What's new in the management of heart failure?
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Heart failure represents a substantial burden for both patients and health services. This syndrome affects up to 4% of the total population and up to 20% of the elderly. It is the most common cause of admission to hospital in patients over the age of 65.

Major progress has been made in the last several decades in the management of this health problem both with regard to improving survival and reducing morbidity. Correct diagnosis is mandatory, preferably with a mechanistic understanding of the pathophysiology. Symptomatic patients often have preserved systolic function especially in women, in the elderly and in patients with hypertension. Therapy consists primarily of diuretics in addition to agents that attenuate pathological neurohumoral activation. The drugs with best documentation are agents that inhibit the renin angiotensin system and adrenergic system. More recently relatively intense inhibition of the renin angiotensin aldosterone system with combined ACE inhibitors and angiotensin receptor blockers often in addition to aldosterone blockers are prescribed routinely in symptomatic patients. Newer agents that inhibit the arginine vasopressin and endothelin systems are also being evaluated.

Importantly, devices that resynchronize left ventricular function and prevent serious ventricular dysrythmia have been shown to be efficacious. A focus on primary prevention and an aggressive approach to the development of atherosclerosis is necessary. Early aggressive mechanical intervention with PCI to limit the size of myocardial infarction and attenuate subsequent remodeling are considered central to optimal therapy. Imaging methods to detect hibernating myocardium and aid in decision making concerning potential revascularisation are commonly employed. Newer biomarkers, especially BNP, serve to identify patients that should be targeted for aggressive management and may also be useful in titrating and monitoring therapy.

Strategic tools for prevention of atherosclerosis in Latvia: health promotion and programme approach

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Statistics of Latvia, one of the new EC countries, show very controversial data on the development of micro- and macroleconomics, as well as on public health. We still have high total mortality (1400/100 000 population), infant mortality (9.9 per thousand live births), low-life expectancy (males: 64.5 yrs; females: 75.7 yrs), low-birth rate (8.55/1000 inhabitants), high prevalence of common cardiovascular risk factors. The prevalence of arterial hypertension among adult population (25–64 yrs) is 44–50%, daily smoking among men – 51%, elevated cholesterol level and Body Mass Index – around 60%. The question is: how to improve the situation?

From the viewpoint of systemic approach, three main complexes of activities should be stressed for prevention of factors influencing the development of atherosclerosis. These are the following: (1) health promotion and monitoring of health behaviour; (2) programme approach, supported internationally by the state and society; (3) implementation of consensus based guidelines for health professionals. Health promotion activities are generally organised by Health Promotion Centre while intervention activities are basically campaigns (Health Weeks, Heart Day, Quit & Win campaigns, workshops etc.) pushed forward by different institutions and NGO. FINBALT Programme serves as the main tool for monitoring of health behaviour. It is a collaborative system for monitoring health behaviour in Estonia, Finland, Latvia and Lithuania. The research purpose is to collect information on health behaviour of individuals, to evaluate actual and potential public health problems associated with health behaviour and to gain accurate information providing basis for future health promotion and health education programmes. Latvia has joined the Programme in the year 1998. The Finnish-Latvian Pilot Project
Degradation of elastin and collagen leads to destruction of the aortic media and supporting lamina. Various matrix metalloproteases (MMPs), derived from macrophages and aortic smooth muscle cells, have found to play important role in aneurysm formation. During AAA formation, the balance of vessel wall remodeling between MMPs and their inhibitors (TIMPs), favors elastin and collagen degradation. MMP-2, MMP-7, MMP-3, MMP-9 and MMP-12 have been found to be increased in aneurysmal aortic tissue. High levels of MMP-2 are found in small aneurysms, suggesting that MMP-2 has an important role in early aneurysm formation. MMP-9 is elevated in aneurysmal aortic tissue as well as in serum of aneurysm patients. Pathogenesis of aortic aneurysms has been studied with experimental aneurysm models, where aneurysm formation has been induced with elastase or calcium chloride. Infrarenal slow injection of elastase causes aortic aneurysm, which is histologically similar with human aortic aneurysms. In MMP-9 knockout rats, calcium chloride injection does not cause aneurysmal dilatation suggesting that MMP-9 is critical in aneurysm formation. After bone marrow transplantation from wild type animals, aneurysm can not be induced with calcium chloride. So far, the mechanism, which initiates the expression of these proteolytic enzymes, is unknown.

Abdominal aorta is more prone to aneurysm formation compared to thoracic aorta. The reason behind this is unknown. It has been differences in wall biology, structure and wall stress are probable important factors behind that difference. Elastase/collagen ratio is higher in thoracic aorta compared to abdominal aorta. Decreased elastin is associated with aortic dilatation. Once aortic diameter has increased, is probable that increased stress causes more dilatation increasing the wall tensile stress further, as well as risk of rupture.

Genetics and immunology have also some role in the pathogenesis of AAA. Abdominal as well as thoracic aneurysms exhibit familial clustering and occur in 10–20% of first-degree relatives. Also, certain HLA subtype has been found to be more common among AAA patients.

Role of infectious agents in atherosclerosis

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Background and main messages: Atherosclerosis is the main reason of cardiovascular (CVD) diseases. It is recognized as inflammatory disease on a world scale. All classical risk factors cannot fully explain such high incidence of CVD in general population. Atherogenesis process resembles many aspects of “chronic inflammation”. This chronic process of inflammation may be promoted by microorganisms: directly, when they infect arterial wall, or infection could influence atherogenesis indirectly through host defence to extravascular infections. Many pathogens are investigated on their etiopathogenetical role in atherosclerosis process but the...
most strong association is found with \textit{Chlamydia pneumoniae} and cytomegalovirus. Both are widely distributed, can experimentally infect blood vessel wall cells, and exhibit persistence, latency and recurrence of infection.

First possible association of \textit{C. pneumoniae} and CVD came from the “serologic study” performed in Finland in 1988. Since then almost 500 papers have been published on this association. Different studies published heterogeneous results that might be due to different criteria for defining CVD and inconsistent criteria used for chronic infection indicators. Few years ago, attention was attracted to antibodies to chlamydial HSP60 and their correlation with CVD, also these proteins (cHSP60) were the antigens where detected in atherosclerotic tissue itself.

Seroprevalence studies were followed by studies in which \textit{C. pneumoniae} was “directly detected in atherosclerotic tissue” by immunocytochemical staining, PCR, electronic microscopy and in several studies this organism has been isolated. Results of cytomegalovirus detection in atherosclerotic tissue are more poor.

“In vitro studies” and animal experiments also support hypothesis that \textit{C. pneumoniae} and cytomegalovirus can be associated with atherosclerosis.

“Clinical treatment studies” with antibiotics showed controversial results, but mostly did not find an effect of antibiotic treatment on adverse cardiac outcome. Studies of treatment of \textit{C. pneumoniae} in animal models of atherosclerosis revealed that best effect of treatment is achieved in acute but not chronic infection.

Conclusions: It is widely recognized that atherosclerosis is a chronic inflammatory disease.

Results of serological studies that investigate possible association between microorganisms and CVD are inconsistent due to lack of standardisation of serological methods and different serological criteria of chronic or persistent infection.

Despite inconsistency in published rates of detection of microorganisms in atherosclerotic tissue, there was clear evidence that infectious agents are present and can be detected in vessels damaged by atherosclerosis. Direct detection of infectious agent indicates possible association between infectious agents and atherosclerosis but does not prove etiological significance.

More investigational studies are needed to prove the role of infectious agents in atherosclerosis process.

Treatment strategy in patients with atherosclerotic disease and high atherothrombotic risk

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Atherothrombosis is an underlying disease process that often results in events such as ischemic stroke, myocardial infarction (MI) and vascular death. Atherothrombosis is a progressive and life long condition often affecting the entire vascular system, it is potentially life threatening and in the long term outcome. Atherosclerosis is characterised by the disruption (rupture, fissure or erosion) of atherosclerotic plaques, which leads to platelet activation and blood clot (thrombus) formation. A rupture of large fissure typically results in formation of a large thrombus. That completely obstructs the vessel resulting in an acute ischemic event such as MI or stroke. A smaller fissure may result in a thrombus that partially or transiently obstructs the artery causing transient ischemia and contributing to the progressive process of plaque growth. A person suffering from any event relating to atherothrombosis has an increased life long risk of the future potentially disabling or life-threatening events caused by the same underlying disease process. These subsequent events may not only be in the same vascular bed (e.g. heart, brain or periphery), but also in other vascular beds.

The major risk risk factors for the development of atherothrombosis are: (1) local factors-elevated prothrombotic factors, blood flow patterns, blood vessel diameter and arterial wall structure; (2) systemic factors – prior vascular events hypertension, hyperlipidemia, hypercoagulable states and homocysteinemia; (3) generalized disorders – obesity and diabetes (Type I and Type II); (4) genetic factors – genetic traits, age and gender; (5) lifestyle factors – smoking, diet and lack of exercise. The most important factors for the development atherothrombotic plaques and therefore for development of atherosclerosis are hypertension, hyperlipidemia, obesity, smoking and diabetes.

There are many effective treatment options in patients at high risk of atherothrombotic events. The following pharmacological treatments for prevention and treatment of atherothrombosis are: (1) ACE inhibitors, which suppress activation of the rennin-angiotensin system; (2) statins, which lower LDL cholesterol and has other positive effects including pleiotropic effects; (3) aspirin, which blocks thromboxane-mediated platelet aggregation; (4) clopidogrel, which inhibits the binding of ADP to platelet receptors thereby reducing ADP induced platelet activity. By inhibiting the platelet P2Y12 receptor for ADP clopidogrel blocks the amplification of platelet aggregation and secretion. Clopidogrel inhibits the following effects of ADP: (a) ADP release from platelet dense granules participates in adhesion activation by interaction with P2Y12, leading to activation of GPIIb-IIIa; (b) ADP-P2Y12 interactions mediate recruitment of circulation platelets to a growing thrombus and, (c) P2Y12 may mediate increased thrombus stability via P-selectin, GP6 and CD40L.

The results of CAPRIE, CURE, PCI-CURE, CREDO and pharmaco-economic analysis suggest that it is cost-effective to prescribe clopidogrel long-term for patients with symptomatic atherothrombosis who are at high risk of further serious vascular events. The incremental cost effectiveness of clopidogrel increases if the patient’s absolute risk of another event is higher.
Cardiovascular diseases (CVD) are the most important non-communicable chronic diseases in both developed and developing countries in terms of morbidity, disability, mortality and health care expenses. Lithuania also faces many serious problems that are being caused by CVD.

In the presentation, the main data on trends in CVD mortality and morbidity, risk factors prevalence and health behavior among Lithuanian adult population will be overviewed.

The data of Lithuanian Health Information center were used to analyze CVD mortality from 1988 to 2001 in Lithuanian population aged 0-64. The trends were analyzed using the method of ordinary linear regression on logarithms of the age standardized annual rates. The data of WHO MONICA and CINDI project Risk factors surveys were used for the evaluation of changes in the prevalence of CVD risk factors. Four cross-sectional surveys (in 1983, 1987, 1993 and 2002) were conducted in urban population aged 35-64 and three in rural population aged 25-64 (in 1987, 1993 and 1999). Since 1994 behavioral factors related to CVD have been monitored within the framework of international Finbalt Health Monitor project. The postal surveys have been carried out every second year in national random samples of Lithuanian population aged 20-64.

In 1988–1994, CVD mortality increased at a rate of 6.1% per year (p < 0.05) in men and at a rate of 3.4% (p < 0.05) in women. From 1994 to 1998, the decreasing trend in CVD mortality was observed only in men (by 9.5% per year, p < 0.05). Since 1999 mortality caused by CVD has been stable.

Since 1994 positive changes in nutrition habits have occurred in Lithuanian population: the consumption of fresh vegetables, vegetable oil and low fat margarine has increased, the intake of animal fat has decreased.

In conclusion, favorable changes in CVD mortality, prevalence of some risk factors and lifestyle habits have been estimated in Lithuania over the last decade. However, the CVD risk profile of Lithuanian population is still high and the implementation of effective health promotion and disease prevention programs is urgently needed.

Stroke incidence, time trends and geographical variations have been in the centre of interest for several years. The possibilities to reduce stroke related morbidity and mortality are constantly looked for. Some questions have been answered and progress in primary and secondary prevention has been made, but the incidence of stroke has remained high, especially in Eastern Europe.

The most realistic overview of stroke incidence worldwide could be achieved by population based incidence studies.

The first epidemiological study on stroke in Estonia was conducted in Tartu from 1970 to 1973. The study demonstrated that the incidence rates of first-ever stroke (184/100 000) and its subtypes are close to the rates reported by other studies carried out in several communities before the 1970s. However, the case-fatality rate at 30 days, especially for brain infarction (BI), was higher than that showed by others.

The crude incidence rate of stroke during the second study in Tartu from 1991 to 1993 was 250/100 000. The rate was higher for women (284/100 000) than for men (209/100 000), after adjustment to the standard European population the predominance of the rate for men became evident. Of total stroke cases, the diagnosis of BI was given to 60% patients, subarachnoid hemorrhage was diagnosed in 6%, intracerebral hemorrhage in 10% of patients and the subtype remained undetermined in 24% of patients.

A remarkable increase in the incidence of stroke was found between the first and second study in Tartu. The rise occurred solely due to the significant increase of the rates in people younger than 70 years. Although, the total incidence rate of stroke increased, the case-fatality rate at 30 days decreased significantly between 1970 and 1993 (from 49 to 30%).

The third population based incidence study of first-ever stroke was conducted from 01 December 2001 to 30 November 2003. During the first year, the crude incidence rate of stroke was 230/100 000, the age adjusted rate to the European population was 195 (214 for men and 181 per 100 000 for women). Sixty-eight patients (29%) died within 28 days of
stroke onset. According to the preliminary results of the third study the incidence and 28-day case-fatality rate of stroke in Estonia has remained high compared to other countries. The high incidence rate of stroke in Estonia might at least partly be related to the high prevalence and inadequate control of the risk factors among the population. However, it has been shown that lower socioeconomic status and psycho-emotional stress play an important role in stroke genesis. Low income may also cause an inadequacy of risk factor control in Estonia.

Role of Duplex-Ultrasound (US) for the investigation of pre-cerebral arteries determining ischemic stroke pathogenesis

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Introduction: Duplex-Ultrasound (US) is the most advanced technology in vascular ultrasound and constitutes the technique for the investigation of brain-supplying arteries. However, the significance of separate Duplex-US diagnostic criteria in ischemic strokes has not yet been sufficiently or precisely identified.

Material and methods: In the neurovascular centre of clinical hospital “Gailezers”, patients with cerebral ischemic stroke undergo Duplex-US with the high technology sonograph Siemens Sonoline Elegra. Duplex-US is routinely used on pre-cerebral and cerebral arteries. It has proven to be a precise method of measuring carotid intima-media thickness (CIMT). In the space of 3 years, 3100 patients were examined using Duplex-US. All patients were diagnosed as suffering from CI, using CT or MR.

Results: Arterial wall investigation with B-mode imaging has yielded important information regarding atherosclerotic plaques: the number, locality, plaque structure, echogenicity, plaque stability (homogeneous smooth-bordered plaques are considered stable; heterogeneous plaques with zones of varying echogenicity, hypoechoic plaques with echogenic spots and niche formations are regarded as unstable).

It has been confirmed that Duplex-US allows precise determination of the degree of stenosis, revealing the cross-section of the artery and measuring the degree of stenosis using the ellipse method. The resulting data was confirmed though angiography. In 2003 and 2004, angiographers performed endarterectomies on 48 patients. Twelve of these were performed on patients using only Duplex-US investigation as the basis for diagnosis. In all cases, the diagnosis was confirmed at the time of surgery.

These diagnostic investigations confirmed that old occlusions could easily be differentiated through B-mode imaging due to echogenic thrombotic material in the vessel lumen. Acute thrombotic occlusions can be difficult to diagnose using B-mode sonography, due to the low echogenicity of fresh thrombus.

Stroke is the third leading cause of death in the U.S. and it is well known that carotid artery stenosis is major pre-disposing factor for stroke. Surgical treatment of patients with carotid stenosis to prevent stroke was first introduced in 1954. Since that time carotid endarterectomy (CEA) has been established as the standard of care for patients with severe carotid stenosis on the basis of prospective randomized clinical trials. These trials, conducted in Europe and the U.S., compared CEA to best medical therapy in both symptomatic (NASCET and ECST trial) and asymptomatic patients (ACAS trial) and proved the efficacy of CEA in reducing the risk of stroke. The benefit of endarterectomy is dependent on a low perioperative stroke/death rate. The upper acceptable limit of stroke/death for symptomatic patients is considered to be 6% and the upper limit for asymptomatic patients is 3%.

Over the last decade, carotid angioplasty–stenting has been introduced with many encouraging clinical reports of low stroke/death rates and this treatment has been adopted at many centers, particularly for high risk patients and patients with carotid restenosis. However, early prospective clinical trials comparing carotid endarterectomy to carotid stenting have been disappointing with either early termination due to high stroke rates in the stenting groups or high stroke/death rates in both the surgical and stented groups. A meta-analysis comparing carotid endarterectomy to carotid stenting revealed a higher stroke/death rate among patients treated with carotid stenting, raising questions regarding the efficacy of this treatment.
However, recent improvements in stent technology and the introduction of cerebral protection devices to prevent embolization have improved the reported results of carotid stenting. A recent systematic review of published literature reports with an aggregate experience with more than 3000 patients suggests that the combined stroke and death rate within 30 days in both symptomatic and asymptomatic patients was 5.5% in patients treated without cerebral protection devices and 1.8% in patients treated with cerebral protection devices. Although the benefit of cerebral protection has not been proved, its use has been incorporated into most current clinical trials of carotid stenting. These trials (such as the Sapphire Trial) have focused on high-risk patients and early results suggest that the stroke/death rate for carotid stenting may be equivalent to carotid endarterectomy. However, the stroke/death rate was high (9%) in both the carotid stenting group and CEA control group, suggesting that this therapy may be equivalent to carotid endarterectomy. Thus, this is the first demonstration that carotid stenting with cerebral protection is equivalent to carotid endarterectomy. However, the stroke/death rate was high (9%) in both the carotid stenting group and CEA control group, suggesting that this therapy may not yet be appropriate for high-risk patients, especially those with asymptomatic carotid stenosis.

Recently, a prospective, multicenter study of carotid stenting with cerebral protection in a broad category of standard risk patients commonly treated in clinical practice has been complete (The CARESS Trial, December issue, JEVT). This study demonstrated that the 30-day stroke death rate for carotid endarterectomy was 2% and that the 30-day stroke death rate for carotid stenting with cerebral protection was also 2%, no different and, thus, equivalent to CEA. This low stroke/death rate was achieved in a broad selection of patients reflective of broad clinical practice and is consistent with the overall 1.8% stroke/death rate reported from multiple studies of carotid stenting with cerebral protection and the 1–2% stroke/death rate for carotid endarterectomy in broad clinical practice, including high-risk patients.

Thus, this is the first demonstration that carotid stenting with cerebral protection is equivalent to carotid endarterectomy with low stroke/death rates in both study groups. It should be noted that long-term results are not yet available and it is likely that carotid stenting will be considerably more expensive than carotid endarterectomy. Thus, the true benefit of carotid stenting and its potential role in the treatment of patients with carotid stenosis remain to be defined.

Inflammation and atherosclerosis

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Inflammation has been implicated as an important component in development of atherosclerosis and acute coronary syndromes (ACS) in particular. Although this concept is widely accepted, many important questions remain yet unanswered.

First of all, the underlying trigger mechanisms of the inflammatory process are not completely understood. Most of the conventional risk factors are associated with increased levels of inflammatory substances and/or markers. Nevertheless, many patients with no traditional risk factors will have elevated markers of inflammation.

Second, it has been unclear to what extent some of the inflammatory markers play role in pathogenesis of cardiovascular (CV) events. Recent scientific evidence suggests that, for example, C-reactive protein (CRP) is not a mere marker of inflammation, but should be regarded also as pro-inflammatory mediator of atherogenesis.

Third, what are the implications of inflammatory marker evaluation in clinical decision-making? High-sensitivity CRP (hs-CRP) has been the most promising inflammatory marker as it meets many criteria for risk factor applicable in clinical use: well-standardized, replicable and widely available assay, supported by strong evidence of association with CV events in numerous prospective studies. The additive prognostic power of hs-CRP in predicting cardiovascular events has recently become a disputed issue. Although hs-CRP had been shown to complement Framingham risk models in prediction of CV events, it was associated with only moderate relative risk of future events compared with hypercholesterolemia and cigarette smoking in a recently published case-control analysis from the Reykjavik study (Danesh et al., NEJM, 2004).

Fourth, search for an “ideal” marker of chronic atherothrombotic inflammation is ongoing. Associations of several other inflammatory markers with CV events have been previously described, e.g., von Willebrand factor, erythrocyte sedimentation rate, white blood cell count, inter-cellular adhesion molecules, serum amyloid A, interleukin-6, interleukin-18 and others. Most of these substances are not perspective as markers for various reasons. Particular interest has recently been drawn to CD40/CD40L signaling dyad as this system plays an important role both in inflammation and thrombosis. Circulating soluble CD 40 ligand (sCD40L) emerges as a potential new risk marker as high levels of sCD40L are shown to identify individuals at increased risk of death among patients with ACS and other patient groups.

Fifth, should the inflammation be a target of drug therapy and, if so, what armamentarium is available and expected in clinical practice? Management of the most traditional risk factors (such as smoking cessation, lipid lowering and weight loss) is associated with decrease in CRP levels. Several pharmaceutical approaches have been found to decrease CRP levels as well: statins, thiazolidinediones, dual cholesterol inhibition, some fibrates, etc. It remains a challenge, however, to distinguish direct anti-inflammatory effects of these therapies from indirect ones such as via lipid-lowering mechanisms. Furthermore, it needs yet to be confirmed that decrease of inflammatory markers such as hs-CRP actually correlates with reduction of CV events as a result of the treatment.

In summary, although inflammation is recognized as a root mechanism underlying atherosclerosis, the intensive research in the field has yielded limited clinical implications. This rapidly expanding research area, however, undoubtedly

has a great potential to improve risk stratification and will help to target treatment at the high-risk patients.

Assessment of endothelial function in the arteries – the clinical tool of the future
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Endothelial dysfunction is well recognized as an initial event in the development of atherosclerosis. Thus, a reliable clinical method for the assessment of endothelial dysfunction would make it possible to recognize pre-clinical stages of atherosclerosis. There are several clinical approaches for the assessment of endothelial function: (1) measurement of biochemical endothelial markers (von Willebrand factor, plasminogen activator, inhibitor complex thrombomodulin adhesion molecules, microalbuminuria, N-oxides, etc.); (2) measurement of morphological and mechanical characteristics of the arterial wall (intima-media thickness, compliance, distensibility, remodelling indexes, etc.); (3) measurement of endothelium-dependent regulation of vascular tone at focal sites of circulation.

The method of flow-mediated dilatation measurement of the brachial artery by high fidelity ultrasound scanning after hyperaemia produced changes in the shear stress of the vessel is widely used in clinical scientific research. The possible clinical implications of this method include long-term follow-up of subjects at high risk of coronary, peripheral or cerebral vascular disease. Another field of its use is the assessment of the effect of cardiovascular drugs on endothelial function. For the first time in the Baltic countries, the endothelial function laboratory was established in the Centre of Cardiology and Angiology, Vilnius University Hospital Santariskiu Klinikos in 1999. It already has the experience of more than 2000 studies of endothelial function in subjects at high cardiovascular risk.

Risk factors (RF) and some clinical factors in various subtypes of cerebral infarction (CI)
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Background: RF commonly has been investigated in stroke at all, without differentiation of ischemic and haemorrhagic strokes or ischemic stroke subtypes. The aim of the study was to determine the most important RF in CI subgroups of atherothrombotic (ATCI) and cardioembolic (CECI) pathogenesis.

Patients and methods: Frequency of RF in 3013 stroke patients (810 CECI and 2137 ATCI) was investigated. In the less number, 90 patients (30 CECI and 60 ATCI), along with other RF, changes in internal carotid arteries (ICA) by duplex ultrasound data (stenoses, atherosclerotic plaques, intima media (IM) thickness), microembolic signals in the middle cerebral artery (MCA) and some clinical factors, as level of C-reactive protein (CRO), changes in the brain by CT data (vascular periventricular leukoencephalopathy, subclinical strokes) were analysed.

Differences between peculiarities of RF in both subtypes were proved by Chi-square test (p < 0.05).

Results: Atrial fibrillation (AF) was the most important RF in CACI subgroup (p < 0.0001). Arterial hypertension (AH) was established in 68.4% of CACI and in 74.1% of ATCI cases (p = 0.002), which shows that AH infrequently accompanies CI of various pathogenesis. Diabetes mellitus (DM) was more significant in ATCI subgroup (p = 0.031). In the both CI subgroups, all patients with DM had changes in ICA – atherosclerotic plaques, stenoses, IM thickness >1 mm. More smokers were among ATCI patients (p < 0.0001), 39.7 and 24.4% accordingly. Hypercholesterolemia manifested more frequently in ATCI than in CACI group (p = 0.0001). CRO level more than 5 mg/l was found in 52.2% of CACI and 63.4% of ATCI patients. In all patients in CACI and in 93.3% of patients in ATCI subgroup IM thickness was >0.7 mm. In ATCI subgroup, clinically relevant stenosis of ipsilateral ICA or MCA was stated in 35% of patients and instable atherosclerotic plaques in ICA – in 8.3% of patients. CACI patients also had significant changes in arteries –33.3% of patients had stenosis or occlusion of ipsilateral ICA or MCA, and 26.7% of patients had instable atherosclerotic plaques in ICA. Proportion of subclinical strokes was greater in CACI subgroup (p = 0.02). Vascular periventricular leukoencephalopathy more frequently was found in CACI subgroup, although more than 90% of the patients had AH.

Conclusion: AF is the ruling RF in CACI subtype and comparatively frequently it is accompanied by AH. More prevalent RF in ATCI subtype is AH, but also other RF as DM, smoking and hypercholesterolemia are important.

Elevation of CRO level has observed both in ATCI and CACI subgroups, however, more significant it is in ATCI subtype.

Elevated IM thickness in ICA has founded in both analysed CI subgroups.

Relevant stenotic changes and instable atherosclerotic plaques in magistral pre-cerebral arteries have stated not only in ATCI but also in CACI cases, which indicates the need for detailed investigation of stroke patients to determine stroke pathogenesis. Frequency of subclinical strokes, which may lead to the worse stroke outcome, was higher in CACI subgroup; this indicates the importance of stroke prevention in AF patients.

Vascular periventricular leukoencephalopathy more frequently have been manifested in CACI subgroup, however more than 90% of the patients had AH.
Homocysteine as a risk factor for atherosclerosis

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Homocysteine (Hcy) is a sulfur-containing intermediate product in the normal metabolism of methionine and is produced in almost all human tissues. Research over the past decade has shown that elevated levels of Hcy have a strong association with all forms of atherothrombotic disease and venous thromboembolism. Additional risk factors (smoking, hypertension, diabetes, and hyperlipidemia) may additively, or by interacting with Hcy, synergistically increase overall risk. Folic acid, Vitamin B₁₂, and Vitamin B₆ deficiencies and reduced enzyme activities inhibit the breakdown of Hcy, thus increasing the Hcy concentration. In addition to these factors, several diseases like decrease of the renal function, proliferating diseases (tumors, psoriasis), hypothyroidism and other conditions (smoking, post-menopausal states, increasing age, several drugs) may cause elevation in Hcy level. Possible mechanisms for promoting atherogenesis and thrombosis include endothelial damage, platelet activation, smooth muscle proliferation, procoagulant effect and oxidative modification of low-density lipoproteins. Endothelial damage appears to be mediated by oxidative stress. Starting at plasma Hcy concentration of approximately 10 μmol/L, the risk increase follows a linear dose–response relationship with no specific threshold level. Recommended target for patients with known atherosclerotic disease is Hcy level <10 μmol/L. Based on various calculation models, reduction of elevated plasma Hcy concentrations by supplementing folic acid, Vitamin B₁₂ and Vitamin B₆, may theoretically prevent up to 25% of cardiovascular events. Ongoing large prospective, randomised controlled trials are investigating the potential beneficial effect of Hcy lowering therapy on cardiovascular morbidity and mortality in subjects with hyperhomocysteinemia.

Atherogenic dysglycemia: whom to treat? How to treat?

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Atherosclerosis tends to occur at younger age among persons with even slightly elevated blood glucose levels. Most of people before diagnosis of type 2 diabetes mellitus (T2DM) have a long period of undiagnosed elevation of fasting and/or 2h plasma glucose levels in an OGTT. Recently published results (Pirags et al., 2003) of the Latvian Diabetes Screening Program performed by 100 family doctors in 4625 persons with increased cardiovascular risk (age over 45 and overweight, hypertension, or other risk factors) showed that 5.5% of them (5.0% of women, 6.5% of men) had impaired fasting glucose (IFG) with fasting plasma glucose levels 6.1–6.9 mmol/L, and 3.8% (3.5% of women and 4.7% of men) had impaired glucose tolerance (IGT) with 2h plasma glucose levels in an OGTT 7.8–11.0 mmol/L. The 8.2% (7.4% of women, 9.2% of men) of them had undiagnosed T2DM with fasting plasma glucose levels above 7.0 mmol/L and/or 2h plasma glucose levels in an OGTT above 11.1 mmol/L. According to the Latvian Diabetes Register, prevalence of diagnosed T2DM in this age group is only 2.9% (3.4% in women and 2.1% in men).

Retrospective analysis of blood glucose levels in more than 630 patients with acute coronary syndrome hospitalised in Riga (320 patients) and Beirut (310 patients) showed that 22% of patients in Latvia versus 37% in Lebanon had T2DM and 31% vs. 16% had IFG (Charbel, 2004).

Epidemiologic data derived from various studies has clearly established the alarming high rate of cardiovascular disease in patients with diabetes and the overall poor prognosis in this group of patients. Not only is the prevalence high, coronary artery disease is more extensive in diabetes patients. At coronary angiography or during autopsy, patients with diabetics have significantly more multi-vessel disease than non-diabetics. As result, total and cardiovascular mortality in diabetics is 3–5 times higher than in their counterparts without diabetes, and life expectancy in diabetics is 5–10 years shorter than in their counterparts.

The UK Prospective Diabetes Study (UKPDS) identified main cardiovascular risk factors in T2DM patients: high LDL cholesterol, low HDL cholesterol, high diastolic blood pressure, smoking, and elevated HbA₁c. Analysis of the data from UKPDS shows that increase of HbA₁c by only 1% leads to:
- increase of the risk of myocardial infarction by 14% (p < 0.0001);
- increase of the risk of stroke by 12% (p < 0.035);
- increase of the risk of amputations by 43% (p < 0.0001);
- increase of the risk of congestive heart failure by 18% (P < 0.021).

Several studies both in pre-thrombolytic and thrombolytic era have clearly demonstrated that in the in-hospital mortality is considerably higher in diabetics compared with their non-diabetic counterparts. In particular, diabetic women have twice the mortality of diabetic men and four times that of non-diabetic men. Early thrombolytic therapy is clearly beneficial in diabetics saving 37 lives per 1000 myocardial infarctions in T2DM compared to 15 lives in non-diabetics. In spite of this, diabetes remains and independent predictor of a fatal outcome at 1 year, with a 1-year mortality of approximately 14.5% in T2DM compared with 9.1% in non-diabetics.

Typical clinical course of T2DM reflects the unsolved problem of diabetic cardiovascular complications:
- dysglycemia or even early diabetes is often ignored by doctors and patients;
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Experience in management of stroke patients in Lithuania

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Background: Stroke is the fourth main cause of death in the Lithuanian population and the main cause of severe disability. During the last decade a lot of efforts was undertaken in order to tackle a difficult situation with cerebrovascular disease in the Republic. The two national programs – Lithuanian Health Program (in operation since 1996) and Lithuanian National Program on Prevention, Diagnostics, Treatment and Rehabilitation of Cerebrovascular Stroke (in operation since 2001) are ongoing. The latter one was initiated by the Lithuanian Stroke Association, which was established in 1997. Lithuanian Stroke Association acts as a force for progress in stroke management in Lithuania, promoting the up-to-date knowledge in the field and encouraging neurologists and other specialists involved in stroke care for more advanced care about the stroke patient.

Main messages: In the Republic, acute stroke care is organised according to the recommendations and guidelines of the AHA and the EUSI, which were adopted to the local situation in 1999. There are six stroke units in the Republic at the moment: the two of them are located in Vilnius, and the remaining four – in four largest cities – Kaunas, Klaipeda, Siauliai and Panevezys. In case there is no stroke unit in a hospital, a stroke patient is admitted to a neurological ward. Subject to indications, stroke patient may be directly admitted to an intensive care unit or neurosurgical ward. In case an acute stroke is suspected, computed tomography has to be performed as soon as possible for all patients unless the device is not available in the place. Thrombolytic therapy can be employed for patients with acute ischemic stroke in two centers in Vilnius and in one in Kaunas. Evacuation of intracerebral haemorrhage as well as clipping of cerebrovascular aneurysms is performed in two centers located in Vilnius and in Kaunas. Endovascular treatment of cerebrovascular aneurysms and malformations is in use in Kaunas. General therapy of all stroke patients includes monitoring and correction of cardiac and pulmonary function, control of hyperthermia, hypovolaemia, hyperglycaemia, hypertension, and increased intracerebral pressure. Early mobilisation of the stroke patients together with the early rehabilitation is generally accepted. After discharge, further rehabilitation (in rehabilitation hospitals, centers or out-patient rehabilitation) is applied in most cases using a “goal-setting” model.

Conclusions: Keeping in mind a fact, that since 1990, mortality rate from stroke decreased by 7% in the Lithuanian population, and 28-day case fatality of stroke decreased by more than 100% in those aged 25–64 years, we may conclude that improved medical intervention contributed a lot to these favourable changes. On the other hand, high mortality and attack rates compared to the average of the EU countries together with a high proportion of severely handicapped stroke survivors indicate that a lot remains to be done in order to improve both the epidemiological situation from the population perspective, and management of stroke from the stroke patient perspective.

Indices of inflammation and other secondary risk factors in the progression of coronary artery disease (CAD)

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1. once diagnosed, early diabetes is not treated aggressively;
2. cardiovascular prevention in diabetics is delayed and ineffective.

Traditionally, step-by-step approach is used for the treatment of patients with atherogenic dysglycemia. First, lifestyle change and medical nutritional therapy is advised. If it fails, oral anti-diabetic drugs are started, initially as monotherapy, later in combination. Insulin therapy, despite being the most potent and durable hyperglycemic intervention available, has generally been saved for last, presumably because of the need to administer it by injection.

Swedish DIGAMI study (Malmberg et al., 1999) demonstrated that both short- and long-term mortality after myocardial infarction is lower in insulin treated diabetic patients with the total relative long-term mortality reduction of 28%. Recently published data from the Belgian study (van den Berghe et al., 2001) in critically ill patients confirmed that intensive insulin therapy aiming normal plasma glucose is significantly increasing patient survival.

Recent discoveries are supporting hypothesis, that described standard approach to atherogenic dysglycemia may be not sufficient to avoid cardiovascular complications in diabetic patients. Several trials are indicating that reduction of even slightly elevated fasting plasma glucose to values <5.4 mmol/L may reduce cardiovascular events. Meta-regression analysis (Coutinho et al., 1999) of 20 published studies in 95,783 patients with mean duration of 12.4 years showed that post-prandial glycemia has even stronger impact on cardiovascular risk than fasting plasma glycemia.

However, there is a need for a large intervention studies showing the effect of early normalization of glycemia on cardiovascular risk in patients with IFG or IGF, and to give explicit answers to the questions:

- Are cardiovascular diseases in T2DM complications of long-standing hyperglycemia?
- Is it possible to normalize glycemia without severe side effects?
Coronary artery disease is the most common cause of morbidity and death in this age group.

Age is an independent risk factor for percutaneous coronary interventions (PCI). Patients aged >75 were poorly represented in randomized trials in the 1980s and 1990s. Data from multicentre and high volume single centre registries account for most reported experience. Selected publications of contemporary practice in the last 5 years indicate several features more common in elderly patients.

Clinical:
1. Atypical presenting symptoms
2. More females F:M ratio ~ 1:1
3. Acute coronary syndromes
4. History of heart failure
5. Prior coronary events – myocardial infarction, PCI, CABG
6. Myocardial infarction complicated by heart failure or cardiogenic shock
7. Co-morbidities – renal, peripheral, vascular, pulmonary, aortic valve disease, anaemia

Procedural characteristics and results:
1. More difficult vascular access
2. Multi-vessel disease
3. "Culprit" vessel PCI i.e. incomplete revascularization
4. Procedural success: 1–2% lower and mortality 2–4 times higher than in younger patients

Post-intervention period: Vascular complications and renal failure were increased 5–10-fold and neurological events 4–6-fold, compared to younger age groups. Mortality at 6–12 months was 4–8 times higher due to co-morbidities and incomplete revascularization.

Results in three publications from leading centres provide a benchmark: Elective PCI – Colombo’s group (Am. J. Cardiol., 2002) patients ≥ 80 years versus 70–79 years. Procedural success 97.3% vs 99.4% (ns). Hospital mortality 2.0% vs 0.5% (<0.01). Mortality at 6 months 7.3% vs 2.0% (<x>0.01). Primary PCI for acute myocardial infarction – Nobuyoshi’s group (Am. J. Cardiol., 2002) patients ≥ 75 years versus <75 years. Reperfusion 93% versus 95% (ns). Hospital mortality 8.4% versus 3.7% (<0.01).

Stenting – Chauhan et al. (JACC, 2001) results from six recent multi-centre trials – 6168 patients ≥80 years versus <80 years. Success 97.4% versus 98.5% (ns). Hospital mortality 1.33% versus 0.1% (<0.001). Major bleeding 4.9% versus 1.0% (<0.001).

From 2000–2003 the PCI register at Cabrini Hospital, Melbourne, recorded 572 consecutive patients aged ≥75, representing 30.6% of procedures. Presentations were stable angina 44%, unstable 42%, acute myocardial infarction 14%. For patients aged 75–79 (n = 339), procedural success, mortality and hospital mortality were 96.9, 0.2 and 1.4% versus 96.6, 1.3 and 3.0% for patients aged 80–92 (n = 233). The results are comparable to those published in the literature.
Do we need a special approach? For unstable coronary syndromes a similar approach seems appropriate for all age groups. For stable angina PCI is offered when symptoms impair daily life, if increased risks are acceptable particularly in patients ≥80 years. “Culprit” lesion PCI is sometimes needed to enable non-cardiac, e.g. vascular or orthopaedic surgery. Co-morbidities, e.g. renal insufficiency must be identified and stabilized if possible to reduce risk.

After intervention special care is needed to prevent bleeding, hypovolaemia and deteriorating renal function.

Conclusions: Elderly patients have increased procedural and late mortality. Success rates are similar in the 75–79 and ≥80 age groups but mortality is higher in octogenarians. PCI can save, prolong and enhance the lives of elderly patients and age alone should not preclude intervention.

Circulatory complications in the neurobiology of body weight regulation

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Despite – or perhaps because of – numerous genetic and acquired factors, human body weight remains remarkably stable notwithstanding environmental variability, leading to the commonly accepted notions of “set point” and “regulated range”. Body weight regulation occurs via negative feedback and is for the most part neurohumoral: local endocrine or adipocyte activity leads to the appearance of peripheral circulating factors which then directly influence hypothalamic nuclei to cause changes in appetite and metabolism. Major long-term feedback signals regulating body weight include the pancreatic hormone insulin and adipocyte cytokine leptin. Short-term meal related signals from the GI system include PYY, GLP-1, CCK and Ghrelin, and adipocytes themselves can release free fatty acids, cortisol, estrone, angiotensinogen and other hemostatic regulators that impact body weight.

The regulatory disorders implicated in obesity are often co-morbid with circulatory disturbances, either causally or as concurrent factors. For example, experimentally-induced pre-diabetic metabolic syndrome has been found to impair the balance between myocardial oxygen delivery and metabolism by tonically vasoconstricting the coronary circulation. Furthermore, in early obesity-associated type II diabetes mellitus, the degree of functional deterioration in coronary circulation appears to be directly correlated with the severity of coronary arteriolar structural remodeling during the development of microangiopathy. While mechanisms are not yet fully understood, loss of endothelial function is clearly associated with micro- and macro-angiopathy. More importantly, recent evidence indicates that improved metabolic control in diabetic patients results in nearly complete restoration of endothelial function.

The independent role of obesity associated with coronary endothelial dysfunction in patients with normal or mildly diseased coronary arteries demonstrates the singular ability of adiposity absent diabetes or dyslipidemia to decrease cardiovascular function. The strong interrelation between metabolic disorders (e.g., obesity) and circulatory events (e.g., hypertension) may in fact point to a common central origin. Nevertheless, the effects of obesity (including insulin resistance) can magnify circulatory pathophysiology, as demonstrated by the correlation between body mass index (BMI) and endothelin-1-dependent vasoconstrictor tone in hypertensive patients. In addition, high BMI has been shown to impair coronary collateral vessel development in patients with chronic myocardial ischemia, leading to increased risk of in-facts and loss of contractile function.

Insulin or other feedback signal disregulation by itself can foster circulatory disorders. Obese hypertensive individuals not only have elevated plasma insulin levels in concert with increased insulin resistance, but they are uniquely responsive to insulin in increasing forearm vascular resistance. On the other hand, leptin directly promotes thrombosis following experimental arterial injury, suggesting that elevated leptin levels may contribute to the risk of atherothrombotic complications in human obesity. Other adipocyte products (e.g., cortisol and angiotensinogen) have also been implicated in cardiovascular dysfunction, although their prevalence in human obesity appears minimal.

In summary, circulatory complications are frequently associated with body weight regulation disorders, both directly and as a result of common risk factors.

Epidemiology and prevention of atherosclerosis – world wide situation

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Despite almost three decades of decline in the incidence of cardiovascular disease (CVD), it is still the most common cause of death in the western world. Epidemiological studies world-wide have identified a number of risk factors for CVD and intervention-studies. Numerous studies have shown that CVD prevention actually works.

In Finland, North Karelia, a comprehensive CVD-prevention programme successfully reduced the burden of the disease dramatically in the early seventies. In Japan, a reduction of salt intake resulted in lower blood pressure levels and drastically reduced stroke mortality. In Poland, a change of dietary fats, related to political changes – resulted in a 20% decline in heart disease mortality. What remains to be solved is a strategy for handling the upcoming epidemic of obeses. In a study by the DECODE study group it has been shown that up to one-fifth of the population in Europe has some sort of dysfunction of their glucose metabolism.
Another challenge in prevention of atherosclerotic diseases is the implementation of the existing knowledge into daily clinical practice. The gap between recommended and actually conducted clinical practice has been analysed in a number of trials. The largest, with almost 5000 patients all across Europe, revealed that more than a third of the patients who did or receive any kind of treatment had blood pressure and serum-cholesterol values above the recommended level. Only half of the patients who received treatment had obtained the recommended treatment goals. New guidelines on cardiovascular disease prevention have been issued by the European Society of Cardiology together with seven other scientific societies. The content of these guidelines will be summarised and a risk-management to together with seven other scientific societies. The content of these guidelines will be summarised and a risk-management computer-programme linked to these guidelines (the HeartScore®-programme) will be shown. It is hoped that a flexible interactive programme may close some of the gap between the recommended and actually conducted preventive care.

Atherosclerotic plaque pathogenesis and artery wall adaptation
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The relationship between atherosclerosis and systemic risk factors such as hyperlipidemia, hypertension, cigarette smoking and diabetes is well known. However, despite beneficial effects of risk factor modification and pharmacologic treatment, localized atherosclerotic lesions are the primary cause of clinical manifestations of vascular disease in the aorta, coronary, carotid and lower extremity arteries. This presentation will review the relationship between hemodynamic and biomechanical forces on the plaque and artery wall in relation to occlusive and aneurysmal atherosclerosis.

Hemodynamic factors are thought to be important modulators of plaque localization and evolution as well as determinants of artery wall adaptive responses. Intraluminal pressure regulates artery wall thickness through its effects on wall tension, and blood flow regulates arterial lumen diameter through changes in wall shear stress. Endothelial cells have a central role in regulating the structural adaptations to sustained alterations in blood flow by their ability to sense changes in flow factors and metalloproteinases, which are required in the remodeling process. Atherosclerotic intimal thickening is reduced in regions of high flow velocity and high wall shear stress, and increased in regions of low-wall shear stress.

It is now evident that atherosclerotic plaques localize preferentially in regions of low shear stress and not in regions of high shear stress. This has been demonstrated in quantitative studies correlating early plaque formation in pressure perfusion-fixed human carotid bifurcations with wall shear stress determinations in analogous geometrically precise flow models. Plaques form where shear stress values are near zero (i.e., at the lateral wall opposite the flow divider), and it has been suggested that a threshold value may exist below which plaque deposition tends to occur. Similar quantitative studies of the human aortic bifurcation have also shown that plaques localize in regions of low rather than high shear stress. Low shear rates may retard the transport of atherogenic substances away from the wall, resulting in an increased accumulation of lipids. In addition, low shear stress may interfere with endothelial surface turnover of substances essential both to artery wall metabolism and to the maintenance of optimal endothelial metabolic function. Low-wall shear stress has also been shown to be a factor in the development of intimal hyperplasia. On the other hand, high shear stress on the surface of a stenotic plaque may play a major role in fracture of the fibrous cap resulting in ulceration, thrombosis and plaque complications causing clinical symptoms.

Aortic wall motion is an important factor in the pathogenesis of experimental atherosclerotic lesions. The amplitude of the stretching movements of the arterial wall associated with the excursion in blood pressure over the cardiac cycle may be a promoting factor in plaque formation. Cyclic stretching stimulates synthesis of matrix components by arterial smooth muscle cells in vitro. Alterations in tensile stress, by flow-induced changes in radius or by changes in blood pressure, result in modification of wall composition appropriate to preserve or restore wall stability. These modeling responses include the elaboration and/or degradation of matrix materials.

Hypertension is a risk factor of atherosclerosis. Experimental studies have indicated that hypertension enhances atherosclerosis. Surgically created aortic coarctations in hypercholesterolemic primates produce hypertension and promote atherosclerosis in the proximal aorta, coronary and carotid arteries. Similar studies using hypercholesterolemic rabbits have also shown increased aortic atherosclerosis proximal to an aortic coarctation. Reduced wall motion by an external rigid support placed either loosely or firmly inhibits plaque deposition despite increased blood pressure, increased pulse pressure, or marked hypercholesterolemia. Thus, wall motion appears to be a critical factor necessary for cellular proliferation, lipid uptake and intimal plaque formation.

Shear stress, or blood flow, is an important regulator in artery dimension and structure, in addition to atherosclerotic plaque deposition. Experimental research has shown that arteries enlarge in response to chronic high flow and shear stress. Structural changes in the arterial wall are necessary. These changes include endothelial cell proliferation, internal elastic lamina degeneration, medial smooth muscle cell proliferation, and arterial dilation with no intimal thickening. When blood flow is reduced to normal in an artery that has enlarged and remodelled in response to high flow conditions, wall shear stress is reduced to very low levels. It has also been shown that under these conditions intimal thick-
Pathobiology of diabetic vascular disease
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The prevalence of diabetes mellitus is rising worldwide and has reached epidemic dimensions. Vascular complications are the leading causes of morbidity and mortality in diabetic patients. In recent years, diabetes mellitus has been even referred to as a vascular disease because of its effect on the vascular endothelial wall. Dysfunction of the microcirculation affects the arterioles and capillaries of the retina, kidneys, and peripheral nerves while dysfunction of the macrocirculation of the coronary and peripheral arterial wall leads to coronary heart disease, myocardial infarction, stroke, peripheral arterial insufficiency, and amputation.

Some date suggest that diabetic atherosclerosis results from similar process seen in non-diabetic atherosclerosis (i.e., inflammation). Alternatively, some contributing mechanisms may be unique to patients with diabetes. Hyperglycemia as a common future of diabetes is a cause of different pathogenic mechanism influencing endothelial dysfunction. Recent date has showed that pro-inflammatory adipocyte cytokines, such as tumor necrosis factor alpha and IL-6 are elevated in type 2 diabetes patients. Also, elevated production of soluble adhesion molecules caused by inflammation of endothelial cells is strongly associated with diabetes.

Although diabetes as an atherogenic risk factor may predispose to coronary artery and cerebrovascular disease, it does not seem to be a risk factor for aneurysm development. Results of the Aneurysm Detection and Management Screening study were published that confirmed the negative association of diabetes and abdominal aortic aneurysm (AAA). These trends are supported by other clinical studies such as the Rotterdam study and Massachusetts study. The reason for the negative association between AAA and diabetes remains unclear.

There could be some speculations that diabetic patients are more likely than those who do not have diabetes to have died with an AAA. However, the Whitehall study did not find a significant positive association between diabetes and dying with diabetes or of AAA. These dates are also supported by other studies. Also, an analysis of prospective data from the Vascular Surgery Registry of Stanford’s University hospital did not show higher mortality rate after endovascular repair of AAA in diabetic patients.

Diabetes appears to have an effect on large arteries that is distinct from atherosclerosis and is characterized by increased aortic stiffness and at least in peripheral arteries, by medial calcification. These changes could stabilize the aorta and resist aneurysm dilatation. However, aortic stiffness has been found to be increased in patients who have an AAA, and no association has been seen between calcification and the expansion rate of AAA.

Increased expression and activity of matrix metalloproteases (MMP’s) have been observed in human aneurysm tissue while little is known about effects of diabetes on MMP’s regulation in aortic tissue. Studies of uterine artery have showed negative association between estrogen receptor expression and collagen in the arteries wall. Also, it is known that treatment with estrogens decrease collagen and increase elastin level in arterial wall and that woman in general are less prone to development of AAA. According these facts higher level of estrogens in obese diabetic patients might be one of the protective factors in development of AAA.

Conclusion: Diabetes and many vascular diseases share an underlying pathophysiology and pathobiology. However, some data demonstrate diabetes distinguish impact on vascular wall and in some cases, such as AAA, diabetes seems to be even protective.