%)	0.56-1.10	1.27-1.29
3-5 (medium risk)	5977	182 (3.0%)	2.62-3.51	2.90-2.94
6 plus (high risk)	4293	480 (11.2%)	10.25-12.16	10.93-11.54
Total	14.799	698 (4.7%)	4.37-5.06	4.72-4.95

*95% Confidence limits for mortality

The advantage of the EuroSCORE was the assessment of the true risk of cardiac surgery in patients without any particular risk factors. For the purposes of this analysis, baseline mortality figures were calculated in patients without known preoperative risk factors (including risk factors that were not found to have a significant impact in this study, such as diabetes and hypertension). When all such patients were excluded, it was satisfying to note the extremely low current mortality for cardiac surgery in Europe: 0% for atrial septal defect repair, 0.4% for CABG, and barely over 1% for single valve repair or replacement. Comparable with other studies some risks factors such as age, sex and left ventricular ejection fraction have been identical. (102), (103)

Knowing the cardiovascular risk factors it is surprisingly that hypertension, diabetes and smoking are missing in this risk score. These major cardiovascular risk factors were also included in other studies. (104), (105), (106)

Extracardiac arteriopathy and severe neurological dysfunction are two relatively new risk factors. Many cardiac surgeons have learnt from experience that these are important determinants of outcome, and this is supported in other works. (107), (108)

The additive (standard) form was first applied, using a number of points for each risk factor. It estimates the percentage of the predicted operative mortality for a patient undergoing a particular operation (Table 6). The additive EuroSCORE can be routinely calculated at the bedside of the patients.

The standard EuroSCORE system consists of three risk groups: low risk (0-2) with expected mortality under 2%, medium risk (3-5) with an expected mortality under 5%, and high risk (≥6) with an expected mortality ≥10%. (109)

During the 2000s, this additive EuroSCORE has been widely used and validated across different centers in Europe and across the world (North America, Japan), making it a primary tool for risk stratification in cardiac surgery. (98), (110)-(121)

However, the validity of this model in Australian, Lithuanian and Turkish population undergoing cardiac surgery was not confirmed. The model overestimated the mortality in these cases. (122), (123), (124), (125)

Gogbashian et al. pooled data from six different studies to get more certainty in risk estimation. Due to the large number of patients with additive EuroSCORE less than or equal to 6, in all of the reviewed articles, it is highly suggestive that additive EuroSCORE performance generally over-estimates mortality at lower EuroSCOREs (EuroSCORE≤6) and under-estimates mortality at higher EuroSCOREs (EuroSCORE>10). (126)

These may lead to serious mistakes in choosing patients for cardiac surgery and may lead to serious consequences with respect to the quality of patient care. To resolve this problem Michel et al. suggested using Logistic EuroSCORE. They demonstrated a better correlation between predicted and observed mortality using logistic EuroSCORE than when using additive EuroSCORE. (109) The logistic model became available in 2003 and proved to be a better risk predictor, for high and very high risk patients, such as in patients that underwent redo operations. (109), (127), (128)

The logistic EuroSCORE model is calculated using the following formula:

$$\frac{e^{(-4.789594+\sum \beta i Xi)}}{1+e^{(-4.789594+\sum \beta i Xi)}}$$

where the number -4.789594 is constant of the logistic regression equation and βi is the coefficient of the variable Xi in the logistic regression data provided in Table 8. If age is considered a continuous variable, Xi=1 if patient age is less than 60 and and Xi increases by one point per year thereafter: hence for age 59 or less Xi = 1, age 60: Xi=2, age 61: Xi=3, and so on.

The logistic model can be easily calculated by a calculator downloaded from the Euro SCORE website (www.euroscore.org).

The EuroSCORE has been used as a risk prediction tool for different purposes.

The both forms of EuroSCORE were used for identification of high risk patients with native valve endocarditis eligible for cardiac surgery. The discriminating ability of the both forms was good (ROC curve 0.74 for the logistic model and ROC curve 0.75 for the additive model). (129)

The EuroSCORE model has been shown to work well in valve surgery across many European countries. (130) Recently published German study by Wendt et al. confirmed that both the additive and logistic EuroSCORE can be used to predict 30-day mortality in patients undergoing isolated aortic valve replacement. (131) Interestingly precise prediction of mortality can be achieved by the single factor "age" but it cannot be used as a global score.

The use of EuroSCORE has expanded its application in the everyday clinical practice. It can be a useful tool for prediction of extended intensive care unit stay, mid and late-term mortality and morbidity after cardiac surgery.

Two different studies demonstrated that prolonged length of stay in the intensive care unit after open heart surgery correlated positively with the EuroSCORE after 2, 5 and 7 days, especially with the logistic model. (132), (133) Long-term mortality, probably the most useful outcome, is rarely assessed, essentially because of the difficulty in following patients over a long period of time. The findings of Nilsson et al corroborate this. They have found that risk models such as EuroSCORE, can predict 1-year mortality. In this study, the authors pointed out that smaller ROC area is expected for 1-year mortality prediction when compared with short-term mortality. This is because the proportion of cardiovascular deaths, among all causes of mortality, is usually lower at 1 year than at 30 days after surgery. (134)

EuroSCORE can be used to predict not only in-hospital mortality, for which it was originally designed, but also 3-month mortality, prolonged length of stay and specific postoperative complications (renal and respiratory failure, sepsis and/or endocarditis) according to Toumpoulis et al. and heart and renal failure, stroke, pneumonia and mediastinitis, according to Hirose. (120), (135)

These outcomes can be predicted accurately using the standard EuroSCORE which is very simple and easy to calculate.

While the accuracy of the additive EuroSCORE has been well established for CABG and isolated valve procedures, its predictive ability in combined CABG and valve procedures has been contradictory. Karthik et al. showed that in patients undergoing combined procedures, the additive EuroSCORE significantly underpredicted the risk compared with the observed mortality. (111)

Recently, one American study published results in which both additive and logistic EuroSCORE were accurate in predicting short and mid-term mortality even in combined coronary artery bypass and aortic valve replacement surgery. (136) According to the regression analysis performed in this study, only the additive EuroSCORE was predictive of mid-term mortality in combined coronary artery bypass and aortic valve replacement surgery patients.

Twelve month major cardiovascular events and all-cause mortality prediction could be improved using combination of preoperative logistic EuroSCORE and postoperative troponin T level. (137) The area under the curve for the prediction of the composite endpoint of the model combining troponin T and the EuroSCORE was 0.72; when based on EuroSCORE alone it was 0.64 ($p < 0.0001$).

Presently, EuroSCORE is the world’s most widely used cardiac surgical risk model, but it was based on patients operated on in 1995. There is evidence that it may be out of date. Although it remains powerful in discriminating between low-risk and high-risk patients, many centers have reported that for them it overpredicts risk (a few centers still say it underpredicts risk).

In acute settings, the logistic EuroSCORE seems to be inappropriate. In a retrospective study in which the patients underwent emergency aorto coronary bypass surgery, the logistic EuroSCORE overestimated the mortality rate. (138) In these conditions creatine kinase-MB/hour-ratio and ST-segment elevation was a more accurate prediction of the operative risk.

The over prediction of the current EuroSCORE risk model can be reduced by reducing the number of variables. One recently published Italian study suggests shorter five risk model consisting of age, left ventricular ejection fraction, serum creatinine, emergency operation and non-isolated coronary operation. The area under the curve (AUC) was 0.76, while the EuroSCORE AUC was 0.75. The 12 risk factors were needed to achieve a good performance only in high-risk patients. Calibration and clinical performance were better in the five-factor model than in the EuroSCORE. (139)

Lately, many retrospective analyses of series with patients who were submitted to aortic valve replacement, found that EuroSCORE overestimates the risk of isolated aortic valve replacement.

Di Giammarco et al. from Italy reported their evaluation of the performance of the EuroSCORE calculator in the prediction of the 30-day outcome after isolated aortic valve replacement, in order to assess its absolute reliability and usefulness as a selection criterion for percutaneous aortic valve implantation. With this aim, they carried out a retrospective statistical analysis on 379 of their patients consecutively submitted for isolated aortic valve replacement during the previous 10 years of surgical activity. Their observed mortality was 5.2%, significantly lower than the 9.4% expected mortality by the logistic EuroSCORE. They concluded that the EuroSCORE appears not to be a valuable model in absolute and relative risk prediction for isolated aortic valve replacement. Therefore, the patient selection for interventional aortic valve replacement cannot be based on the EuroSCORE. (140)

Similarly to this study, two other retrospective analyses of series of patients that were submitted for isolated aortic valve replacement, found that the EuroSCORE overestimates the risk of isolated aortic valve replacement. (141), (142)

An analysis of a subgroup of 6305 patients submitted to isolated AVR registry of the German Society of Thoracic and Cardiovascular Surgery from 2006 and 2007 revealed an overall hospital mortality of 3.9% whereas the logistic EuroSCORE predicted 7.3% which supports the substantial lack of predictive value of the EuroSCORE. (143)

The Italian CABG Outcome Project has found that the logistic EuroSCORE overestimation remains constant through the six risk classes of isolated CABG analyzed, with an observed over predicted mortality ratio of 0.4. (144) They have concluded that when properly recalibrated, the logistic EuroSCORE model can be exported to the Italian population and used to rank hospital performance and evaluate preoperative risk of patients undergoing open-heart surgery.

The North West Quality Improvement Programme in Cardiac Interventions has found different recalibrations for different operative groups. (145) The Society of Cardiothoracic surgery in Great Britanie and Ireland have responded to the over-prediction of logistic EuroSCORE by undertaking a complex recalibration whereby they have looked at the comparisons between the observed mortality and those predicted in each operative group to derive a series of recalibration coefficients. These were then applied to the analyses of national data for hospitals and surgeons, which are available to the public.

We have to have in mind, that EuroSCORE was not intended to be used as a substitute tool for therapeutic decision making by physicians regarding elderly and high risk patients. This is one of the reasons why in these studies EuroSCORE showed lack of efficacy. However, this should not be disappointing for the physicians. Rather than abolishing the EuroSCORE, it appears more adequate to modify it, since it is an evidence-based powerful tool for risk prediction for the group of patients for which it was originally constructed.

There have been several studies from individual centers as well as regional studies examining the effectiveness of the EuroSCORE at the local level.

To examine the validity of the EuroSCORE among the Czech cardiac population we performed a prospective study evaluating the abilities of this European score in consecutive group of patients, candidates for cardiac surgery.

Table 8. European System of Cardiac Operative Risk Evaluation (EuroSCORE) risk factors: Additive and Logistic EuroSCORE model.

Patient Factors	Additive EuroSCORE	Logistic EuroSCORE
Age 60+ (per half decade) (60-64 = 1, 65-69 = 2, etc.)	1	0,0666354
Sex	1	0,3304052
Chronic pulmonary disease	1	0,4931341
Extracardiac arteriopathy	2	0,6558917
Neurological dysfunction	2	0,841626
Previous cardiac surgery	3	1,002625
Serum creatinine >200 μmol/ L	2	0,6521653
Active endocarditis	3	1,101265
Critical preoperative state	3	0,9058132
Cardiac Factors		
Unstable angina	2	0,5677075
LV dysfunction moderate or LVEF 30-50%	1	0,4191643
LV dysfunction poor or LVEF<30%	3	1,094443
Recent myocardial infarction	2	0,5460218
Pulmonary hypertension	2	0,7676924
Operation Factors		
Emergency	2	0,7127953
Other than isolated CABG	2	0,5420364
Thoracic aorta surgery	3	1,159787
Postinfarction septal rupture	4	1,462009

Abbreviations: LV = left ventricular; LVEF = left ventricular ejection fraction; CABG = coronary artery bypass grafting

2.1. EuroSCORE before cardiac surgery among Czech cardiac population

2.1.1. Methods

Data were prospectively collected from a total of 460 consecutive patients who were presented to the cardiac surgeon as cardiac surgery candidates between September 2004 and March 2005 at the Cardiocenter, University Hospital Vinohrady, Prague, the Czech Republic. (146)

From this group, 272 patients (59%) were indicated for cardiac surgery and 188 patients (41%) were refused for cardiac surgery.

Cardiac surgery candidate patients were refused due to: diffuse coronary atherosclerosis too extensive for surgery (n = 40; 22%), high operative risks (n=89; 47%) or other reasons (n=59; 31%).

The group of patients refused for cardiac surgery due to high operative risks comprised patients with a combination of polymorbidity, higher age (> 75 years), and ejection fraction less than 30%.

The group of patients refused due to other reasons involved either patients with borderline (intermediate) atherosclerosis lesions, a mild, minimal and stable symptoms at the time of referral to surgery or patient who refused the surgery.

Diffuse coronary atherosclerosis indicates a diffuse stenosis approaching the periphery of the coronary blood vessels. High operative risk due to polymorbidity means coexistence of advanced stages of multiple organ diseases (e.g. CNS, pulmonary, renal, peripheral arteries, hepatic etc.).

There were no exclusion criteria.

The measured outcome was the mortality, defined as death within 30 days from operation or later than 30 days if still in hospital, while for refused patients mortality was defined as death during the hospital stay or 30 days after discharge. To assess the risk factors for mortality in patients, candidates for cardiac surgery we used both additive and logistic model of the

European system for Cardiac Operative Risk Evaluation (EuroSCORE). Definitions of the risk factors were identical to the EuroSCORE definitions. (66)

The additive EuroSCORE has been routinely calculated at the bedside of all patients presented to the cardiac surgeon, while the logistic model has been calculated by a calculator downloaded from the Euro SCORE website (www.euroscore.org).

Thirty-day mortality information was obtained by contacting the patient or a family member by telephone. The result from the surgery, and clinical outcome after the surgery, were taken into account in the operated patients.

2.1.2. Statistical analysis

Quantitative and score variables were summarized in terms of mean values and SDs. Chi square test was used to compare categorical values between groups. Changes in quantitative variables between the groups were assessed with the student t test. Discrete variables are expressed as counts and percentages. Using the Univariate Cox regression analysis we tested whether the survival time depends on the standard and the logistic EuroSCORE.

The C statistic method (receiver operating curve) was used to assess the discriminatory ability of standard and logistic EuroSCORE. The area under the receiver operating characteristics curve was calculated as an indicator for how well the EuroSCORE could discriminate patients who lived from those who died. The discriminatory power of the model is deemed excellent if the area under the receiver operating characteristic curve is 0.80, very good if it is greater than 0.75 and good if greater than 0.70. Statistical analyses were performed using the statistical SPSS 13.0 Software. A p value of less than 0.05 was considered significant.

2.1.3. Results

Table 9 compares the variables utilized by the EuroSCORE model. Refused patients experienced poorer left ventricular function (EF<30%), chronic pulmonary disease, serum creatinin >200 μmol/L and significantly higher EuroSCORE ($p<0.001$).

Eleven patients (4%) of the patients indicated for cardiac surgery refused to be operated. They were included in the group of refused patients. Two patients indicated for cardiac surgery died before the operation. These deaths were excluded from the study, leaving a total of 458 patients for evaluation.

Finally, 259 patients (57%) were operated and 199 patients (43%) were refused for cardiac surgery (125 patients (63%) were treated conservatively and 74 patients (37%) were treated by percutaneous coronary intervention, (PCI)).

One hundred eighty patients (69%) underwent coronary artery bypass surgeries, 54 patients (21%) underwent valve operations, 3 patients (1%) underwent thoracic aorta surgery and 22 patients (9%) underwent combined surgeries. Sixty-one patients (82%) treated by PCI received at least one stent, the mean number of implanted stents was 1.3 ± 0.5. The implantation failed in 4 patients (5%) and dissection of the coronary vessel was performed in one patient (1%). Two patients (3%) had a nonfatal periprocedural myocardial infarction. None of the patients died during the first 24 hours after the PCI intervention. The patients treated conservatively received only medications.

2.1.4. Clinical outcome

The mean follow up was 36±10 days. The overall observed mortality was 26 patients (6%). Out of them, in-hospital mortality was 17 patients (65%), and overall observed mortality after discharge in or out of hospital was 9 patients (35%).

2.1.5. Validation of EuroSCORE

There was no significant difference between the observed and predicted mortality neither the entire cohort nor in the subgroups.

Mean Additive EuroSCORE in the entire cohort was 4.6, while the logistic EuroSCORE was 5%. Of the 259 operated patients, there were 12 deaths or 5%. Both the Additive EuroSCORE and the logistic EuroSCORE predicted 10 deaths (4%). The chi square test P value of the total number of observed versus expected deaths in the subgroup of operated patients was 0.663 in both cases (Table 10). Among the 199 refused patients, we observed a mortality of 14 deaths (7%). The additive EuroSCORE predicted 10 deaths (5%), while the logistic EuroSCORE predicted 13 deaths (7%). The chi square test P value of the total number of observed versus expected deaths was 0.400 and 0.842 respectively (Table 10).

The deceased patients had a statistically higher additive and logistic EuroSCORE than the survivors in the surgical subgroup ($p<0.001$), as well as the survivors in the subgroup of the refused patients ($p<0.05$).

The patients with additive EuroSCORE > 5 had a significantly worse prognosis than patients with EuroSCORE ≤ 5 in both subgroups (Figure 7).

2.1.6. Discriminatory ability – C statistic

EuroSCORE showed good discriminatory ability in predicting short-term mortality. Figure 8 and Figure 9 show the areas under the receiver operating characteristic curves for both the standard and the logistic EuroSCORE in both subgroups of patients.

Table 9. Baseline characteristics of the patients, candidates for cardiac surgery

Patient Factors	**Operated patients (n=272; 59%)**	**Refused patients (n=188; 41%)**
Age (mean ± S.D.)	65±10	69±10
Sex (female), n(%)	75(28)	58(31)
Chronic pulmonary disease, n(%)	19(7)	35(19)
Extracardiac arteriopathy, n(%)	28(10)	30(16)
Neurological dysfunction, n(%)	4(1)	6(3)
Previous cardiac surgery, n(%)	0	1(0.5)
Serum creatinine >200 µmol/ L, n(%)*	4(1)	15(8)
Active endocarditis, n(%)	1(0.4)	0
Critical preoperative state, n(%)	2(0.7)	0
Cardiac Factors		
Unstable angina, n (%)*	24(9)	6(3)
LV dysfunction moderate or LVEF 30-50%, n(%)	75(28)	70(37)
LV dysfunction poor or LVEF<30, n(%)* Mean EF (±S.D.)*	6(2) 54±11	24(13) 48±15
Recent myocardial infarct, n(%)	54(20)	49(26)
Pulmonary hypertension, n(%)	1(0.4)	5(3)
Operation Factors		
Emergency, n(%)	7(3)	0
Other than isolated CABG, n(%)	78(30)	0
Surgery on thoracic aorta, n(%)	3(1)	0
Postinfarct septal rupture, n(%)	2(0.7)	1(0.5)
Mean Additive/ Mean Logistic EuroSCORE*	4.1/3.95	5.6/7.1

*p<0.001; Abbreviations: S.D. – Standard Deviation

Table 10. Predicted vs. observed mortality in the entire cohort, in operated and refused patients

	Entire cohort (n=458)		**Operated patients (n=259; 57%)**		**Refused patients (n=199; 43%)**	
Predicted mortality	Add. ES	Log. ES	Add. ES	Log. ES	Add. ES	Log. ES
	21(4.6%)	23(5%)	10(4%)	10(4%)	10(5%)	13(7%)
Observed mortality	26(6%)		12(5%)		14(7%)	
P value	0.454	0.660	0.663	0.663	0.400	0.842

Abbreviations: Add. – Additive, ES – EuroSCORE, Log. – Logistic.

Figure 7. Mortality according to the EuroSCORE level in both subgroups
Open bars – patients with EuroSCORE ≤ 5, closed bars – patients with EuroSCORE > 5.

*p < 0.01

**p < 0.05

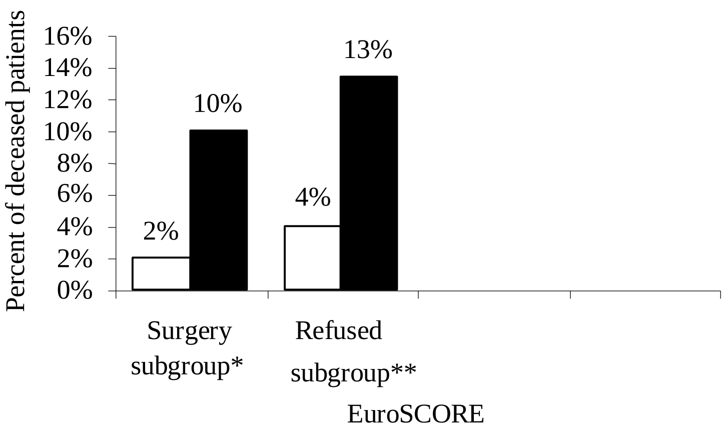


Figure 8. Receiver operating characteristic curves for short-term mortality after cardiac surgery.

Figure 8a Additive EuroSCORE: area 0.755 [0.659-0.850]
Figure 8b Logistic EuroSCORE: area 0.762 [0.668-0.857]

Figure 8a

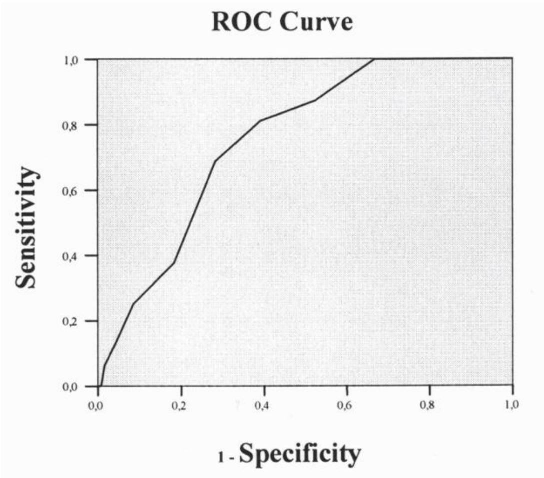
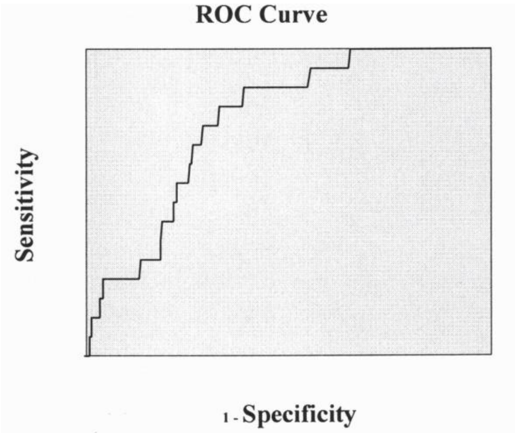


Figure 8b



3. EuroSCORE before percutaneous intervention

EuroSCORE was originally designed to predict postoperative mortality after cardiac surgery in the adult population. After it was approved as the risk score with best discriminatory capacity among the existing risk scores, it continued to be applied as a risk predictor for different other measures for cardiac surgery success, such as mid and late-term mortality, postoperative length of stay and postoperative complications.

More recently, several small-sized studies suggested that EuroSCORE could also be used for baseline percutaneous coronary intervention (PCI) risk stratification in selected high-risk procedures such as left main coronary artery stenting. (147), (148), (149), (150)

Furthermore, recent studies suggested that EuroSCORE could be used as selection criterion for specific risk-reduction strategies in very high-risk patients, such as off-pump strategy during CABG and pre-procedural use of intra-aortic balloon pump during unprotected left main PCI. (151), (152)

A broader validation of the EuroSCORE to predict outcome in unselected patients with coronary artery disease (CAD) undergoing PCI, similar to that obtained for coronary surgery, may provide an immediate, better stratification of individual revascularization-related risks. Romagnoli et al. prospectively assessed the predictive power of the EuroSCORE in the prediction of peri-procedural mortality in 1173 consecutive patients undergoing percutaneous coronary intervention. The area under the ROC curve for the EuroSCORE system was 0.91 (95% CI 0.86 to 0.97), indicating a good ability of the model to discriminate patients at risk of dying during the hospitalization after percutaneous coronary intervention.

In this study, similar results were obtained applying both the additive and logistic EuroSCORE models. These findings were probably due to the small number of patients at very high risk in the study population (for example, additive EuroSCORE >14, logistic EuroSCORE >30.00).

Thus, in the era of large randomized trials matching surgical versus percutaneous revascularization approaches, the use of a common risk-prediction model as EuroSCORE, might facilitate the objective comparison of procedural outcomes following PCI and coronary artery bypass surgery.

The EuroSCORE model was originally designed to predict surgical in-hospital mortality, thus explaining the absence of angiographic variables in risk score computing. Therefore, the accuracy of the EuroSCORE system could be further increased by adding to this model some specific angiographic features that are known to influence complication rate during the procedure. (153), (154) So, significant improvement in the prediction of cardiac mortality could be achieved with the inclusion of EuroSCORE in a SYNTAX score-based model. Clinical and angiographic information are both important for assessing individual risk of patients undergoing PCI. (155)

Another work by Lehmann et al. showed that EuroSCORE, can be routinely used to estimate not only the perioperative risk of patients undergoing CABG, but also to predict short- and long-term prognosis of patients undergoing multivessel PCI in acute and elective settings. (156)

The discriminative ability of the EuroSCORE, Parsonnet, and GRACE risk scores in unselected patients with acute coronary syndrome undergoing emergent left main PCI was good. Comparing the EuroSCORE and Parsonnet scoring systems, it seems that they have no discriminative value in low and moderate risk patients, while the GRACE risk score discriminated risk among intermediate and high risk patients. (157)

The EuroSCORE risk stratification system was developed and validated within eight European populations. Since, there should be caution in the utilisation of any particular risk stratification system outside the countries of origins, it is important to carefully evaluate the validity of such system amongst foreign population, such as the Czech population.

A common practice in Vinohrady cardio centre is therapeutic decision made in close collaboration of cardiologists and cardiac surgeons considering not only cardiac but also all other comorbidities of the individual patient. In each patient report, the additive and logistic EuroSCORE are provided.

In our study we investigated for the first time validity of the both forms of EuroSCORE among the patients that underwent PCI and were treated medically. In such subset population, EuroSCORE showed good discriminatory capability for short-term mortality (area under ROC 0.695 for the additive model and 0.762 for the logistic model) (Figure 9)

Observed mortality was 7%, while the predicted mortality for the additive EuroSCORE was 5% (p=0.4) and 7% (p=0.842) for the logistic EuroSCORE. It seems that the logistic EuroSCORE tend to be more accurate in prediction of short–term mortality in patients that are not operated.

In conclusion, the present study, within the limitations of being single centre and based on a restricted number of adverse events, is the first to prove the applicability of the EuroSCORE risk model in patients undergoing percutaneous coronary revascularization. Thus, the EuroSCORE may help cardiologists and cardiac surgeons alike to individualize the risk profile of patients in order to better define the revascularization strategy and to appropriately counsel the patient.

Figure 9. Receiver operating characteristic curves for short-term mortality in the refused patients.

Figure 9a Additive EuroSCORE: area 0.695 [0.562-0.828]
Figure 9b Logistic EuroSCORE: area 0.716 [0.590-0.842]

Figure 9a

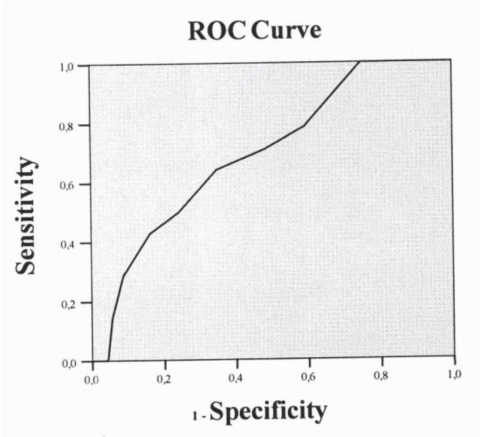
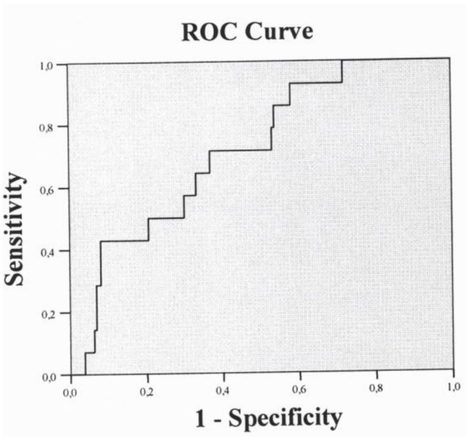


Figure 9b



4. Conclusions

Scoring systems have been developed in almost all subspecialties of clinical medicine. The major risk of a scoring system is to systemically determine factors that may identify patients at risk, or determine efficacy of diagnostic and therapeutic procedures. They provide comparative measures between different centers and countries. In addition, they facilitate the establishment of systems for quality assurance in a given treatment. However, scoring systems never intended to substitute the clinical decision making of physicians in the context of an individual patient.

In this work, we examined the most used and powerful risk prediction tool in Europe – the EuroSCORE. This work confirmed the EuroSCORE as a valuable risk prediction tool for all cardiac surgery in Czech Republic. We found good discrimination of the both forms of EuroSCORE with ROC area of 0.75 for the additive form and 0.76 for the logistic form for short-term mortality after all cardiac surgery. The observed and predicted mortality were similar (p=0.663). This means that patient selection for cardiac surgery in the Czech Republic can be based on the EuroSCORE. Despite, the already known indications for EuroSCORE use, we found that the EuroSCORE can be used as an effective risk prediction tool even in patients treated by percutaneous coronary intervention and conservatively treated patients.

The recently published articles about overestimation of the EuroSCORE, could be from three main reasons: Firstly, the EuroSCORE is already outdated, as it was developed from data regarding patients operated almost a decade and a half ago, and the results of surgery have improved significantly since then, especially in the elderly. Following the improvement of the surgery techniques and changes of the patients risk profiles, the EuroSCORE should be updated. The important thing is that the current EuroSCORE models present valuable and applicable base for further modifications.

Another reason is that the data originated from only eight European countries and only a few centers contributed from each one of these countries. Any particular risk stratification system outside the countries of origin should be utilized with great caution, and it is important to carefully evaluate the validity of such system among foreign population. We investigated the applicability of both models of EuroSCORE among Czech cardiac population and found out that it is a valuable risk stratification model in predicting short-term mortality.

Thirdly, and most important, the EuroSCORE was especially developed for cardiac surgery in general, especially for coronary revascularization procedures, the majority of data belonging to this group of patients, and not specifically for aortic valve replacement.

The purpose of the EuroSCORE is not only to allow a precise assessment of individual operative mortality, but also to analyze care for a center or a country as an overall score concerning cardiothoracic surgery and percutaneous coronary intervention. The main concern in the everyday practice is to be able to stratify patients according to their risk profiles into high risk and low risk populations, and make decisions based on this information for resource allocation and probable invasive treatment designed to reduce, if possible the risk of morbidity and mortality.

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5. Appendix – other publications of the candidate

1. Klinceva M, Widimský P, Pesl L, Stásek J, Tousek F, Vambera M, Bílková D. Prevalence of stress-induced myocardial stunning (Tako-Tsubo cardiomyopathy) among patients undergoing emergency coronary angiography for suspected acute myocardial infarction. Int J Cardiol. 2007 Sep 3;120(3):411-3.
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5.1. Prevalence of stress-induced myocardial stunning (Tako-Tsubo cardiomyopathy) among patients undergoing emergency coronary angiography for suspected acute myocardial infarction

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Abstract:

Stress-induced myocardial stunning is defined as a syndrome of acute chest pain, ST-T changes on the ECG and transient left ventricular apical wall motion abnormalities mimicking acute myocardial infarction but with surprisingly normal coronary angiography findings.

The aim of this retrospective study is to assess the prevalence of stress-induced myocardial stunning among patients undergoing urgent coronary angiography for suspected acute myocardial infarction.

During a four-year period (2002-2005), a total of 5876 patients underwent urgent coronary angiography for suspected acute myocardial infarction at three tertiary centers. Four patients fulfilled the diagnostic criteria for stress-induced myocardial stunning. Thus, the cath-lab prevalence of stress-induced myocardial stunning (i.e. among patients undergoing urgent coronary angiography for suspected acute myocardial infarction) was estimated as 1 per 1469 ST-elevation coronary angiograms (i.e. 0.07%). The estimated annual population incidence of this rare disorder was calculated as 0.00006%.

Stress-induced myocardial stunning is an extremely rare syndrome among patients undergoing emergency coronary angiography for suspected acute myocardial infarction.

Stress-induced myocardial stunning is defined as a syndrome of acute chest pain, ST-T changes on the ECG and transient left ventricular apical wall motion abnormalities mimicking acute myocardial infarction but with surprisingly normal coronary angiography findings. Originally it was named by Dr. Dote and his colleagues as Tako-Tsubo cardiomyopathy, after a fishing pot with a round bottom and narrow neck that is used for trapping octopuses in Japan [1]. Recently this syndrome has also been described among the white population [2].

However, the prevalence of stress-induced myocardial stunning among patients undergoing urgent coronary angiography for suspected acute myocardial infarction is not known. Thus, we retrospectively reviewed all 5876 patients who underwent urgent coronary angiography for suspected acute myocardial infarction at three tertiary cardiology centers in the Czech Republic (Prague - Vinohrady, Hradec Králové and České Budějovice) during a four-year period (2002-2005). The diagnostic criteria for stress-induced myocardial stunning were: acute chest pain with ST-T changes compatible with acute myocardial infarction, absence of any >50% stenosis on coronary angiography and transient apical left ventricular asynergy. Patients with acute febrile illness were excluded due to difficult separation from acute myocarditis.

Only 4 of the 5876 patients undergoing urgent coronary angiography for suspected acute myocardial infarction fulfilled the criteria for stress-induced myocardial stunning. Thus, the cath-lab prevalence of stress-induced myocardial stunning (i.e. among patients undergoing urgent coronary angiography for suspected acute myocardial infarction) was estimated as 1 per 1469 ST-elevation coronary angiograms (i.e. 0.07%). The three centers catheterize urgently 87% of all ST-elevation myocardial infarctions in the region with a total population of 1 628 000 citizens. Thus, the estimated annual population incidence of this rare disorder was calculated as 0.00006%.

Case no.1: An eighty-two years old woman was admitted with acute dyspnoe, ST elevation in II, III, aVF, V3-5 on ECG, troponin level 10.7 μg/l and CK-MB level 1.17 μkat/l. Coronary angiography showed minimal non-obstructive irregularities, while left ventriculography demonstrated apical akinesia with basal hyperkinesis and ejection fraction 43%. Echocardiography one day after the episode showed hypokinesis of the apical part of the left ventricle and improvement in the function to 50%. The patient was discharged 4 days later. She died suddenly at home 2 months after the episode.

Case no. 2: Sixty-three years old female with suspected acute myocardial infarction (ST elevation in V2-4, with troponin 0.6 μg/l and CKMB 0.81 μkat/l) and chest pain after severe emotional stress, underwent urgent coronary angiography. Coronary arteries were normal and left ventriculography showed anteroapical akinesia. Echocardiography 5 days later showed normal left ventricular function. Patient was discharged 8 days after the attack.

Case no. 3: Fifty – five years old man with chest pain after severe emotional stress was admitted to the catheterization laboratory with ST elevation in V2-6 and troponin-T 0.5 μg/l; CKMB 1.5 μkat/l. Urgent coronary angiography was normal, while left ventriculography showed anteroapical akinesia and hyperkinesia in the other segments. Echocardiography findings confirmed the finding anteroapical akinesia and basal hyperkinesis with ejection fraction 55%. Left ventricular kinesis improved 2 days after the episode, confirmed by echocardiography examination. The patient stayed at the hospital 9 days.

Case no. 4: Seventy years old woman with chest pain, after psychical stress in the last days was admitted to the coronary angiography unit with ECG changes (ST elevation in V1-V3, neg. T in V4-V6) and increased troponin (0.96 μg/l). Left ventriculography demonstrated apical akinesia and basal hyperkinesis. The patient left the hospital on the 7th day with a normal echocardiogram and 70% ejection fraction.

Among the Japanese population, Dote et al. in 1991 estimated the prevalence of this dysfunction as 1% among all acute myocardial infarctions treated invasively (1). This is 14-times higher frequency when compared to our data. However, the Japanese study is a single center registry, comprising a small number of patients. Our data are likely to be more relevant due to the fact, that patients from three centers with a defined population service area were included and due to the routine immediate cardiac catheterization performed in 87% of STEMI in the Czech Republic.

Thus, we conclude, that stress - induced myocardial stunning is an extremely rare distinct syndrome in European patients undergoing emergency coronary angiography for suspected acute myocardial infarction. In most cases it has a good prognosis with complete recovery within a few weeks. Nevertheless doctors should be cautious, due to the possibility of a sudden cardiac death as shown in one our patient.

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Figure legend:

Figure 1. Ventriculographic assessment of cardiac function at admission in a patient with Stress Cardiomyopathy.

End diastolic (A) left ventriculogram of patient 2 shows extensive akinesia of the apical wall of the left ventricle. End systolic (B) left ventriculogram of patient 2 shows balloon like asynergy of the apical region with hypercontraction of the basal segments of the ventricle. This ventriculogram is representative for all the patients with stress-induced myocardial stunning in the study.

Figure 1A.

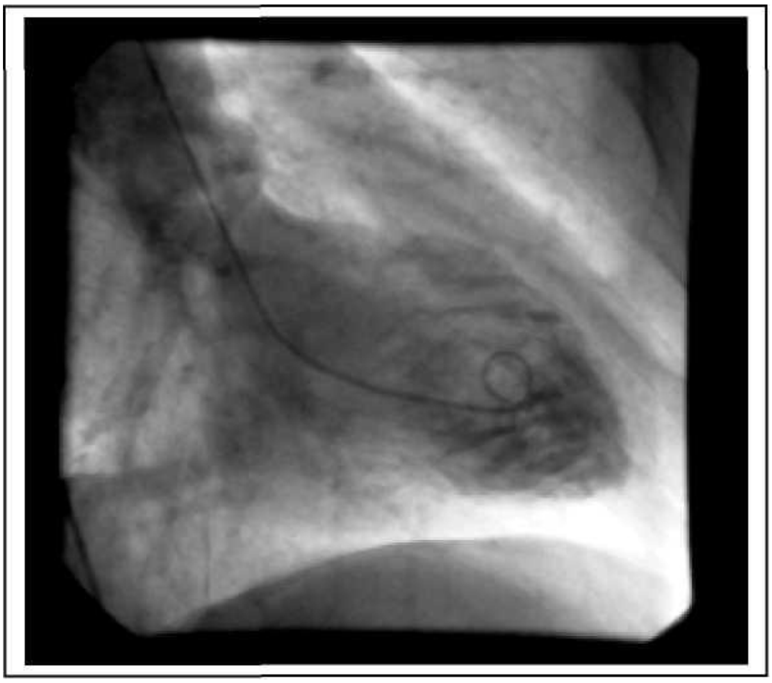
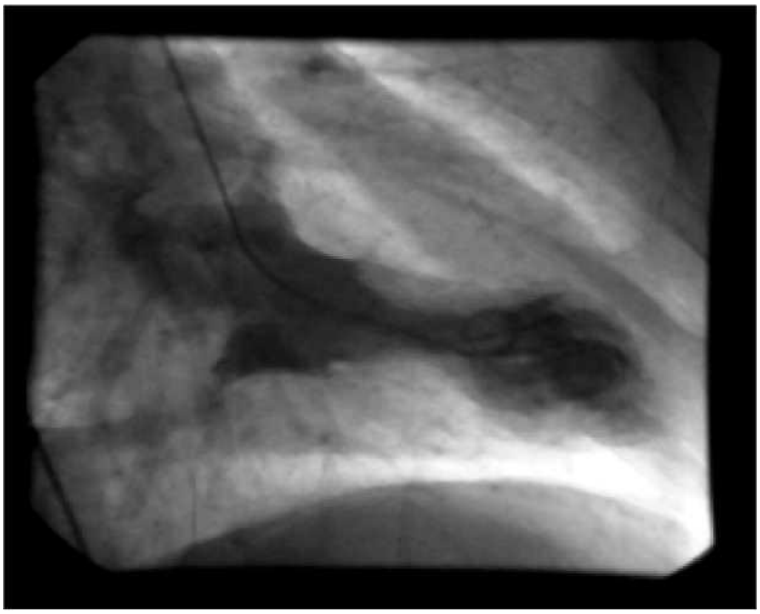


Figure 1B



5.2.Reperfusion therapy for ST-elevation acute myocardial infarction in Europe

Description of the current situation in 30 countries.

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**see Appendix for the full list of contributors.*

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Abstract

Background. Patient access to reperfusion therapy and the use of primary percutaneous coronary intervention (p-PCI) or thrombolysis (TL) varies considerably between European countries. The aim of this study was to obtain a realistic contemporary picture of how patients with ST-elevation myocardial infarction (STEMI) are treated in different European countries.

Methods. The chairpersons of the national working groups / societies of interventional cardiology in European countries and selected experts known to be involved in the national registries joined the writing group upon invitation. Data were collected about the country and any existing national STEMI or PCI registries, about STEMI epidemiology and treatment in each given country and about PCI and p-PCI centers and procedures in each country. Results from the national and/or regional registries in 30 countries were included in this analysis.

Results. The annual incidence of hospital admission for any acute myocardial infarction (AMI) varied between 90 – 312 / 100 thousand / year, the incidence of STEMI alone ranging from 44 – 142. Primary PCI was the dominant reperfusion strategy in 16 countries and thrombolysis in 8 countries. The use of a p-PCI strategy varied between 5 – 92% (of all STEMI patients), the use of thrombolysis (TL) between 0 – 55%. Any reperfusion treatment (p-PCI or TL) was used in 37 – 93% of STEMI patients. Significantly less reperfusion therapy was used in those countries where TL was the dominant strategy. The number of p-PCI procedures per million per year varied among countries between 20 – 970. The mean population served by a single p-PCI center varied between 0.3 – 7.4 million inhabitants. In those coutries offering p-PCI services to the majority of their STEMI patients this population varied between 0.3 – 1.1 million per center.

In-hospital mortality of all consecutive STEMI patients varied between 4.2 – 13.5%, for patients treated by thrombolysis between 3.5 – 14% and for patients treated by p-PCI between 2.7 – 8%.

The time reported from symptom onset to the first medical contact (FMC) varied between 60 – 210 minutes, FMC – needle time for thrombolysis between 30 – 110 minutes and FMC – balloon time for p-PCI between 60 – 177 minutes.

Conclusions. Most North, West and Central European countries used p-PCI for the majority of their STEMI patients. The lack of organised p-PCI networks was associated with fewer patients overall receiving some form of reperfusion therapy.

Introduction.

Primary PCI and thrombolysis represent two alternative reperfusion strategies for ST elevation acute myocardial infarction (STEMI). Commonly, thrombolysis is considered to be more widely available and can be started faster then primary PCI. In many randomized clinical trials (*ref. 1-6*) primary PCI has been shown to be superior to thrombolysis in reducing mortality, reinfarction and stroke. This benefit is related to a much higher early mechanical reperfusion rate (cca 90%) compared to pharmacological reperfusion rate (cca 50%), to the ability of simultaneously treating the underlying stenosis and finally to the lower risk of severe bleeding. The most recent European Society of Cardiology (ESC) guidelines (*ref. 7, 8*) recommend primary PCI as the preferred treatment whenever it is available within 90-120 minutes of the first medical contact. The aim of this project was to analyze the use of reperfusion treatments across Europe at the time when these new ESC guidelines were published.

Methods.

The European Association for Percutaneous Cardiovascular Interventions (EAPCI) invited the chairpersons of the national working groups / societies of interventional cardiology in all 51 European Society of Cardiology (ESC) countries and selected experts known to be involved in the national registries of ST-elevation acute myocardial infarction (STEMI) to join this project. Positive replies were received from 30 countries. Data were collected about the country and any existing national STEMI or PCI registries, about STEMI hospital admissions and treatment in each given country and about PCI and primary PCI centers and procedures in each country. Specifically, each participating national working group (or society) provided the precise number of all existing PCI hospitals in the given country and how many of them offer non-stop (24/7) primary PCI services. Primary PCI center (24/7) was defined as PCI hospital not using thrombolysis for the treatment of STEMI patients, in other words hospital performing primary PCI in all STEMI patients, 24 hours / day and 7 days / week.

Results from 30 European countries were included in this analysis *(tables 1 and 2)*. These data reflect the situation in years 2007-8 for most countries, but in 2006 or 2005 for a few, in whom the most recent data were not available.

Those national data already published are listed in the references section (ref. 9-27) and the names of ongoing registries and/or surveys are listed in the appendix and more details in table 1.

Besides obtaining the numbers from the individual countries, the contributors were also asked to describe subjectively, what they consider to be the main barriers for better p-PCI implementation and to comment on the possible influence of hospital / staff reimbursement on the local situation.

Statistical analysis. Data are presented in the descriptive format as we received them from each individual country (see appendix for the list of contributors). The SPSS 12.0 statistical package was used to fit the linear regression lines in fig. nr. 3.

Results.

Annual incidence of hospital admission for acute myocardial infarction. The annual incidence of hospital admission for *any* acute myocardial infarction (AMI) varied between 90 – 312 / 100 000 inhabitants / year and the incidence of hospital admissions for *STEMI* alone between 44 – 142 / 100 000 inhabitants / year *(table 2)*.

Reperfusion strategy use. Primary PCI is the dominant reperfusion strategy in 16 countries and thrombolysis in 9 countries. From five countries (Denmark, Estonia, Lithuania, Norway, Spain) only information about primary PCI (and not about thrombolysis) was available. The use of a p-PCI strategy varies between 5 – 92% (of all STEMI patients), the use of thrombolysis (TL) between 0 – 55%. Any reperfusion treatment (p-PCI or TL) is used in 37 – 93% of STEMI patients *(fig. 1)*. Overall, in those countries using TL as the dominant strategy, the overall population receiving some form of reperfusion therapy is lower (only 55% patients are treated, although this varied considerably from country to country).

The population need for primary PCI services. The number of primary PCI procedures per 100 000 inhabitants per year *(table 3, fig. 2)* ranged from 2 – 97. The mean population served by a single p-PCI center *(table 4)* varies between 0.3 – 7.4 million inhabitants. In those coutries offering p-PCI services to the majority of their STEMI patients this population varies between 0.3 – 1.1 million per center. There was a weak correlation between numbers of PCI procedures and the gross domestic product per capita *(fig. 3, table 3).*

Mortality. The in-hospital mortality of all consecutive STEMI patients *(table 5)* varies between 4.2 – 13.5%, for patients treated by thrombolysis between 3.5 – 14% and for patients treated by primary PCI between 2.7 – 8%.

Time delays. *(table 6, fig. 4-5)* The time from symptom onset to the first medical contact (FMC – defined as the time of diagnostic ECG) ranged from 60 – 210 minutes, FMC – needle time for thrombolysis between 30 – 110 minutes and FMC – balloon time for p-PCI between 60 – 177 minutes. These FMC – balloon times are given for all primary PCI procedures, irrespective whether the patient underwent interhospital transfer or was directly admitted to the PCI hospital.

STEMI initial presentation. Only approximately half of the patients arrive at the hospital via an EMS ambulance. This proportion varies considerably between countries: from 17% (Greece) to 85% (United Kingdom) – see *fig. 6*.

<u>Discussion.</u>

Geographic differences, heterogenity of care. Primary PCI is now the dominant treatment of STEMI in the majority of countries: Scandinavia (NO, DK, SE, FIN), Central Europe (CZ, SLO, PL, HU, AT, HR), West Europe (DE, BE, FR, CH and NL), Italy and Israel. Several countries have the infrastructure available but do not use it sufficiently to treat most of their AMI patients – this holds true especially for the South Europe (Greece, Bulgaria, Portugal, Spain, Turkey) and for the United Kingdom and Slovakia (however, national programs for p-PCI implementation have already started in these latter two countries). The described „North-South gradient“ in primary PCI services is typically seen in Italy: the Northern part of Italy has p-PCI rates similar to Central or West Europe, while the Southern part of Italy has rates similar to Greece or Turkey. Unfortunately, no or few data have been obtained from Ireland, Iceland, East Europe (Belarus, Ukraina, Russia, Moldova, Bosnia i Herzegovina, FYROM, Albania, Georgia) and from the Mediterranean non-European countries (ESC members).

The heterogeneity of care is known from international registries – e.g. the GRACE registry showed that the care-seeking behavior in patients with acute coronary disease differs among countries or continents. (*ref. 28*)

Annual incidence of acute myocardial infarction. The annual incidence of hospital admission for <u>*any*</u> acute myocardial infarction varied considerably, as was the case for the incidence of <u>*STEMI*</u> alone. Those countries with the most precise data (e,g, covering 100% of the population either in the whole country or in selected regions / counties – see table 1) reported the incidence close to the overall mean numbers (cca 1900 for all AMIs and cca 800 for STEMIs). In other words, the annual incidence of cca 1900 hospital admissions for any AMI per year per million population seems to be typical for the European population. This can be used for planning infrastructure because most of these patients will need coronary angiography and subsequent PCI or CABG during their hospital stay.

Reperfusion strategy use. It is of note that primary PCI is already today the leading reperfusion strategy in most European countries. Several countries can serve as evidence that p-PCI can be offered to as many as 70-90% of all STEMI patients in the whole country. An increased use of primary PCI as the preferred reperfusion therapy is identified by this data when compared with the second Euro Heart Survey on Acute Coronary Syndromes (EHS–ACS-II) (*ref. 29*). Results of our study reverse the traditional opinion, that thrombolysis is the strategy more suitable for widespread application. The opposite is true: reperfusion as a whole is offered to less of the STEMI population in those countries using thrombolysis as the dominant strategy. This is probably related to the many contraindications for thrombolytic therapy and also to the fear of using thrombolysis in patients over 75 years of age, who present a significant proportion of all STEMI patients today (e.g. 31% of all hospitalized AMI patients in the Netherlands – *ref. 30*). Thus p-PCI, despite its apparent logistic complexity, offers far broader population reach.

The population need for primary PCI services. The number of primary PCI procedures per million per year in these countries, covering their population needs, varies between cca 600-900 per million. In these coutries one PCI center is serving a population of cca 0.3 – 0.8 million per center. These numbers might serve as a reference for planning the infrastructure.

Mortality. The data on mortality betwen countries cannot be directly compared due to the different methodology of the national registries or surveys. The Czech Republic can serve as an example of these methodologic limitations: the in-hospital mortality after p-PCI in the national PCI registry reported by the cardiologists was 3.5%, while after matching the data with the national deaths registry this number rose to 6.7%. This can be explained by the fact that cardiologists are frequently entering the registry data immediately after the procedure, when the patient is subsequently moved from the interventional cardiology unit to another unit (long-term facility, local community hospital, cardiac surgery, long-term rehabilitation unit, etc.) and thus they do not reflect the true (total) hospital outcome.

As with all registries, these data must be interpreted with great caution. The demographic features of patients treated by p-PCI may well be different from those treated by thrombolysis. In the National Infarct Angioplasty Project (NIAP) study in the United Kingdom for example, the patients treated by p-PCI were younger than those treated by thrombolysis, suggesting a tendency to use p-PCI in fitter patients who have a lower predicted mortality regardless of treatment strategy. Conversely it is also possible that some of the difference is due to the „real world“ inclusion of higher risk patients, for whom the differential benfits of PCI might be greater. The highest risk patients (elderly, cardiogenic shock, polymorbid, etc.) are usually excluded from the randomized trials and p-PCI is certainly an optimal treatment for this high risk group, while thrombolysis is associated with high mortality or high complication rates in cardiogenic shock or elderly patients.

The lack of information about the baseline characteristics of individual patients in our study and subsequently the inability to statistically compensate for probable differences between the two reperfusion groups, prohibit us from making any adjusted comparison of mortality outcome between p-PCI and thrombolysis. However, properly analysed consecutive STEMI patients from a whole European country (Sweden) showed that p-PCI was superior to thrombolysis with lower 30-day and 1-year mortality *(ref. 31)*. The mortality benefit was somewhat greater in this “real life“ study compared to randomized trials, which is to be expected as high risk patients that benefit the most from reperfusion therapy usually are excluded from randomized trials, a matter previously shown in STEMI patients *(ref. 32)*.

Time delays. If 30 minutes (as an expected minimal time to achieve pharmacologic reperfusion) are arbitrarily added to FMC – needle time, then thrombolysis is only minimally faster in opening the coronary artery when compared to p-PCI in our study. The importance of time delays can be easily demonstrated on the situation in France: the time delays in reperfused patients are short and thus the mortality is low. Furthermore, the difference (125 min. – see table 5) between the short thrombolysis- related delay and the long PCI-related delay causes no significant difference in mortality between the two treatment strategies in this country *(ref. 33)*. In other words: p-PCI is superior to thrombolysis only when the time difference between these two strategies is below 2 hours. We are fully aware, that this survey cannot directly compare thrombolysis and p-PCI. Both treatments can certainly be offered more expeditiously than was shown in this study. This should be one of the main goals for future improvements.

Primary PCI volume per center and per operator may influence the outcomes, especially of STEMI patients, where the complexity of care is more important compared to elective PCI. Unfortunately, this study was not designed to collect such data. The experience from countries, using primary PCI for vast majority of their STEMI patients shows, that a population between 0.3 and 1.1 million per one primary PCI (i.e. non-stop, 24/7) center results in cca 200 – 800 primary PCI procedures / year / center. This may be considered optimal. Population per center < 0.3 million results in low numbers of STEMI and thus the experience of the team may not be sufficient. A population significantly greater than one million results in „overload“ of the center by too many infarcts (of course only if all infarcts from that region are admitted to this center). The PCI volume per operator is probably less important than PCI volume per center as there are very few low volume operators in the high volume centers. The optimal case load may be anywhere between 50 – 100 primary PCIs / operator / year.

Reimbursement. In most European countries (Austria, Croatia, Czech Republic, Denmark, Germany, Greece, Hungary, Italy, Izrael, Lithuania, Netherlands, Norway, Poland, Portugal, Serbia, Slovakia, Slovenia, Sweden, Switzerland) the reimbursement systems supports primary PCI - i.e. the PCI hospital is reimbursed adequately, the non-PCI hospital in general does not lose money by sending patients for primary PCI and Emergency Medical Services (EMS) transfers are reimbursed. In some countries PCI centers receive reimbursement for primary PCIs, but the small hospitals lose money when STEMI patients are admitted initially to PCI centers (Belgium, Bulgaria, Spain, Turkey, United Kingdom) or interhospital transfer is not appropriately reimbursed (Belgium, Bulgaria). In only one country (Romania) PCIs (any) are not adequately reimbursed in general (low limits on numbers of centers and procedures).

Barriers for the implementation of primary PCI in Europe. Reimbursement is only rarely a real problem (see above). EMS interhospital transport is not supported by adequate reimbursement in some countries, and in smaller districts only a single EMS ambulance is in service during the off-hours and cannot go outside this district. Low staffing levels (lack of interventional cardiologists and/or nurses and other support staff) prevent many smaller PCI hospitals running a non-stop (24/7) primary PCI services. A conservative attitude of internists and even some noninvasive cardiologists, who still prefer to use thrombolysis instead of sending their patients to other cardiologists, is the most frequently quoted barrier, along with the insufficient motivation of interventional cardiologists and/or nurses to run the non-stop (24/7) services even when the staffing is sufficient (they are often not paid adequately for this activity). The use of helicopters for ***short*** distance transfers actually prolongs the delays and should in general be avoided; helicopter transfer is extremely useful for patients with ***long*** distance transfers but is expensive. In several countries (Austria, Croatia, Czech Republic, Norway, Sweden) the good cooperation between the national society of cardiology, government and insurance companies (health care funds) significantly contributed to the development of p-PCI services.

This survey suggests that medical and non-medical staff are the main barriers for wider p-PCI implementation: with reasons ranging from low staffing levels (lack of interventional cardiologists and/or nurses and other staff groups) through to the conservative attitude of many physicians and to the insufficient motivation of interventional cardiologists and/or nurses to run demanding non-stop (24/7) services. In some countries the lack of a systematic training program has resulted in a lack of interventional cardiologists and foreign cardiologists have been invited to work there in order to fill this gap. An inappropriate reimbursement system is the limitation of p-PCI only in a few countries. Some of these problems might be overcome by organizing cooperating networks of PCI hospitals in close vicinity and organized by the local ambulance system (EMS) as shown from the VIENNA STEMI network *(ref. 34)*. The formation of local networks might help to reach the goal *(ref. 35)*.

Limitations of this analysis. While data from 30 countries were included in this analysis, the number of centres that participated in some of the national registries or surveys may not be representative of the countries' total populations. In addition, data were not gathered during the same period of time (data from countries are based on 2005, 2006 or 2007 registries or surveys depending on what was available in each country at the time of this manuscript preparation). Furthermore, different inclusion criteria to national registries and surveys may lead to selection bias in the patient population. This manuscript cannot objectively compare p-PCI versus TL. It is possible that hospitals using primary PCI have better resource allocation and organization that allows for better overall management of all aspects of AMI, e.g. staffing of these centers may play an important role. Furthermore, we did not have individual patient level data and it may well be that the patients treated by p-PCI and thrombolysis are not matched (e.g. p-PCI patients might be younger than the lytic cohort) and thus caution is needed in making such non-randomised comparisons. The presented data are unvalidated, derived from national registries or surveys that might not have identified all patients with AMI or STEMI. The various registries used here differ from each other in their methodology, this being the major limitation that led us to the decision not to use sophisticated statistics in this manuscript.

Due to the facts, that this is a retrospective analysis of multiple national registries, there is a lack of rigor in defining the same entry criteria to these variable registries. Furthermore, the data about all hospital admissions (including non-PCI hospitals) were available only from 16 countries. In the remaining 14 countries data were limited mostly to PCI centers (plus partial information about admissions to non-PCI hospitals).

However, despite these limitations we believe that these data are the best available and have clear clinical relevance.

Conclusions.

The annual incidence of hospital admission for AMI in Europe is cca 1900 patients per million population with an incidence of STEMI of about 800 per million. A nationwide primary PCI strategy for STEMI results in more patients being offered reperfusion therapy. North, West and Central Europe have already well developed primary PCI sevices, offering primary PCI treatment to 60-90% of all STEMI patients. South Europe and the Balkans are still predominantly using thrombolysis - associated with this is a higher proportion of patients left without reperfusion treatment. Countries performing annually >600 primary PCIs per million population and having a mean population per one p-PCI center <750 000 are able to meet the needs of all their STEMI patients. Countries in which (nearly) all existing PCI centers offer 24/7 p-PCI services appear to exhibit the best results. Overall, there is a substantial heterogenity of practice in Europe and there are many opportunities to improve the care.

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Belgium (Belgian STEMI registry, Belgian Working Group Interventional Cardiology registry): Marc Claeys, Victor Legrand

Bulgaria: Slaveyko Djambazov, Vasil Velchev

Croatia (Croatian Cardiac Society, WG for Acute Coronary Syndromes, Hospital PCI registries, Zagreb Registry of Acute Myocardial Infarction, Croatian Institute for Public Health): Davor Miličić, Vjeran Nikolić Heiztler, Zdravko Babić, Mijo Bergovec, Vlasta Hrabak Žerjavić, Verica Kralj

Czech Republic (CZECH registry, National PCI registry - NRKI): Petr Widimsky, Petr Kala, Michael Zelizko, Michael Aschermann, Petr Jansky, Frantisek Tousek, Frantisek Holm

Denmark: Steen Dalby Kristensen, Anders Junker

Estonia: Toomas Marandi

Finland: Juha Hartikainen

France: Jean Fajadet, Nicholas Danchin, Martine Gilard, Didier Blanchard

Germany (Deutsches Herzinfarkt-Register, Herzbericht 2007: Uwe Zeymer, Volker Schaechinger, Anselm Gitt, Michael Boehm

Greece (HELIOS registry, Hellenic Heart PCI registry): George Andrikopoulos, Georgios Papaioannou

Hungary (Database of the National Health Insurance Fund, National primary PCI registry): Bela Merkely, David Becker

Israel (ACSIS registry): Alexander Battler, Basil Lewis, Shlomo Behar

Italy (SICI GISE PCI registry, LOMBARDIMA registry, BLITZ 3 survey, IN-ACS Outcome registry, Italian National Health Service, Veneto region registry, Ministero del Lavoro, Salute e Politiche Sociali, Istituto Superiore di Sanità): Stefano De Servi, Marco Tubaro

Latvia (Latvian registry of ACS): Andrejs Erglis

Lithuania: Ramunas Navickas

F.Y.R. Macedonia: Milka Klinčeva

Netherlands: Karel T. Koch, Willem J. ter Burg

Norway: Lars Aaberge

Poland (PL-ACS Registry, WG on Cardiovascular Interventions registry): Grzegorz Opolski, Adam Witkowski, Lech Polonski

Portugal: Joao Morais

Romania (RO-STEMI registry): Dan Deleanu, Gabriel Tatu-Chitoiu

Serbia (National ACS registry): Miodrag Ostojič, Zorana Vasiljevič

Slovakia (SLOVAKS registry): Martin Studenčan, Anna Baráková, Peter Hlava, Ján Murín, Gabriel Kamenský, Gabriela Kaliská.

Slovenia (National survey 2007, Ljubljana registry): Marko Noč

Spain: Jose Antonio Baz, Amadeo Betriu, Josephina Mauri Ferre, Agustin Albarrang, Felipe Hernandez

Sweden (RIKS-HIA / Swedeheart registry): Ulf Stenestrand

Switzerland (Swiss PCI registry, AMIS Plus registry): Paul Erne, Dragana Radovanovic, Stephan Windecker, Eric Eeckhout

Turkey (TUMAR registry): Omer Kozan, Rasim Enar

United Kingdom (MINAP registry, BCIS registry): Mark de Belder, Peter Ludman, John Birkhead

Figure 1: Hospitalized STEMI treatment in Europe (data from national registries or surveys). 100% = all hospitalized STEMI patients in each given country. Green color = STEMI patients treated by primary PCI, red color = STEMI patients treated by thrombolysis, black color = STEMI patients not treated with any reperfusion.
Countries abbreviations: CZ = Czech Republic, SLO = Slovenia, DE = Germany, CH = Switzerland, PL = Poland, HR = Croatia, SE = Sweden, HU = Hungary, BE = Belgium, IL = Israel, IT = Italy, FIN = Finland, AT = Austria, FR = France, SK = Slovakia, LAT = Latvia, UK = United Kingdom, BG = Bulgaria, PO = Portugal, SRB = Serbia, GR = Greece, TR = Turkey, RO = Romania.

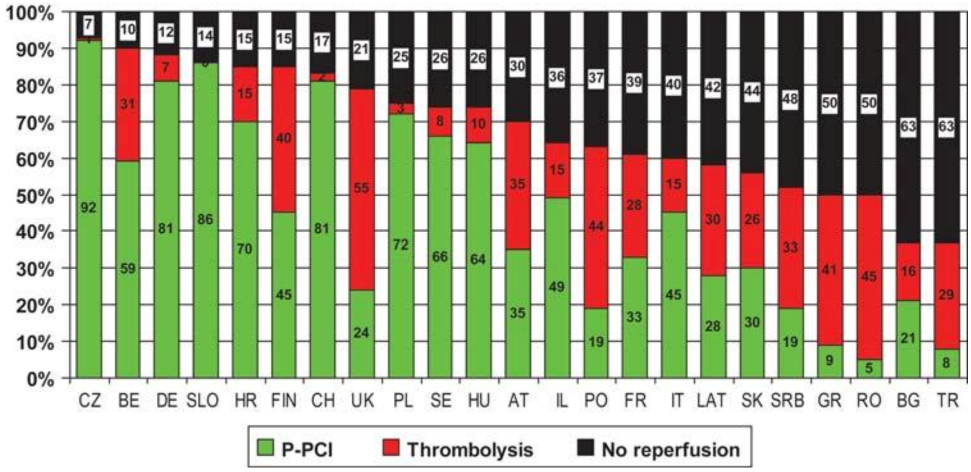


Figure 2: Primary PCIs per year per million inhabitants in European countries. Grey color = no data available, blue colors = countries participating in this study.

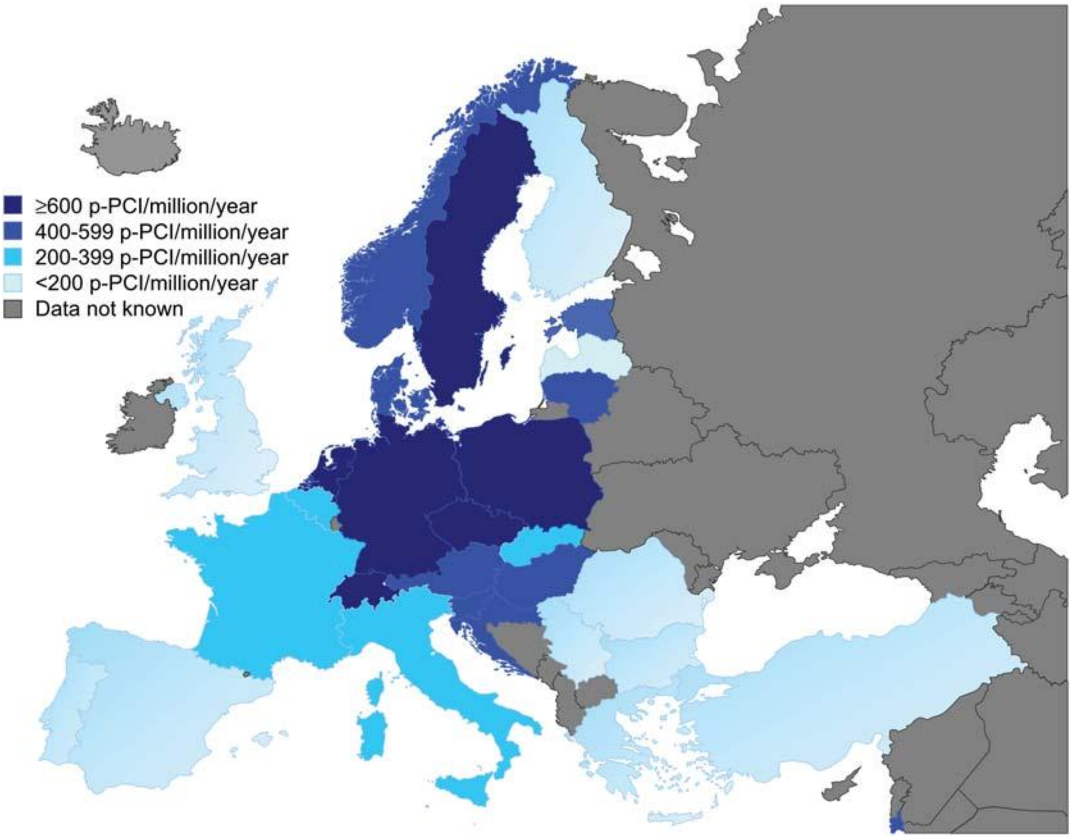
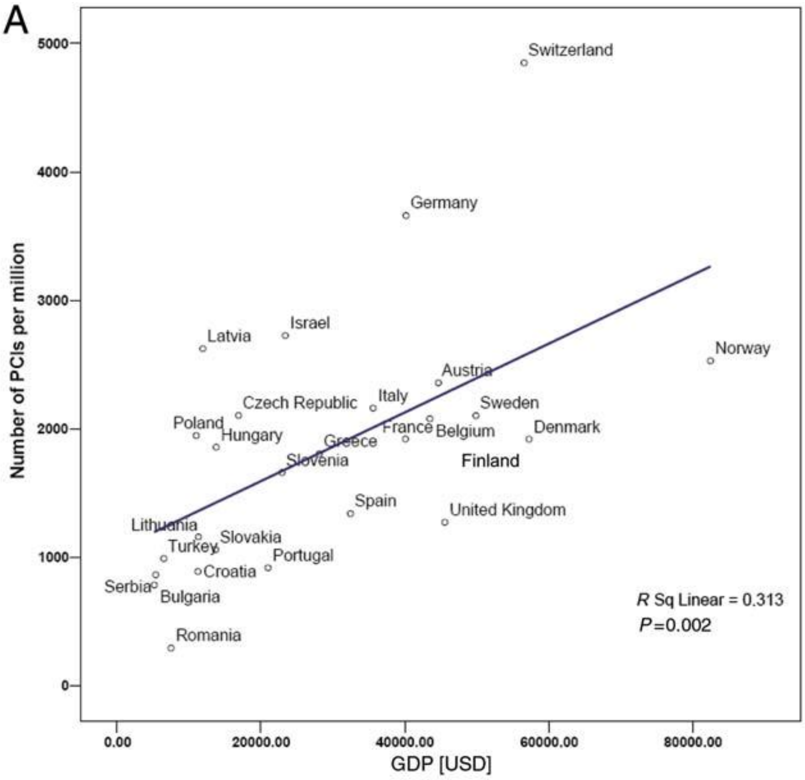


Figure 3: Correlation between the annual number of PCI procedures per million population and the gross domestic product per capita in European countries.
a) All PCI procedurtes.
b) Primary PCI procedures.



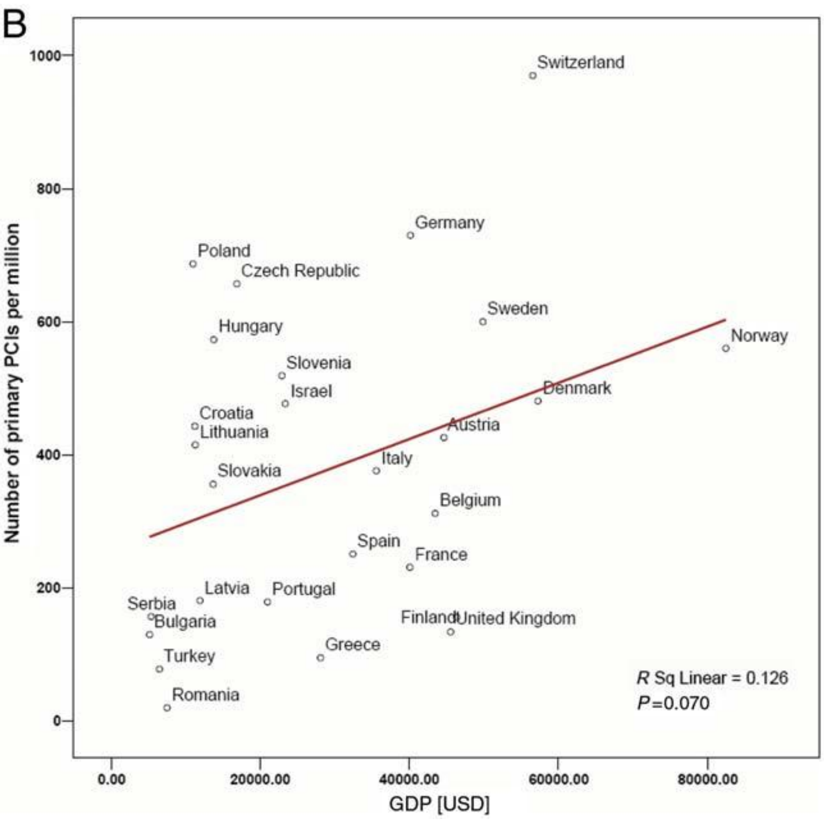


Figure 4: Time delays in patients treated by thrombolysis: „symptom onset – first medical contact“ and „first medical contact – start of thrombolysis“ time.

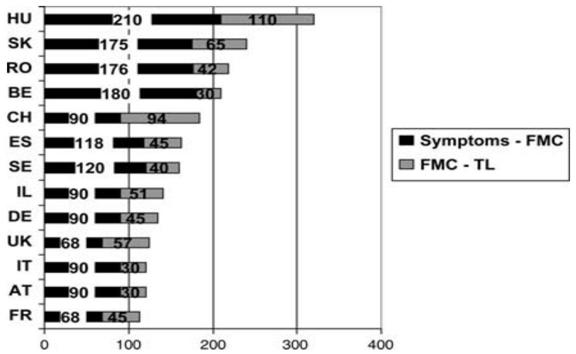


Figure 5: Time delays in patients treated by p-PCI: „symptom onset – first medical contact“ and „first medical contact – balloon“ time.

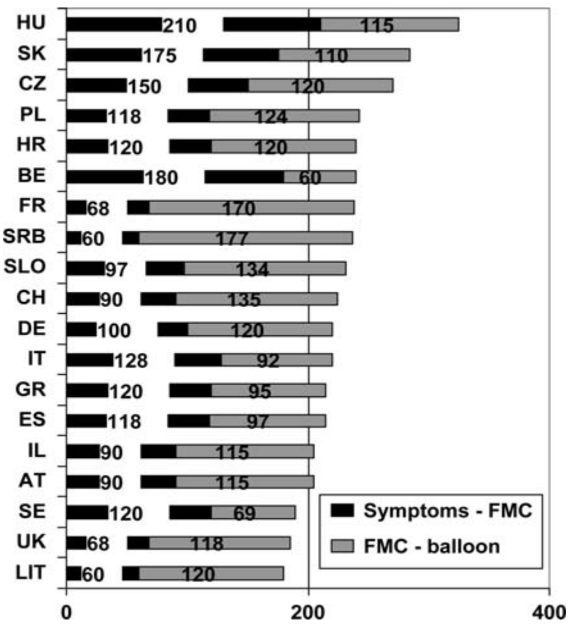


Figure 6: Percentace of STEMI patients arriving to the first hospital via EMS services.
In the UK, Norway, Switzerland and Sweden physicians are only in ambulance helicopters, paramedics are in ambulance cars. In all other countries physicians are in most or all EMS ambulances (cars and helicopters).

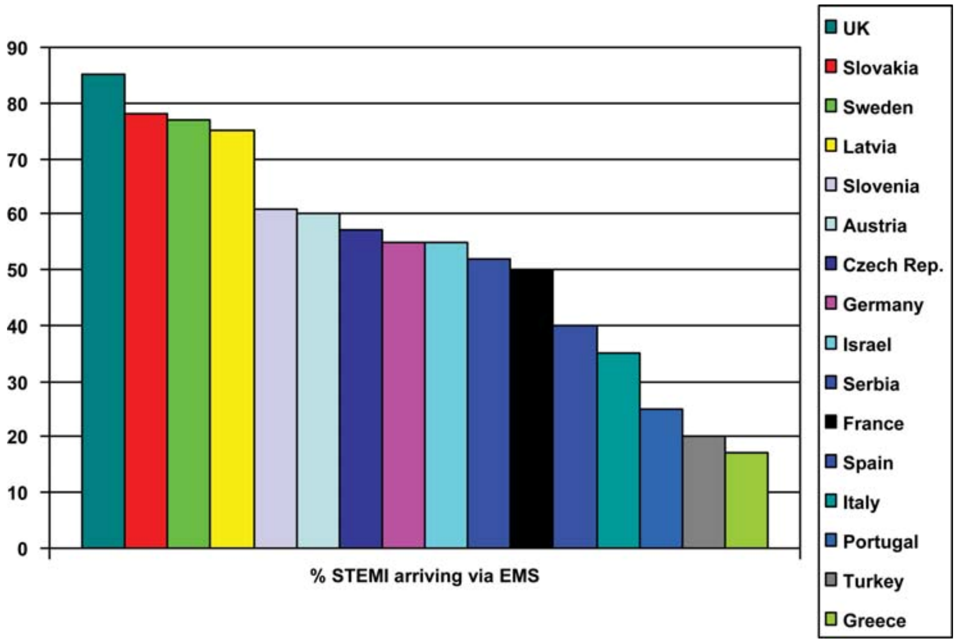


Table 1: National registries and other sources of the countries' data for this study.

Country	Year	STEMI registry (name, ref.)	PCI registry (name, ref.)	Other registry or survey (name, ref.)	Expert estimate only	Completeness of STEMI capturing per period and region
Austria	2005-7	VIENNA STEMI registry *(ref. 34)*	Austrian Heart Catheter Registry *(ref. 36)*	Austrian Acute PCI Registry *(ref. 37)*	---	100% in Vienna region, cca 50% for Austria
Belgium	2008	Belgian STEMI registry	Belgian Working Group Interventional Cardiology registry			50%
Bulgaria	2007	National Health Insurance Fund	National Health Insurance Fund, Bulgarian WG Interventional Cardiology	---	---	100%
Croatia	2005-8	Croatian Cardiac Society, WG for Acute Coronary Syndromes	Croatian Cardiac Society; Hospital PCI Registries	Zagreb AMI Registry; Croatian Institute of Public Health		90% for STEMI; 100% for PCI
Czech Republic	2005-7	CZECH registry (all ACS - *ref. 19)*	NRKI registry.	---	---	100% for all ACS in the CZECH registry.
Denmark	2007	None.	Danish Heart Registry	-	For AMI not undergoing PCI	100% for p-PCI
Estonia	2008	Estonian Myocardial Infarction Registry, WG on Acute Coronary Syndromes	---	---	---	100%
France	2005	FAST-MI *(ref. 33)*	FAR	---	---	60% of ICUs
Finland	2006	---	---	Registry of Cardiovascular Diseases, National Institute for Health and Welfare *(ref. 18)*	---	cca 90 % for all AMI
Germany	2007-8	German Myocardial infarction registry *(ref 46)*	---	Herzbericht 2007 *(ref. 47)*	--	25 %
Greece	2006	HELIOS *(ref. 14, 16)*	---	Hellenic Study of AMI *(ref. 15)*	---	100%
Hungary	2004-8	National Health Insurance Database	Registry of the Working Group of Interventional Cardiology	PCI Network in the Middle-Hungarian region (Budapest)	---	100% for all
Italy	2006-8	VENERE *(ref.41)*, In-ACS (2007) BLITZ 3 (2008)	GISE Registry (GISE=Italian Society of Interventional Cardiology)	Istituto Superiore di Sanità (ISS)	---	100% in Veneto Region p-PCI 100% in GISE (all Italy) 80% in BLITZ 3
Israel	2006	ACSIS	---	---	---	100%
Latvia	2008	Latvian registry of acute coronary syndromes	Latvian registry of acute coronary syndromes	---	---	100%
Lithuania	2007-8	---	Lithuanian PCI registry	---	Yes for	100% for p-PCI only

					AMIs without PCI	
F.Y.R.Macedonia	2007-8	--	Hospital based registries in all existing PCI centers	--	---	95% in Skopje, cca 80% for Macedonia
Netherlands	2008	---	Dutch National PCI Registry (BHN)	---	---	---
Norway	2007	---	PCI -hospital based registries	---	For patients not treated by PCI.	Not known (PCI data only)
Poland	2004-7	PL-ASC Registry	PCI registry of the WG on Cardiovascular Interventions of the Polish Cardiac Society		---	100%
Portugal	2008	National ACS Registry 2002 *(ref. 43),* updated 2009 *(ref. 44)*	---	---	---	N.A.
Romania	2007-8	RO-STEMI	---	---	---	100%
Serbia	2007	National Institute for health	Working group on interventional cardiology *(ref. 42)*			100%
Slovakia	2007	SLOVAKS registry	Registry of the Working Group Interventional Cardiology (Slovak Society of Cardiology)	---	---	46% of all STEMI and 100% of p-PCI in Slovakia
Slovenia	2007	National survey	National survey	---	---	100%
Spain	2007	---	Registro Español de Hemodinámica y Cardiología Intervencionista *(Ref. 45)*	---	Yes for AMIs without PCI	N.A.
Sweden	2007	RIKS-HIA	SCAAR	---	---	100%
Switzerland	2007	AMIS Plus (STEMI/NSTEMI/UA registry, *ref. 48-50*)	Swiss PCI survey *(ref. 51)*	---	---	100% for p-PCI, 43% for STEMIs
Turkey	2007	TUMAR registry	---	---	Yes, partly	N.A.
United Kingdom	2005-8	Myocardial Ischaemia National Audit Project (MINAP) *(ref 38)*	British Cardiovascular Intervention Society (BCIS) *(ref 39)* and Central Cardiac Audit database (CCAD) *(ref 40)*	---	---	100%

Table 2: Population data and acute myocardial infarction annual incidence.
STEMI = ST elevation acute myocardial infarction, AMI = acute myocardial infarction, N.A. = not available.

Country	*Country population* *(www.populationmondiale.com)*	*Hospitalized STEMI / year*	*STEMI / 100 thousand / year*	*Hospitalized AMI (any)*	*AMI / 100 thousand / year*
Austria	8 199 783	7 800	95	16 000	195
Belgium	10 584 534	7 000	66	12 000	114
Bulgaria	7 640 238	8 726	114	11 285	148
Croatia	4 493 312	3 600	82	N.A.	N.A.
Czech Republic	10 228 744	6 761	66	20 048	196
Denmark	5 468 120	N.A.	N.A.	N.A.	N.A.
Estonia	1 315 912	1 751	133	3 502	266
France	62 448 977	35 000	55	65 000	105
Finland	5 300 484	4 674	88	16 446	310
Germany	82 217 837	100 000	121	208 000	250
Greece	10 706 290	11 780	110	19 853	185
Hungary	9 956 108	8 900	89	18 500	186
Italy	58 147 733	67 500	1 16	147.500	254
Israel	7 337 000	5 500	75	10 000	136
Latvia	2 270 894	1 437	63	N.A.	N.A.
Lithuania	3 575 439	3 000	84	N.A.	N.A.
F.Y.R. Macedonia	2 049 613	1765	86	N.A.	N.A.
Netherlands	16 405 399	N.A.	N.A.	N.A.	N.A.
Norway	4 703 779	3900	83	12 650	276
Poland	38 518 241	50 000	130	90 000	234
Portugal	10 642 836	11 104	104	N.A.	N.A.
Romania	22 276 056	10 000	45	20 000	90
Serbia	7 400 000	6 079	82	8 655	117
Slovakia	5 447 522	3 635	67	7635	140
Slovenia	2 009 245	1 210	60	N.A.	N.A.
Spain	45 116 894	40 000	89	120 000	266
Sweden	9 031 088	6 000	66	21 000	232
Switzerland	7 593 494	N.A.	N.A.	11 337	149
Turkey	70 586 256	100 000	142	220 000	312
United Kingdom	60 776 238	27 000	44	105 000	173

Table 3: Percutaneous coronary interventions (PCI) per one million inhabitants compared with gross domestic product (GDP) per capita
(in US dollars, according to the UN statistics for 2007, http://unstats.un.org/unsd/demographic/products/socind/inc-eco.htm**).**

Country	*All PCIs / year*	*All PCIs / million*	*Primary PCIs / year (% of all PCIs)*	*Primary PCIs / million*	*GDP per capita (US$)*
Austria	19 342	2 358	3 500 (18%)	426	44 652
Belgium	22 000	2 079	3 300 (15%)	312	43 469
Bulgaria	6 000	785	1 801 (30%)	236	5 177
Croatia	4 000	890	1 150 (22%)	255	11 256
Czech Republic	21 531	2 105	6 720 (31%)	657	16 880
Denmark	10 500	1 920	2 691 (26%)	481	57 256
Estonia	2 471	1 878	485 (20%)	369	15 932
France	120 000	1 921	14 400 (12%)	231	40 089
Finland	8 894	1 678	826 (9%)	156	46 370
Germany	299 600	3660	60 000 (20%)	730	40 162
Greece	19 311	1 804	1 022 (5%)	95	28 111
Hungary	18 500	1 858	5 700 (31%)	573	13 777
Italy	128 428	2 161	22 421 (17%)	376	35 585
Israel	20 000	2 726	3 500 (17%)	477	23 382
Latvia	5 956	2 624	410 (7%)	181	11 930
Lithuania	4 143	1 159	1 485 (36%)	415	11 307
F.Y.R.Macedonia	2516	1227	981(39%)	478	3 703
Netherlands	36 367	2 217	11 201 (31%)	683	46 669
Norway	11 890	2530	2632 (22%)	560	82 464
Poland	75 024	1 948	26 457 (35%)	687	11 007
Portugal	9 873	919	1 902 (19%)	179	20 990
Romania	6 560	294	450 (7%)	20	7 523
Serbia	6 395	864	1 161 (18%)	157	5 382
Slovakia	5 730	1061	1924 (34%)	356	13 701
Slovenia	3 336	1 661	1 043 (31%)	519	22 936
Spain	60 457	1 340	11 322 (19%)	251	32 450
Sweden	19 000	2 103	5 421 (29%)	600	49 873
Switzerland	36 817	4 849	7 363 (20%)	970	56 578
Turkey	70 000	991	5 500 (8%)	78	6 511
United Kingdom	77 373	1 273	8 153 (11%)	134	45 549

Table 4: Numbers of PCI centers and population per one center.
Primary PCI center (24/7) was defined as PCI hospital not using thrombolysis for the treatment of STEMI patients, in other words hospital performing primary PCI in all STEMI patients, 24 hours / day and 7 days / week.

Country	*PCI centers all*	*Population per any PCI center*	*Primary PCI centers (non-stop, 24/7)*	*Population per primary PCI center (24/7)*
Austria	34	282 751	24	341 000
Belgium	36	294 015	30	352 817
Bulgaria	21	363 820	9	850 000
Croatia	10	449 331	8	561 664
Czech Republic	22	464 943	22	464 943
Denmark	7	781 160	5	1 093 624
Estonia	3	438 637	2	657 956
France	210	297 376	200	312 245
Finland	24	220 853	2	2 650 242
Germany	430	190 000	310	265 000
Greece	40	267 657	10	1 071 000
Hungary	16	622 257	13	765 854
Italy	242	240 270	164	354 559
Israel	22	333 500	16	458 563
Latvia	5	454 179	1	2 270 894
Lithuania	6	595 906	3	1 191 813
F.Y.R.Macedonia	3	683 204	3	683 204
Netherlands	22	745 700	22	745 700
Norway	8	587 500	6	783 963
Poland	95	405 455	74	520 516
Portugal	19	560 158	9	1 182 555
Romania	12	1 856 338	0	N.A.
Serbia	9	822 222	1	7 400 000
Slovakia	6	916 666	4	1 375 000
Slovenia	5	401 849	2	1 004 745
Spain	129	349 743	56	805 658
Sweden	29	311 417	13	694 699
Switzerland	27	281 240	20	379 675
Turkey	157	449 592	35	2 016 742
United Kingdom	98	620 165	23	2 642 445

Table 5: In-hospital mortality (in %) of acute myocardial infarction.

Country	*All STEMIs*	*STEMIs treated by primary PCI*	*STEMIs treated by thrombolysis*	*All AMIs (STEMI + non-STEMI)*
Austria	12	5	8	NA
Belgium	6.6	5.1	7	N.A.
Bulgaria	N.A.	N.A.	N.A.	N.A.
Croatia	10	5	7	N.A.
Czech Republic	8.6	6.7	N.A.	6.3
Denmark	N.A.	N.A.	N.A.	N.A.
Estonia	N.A.	N.A.	N.A.	N.A.
France	6.6	5.0	4.3	5.4
Finland	11.9	NA	NA	11.8
Germany	6.8	5.3	7.8	6.1
Greece	8.9	3.6	5.1	7.7
Hungary	9.1	5.7	13	13.5
Italy	13.5	3.1	3.5	11.1
Israel	4.2	N.A.	N.A.	2.8
Latvia	11.7	2.3	10.1	10.9
Lithuania	N.A.	6	N.A.	N.A.
F.Y.R.Macedonia	N.A.	4	7	N.A.
Netherlands	N.A.	N.A.	N.A.	N.A.
Norway	NA	3.5	NA	8.5
Poland	8.5	4.2	12	7.5
Portugal	7.8	N.A.	N.A.	6.0
Romania	13	7	8.5	N.A.
Serbia	9.9	3.3	9.3	10.7
Slovakia	9.4	3.2	11.1	N.A.
Slovenia	N.A.	6.2	N.A.	N.A.
Spain	N.A.	4	N.A.	N.A.
Sweden	6.2	3.8	8.8	5.2
Switzerland	6.2	3.6	4.5	5.0
Turkey	11	8	14	14
United Kingdom	9	3.7	7.3	8.7

Table 6: Median time delays (in minutes) in reperfusion therapy.
(In some countries, the FMC time is not reported and instead, the door-needle or door – balloon times are in the table below).

Country	*Symptoms onset – First medical contact (FMC) time*	*FMC – thrombolysis (needle) time*	*FMC – primary PCI (balloon) time*
Austria	90	30	115
Belgium	180	30	60
Bulgaria	N.A.	N.A.	N.A.
Croatia	140	N.A.	120
Czech Republic	150	N.A.	120
Denmark	N.A.	N.A.	N.A.
Estonia	N.A.	N.A.	N.A.
France	68	57	170
Finland	NA	NA	NA
Germany	100	45	120
Greece	180	N.A.	95
Hungary	210	110	115
Italy	117	30	88
Israel	90	73	92
Latvia	NA	NA	NA
Lithuania	60	N.A.	120
F.Y.R.Macedonia	147	N.A.	154
Netherlands	NA	NA	NA
Norway	NA	NA	NA
Poland	118	N.A.	124
Portugal	NA	60	86
Romania	176	42	N.A.
Serbia	60	N.A.	177
Slovakia	175	65	110
Slovenia	97	N.A.	134
Spain	118	45	97
Sweden	120	40	69
Switzerland	90	94	135
Turkey	N.A.	N.A.	N.A.
United Kingdom	68	55	118

6. Conclusions to the PhD thesis

Current interventional approach to the coronary artery disease is based on routine use of percutaneous coronary intervention. Offering less aggressivity it became widely used interventional method. Despite that, there is still risk related from the procedure.

In this thesis, we investigated the applicability of the risk stratification tool EuroSCORE in patients that underwent CABG, PCI and/or medical treatment. We proved that EuroSCORE can serve as risk stratification tool in **both** revascularization strategies as an appropriate tool. Thus, the EuroSCORE may help cardiologists and cardiac surgeons alike to individualize the risk profile of patients in order to better define the revascularization strategy and to appropriately counsel the patient, reducing the morbidity and mortality.

Routine immediate cardiac catheterization performed in 87% of STEMI in the Czech Republic enables us to discover new distinct syndromes, such as stress-induced myocardial stunning (Tako-Tsubo syndrome). Huge number of cardiac catheterizations performed in three different environments in Czech Republic allowed us to precisely estimate the prevalence and annual incidence of this very rare syndrome among white population.

Primary PCI is currently the most used revascularization method in Europe for STEMI treatment. This revascularization method has been shown to be superior to thrombolysis in reducing mortality, reinfarction and stroke. Its use needs good organized PCI network and knowing of the guidelines. The lack of organised primary percutaneous coronary intervention networks is associated with fewer patients overall receiving some form of reperfusion therapy. The best results are achieved in countries with PCI centers that offer 24/7 primary percutaneous coronary intervention services.

Current interventional approach to coronary artery disease spread doctor’frontiers, improving the quality of patient care and reducing the costs.